60 years anniversary

Acad. S.Yu. Yunusov Institute of the Chemistry of Plant Substances AS RUz

12th International Symposium on the Chemistry of Natural Compounds

ABSTRACTS

September 7-8, 2017
Tashkent, Uzbekistan

SPONSORS

The Organizing Committee of 12th International Symposium on the Chemistry of Natural Compounds acknowledges with gratitude the support of the following companies and organizations

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SYMPOSIUM TOPICS

1. Chemistry, biology and technology of natural compounds and their derivatives.
2. Development of original natural medicinal preparations.

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Tel.: (99871) 262-73-58, 262-59-13, e-mail: conf.ixrv.2016@rambler.ru

Plenary Presentations

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ЗАО ФАРМЦЕНТР ВИЛАР (РФ),
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АЛЛАПИНИН®

ОТЕЧЕСТВЕННЫЙ АНТИАРИТМИЧЕСКИЙ ПРЕПАРАТ

Бромистоводородная соль алкалоида лаппаконитина, выделяемого из травы *Aconitum leucostomum* (аконит белоустый) и *Aconitum septentrionale* (аконит северный)

Корневища с корнями *Aconitum septentrionale* Koelle (борца северного)

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Препарат оказывает антиаритмическое действие, угнетая быстрый ток ионов натрия внутрь клетки. **Аллапинина®** относится к классу 1 антиаритмических препаратов.

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Таблетки по 25 мг, №30 и инъекционный раствор - ампулы по 2,0 мл, 0,5%, №10.
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E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - АО "O'ZKIMYOFARM"

АКСАРИТМИН

АНТИАРИТМИЧЕСКИЙ ФИТОПРЕПАРАТ

Действующее вещество:
Сумма алкалоидов, получаемая из растения Acontium septentrionale (борец северный)

Эффективен при аритмиях на фоне инфаркта миокарда и при различных хронических заболеваниях сердечно-сосудистой системы

Фармокологические свойства:

Оказывает антиаритмическое действие в отношении предсердных и желудочковых нарушении ритма сердца, обусловленных различными механизмами.

Аксаритмин проявляет местно-анестезирующее, анальгезирующее, противовоспалительное и седативное действие.

Показания к применению:

Желудочковая и наджелудочковая экстрасистолия, пароксизмы мерцания и трепетания предсердий, пароксизмальная наджелудочковая и желудочковая тахикардия, в том числе при синдроме Вольфа-Паркинсона-Уайта.

Преимущества:

По сравнению с существующими антиаритмическими средствами Аксаритмин проявляет более высокую эффективность при лечении больных с хроническими и жизненно-опасными желудочковыми тахиаритмиями. Препарат превосходит по эффективности хинидин, дизопирамид, кордарон, этмозин и этацизин.

Форма выпуска:

Таблетки покр. оболочкой
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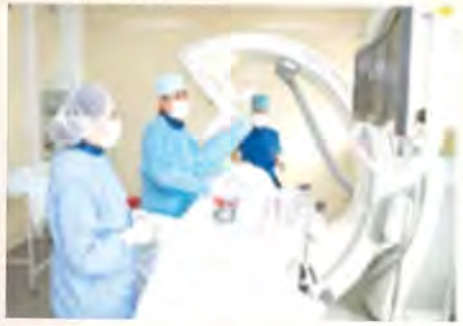

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Факс: (+99871) 262 73 48;
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РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - АО "O'ZKIMYOFARM"

АНТИАРИТМИН

АНТИАРИТМИЧЕСКОЕ СРЕДСТВО

ЭФФЕКТИВЕН ПРИ АРИТМИЯХ НА ФОНЕ ИНФАРКТА МИОКАРДА И ПРИ РАЗЛИЧНЫХ ХРОНИЧЕСКИХ ЗАБОЛЕВАНИЯХ СЕРДЕЧНО-СОСУДИСТОЙ СИСТЕМЫ

Действующее вещество: Сумма алкалоидов, получаемая из растения *Aconitum septentrionale* (борец северный).

Aconitum septentrionale

Показания к применению: Аритмия на фоне инфаркта миокарда, при различных хронических сердечно-сосудистой системы. Для экстренного купирования приступов угрожающих жизни тахиаритмий.

Преимущества: По сравнению с существующими антиаритмическими средствами **Антиаритмин** проявляет более высокую эффективность при лечении больных с хроническими и жизненно-опасными желудочковыми тахиаритмиями. Препарат превосходит по эффективности Хинидин, Дизопирамид, Кордарон, Этмозин и Этацизин. Преимуществом **Антиаритмина** является его успешное применение при выраженной синусовой брадикардии, синдроме слабости синусового узла, синдроме уширения интервала Q-T на фоне сниженного артериального давления. У больных с сердечной недостаточностью **Антиаритмин** практически не вызывает изменений сократительной функции миокарда, что выгодно отличает препарат от других антиаритмических средств. **Антиаритмин** эффективен и в тех случаях, когда другие противоаритмические средства не помогают.

Форма выпуска: Инъекционный раствор - ампулы по 2,0 мл, 0,5% №10.
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Факс: (+99871) 262 73 48;
Тел.: (+99871) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
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РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

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Экдистен – тонизирующий, адаптогенный и актопротекторный препарат

Природное соединение, получаемое из корней растения левзея сафлоровидная

ПРИМЕНЯЕТСЯ ПРИ:

- астенических и астенодепрессивных состояниях
- при длительных интоксикациях
- соматических и инфекционных заболеваниях
- при неврастениях, неврозах
- гипотонии, повышенной утомляемости

Товарный знак “Экдистен” зарегистрирован на территории РУз

Длительный прием экдистена даже в высоких дозах (по 8-10 таблеток в день в течение 1-2 месяцев) не вызывает нарушений в содержании основных гормонов организма в крови, не оказывает какого-либо побочного влияния на печень.

ЭКДИСТЕН не является допингом и может применяться без каких-либо ограничений с точки зрения антидопингового контроля.

Использование экдистена (2-4 табл.) одновременно с приемом дополнительного белка и витаминов B6, B12 способствует выраженному анаболическому действию

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e-mail: plant_inst@icps.org.uz
www.uzicps.uz

РАЗРАБОТЧИК И ПРОИЗВОДИТЕЛЬ СУБСТАНЦИИ И БАД:
ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ
ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз

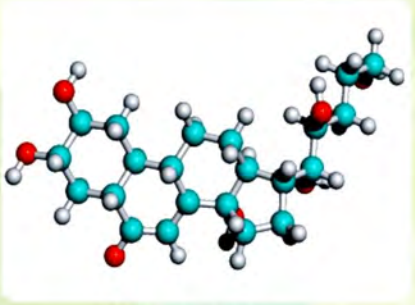
ЭКСУМИД

Биологически активная добавка к пище

Тонизирующий препарат
стероидной природы
Сумма фитоэкдистероидов
из надземной части *Ajuga turkestanica*

ЭКСУМИД назначают при:

- чрезмерном умственном и физическом напряжении
- интенсивных спортивных нагрузках
- астенических и астенодепрессивных состояниях
- длительных интоксикациях
- соматических и инфекционных заболеваниях
- неврастениях
- неврозах
- гиопотонии
- повышенной утомляемости



Экдистерон

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Тел: (+998 71) 262 59 13, 262 05 48; факс: (+998 71) 262 73 48
e-mail: plant_inst@icps.org.uz
www.uzicps.uz

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

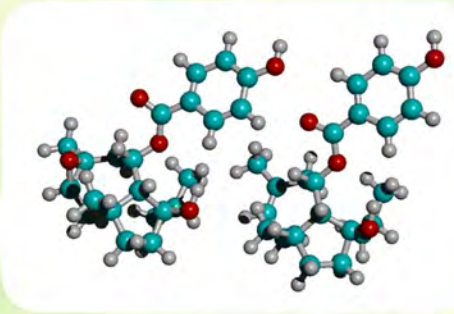
ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - АО "O'ZKIMYOFARM"

ТЕФЭСТРОЛ

ЭСТРОГЕННЫЙ ПРЕПАРАТ РАСТИТЕЛЬНОГО ПРОИСХОЖДЕНИЯ

ТЕФЭСТРОЛ – смесь сложных эфиров двух терпеноидных спиртов Ферутинина и Тенуферидина

Ferula tenuisecta Eug.Kor.



Тенуферидин Ферутинин

- **Проявляет высокую эстрогенную активность во всех звеньях гипоталамо- гипофизарно-яичниковой системы**
- **Не влияет на артериальное давление и дыхание**
- **Не обладает канцерогенностью, тератогенностью и кумулятивностью**
- **Активирует процессы синтеза и секреции фолликулостимулирующих и лютенизирующих гормонов в гипофизе**
- **Малотоксичен**
- **Проявляет седативный эффект**
- **Не изменяет секрецию эндогенных эстрогенов**

Форма выпуска: таблетки по 5 мг, №10, №30
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e-mail: plant_inst@icps.org.uz
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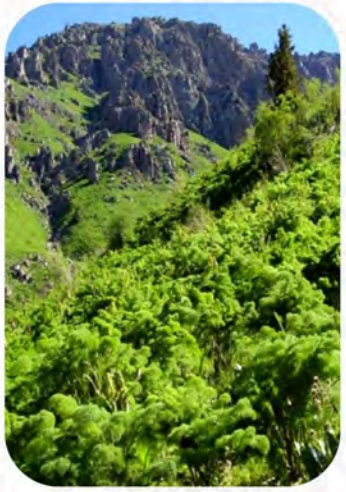
РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ДХО “NIKA PHARM” (РУз)

ФЕРУЛЕН

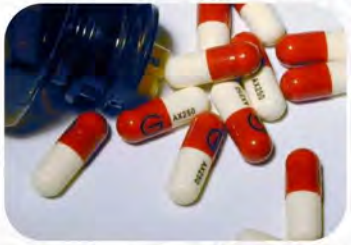
Фитопрепарат для лечения аденомы и рака предстательной железы

ФЕРУЛЕН получают из корней растения
Ferula tenuisecta Eug.Kor.



- избирательно действует на андрогензависимые органы
- нормализует ипредотвращает дальнейший рост ткани предстательной железы
- нормализует мочеиспускание
- сохраняет сексуальную функцию

Фармакологические свойства ФЕРУЛЕНА



Препарат обладает выраженным антипростатическим действием:

- уменьшает массу андрогензависимых органов: вентральной простаты
  передней простаты
  семенных пузырьков
  семенников

- угнетает секрецию тестостерона

- не оказывает существенного влияния на центральную нервную систему системное артериальное давление

Форма выпуска:
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Р. 00279/09/15

100170 г. Ташкент, ул. М.Улугбека, 77
Тел: (+998 71) 262 59 13, 262 05 48; факс: (+998 71) 262 73 48
e-mail: plant_inst@icps.org.uz
www.uzicps.uz

ACHIEVEMENTS AND PERSPECTIVES IN NATURAL COMPOUNDS STUDY

Sh. Sh. Sagdullaev

S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
100170, Tashkent, M. Ulugbek st., 77, e-mail: sh_sagdullaev@rambler.ru

Due to the relative immobility, the biochemical adaptation of plants in the ecosystem is the main survival way. It is based on the plants ability to synthesize biologically active substances of secondary metabolism, making them inedible for herbivorous insects and mammals; thus, they play a crucial role in the plants and animals coevolution.

In this regard, the study of biologically active secondary metabolites of plants is important in two aspects: first, to obtain a fundamental knowledge on the living organism structure and functioning, and, second, to search rationally for new biologically active substances for the effective drugs creation and their subsequent manufacture. The main classes of secondary metabolites of plants include alkaloids, terpenoids and phenolic compounds.

Alkaloids. As a result of ongoing systematic studies at the Institute of the Chemistry of Plant Substances, more than 300 promising alkaloid plants have been identified, of which 1270 alkaloids have been isolated, and 650 new structures have been established. It was revealed that the isolated alkaloids possess antiarrhythmic, anticholinesterase, sedative-tranquilizing, analgesic, anti-inflammatory, antihypertensive, anticonvulsant, anti-tuberculosis, expectorant, psychotropic and other types of activity. 35 medicines for medicine and more than 60 bioreactives were created. To ensure the practical availability of a number of alkaloids, relatively simple and effective approaches to the complete synthesis of benzylisoquinoline, quinazoline, isoquinoline, spiropiperidine, indole and other types of alkaloids have been developed.

Terpenoids. In general, over 1000 terpenoids have been isolated from the plants of Asteraceae, Apiaceae and Labiatae families (430 of which are new). On their basis, antiatherosclerotic, estrogenic, angioprotective, lipid-lowering, anti-inflammatory, cardiotonic, immunostimulating, tonic and antitumor drugs have been developed.

Phenolic Compounds. Over 200 species of plants with high content of coumarins, flavonoids, lignans and proanthocyanidins have been investigated, over 500 compounds identified (270 of which are new); cholagogue, hypoazotemic, antispasmodic, cardiotonic, hypolipidemic, antihypoxic, photosensitizing and anti-inflammatory drugs have been created.

Relatively simple and environmentally friendly technologies for obtaining the substances of these preparations have been developed, and their manufacture is established on the basis of the Pilot Production of the Institute.

Phytochemical studies carried out by the Institute of the Chemistry of Plant Substances have created a significant reserve for the pharmaceutical industry in the Republic of Uzbekistan and contributed to the new and unique export-oriented domestic medicines development.

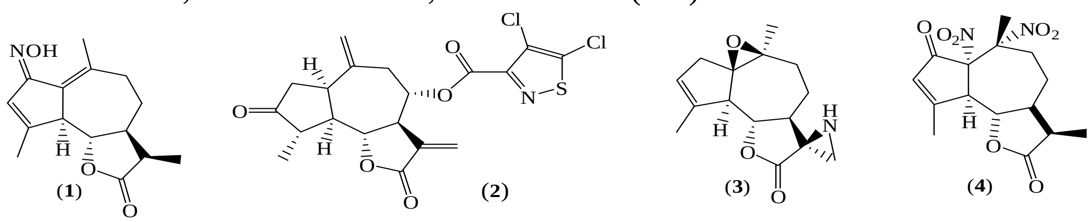
NITROGEN-CONTAINING SESQUITERPENE LACTONES

S. M. Adekenov

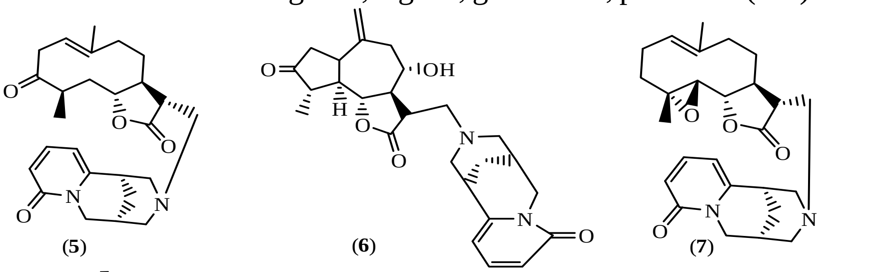
JSC “International research and production holding “Phytochemistry”, Republic of Kazakhstan, Karaganda, 100009, Gazaliyev str. 4, tel./fax: +7(721 2) 433127, e-mail: arglabin@phyto.kz

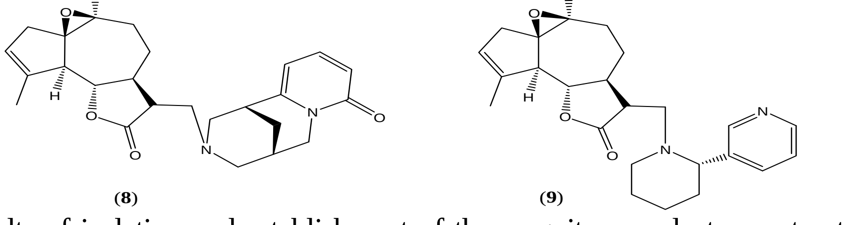
Among natural sesquiterpenoids there is a specific type of nitrogen-containing sesquiterpene lactones, which can be found in the species of *Asteraceae*, *Magnoliaceae* families. Thus, nitrogen-containing sesquiterpene lactones are isolated from *Acanthospermum glabratum* (DC) Willd, *Saussurea lappa* Clarke, *Saussurea pulchella* Fisch., *Ixeris sonchifolia* (Maxim.) Hance.

Generalization of conducted experiments and available literature data shows that nitrogen-containing derivatives of sesquiterpene lactones are obtained mainly by the following fragments of their molecules: α-methylene-γ-lactone cycle, keto-group, and olefinic bond. On the basis of sesquiterpene lactones, we synthesized more than 50 new nitrogen-containing derivatives of sesquiterpene lactones of arglabin, alantolacton, argolid, achillin, grosheimin, leucomisin, parthenolid, santonin, stizolicin etc. by azidation reaction, amination reaction, oximation reaction, nitrozolchloration, Heck reaction (1–4).



Amination by primary and secondary amines by the type of Michael reaction, which is performed regio- and stereoselectively only by conjugated olefinic bond of γ-lactone cycle, is one of comparatively promising field of synthesis of nitrogen-containing compounds of this class. This approach also allows to obtain water soluble derivatives, that is very important on practice. Obtaining of dimeric compounds based on natural compounds and studying their biological activity are also not without interest. Cytizine and anabasine alkaloids are used as nucleophile. We synthesized new bimolecular derivatives on the basis of arglabin, argolid, grosheimin, partenolid (5–9).





Thus, the results of isolation and establishment of the sesquiterpene lactones structure from raw materials of Kazakhstan, directed chemical modification of sesquiterpene lactones molecules in terms of the synthesis of new nitrogen-containing derivatives of represented natural compounds, are the precondition for production of new effective medicinal preparations with pharmacological action.

AROMATIC PLANTS AND ESSENTIAL OILS OF CYPRUS

K. Husnu Can Baser

Near East University, Faculty of Pharmacy, Department of Pharmacognosy,
Lefkosa (Nicosia), N. Cyprus, e-mail: khcbaser@gmail.com, www.khcbaser.com

Cyprus is the 3rd largest island in the Mediterranean Sea with a land cover of 9.251 sq.km. Being in eastern Mediterranean it is under the influence of the floras of Asia, Africa and Europe. Flora of Cyprus is well documented with 1.610 species and altogether 1.738 taxa. 108 species (143 taxa) are endemic plants comprising 6.7% (8.2%) of the flora. The families Asteraceae (66), Lamiaceae (39) and Apiaceae (29) are important for the aromatic flora.

We have been systematically investigating essential oils from aromatic plants of Cyprus and here I shall present our results on the essential oils of the following species: *Anthemis tricolor, Asphodelus aestivus, Chenopodium murale, Helichrysum conglobatum, Lagoecia cuminoides, Lathyrus* spp., *Origanum cordifolium, Origanum majorana, Phlomis brevibracteata, Phlomis cypria var. cypria, Pimpinella cypria, Sideritis cypria, Teucrium cyprium, Teucrium kyrenia, Teucrium micropodioides, Teucrium salaminium, Thymus capitatus, Zosima absinthifolia*.

ISOLATION AND BIOLOGICAL ACTIVITIES OF DITERPENOIDIC COMPOUNDS FROM THE MEDICINAL HERBS OF CENTRAL ASIA

H. A. Aisa

Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1,Urumqi 830011, Xinjiang, P. R. China, e-mail: haji@ms.xjb.ac.cn

Diterpenoidic compounds occurring in plants of the genus *Euphorbia* are the focus of natural product drug discovery because of the wide range of their therapeutically relevant biological activities and their great structural diversity, resulting from various macrocyclic and polycyclic skeletons and oxygen containing functionalities, including different aliphatic and aromatic acids. In our research for diverse and bioactive constituents from the genus *Euphorbia*, a phytochemical investigation was conducted on the plant of *Euphorbia sororia*, *Euphorbia macrorrhiza*, *Euphorbia soongarica*, and *Euphorbia alatavica* which are widely distributed in Central Asian. Among these herbs, 39 new diterpenoids, which belong to seven skeleton-types, including jatrophane, jatropholane, premyrsinane, lathyrane, euphoractin, casbene and pimarane diterpenoids, together with 33 known diterpenoids were isolated. Chemoreversal effects of these diterpenoids on multidrug resistance were evaluated in KBv200 and MCF-7/ADR cells that overexpress P-glycoprotein (P-gp), only to find several compounds have different degrees of chemosensitization. Remarkbly, two compounds (ES-2, and ES-18) exhibited most potent chemoreversal abilities than the classical P-gp inhibitor verapamil. Mechanistic investigations showed that compound ES-2 reversed multidrug resistance through suppressing the activity of P-gp and restraining the expression of P-gp, whereas compound ES-18 possessed a high affinity toward binding to substrate recognition site of P-gp without lowering its expression. The present study demonstrates that diterpenoids can be employed as promising modulator of P-gp-mediated drug resistance in cancer cells.

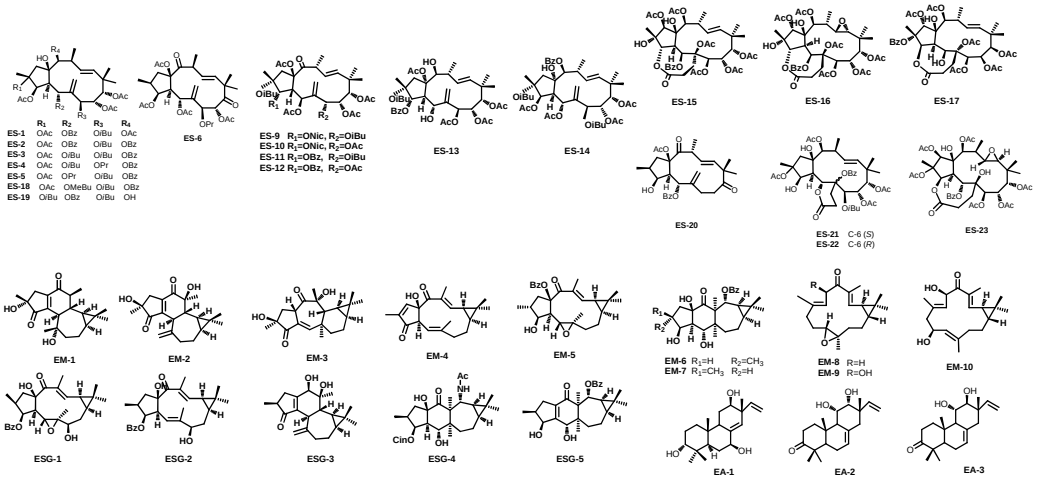


Fig. 1. Structures of 39 new diterpenoidic compounds were isolated from *Euphorbia sororia* (ES-1 to ES-6, ES-9 to ES-23), *Euphorbia macrorrhiza* (EM-1 to EM-10), *Euphorbia soongarica* (ESG-1 to ESG-5), and *Euphorbia alatavica* (EA-1 to EA-3), respectively.

Acknowledgment. The investigation was funded by International Cooperation and Exchange of the National Natural Science Foundation of China (NO. 31110103908), Central Asia Drug Discover and Development Centre of Chinese Academy of Sciences.

USING PHYTOLECTINS IN CLINICAL PRACTICAL MEDICINE

V. F. Korsun, E. V. Korsun, V. M. Lachthin

Department of herbal medicine Institute of Oriental medicine of the Russian University of friendship of peoples; Institute Phytotherapy, Russia, Moscov, www.fitokor.ru; e-mail: korsun_vf@mail.ru

The progress and achievements in this area of the science is closely connected with development of the new methods of the studies. One of them are a determination фито lectines - a squirrel, possessing characteristic reversible and electoral to link the carbohydrates, not causing their chemical conversion. Using lectines for decision of the main problems immunoligy, oncology, virologies, diabetology, celluar biology is one of the perspective methdological approach. Due to its unique characteristic lectines become object of the intensive study and broad introduction in different area biological and medical studies.

The Author are presented experimental data and results of the clinical observations, got for the last 10 years on use the facility and preparation, containing phytolectines. It was noted that such plants, as *Melissa, Agastache rugosa, Spearmint, Pot marigold, Common ground, corn silk, Sage, Heather* and others possess expressed antiherpetics and antiinfuciens characteristic. The Data of the plant, as well as fireweed show the expressed activity in respect of virus of the hepatitis ets. Fitolektiny in mushroom *Inonotus, Pleurotus* and *Ganoderma* useful in complex treatment of the row of the viral diseases (herpes, chlamidiosis, psoriasis), as well as at row oncologics disease of the digestive tract. The preparations *Common betony, Beans, Medicinal goats-beard, Jerusalem* artichoke have shown denominated antidiabetics effect. Biologically active additive to food "Schitovid", containing sheet of the currant, Green tea, Boer algae and sheet of the Melissa with proved by effect useful under hypothyroidism and autoimmune thyroidism.

The data and other preparations and facility, containing phytolectines - determined step to absolutely new approach to modern molecular (the receptoric) pharmacotherapy and phytoreabilitation sick with different diseases of the civilizations inflammatory, tumoral and viral (herpes, influenza, psoriasis, viral hepatitis, reumatoides arthritis, sterility, sugar diabetes, obesity and oth,) of the nature.

FROM INSECT PHEROMONE SYNTHESIS TO PREPARATIONS

G. Yu. Ishmuratov, M. P. Yakovleva, N. M. Ishmuratova, G. A. Tolstikov

Ufa Institute of Chemistry of the Russian Academy of Sciences, prospect Oktyabrya, 71. c. Ufa, 450054, Russia, tel.: (347) 235 58 01, e-mail: insect@anrb.ru

The report summarizes the results obtained by the Laboratory of Insects' Bioregulators (Ufa Institute of Chemistry of the Russian Academy of Sciences) in the streamlined synthesis of honey bee and pest insect pheromones and development of preparations on their basis for beekeeping and pest population control.

Insect pheromones are biologically active substances secreted by insects into the environment and specifically affecting the behaviour and physiological state of other individuals from the same species. They are functionally diversified and include sex, aggregation, trace, alarm and queen pheromones. Since pheromones are produced in the insect bodies, most frequently in nanogram amounts, the only way to obtain them for practical purposes is a multistage chemical synthesis (usually 8 to 10 stages). In so doing, the problems to be solved are typical for the streamlined organic synthesis. These are availability and low cost of parent compounds; chemo-, regio- and stereoselectivity of separate stages; production effectiveness and high yields. Special attention is given to complete structural and stereochemical compatibility with the natural bioregulators and artificial pheromone purity, which is to be no less than 98–99 pc. In turn, the doubtless merits of pheromone production now organized is its science linkage and small-series production (in kilograms and sometimes even in grams) allowing us to use common laboratory equipment in the pheromone synthesis without any problem with waste and sewage disposal.

In our research on the streamlined synthesis of insect pheromones, we used both artificial (cyclic and linear oligomers, co-oligomers, telomeric butadiene and isoprene, 4-methyl tetrahydropyran, acetylene and its derivatives) and natural (*l*-menthol, α-(+)-pinene, (S)-(+)-dihydromyrcene, Δ^3-carene, geraniol, citral) substrates with a high synthesizing potential.

Progress has been achieved in a promising research area, namely, a streamlined synthesis of low-molecular-weight insect bioregulators, including the development of high-tech procedures for obtaining a large group of universal acyclic-type block-syntones and designing original and efficient schemes on their basis to synthesize acetogenin, isoprenoid and macrolide pheromones of more than 60 species of agricultural and forest insect pests. As a result, there has been organized a wide-scale production and practical introduction of patented and certified pheromone preparations Armigal (almost 1 million dispensers per year at an application rate of 6 devices per ha) and Kunemon (almost 200 thousand glue traps per year at an application rate of 1 trap per 150 cubic metres) to regulate populations of the cotton bollworm and the mill moth, respectively.

Using the theory of insect communication by pheromones, a promising research area has been formed and developed to create beekeeping medications on the basis of synthesized honey bee metabolites multifunctional pheromone of the honey bee – 9-oxo-2*E*-decenoic acid – and the active component of royal jelly – 10-hydroxi-2*E*-decenoic acid, including the development of efficient methods for their synthesis and investigations into pharmacological activity and application techniques.

STRUCTURAL TRANSFORMATIONS OF CYCLE A OF TRITERPENOIDS IN THE SYNTHESIS OF BIOLOGICALLY ACTIVE COMPOUNDS

V. V. Grishko

Institute of Technical Chemistry of Ural Branch of the RAS, Perm, Russia,
e-mail: grishvic@gmail.com

The naturally occurring compounds with biological activity are conventionally used as multifunctional platform for the process of synthetic transformations in medicinal chemistry. Among polycyclic triterpenoids produced by plants, betulin as pentacyclic lupane alcohol has the highest synthetic potential for development of therapeutically promising new agents on its basis.

In the present study, semi-synthetic A-secotriterpenoids with fragmented C-2–C-3 bond synthesized from betulin and its available derivatives (betulonic acid, methyl ester of betulonic acid and allobetulon) as the basic compounds were used to produce original triterpenoids with multiple pharmacophoric groups in the cycle A. The presence of the activated methylene group in the alpha-position to the cyano-group in the basic 1-cyano-2,3-secotriterpenoids enabled to use intramolecular cyclization reaction including regioselective contraction or expansion of the cycle A as the key reaction in skeletal modifications of the triterpene backbone. This approach enabled to obtain various triterpene derivatives with pharmacophoric fragments: alkene-nitrile, enamine, ketonitrile, hydroxy ketone, enol or cyano-enone.

The conducted investigations based on available triterpenoid betulin resulted in the synthesis methods of new triterpene derivatives of lupane and oleanane type with diversely-functionalized cycle A. The synthesized compounds were *in vitro* tested for their cytotoxic, antiviral and immunomodulatory effects. Also, main regularities of the target activity as dependent on the structure of the compounds were revealed. The mechanism of cytotoxic action of the most active cytotoxic derivatives as promising antitumor agents was investigated.

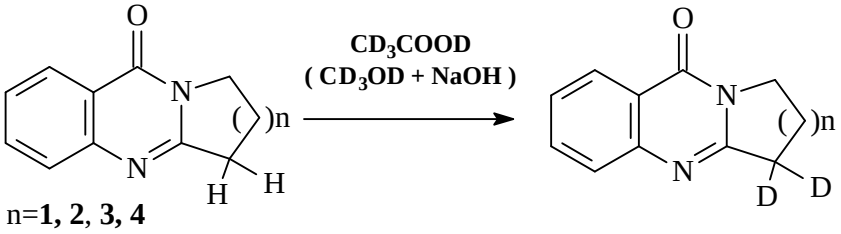
Acknowledgment. This work was financially supported by the Basic Research Program of Ural Branch of the Russian Academy of Sciences (Grant No. 15-21-3-2), the Russian Science Foundation (Project Nr. 16-13-10245) and the Russian Foundation for Basic Research (Project Nr. 16-03-00865-a, 14-03-96007-r_ural-a).

ON ELECTROPHYLIC ACTIVITY AND DEUTERIUM EXCHANGE OF α-METHYLENE GROUP PROTONS OF TRYCYCLIC QUINAZOLINES

M. G. Levkovich, B. Zh. Elmuradov, Kh. M. Shakhidoyatov, N. D. Abdullaev

S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, 100170, Mirzo-Ulugbek str., 77,
e-mail: mlevkovich@rambler.ru, b_elmuradov@mail.ru

Even in the early stages of the research of *Harmala* alkaloids an activity of α-methylene group of polymethylene cycle was marked. In more recent studies deoxyvasicinone, mackinazolinone and their synthetic homologues with 7- and 8-membered polymethylene rings it was revealed a pronounced dependence of activity on environmental conditions and polymethylene ring size. In parallel with these studies in some environments a strange feature of these compounds has been detected – exchange of α-methylene protons to deuterium atoms (*D*-substitution):



It caused depth study of *D*-substitution and possible causes of chemical activity in methylene groups. In this work *D*-exchange has been studied by NMR means, and it was revealed a dependence of substitution rate and process conditions: environment, temperature, concentration, presence of additional substituents in the molecules.

It is possible to determine the number of physical and chemical parameters of the observed phenomenon and to consider the probability of occurrence of its various mechanisms. In particular a need has been established the presence of *D*-substitution initiators: in these case molecules were CD_3COOD or NaOH. By means of molecular modeling have been considered various options for the *D*-substitution process and selected the most likely - the initiators of the molecules form with quinazolone a temporary (dynamic) molecular complexes, which after the collapse occurs the initial quinazolones with proton deficit in the α-methylene group. This explains the inclination of the studied compounds to *D*-substitution (or H-substitution also observed in the present work), and the electrophilic substitution of hydrogen atoms of α-methylene group.

DIRECT MODIFICATION OF BIOLOGICALLY ACTIVE COUMARINS AND SESQUITERPENOIDS VIA THE TRANSITION METAL CATALYSIS REACTIONS

E. E. Shults, S. S. Patrushev, A. V. Lipeeva

Novosibirsk Institute of Organic Chemistry, Siberian Branch of the RAS,
fax: +7 (383) 330 9752, e-mail: schultz@nioch.nsc.ru

Methods of functionalization of some plant metabolites or their derivatives, *viz*., the eudesmane-type methylene lactones and coumarins using the transition metal catalyzed reactions are discussed.

The cross-coupling reaction of eudesmane-type methylene lactones (isoalantolactone, alantolactone, 4,15-epoxyisoalantolactone, 4,15-(*gem*-dichloromethelene)isoalantolactone with bromoxanthines (8-bromocaffeine, 8-bromotheobromine, 8-bromo-3-butyltheobromine, 8-bromotheophylline, 9-benzyl-8-bromotheophylline, 8-bromo-9-butyltheophylline) under [Pd] catalysts resulted in the synthesis of the corresponding (*E*)-13-(2,6-dioxo-2,3-dihydro-1*H*-purin-8-yl)eudesma-4(15),11(13)-dien-8β,12-olides and 11-(2,6-dioxo-2,3-dihydro-1*H*-purin-8-yl)-13-normethyleudecma-4(15)-7(11)-dien-8α,12-olides. The yields and ratios of the cross-coupling and isomerization products depended on the reaction conditions, the structure of methylene lactone and the substituents in the xanthines. A synthetic route for obtaining 6-methylaminomethyl substituted furo[2,3-d]pirimidines including the Sonogashira reaction of (11*R*)-[5-bromouracyl-yl]eudesma-4(15)-en-8β,12-olides with alkynes, Cu-catalyzed Mannich reaction of (11*R*)-[(5-ethynyl)uracyl-1-yl]eudesmanolide with amines and formaldehyde and cyclization reaction.

The trifluoromethylsulfonyl derivatives of plant coumarins – peucedanin and peuruthenicin were studied in the Sonogashira reaction with terminal alkynes. Synthesis of 7,7′-linked bicoumarins, 3,3′-linked bi(2-isopropyl)psoralens as well as 1*H*-1,2,3-triazole linked coumarin-2,3-dihydrofurocoumarin and furocoumarin-2,3-dihydrofurocoumarin hybrids was performed by two alternative pathways, either involving a catalyzed transformations of the ethynyl derivatives of plant coumarins – peucedanin or peuruthenicin. The Sonogashira reaction of 7-ethynyl coumarins or 3-ethynyl-2-isopropylpsoralen with the subsequent coumarin triflates led to 7,7′-linked bicoumarins or 3,3′-linked bipsoralens. 1,2,3-Triazole linked coumarin-2,3-dihydrofurocoumarin or furocoumarin-2,3-dihydrofurocoumarin hybrids were synthesized by a regioselective Cu-catalyzed cycloaddition reaction of 2-azidooreoselone with 7-alkynylcoumarins or 3-ethynyl-2-isopropylpsoralen. Pharmacological screening of synthesized bicoumarins for anticoagulant activity *in vivo* revealed that coumarin–dihydrofurocoumarin hybrids linked with a 1,2,3-triazole ring were the most active compounds. Docking studies were undertaken to gain insight into the possible binding mode of these compounds with the coagulation factor Xa (FXa) binding site.

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BIOACTIVE NATURAL COMPOUNDS FROM TRADITIONAL CHINESE MEDICINES

Jun-Li Yang, Yan-Ping Shi

CAS Key Laboratory of Chemistry of Northwestern Plant Resources, Lanzhou Institute of Chemical Physics (LICP), Chinese Academy of Sciences (CAS), Lanzhou 730000, P. R. China

Traditional Chinese Medicines (TCMs) are the treasure of the Chinese nation, and it is extremely valuable for human to fight with diverse diseases over the past few thousand years. Research on the chemical constituents of TCMs is vital for understanding the function of TCMs, and the studies on the biological activities of these natural compounds is the first step to explore the functional components of TCMs. As the important biological sources, TCMs have been considered as the resource of new lead compounds, and it is promising to explore bioactive natural compounds and the lead compounds from TCMs. In recent years, our group focused on the discovery of new anti-aging and anti-viral natural compounds from the TCMs collected in Western China. Guided by the high-content screening and LC-MS/MS methods, we have systematically studied the chemical constituents and their biological activities of *Oxytropis falcate*, *Ligularia* species, *Inula britannica*, and *Dictamnus dasycarpus*. As results, thousands of terpenoids and their glycosides with diverse carbon skeletons and bioactivities have been isolated and evaluated for their anti-aging and antiviral activities. These materials and data have been applied for the quality control, function evaluation, and lead compounds discovery of the above TCMs.

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DESIGN OF ORIGINAL MEDICINES AS THE BASIS OF HOMELAND SECURITY OF THE RUSSIAN FEDERATION IN THE FIELD OF PUBLIC DRUG SUPPLY

Ya. A. Kostyro[1], V. V. Kostyro[1], E. S. Gogol′[1], V. V. Davaa[2], E. N. Petrova[1], A. O. Savinova[3], N. N. Trofimova[1], S. A. Lepekhova[4], K. V. Alekseev[5], V. A. Babkin[1], V. K. Stankevich[1], B. A. Trofimov[1]

1) A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences; 1 Favorsky Street, Irkutsk 664033, Russia; e-mail: yanakos@irioch.irk.ru
2) Republican medical college; 2A Kechil-ool Street, Kyzyl, Republic of Tyva 667003, Russia
3) JSC “Specialized Industrial Company IrIOH”; 295 Baikal Street, Irkutsk 664050, Russia
4) Irkutsk Scientific Center of Surgery and Traumatology; 1 Fighters Revolution, Irkutsk 664003, Russia
5) V. V. Zakusov Research Institute of Pharmacology, Russian Academy of Medicinal Sciences; 8 Baltyskaya Street, Moscow, 125315, Russia

Currently the Government of the Russian Federation (RF) pays much attention to the issue of homeland security in the sphere of public drug supply.

Within the framework of a sectorial program on import substitution in the pharmaceutical industry [1], original substances, exerting a wide range of pharmacological activity (antimicrobial [2], hypolipodemic and anticoagulant [3, 4], anti-inflammatory and wound healing [5], have been developed at Irkutsk institute of chemistry SB RAS.

These substances have been employed for design of various drug formulations, which are effective against such socially significant diseases as atherosclerosis, acute and chronic venous insufficiency, diabetes mellitus, infected wounds and burn injuries.

The conducted preclinical trials have shown safety and high therapeutic efficacy of the original pharmaceutical compositions.

The penetration of original domestic medicines having a wide variety of pharmacological activities into the pharmaceutical market of the RF completely corresponds to requirements of import substitution in the field of pharmaceutics and will strengthen a homeland security of the Russia in the sphere of public drug suply.

Acknowledgment. This work is supported by the Program of the Presidium of Russian Academy of Sciences "Fundamental Sciences for Medicine" 2009–2014, 2016.

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ESIGN OF MULTIFUNCTIONAL BIOMOLECULES BASED ON TERPENOPHENOLS, POLYSACCHARIDES AND PORPHYRINS

A. V. Kutchin, D. V. Belykh, E. V. Buravlev, M. A. Torlopov, E. V. Udoratina, I. S. Khudyaeva, T. K. Rocheva, I. Yu. Chukicheva

Institute of Chemistry, Komi Science Centre, 167000, Russia, Republic of Komi, Syktyvkar, Pervomaiskaya st.,48

Natural and semi-synthetic porphyrins and terpenoids, hydrophilic polymers are attractive platform for the synthesis of new biologically active compounds, including potential drug candidates.

Currently, the production of hybrid molecules which combine the pharmacological properties with the targeted delivery and capability structural interactions with biosystem as well as the production of molecules containing multiple reaction centers are of great interest. The biological effect of these multifunctional compounds in many cases significantly exceeds the efficiency of used analogues.

In order to find new more effective and less toxic therapeutic regulators of redox processes new hybrid biomolecules containing pharmacophore groups are synthesized. They include terpenophenols and its nitrogen, oxygen and sulfur-containing functional derivatives showing antioxidant, antiradical, anti-inflammatory, hepatoprotective, rheological and anti-platelet properties. In addition, hybrid molecules containing chlorin or porphyrin macrocycle (including macrocycle with metal cation in coordination sphere) generating singlet oxygen under photosensitization and determining the possibility of a molecule to participate in redox processes and determining the affinity to malignant neoplasms and the dark antitumor cytotoxicity.

Series of conjugates containing chlorin and isobornylphenol fragments, interconnected by spacers of various lengths, was synthesized on the basis of methylpheophorbide *a* and an assessment of the toxicity and antioxidant activity of synthesized compounds was carried out.

Another example involves macromolecular antioxidants based on hydrophilic biopolymers in which fragments of substituted phenols are grafted chemically to the polymeric matrix. The advantages of such compounds are: correction of solubility; providing of prolonged action; increase of the antioxidant activity; decrease of the toxicity levels.

The report will present the results of the synthesis of low molecular weight hybrid biomolecules and polymer hybrid biomolecules based on semi-synthetic terpenoids, polysaccharides, and porphyrins; as well as the development of new pharmaceutical substances and drugs using the most promising from synthesized compounds as the active ingredients.

Studies of toxicity and pharmacological properties are conducted jointly with the Institute of Biochemistry and Genetics Ufa Science Centre of the Russian Academy of Science and the Institute of Biology Komi Scientific Centre Ural Branch of the Russian Academy of Sciences.

Acknowledgment. Work is carried out with the support of Russian Science Foundation (project № 16-13-10367).

THE STRUCTURAL DIVERSITY AND STATE OF KNOWLEDGE OF FLAVONOIDS OF THE GENUS *Scutellaria* L.

E. Kh. Botirov[1], A. M. Karimov[2]

1) Surgut State University, Russia, e-mail: botirov-nepi@mail.ru
2) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances Academy of Sciences of the Republic of Uzbekistan

Scutellaria L. is a plant genus of the family *Lamiaceae* that comprises about 350 species that are broadly distributed in temperate, subtropical, and tropical zones of Europe, North America, and eastern Asia. Plants of this type are widely used in folk medicine for thousands of years. *S. baicalensis* roots and grass *S. barbata* included in Chinese and Japanese Pharmacopoeia. The above-ground part of the *S. galericulata* in folk medicine in Siberia used for nausea, dyspepsia, gastrointestinal disorders, with hypertensive disease, malaria, bleeding and acute respiratory infections. The above-ground part of the *S. scordifolia* in Tibetan medicine is used in pneumonia, myocarditis, tachycardia, polyarthritis, as an antipyretic. Pharmacological studies confirmed that extracts and individual flavonoids of *Scutellaria* possessed antitumor, antiviral, hepatoprotective, antioxidant, antiinflammatory and anticonvulsive, properties.

The report presents data of scientometric analysis of data on the level of study of flavonoids of species of the genus *Scutellaria* of the world's flora, compiled information on hemiatrophia flavonoids.

An analysis of the literature data on the chemical composition of plants of the genus Scutellaria flavonoids demonstrates its diversity. There are currently studied flavonoids for more than 60 species of the genus *Scutellaria,* from which isolated and identified 322 flavonoids, including flavones - 196, flavanones – 71, flavanonols - 11, chalcones - 10, flavonols - 17, isoflavones - 5 flavolignans - 7, biflavonoids - 5. The most common and, therefore, a detailed study is S. baicalensis. To date, various parts *S. baicalensis* found 151 flavonoids, including flavones -110, flavanones - 22, flavanonols - 5, flavonols - 9, isoflavones - 4, chalcone -1. According to the number of detected flavonoids followed plants *S. indica* - 61, *S. barbata* - 51, *S. amoena* - 38, *S. prastrata* - 35, *S. galericulata* - 29, *S. discolor* - 27 and *S. ramosissima* and *S. supina*, of which allocated to 24 flavonoid.

Scientometric studies indicate the constantly growing interest in the study of species of the genus Scutellaria L. by scientists of various branches of science – phytochemists, biologists, pharmacologists, and others. Investigation of flavonoids promising species *Scutellaria* L., revealing the relationship between their molecular and structural parameters, the establishment of a number of regularities in the structure - biological activity and finding ways to relate to the application of topical problems of modern phytochemistry in medical practice.

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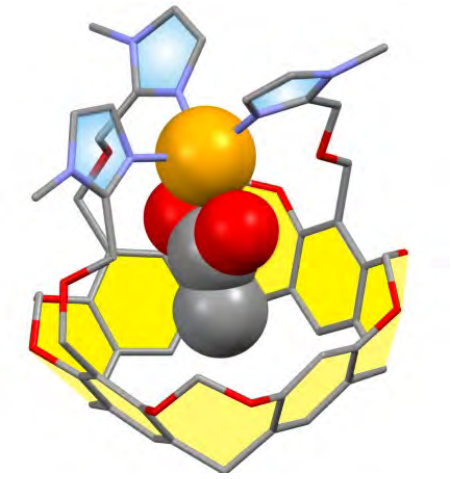
BIOMIMETIC MODELLING OF THE (MONONUCLEAR) METALLOENZYME ACTIVE SITE

Aleksandar Višnjevac

Institut "Ruđer Bošković", Bijenička cesta 54, HR-10000 Zagreb, Croatia
e-mail: aleksandar.visnjevac@irb.hr

Although bioinorganic chemistry examines the role that, generally, metallic and non-metallic elements beyond the big six (CHNOPS) play in biological systems, metalloenzymes and metalloproteins remain its main topic [1]. Biomimetic chemistry aims to create novel chemical species inspired by the natural systems such as metalloenzymes. This translates to the catalysts design, but *en-route*, very often secrets of the mechanisms used by the natural systems are discovered [2]. As an example of the supramolecular approach in biomimetic modelling [3], the syntheses, structural characterizations, and chemical activity studies of "bowl complexes", based on the resorcin[4]arene scaffold with three imidazole-containing coordinating arms grafted at the large rim, are presented. These complexes are biomimetic models of a ubiquitous mononuclear active site where three amino-acid residues hold the metal ion, leaving its one or two coordination sites available for the reversible guest (substrate) binding. The trisimidazole ligand RIm3 was prepared [4], as well as its complexes with Zn(II), Cu(I) [5] and Cu(II). Spectroscopic studies and X-ray single crystal analysis revealed a 5-coordinate environment for the Zn(II) and Cu(II) centres provided by three imidazole arms, and two extra donors, one embedded inside the resorcinarene cavity, the other in *exo* position. These two labile sites are occupied by solvent molecules or residual water, and are readily displaced by carboxylate donors, the position of which (*endo* or *exo*) is under tight control of the bowl-cavity. The reaction of RIm3 ligand with Zn(II) or Cu(II) acetates led to the formation of the complexes with the acetate anion irreversibly embedded inside the cavity. Cu(II) acetate complex was characterized by the X-ray single crystal analysis [6].



Its molecular structure features a rigidified resorcinarene bowl, which reveals an approximate, non-crystallographic, 4*mm* point symmetry, and can easily host small guest molecules.

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BIOACTIVE METABOLITES FROM SYMBIONT CULTURES

Ren Xiang Tan

1) School of Pharmacy, Nanjing University of Chinese Medicine, Nanjing 210023, P. R. China
2) Institute of Functional Biomolecules, State Key Laboratory of Pharmaceutical Biotechnology, Nanjing University, Nanjing 210023, P. R. China, e-mail: rxtan@nju.edu.cn

The impact of natural products on drug discovery pipelines keep kindling our interest in structurally unpredictable low-molecular-weight biomolecules which remain a promising source of pharmaceutical leads. But, scientists are being frustrated by reisolations of known compounds from new organism collections. This is not surprising since countless natural products have been identified since the characterization of morphine in 1806. Thus, the affordability and chemical space expansion of minor new natural products become a great concern, and chemical synthesis has been performed to produce organism-originated complex molecules and natural product-like compounds with privileged scaffolds. To add more skills to the existing arsenal of searching for high-value chemicals such as drug leads, this talk will present the discovery and biosynthesis of bioactive secondary metabolites from the cultures of symbionts obtained from plants, insects, and fishes.

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SEARCH FOR BIOACTIVE NATURAL PRODUCTS FROM *Zephyranthes candida* USING A BIOASSAY BASED ON INHIBITION OF HYPHAE FORMATION IN *Streptomyces* 85E

Guangmin Yao

Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, P. R. China, e-mail: gyap@mail.hust.edu.cn

Natural products play an important role in new drug discovery. In an ongoing search for bioactive compounds from Chinese medicinal plants by a bioassay based on inhibition of hyphae formation in *Streptomyces* 85E, the extract of *Zephyranthes candida* (Lindl.) Herb. showed potent inhibitory activities against hyphae formation in *Streptomyces* 85E.

Aamaryllidaceous bulbous herb, is native to South America, and naturalized in South China as an ornamental and a herbal medicine for the treatment of infantile convulsions, epilepsy, and tetanus. Previous phytochemical studies on the bulbs of *Z. candida* lead to the isolation of alkaloids and ceramides. However, studies on the whole plants are rare.

Bioassay-guided isolation of the whole plants of *Z. Candida*, collected at Shiyan, Hubei, China, in Jun 2010, revealed the presence of seven new and eight known alkaloids. And some of them showed potent cytotoxicity against five human cancer cell lines. Further studies revealed that *N*-methylhemeanthidine chloride (NMHC) inhibits pancreatic cancer cell proliferation via down-regulating AKT activation *in vitro* and *in vivo*. Interestingly, NMHC slectively inhibits AML cell proliferation *in vitro* and *in vivo*, and the action mechanism is activating the NOTCH signaling pathway, and NMHC is a novel NOTCH agonist. And the semi-synthesis of NMHC was investigated. In addition, in order to prepare *N*-phenylethylcrinasiadine derivatives, we developed transition-metal-free method to synthesize phenanthridinones from biaryl-2-oxamic acid under radical conditions, and synthesized several phenanthridinone derivatives. Their SAR was studied, and a more ative phenanthridinone derivative was found.

In order to enrich the bioactive NMHC, the whole plants of *Z. candida* were re-collected in October, 2011. In the current investigation, total 54 alkaloids including 3 new skeleton types and 27 new alkaloids, and 2 new flavanes were isolated. New isolates were evaluated for their antitumor, anti-inflamatory, and acetylcholinesterase inhibitory activities, and some of them exhibited potent activities. In addition, their SAR will be discussed.

Our investigation on these two collections of the whole plants of *Z. candida* at two different seasons revealed that the alkaolodial components of *Z. candida* vary with seasons.

Acknowledgment. This work was financially supported by the National Natural Science Foundation of China (No. 31170323), Wuhan Youth Chenguang Program of Science and Technology, China (No. 201271031389).

GOSSYPOL – A VERSATILE BUILDING BLOCKS FOR ADVANCED DRUG DESIGN AND DISCOVERY

Lan Zhang[1,2,3], Lu Xu[1,2,3], Lulu Wang[1,2,3], Yagang Zhang[1,2,3*]

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Urumqi, Xinjiang 830011, P. R. China
2) Xinjiang Technical Institute of Physics and Chemistry, CAS, Xinjiang, 830011, P. R. China
3) University of the Chinese Academy of Sciences, Beijing 100039, P. R. China

Gossypol (1,1′,6,6′,7,7′-hexahydroxy-3,3′-dimethyl-5,5′-diisopropyl-(2,2′-binaphthalene)-8,8′-dicarboxaldehyde, $C_{30}H_{30}O_8$) is a polyphenolic aldehydic compound extracted from cotton plants. Although studies have indicated that gossypol was toxic to monogastric animals as well as young ruminants, the unique and elegant structure of Gossypol makes it a versatile building block for advanced drug design and discovery. Gossypol was used in contraception. Studies showed that Gossypol and its derivatives had series of interesting biological activities including anti-cancer, anti-virus, anti-protozoan parasites, anti trypanosoma, antimalaria and anti-inflammatory. As a bio-based abundant precursor, series of Gossypol derivatives can be conveniently synthesized including ether derivatives, ester derivatives, gossypolone derivatives, Schiff's base gossypol, apogossypol and its derivatives, gossylic acid derivatives, azo derivatives, gossylic nitrile derivatives and halogen derivatives. The preparation of these gossypol derivatives and their biological activities will be discussed.

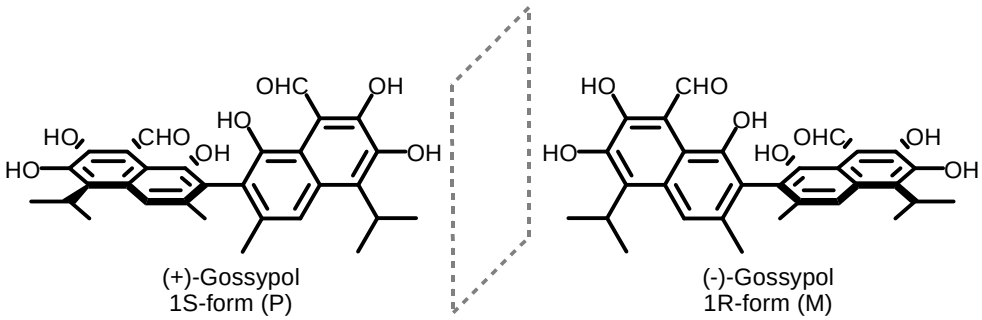

Fig. 1. The structure of gossypol enantiomers corresponding to absolute configuration of gossypol atropisomers, (P) and (M) according to the helicity rule.

Acknowledgment. This work was financially supported by National Natural Science Foundation of China (21472235, 21464015), Xinjiang Distinguished Youth Scholar Program (qn2015jq012) and "One Thousand Talents" Program (Y32H291501) of China.

THE SYNTHESIS AND MODIFICATION OF ALKALOIDS AS RESERVE FOR FURTHER ICPS DEVELOPMENT

Yu. R. Mirzaev, V. I. Vinogradova, Sh. Rahimov, Sh. N. Jurakulov, Z. I. Sanoev

Institute of Chemistry of Plant Substances, Mirzo Ulugbek st, 77, Tashkent, 100170

The main achievement of ICPS is the deep elucidation of chemical composition of major plants growing mainly in Central Asia. First of all, it is related with successful studies of ditherpenoid alkaloids and ecdisteroids of certain local plants. Some substances of mentioned plants are exporting abroad and provided financial independence of the Institute. It needs to point, that base of mentioned Institute achievements were made in past century. Later Institute′s achievements became modest. One of the means of Institute scientific activity revive is obviously the strength of synthesis of new and modification of known biological active compounds. For example, in the Institute complete synthesis of quinasolone and quinasoline alkaloids of Peganum harmala is real and pharmacologist obliged to determine their application. Besides, the modification of N-cholinostimulating agent Cytisine, have gave the series of new compounds with N- and M-cholinopositive and cholinonegative action, that reach 20–40% of tubocurarine, atropine and carbacholine activity with more expressed pharmacological width. Deep pharmacological studies of mentioned series would be fruitful as fundamenthal so practice study. Another example related with series of synthetic phenylisoquinoline compounds. Pharmacologic studies have discovered their relativity to the number of neuroreceptors, such as dopamine-, 5HT-, M-cholino- and α-adrenoreceptors. It is known, these receptors take part in regulation of psychosomatic state. The compounds F-16 and F-29 supposed for patent defense in quality of original anxiolytic and antipsychotic compounds. In the Institute have been discovered the selectivity of some compounds to M_2 subtype of muscarinic receptors. Synthesed in the Institute 3-a-chlorimperialine was for thirty times more power, than native alkaloid. Fundamental pharmacologic studies conducted in the Institute have showed possibility of create at least four branches of medical preparation on the base of M_2-cholinoblockers. Semisynthetic 3-a-chlorimperialine recognized in world as aethalone of central M2-cholinoblockers and base for create psychotropic drugs.

CHEMICAL COMPONENTS FOUR REPRESENTATIVE OF FAMILY LAMIACEAE -*Scutellaria holosericea, S. schachristanica, S. gutata, Dracocephalum komarovii* AND THEIR BIOLOGICAL ACTIVITY

K. A. Eshbakova[1,3*], Z. O.Tashmatov[2,4], Kh. Sh. Kamoldinov[2,4], C. Z. Omonturdiev[5], Sh. S. Khushmatov[5], H. A. Aisa[2,3*]

1) S.Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences, 100170, Tashkent, Republic of Uzbekistan, e-mail: e_komila@yahoo.com
2) Key Laboratory of Plant Resources and Chemistry of Arid Zone, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi, Xinjiang, P. R. China, e-mail: haji@ms.xjb.ac.cn
3) Key Laboratory of Xinjiang Indigenous Medicinal Plant Resources Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi, P. R. China;
4) University of Chinese Academy of Sciences, TWAS, 19 Yuquan Road, 100049, Beijing, P. R. China
5) Institute of the Bioorganic Chemistry, Academy of Sciences, 100125, Tashkent, Republic of Uzbekistan

Plants of the family Lamiaceae widely distributed in the flora Uzbekistan and used in the folk medicine. Study their chemical components and identify biological activity of current interest.

We have studied four representative of family Lamiaceae: three species of *Scutellaria* and *Dracocephalum komarovii. Scutellaria schachristanica* and *Dracocephalum komarovii* are endemic plants for Uzbek flora. Aerial parts these plants we have isolated a new and known compounds in relation to flavonoids, sterols, terpenoids and iridoids.

The isolated compounds showed highly hinotropic, antihypertensive and spasmolytic effects and founded flavonoids with an increase in the chemical structure of OH group increases kardioinotropnoe positive effects, but with the increasing number of group's increases -OCH_3 negative inotropic effects.

MONOTERPENE GLYCOSIDES, IRIDOIDS AND SECOIRIDOIDS FROM PLANTS OF TURKEY

İhsan Çaliş

Near East University, Faculty of Pharmacy, Department of Pharmacognosy, Nicosia, N. Cyprus, e-mail: ihsan.calis@neu.edu.tr

Iridoids have a cyclopentane-tetrahydropyran ring system of which 10-hydroxy geraniol or 10-hydroxy nerol are the biosynthetic precursors. This simplest basic body of the series, the iridodial ($C_{10}H_{16}O_2$) has firstly been found in the defense secretion of *Iridomyrmex* species (ants). Therefore, iridoids are mainly C_{10} compounds and represent mostly monoglucosidic structures. Rarely, C_8 and also C_9 iridoids are also found. Valepotriates and and plumerisin are typical examples for nonglycosidic iridoids. Secoiridoids are formed from iridoids (loganin) by cleavage of the bond between C-7 and C-8 of the cyclopentane ring yielding secologanin which is a key intermediate in the biosynthesis of some alkaloids. Secologanin is also the biosynthetic precursor of the Oleaceae- and Gentianaceae-type secoiridoids, such as oleuropein and gentiopicroside, swertiamarin, sweroside and their esters, respectively. Distributions of iridoids within the plant families are limited to subclasses of Dicotyledones of Angiospermae, especially to Sympetalae. Despite their simple structures, iridoids and secoiridoids show a rich structural diversity.

Along the above mentioned lines, phytochemical studies have been performed on plants registered in the Flora of Turkey, which represents more than 9.000 species and 12.000 taxa [1–3]. In this presentation, a brief summary will be given for the studies showing highlights in the structural diversity of monoterpene glycosides from plant species belonging to the families *Caprifoliaceae* (*Lonicera* spec., *Viburnum* spec.), *Scrophulariacea* (*Euphrasia pectinata, Lagotis stolonifera*, *Scrophularia* and *Pedicularis* spec.), *Plantaginaceae* (*Plantago* and *Globularia* spec.), *Gentianaceae* (*Gentiana* sp.), *Oleaceae* (*Fraxinus angustifolia, Olea europea*), *Rubiacae* (*Putoria calabriaca, Wendlandia ligstroides*), *Verbenaceae* (*Clerodendrum inerme*) and selected plants from various subfamilies of *Lamiaceae* [*Ajuga* (AJ), *Eremostachys* (LA), *Lamium* (LA), *Leonurus* (LA), *Phlomis* (LA), *Scutellaria* (SC), *Sideritis* (LA), *Stachys* (LA), *Teucrium* (TE), *Nepeta* (NE)].

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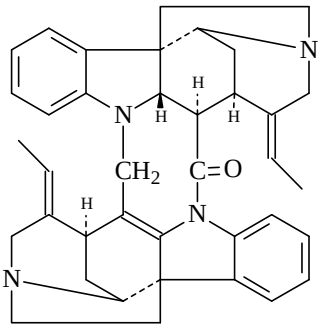
TRANSFORMATION OF A-METHYLENE INDOLENINE ALKALOIDS

P. Kh. Yuldashev

Institute of the Chemistry of Plant Substances, Academy of Sciences of Uzbekistan
77, M. Ulugbek str., 100170 Tashkent, e-mail: fattakhyuldashev@rambler.ru

Indoline alkaloid vincanine$C_{19}H_{20}N_2O$ was first isolated from the roots of *Vincaerecta*. Continuing work on the preparation of biologically active compounds, among the derivatives of the indoline alkaloids of vincanine, we studied reaction of its tranformation.

Vincanine, upon reduction with zinc in sulfuric acid, forms two bimolecular products: 2,16-dihydro-19-oxonordihydrotoxypherine (**1**) and 2,16,2′,16′-tetrahydronordihydrotoxypherine (**2**).



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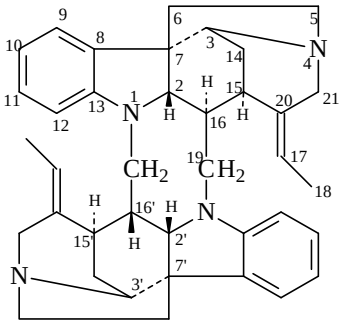

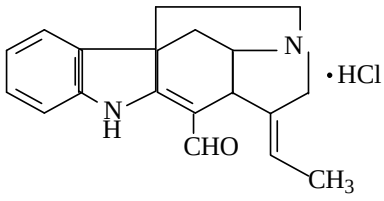

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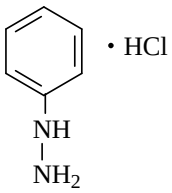

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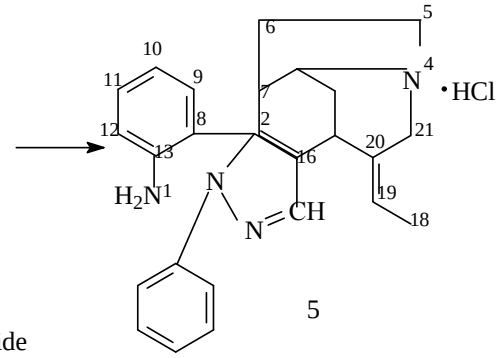
Vincanine hydrochloride Phenylhydrazine hydrochloride



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Formed 1,2-secovincanine-2,17-phenylhydrazone **5** is toxic for tumor cells and is not toxic to normal cells.

ECO SCIENCE FOUNDATION - A CATALYST FOR SCIENCE, TECHNOLOGY AND INNOVATION BASED ECONOMIC DEVELOPMENT IN ECO REGION

Manzoor Hussain Soomro

ECO Science Foundation
Constitution Avenue, Sector G-5/2, Islamabad 44000, Pakistan,
e-mail: president.ecosf@eco4science.org, manzoorhsoomro@gmail.com

Economic Cooperation Organization (ECO) is an Intergovernmental Organization of 10 countries; Afghanistan, Azerbaijan, Iran, Kazakhstan, Kyrgyzstan, Pakistan, Tajikistan, Turkmenistan, Turkey and Uzbekistan. The ECO is meant for economic wellbeing and cultural integration of the peopleas well as for promotion of trade in the region. It has a number of Specialized Agencies likeECO Cultural Institute in Tehran; ECO Educational Institute in Ankara, ECO Science Foundation in Islamabad; the ECO Development Bank in Istanbul and so on.

ECOScience Foundation (ECOSF) established in Islamabad Pakistan is mandated to promote Science, Technology, Innovation and Science Education leading to economic development and integration of the community. Thus it supports scientific research and related activities,such as; funding of collaborative research projects in priority areas of energy, water, food security and climate change etc. in line with “ECO Vision 2025”, organization and funding of science conferences, capacity building workshops and provides travel grants to scientists for participation in various such forums within ECO member countries. The world has always been in search of a system of science teaching, tailored to create thinkers, inquirers and discoverers, needed to fuel the scientific revolution of the day. Since the Great Scholars & Scientists are actually nurtured at schools and the concept of "inquiry" i.e., critical thinking and critical observation which fosters the understanding of scientific and technological innovations needs to be inculcated among the young generation at primary and secondary school levels. Thus to provide a stronger research base,the Foundationemphasizes on nurturing Inquiry Based Science Education (IBSE) at school level, in collaboration with its collaborators and partners. The main collaborators of ECOSF include; the Academies ofSciences of each country, *La main a la pate* (LAMAP) Foundation of France, International Science Technology and Innovation Centre for South-South Cooperation under the auspices of UNESCO (ISTIC) Kuala Lumpur-Malaysia, Inter Academy Partnership Science Education Program (IAPSEP), UNESCO, TWESCO and many more. The ECOSF thus plays the role of a catalyst to trigger collaborative programmes for Science, Technology & Innovation (STI) and IBSE based economic development in the 10 countries of ECO region. The presentation will elaborate the programmes and initiatives of ECOSF for the scientific community to benefit from them.

EFFECTS OF NAGILACTONE B ON ATHEROSCLEROSIS

Y. Gui, S. Yao, H. Yan, L. Hu, C. Yu, F. Gao, C. Xi, H. Li, Y. Ye, Y. Wang

State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, 201203, Shangha, P. R. China, e-mail: ypwang@simm.ac.cn

Aims: Atherosclerosis is the most common cause of cardiovascular diseases, such as myocardial infarction and stroke. We hypothesized that nagilactone B (NLB), a small molecule extracted from the root bark of Podocarpus nagi (Podocarpaceae), suppresses atherosclerosis in an atherosclerotic mouse model.

Methods and results: Male apoE-deficient mice on C57BL/6J background received NLB (10 and 30 mg/kg) for 12 weeks. Compared with the model group, NLB treatment (10 and 30 mg/kg) significantly reduced en face lesions of total aorta areas. In RAW264.7 cells, NLB significantly ameliorated cholesterol accumulation in macrophages via enhancing apolipoprotein A-I and HDL-mediated cholesterol efflux. Mechanistically, NLB induced messenger RNA and protein expression of the ATP-binding cassette transporter A1 (ABCA1) and G1 (ABCG1) in RAW264.7 and THP-1 cells. Liver X receptor (LXR) site mutations in the mouse ABCA1 promoter abrogated NLB-mediated luciferase reporter activity. LXRα and LXRβ small interfering RNA suppressed NLB-mediated induction of ABCA1 expression. Consistent with in vitro results, NLB induced ABCA1 expression and suppressed macrophage areas in the aortic sinus. Moreover, NLB treatment did not induce the protein expression of LXR in liver. Hepatic and intestinal cholesterol accumulation was significantly alleviated on NLB treatment. Besides, NLB significantly improved plasma lipid profiles in apoE-deficient mice.

Conclusion: Selective LXR activation in macrophages with NLB induces ABCA1- and ABCG1-mediated cholesterol efflux while exerting minimal effects on lipogenesis and lipid accumulation in liver, resulting in regression of atherosclerosis, and therefore might be a promising strategy for therapeutics.

A BI-MODAL ACTIVATION MECHANISM UNDERLIES SCORPION TOXIN INDUCED PAIN

Lai Ren, Yang Shilong

Key Laboratory of Animal Models and Human Disease Mechanisms of Chinese Academy of Sciences/Key Laboratory of Bioactive Peptides of Yunnan Province, Kunming Institute of Zoology, Kunming, Yunnan 650223, P. R. China, e-mail: rlai@mail.kiz.ac.cn

Venomous animals use peptide toxins for hunting and self-defense. To achieve these goals, toxins need to bind to their targets with high affinity due to the small amount a single bite or sting can deliver. The scorpion toxin BmP01 is linked to sting-induced excruciating pain; however, the reported concentrations for activating TRPV1 channel or inhibiting Kv channels (both in мM range) appear too high to be biologically relevant. Here we show that the effective concentration of BmP01 is highly pH-dependent – it increases by about 10-fold in inhibiting Kv channels upon a one-unit drop in pH, but decreases over 100-fold in activating TRPV1. Mechanistic investigation revealed that BmP01 binds to one of the two proton-binding sites on TRPV1 and, together with proton, uses a one-two punch approach to strongly activate the nociceptive channel. As most animal venoms are acidic, proton-facilitated synergistic action may represent a general strategy for intoxication.

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A GLOBAL VIEW ON REGISTRATION OF HERBAL PRODUCTS

Kelvin K.C. Chan

Liverpool John Moors University, Liverpool L3 3 AF, United Kingdom; University of Sydney, Technology, NSW2006; and Western Sydney University, NSW 2560, Australia, e-mail: profkchan@gmail.com; kelvin; chan@sydney.edu.au

Problems and difficulties are recognised by manufacturers in coping with regulatory requirements to implement the QSE of herbal medicinal products containing unidentified chemical entities in the finished products; as the actual bioactive components are seldom known [1]. Therefore the Good Agricultural & Collection Practice (GACP) is the key role to provide tracibility of the starting materials used for producing the finial product for registration. Pharmacopoeia standard of starting materials for research and manufacturing is the minimimum requirement to comply with the regulatory guidelines for registration purpose [2].

How should research and development (R&D) of herbal medicine be directed to comply regulatory mandates on registration of herbal products as medicines? How regulatory agencies have affected the types of herbal remedies available in the market? International authorities such as the EMA (EU), FDA (USA), MHRA (UK), NHPR (Canada), and TGA (Australia), and local authorities such as SFDA (PRC) and Hong Kong SAR (PRC) [2, 3] have guidelines for registration of herbal products. These are vasely different that it not easy to cope with as observed by The Work-Package 7 (WP7) of the 3-year EU-funded project on Good Practice in TCM Research in the Post-genomic Era. WP7 on R&D of Chinese Herbal Medicines published their findings [4] and advised that: (1) the lessons learnt from global regulation of herbal medicines, in particular those from traditional Chinese Medicine (TCM), will provide valuable insights for regulation of other traditional medicines, (2) before taking any regulatory action, readers are advised to consult current official legislation and guidance and/or to seek appropriate professional advice, and (3) the WHO is well placed to co-ordinate a consultation process with the aim of putting forward suggestions for harmonisation to key regulatory agencies.

This lecture will focus on examples from recent development of pharmacopoeia standards of starting Chinese materia medica to recently registered TCM herbal medicines admitted to the EU market for registration.

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DEVELOPING NEW SIMULATION METHODS FOR IDENTIFYING NEW PROTEIN CONFORMATION FOR DRUG DESIGN AND DISCOVERY

Weiliang Zhu

Drug Discovery and Design Center, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, 201203, Shanghai, P. R. China,
e-mail: wlzhu@simm.ac.cn

Target protein may have different conformations that could be used for drug discovery and design. Although more and more protein structures have been determined by experimental methods, the functional conformation may significantly be different from the structure at its crystal state. Therefore, it is meaningful to predict functional conformation of target protein by theoretical approaches. However, it is still a great challenge to simulate protein conformation change. Conventional molecular dynamics simulation methods can only simulate small protein systems as simulating large protein system requires too much computational resources that is not affordable to common project.

In the last 5 years, we developed 3 different new approaches for improving the efficiency and accuracy of the simulation of protein conformation change. Testing these new methods on different protein systems showed that not only they could significantly reduce the computational resources in comparison with the traditional molecular dynamics simulation, but also they achieved consistent result with that from conventional MD and experimental studies. Therefore, these results demonstrated that the new methods may have great potential in investigating conformational change of large protein systems for providing more reasonable protein conformation for drug discovery and design.

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THE OSTEOGENIC PROPERTIES OF DANGGUI BUXUE TANG, A CHINESE HERBAL DECOCTION CONTAINING ASTRAGALI RADIX AND ANGELICAE SINENSIS RADIX: GENOMICS ANALYSIS OF SPECIFIC CHEMICAL KNOCK-OUT HERBAL DECOCTION

Amy G. W. Gong, Tina T. X. Dong, Karl W. K. Tsim

Division of Life Science and Center for Chinese Medicine, The Hong Kong University of Science and Technology, Clear Water Bay, Hong Kong; HKUST Shenzhen Research Institute, Hi-Tech Park, Shenzhen 518000, P. R. China, e-mail: botsim@ust.hk

Danggui Buxue Tang (DBT), a Chinese herbal decoction, contains 2 herbs of Astragali Radix (AR) and Angelicae Sinensis Radix (ASR) at the ratio of 5:1. Clinically, DBT was utilized to mitigate menopausal osteoporosis; however, the signaling mechanism and the active compounds contributed in bone formation remained unclear. Calycosin and ferulic acid, being the most abundant distinct chemicals in AR and ASR, respectively, were depleted specifically from DBT by HPLC separation. Authentic DBT, a calycosin-depleted DBT ($DBT_{\Delta cal}$) and a ferulic acid-depleted DBT ($DBT_{\Delta fa}$) were applied onto cultured rat osteoblasts. Mineralization assay illustrated that both DBT and $DBT_{\Delta fa}$ significantly induced osteoblast differentiation, while $DBT_{\Delta cal}$ exhibited a reduced activation in mineralization. The total RNA from herbal decoction-treated osteoblasts was isolated for transcriptome analysis by RNA-seq. The gene expressions of osteogenic markers during differentiation, including Alpl, Runx2, Sparc, Sp7 and Spp1, were significantly increased under the treatments of DBT and $DBT_{\Delta fa}$. Signaling pathway analysis by KEGG and GO-Elite revealed that 11 pathways were activated by DBT, including MAPK/ERK and Wnt/в-catenin signalings, as compared to the untreated control; these signaling pathways were the well-known cascades for osteoblast formation. In contrast, $DBT_{\Delta cal}$ was not able to trigger Wnt/в-catenin signaling. Thus, our findings indicated that calycosin could be an indispensable chemical in DBT to orchestrate multi-components of DBT as to achieve maximal osteogenic properties.

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UNCOVERING NOVEL SIGNALING MECHANISMS USING NATURAL SMALL MOLECULES AS THE CHEMICAL PROBES

Xiaojiang Hao[1], Lin Li[2], Quan Chen[3], Chonglin Yang[4]

1) Kunming Institute of Botany, Chinese Academy of Sciences, P. R. China, e_mail: haoxj@mail.kib.ac.cn
2) Shanghai Institutes for Biological Sciences Chinese Academy of Sciences, P. R. China, e-mail: lli@sibs.ac.cn
3) Institute of Zoology, Chinese Academy of Sciences, P. R. China, e-mail: chenq@ioz.ac.cn
4) Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, P. R. China, e-mail: clyang@genetics.ac.cn

Natural products of plants of plants, in generally, are considered as a rich source of novel structural and bioactive small molecules. Especially, the structural characters of natural products could inspire us to identify the suitable chemical probe to uncover some underlying mechanisms of cellular signaling pathways. Combination of chemical and biological research groups promotes us to approach on this goal. S-3, a diterpenoid derived from spiramine alkaloids isolated from *Spiraea japonica* complex, helped us to reveal some novel mechanisms of the signaling pathways such as a specific inhibition of Wnt/в-catenin signaling [1,2], a Bax/Bak-independent mechanism of cytochrome c release and apoptosis [3], and an unconventional process of mitochondrial fusion [4]. Recently, aimed to promote biogenesis of lysosome using natural small molecules, we uncovered that protein kinase c controls lysosome biogenesis independently of mTORC1 [5]. By identifying small molecules HEP-14 and HEP-15, the Ingenol-type diterpenoids isolated from *Euphorbia peplus*, we revealed that PKC couples TFEB activation with ZKSCAN3 inactivation through two parallel signaling cascades to enhance lysosome biogenesis, which provides insights into previously reported effects of PKC on lysosomes.

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BAVACHININ, A COMPOUND FORM CHINESE MEDICINE *Psoralea corylifolia,* WITH ITS PAN-PPAR AGONIST EFFECTS

Yiming Li

School of Pharmacy, Shanghai University of TCM, 1200 Cailun Road, 201203, Shanghai, P. R. China, e-mail: ymlius@163.com

Pan-peroxisome proliferator-activated receptors (PPAR) agonists have long been desired as therapeutic drugs against metabolic syndrome. However, limited efficacy and undesirable adverse effects have hindered the development of PPAR agonists. In this study, we identified bavachinin as a novel natural pan-PPAR agonist from the traditional Chinese anti-diabetic herb *Malaytea scurfpea* fruit. Mouse and monkey studies show bavachinin exhibited properties desired for an anti-diabetic PPAR-target agonist without weight gain and hepatotoxicity, which are distinct from known synthetic PPAR-γ modulators. Intriguingly, bavachinin did not antagonize, but rather synergize with synthetic PPAR-α and -γ agonists on PPAR transcriptional activities. We also performed dose-response mouse tests to certify their synergism in lowering glucose and TG levels. Furthermore, we demonstrated that bavachinin shared the same stronger canonical site as rosiglitazone and had the other alternate binding site in PPAR-γ via cellular, NMR and docking methods. Our structural analysis revealed that the 6-prenylatedflavanone skeleton and 4′-hydroxy and 7-methoxy groups of bavachinin were crucial to its bioactivities. It is the first time to report the synergistic effects between PPAR agonists by activating the alternate binding site. The synergism between bavachinin and synthetic PPAR-α or -γ agonists might increase efficacy and decrease toxicity of the market drugs with a lower-dosage.

CHEMICAL COMPONENTS AND BIOACTIVE PROPERTIES OF *Coreopsis tinctoria*

Jun Li, Haji Akber Aisa*

The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi 830011, P. R. China, e-mail: haji@ms.xjb.ac.cn*; lijun702@ms.xjb.ac.cn

Coreopsis tinctoria, also called "snow chrysanthemum" in China due to its distribution of the high altitude on the Karakorum mountains in Xinjiang Province, is a member of the Asteraceae or Compositae family, which originated from the midwest of American and presently has been spread all over the world. Besides the usage of ornamental plant, *C. tinctoria* has been known as a folk functional food for anti-diabetes and anti-hyperlipid.

In our present study on the chemical components and bioactive properties of *C. tinctoria*, 22 compounds including 20 flavonoids and two phenylpropanoids were isolated and identified, and six of them were discovered from this plant for the first time. Moreover, some of these flavonoids were revealed to exhibit good anti-diabetic activity.

BIOCIDAL PEPTIDES FROM THE ENDEMIC PLANTS OF CENTRAL ASIA AND THEIR APPLICATION

A. Yili[1], Sh. I. Salikhov[2], A. Aisa[1]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, Urumqi 830011, Xinjiang, P. R. China, e-mail: abu@ms.xjb.ac.cn
2) Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan

It is generally known that so many infectious diseases are treated with antibiotics. However, the increasing of drug-resistant of bacteria also makes us face the danger more and more. There is a way to solve this problem- search of new compounds which having completely different mechanism of action against to infectious diseases. In this sense, antimicrobial peptides are considered an alternative to be widely used now in medicine synthetic antibiotics because of completely different mechanism of action to pathogenic microorganisms.

Therefore, study the properties of the natural antimicrobial peptides: nontoxic organism, no drug-resistant against to pathogenic microorganisms, functional targeted, high therapeutic effectiveness, completely different from antibiotics, will lead to creation of a new generation of drugs. Search peptides with antibacterial, antifungal, antitumor and other activities from endemic plants of Central Asia such as Apiaceae and *Cicer arietinum* L. seeds are urgent issues of bioorganic chemistry, pharmacology and pharmacy. And creation of new peptides production technology has a special significance.

Therefore, the systemically studies and pharmaceutical extraction of polypeptides and proteins from edemic plants of Central Aisa can be regarded as one of the valuably potential pharmaceutical raw materials, and could be applied for valuable food additives and pharmaceutical products.

Acknowledgment. Thanks for financial support to the project of “Supporting Xinjiang 201491160” and 2014 "the light of the western" talent training plan; Thank for the Central Asia Drug Research and Development Center of the Chinese Academy of Sciences and the Training Project of Xinjiang Autonomous Region for Technological Innovation of Youth Talents for financial support.

THE NATURAL PRODUCTS RESEARCH ON TUJIA ETHNOMEDICINE

Wei Wang

TCM and Ethnomedicine Innovation & Development Laboratory, Sino-Luxemburg TCM Research Center, School of Pharmacy, Hunan University of Chinese Medicine, Changsha 410208, P. R. China, e-mail: wangwei402@hotmail.com

Tujia ethnic nationality is an inland minority of China, who lived in the Wuling mountains area (including Hunan, Hubei, Chongqing and Guizhou Provinces) for generations.

The warm and humid climate of Wuling mountain area resulting high incidence of rheumatic diseases in local residents.

They have developed their special ethnomedicine for the prevention and treatment of kinds of disease during thousands of years. The Tus people trust the effect of the Tujia ethnomedicine and many folk medicines are still used widely in their ghetto so far. Tujia ethnomedicine is an important part of traditional Chinese medicine, it has an unique Tujia ethnomedicine theory "three yuan" theory and peculiar drug classification, such as "72-Qi herb", "36 -Blood herb", "72-Lotus herb", "72 Huanyang herb" and so on. We investigated some of these unique Tujia ethnomedicines, did chemistry, efficacy and quality control studies on several typical Tujia ethnomedicine and got some interesting results.

Oral Presentations

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ДХО "NIKAPHARM" (РУз)

Флатерон

АНТИАТЕРОСКЛЕРОТИЧЕСКОЕ СРЕДСТВО

Флатерон – препарат, полученный из растения *Thermopsis alterniflora* (термопсис очередноцветковый)

Thermopsis alterniflora

Действующее вещество:
Сумма флавоноидов, в основном лютеолина и формононетина, получаемая из дикорастущего растения *Thermopsis alterniflora* .

Показания к применению:
Флатерон рекомендуется применять для профилактики и лечения нарушений липидного обмена, атеросклероза, атеросклеротических поражений сосудов мозга, коронарных и периферических сосудов, ишемической болезни сердца с сопутствующей гиперлипидемией (преимущественно с гиперхолестеринемией).

Преимущества:
По гиполипидемической активности Флатерон в экспериментальных условиях превышал или был вполне сопоставим с действием мисклерона (Венгрия), по ангиопротекторной активности Флатерон превосходил продектин (Венгрия).

Форма выпуска:
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Р. 00199/07/15

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Факс: (+99871) 262 73 48;
Тел.: (+99871) 262 59 13, 262 05 48
E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ЗАО ВИФИТЕХ (РФ),
ЧНПП "RADIKS" (РУз)

ГАЛАНТАМИНА ГИДРОБРОМИД

Антихолинэстеразный фитопрепарат

Ungérnia Victoris Wed.

Бромистоводородная соль алкалоида галантамина, получаемого из растения *Ungérnia Victoris* (унгерния Виктора)

Показания к применению: Галантамина гидробромид применяется в токсикологии, анестезиологии, хирургии, неврологии, психиатрии, рентгенологии и физиотерапии. Препарат назначают при двигательных и чувствительных нарушениях, связанных с невритами, полиневритами, радикулитами; при остаточных явлениях после перенесенного инсульта и поражений тканей мозга инфекционно-воспалительного, токсического и травматического генеза (менингит, миелит, менингоэнцефалит); при психогенной и спинальной импотенции и другой патологии нервной проводимости. В восстановительном периоде острого полиомиелита и при детских церебральных параличах применение препарата способствует восстановлению двигательных процессов и улучшению общего состояния больных.

Галантамина гидробромид рекомендован для лечения миастении, миопатии, атонии кишечника и мочевого пузыря, прогрессирующей мышечной дистрофии, деменции альцгеймеровского типа легкой или умеренной степени, закрытоугольной глаукомы. Препарат применяют при отравлении холинолитическими средствами и морфином, для функциональной рентгенодиагностики при заболеваниях желудка и кишечника.

Форма выпуска:
Таблетки по 5 мг и 10 мг, №50,
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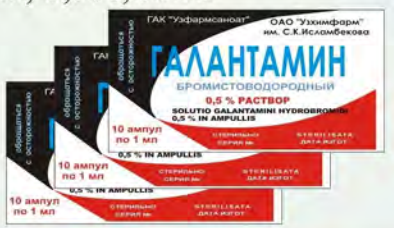
Р. 04/415/6



Ташкент, 100170, ул. Мирзо Улугбека, 77.
Факс: (99871) 262 73 48;
Тел.: (99871) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК И ПРОИЗВОДИТЕЛЬ ДИАГНОСТИКУМОВ:

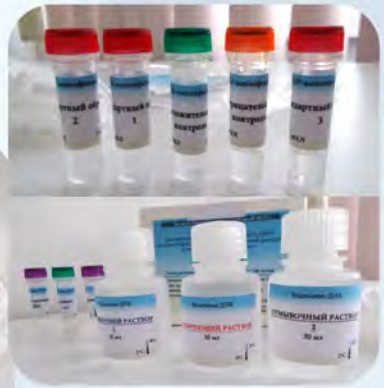
ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ

ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз

ПЦР НАБОРЫ ДЛЯ ВЫЯВЛЕНИЯ ДНК ВИРУСА ГЕПАТИТА В (HBV) и РНК ВИРУСА ГЕПАТИТА С (HCV)

методом гибридизационно-флуоресцентной детекции в режиме «реального времени»

Наборы реагентов для диагностики гепатитов В и С в клинических образцах методом ПЦР (полимеразной цепной реакции)



ПЦР набор для диагностики гепатита С

Набор обладает высокой специфичностью и чувствительностью к гену вируса гепатита С. Время проведения анализа (с начала постановки ПЦР и до получения результатов) составляет 2 часа

ПЦР набор для диагностики гепатита В
Обладает высокой специфичностью и чувствительностью к гену вируса гепатита В. Время проведения анализа (с начала постановки ПЦР и до получения результатов) составляет два часа.

ПЦР набор для диагностики гепатита С
Набор обладает высокой специфичностью и чувствительностью к гену вируса гепатита С. Время проведения анализа (с начала постановки ПЦР и до получения результатов) составляет 2 часа

С помощью ПЦР диагностикумов возможного проведения ранней диагностики заболевания, что позволит провести эффективный курс лечения

100170 г. Ташкент, ул. М.Улугбека, 77
Тел: (+998 71) 262 59 13, 262 05 48; факс: (+998 71) 262 73 48
e-mail: plant_inst@icps.org.uz
www.uzicps.uz

РАЗРАБОТЧИК И ПРОИЗВОДИТЕЛЬ ДИАГНОСТИКУМОВ:

ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ

ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз

ИФА анти – LUES

ИФА анти – LUES - тест-система иммуноферментная для выявления антител к возбудителю сифилиса *Treponema pallidum* в сыворотке (плазме) крови человека.

Срок годности – 1 год

Регистрационное удостоверение ТВ/Х 00007/04/15
Набор рассчитан на 96 определений, включая анализ контрольных образцов, и содержит все необходимые для проведения анализа реагенты.

Ташкент, 100170, ул. Мирзо Улугбека, 77.
Факс: 998(71) 262 73 48;
Тел.: 998(71) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК И ПРОИЗВОДИТЕЛЬ ДИАГНОСТИКУМОВ:

ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ

ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз

ИФА-HBsAg

ИФА–HBsAg – тест-система иммуноферментная для выявления поверхностного антигена вируса гепатита В (HBsAg) в сыворотке (плазме) крови человека.

Чувствительность – 0,1 МЕ/мл

Срок годности – 1 год

Регистрационное удостоверение ТВ/Х 00008/04/15
Набор рассчитан на 96 определений, включая анализ контрольных образцов, и содержит все необходимые для проведения анализа реагенты.

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Тел.: 998(71) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК И ПРОИЗВОДИТЕЛЬ ДИАГНОСТИКУМОВ:

ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ

ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз

ИФА анти - HIV

ИФА анти – HIV - тест-система иммуноферментная для выявления антител к вирусам иммунодефицита человека I и II типов (ВИЧ – 1 и ВИЧ - 2) в сыворотке (плазме) крови человека (3 поколение).

Срок годности – 1 год

Регистрационное удостоверение ТВ/Х 00009/04/15
Набор рассчитан на 96 определений, включая анализ контрольных образцов, и содержит все необходимые для проведения анализа реагенты.

Ташкент, 100170, ул. Мирзо Улугбека, 77.
Факс: 998(71) 262 73 48;
Тел.: 998(71) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК И ПРОИЗВОДИТЕЛЬ ДИАГНОСТИКУМОВ:

ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ

ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз

ИФА – HIV - АГ/АТ

ИФА – HIV - АГ/АТ- тест-система иммуноферментная для одновременного выявления антигена р24 ВИЧ и антител к вирусу иммунодефицита человека, в сыворотке (плазме) крови человека (4 поколение).

Срок годности – 1 год

Регистрационное удостоверение № ТВ/М 00027/09/15

Набор рассчитан на 96 определений, включая анализ контрольных образцов, и содержит все необходимые для проведения анализа реагенты.

Ташкент, 100170, ул. Мирзо Улугбека, 77.
Факс: 998(71) 262 73 48;
Тел.: 998(71) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК И ПРОИЗВОДИТЕЛЬ ДИАГНОСТИКУМОВ:

ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ

ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз

ИФА анти – HCV

ИФА анти – HCV - тест-система иммуноферментная для выявления антител к вирусу гепатита С в сыворотке (плазме) крови человека.

Срок годности – 1 год

Регистрационное удостоверение ТВ/Х 00006/04/15
Набор рассчитан на 96 определений, включая анализ контрольных образцов, и содержит все необходимые для проведения анализа реагенты.

Ташкент, 100170, ул. Мирзо Улугбека, 77.
Факс: 998(71) 262 73 48;
Тел.: 998(71) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ДХО "NIKA PHARM" (РУз)

ФЛАНОРИН

Гепатозащитное средство

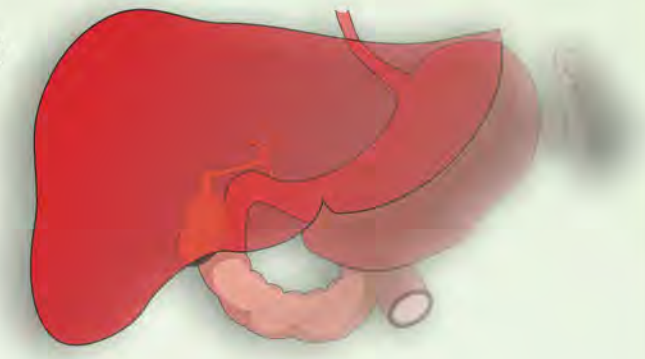
Фланорин представляет собой суммарный флавоноидный препарат, выделенный из *Pseudosophora alopecuroides*.

Pseudosophora alopecuroides

Фланорин оказывает благоприятное влияние на функциональное состояние печени при её токсических и вирусных поражениях.

Показания для применения:

Острые и хронические заболевания печени
- токсические и вирусные гепатиты
- цирроз
- гепатохолециститы
- жировое перерождение печени
- поражение печени с функциональными нагрузками, вызванными отравлениями
- состояния , связанные с повышенным притоком веществ, обременяющих функцию печени



Форма выпуска:

таблетки по 50 мг №100
Р. 01558/06/17

Ташкент, 100170, ул. Мирзо Улугбека, 77.
Факс: (+99871) 262 73 48;
Тел.: (+99871) 262 59 13, 262 05 48
E-mail: Plant-inst@rambler.ru
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REACTION OF DEOXYVASICINONE AND MAQUINAZOLINONE WITH FORMALDEHYDE

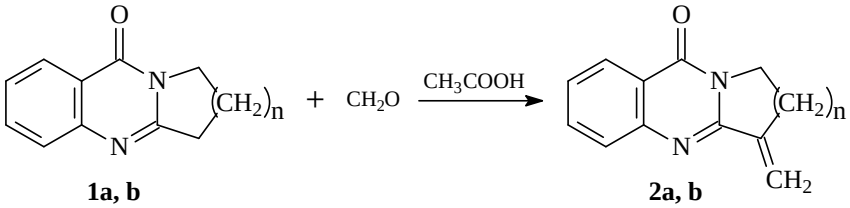
Sh. N. Zhurakulov, M. G. Levkovich, V. I. Vinogradova

Acad.S.Yu.Yunusov Institute of the Chemistry of Plant Substances, AS RUz,
100170, Tashkent, Uzbekistan, e-mail: j.sherzod.78@mail.ru

Tricyclic quinazoline alkaloids are widespread in plants *Peganum, Adhatoda, Galega, Galium, Nitraria* and other species. In addition to monomeric bases, dimeric alkaloids dipegine and dipeginole that contain the rests of deoxyvasicinone and deoxypeganine found in *Peganum harmala*.

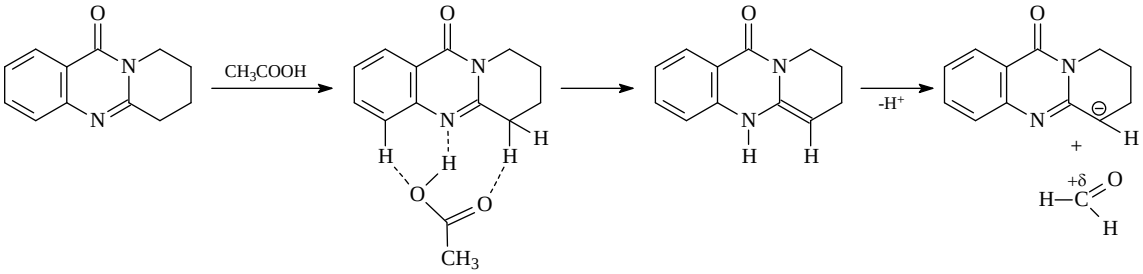
We have continued the investigation of the reaction of interaction between deoxyvasicinone and maquinazolinone and 30% formalin in benzene and methanol-acid medium in heating. In spite of a high reaction ability of C-3 (**1a**) or C-4 (**1b**) atoms, we don't observe the product formation.

When a glacial acetic acid used as a solvent, the reaction with formalin led to formation of methylidene products of deoxyvasicinone and maquinazolinone, and few mixture of bis-product and a primary alcohol. It may be due to a possible formation of deoxyvasicinone and maquinazolinone complexes with acetic acid that was proved by NMR experiment with deiteroacetic acid increasing the activity of C-3 (**1a**) or C-4 (**1b**) atoms.



1a, b **2a, b**

1a, 2a: n=1
1b, 2b: n=2



The structures of the obtained substances were proved by IR and NMR spectra.

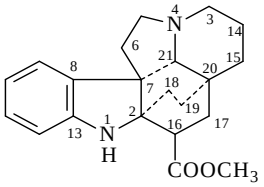
COORDINATION OF NITROGEN IN INDOLE ALKALOIDS KOPSININE, PSEUDOKOPSININE, ERVINCININE AND VINCADIFFORMINE TYPE

Sh. M. Adizov, B. Tashkhodjaev, P. Kh. Yuldashev, V. M. Malikov

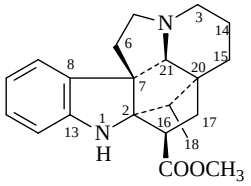
S. Yunusov Institute of the Chemistry of Plant Substances Academy of Sciences of Uzbekistan, 77, M. Ulugbek str., 100170, Tashkent, e-mail: adizovsh@gmail.com

Preparaton of water-soluble salts of alkaloids are actually dependant on the nature of the substrate, the solvent medium and the reacting salt. These factors affected not only to salt formation, but also to the formation of intra- and intermolecular hydrogen bonds, which is important for appearance of biological activity. The kopsinine and pseudokopsinine can form double salts under special conditions, but relationship between vincadifformine-mono salts and ervincinine, ervinidinine in commom conditions do not form salts.

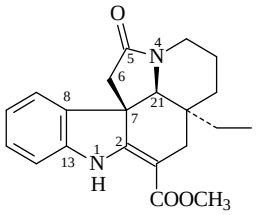
Coordination of the N1 and N4 nitrogen atoms of the indole alkaloids pseudokopsinine, kopsinine, vincadifformine is important in the salt formation. In pseudokopsinine, kopsinine lone pair of N4 tetrahedral nitrogen electrons is always directed to α- and protonation (or methylation) in these alkaloids is on the α-direction, maintaining the conventional *R*-configuration.



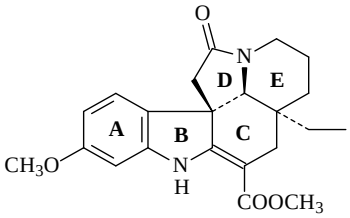
Kopsinine



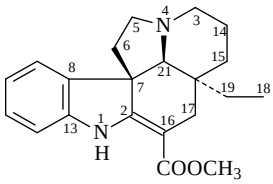
Pseudokopsinine



Ervinidinine



Ervincinine



(–)-Vincadifformine

However, in (–)-vincadifformine, its 14,15-epoxy derivative katovalinine and dimeric derivative vincadifformine, from available in the Cambridge Crystallographic Data Centre, the sp^3-hybridized atom N4 is inverted and its lone pair electrons directed towards β-direction (nitrogen took conventional *S*-configuration).

The molecules of ervinidinine (5-oxo-vincadifformine), ervincinine (5-oxo-11-methoxyvincadifformine) as distinct from (–)-vincadifformine, N4 nitrogen atom adjacent to the carbonyl group at C5. As expected adjacency of indole alkaloids N4 carbonyl group leads to the nitrogen atom to planar configuration. For that reason ervinidinine and ervincinine in common conditions do not form salts.

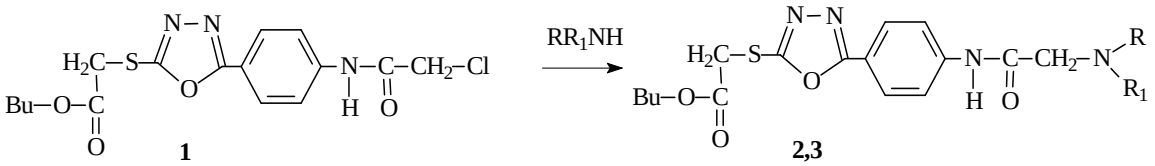
Thus, in the molecular structure of (–)-vincadifformine the inversion occurs at the nitrogen atom N4 in transition from the base into the salt. In ervinidinine and ervincinine molecules the conjugation of π-electrons of the carbonyl group with a lone pair of electrons on N4 nitrogen leads to trigonal planar coordination of N4.

NOVEL DERIVATIVES OF 2-ALKYLTHIO-5-(4-CHLORO-ACETYLAMINOPHENYL)-1,3,4-OXADIAZOLES

D. S. Ismailova

S. Yu. Yunusov Institute of the Chemistry of Plant Substance, AS RUz,
Tashkent, Republic of Uzbekistan, e-mail: d.jalilova@mail.ru

Continuing our investigations on studying of chemical modification of 5-(4-aminophenyl)-1,3,4-oxadiazol-2-thione derivatives [1] and to synthesize new compounds, we carried out reaction of α-[5-(4-chloroacetylaminophenyl)-1,3,4-oxadiazol-2-ylthio]-acetic acid butyl ester with heterocyclic (cytisine) and aliphatic (diethylamine) amines. Syntheses were carried out in dry benzene and acetone with changing an oxadiazolthione and an amine ratio, and a temperature of the reaction. It was established that the optimal conditions were interaction at boiling temperature of benzene and reagents ratio 1:2:



1 **2,3**

2, R=R$_1$=C$_2$H$_5$; **3**, R+R$_1$= residue of cytisine

Therefore, we synthesized and the structures of the synthesized compounds α-[5-(4-diethylacetylaminophenyl)-1,3,4-oxadiazol-2-ylthio]-acetic acid butyl ester and α-[5-(4-cytisineacetylaminophenyl)-1,3,4-oxadiazol-2-ylthio]acetic acid butyl ester are characterized by ^{1}H NMR spectra, physical and chemical data, which were not described in the literature. We continue works in this field.

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1. D.S.Ismailova**,** Kh.M.Bobakulov, E.R.Kurbanova, A.A.Ziyaev, Kh.M.Shakhidoyatov. Alkylation of 5-(*o*,*p*-aminophenyl)-1,3,4-oxadiazol-2(3H)-thiones // *Abstract book of the young scientist conference "Actual issues of the chemistry of natural compounds" devoted to the memory of acad. S.Yunusov*, March 12, 2015, p.48.

ANALYSIS OF SULFATCYL EYE DROPS BY THE METHOD OF RAMAN SPECTROSCOPY

N. B. Saidkarimova

The Tashkent Pharmaceutical Institute, Tashkent, Republic of Uzbekistan,
e-mail: nodira_botirovna@mail.ru

Introduction. The quality of medicines is considered as activity and safety of the human body, purity, and quantity. It is one of the main features of the product, which is being taken by the patient. Furthermore, the insurance of the quality of drugs is very complex problem of social life. It stands under the State control in many countries. Currently a number of modern methods, such as mass spectroscopy, HPLC, GC, IR, UV-spectroscopy and others are used in the evaluation of the quality of medicines. In particular, the Raman spectroscopy is also one of the promising method in pharmaceutical practice. Raman spectroscopy has strong potential for use in the fast, nondestructive analysis of tablets, powders, solution and gases.

Purpose. To use the new drug analysis method - Raman spectroscopy in pharmacy.

Materials and methods. For obtaining Raman spectrum a R532 Raman spectrometer (Enhanced Spectroscopy, USA) was used. The object of the analysis was Sulfatcyl eye drops.

Results and discussion. This study shows that the Raman spectrum of the eye drops Sulfatcyl sodium give an absorbtion lines at 823 cm^{-1} for C–S bonds, at 1128 cm^{-1} for sulfonamid group, at 1596 cm^{-1} -NH_2 group, and at 3366 cm^{-1} for H_2O.

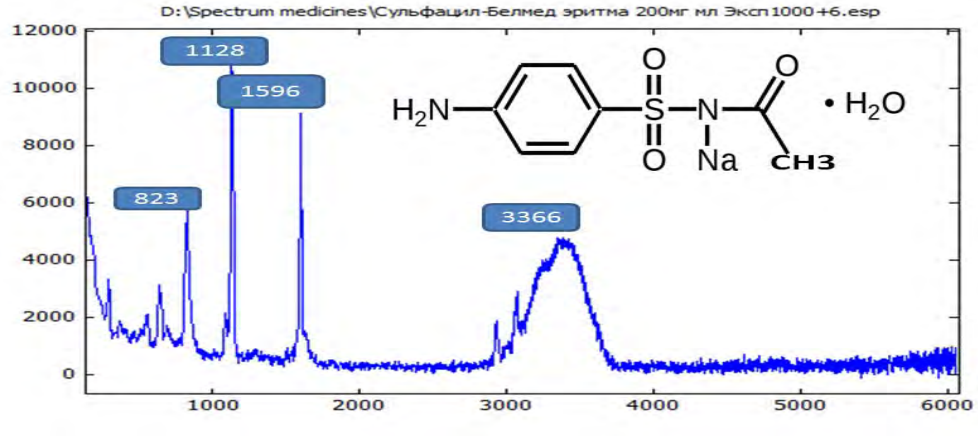


Fig. 1. Spectrum of the eye drops Sulfatcyl sodium

Conclusion. For the first time Raman spectrum of the eye drops Sulfatcyl sodium obtained and analyzed. According to this, characteristic peaks of medicine are appropriate to the specific functional groups in the structure of Sulfatcyl sodium.

NEW CYTOSTATIC BASED ON TROPOLONE ALKALOIDS WITH STIMULATION SFUS

Sh. N. Ibragimov, Z. M. Enikeeva

National scientific center of oncology at the Ministry of Health of RUz, 383, str. Farobiy, Tashkent, Uzbekistan

This work is studying at NSCO MH of RUz, on modification tropolones alkaloids, gave specify results: carried out synthesis and biological properties of new compound are studied, based on tropolones alkaloids colchicine and colchomine with various substitute in tropolones and heptadienic rings of alkaloids, which has less toxicity and high cytostatic activity in vitro, to detected at NCI USA.

Based on studying of antitumor activity in vitro in NCI, and then in vivo on animals with number subinoculation tumours are selected 15 substances with high activity for the further application at practical oncology.

These substances at 14–360 times less toxic, than colchicine, their antitumor effect exceeds as activity colchicine and colkhamine at 20–70%, and in some cases known cytostatic, including tubulin interactive (taxol, etoposide, vincristine) and alkylating preparations (doxorubicin, cisplatin, cyclophosphan) are used as control.

After expanded studying of antitumor activity of some substances in vivo and corresponding pharmaco-toxicological and pharmacopoeia researches at Central administrative on control quality of medical products and medical technics of MH of RUz 4 drugs: decocine, colchiprit (K-20), decovine and colkhaminol. Decocine has passed 1 phase of clinical tests as an antitumor preparation for skin cancer treatment, its clinical application has shown high percent of suppression of growth of tumour (at $T_{I\text{-}III}$ efficiency statistically authentically reaches 91.17%, in stages $T_{II\text{-}IY}$, at application of Decocine together with an irradiation – 77.76%).

By results of studying the mechanism of action 15 of new preparations are shown that all studied new preparations possess number of properties damaging tumor: mitotic activity, highly - alkylating, promote internucleosome to degradation and DNA fragmentation, inhibited topoisomerases I and II, as causes their high antitumor effect, i.e. possess the expressed cytotoxic action, with new preparations activity topoisomerases more chokes, and stimulated p53 - inductor apaptoze, the more low caused ability of overcoming of medicinal stability, and above, than at etoposide and doxorubicin.

Thus ability to emission SFUs protects an organism from consequences of their cytotoxic action. Substances with high level of SFUs, along with the expressed antineoplastic action, don`t reduce immunity after the spent treatment, at all substances high degree of overcoming of resistance is observed. There are substances with absence mutagenicity.

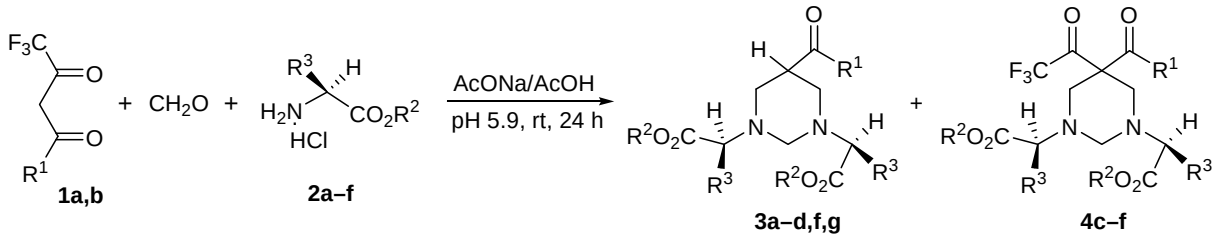
So 7 substances, and more all K-48, don′t reduce immunity and hemopoiesis that is caused by their ability to increase in quantity SFUs to 20–40 unit. Thus, representation that new substances concern new class of multifunctional antitumor preparations with property to induce SFUs is formed.

NATURAL α-AMINOACIDS IN THE SYNTHESIS OF CHIRAL FLUORINATED HEXAHYDROPYRIMIDINES

N. N. Gibadullina[1], D. R. Latypova[1], V. A. Dokichev[1,2]

1) Ufa Institute of Chemistry of the Russian Academy of Sciences, 71 Prosp. Oktyabrya, Ufa, 450054, Russian Federation
2) Ufa State Aviation Technical University, 12 K. Marx Street, Ufa, 450008, Russian Federation

In continued research on the synthesis of hexahydropyrimidines interaction of fluorinated 1,3-dicarbonyl compounds (ethyl 3-oxo-4,4,4-trifluorobutanoate (1a), 1,1,1-trifluoropentane-2,4-dione (1b)) with formaldehyde and esters of natural amino acids by Mannich type reaction was studied using an acetate buffer AcONa-AcOH (pH 5.9). As used aminoesters hydrochloride methyl ester *l*-alanine (2b), *l*-valine (2c), *l*-leucine (2d) and ethyl ester glycine (2a), *l*-phenylalanine (2e) and *l*-tyrosine (2f).



Entry	CH-acid			Amino ester		Isolated yields (%)	
		R^1		R^2	R^3	**3**	**4**
1	**1a**	OEt	**2a**	Et	H	**3a** (62)	–
2	**1a**	OEt	**2b**	Me	Me	**3b** (56)	–
3	**1a**	OEt	**2c**	Me	$CH(Me)_2$	**3c** (10)	**4c** (48)
4	**1a**	OEt	**2d**	Me	$CH_2CH(Me)_2$	–	**4d** (68)
5	**1a**	OEt	**2e**	Et	CH_2Ph	–	**4e** (46)
6	**1b**	Me	**2a**	Et	H	–	**4f** (70)
7	**1b**	Me	**2f**	Et	$CH_2C_6H_4OH$-4	**3g** (46)	**–**

Novel derivatives of 1,3,5- and 1,3,5,5-substituted hexahydropyrimidine, including those containing trifluoroacetyl group at the 5 position of the heterocycle was obtained, promising as chiral synthons for the production of biologically active substances.

Acknowledgment. This work was financial supported by the Russian Science Foundation (grant no. 14-33-00022)

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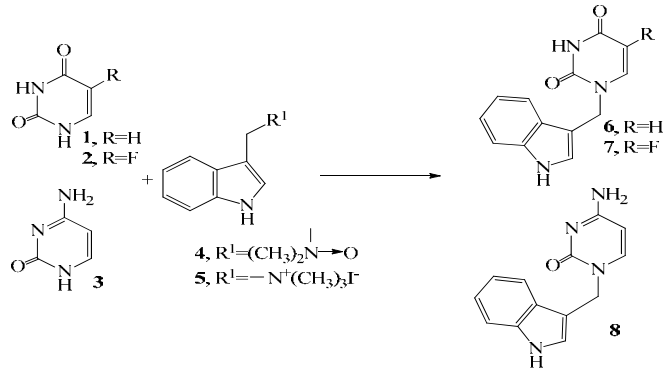
1. Latypova D.R., Badamshin A.G., Lobov A.N., Dokichev V.A. Russ. J. Org. Chem., **2013**, *49*, 843.

X - PHILIC AND IPSO - SUBSTITUTION REATIONS OF URACILS

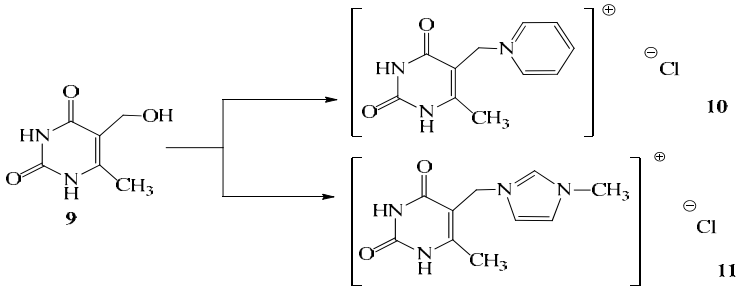
I. B. Chernikova, G. A. Salikhova, M. S. Yunusov

Ufa Institute of Chemistry of the Russian Academy of Sciences, 450054,
Ufa, Prospekt Oktyabrya, 71

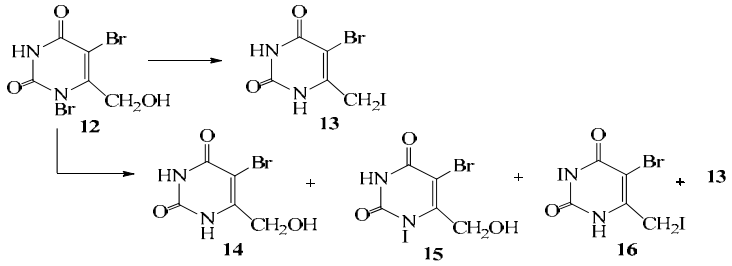
Reaction of uracil (**1**), 5-fluorouracil (**2**) and cytosine (**3**) with *N*-oxide gramine (**4**) or its iododmethylat (**5**) in DMF at 130°C for 7 hours leads to *N*-1-skatilderivatives **6**, **7** and **8** in moderate yields.



The reaction of 5-hydroxy-6-methyluracil (**9**), MsCl and pyridine or *N*-methylimidazole at room temperature for 5 hours gives the quaternary ammonium salts **10** and **11** in high yields.



Treatment of 5-iodo-1,3,6-trimethyluracil or 5-bromo-1,3,6-trimethyluracil with 5% H_2SO_4 in presence of an excess of KI at 80°C for 5 hours leads to the sole product of the reaction 1,3,6-trimethyluracil. Similar treatment of *N*-bromo-5-bromo-6-hydroxymethyluracil (**12**) gives a mixture in which the main component is 5-bromo-6-iodouracil (**13**). The reaction **12** with excess of KI in methanol at 50 ° C, depending on the reaction time, leads to 5-bromo-6-hydroxymethyluracil (**14**), *N(1)*-iodo-5-bromo-6-hydroxymethyluracil (**15**), *N(3)*-iodo-5-bromo-6-iodouracil (**16**), 5-bromo-6-iodouracil (**13**).



Acknowledgment. This study was supported by from Grant RSF 14-13-01307 and program Division of Chemistry and Materials Science of the Russian Academy of Sciences for 2016.

STRUCTURE OF THE NEW GERMACRANOLIDE – MEREZOLIDE

S. V. Serkerov, A. N. Aleskerova

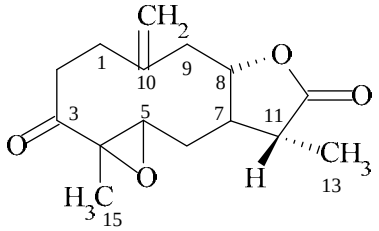
Botanical Institute of Azerbaijan NAS, Badamdar highway 40, Baku AZ1073
e-mail: s.serkerov@mail.ru

Sesquiterpene lactone ($C_{15}H_{20}O_4$, mp 123–125°C), isolated from the aerial part of *Artemisia kobstanitsa* Rzazade called merezolide has an absorption bands of CO-group γ-lactone ring (1795 cm^{-1}), six-membered CO–ketone group ring (1705 cm^{-1}) in the IR-spectrum. Intense band at 915 cm^{-1} in the IR-spectrum makes it possible to characterize double bond as methylene.

NMR spectrum of lactone have a signal at CH_3–CH<-group (d, 1.08 ppm, J = 7.00 Hz, 3H), methyl group at the oxide cycle (s, 2,20 ppm, 3H) and exocyclic methylene group (s, 4.80 and 4.95 ppm, 1H each, CH_2=C<)

In the area range of 2.40–4.00 ppm. spectrum has shown four one-proton signals: 2.50 (m), 2.76 (m), 2.90 (q, J_1 = 3.90; J_2 = 12.0 Hz) and 3.83 ppm (sextet, J_1 = 3.90; J_2 = 11.10; J_3 = 15.3 Hz). The quartet of them at 2.90 ppm intended typical proton chemical shifts with the oxide cycle. Sextet at 3.83 ppm caused by lactone proton interacting with three vicinal protons.

From these biogenetic considerations, and interpretation ofdata of the NMR spectrum chemical shifts and spin-spin constant of interaction of protons H-5, H-7, H-8 merozolide probably structure of 3-keto-4(5)-epoxy-8β,7α,11β(H)-germacra-10,14-en-8,12-olide (I).



ANTHOCYANINS OF FLOWERS OF *Polygonum patulum* M.B.

E. E. Dzhafarova[1], S. V. Serkerov[2], L. A. Mustafaeva[1]

1) Institute of the NANA Genetic resources to Mr. Buck, Azadlyg Ave
2) Institute of Botany of NANA, to Baku, Badamdar Highway, 40 AZ1073,
e-mail: eldar_novruzov@yahoo.co.uk

Species of the genus *Polygonum* L. in folk and scientific medicine used to treat gout, diabetes, nasal polyps, cancers, kidney stones and gall stones, and others diseases. Therapeutic effect of *Polygonum* species associated with the high content of polyphenolic compounds, anthocyanins. Anthocyanins, along with other substances polyphenol nature (catechins, flavonoids) have – antioxidant, antiradian effect, anticarcinogenic, interferon activating, antibiotic and other properties. We investigated the qualitative and quantitative composition of anthocyanins of flowers of *Polygonum patulum* M.B.

Flowers of *Polygonum patulum* collected in the phase of mass flowering at the edge of the forest of Hulug village Gusar region. Anthocyanins of flowers isolated by extraction with a mixture of methanol with concentrated hydrochloric acid (99: 1). The residue was treated with chloroform and analyzed by chromatography in systems of paper: I – butanol-acetic acid-water (4:1:2), II – water-conc.HCL-acetic acid (82:3:15). In chromatograms were found three anthocyanin substances. Based on mobility, two of them referred to diglucoside and one - to the monoglycoside. Judging by the color in the visible region and the UV-light can be assumed that they are derivatives of cyanidin and pelargonidin. After hydrolysis were found 2 aglycones. First identified as aglycone cyanidin, the second - pelargonidin . The identity of the first aglycone cyanidin confirmed by comparison with the chromatography data and UV - inspectors with that of authentic sample of cyanidin and literature data. By comparing with the authentic sample pelargonidin second aglycone identified with pelargonidin.

The quantitative content of anthocyanins in flowers determined by using photoelectrocolorimetric method by using a calibration curve for cyanidin. Cyanidin obtained from *Rosa* flowers. It was established that in the phase of mass flowering flowers contain anthocyanins 980 mg % (in wet weight).

It should be noted that the composition of the anthocyanin *Polygonum aviculare* L. flowers investigated for the first time.

ISOLATION AND STUDY OF CONTENT OF FLAVONOIDS OF LEAVES *Sambucus ebulus* L.

M. B. Zulfugarova[1], E. N. Novruzov[2]

1) Azerbaijan Medical University, Baku
2) Institute of Botany of NANA, to Baku, Badamdar Highway, 40 AZ1073,
e-mail: eldar_novruzov@yahoo.co.uk

Types of elder *Sambucus* L. regarded as essential medicines, food plants and are used in cardiovascular, oncology kidney and liver, and diabetes mellitus.Extract of flowers have an effect on reducing hemagglutination and reproduction of group forms A and B virus, flavonoids are associated with the H1N1 cholerae, including swine and avian influenza.

It was studied qualitative and quantitative composition of the flavonoid content of leaves *Sambucus ebulus*. Flavonoids were extracted from the dried powdered leaves with 70% alcohol. From the aqueous residue aqueous-alcoholic extraction amount of flavonoids extracted with ethyl acetate–ether (12:1). The method of TLC on "Silufol" - UV 254 , it was found 11 phenolic origin substances, color, visible light UV and ionizing complexing reagents found that 7 of them are flavonoids, two of which are aglycones. By column chromatography on polyamide sorbent received 6 individual substances.

According to R_f value in different systems, as well as a positive reaction, Bryant (cyanide test) 2 of them is related to the aglycone 3 to glycosides. As a result, chromatographic, spectral analyzes, comparison of these data with published data and data notorious samples aglycones identified as quercetin and kaempferol.

On a base data of chromatography and spectroscopy ionized and complexing agents, and the results of the full and partial acid hydrolysis, to compare them with authentic and literary data flavonoids identified as isoquercetin, giperozid, rutin, and luteolin-7-glucoside.

Revealed that the main part of the sum of flavonoids rutin and astragalin. The content of flavonoids in the leaves varies from 0.98–1.43% in the air - dry weights of raw materials.

SUPRAMOLECULAR COMPLEXES OF ANABAZINE, CYTISINE, *d*-PSEUDOEPHEDRINE, AND LUPININE WITH β-CYCLODEXTRIN

T. M. Seilkhanov[1], O. A. Nurkenov[2], O. T. Seilkhanov[2]

1) Sh. Ualikhanov Kokshetau State University, Republic of Kazakhstan, 020000, Kokshetau, 76 Abay St, e-mail: tseilkhanov@mail.ru
2) Institute of Organic Synthesis and Coal Chemistry of the Republic of Kazakhstan, Republic of Kazakhstan, 100008, Karaganda, 1 Alikhanov St.

Nowadays, due to the intensive development of the pharmaceutical industry the development of new forms of drugs becomes very important. Global trends in the use of medicines show gradually occurring replacement of obsolete drugs by more effective and safe medicines of new generations. The pharmaceutical industry today and in the future with great perspectives binds encapsulating drugs with the help of effective receptors, which allow to obtain solid dosage forms from liquids, promote to the stabilization of active substances to the action of light and heat, increase the solubility of the drug, improves its bioavailability, mask undesirable odors and taste. Encapsulation of pharmaceutical drugs produces prolonged, programmed and transdermal effects and increases the possibility of targeted drug transport in the body directly to the site of its action. In this context, supramolecular self-assembly and study of the structure of inclusion complexes of pharmaceutically active anabazine, cytisine, *d*-pseudoephedrine and lupinine with β-cyclodextrin is an urgent task of modern chemistry and medicine.

The increased interest in cyclodextrins is due to their cyclic structure and ability to form supramolecular complexes such as the inclusion of host-guest with the test hydrophobic guests with the help of the expense of the internal cavity. As long as the size and structure of the (geometric complementarity) interacting components plays a big role in Supramolecular Chemistry for inclusion complexes with the studied natural pharmaceutically active substrates was selected β-cyclodextrin.

Supramolecular self-assembly inclusion complexes anabazine, cytisine, *d*-pseudoephedrine and lupinine with β-cyclodextrin was conducted by reacting equimolar amounts of the reactants in the aqueous-alcoholic solutions.

To study the supramolecular inclusion complexes NMR method was used. NMR spectroscopy study inclusion complexes based on determining the difference in ^{1}H chemical shifts and ^{13}C receptor substrates and in a free state in the composition as a result of the inclusion complexes of the intermolecular interaction.

It is shown that in all investigated cases form inclusion complexes of the 1 substrate molecules 1 receptor molecule to the occurrence of the most hydrophobic substrate fragment into the inner sphere.

BIOLOGICALLY ACTIVE COMPOUNDS FROM PLANTS OF THE GENUS *Climacoptera*

A. K. Kipchakbayeva[1], B. K. Yeskaliyeva[1], G. Sh. Burasheva[1], H. A. Aisa[2]

1) Al-Farabi Kazakh National University, Faculty of Chemistry and Chemical Technology, Almaty, 050040, Kazakhstan, e-mail: balakyz@mail.ru
2) Xinjiang Technical Institute of Physics and Chemistry of CAS, Urumqi, 830011, P. R. China

Currently, 15–20% of drugs are produced by Kazakhstan′s pharmaceutical companies, so increasing of domestic drugsand suggesting of new methods of isolation of biologically active complexes are a priority and actual task. Therefore, a great theoretical and practical interest play plants of *Chenopodiaceae* family, *Climacoptera* genus, which are widespread in Kazakhstan and some of them are endemic plants.

For the first time in the framework of fundamental program the aerial parts of the plants *C. ambylostegio, C. subsrassa* and *C. korshinskyi*, which growing in the Almaty region were studied. A comparative study of the component composition and quantitative content of three plants. As a result, allocated 9 macro - and microelements, 20 amino acids, 8 fatty acids, 35 lipophilic compounds, 16 flavonoids, 1carbohydrate, 1 purine substance and 5 saponins. According to the analysis of the *Climacoptera subcrassa* has a high content of flavonoids.

Investigation of lipophilic composition of the plants by the method of supercritical fluid CO_2 extraction. A comparative analysis of essential oils using GC-MS. Establishment of the chemical composition of *Climacoptera* lipophilic compound revealed the presence of 70 compounds. In *C. subcrassa* identified 11 components, while in *C.korshinskyi* – 16 components were identified and *C. ambylostegio* – 8 component. For the isolation of biologically active complexes effective solvents, the optimal block scheme of separation of substances, material balance and laboratory regulations were proposed. For effective separation of butanol extract of a plant of genus *C.subcrassa* used as a macroporous AB-8. A quantitative analysis of flavonoid complex by HPLC was done, as a result 8 flavonoids were determined.

As a result of scientific research isolated 23 individual substances, which structures established by modern spectral analysis methods.

9 biologically active complexes for bioscreening for various activities were elaborated. As a result of bioscreening of biologically active complex showed antioxidant and antibacterial activities. Main components of an antioxidant activity are flavonoids, quercetin glycosides and isorhamnetin. For antibacterial effect of biologically active complex are responsible arbutin, hypsogenin glycosides and adenine.

First identified phytotoxic activity of the ethyl acetate extract of plants of the genus *Climacoptera*.

TERPENOIDS OF *Artemisia* SPECIES PLANTS OF THE NORTH AND CENTRAL ASIA

L. D. Radnaeva[1,2], S. V. Zhigzhitzhapova[1,2]

1) Baikal Institute of Nature Management SB RAS, Sakhyanovoy 6 str., Ulan-Ude, Russia, 670000, e-mail: radld@mail.ru
2) Buryat State University, Smolina 24a str., Ulan-Ude, Russia, 670000

Artemisia L. (*Asteraceae*) is one of the largest and widely distributed genus reperesenting with more than 400 species. Species of the genus are herbs or small shrubs, with special organoleptic characteristics. They are mainly found in Asia, Europe and North America. *Artemisia* species are well known for their volatile oil that is used in the food and pharmaceutical industries and in folk medicine to treat gastrointestinal diseases. We have jointly studied 15 species of the genus *Artemisia* plants growing on the territory of Russia and China. The chemical compositions of essential oils from various Artemisia sp. in the flora of Qinghai and Buryatia have been analyzed in previous studies. In the current studies, we reported for the the composition of essential oils, to proivide more information for potential applications of *Artemisia*.

The essential oil produced in this study was extracted from the entire aerial parts of the plant. The essential oil was analyzed by GC-MS. The chemical composition data were subjected to multivariate statistical analysis using principal component analysis (PCA). All statistical analyses were conducted using Sirius ver. 6.0 software.

The PCA based on the structural groups of components in essential oils of *A. vulgaris* from different countries showed that the moisture conditions at the collection site were the main factor contributing to variation. Three clusters could be distinguished on the biplot. Samples from European countries with a humid climate (Croatia, Serbia, and France) comprised the first cluster, and were characterized by high contents of β-thujone and sabinane monoterpenes in their essential oils. Samples from three semihumid territories - Anatolia (Turkey), Nilgiri (India), and South Ural (Bashkortostan) - formed the second cluster. The third cluster represented samples from semiarid and arid areas - Krasnoyarsk, Buryatia, Mongolia, and Iran. Sesquiterpenes were the predominant component of essential oils extracted from these samples. The samples collected from the Qinghai-Tibet Plateau were located between the “European” and “Siberian” chemotypes. The climate of the Qinghai–Tibet Plateau is semiarid and arid, but the collected plants were growing in an intrazonal ecotope (fallow land). Therefore, the essential oil profile does not fully reflect zonal climatic features.

Components of essential oil in *Artemisia* are determined by genes and the environmental factors. The main components of essential oils of *A. vulgaris* were similar, regardless of the growth site, the year of collection, and the method of VOC extraction. Plants grown in drier conditions tended to produce higher quantities essential oil and sesquiterpenes with greater structural diversity.

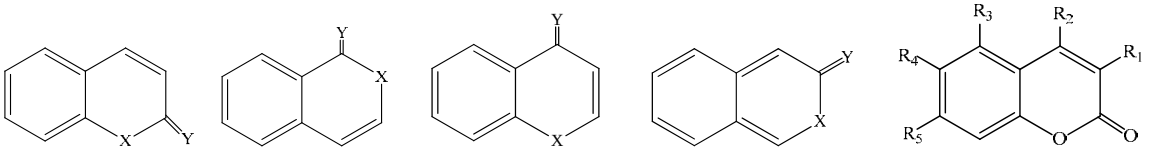
Acknowledgment. This research was supported by Programs of Basic Scientific Research of the State Academies of Sciences and Russian Foundation for Basic Research (Grant No. 15-44-04230). We thank Elena Dylenova for language editing, prof. Shilong Chen, PhD. Zhang Faqi for help in collecting samples.

A STUDY ON THE AROMATICITY OF COUMARIN, CHROMONE AND RELATED COMPOUNDS

Abulikemu Keremu

School of Chemistry and Chemical Engineering, Xinjiang University, Urumqi 830046, P. R. China, e-mail: ablikim.kerim@163.com

Coumarins are common both in chemical laboratories and in nature. In this paper, the global aromaticity of coumarin, isocoumarin, thiocoumarin, chromone, thiochromone, and certain hydroxycoumarins were studied using the topological resonance energy (TRE) method [1, 2]. The bond resonance energy (BRE) and circuit resonance energy (CRE) methods were used to evaluate local aromaticity [1, 2]. Analysis was made of the effects and the arrangement of heteroatoms on the global and local aromaticity of the molecules under consideration. Our TRE results show that all these compounds are globally aromatic systems with positive TREs. The relative aromaticity of all compounds we explain using the topological charge stabilization (TCS) rule [3]. Because they conform to the TCS rule, coumarins, chromones, and their hydroxylated derivatives naturally occur in the world and exhibit stable molecular systems. Our BRE and CRE results show that in each of the compounds shown in Figure 1, the left six-membered ring exhibits larger local aromaticity than both the right six-membered ring and the peripheral ring. Ring current results predict that a strong diamagnetic current will flow around the whole molecular perimeter.



1 X=Y=O
2 X=S, Y=O
3 X=O, Y=S
4 X=Y=S

5 X=Y=O
6 X=S, Y=O
7 X=O, Y=S
8 X=Y=S

9 X=Y=O
10 X=S, Y=O
11 X=O, Y=S
12 X=Y=S

13 X=Y=O
14 X=S, Y=O
15 X=O, Y=S
16 X=Y=S

17 R_1=OH; R_2=R_3=R_4=R_5=H
18 R_2=OH; R_1=R_3=R_4=R_5=H
19 R_1=R_2=OH; R_3=R_4=R_5=H
20 R_2=R_4=OH; R_1=R_3=R_5=H

Fig. 1. The structure of the compounds in this study

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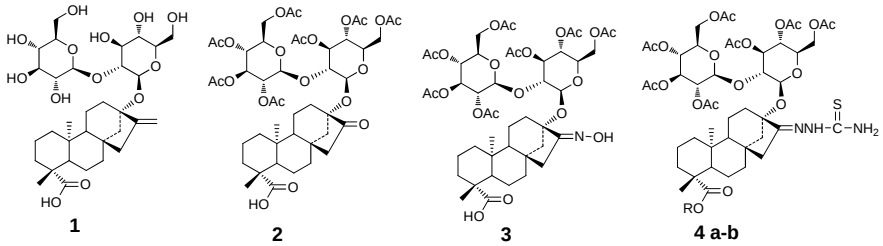
FUNCTIONALISATION OF THE DOUBLE BOND IN THE GLYCOSIDE STEVIOLBIOSIDE FROM THE PLANT *Stevia rebaudiana*

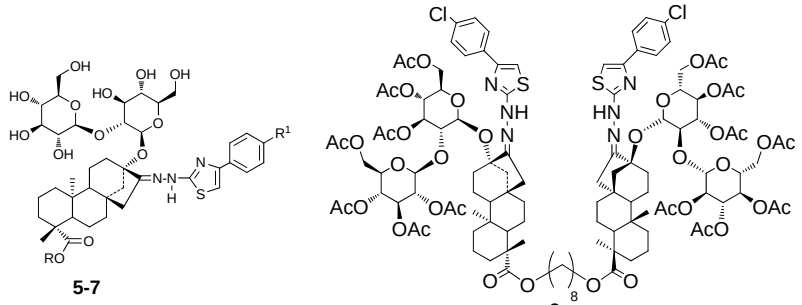
R. R. Sharipova, I. Yu. Strobykina, V. E. Kataev

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Centre, Russian Academy of Sciences, 420088, Russian Federation, Kazan, Arbuzov str. 8
e-mail: radmila@iopc.ru

The C^{16}=C^{17} bond in the glycoside steviolbioside **1** from the plant *Stevia rebaudiana* was oxidized for the first time. Ketone **2**, oxime **3**, thiosemicarbazones **4 a**–**b**, and thiazolylhydrazones **5**–**8** of steviolbioside with a heptaacetylated sophorosyl fragment, as well as binuclear **9 a**–**c** and tetranuclear macrocyclic derivatives **10 a**–**c** of this rebaudioside were synthesized.

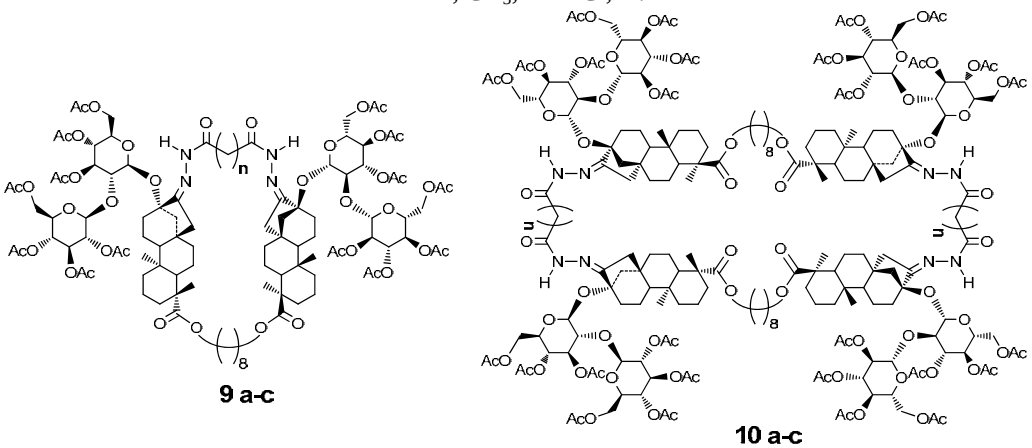


1 **2** **3** **4 a-b**



5-7 **8**

R = H, CH_3; R^1 = Cl, H.



9 a-c **10 a-c**

n = 4, 6, 8

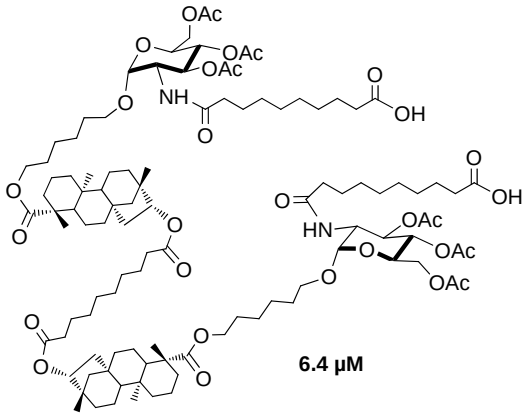
Acknowledgment. This study was performed under financial support of the Russian Science Foundation (Grant №14-50-00014).

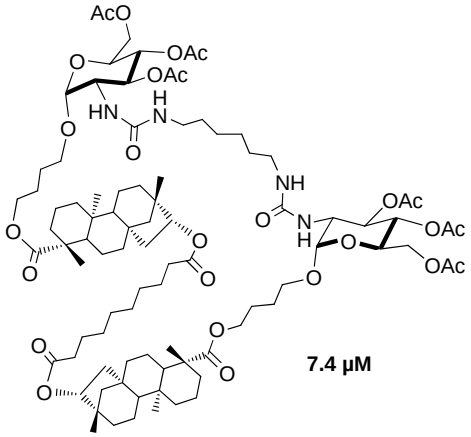
THE NEW GLYCOTERPENOIDS COMPRISING GLUCOSAMINE AND DITERPENOID ISOSTEVIOL SYNTHESIS AND ANTITUBERCULOSIS ACTIVITY

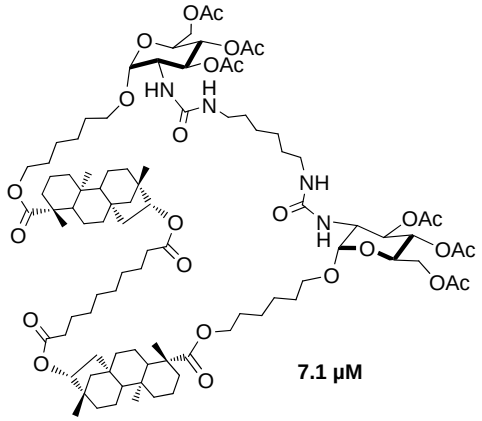
B. F. Garifullin[1], I. Yu. Strobykina[1], R. R. Sharipova[1], M. A. Kravchenko[2], O. V. Andreeva[1], V. E. Kataev[1*]

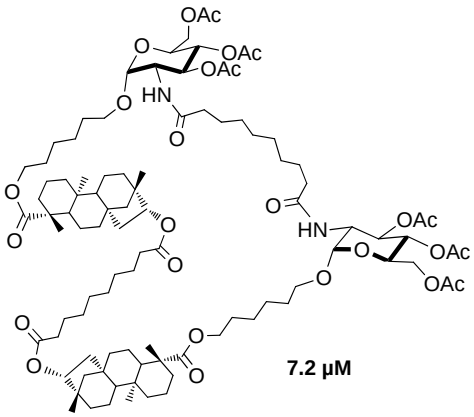
1) A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Centre, Russian Academy of Sciences, 420088, Russian Federation, Kazan, Arbuzov str., 8, e-mail: garifullin.bulat@iopc.ru
2) Ural Research Institute for Phtisiopulmonology, Ministry of Health Protection of the Russian Federation, 620039, Russian Federation, Yekaterinburg, XX Parts′ezda str., 50

The glycoterpenoids comprising glucosamine and diterpenoid isosteviol moieties were synthesized and evaluated for inhibition activity against *M. tuberculosis* H37Rv. Structural formulas of some glycosides and their in vitro inhibitory activities against the growth of *M. tuberculosis* H37Rv (MIC 101.5 μM for pyrazinamide in control) are presented below.









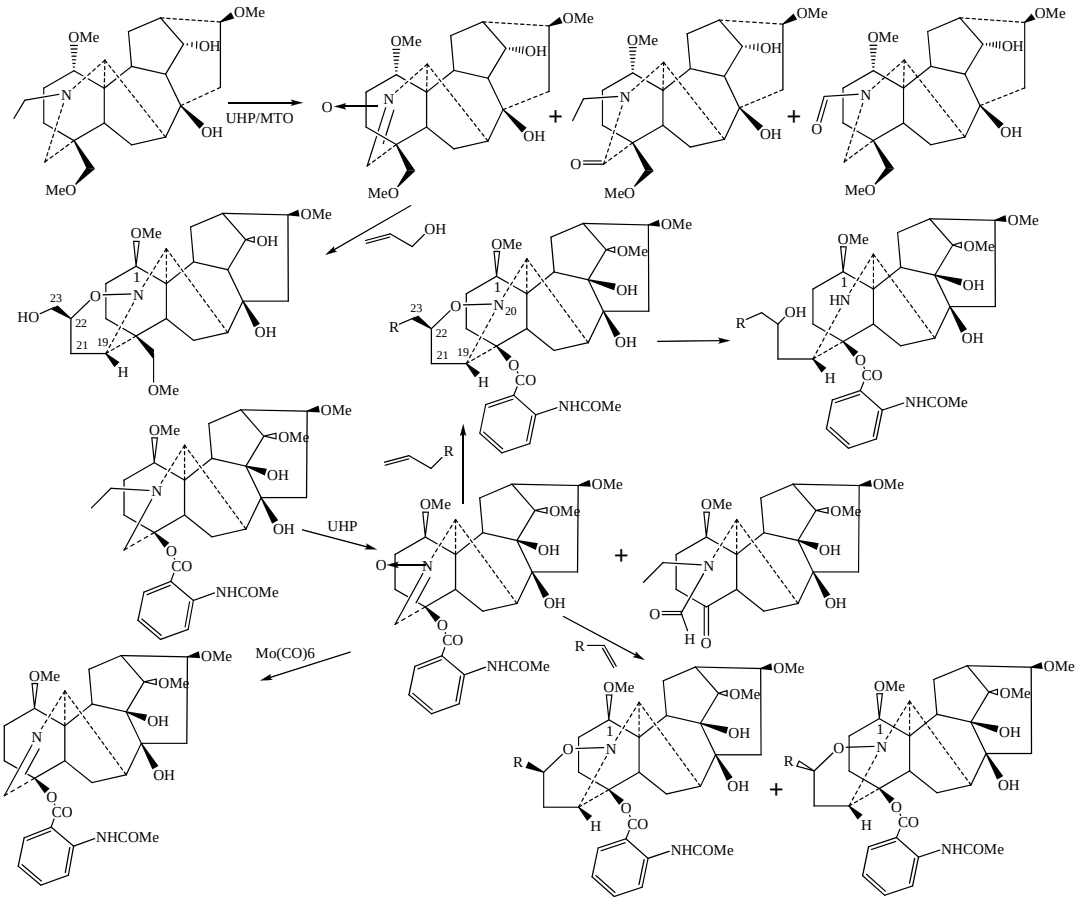
Acknowledgment. This study was performed under financial support of the Russian Science Foundation (Grant №14-50-00014).

SOME TRANSFORMATION OF DITERPENOID ALKALOIDS

E. M. Tsyrlina, T. M. Gabbasov, M. S. Yunusov

Ufa Institute of Chemistry of the Russian Academy of Sciences
450054, Ufa, pr. October, 71, fax: 7 (347) 235 60 66, e-mail: tsirlina@anrb.ru

A number of transformations of diterpenoid alkaloids have been carried out using the reactions of oxidation, 1,3-cycloaddition. Oxidation of diterpenoid alkaloids with a hydrogen peroxide-urea complex (UHP) under various conditions yields corresponding nitrones.The interaction of a nitrones based on lappaconitine or talatisamine with unsaturated compounds by the reaction of 1,3-cycloaddition yielded a number of previously not described isoxazolidines. The stereochemistry of the products of 1,3-cycloaddition was defined.



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FLAVONOIDS OF PLANTS OF THE GENUS *Scutellaria* GROWING IN UZBEKISTAN

A. M. Karimov[1,3], E. Kh. Botirov[2]

1) S. Yu.Yunusov Institute of the Chemistry of Plant Substances, Tashkent, Uzbekistan Academy of Sciences Republic of Uzbekistan
2) Surgut State University, Surgut, Russia, e-mail: botirov-nepi@mail.ru
3) Namangan State University, Namangan, Uzbekstan

Genus *Scutellaria* L. (family *Lamiaceae*) represented by 360 species is widely distributed in temperate, subtropical and tropical regions. Many of them have a wide spectrum of biological activity and used both in formal andin folk medicine. On the territory of Uzbekistan 32 species of *Scutellaria* L. grow, some of which are used in folk medicine for the treatment of epilepsy, allergies, neurosis, hypertension and other diseases.

Pharmacological studies confirmed that extracts and individual flavonoids of *Scutellaria*possessed antitumor, antiviral, hepatoprotective, antioxidant, antiinflammatory and anticonvulsive, properties. Flavonoids of *Scutellaria* genus is represented by flavones, flavanones, flavonol, chalcones, isoflavones, bioflavonoid and flavolignans. We conducted a scientometric analysis of research data on flavonoids of species of the genus *Scutellaria* L. of the world flora, andinformation on the composition of flavonoids of 63 species of *Scutellaria*, the distribution in plants, the structure and sources of 327 flavonoidsprovided. Scientometric studies indicate the constantly growing interest in the study of species of the genus *Scutellaria* L. by phytochemists, biologists, pharmacologists, and others.

We studied the composition of the flavonoids of the aerial part and roots of 7 species of the genus *Scutellaria* growing in Uzbekistan (*S. adenostegia* Briq., *S.comosa*Juz., *S. haematochlora* Juz., *S. immaculata* Nevski ex Juz., *S. intermedia* Popov, *S. nepetoides* Popov ex Juz., *S. ocellata* Juz.). Using chemical and spectral methods of studies the structures of the new compoundsestablished: 7-hydroxy-5,8-dimethoxyflavone 7-*O*-β-*D*-glucopyranoside, 5,7-dihydroxy-8-methoxyflavone 7-*O*-β-*D*-glucopyranoside, 5,7,2′-trihydroxyflavone 2'-*O*-β-*D*-glucuronoside, 5,7,2′-trihydroxy-8-methoxyflavone 2′-*O*-β-*D*-glucuronopyranoside and 5,7,8-trihydroxyflavone 7-*O*-β-*D*-galacturonopyranoside.

The research results will be applied in further development of technologies of new drugs.

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SYNTHESIS OF DERIVATIVES OF 20-HYDROXYECDYSONE HYPOGLYCEMIC ACTIVE

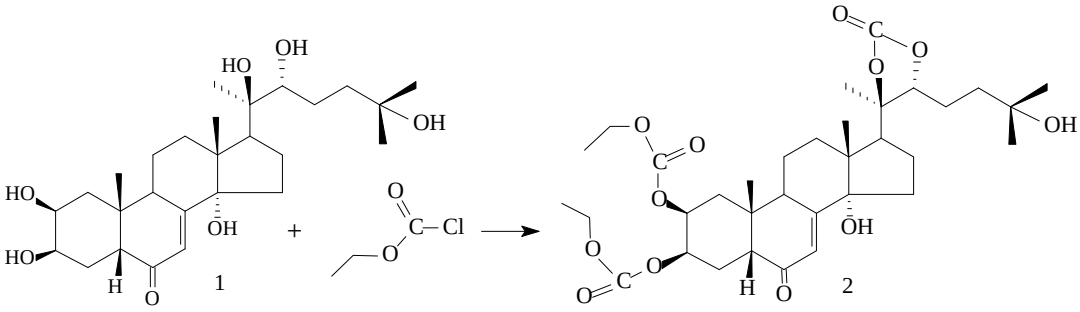
I. D. Bobaev[1], A. N. Blinnikov[2], I. V. Zavarzin[2], Kh. M. Bobakulov[1], N. Sh. Ramazanov[1], N. Kh. Yuldasheva[1], Z. A. Khushbaktova[1], V. N. Syrov[1]

1) S. Yu. Yunusov Institute of the Plant Substances AS RUz, Tashkent, e-mail: bobaev-isom@mail.ru
2) N. D. Zelinsky Institute of Organic Chemistry RAS, Moscow

Phytoecdysteroids are an important class of biologically active compounds with a wide range of biological and pharmacological effects. The prevalence of phytoecdysteroids among plants of Uzbekistan, their biological activity and pharmacological application are shown in a number of works.

Acetylated ecdysteroids have pronounced wound healing, antimicrobial properties, and immunomodulatory effects.

A method has been developed for the preparation of an agent having hypoglycemic activity, which comprises the synthesis of 2,3-*O*-di-(ethyl carbonate)-20,22-*O*-carbonate-20-hydroxyecdysone (**2**) by reacting 20-hydroxyecdysone (**1**) with ethyl chloroformate in pyridine, successively stirring at room temperature.



From the mixture of compounds **1** and **2**, individual compound **2** was isolated by column chromatography.

Purified 2,3-*O*-di-(ethyl carbonate)-20,22-*O*-carbonate-20-hydroxyecdysone (**2**) was analyzed by ^{1}H, ^{13}C, NMR spectra and Dept, Hetcor experiments.

The structure of 2,3-*O*-di-(ethyl carbonate)-20,22-*O*-carbonate-20-hydroxy-ecdysone (**2**) follows from the spectral data: the structure of *O*-tetra-substituted 20-hydroxyecdysone as *O*-ethyl carbonate is proved from data ^{1}H NMR spectrum. It should be noted that the chemical shifts have signals of 4.84 (C-2), 5.09 (C-3), 4.33 (C-22) and in the ^{1}H NMR spectrum of the tetraester **2**. This allows the addition of four residues of 2,3-*O*-di-ethyl carbonate and 20,22-*O*-carbonate at C-2, C-3, C-20 and C-22.

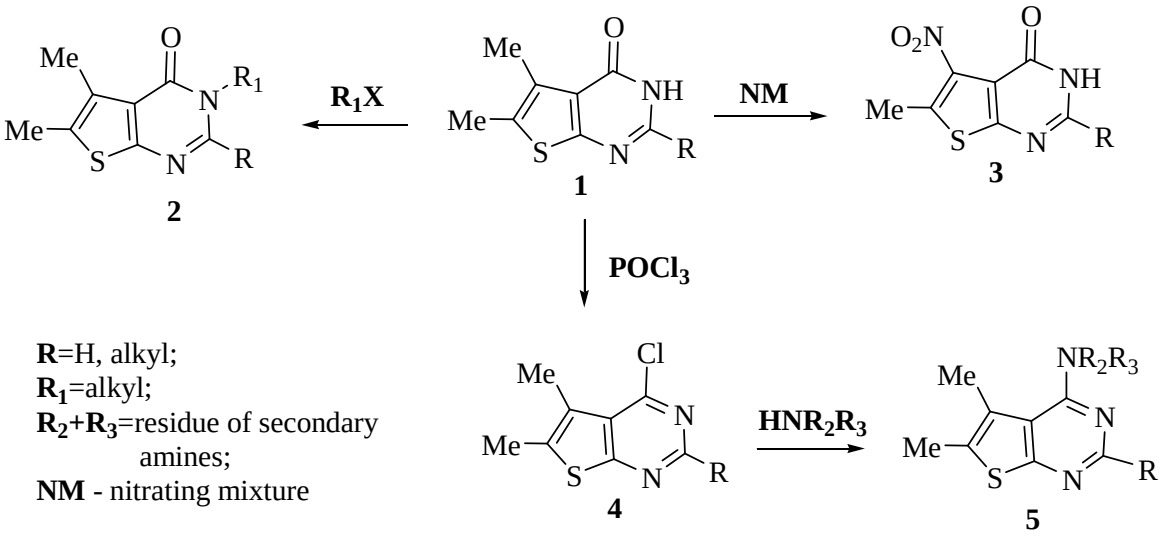
The conducted studies showed that after a single injection of 2,3-*O*-di-(ethyl carbonate)-20,22-*O*-carbonate-20-hydroxyecdysone in 3 hours (the peak of action of the drug), a decrease in the level of glucose in the blood of experimental animals by 32%. In the group of animals treated with 20-hydroxyecdysone and adebitol, only a 14.8% and 15.7% decrease in blood glucose was observed.

INTERACTION OF SUBSTITUTED THIENO[2,3-D]PYRIMIDIN-4-ONES WITH ELECTROPHILIC AND NUCLEOPHILIC REAGENTS

I. S. Ortikov[1], D. Kh. Akramov[1], B. B. Zhurayev[2], B. Zh.Elmuradov[1]

1) S. Yunusov Institute of the Chemistry of Plant Substances AS of the Republic of Uzbekistan,Tashkent, 100170, Mirzo-Ulugbek st., 77, e-mail: b_elmuradov@mail.ru
2) Mirzo-Ulugbek National University of Uzbekistan, Chemical Faculty, Tashkent 100195, Uzbekistan

Thieno[2,3-d]pyrimidin-4-ones (TPs, **1**) are widely distributed in the field of heterocyclic compounds. Due to ambifunctional fragments and different reactive groups these heterocyclic compounds have plural reactivity and it gives an opportunity to carry out various reactions with electrophilic and nucleophilic reagents. Besides among of the substituted thieno[2,3-d]pyrimidin-4-ones there are some perspective biological active compounds, which are widely used in agriculture and medicine. Continuing our investigations on modification of bycyclic TPs in the present work we have carried out synthesis and studied an interaction of compounds **1** with alkyl halides, nitrating mixture and $POCl_3$ and some modification of the synthesized compounds:



R=H, alkyl;
R_1=alkyl;
R_2+R_3=residue of secondary amines;
NM - nitrating mixture

Interaction of substituted TPs (**1**) with alkyl halides gives N3-alkyl derivatives (**2**), aromatic electrophilic *ipso*-substitution with nitrating mixture (NM) - targeted heterocyclic 5-nitro-TPs (**3**), with $POCl_3$ the 4-chloro-TPs (**4**), which are smoothly react with different aliphatic and aromatic amines to give corresponding heterocyclic amines (**5**). The structure of the synthesized compounds was confirmed by physical methods of research.

FORMATION OF FINE POLYACRYLONITRIL FIBER

N. U. Umarova, Sh. Kh. Shamanov, S. Kh. Khasanova, I. A. Nabieva

Tashkent Institute of Textile and Light Industry

The main solvent for mixtures of a polyacrylonitrile (PAN) copolymer and a solution of natural silk waste (NSH) is sodium thiocyanate. It should be noted that for small (about 1%) NS additives, concentrated PAN solutions are stable practically during the year. However, they are characterized by some turbidity. Structural and mechanical properties of 12% solutions (with an NS content of up to 50%) do not change even for several months. When NS is added to the PAN, the precipitation bath does not deepen into the capillary channel. Apparently, for these solutions, compression of the spinning dope jet and fiber breakage occur after exiting the capillary due to the slow precipitation of the polymer from the solution.

Under the selected conditions, laboratory samples of silk-nitron fiber were produced. For comparison, under the same conditions, the nitrone was formed without the inclusion of natural silk. The fiber was formed in the laboratory spinning machine MUL. For molding, a polymer of 12% polymer concentration in the solution dissolved in rhodanate sodium was used. The viscosity of the spinning solution of PAN is 172 sec (by ball), and the mixture of PAN-NSH (90:10) – 158 sec.

Studies have shown that the introduction of semi-rigid natural silk into the polyacrylonitrile copolymer causes a higher orientation of the structural elements of the fibers. An analysis of the results of the physical and mechanical properties of the fibers showed that when NS is included in the structure, the PAN leads to an increase in strength and, especially, resistance to double bending to 20% of the NS content in PAN. With an increase in the content of natural silk in PAN, moisture absorption increases, if a PAN fiber at a relative humidity of 60% and a temperature of 20°C can absorb 3.34% of water, then a SNV containing 10% NS is 3.97%.

When dyeing nitron with cationic dyes and, especially blue, usually intense colors are obtained, characterized by unevenness. Therefore, the development of technology that provides a uniform coloration is of great practical importance. The quality of coloring of the stained samples with cationic blue 2K, obtained in laboratory conditions, was tested, and the color difference, the unevenness of dyeing and the color stability to the action of certain physicochemical effects were determined. The dye, fixed on the protein, is retained only by the ionic bond, for a given dye the role of the substrate - nitron - loses its significance.

The results obtained show that the heterogeneity and unevenness of the dyeing of SHVV decreases by a factor of 1.5–3.5 compared to the control fiber. The reason for this may be the complex effect of the components of the spinning solution. Stability of coloring to various influences of the control and SHNW samples is the same.

GRIFININE, A NEW QUINOLINE-2-ON ALKALOID FROM THE PLANT OF *Haplophyllum griffithianum*

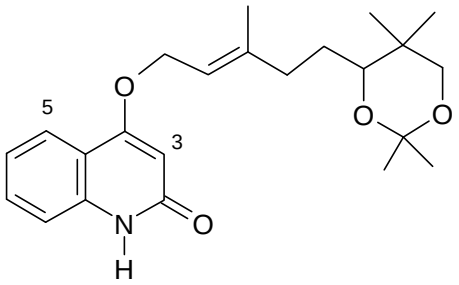
D. R. Kodirova[1,2], H. A. Rasulova[3], Sh. Sh. Sagdullaev[3], H. A. Aisa[1]

1) Key Laboratory of Plant Resources and Chemistry of Arid Zone, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi 830011, P. R. China
2) University of Chinese Academy of Sciences, Beijing 100039, P. R. China
3) S.Yu. Yunusov Institute of Chemistry of Plant Substances, AS RUz, 100170, Tashkent, e-mail: dilobar.kodirova@gmail.com

Haplophyllum griffithianum (family *Rutaceae*) was first investigated by us. From the aerial parts and roots of *H. griffithianum* eleven bases and two steroid compounds were isolated. Known alkaloids - diktamnine, skimianine, dubinidine, dubinine, dubamine, flindersine, folifine and N-methylhaplopholin were isolated from the plant for the first time, as well as new alkaloids of gerfitine, gerfitinine, griffitine, belonging to the type of furanoquinoline and furanoquinolin-4-one, respectively. The structures of these alkaloids were established by their spectral data (UV, IR, ^{1}H, ^{13}C NMR) and X-ray diffraction. We continued the separation of the chloroform main fraction of the total alkaloids, obtained from the aerial part of the *H. griffithianum* plant collected in the vicinity of the Khondiz, Surkhandarya region.

From the alcohol fraction, by re-chromatography on silica gel, a new base grifinine (1) was isolated, m.p. 158°C, $C_{22}H_{29}NO_4$ composition of M 371 (mass spectrum).

The structure of griffin was established by studying the data of the spectra of UV, IR, mass, NMR ^{1}H, ^{13}C, DEPT, which were compared with the literature data of bukharaine acetonide.



Grifinine refers to the type quinolin-2-on and found in the plant for the first time.

TOTAL SYNTHESISOF (±)-RUPESTINE G

Abdullah Yusuf[1,2,3], Jiangyu Zhao[1], H. A. Aisa[1*], Guozheng Huang[1*]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions, and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, South Beijing Road 40-1, Urumqi, 830011, P. R. China
2) University of Chinese Academy of Sciences, 19 A Yuquan Rd, Beijing, 100049, P. R. China
3) College of Chemistry and Environmental Science, Kashgar University, Kashgar, 844000, P. R. China, e-mail: haji@ms.xjb.ac.cn; g.huang@ms.xjb.ac.cn

Guaipyridinesesquiterpene alkaloids are a collection of natural products with unusual structure consisting of a fused pyridine ring and seven-membered carbocycle [1]. Most of those alkaloids exhibit potent pharmacological activities and might serve as leads for further drug development. For example, cananodine, a representative guaipyridine alkaloid isolated form the fruits of *Canangaodorata*, shows sub-micromolar activity against Hep G2 human hepatocarcinoma cell lines [2]. Recently thirteen new guaipyridinesesquiterpene alkaloids, *i. e*. rupestine A-M were isolated by our group from *Artemisia rupestris* L., which is a well-known traditional Chinese medicinal plant used for detoxification, antitumor, antibacterial, antivirus and protecting the liver [3,4]. The similar structures of rupestine A-M as compared to cananodine in guaipyridine bicyclic core indicate possible hepatocellular carcinoma cytotoxic activity. But further biological evaluations were limited by their scarce availability from natural sources. Hence, the total synthesis approach for these alkaloids is requisite.

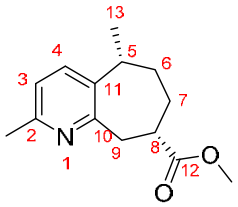


Fig. 1. Structure of Rupestine G

We recently accomplished a ten-step synthetic procedure for total synthesis of (±)- rupestine G (Fig. 1) and its epimers. A cheap chemical, 5-bromo-2-methylpyridine was used as starting material and the heptatomic ring was constructed by using Grubb′s Catalysts II-catalyzed RCM reaction [5]. Rupestine G and its epimers were separated by chiral high performance liquid chromatography separation. Absolute configuration of rupestine G and its epimers were determined by comparison of the experimental ECD and calculated ECD [6]. Conversion of ruspestine G into other rupestines is under inverstigation in our group. Biological evaluation of rupestine G and its epimersareaslounderway and willbe reported in due course.

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CHEMICAL CONSTITUENTSFROM *Nigella glandulifera*

Xixi Liu[1,3], Xuelei Xin[1,2], Haji AkberAisa[1,2*]

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang 2) Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi 830011, P. R. China
3) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China, e-mail: haji@ms.xjb.ac.cn

Nigella glandulifera Freyn, belongs to the *Nigella* genus of *Ranunculaceca* family, is widely cultivated in the western region of China mainly in Xin Jiang [1]. *N. glandulifera* seeds have been used as Uighur folk medicine for remedy various ailments including diabetes, cold, edema, urinary calculus, bronchial asthma and edible condiment for hundreds years [2]. In our previous work, several interesting constituents have been identified with distinct biological activities [3, 4].

Therefore, we continued to study the chemical composition of this medicinal plant, aimed to discover new bioactive natural products.

Chemical constituents, a new ester compound (**1**) and two known compounds (**2** and **3**), were isolated from the seeds of *Nigella glandulifera*. Their structures (Fig. 1) were elucidated by MS, 1D and 2D NMR spectra.

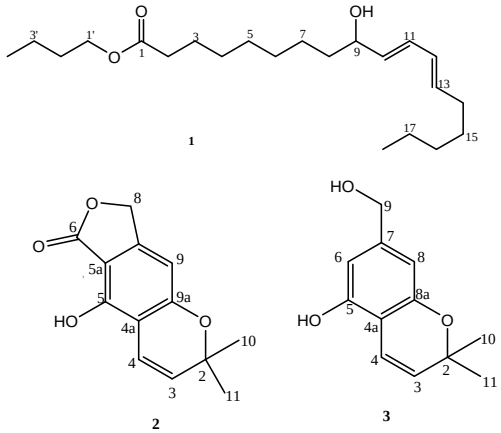

Fig. 1. Chemical structures of compounds **1–3**

Acknowledgment. We gratefully acknowledge the Natural Science Foundation of Xinjiang, China (2014211B045) for financial support.

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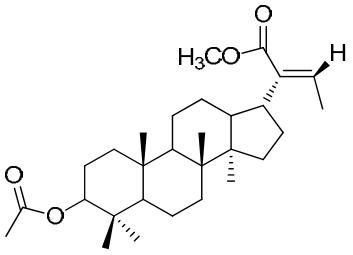
NEW TRITERPENOIDS FROM *Euphorbia alatavica*

Rushangul Rouzimat[1,2], Nurmuhammat Kehrimen[1], H. A. Aisa[1,3*]

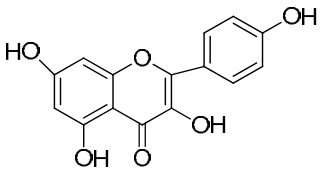
1) Key Laboratory of Plant Resources and Chemistry in Arid Regions,
Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences,
Beijing South Road 40-1,Urumqi 830011, Xinjiang, P. R. China
2) Key Laboratory of Xinjiang Indigenous Medicinal Plants Resource Utilization,
Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences
3) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China
e-mail: haji@ms.xjb.ac.cn

Euphorbia is a large genus consisting of more than 2000 species widely distributed in the world, of which about 200 species distributed in Central Asia and China [1]. *Euphorbia alatavica* Boiss, belonging to the Euphorbia genus, is a perennial herb, widely distributed in the Xinjiang Uighur Autonomous Region of China and Central Asia [2]. To the best of our knowledge, there is only our group is studying the phytochemical constitutes of *E. alatavica*, andrecentlywe have reported the isolation of two new triterpenoids from this plant [3].

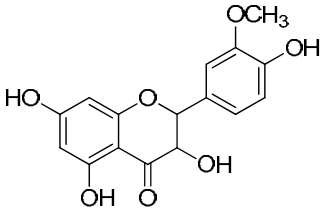
In this study, our group isolated one new nor-dammarane type of triterpene and two known flavonoids [4, 5] from the areal part of *E. alatavica*. Their structures were elucidated by MS, 1D and 2D NMR techniques. Follow is the chemical structure of isolated compounds:



Compound 1



Compound 2
kaempferol



Compound 3
Isorhamnetin

Acknowledgment. The investigation was funded by International Cooperation and Exchange of the National Natural Science Foundation ofChina (NO. 31110103908) and Central Asia Drug Discovery and Development Centre of Chinese Academy of Sciences.

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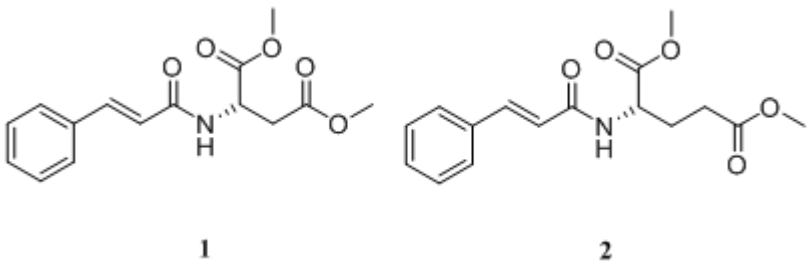
TWO NEW CINNAMAMIDES FROM *Lavandula angustifolia*

Nigary Yadikar[1], Khayrulla Bobakulov[2], H. A. Aisa[1*]

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi 830011, P. R. China, e-mail: haji@ms.xjb.ac.cn
2) Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100170, Uzbekistan

Lavandula angustifolia Mill., which was native to the Mediterranean region, has been intensively cultivated in Yili region of Xinjiang (Northwest of China), nowadays. The essential oil is considered to be its major component, but some phytochemical studies on nonvolatile components of *Lavandula* species are documented, such as phenolic acids [1], flavones [2], arylbenzofurans [3], isobenzofurans [4], benzolactones [5], phenylpropanoids [6], and so on.

In a continuous search for bioactive constituents, our research has been performed to determine non-volatile compounds in remaining material after the essential oil of the title plant being distillated, and many phenolic acid derivatives had been isolated and purified by various chromatographic techniques. Two novol natural cinnamamides lavanduamide A (**1**) and lavanduamide B (**2**) were given (Fig. 1), and their structures were elucidated on the basis of physicochemical properties and spectral data of UV, MS, 1D and 2D NMR spectroscopy.



1 **2**

Fig. 1. Strucutres of cinnamamides 1 and 2

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TWO NOVEL FLAVONOID GLYCOSIDES FROM *Astragalus turkestanus* AND *A. xanthomeloides* (*Leguminosae*)

Abdulaziz A. Janibekov[1*], Fadia S. Youssef[2], Mohamed L. Ashour[2], Nilufar Z. Mamadalieva[1]

1) Institute of the Chemistry of Plant Substances, Academy of Sciences, Mirzo Ulugbek str. 77, Tashkent 100170, Uzbekistan
2) Department of Pharmacognosy, Faculty of Pharmacy, Ain Shams University, Abbassia, Cairo 11566, Egypt

Astragalus represents one of the popular genera of flowering plants belonging to the Leguminosae. *Astragalus turkestanus* Bge. and *A. xanthomeloides* Eug. Kor. et M. Pop. are two species endemic to the Uzbek Flora. Tracing the current literature, nothing was found regarding either the chemical composition or the biological activities of *A. turkestanus.* However, only two compounds namely, *D*-pinitol (or 3-*O*-methyl-*D*-chiroinositol) and kaempferol-3-*O*-α-*L*-rhamnopyranosyl-(1→6)-β-*D*-galactopyranoside-7-*O*-α-*L*-rhamnopyranoside were isolated from *A. xanthomeloides* [1, 2].

The aerial parts of *A. turkestanus* and *A. xanthomeloides* were collected from the Qashqadaryo and Tashkent regions of Uzbekistan in 2015. Comprehensive phytochemical investigation of the total methanol extracts of the aerial parts of *A. turkestanus* and *A. xanthomeloides* resulted in the isolation and structural elucidation of two novel flavonoid glycosides 7-methoxy kaempferol-3-*O*-α-*L*-arabinosyl-(1→6)-β-*D*-galactopyranoside (**1**) from the former and kaempferol-3-*O*-α-*L*-rhamnopyranosyl-7-*O*-α-*L*-rhamnopyranosyl-(1→6)-β-*D*-galactopyranoside (**2**) from the latter in addition to other five known compounds that are isolated for the first time from the respective *Astragalus* species. They are a mixture of β-sitosterol glucoside (**3**) and stigmasterol glucoside (**4**) in addition to *D*-pinitol (**5**) from *A. turkestanus,* whereas an oleanane type triterpenoidal saponin, azukisaponin V (**6**) and a flavonoid glycoside, 7-methoxy kaempferol-3-*O*-β-*D*-glucopyranoside (**7**) were isolated from *A. xanthomeloides*. Concerning the two novel compounds, they are comprehensively elucidated using UV, HR-ESI-MS, 1D and 2D NMR techniques.

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HIGH PERFORMANCE LIQUID CHROMATOGRAPHY - ELECTROSPRAY - QUADRUPLE - TIME - OF - FLIGHT TANDEM MASS SPECTROMETRY ANALYSIS OF CHEMICAL CONSTITUENTS

Mamatjan Abduwaki, Ubul Turdi, Arxidin Mamat

Xinjiang Uygur Medical School, 848000, Hotan, P. R. China

To analyze and identify the main chemical constituents of the extractof Herba dextran by high performance liquid chromatography-electrospray-quadrupole-time-of-flight mass spectrometry (LC-ESI-Q-TOF-MS / MS).

Purification of the main components was carried out by reversed-phase HPLC gradient elution with Poroshell 120-C18 (2.7 mm × 100 mm, 2.7 μm). The electrospray ionization source was used to elute the chromatographic effluent. Detection, four - pole flight time tandem mass spectrometries for the main chromatographic peaks were assigned.

The structure of 22 compounds was identified by two - stage high - resolution mass spectrometry combined with reference data and related literature.

LC-ESI-Q-TOF-MS / MS can qualitatively analyze the main components of hard-scented herbs from the aspects of retention time, exact relative molecular mass, molecular formula and secondary structure debris. In order to find out the activity

The substance provides a quick and accurate analytical method.

RADIOPROTECTIVE ACTIVITY OF POLYPRENOLS FROM *Alceae nudiflora*

N. V. Tursunova, V. N. Syrov, Z. A. Khushbaktova, M. D. Rahmatova, N. K. Khidyrova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, Tashkent,
e-mail: natalya-tursunova@mail.ru

Recent years in terms of environmental pollution and improve the overall background radiation of the Earth the world community of scientists pay great attention to search ways of protection from the effects of chronic ionizing radiation of low intensity in nature. In this case use of biologically active natural compounds, e.g., antioxidants, adaptogens, immunomodulators instead a non-toxic radioprotective short-acting drugs seems promising. These substances increase the non-specific resistance and can be used for a long time. The plant polyprenols as immunomodulators and membrane protectors are of special interest as a potential radioprotective substances.

We have investigated the antimutagenic, immunoprotective and hemostimulating effects of polyprenols' sum from the aerial part of the *Alceae nudiflora* widespread in the Central Asia. The preparation was administered as a water-oil emulsion orally to white not purebred mice of both sexes weighing 20–22 g in a pilot researches under condition of 5 Gy irradiation in the hot season (June to July) for 3 weeks (one week before irradiation and two weeks after irradiation). After 3 weeks animals were subjected to decapitation under light ether anesthesia and bone marrow, organs of the lymphatic system and blood were evaluated. In bone marrow it was determined the degree of genomic and chromosomal abnormalities, apoptosis and expression of proliferative processes. Histomorphological study was conducted in spleen. Some indicators of leucopoiesis and erythropoiesis were determined in blood. The number of cells of the immune system organs and its reactivity was defined. Results of the experiments showed that preventive and therapeutic administration of polyprenol sum reduced adverse effects of radiation. In this group a 2-fold reduction of rate genomic disorders compared to control values of untreated animals and chromosomal changes in 33.3% less than in the control was observed. The degree of bone marrow cells proliferation was similar to the values of intact animals, while the apoptotic index in treated group differed little from the control. The polyprenol sum changed the number of blood cells in mice characteristic to leucopoiesis processes recovery, namely, neutrophils count in 1.8 times and monocytes count in 5 times was higher than reference values. The lymphocyte content does not differ from those of intact animals; the number of blast lymphocytes was 50% of the total number. Structural and functional state of the spleen lymphoid apparatus conformed to the standards and indicated the immunogenesis activation. Simultaneously, it has been found a high antibody-stimulation of spleen cells. Also in this group of animals the number of lymph nodes cells (in 3 times compared to control) increased. At the same time, influence of polyprenols on severity of erythropoiesis process was moderate.

Thus, sum of polyprenols from *A. nudiflora* activated protective resources of the body in single exposure to radiation at a dose of 5 Gy and was able to prevent some of its effects in the additional burden by high seasonal temperatures.

EXPEDIENCY OF USE ECDYSTEROID-CONTAINING PREPARATIONS TO IMPROVE THE RESISTANCE OF THE ORGANISM

V. N. Syrov

Institute of the Chemistry of Plant Substances, Academy of Sciences,
Republic of Uzbekistan, Mirzo-Ulugbek str., 77, Tashkent, 100170 Uzbekistan,
e-mail: zainab@icps.org.uz

In recent years the problem of prevention of overwork as a form of pre-pathological condition of the body takes on the fully new aspects in connection with the change in the nature of human labor and the expansion of its scope of application.

Therefore, the creation of new medicaments for the correction in these conditions disturbed adaptive reactions that prevent the effects of adverse environmental influences, and high physical and emotional load is urgent task nowadays. Considerable interest in this area may be represented by ecdysteroid-containing remedies ecdysten and ayustan, and biologically active food supplements - ecdysten plus and eksumid developed at the Institute of Chemistry of Plant Substances of the Academy of Sciences of Uzbekistan. They are based on the substance of ecdysterone, turkesterone, cyasterone and other compounds in this class, isolated from *Rhaponticum carthamoides, Rh. integrifolum*, *Ajuga turkestanica*, *Silene brahuica*.

All of them are classical adaptogenic agents with varying degrees of severity of effect. They increase physical performance, psycho-emotional stability, resistance of the body to various stresses and climatic conditions, accelerate regenerative processes. The basis of ecdysteroid-containing preparations and biologically active food supplements action mechanism is stimulation of protein synthesis in various organs and tissues, in particular enzymes of gluconeogenesis. This explains the rapid re-synthesis of glucose from lactic acid, which is the main factor limiting performance, decreasing the degree of acidosis, lacticemia, reducing oxygen debt and normalizing aerobic productivity of cells after intensive exercises. All ecdysteroid-containing preparations increase endurance in individuals engaged in heavy physical work, in sportsmen during prolonged debilitating stress and rehabilitation after intoxications, radiation injuries. Ekdisten, ayustan and biologically active supplements containing ecdysteroids stimulated processes of immunogenesis and interferonogenesis, increase the tolerance to hyperthermia, promote the formation of nitric oxide in the body, and have a positive effect on carbohydrate-phosphorus and lipid metabolism. Ecdysteroid-containing preparations are practically non-toxic, do not have any hormonal and side effects, and have expressed tonic effect.

Their widespread practical use to extend the boundaries of adaptation and resistance of the organism to the effects of many factors of extreme fits well in facing the problem of modern medicine - development and improvement of “Pharmacology of the healthy human”.

STUDY OF THE TOXICITY OF IMMUNOCOR PREPARATION

A. A. Azamatov, J. Rejepov, F. M. Tursunkhodjaeva, A. A. Suyarov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, AS RUz, 100170, Tashkent, Uzbekistan, e-mail: akademic1986@list.ru

Immunocor preparation consists of a polysaccharide sum isolated from the bur-marigold herb. Suyarov A.A. (2015) has established that the preparation renders a stimulating action on humoral immunity and lymphoid organs in intact and immunodeficiency animals. By immunostimulating activity Immunocor exceeds the commercial preparation Immunal.

We investigated the acute, sub-acute toxicity and local irritating action of Immunocor (1).

It was established that the drug substance and tablets are low toxic in relation to the acute toxicity evaluated on mice and rats in intragastrinal introduction. Sex and specific differences in the drug tolerance were not observed. Long per oral introduction (30 days) at the doses of 15-150-300 mg/kg was good tolerated, and had no toxic effects on the experimental rats.

The preparation is not cumulated in repeat introductions, and not irritated the skin and mucous membranes.

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ANTI-INFLAMMATORY EFFECTS OF DITERPENOID ALKALOIDS ON FORMALIN RAT MODEL

F. M. Tursunkhodjaeva, N. B. Sokhibova

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances, AS RUz, 100170, Tashkent, Uzbekistan, e-mail: ftm40438@gmail.com

Earlier we have analyzed the analgesic mechanisms of a number of diterpenoid alkaloids with different types of carbon skeleton (1). The present work is aimed at the evaluation of anti-inflammatory effects contribution to their antinociceptive activity. The investigated substances were provided by Prof. B. T. Salimov and Dr. M. N. Sultankhodjaev (ICPS AS RUz). Aseptic inflammation was caused by subplantar injection of 1% formalin. The alkaloids were introduced to rats intraperitoneally.

Anti-inflammatory effects of the most active investigated substances represented in the Table. Analgesic activity of these substances in mice acetic writhing test (1) that was higher than that of sodium metamizole and acetylsalicylic acid is notable. It may be supposed that the anti-dropsical and anti-inflammatory effects make a great contribution to the antinociceptive activity of these alkaloids.

TABLE 1. **Anti-inflammatory effect of diterpenoid alkaloids on rat formalin model (N=6, p<0.05)**

Alkaloid	Dose, mg/kg	Anti-inflammatory effect, %	LD_{50}, mg/kg i.p.
Sodium metamizole	100	57.90	119
1-*O*-benzoylisotalatisidine	12	57.87	120
1-*O*-benzoylnapelline	14	39.50	140
Acorine	5.4	39.00	54
Atisine azomethine	5	38.50	50
Acsinatine	8	35.00	80
Talatisine	10	32.60	100
N-deacetyllappaconitine	3	31.00	35
6-*O*-benzoylheteratisine	2	30.60	21.5
Ajacine	3.6	28.80	35.4
Dihydroatisine	9	24.60	90

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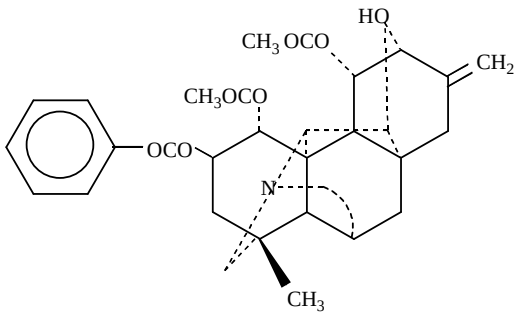
NEW ASPECTS IN PHARMACOLOGY OF DITERPENOID ALKALOID TAJACONINE

F. M. Tursunkhodjaeva, F. N. Dzhakhangirov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, AS RUz, 100170, Tashkent, Uzbekistan, e-mail: ftm40438@gmail.com

Tajaconine, a hetisine-type diterpenoid alkaloid, was isolated from *Aconitum zeravschanium, A. firmum* and *A. anthoroideum* (1, 2).



Its high curariform and local anesthetic activity has been shown earlier (3, 4). The alkaloid rendered a high antiarrhythmic action on rat aconitine model and had a wider therapeutic range (LD_{50}/ED_{50}) than that of antiarrhythmics quinidine, ajmaline, and rithmilen (5).

In our experiments, tajaconine has shown a high analgesic action in mice acetic writhing test with ED_{50} 3.4 mg/kg in s.c. injection. ED_{50} of sodium metamizole and acetylsalicylic acid in this test were 11.4 and 205 mg/kg, accordingly. In a hot plate test, tajaconine at a dose of 5 mg/kg in s.c. injection in 30 minutes after injection increased a pain threshold in mice for 2.3 times, while morphine – for 2.7 times. LD_{50} of tajaconine in i.p. the injection was more than 100 mg/kg.

Investigation of nootropic action on the model of exploratory activity of mice with cognitive functions disturbance caused by nicotine (0.5 mg/kg s.c.) shown that tajaconine decreases both the total time of the maze exploration (for 85%) and a number of repeat visits of maze arms, that proves its nootropic action.

A high analgesic and nootropic activity of the alkaloid may be explained by its ability to block N-cholinoreceptors in CNS.

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GROWTH REGULATING ACTIVITY OF PECTIN POLYSACCHARIDES OF *Silybum maryanum* AND *Lagochilus inebrians*

R. P. Zakirova, N. N. Kuchkarova, K. S. Zhauynbaeva, R. K. Rahmanberdyeva

S. Yu.Yunusov Institute of the Chemistry of Plant Substances AS RUz, 100170, Tashkent, Republic of Uzbekistan, e-mail: ranozakirova@mail.ru

It is known that many plant-growth regulators increase seed germination; promote the formation of healthy, strong seedlings that finally leads to increasing crop yields. To date, among the natural growth regulators of plants polysaccharide compounds were found. Polysaccharides regulate the extension of cells and control the processes of morphogenesis, stimulate functional activity of cells, increase the seeds power. These properties attract an interest to polysaccharides as immunomodulatory and growth-regulating agents.

The goal of this paper was to establish the growth-regulatory activity of polysaccharides extracted from the plant *Silybum maryanum* and *Lagochilus inebrians*.

Experiments were carried out on the seeds of wheat varieties “Tatiana” and cucumber varieties "Uzbekistan". Seeds treated with aqueous solutions of polysaccharides in concentrations of 0.01%, 0.001% and 0.0001% for 18 hours were grown in Petri dishes. The seeds presoaked in 0.001% solution Novosil drug and water were used as the standard and the control, accordingly. The biological activity of polysaccharides was evaluated on the growth of aerial and underground organs of seedlings. Auxin activity was determined by the growth of wheat coleoptiles. The results were subjected to statistical analysis by the program Original Pro.

Tests conducted on the wheat seedlings have shown that the polysaccharide derived from *L. inebrians* at a concentration of 0.001% and 0.0001% increased growth of roots at the level of the standard and greater than the control variant on 15% and 11%, accordingly. Stimulating the growth of the stem by treating the seeds with polysaccharides of *S. maryanum* was not observed. Their length was almost at the level of control.

In experiments on seedlings of cucumbers high growth stimulating activity has been showed by polysaccharide of *S. maryanum* at a dose of 0.01%. Root was longer than the control variant on 78.5%, the shoot length - on 77.5%. By effect the polysaccharide at the concentration of 0.001% of the root length was greater than the control on 54.5%.

Tests on auxin activity have showed that the maximum length of coleoptiles of wheat has been produced at 0.01% concentration on investigating two polysaccharides. By exposing with the compound of *Silybum maryanum* extension segments was 8.0 mm, and greater than control on 42.8%, by exposing with the compound of *Lagochilus inebrians* extension segments was 7.9 mm, and greater than control on 41.0%, in the standard version (2,4D 1h10-6) it was 7.6 mm.

ANTIPROTOZOAL ACTIVITY OF LACTONES EXTRACTED FROM PLANTS OF CENTRAL ASIAN REGION

J. I. Islamova, I. D. Sham′yanov, Z. A. Khushbaktova, V. N. Syrov

Institute of the Chemistry of Plant Substances, Academy of Sciences, Republic of Uzbekistan, Mirzo-Ulugbek str., 77, Tashkent, 100170, Uzbekistan, e-mail: zainab@icps.org.uz

The effects of lactones leucomisin and austricin isolated from *Artemisia leucodes Schrenk, repin*, acroptilin and girkanin – from *Acroptilon repens* (L.) *Dc*, tanachin and tavulin from *Tanacetopsis mucronata* (Rgl. et Schmalh.) S.Koval, tachillin and tanapsin from *Tanacetum pseudoachillea* S. Winkl., artemisinin from A*rtemisia annua* and alantolactone from *Inula grandis* Schrenk screened for antigiardial activity. To reproduce the experimental model of giardiasis the animals were inoculate orally with a suspension containing cysts and trophozoites of *Giardia muris* 5×10^3 in 0.5 mL [4.560–561].The suspension is prepared from the contents of the small intestine of spontaneously infected mice (Roberts-Thomson, Mitchell, 1978) [5,42-46.]. Studied lactones were injected to mice 5 days by special atraumatic probe into the stomach as an aqueous emulsion with arabic gum 20 mg/kg starting 5^{th} day post-infection. All experiments were performed in accordance with the "European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes" (Strasbourg, 1986).Groups of mice were euthanized at various time points, and the proximal 10-cm sections of their small intestines were removed and placed in 5 ml of physiological solution on ice. The small intestines were minced, and after 15 min on ice, the parasites were counted with a hemocytometer.

The experiments have shown that some of the studied compounds exhibit relatively high antigiardial activity. Thus, the intense-efficacy of repin, acroptilin, girkanin, tachillin, tanapsin and artemisinin was as follows: 81.5; 77.5: 72.8; 69.7; 67.4 and 82.6%, respectively. Other studied compounds of this class showed a less pronounced, but also completely reliable antigiardial effect. Intense-efficacy of leucomisin and austricin was 46.1 and 48.9%; tanachin and tavulin- 58.0 and 56.8%, alantolactone – 61.6%. Previously the same similar activity of these lactones was detected against *Entamoeba histolitica* and *Trichomonas vaginalis*.

It was established that most of the studied ranks of lactones considered more pronounced activity was observed for compounds containing exocyclic methylene group in conjunction with CO-group of lactone. Restoring exocyclic methylene reduced antiprotozoal activity. In addition, increasing of antiprotozoal activity of lactones may be due to the presence and position of epoxy group (repin, acroptilin et al.) or the presence of a chlorine atom and its position in the molecule (girkanin, akroptilin, elegin). A certain value for the manifestation of antiprotozoal actions can have the position of the lactone ring of compounds. The antigiardial activity of lactones depended on also of the presence of peroxide group in their structure (artemisinin).

Thus, these findings not only open the search of sesquiterpene lactones with high antigiardial activity, but also create a real opportunity to develop effective antigiardial drugs on their basis, especially if the currently existing drugs lose their effectiveness due to increased resistance of these protozoa parasites.

METHODS FOR IDENTIFICATION OF SYNTHETIC DRUGS – SPICES IN EXPERT RESEARCHES

L. T. Pulatova, F. S. Jalilov

Higher Military Customs Institute of SCC RUz, Tashkent, e-mail: lorena_97@mail.ru

Nowadays, identification of synthetic cannabinoids in the "spices" which are a part of various objects of illicit movement through a customs border of the Republic of Uzbekistan is a complex challenge and requires use of modern high-informative methods of research. There are approaches directed on detection and determination of several chosen target analytes, and also more difficult methods of detection of groups of the unknown substances close on chemical structure. A group of analytical methods, especially for identification of substances, provide use of instrument providing and require longer time.

One of the most powerful and universal ways of research of structure of unknown substances, in particular "spices", in expert laboratories is the GC-MS with high-selective division of the studied mixtures, a possibility of identification of unknown substances on signals of molecular and fragmentary ions in mass spectra and high sensitivity.

In the presented work, extraction of active ingredients was carried out by organic solvents, in particular, chloroform, ethanol, or methanol. For optimization of extraction of active ingredients ultrasonic processing is applied. Use of chloroform as an extragent has allowed to exclude extraction of the accompanying substances presented in the composition of investigated dried and crushed substance of plant origin of chartreuse color with a specific smell of a pharmaceutical chamomile (object No 1), and also a substance of brownish-yellow color with the mixed smell of pharmaceutical herbs and tobacco (object No 2). The chromatograms and mass spectra demonstrated that:

in the extract of object No.1 the peak of holding 2.581 min and a mass spectrum characteristic of the substance NM-2201 is revealed over time (naphthalene-1-yl-1-(5-fluoropentyl) - 1H-indole-3-carbonic acid);

in extract of object No.2 peaks with times of holding 23.87 and 26.71 min and mass spectra characteristic of AB-CHMINAKA (N-[1-(aminecarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazol-3-carboxamide, and NM-2201 (naphthalene-1-yl-1-(5-fluoropentyl) - 1H-indole-3-carbonic acid) are revealed.

Results of research have allowed study the processes of formation of mass spectra; determine the consistent patterns connecting the structure of analytes and m/z values, and relative intensity of signals in mass spectra.

MOLECULAR DOCKING OF BASIC COMPONENTS OF LIPID-LOWERING DRUG FLATERON

V. P. Bruskov, Z. A. Khushbaktova, N. D. Abdullaev

S.Yu. Yunusov Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uzbekistan, Tashkent, Republic of Uzbekistan

Lipid-lowering drug flateron contains six main natural components: apigenin, luteolin, chrysoeriol, cynaroside, termopsoside and formononetin related to flavonoids.

Acyl-CoA cholesterol acyltransferase, 3-hydroxy-3-methylglutaryl-CoA reductase, the endothelial NO-synthase (eNOS), and cyclooxygenase (COX-1, COX-2)) are probable targets of hypolipidemic actions of many flavonoids. In order to identify the molecular mechanism of flateron action we made molecular docking components listed in the biological target.

TABLE 1. **Lowest Binding Energy (kkal/mol)**

	AXAT	HGM CoA reductase	COX-1	COX-2
Apigenin	–7.44	–6.65	–8.49	–8.42
Cynaroside	–8.76	–7.70	–8.13	–9.44
Formononetin	–7.06	–6.90	–8.16	–7.99
Chrysoeriol	–7.54	–7.42	–8.72	–860
Luteolin	–7.49	–7.46	–8.91	–8.23
Termopsoside	–8.47	–7.66	–7.62	–9.13

The study of action mechanism of flavonoids - components of flateron formulation using the apparatus of molecular dynamics, quantum chemistry docking and showed a high degree of binding apigenin, luteolin, chrysoeriol, cynaroside, termopsoside and formononetin with the above enzymes. This sugar-cynarozide and termopsoside significantly inhibit 3-hydroxy-3-methylglutaryl-CoA reductase, which is the target of such cholesterol-lowering drugs as statins (with cynaroside and termopsoside not have side effects attributed to statins), and are selective blockers of cyclooxygenase type 2, providing anti-inflammatory effects.

MECHANISMS OF NEOANGIOGENESIS IN THE BRAIN OF RATS WITH EXPERIMENTAL ISCHEMIC STROKE

Kh. A. Rasulova

Tashkent Pediatric Medical Institute, Uzbekistan

Angiogenesis is a formation of new blood vessel networks, which is necessary for a long-term adaptation of vital organs after damage. In this case, there is a partial production of various growth factors in the blood, determination of which could have important clinical-diagnostic value.

The purpose of present paper was to study the level of vascular endothelial growth factor (VEGF) in blood serum and to prove morphologically the process of neoangiogenesis in the brain of rats, in which a model of experimental ischemic stroke (EIS) was reproduced.

Materials and Methods. Forty-two male outbred white rats weighing 220–280 g were taken for the experiments. The model of EIS was reproduced by ligating the left common carotid artery. In 10 rats, skin incision of the neck over the carotid artery was made followed by suturing of the skin (false-operated group). 11 rats were intact. The level of VEGF in blood serum was determined by enzyme linked immunosorbent assay. After decapitation, the pieces of brain tissue were immediately immersed in 2.5% solution of glutaraldehyde for fixation. After embedding in Epon-Araldite mixture ultrathin sections were stained with methylene blue and fuchsin. Microscopic images were taken using light-optical microscopy with fixed digital camera. The studies were conducted in the dynamics of EIS at the 1^{st}, 3^{rd} and 7^{th} days of experiments.

Results. The level of VEGF significantly increased after EIS, exceeding the value of control rats in 2.87 times ($P < 0.001$). Morphologically in the brain we noted constricted capillaries, stagnation of blood in the sinus, mild endothelial dysfunction, swelling of the brain tissue and the appearance of new collaterals already at 3^{rd} day, increasing by the 7^{th} day of experiment.

Conclusions. The results obtained indicate the development of endothelial dysfunction in ischemic stroke with activation of neoangiogenesis in experimental animals. Thus, hypoxia, ischemia and hemodynamic stress are potent stimulators of neoangiogenesis in EIS that can be considered as a protective mechanism. Certainly, the exploration of possibilities of therapeutic effects on this process (therapeutic angiogenesis) is a promising and perspective issue of today.

GETTING TO DISPLACE THE FLUORESCENT PROBE FOR RT-PCR ANALYSIS WITH A LOW BACKGROUND FLUORESCENCE

A. A. Mahnyov, D. R. Mansurov, S. A. Ikramov, O. B. Alimuhamedova, G. A. Piyakina

S. Yu. Yunusov Institute of the Chemistry of Plant Substances
Bd. 77, Mirzo Ulugbek str., 100170 Tashkent

For the development of any modern quantitative RT-PCR test system is the most important component of a fluorescent probe, which is directly responsible for the formation of a specific signal during the PCR reaction by which determine the amount of DNA/RNA in the sample. One of the simplest and most effective probes are "displacing probes."

Displacing probes are the part of a pair of oligonucleotides, which are complementary to each other, one of which carries a fluorophore (oligonucleotide A) and the other one - the fluorescence quencher (oligonucleotide B). In the absence of the target, probe the forms duplex in which fluorescence is suppressed. During the accumulation of the reaction product complementary to the probe, the process of re-association of the probe begins to compete with the hybridization of oligonucleotides to the target process, which leads to an increase of fluorescence. In the case of polymerases with 5'-exonuclease activity, the oligonucleotides hybridized to the target are destroy, that lead to a further increase in the specific signal. As advantages of the method, the easy synthesis and the relatively low price of samples can be considered. The main drawback of the method is a high level of background fluorescence.

In order to reduce background fluorescence (increase specificity fluorescence and fluorescence output) to the oligonucleotide A which carries fluorophore we attached an additional quencher molecule at the 3' end of the sequence. Thus, the fluorescence quenching will occur not only in time re-association, but in the process of probe hybridization with a target, which significantly reduce background fluorescence.

The experiment was carried out with plasmid pET19b, which used as an internal control for RT-PCR analysis.

As a result we revealed that the initial level of background fluorescence when the probe is used at a concentration of 250 nM pET19bZMd is 5000 fl, while pET19bZSt probe at the same concentration gives fluorescence value of 7500 fl. The background fluorescence reduced for 1.5 times in compare to the specific signal level between the two probes at the end of the PCR reaction. For probe pET19bZMd final fluorescence level was 25,000 fl, for pET19bZSt probe of 12,000 fl. The specific signal increased two-fold.

Thus, the obtained displacement type probe had a low background fluorescence and higher specific output signal in comparison with the standard preempt probe, which leads to increasing in the specific signal of quantitative PCR analysis.

NATURAL COMPOUNDS FOR THE DEVELOPMENT OF GRAIN SEEDS PROTECTANTS

S. S. Khalikov[1], E. S. Meteleva[2], A. V. Dushkin[2], O. I. Teplyakova[3], N. G. Vlasenko[3]

1) Institute of Organoelement Compounds RAS, 28, Vavilova str., Moscow, Russia; e-mail: salavatkhalikov@mail.ru
2) Institute of Solid State Chemistry and Mechanochemistry Siberian Brunch of RAS, 18, Kutateladze str., Novosibirsk, Russia
3) Siberian Researches Institute of Soil Management and Chemicalization of Agriculture of SFSCA RAS, Krasnoobsk, and Novosibirsk Region, Russia

The using of modern protectants should ensure the protection of seeds from external and internal infections, the plague pathogens in the soil and reduce the negative impact of seed of injury due to the intensification of its protective properties and prevent the development of pathogens. Protectants must be toxic to pathogens is well kept on the surface of the seed, not to reduce their germination. During protection of seeds the relatively small amounts of active substances should be applied uniformly on the seed. In order to achieve the optimum biological action against the disease, these protectants must be highly efficient and have a good formulation, providing an effective processing technology. In this regard, prospective and current development should be considered multifunctional protectants. We propose the use of mechanochemical modification technology known and used in practice of pesticides during their co-treatment with natural compounds such as polysaccharides and saponins. This innovative approach is based on the formation of supramolecular complexes of active substances (Tebuconazole, Carbendazim, Benomyl, etc.,) with increased permeability of the membrane, thereby increasing the penetration of active ingredients in the caryopsis. Simultaneously, increasing the transport of nutrients and water in a plant cell, stimulating the growth and development of the plants themselves.

Obtained protectants have high water solubility and a broader spectrum of activity than the pesticides used in practice. New protectants have not only high biological effectivity against common root rot (pathogens - *B. sorokiniana*, *Fusarium* spp.,), but they increase the germination of seeds of crops, increase the height and biomass of seedlings and plants. Typically, the using of these protectants helps improve the basic elements of yield structure - the length of the ear, the number of spikelets and grains per ear, grain weight from one ear and 1000 grain weight. As result, we can see the affects to the yield of the formation, which in these experiments either comparable to that with known commercial preparations, or significantly greater than it.

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ASPECTS OF REFRACTORY ANAEMIA OF INFLAMMATION IN CHILDREN WITH CHRONIC HEPATITIS B

F. I. Inoyatova, G. Z. Inogamova, A. Kh. Akhmedova, N. K. Valieva, F. G. Abdullaeva, V. I. Sabitova, N. A. Ikramova, Kh. M. Kadirkhodjaeva

Republic Specialized Scientific Practical medical Center of Pediatrics
under the Ministry of Health of the Republic of Uzbekistan
Tashkent, Chimbay street-2, Talant, 3

The aim is to study the informational content of ferrokinetic markers in the diagnosis of refractory anaemia in children with chronic hepatitis B (CHB).

Material and methods. The study involved 75 patients with CHB, ages 3 to 18 with refractory anaemia of inflammation 82.7% boys and 17.3% girls. Ferrokinetic markers were determined in serium by ELISA: ferritin (Ft), soluble transferrin receptor (sTfR), «Biochemmack», Moscow. The ratio of transferrin saturation (TSR) in urine is calculated: sTfR / log Ft. Hemosiderin (HS) was defined in urine by using the reaction of Prussian blue. The control group consisted of 20 practically healthy children.

Results. Analysis of ferrokinetic markers showed that the differences were obtained by the deciphering of the TSR. All patients were assigned to gradation: 14 (18.6%) patients with TSR below 0.2, 29 (38.6%) patients had TSR level ranging from 0.2 to 0.5, and 32 (42.6%) patients – with TSR higher than 0.5. On the background of significant difference with control, the dynamics of increasing of the Ft was detected up to 135.3±1.92 ng/mL, 142.3±2.36 ng/ml and 15.0±1.81 ng/mg, and decreasing of sTfR until 1.34±0.06 mkg/ml, 1.20±0.04 mkg/ml and 1.09±0.01 g/ml, respectively, by the patients of III, II and I groups with control of 62.2±1.21 ng/mg ($p < 0.001$). Herewith, all patients with TSR above 0.5 and 68.9%, with TSR from 0.2 to 0.5 had normocytic type of anaemia (84.46±0.74 fL and 83.81±1.42 fL respectively), whereas the majority (71.4%) of children with TSR below 0.2 had microcytic anaemia (74.46±1.42 fL). The explanations to that we see in the reduction of hepcidin synthesis in hepatocytes, wich is the main regulator of Fe metabolism in the body. At the same time, the presence of HS in examined patients' urine revealed in 29.3% of cases, wherein all of these children had TSR below 0.5. Moreover, with decreasing of the TSR the frequency of incidence of HS in the urine was growing, and reached up to 92.8% in children with TSR below 0.2 ($p < 0.001$ for the comparison group and the control group).

Conclusion. Considering the diagnostic significance of ferritin in the assessment of iron overload degree in children and its comparability with gradations of TSR we have found that there are three variations of refractory anaemia of inflammation in children with chronic hepatitis B: mild (TSR higher than 0.5), moderate (TSR above 0.2-0.5), and severe (TSR less than 0.2) degree. The diagnostic value of HS in the urine becomes significant only in the cases of severe iron overload in children with chronic hepatitis B.

PHYTOTOXIC AND INSECTICIDAL ACTIVITIES OF EXTRACTS FROM PLANTS GENUS OF *Climacoptera* AND *Kochia*

B. K. Yeskaliyeva[1], G. A. Seitimova[1], G. Sh. Burasheva[1], M. I. Choudhary[2]

1) Al-Farabi Kazakh National University, Faculty of Chemistry and Chemical Technology, Almaty, 050040, Kazakhstan
2) H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi-75270, Pakistan, e-mail: balakyz@mail.ru

Weeds have always been thought as one of the most serious agricultural and environmental problems. In agriculture, the control of weeds and their harmful effects is usually achieved by using herbicides belonging to different classes of organic synthetic chemicals. Some serious flaws are associated with the use of these synthetic pesticides including problems to human health and produces heavy environmental pollution. In Kazakhstan, approximately 2.5 million hectares of grain are heavily infested with weeds. Government subsidies for herbicide purchase of US$2-3 million/year resulted in herbicide use on 1.4 million hectares. These problems have resulted in the renewed interest in the development and use of botanical pesticides, which could be an appropriate and non-hazardous alternative to the currently used synthetic agrochemicals as the natural products.

Therefore, all extracts of *Climacoptera obtusifolia* and *Kochia prostrata* were checked for phytotoxic activity. Complete growth inhibition (100%) of *Lemna minor* was demonstrated by the dichloromethane, ethyl acetate and butanol fractions of *Climacoptera obtusifolia* at 1000μg/ml. In addition to that, the phytotoxic potential of hexane fraction was also worth mentioning: 93% at 1000μg/mL. Methanol fraction of *Kochia prostrata* exhibited significant phytotoxic activity against growth of *Lemna minor* with 100 % growth regulation at 1000 μg/mL, *n*-hexane, dichloromethane and ethyl acetate fractions showed 31, 69 and 93 % at 1000 μg/mL, respectively.

Regarding the results of insecticidal activity of both plants' various solvent fractions, moderate activity was exhibited by hexane (40%), dichloromethane (20%), ethyl acetate (20%) fractions of *Kochia prostrata* and dichloromethane (20%), butanol (40%) fractions of *Climacoptera obtusifolia* against *Rhyzopertha dominica*. On the other hand, none of the tested samples showed any activity against various insects used in the assay.

Based on the phytotoxicity, the aerial parts of the halophyte plants could be a significant source of natural herbicide for sustainable weed control.

NEUROPROTECTIVE EFFECTS OF POLYPRENOLS IN ISCHEMIA OF THE BRAIN AND VITAL STRESS IN RATS

P. D. Shabanov, N. S. Bakunina, S. V. Azarenko

Military Medical Academy, 6, Acad. Lebedev street, St.Petersburg, 194044, Russia,
e-mail: pdshabanov@mail.ru

Ropren® is a 95% concentrate of polyprenols, which is obtained from green conifer needles (*Picea abies* L. Karst). It is recommended as a hepatoprotective medication of plant origin. We have previously shown that Ropren not only has hepatoprotective, but also neuroprotective properties in the model of subacute hepatosis with encephalopathy caused by CCl_4 in rats. This paper presents data on the anti-ischemic and energy-stabilizing effects of Ropren in ischemia of the brain and vital stress in rats.

In the first experiment, the rats were anesthetized with nembutal, both carotid arteries were ligated and for 7 days they were injected daily with Ropren intraperitoneally at doses 4.3 or 11.6 mg/kg. An hour after the last injection neurological status of ischemic animals was assessed using the McGraw scale and the concentration of creatine phosphate, adenine nucleotides and energy charge, lactate and pyruvate in brain tissue was estimated. The nootropic drug piracetam (200 mg/kg) was used as the comparator. In the second experiment, the rats (n=21) were exposed to a single acute psychotraumatic situation by placing them into the cage with a tiger python. The python devoured a rat in the presence of 20 others, so it get an acute psychotraumatic exposure.

The treatment resulted in a marked improvement of the neurological status of ischemic animals, normalization of brain energy metabolism (concentration of creatine phosphate, adenine nucleotides and energy charge) and decrease of lactic acidosis. Piracetam injections caused slowness of movements in 17% of the rats, 8% showed circling behaviour and it also created limb paresis. All animals treated with Ropren didn't have any signs of paralysis in the extremities. Only in 10% of cases paresis was registered at 4.3 mg/kg dose injection. When Ropren was injected at the dosage of 4.3 mg/kg, 20% of the rats showed slowness of movements and hypotonicity, 10% - circling behaviour. Following 11.6 mg/kg dose injections of Ropren, symptoms such as slowness of movement and weakness of limbs were observed in only 8% of rats. The positive effect was more pronounced after Ropren injections of 11.6 mg/kg dose, exceeding the effect of the comparator drug – piracetam. Following the usage of piracetam on the 7th day after occlusion of the common carotid arteries 67% of rats survived, as with Ropren given at 4.3 mg/kg dose - 56% and at 11.6 mg/kg dose - 63% of animals survived, respectively. Cerebral ischemia and, hypoxia as a consequence, led to significant depletion of the energy resources of the brain, even though by this time it was already very deficient. The content of macroergs sharply decreased (ATP, creatine phosphate), the number of unoxidized products (ADP, AMP, lactate) increased, the organism's energy charge decreased and lactic acidosis developed. The latter is due to a 5-fold increase in the level of lactic acid in the brain. In these cases piracetam decreased lactic acidosis only by 46.5% and ropren by 62% at 11.6 mg/kg respectively (i.e. by almost two-thirds). The same dosage of Ropren increased the content of creatine phosphate by 73% (piracetam – by 60%) and concentration of ATP in brain tissues by 173%. Both Ropren and the comparator drug piracetam affected the level of ADP quite similarly, lowering it by 40–43%. Thereby, both piracetam and Ropren normalised the energy charge, reflecting the general state of energy metabolism in the brain. In general, we managed to demonstrate proximity in the pharmacological effects of piracetam and Ropren (especially at a dose of 11.6 mg / kg) in cases of cerebral ischemia. In the experiment with vital stress, the psychotraumatic exposure dramatically disturbed rat behavior assessed in the open field, elevated plus maze and resident-intruder tests. Ropren administered within 1 week after exposure recovered the majority of behavioral indexes investigated.

The results obtained demonstrated the neuroprotective and energy-stabilyzing effects of Ropren in ischemia of the brain and vital stress in rats. This is consistent with previously collected data on the protective effect of Ropren in cases of toxic damage of internal organs (mainly liver) and encephalopathy. The results can be used in clinical practice for treatment of neurodegenerative diseases and the effects of ischemic and brain injury.

PEPTIDE ANTAGONISTS OF OREXIN OX(1) RECEPTORS MODULATE THE REINFORCING SYSTEMS OF THE BRAIN IN A RAT SELF-STIMULATION MODEL

P. D. Shabanov, A. A. Lebedev, V. I. Morozov

Institute of Experimental Medicine, 12, Acad Pavlov st., St.Petersburg 197376, Russia,
e-mail: pdshabanov@mail.ru

The orexin (hypocretin) family of hypothalamic neuropeptides has been participated in reinforcement mechanisms relevant to both food and drug reward. There are dense concentrations of orexin receptors in the extended amygdala and mesocoricolimbic structures implicated in drug reinforcement processes. Behavioral studies with antagonists at the orexin A-selective receptor OX(1) have demonstrated its involvement in behavioral sensitization, conditioned place-preference, self-administration and reinstatement of drugs abuse. Because of suggestion, that OX1 and D2 dopamine receptors could form heteromeric complex, for example, orexin A + quinpirol, a D2 dopamine agonist, or SB-408124, an antagonist of OX1 receptors, with sulpiride, we used both latter drugs in our experiments to prove or disprove this admission. The possible interaction between orexin OX1 and dopamine D2 receptors in alcohol abuse has recently shown in the experiment on rodents.

The purpose of the investigation was to clear if SB-408124 and antorex, the new antagonists of the orexin A-selective receptors OX(1), one of them synthetic (SB-408124) and the other peptide (antorex), injected into the central amygdala can interact with antagonist D2 receptor sulpiride on inhibition of reinforcing effects of amphetamine on self-stimulation of the lateral hypothalamus in rats.

The 51 Wistar male rats were implanted bipolar electrodes into the lateral hypothalamus to study self-stimulation reaction in the Skinner box. Simultaneously, the microcannules were implanted into the central nucleus of amygdala (CA) to inject the drugs studied (1 μg in 1 μl in volume for each injection). Antagonists of the orexin A-selective receptors OX(1) SB-408124 and antorex were administered intrastructurally (into CA) and antagonist of D2 receptor sulpiride was injected intraperitoneally followed by pharmacological analysis.

Both SB-408124 and antorex injected into the extended amygdala region (CA) alone had no effect on self-stimulation of the lateral hypothalamus. Sulpiride in low dose (5 mg/kg) did not affect both the spontaneous and amphetamine-activated self-stimulation (1 mg/kg). Amphetamine as a rule increased self-stimulation measured as lowering the threshold and enhancing the frequency. Amphetamine-induced stimulatory effects on intracranial self-stimulation were reduced by injections of SB-408124 into the CA up to the background level. The same effect was registered for antorex. Simultaneous administration of SB-408124, an antagonist of the orexin A-selective receptors OX(1), and sulpiride i.p. (5 mg/kg) inhibited amphetamine-induced self-stimulation in more degree than background level, that was sulpiride potentiated the inhibitory effect of SB-408124. The same but not so significant effect was received when antorex was used. These data demonstrate that OX(1) receptors play an important role in regulating the reinforcing and reward-enhancing properties of amphetamine and suggest that orexin transmission (neuromodulation) is likely essential for establishing and maintaining the amphetamine habit in human addicts. However, the observations that OX1 antagonism reduces brain reward and blocks stress- and cue-induced reinstatement of drug-seeking suggesting that class of compounds may be useful additions to stress-reduction and other behavioral therapies in the treatment of substance abuse disorders.

The findings suggest that the combined use of low doses of D2 antagonists (like sulpiride) and antagonists of the orexin A-selective receptors OX(1) (like SB-408124 or antorex) are necessary to reorganize the central mechanisms underlying the addiction state to target correction of addictive disorders. Supported by RFBR grant # 16-04-00954a.

DEVELOPMENT OF COMPOSITION OF BIOMAYRIN CAPSULES

N. E. Mamatmusaeva, Sh. A. Shomuratov, B. T. Sagdullaev, A. S. Turaev

Institute of Bioorganic Chemistry of the Academy of Sciences of Uzbekistan, Tashkent, 100125, MirzoUlugbek, 83

Recent years due to the massive uncontrolled migration of the population of countries with less developed infrastructure to the developed ones, tuberculosis hasbecome more frequent over the world.

Tuberculosis refers to the most severe intracellular infections caused by *Mycobacteriumtuberculosis* bacillus. As it is known, low-molecular synthetic drugs are highly toxic and do not have the ability to selectively penetrate into phagocytes (cell-eaters) containing a pathogen of tuberculosis, also they are rapidly excreted from the body without providing prolonged action, since they have only an effect on extracellular pathogens of tuberculosis. Therefore, in the treatment and maintenance of a constant therapeutic concentration of anti-tuberculosis drugs (ATD) in the blood of patients, multiple administration of ATD is required, which often accompanied by the development of severe toxic-allergic reactions leading to withdrawal of therapy or disruption of drug regimens. In addition, regular use of anti-tuberculosis drugs in a large dosage leads to the development of multiple drug resistance.

The anti-tuberculosis preparation of the combined action "Biomayrin" has been developed at the Institute of Bioorganic Chemistry of the Academy of Sciences of Uzbekistan, by chemical binding of isonicotinic acid hydrazideto the modified dialdehyde of polygalacturonic acid, followed by the incorporation of ethambutol and rifampicin into the macromolecule through ionic binding.

The purpose of this work is to develop the optimal composition of the Biomayrin capsules. Technological properties such as the shape and particle size (using microscopic analysis), fractional composition, compressibility, compression ratio, bulk density (freely poured) and (with compaction), angle of naturalinclination, flowability (with vibration) and (without vibration) as well as residual moisture have been studied. In the first series of experiments it was found, that the particles of the tested substance had a plate-like and a rod shape; the fractional composition had satisfactory results for the substance; the compressibility of the substance was 1.66 g/mm; compression ratio 2.95,; bulk density (freely poured) 688 kg/m^3, bulk density (with compaction) 870 kg/m^3; angle of natural inclination 42.7°;flowability (with vibration) 3.1 g/s, flowability (without vibration) could not be determined; and residual moisture 4.8%.

As can be seen from the results of investigations, the value of flowability of a substance under vibration is at a minimum level, and the flowability without vibration could not be determined, in addition the magnitude of the angle of natural inclination was higher than the recommended value.That indicates the technological properties of the substance should be improvedusing antifriction agents. To improve them, reduce the undesirable effects of the plate form of the particles of the substance and increase its flowability, we studied the effect of various antifriction agents on the technological properties of the capsule mass (calcium stearate, stearic acid, potato starch, talc, aerosil and PEO-4000 polyethylene oxide). Antifriction substances were added in amounts satisfied to permissible requirements and corresponded to the previously obtained a priori information.

The composition of a capsule was determined: isoniazid 90.0 mg ± 3%, rifampicin 102.0 mg ± 3%, ethambutol 90.0 mg ± 3%, polygalacturonic acid 318.0 mg, calcium stearate 6.0 mg. The average weight of one capsule was 606 mg.

CONIFEROUS WOOD GREENERY POLYPRENOLS FOR MEDICINE

V. N. Syrov[1], Z. A. Khushbaktova[1], T. V.Hurshkainen[2], A. A. Koroleva[2], A. V. Kutchin[2]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances of Academy of Sciences of the Republic of Uzbekistan Tashkent, Uzbekistan, e-mail: zainab@icps.org.uz
2) Institute of Chemistry Komi Science Center of Ural Division of RAS, Syktyvkar, Russia

Wood and wood greenery are perspective sources of polyisoprenoids when maintenance of polyprenols makes from 0.001 up to 2 % to absolutely dry raw material weight. The unique biological role of polyisoprenoids in vital functions of living organisms defines urgency of development of effective methods of their extraction from plants raw material and research of this class of compounds.

The effective way for isolation of polyprenols from coniferous greens, and from sulphatic soap - a by-product of pulp-and-paper manufacture is developed in Institute of Chemistry of Komi SC UD of the Russian Academy of Science. On the basis of ICPS AS RUz the biological tests of polyprenols obtained from *Abies*, *Picea* wood greenery and also from sulphatic soap are carried out. Hepatoprotective activity of *Abies* polyprenols at defeat of a liver by alcohol, and stress-protective effect are established.

The purpose of this work is studying *Abies* polyprenols as wound-healing means. Experiments were spent on mice (male in weight 19-20 g). Planer (full-thickness) skin wounds at mice reproduced in the field of a back by means of a special round stamp (diameter of 9 mm). Supervision over process of healing of experimental wounds spent before their full healing. Polyprenols applied on wound defects of leather a uniform layer once in day daily during all experiment. Wound surface at control groups of animals did not treat (control I) and greased with sunflower oil (control II). As a preparation of comparison used sea-buckthorn oil. *Abies* polyprenols have shown the expressed stimulating action on regenerative processes in a skin wound. So, at reproduction pure full-thickness skin wounds put on depilating skin of a back, from first days of inflammatory reaction around of them has been expressed noticeably more poorly, and process of regeneration from the very beginning went more actively, than in the control. At mice smaller puffiness, poor wounds exudate, active development of granulation was marked. In parallel of connecting tissue development and wounds vascularization expressed epithelization of wound defect (growing epithelium was clearly visible as a white rim on a dark red background of formed granulations) was observed. Full healing wound defects in control I occured on the average on 28th, in the control II - for 27th day; under action of *Abies* polyprenols or sea-buckthorn oil - on 18th and for 23th day, accordingly. Wound-healing effect in relation to the control II in the first case made 33.3%, and in the second 15.8%. Hence, *Abies* polyprenols surpass sea-buckthorn oil on ability activate a regenerative processes in a wound. Thus, *Abies* polyprenols render the expressed positive influence on process of healing of skin wounds (reduction of an inflammatory hypostasis, strengthening of the counteraction with the subsequent acceleration of filling of wounds by granulation tissue and them epithelization) and represent the certain interest as effective wound-healing means.

COMPARATIVE STUDY OF FLAVONOIDS ANTIOXIDANT ACTIVITY *in vitro*

D. A. Narbutaeva[1], O. S. Charishnikova[2], V. N. Syrov[1], Z. A. Khushbaktova[1]

1) S. Yu.Yunusov Institute of Chemistry of Plant Substances, AS RUz
e-mail: zainab@icps.org.uz
2) Educational-Experimental Centre of High Technologies, Tashkent, Uzbekistan

Flavonoids is a wide-ranging class of low molecular weight polyphenolic compounds. They arethe main components of many drugs, which mechanism of action is the inhibition of lipid peroxidation (LP). Lipid peroxidation plays a significant role in the pathogenic processes in our organism, in particular, in diseases of cardiovascular and hepatobiliary systems.Therefore, we decided to check is there any correlation between flavonoids structure and their antioxidant activity,which mightbe helpfulin the prospect for the use of individual representatives of this class of compounds, for the creation of new effective drugs.

It was found that among a number of studied isoflavones (orobol, formononetin, genistin, ononin, and biohanin) only orobol at a concentration of 2.5×10^{-5} M inhibited the formation of one of the end products of LP - malonicdialdehyde (MDA) by 67%. For these experiments, we used the model of iron-induced ascorbate-dependent LP *in vitro* using rat liver homogenate.Other compounds, in contrary, showed little pro-oxidant effect. Experiments with some flavones such as luteolin, chrisoeryol, cynaroside, thermposopide and gyspidulinshowedthat only luteolinwas highly active and inhibited LPby 63.7%.Other compounds were weakly active.

The most pronounced antioxidant activity (AOA) among the studiedcompounds hadflavonols.Galangin, quercetin, morin, myricetin, isoramnetin, limocitrineinhibited the formation ofMDA by 86.3, 78.1, 80.6, 83.5, 80.9, 69.5 %, respectively.The effectof rutin, myricetin-3-glucosideand haplogenin-7-glucoside was slightly weaker than in previous group (24.1, 40.3 and 26.7 %, respectively). All the results were statistically significant.

Among a number of examined flavonones (pinocembrin, glabranin, isoglabranin, isobavachin, glabrol, vesibinol, lemanin) onlyglabrol (80.8%) and lemanin (73.5%) showed significant AOA. Interesting, combined application of the numberof flavonoids such as apigenin, luteolin, chreoiseryl, cynaroside, thermposopide, formononetin, with thedifferent AOA, isolated from *Thermopsisalterniflora*decreased the level of MDA to the basal level (*in vitro*), so the effect was 100 %. Experiments performed on the membranes of isolated rat liver mitochondria.

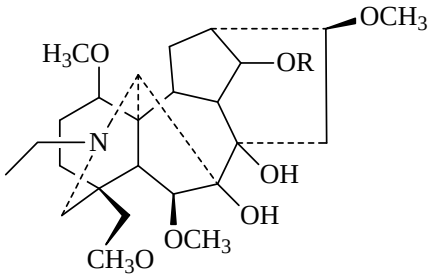
In this study, we discuss the importance of the chemical structure of the main nucleus (isoflavone-flavone), the number and arrangement of free OH groups in rings A and B, as well as the glycosylation and polymethoxylation of flavonoids for the optimal selection of certain compounds of this series suitable for practical use.

ON PHARMACOLOGY OF DITERPENE ALKALOIDS BROWNIINE, *C*(14)-*O*-ACETYLBROWNIINE AND *C*(14)-*O*-BENZOYLBROWNIINE

F. N. Dzakhangirov[1], A. A. Azamatov[1], V. F. Tukhtasheva[1], B. B. Zhao[2], J. Y. Zhao[2], H.A. Asia[2], B.T. Salimov[1]

1) S.Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, Republic of Uzbekistan, e-mail: akademic1986@list.ru
2) Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, P. R. China

The comparative pharmacological investigation of alkaloids browniine (**1**), *C*(14)-*O*-acetylbrowniine (**2**) and *C*(14)-*O*-benzoylbrowniine (**3**), isolated from *Consolida* and *Delphinium* plants have been carried out.



R = - H (1)
R = - $COCH_3$ (2)
R = - COC_6H_5 (3)

LD_{50} in intravenous injection for mice was **1** - 70 mg/kg, **2** - 57 mg/kg, **3** - 17.5 mg/kg. Resorptive action of **1** and **2** differ than **3** ones. In acute experiments on anaesthezied cats the substances displayed short-time hypotensive action attributed to H-AcCh-bloking effect. ED_{50} of nerve impulses conduction in cats upper neck sympatic ganglia was **1** - 4,5, **2** - 4,8 and **3** - 2,5 mg/kg for **1**, **2**, **3** accordingly. In high doses **3** caused inhibition of basic cardiac functions (excitability, conductivity, contractibility, refractory, automatism) and lead to arrhythmia.

In vitro on isolated fragments of rats and rabbits intestine the substance **3** displayed expressed myotrop spasmolytic action surpasses **1** and **2** ones for more than 40 times.

In contrast to **1** and **2**, the substance **3** displayed expressed antiarrthymic activity on different animals on aconitine, calcium chloride, barium chloride, strophanthin K, heart sections electric irritation and coronary artery occlusion models. On antiarrythmic activity, effectivity and therapeutic width it surpasses **1** and **2** for 60 times and more, and antiarrhythmic drugs of I class quinidine, procainamide, rhythmilene, ethmothine, ajmaline for 10 times and more. On electrophysiological action on myocardium the substance **3** is attributed to I class of antiarrthythmic drugs. On isolated neurons of rats sensor ganglia and cardiomyocytes in concentrations 10^{-6} – 10^{-5} M **3** inhibits intake TTX-sensitive sodium current.

In contrast to **1** and **2**, the substance **3** displayed sedative, antinociceptive, anti-inflammatory and hypothermal effects. On analgesic activity **3** surpasses acetylsalicylic acid and metamizole sodium. In contrast to metamizole sodium, **3** decreased the ability of CNS to summation of sub-threshold impulses and increased the pain threshold of rats and mice to thermal and electric irritation.

PREVENTION OF CANCER DEVELOPMENT BY PRODUCTION OF ANTIMUTAGENIC HERBAL MEDICINES

B. Iriskulov, B. Abdullaev

Department of Pathology, Tashkent Medical Academy, Farobi 2, Almazar District, Tashkent, Uzbekistan, 100109; e-mail: author.uzb@mail.ru

Background. Nowadays, it is proved that mutation in somatic cells are not only involved in carcinogenesis and genotoxicity, but also involved in the commencement and pathogenesis of several chronic degenerative diseases, such as hepatic disorders, arthritis, diabetes, neurodegenerative and cardiovascular disorders, chronic inflammation and in the process of ageing. One of the best pathways to diminish the detrimental effects of mutagens is by the use of natural antimutagens, which is so-called like G-bombs (green bombs). There are continued efforts all over the world to investigate rich biodiversity of comestible as well as medicinal plants and other edible non-toxic plants in pursuit of the most effective phytoantimutagens. These bioactive compounds relate to a diversity of different chemical groups like phenolics, anthocyans, pigments, allylsulfides, flavonoids, glucosinolates, tannins, phytosterols, protease inhibitors and phytoestrogens. Many of these substances stimulate, except antimutagenic and anticarcinogenic properties, additional profitable effects such as activation of the immune system and/or protection against cardiovascular diseases.

Antimutagens. Antimutagens can prevent the transformation of mutagenic substances into mutagen, inactivate the mutagen or otherwise preclude the reaction between mutagen and DNA. Another kind of antimutagens may induce, repress or inactivate directly or indirectly the enzymes of the DNA repair recombination and replication pathways. The antimutagens can be classified as desmutagens and bioantimutagens.

Natural Antimutagenic Agents. Additional research in the last two decades on the detection and characterization of antimutagenic compounds from edible, non-edible and medicinal plants and marine organisms has demonstrated a great diversity. Numerous authors have suggested that natural antimutagens may relate to any of the following major class of substances. Major emphasis has been laid on the saponins, flavonoids, coumarins, phenolics, anthraquinones, tannins, carotenoids, terpenoids and several others all of which are secondary plant metabolites. More than 500 compounds belonging to at least 25 chemical classes have been recognized as possessing antimutagenic/protective effects. In last years, there has been an increased interest in determining the anticarcinogenic and antimutagenic constituents of both dietary and medicinal plants worldwide.

Conclusions. There is a need to find natural antimutagenic agents having the potential to prevent or at least delay the onset and severity of genetic damage, which can be integrated into the regular diet of an individual. Potentially, antimutagenic plants include a number of common or ethnic group restricted edible plants, including pulses, cereals, vegetables and spices and medicinal herbs and health tonic plants. Consumption of fruits, dietary green leafy vegetable, carrots, nuts, beverages and green tea etc. can communicate required protection against the genotoxic effects of mutagens present in drugs, food, cosmetics, industrial waste etc. and in that way help in prevention of cancer and other degenerative disease as atherosclerosis, diabetes mellitus, ischemic heart disease, rheumatoid arthritis, neurological disorders etc.

ANTIOXIDANT ACTIVITY OF COMPLEXES GLYCYRRHIZINIC ACID WITH FLAVONOID QUERCETIN

N. A. Ergashev, E. J. Komilov, M. I. Asrarov, U. D. Matchanov, R. S. Esanov

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, 100125, Tashkent, Mirzo Ulugbek str., 83

Nowadays, a special role of the processes of lipid peroxidation (LPO) of biological membranes is shown in norm and in various pathological conditions. In this regard, the study of regulation of free radical processes of LPO at the level of mitochondria, with various biologically active substances, remains topical. Thus, antioxidant activities of quercetin and its complex with glycyrrhizic acid have been investigated. According to literature data it is well known that quercetin has a very high antioxidant activity, however the antioxidant activity of glycyrrhizic acid is weakly expressed in comparison with quercetin.

The purpose of this work was to determine the optimal molar ratio of water-soluble supramolecular complexes of glycyrrhizic acid with quercetin, for further deep study of pharmacological and toxicological properties of obtained complexes.

Data obtained shows that quercetin at a concentration of 15 μM completely inhibits LPO process induced by the Fe^{2+}/ascorbate system in rat liver mitochondria. However, under the same conditions, glycyrrhizic acid inhibits LPO at a concentration of 150 μM, which is 10 times more effective comparing with concentration of quercetin. The supramolecular complex of these compounds, in the ratio of GA:Q = 2:1 and GA:Q = 4:1, inhibited LPO in mitochondria of rat liver at the concentration of 33 μg/ml. This data shows a certain weakening of antioxidant activity of supramolecular complexes of glycyrrhizic acid with quercetin in comparison with quercetin itself. These data do not provide a basis for weakening the effectiveness of synthesized new water-soluble complex compounds.

FERULEN – A THE NEW PHYTO DRUG FOR THE TREATMENT OF PROSTATE ADENOMA AND CANCER

J. Rejepov, F. N. Dzakhangirov, V. F. Tukhtasheva

S.Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, Republic of Uzbekistan, e-mail: Visolaft@mail.ru

Ferulene consists of the sum of sesquiterpene esters alcohols obtained from the plant *Ferula tenuisecta* Eug. Kor. Under the experimental conditions on females, Ferulen has a pronounced estrogenic activity that is not inferior to the drug Tefestrol used in medical practice. In males Ferulen selectively acts on male genital organs: -much weight of androgen-dependent organs (prostate gland, seminal vesicles, and testicles), inhibits the secretion of testosterone. By it antiprosthatic activity and efficiency, Ferulen is superior to Sinestrol, Diethylstilbestrol, Prostamol Uno, and it acts at the level of surgical castration.

The drug belongs to the IV class of low-toxic substances (LD50 when administered per os> 5000 mg / kg) does not significantly wobble on blood pressure, respiration, peripheral autonomic nervous system and ECG. It has moderate immunomodulatory, anti-inflammatory and prolongs the time of blood coagulation.

Clinical efficacy was tested in patients diagnosed with prostate cancer of stages I-IV on the basis of the RTC MH RUz (Tillashaikhov M.N.) and Tash. Hor. Onko. The dispensary (chief physician Prof. Gafurakhunov MA)

After the course use of Ferulen noted:

-Improving the overall well-being of patients

-Complete elimination or significant reduction of disuric phenomena (difficulty urinating, blood in the urine, pain luring urination ing, frequent urge to urinate) in 96% of the patients

-Reduction of prostate gland volume takes plorein 62.5% of the patients

- Complete normalization or reduction of the initial increase in PSA levels by more than 50% in 82% of the population

- Decrease in testosterone and LH levels.

At high therapeutic efficacy, Ferulen had a minimal number of side effects not requiring at withdrawal of the drug. According to clinical efficacy and tolerability Ferulen significantly exceeded the reference drug Diethylstilbestrol.

One of the important advantages of Ferulen is a convenient dosage form (tablets, capsules) and low cost of the drug

The work was done with the financial support of the State Committee for Science and Technology of the Republic of Uzbekistan and the IP of ICPS Academy of Sciences of Uzbekistan.

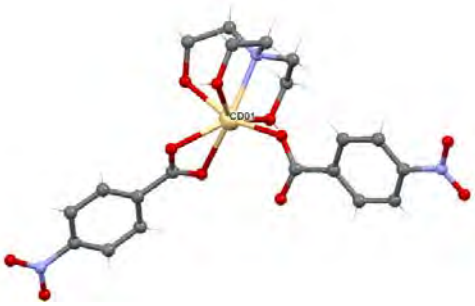
BIOLOGICAL ACTIVITY OF METAL COMPLEXES ON THE BASE OF 4-NITROBENZOIC ACID AND ETHANOLAMINES

A. B. Ibragimov

Institute of General and Inorganic Chemistry of Uzbekistan Academy of Sciences
e-mail: aziz_ibragimov@mail.ru

Priority is receiving cheap drugs a synthesis of which is simple and demonstrates several types of biological activity. For example, such drugs are ones showing at the same time both types of anti-fungicide and growth stimulating activities. The new substances received by us are related to this category. It is well known that 4-nitrobenzoic acid and some metals demonstrate antimicrobic properties while ethanolamines have a good growth stimulating activity. Knowing this we synthesized several new mixed-ligand metal complexes on the base of these ligands which possessed a double biological effect.

The mononuclear Cu (II) complex with *p*-nitrobenzoic acid and monoethanolamine



The mixed ligand Cd (II) complex with *p*-nitrobenzoic acid and triethanolamine

We tested a biological action of the obtained compounds at Institute of microbiology and Institute of the general and inorganic chemistry of Uzbekistan Academy of Sciences.

Indeed, researches have shown that we managed synergism of biological effect and prepared growth stimulating and anti-fungicide compounds. In figures some new mixed-ligand metal complexes with double biological activity are shown.

All received mixed ligand metal complexes are characterized by physical methods of the investigations such as FTIR, LC-MS mass-spectrometry and XRD. They are deposited to the Cambridge structural database as new compounds. Researches and synthesis of the new mixed ligand metal complexes on the base of benzoic acids and ethanolamines are in progress in our lab.

ACUTE MYELOID LEUKEMIA WITH TRISOMY 11: A MOLECULAR -GENETIC STUDY

Kh. Ya. Karimov, S. K. Kurganov, K. T. Boboev

Scientific-Research Institute of Hematology and Blood Transfusion, Tashkent, Republic of Uzbekistan., City of Tashkent, Chilonzor district, st. Bunyodkor, 42-a, e-mail: info.niigem@minzdrav.uz

The KMT2A (MLL) gene is located at the 11q23 locus and encodes a DNA-binding protein that methylates histone H3 lys4 (H3K4) positively regulates expression of target genes, including multiple HOX genes.

Partial tandem duplications (PTD) of the MLL gene have been associated with trisomy 11 in acute myeloid leukemia (AML) and have also been reported for karyotypically normal AML.

The purpose. To evaluate the effect of additional Trisomy 11 mutations in patients with AML.

Materials and methods. In order to test the incidence and prognostic importance of this molecular marker, we have analyzed 10 was patients. A total of 230 (10 patients * 23 markers) tumor markers were analyzed in the study.

The material of the study was patients with a clinically established diagnosis of AML, observed in the hematology department of the Research Institute of Hematology and Blood Transfusion of the Ministry of Health of the Republic of Uzbekistan. Preliminary diagnosis of AML is established on the basis of clinical and laboratory (morphological and cytochemical) studies of blood and bone marrow. For the analysis, a set of "LC-biochip" chosen, which 13(23 isoforms) most known chimeric oncogenes acute leukemia (AL): t(12;21) ETV6-RUNX1, t(1;19) TCF3-PBX1, t(9;22) BCR-ABL1, t(4;11) MLL- AF4, t(15;17) PML-RARA, t(8;21) RUNX1-RUNX1T1, inv(16) CBFB-MYH11, t(9;11) MLL-MLLT3, t(10;11) MLL-MLLT10. Also, there is of identification of MLL genes for common exones 8-11.

Analysis of MLL-PTD of tumor cells on the biochip included the following steps: isolation of DNA from peripheral blood leukocytes of patients, carrying out a two-stage (nested) PCR; Introducing a fluorescent label into the second-stage PCR product using fluorescently labeled primers; Hybridization of the labeled PCR product on the biochip; Image analysis on the device with Imageware software.

Results. Study 10 patients, the following results were obtained: in 3 cases (33.3%), structural rearrangements of the t (9;22) genes were revealed BCR/ABL p190, t (10;11) MLL/AF10, and t (8;21) AML/ETO. Other cases (66.6%) revealed a normal karyotype. Of the a normal karyotype patients examined, mutations with trisomy 11 were detected in two (20.0%) cases, which allowed to accurately diagnose AML. All other samples apparently contained other somatic mutations and they will be identified by other molecular methods (PCR, FISH immunophenotyping, sequencing, etc.). It should be emphasized that this mutation, in itself, is not able to cause leukemia, therefore, to fully confirm the diagnosis, it is necessary to investigate additional (secondary) mutations.

Conclusion. Although our analyses are limited by a relatively small sample size, our study sheds new light on the mutational background of this prognostically adverse subset of AML patients with sole +11.

ROLE OF TYROSINASE GENE, TYR, IN MECHANISM OF VITILIGO ONSET AND PROGRESSION

T. S. Saatov, Z. Z. Ibragimov, B. T. Saatov

Institute of Bioorganic Chemistry, Uzbekistan Academy of Sciences,
83, Mirzo Ulugbek Street, 700125, Tashkent, Republic of Uzbekistan
e-mail: t.saatov@yandex.ru

Vitiligo is an acquired dermatosis of chronic course with typical manifestations in the form of white patches resulting from sharp reduction or absence of melanin, a pigment. The findings from recent epidemiological studies definitely indicate intensive growth in incidence of vitiligo worldwide, Uzbekistan included. Tyrosinase, an enzyme of melanocytes, takes a special place in pathogenesis of vitiligo. Tyrosinase catalyzes conversion of tyrosine, an amino acid, into melanin in the special pigment cells, melanocytes.

Of note, involvement of tyrosinase in onset of vitiligo is unestablished yet.

The work was initiated to study TYR gene rs 1393350 polymorphism and association of the polymorphism with the susceptibility to vitiligo.

Materials and methods. We examined 58 patients diagnosed with vitiligo. Forty healthy Uzbeks were included into the control group. “Ampli-Prime RIBO-prep” (Next-Bio, Russia) was used to isolate genomic DNA from peripheral blood. DNA qualitative and quantitative assessment was performed by means of NanoDrop 2000 (USA) spectrophotometer. TYR gene rs 1393350 polymorphism was genotyped by means of Rotor Gene 6000 (Australia) with commercially available kits of DNA- Technology company (Moscow, Russia). The data were statistically processed by Doctor Stat 2013, Version 1.9 program package.

Results and discussion. Frequency of TYR gene polymorphism alleles and genotypes in patients with vitiligo and the controls was different. G allele frequency in patients with vitiligo and the controls was 73.3% and 80.0%, respectively. Frequency of unfavorable, mutant A allele of TYE gene was insignificantly higher in patients with vitiligo than in the controls. Presence of A allele in TYR gene rs 1393350 polymorphism indicates higher risk for onset of vitiligo by 1.5 times ($\chi2$=1.17; p=0.28; OR=1.46; 95%CI: 0.74-2.89). Distribution of wild homozygous G/G TYR gene genotype in patients with vitiligo was distinctly lower than in the controls, 53.4% и 65%, respectively ($\chi2$=1.3; p=0.5; OR=0.62; 95%CI: 0.27-1.41). Unfavorable, heterozygous G/A genotype in TYR gene rs 1393350 polymorphism in patients was more than 1.6 times higher than in the controls.

Our findings in frequency of TYR gene rs 1393350 polymorphism in patients with vitiligo helped establish presence of mutant homozygous A/A genotype (6.9% versus 5.0% in the controls ($\chi2$=0.33; p=0.56; OR=1.68; 95%CI: 0.28-9.9). The data can be the evidence for involvement of A/A genotype in susceptibility to vitiligo, increasing risk of its onset almost by 1.7 times, as compared with G/G genotype.

The findings allow concluding that functionally unfavorable A/G, A/A genotypes and A allele are dependent genetic markers for vitiligo risk in the Uzbek sample.

ACTIVE SCREENING OF ALPINIA OXYPHYLLA BY PLASMID TRANSFECTED CELLS AND STEM CELLS

Rui Tan

College of Medicine, Southwest Jiaotong University, No. 111, North 1st Section of Second Ring Road, Jinniu District, Chengdu City, Sichuan Province, PRC,
e-mail: tanrui@home.swjtu.edu.cn

A simple screening model for ICVD is necessary for discovering active compounds and lead compounds. ICVD treatment is mainly related to the body adaptability of neurons protection or regeneration, and the involved functional gene is NGF (Nerve growth factor, NGF). In our research, cell-based reporter models with NGF promoter were constructed to screen the drugs systematically and effectively. Stem cells are used to detect the differentiation direction of treated cells in nerve regeneration.

Two reporter systems were constructed, and red fluorescent protein model (E2) was for the rapid observation and luciferase model(Luc) for the quantitative determination. After the positive stimulus treatment, increased expression of luciferase was observed and the high doses showed statistical significance as Fig.1. Compounds from *Alpinia oxyphylla* were screened by Luc model, tectochrysin shows a biological activity that can increase the transcription level of the NGF promoter as Fig.2.

Rat bone marrow mesenchymal stem cells (rMSCs) are induced by tectochrysin between 24h to 7d. Transcription level of five indicator genes was detected by RT-qPCR to find the differentiation direction of treated stem cells. Nestin and Vimentin transcription level is raised at rMSCs treated by 1мM tectochrysin for 3d. However, transcription level exaltation of NSE and GalC are not observed.

The promoter sequences contain variety of binding sites, so it is possible to reconcile specificity and efficiency in drug screening, which is beneficial for the later mechanisms investigations, especial for transcription regulation. The biological activity tectochrysin was surmised that can improve the level of Nestin and Vimentin. A material basis for the neuroprotection of the *Alpinia oxyphylla* was conjectured, and an example is provided for the rapid screening of small molecule compounds from natural medicine.

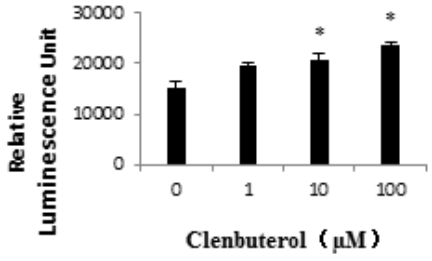


Fig. 1. Luc model modification.

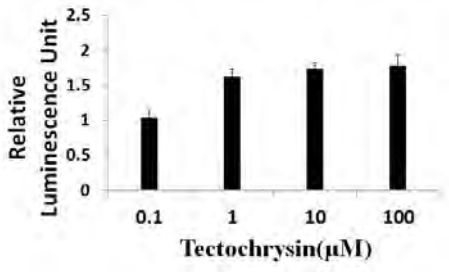


Fig. 2. Result of tectochrysin.

NATURAL ACTIVE INGREDIENT OF EDIBLE BIRD'S NEST (EBN) ON SKINCARE FUNCTIONS

Gallant K. L. Chan, Zack C. F. Wong, J. J. Sun, Elizaveta Gridneva, Karl W. K. Tsim

Division of Life Science and Center for Chinese Medicine, The Hong Kong University of Science and Technology, Clear Water Bay, Hong Kong; HKUST Shenzhen Research Institute, Hi-Tech Park, Shenzhen 518000, P. R. China, e-mail: gallant@ust.hk

Edible bird's nest (EBN; Yan Wo) is an ancient Chinese delicacy, made of the salivary secretion of specific swiftlets (such as *Aerodramus fuciphagus)*, which has been consumed for several hundred years. Until now, EBN is still a popular luxurious food supplement for women in oriental regions. According to the traditional Chinese medicinal descriptions, EBN can promote the "Qi", which is corresponding to the lung/respiratory functions; and hence which improves the healthiness of skin. However, the underlying mechanism of this medicinal theory is still largely unknown. Here, we demonstrated the potential bioactive ingredients of EBN have responsible for the skincare functions such as skin whitening and anti-aging.

Tyrosinase inhibition assay was applied to determine the skin whitening function of different EBN. White and Red EBN showed obvious inhibition effect on tyrosinase activity, while the inhibition effect of Grass EBN is not significant. No inhibition effects on tyrosinase activity for all adulterants. From our previous study, different amounts of free N-acetyl neuraminic acid (NANA) were found in different types of EBN. Thus, the skin-whitening assay was applied using NANA. Resulted showed that NANA was able to inhibit tyrosinase activity in a dose-dependent manner and performed a mixed type of inhibition. On the other hand, total anti-oxidation capacity of the EBN was examined by Cu^{2+} reduction quantified by Trolox standards. The protein of EBN was found to be responsible for the anti-oxidation function, which eventually led to anti-aging function.

A collaboration project between the university and cosmetics company was then launched for the optimization of EBN extract on skin whitening function. During the optimization, the contents of NANA and protein were monitored at different stages of production. Extraction time, temperature, ratio of water and other biochemical parameters were adjusted to maximize the contents of NANA and protein extract. After optimization, the increased content of NANA and protein were 4.9 and 29 folds respectively, as comparing to the original EBN extract. In parallel, the skin whitening effect was increased by 12 % after optimization. While the anti-oxidation capacity of the optimized EBN extract was increased by 5 folds of the original EBN extract. Seemingly, NANA is the precious natural active ingredient present in EBN which account for its renowned skincare functions.

Acknowledgment. This research was supported by RGC (661110, 662911, 660411, 663012, 662713), ITC (UIM/254, UIM/302), TUYF Charitable Trust (TUYF12SC02, TUYF12SC03, TUYF15SC01) and The Hong Kong Jockey Club Charities Trust and Foundation of The Awareness of Nature (TAON12SC01).

INDUSTRIAL PRODUCTION OF NATURAL DRUGS: ACTUAL PROBLEMS AND PROSPECTS OF DEVELOPMENT

I. N. Zilfikarov[1,2], M. A Marchenko[2], S. A. Postelnikov[2]

1) All-Russian Science Research Institute of Medicinal and Aromatic Plants (FGBSI VILAR), 117216, Moscow, Grina str., 7, building 1, e-mail: dagfarm@mail.ru
2) CJSC «VIFITEH», 142279 Russia, Moscow Region, Obolensk, SSC PMB, 84

Medicinal drugs from natural raw materials of plant, mineral and animal origin represent a wide range of the modern nomenclature of medicines. These include, first of all, drugs with proven safety and pharmacological activity, with a stable component composition, standardized according to the main quality indicators provided for the corresponding dosage form, as well as serially produced in the conditions of an industrial enterprise. The creation of conditions under which a pharmaceutical enterprise produces high-tech products, such as natural medicines that meet modern quality standards, and with minimal inter-series deviations, is an actual scientific and scientific-technological problem. The assortment of products of the Russian pharmaceutical company CJSC "VIFITEH" includes more than 80 names of ready-made medicines and about 100 substances, mostly of plant origin. In the course of many years of work on the creation of normative (ND) and technical documentation, the tasks of adapting and developing technological methods and methods of standardization in production conditions have been successfully accomplished: the harmonization of NDs with national and international standards, the improvement of analysis techniques, the revision of the quality standards of drugs, To medical use more than 20 years ago, etc.

Scientific researches carried out jointly with the FGBSI VILAR include the development and improvement of methods for standardization of medicinal plant raw materials (MPRM) and phytopreparations (PhP) of industrial importance; creation of new drugs from natural sources of biologically active substances (BAS).

The objects of the study are MPRM and PhP from ivy (*Hedera helix* L.), aloe (*Aloe arborescens* Mill.), immortelle (*Helichrysum arenarium* L.), eucalyptus (*Eucalyptus viminalis* Labill), pion (*Paeonia anomala* L.), passiflora (*Passiflora incarnata* L.), sage (*Salvia officinalis* L.), licorice (*Glycyrrhiza glabra* L.), ginkgo (*Ginkgo biloba* L.), serenoa (*Serenoa repens* J.K. Small), plantain (*Plantago ovata* L.), etc. The methods: physical and chemical research methods - spectrophotometry, refractometry, high-performance liquid chromatography (HPLC), gas-liquid chromatography (GLC), thin-layer chromatography (TLC), densitometry, gravimetry, titrimetry, etc., methods information-analytical, statistical method, etc. Numerous studies have resulted in unified approaches to the analysis of MPRM samples and corresponding PhPs, which correspond to the so-called "through" standardization and the relationship "chemical composition - biological activity." New methods for the qualitative and quantitative determination of BAS have been developed or revised, relevant NDs have been revised to normalize the quality of feedstock, intermediates and finished medicines. The results allows to improve approaches to standardization MPRM, taking into account the purpose, methods of reprocessing, the composition of the target products, taking into account the pharmacological activity. Other results of such approaches are the reduction of risks, the improvement of the quality and safety of manufactured products, and the stable serial production of finished products.

IMPLICATIONS OF PHARNESYLTRANSFERASE AND ITS INHIBITORS AS A PROMISING STRATEGY FOR CANCER THERAPY

S. G. Klochkov

Institute of Physiologically Active Compounds of Russian Academy of Sciences,
142432, Russia, Moscow region, Chernogolovka, IPAC RAS, e-mail: klochkov@ipac.ac.ru

The Ras superfamily consists more than 100 proteins, involved in the regulation of proliferation, differentiation, cell adhesion and apoptosis of cells. Each mammalian cell contains at least three associated genes, H-ras, K-ras and N-ras. Some of these proteins are small G proteins that deliver signals from cell-surface receptors, such as growth factor receptors, and then transmit the signals to several different pathways, ultimately affecting mitogenic functions such as DNA synthesis, cytoskeletal organization and lipid metabolism.

The incidence of mutated Ras gene isoforms in human tumors is about 30%. For example, the K-ras gene is mutated in pancreatic cancer (90%), colorectal cancer (44%). Farnesylation is a type of lipid modification called protein prenylation that is critical for biological functionality, including membrane association of Ras proteins. Farnesyltransferase (FTase) is a cytoplasmic protein that catalyzes this process which involves the transfer of a 15-carbon farnesyl group to a cysteine amino acid in the carboxyl end of Ras proteins.

Known farnesyltransferase inhibitors (FTIs) are classified based on the mechanism by which they inhibit a target enzyme: i) peptide analogues, designed to mimic and compete with the typical CAAX motif that characterizes FTase peptide substrates; ii) farnesyl pyrophosphate (FPP) analogues, designed to compete with the FPP substrate; iii) bisubstrate analogues, that combine properties of both FPP and CAAX peptide substrates; and iv) nonpeptidomimetic inhibitors. FTIs that are being investigated in clinical trials include lonafarnib, tipifarnib, L778123, BMS-214662, and salirasib and up to date FTIs are promising basis for new antineoplasts development.

The one of probable mechanisms of sesquiterpene lactone action on tumor cells is the apoptosis induction through the inhibition of key enzyme farnesyltransferase. The most known lactone with farnesyltransferase inhibition activity is well known arglabin. We developed a series of natural and modified sesquiterpene lactones and tested them on cytotoxicity, apoptosis induction, ability to inhibit farnesyltransferase and other connected activities. Our experiments reveal several natural and modified lactones with high cytotoxic activities (nanomole level), apoptosis induction, farnesyltransferase inhibition. This data allows us to suggest that antineoplastic effects of the sesquiterpene lactones is wider than the Ras-inhibition and is connected also with inhibition of Ras/MAPK and PI3K signal transduction pathways. It was demonstrated the prospect of using sesquiterpene lactones for developing of effective antineoplasts on their basis.

INFLUENCE OF WATER REGIME ON CHANGES OF CHLOROPHYLL CONTENT IN COTTON LEAVES

N. N. Sanaev, Sh. Yunuskhanov, T. A. Bozorov

Institute of Genetics and Plant Experimental Biology, Academy of Sciences of Uzbekistan, Yukori-Yuz, Kibray Ds., Tashkent region, Uzbekistan

Water deficiency significantly affects on intensity of photosynthesis and alteration in metabolic processes in many agricultural crops, especially in cotton, that result in decreasing of crop production. In order to make a comparative study of water deficiency, we created water deficiency regimes such as 0-1-0 (only once during flowering), 0-2-1 (beginning of the flowering, boll formation and boll opening), 1-3-1 (flower formation, flowering, flower opening). In all cases chlorophyll content were determined by SPAD-502 counter and SF-16 spectrophotometer. SPAD-502 counts chlorophyll amount from 2x3 leaf surface. To determine content of chlorophyll a and b and compare results from SPAD-502 and SF-16, we counted chlorophyll content from 3th leaf from the top of plant by two equipments. Results showed that content of chlorophyll a were 3-fold more than b in 1-3-1 regime, whereas chlorophyll b was higher in 0-2-1 and 0-1-0 regimes that effect on increasing number of total chlorophylls.

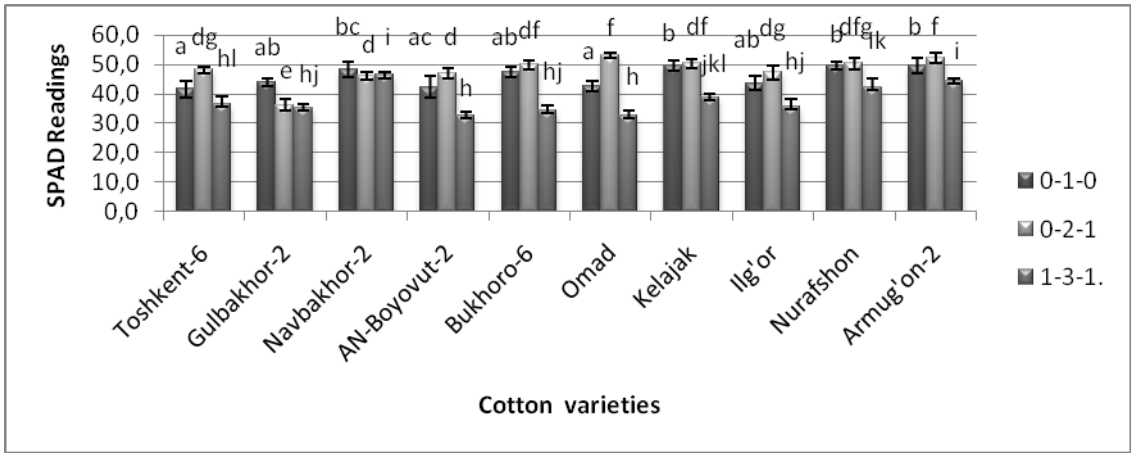


Fig. 1. Chlorophyll content determined by SPAD-502 in different water deficiency regimes. Letters indicate significant difference among the regimes following an ANOVA (Fisher'PLSD; P<0.05).

The results provided on Figure 1 indicated that total chlorophyll content was lower in 1-3-1 regimes, and varied in cotton varieties in 0-1-0 and 0-2-1 regimes. Variety of Gulbakhor-2 known as drought tolerant demonstrated higher accumulation of chlorophyll. Chlorophyll content was not change in all regimes for variety of Navbakhor-2. Varieties of Tashkent-6 and Omad showed higher chlorophyll accumulation in 0-2-1 regime.

Helianthus tuberosus L. THE COMPOSITION, PROPERTIES AND METHOD OF PROCESSING AND APPLICATION

D. A. Rahimov, S. A. Salikhov, B. B. Abduazimov

S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Uzbek Academy of Science, Tashkent

A great success has been achieved by Uzbek scientists in breeding plants of *Helianthus tuberosus L*. and in revealing its healing properties. The sorts of "Fayz baraka" and “Mujiza”, which were derived by Uzbek breeders, are added to the Register of sowing crops of Uzbekistan by the State Committee of the Republic of Uzbekistan.

In different organs of the plant the content of chemical substances is distributed unequally and carbohydrates the dominate of the quantitative presence in the tubers.

The researchers have examined the content and the composition of the alcohol-soluble sugars (ASS), water-soluble polysaccharides (WSPS) - inulin, fructooligosaccharides (FOS), pectin (PC) and hemicellulose (HMC) in stems, leaves and tubers of the above mentioned plant sorts.

We have also studied the quantitative presence of protein and amino acids in tubers of *Helianthus tuberosus L*. Protein has made up to 5.45% of the content of “Fayz Baraka” and up to 19.2% of “Mujiza’s”. Proteins contain the full specter of the essential amino acids that characterizes the quality of the usefulness of protein (nutritional, health, etc.).

The presence of water-soluble polysaccharides in the tubers of “Fayz Baraka” and “Mo’jiza” was spotted at 26.1-14.5% and at15.8-9.3% respectively.

The concentration of macro and micro-elements in the tubers of “Fayz Baraka” and “Mujiza” was determined using inductively coupled plasma mass spectrometry (ICP-MS), which is important for characterizing their nutritional value.

Results of the analysis on the content of microelements in the tubers showed a balanced microelement composition and existence of the majority of the necessary elements like Si, Fe, Mg, K, Zn, Cu, P, etc.

The widespread use of *Helianthus tuberosus L*. is defined by its unique chemical composition and the presence of biologically active substances, which makes it possible to use in medicine, food and agriculture industry.

The methods of processing of the tubers of *Helianthus tuberosus L*., extraction of inulin, fructooligosacharides and juice from *Helianthus tuberosus L*. were patented in the Republic of Uzbekistan.

Special attention is paid to the foundation of the industry of *Helianthus tuberosus L*. and to the prospect of inulin and FOS production in Uzbekistan.

CAROTENOIDS AND STEROLS OF SEVERAL FORMS OF *Sea buckthorn* L.

Sh. M. Mamedova, E. N. Novruzov

Institute of Botany of NANA, to Baku, Badamdar Highway, 40 AZ1073,
e-mail: eldar_novruzov@yahoo.co.uk

Continuing the study of *Hippophae rhamnoides* L. (sea buckthorn) growing in Azerbaijan, we have found that in the north - western Azerbaijan, in a valley Kishchay grow 10 sea buckthorn forms, which differ in shape, size, color, fruit, leaf size, habit and power of the bush, the number of spikes and other characteristics. Carotenoids and Sterols are the main active ingredients of sea buckthorn oil. We investigated the quantitative content and quality of the fruit of identified forms. It is found that the shapes differ both in content and qualitative composition. The content of carotenoids in fruits varies from 7.8 mg to 12.6% (by weight of crude fruit).

The qualitative composition of carotenoids established by TLC on "Silufol". The highest amount of carotenoids (10 components) found in the forms 3. The amount of carotenoids (3 forms) was separated by column chromatography on aluminum oxide. We identified 10 individual carotenoids, which are the results of chromatography, UV - spectra are set as α-, β-, γ- carotene, lycopene, polycis lycopene A, zeaxanthin, cryptoxanthin, fitoflolin taraxacin and lutein. It was found that α,β-carotene, cryptoxanthin, zeaxanthin are present in all studied forms of lycopene polycis lycopene A, found in the forms 2,5,8. In the qualitative composition and quantitative content of carotenoids are the most promising forms of 2,5,7,8.

In the hexane extract after saponification detected 3 substance of steroid nature. One of them individually isolated form and identified as β-sitosterol. The content of β-sitosterol in the fruits studied forms ranges from 0.57 to 0.78 % for all dry fruit. It was found that the different forms different of the composition of carotenoids. β-carotene, zeaxanthin, lutein and taraksantin present in the fruits of all studied forms.

COMPONENT COMPOSITION OF ESSENTIAL OIL OF *Artemisia issayevii* RZAZADE AND ITS ANTIMICROBIAL ACTIVITY

A. N. Aleskerova, S. V. Serkerov

Institute of Botany of ANAS, Baku, Badamdar highway 40, AZ 1073
e-mail: adelyaaleskerova @mail.ru

The genus *Artemisia* (*Artemisia* L.) is widely distributed in all geographical and ecological zones and includes more than 500 species on the globe. In the CIS the most common range of European, Caucasian and Central Asian species of wormwood . Wormwood , as evidenced by many researchers to be rich in essential oils , which can be used in folk and official medicine as antibacterial , anti-inflammatory, antiulcer , antiviral , antispasmodic , and other means. Essential oils of various species of the genus Artemisia L. is widely used as a disinfectant antiparasitic agent, wound healing, fungicidal as well as for flavoring food products , perfumery - cosmetic and medical industries.

For the first time was study the scope of the Artemisia species issayevii Rzazade circulated in the flora of Azerbaijan.

By chromatography- mass - spectrometry was studied component composition of essential oil of endemic species of *Artemisia issayevii* Rzazade growing in Azerbaijan. In the essential oil of *Artemisia issayevii* found 37 components (dominant in %: camphor - 37,21 and 1,8-cineole - 31.72)

We studied the antimicrobial activity of essential oils. The object of research was test - germs that cause diarrheal infections and inflammation. Was used the modern bacteriological and serological methods. The antibacterial effect of the essential oils studied by the disk and emulsion-contact methods. Were chosen most frequently encountered and multiresistant microorganisms such as gramm-positive *St.aureus* and yeast fungi of the genus *Candida* and gramm-negative *Klebsiella* and *Ps. aeruginosa*. The action of the essential oil in accordance with the etiology of various pathogens has been different. The greatest impact of essential oils on the pathogenic properties has been found in the etiology of respiratory *Klebseilla* strains. On the biological properties of the blue - green purulent sticks as the respiratory and intestinal etiology action of essential oils was equally high. Pathological properties characteristics of strains of Staphylococcus St. intestinal etiology after the action of essential oils greatly weakened.

The widest range of essential oils activity was against *S. aureus, Ps. aeruginosa, Klebsiella* and *Candida.*

INVESTIGATION OF COMPOSITION AND BIOLOGICAL ACTIVITY OF ESSENTIAL OILS FROM EAST ASIA PLANTS

Ye. M. Suleimen[1], Zh. B. Iskakova[1,2], N. K. Tursynova[1], R. V. Dudkin[3,4,5], P. G. Gorovoy[3], A. B. Myrzagaliyeva[6]

1) The Institute of Applied Chemistry, L.N. Gumilyov Eurasian National University, Kazakstan, Astana, Satpayev st, 2; e-mail: suleimen_em@enu.kz
2) Kazak University of Technology and Business
3) G. B. Elyakov Pacific Institute of Bioorganic Chemistry, Far East Branch, Russian Academy of Sciences
4) Botanical Garden-Institute, Far East Branch, Russian Academy of Sciences
5) Far East Federal University, Russian Federation
6) S. Amanzholov East Kazakstan State University

The component composition of the 54 species vascular plants of the families Cupressaceae, Umbelliferae, Labiatae, Compositae, collected in the territory of Kazakstan and the Russian Far East were investigated by GC/MS method.

Family Cupressace: *Juniperus sibirica* Burgsd., *Juniperus sabina* L.

Family Umbelliferae (= Apiaceae): *Sanicula chinensis* Bunge, *Aegopodium alpestre* Ledeb., *Spuriopimpinella calycina* (Maxim.) Kitag. (synonims *Pimpinella calycina* Maxim., *Pimpinella brachycarpa* Nakai), *Libanotis buchtormense* (Fisch. ex Hornem.) DC., *Libanotis seseloides* (Fisch. et Mey.) Turcz. (syn. *Seseli seseloides* (Turcz.) Hiroe), *Cnidium dahuricum* (Jacq.) Turcz. ex Fisch. et Mey., *Conioselinum chinense* (L.) Britt., Pogg.et Sterns (syn. *Conioselinum kamtschaticum* Rupr.*), Angelica anomala* Avé-Lall. (syn. *Angelica jaluana* Nakai), *Angelica cincta* N. Boissieu (syn. *Angelica amurensis* Schischk., *Angelica sachalinensis* Maxim.*), Angelica czernaevia* (Fisch. et C. A. Mey.) Kitag. (syn. *Angelica laevigata* Benth. et Hook)., *Angelica dahurica* (Fisch. ex Hoffm.) Benth. et Hook.fil. ex Franch. et Savat., *Angelica ursina* (Rupr.) Maxim., *Angelica viridiflora* (Turcz.) Benth. ex Maxim., *Coelopleurum gmelinii* (DC.) Ledeb. *(syn. Angelica gmelinii* (DC.) M. Pimen.), *Glehnia littoralis* Fr. Schmidt, *Peucedanum alsaticum* L., *Peucedanum deltoideum* Makino ex Yabe, *Peucedanum elegans* Kom., *Heracleum voroschilovii* Gorovoi.

Family Labiatae (= Lamiaceae): *Scutellaria regeliana* Nakai, *Nepeta manchuriensis* S. Moore, *Nepeta densiflora* Kar. et Kir., *Dracocephalum argunense* Fisch. ex Link, *Stachys chinensis* Bunge, *Thymus przewalskii* (Kom.) Nakai, *Salvia stepposa* Shost., *Phlomis maximowiczii* Regel, *Rabdosia excisa* (Maxim.) Hara (syn. *Plectranthus excisus* Maxim.).

Family Compositae (= Asteraceae): *Achillea micrantha* Willd., *Achillea nobilis* L., *Artemisia argyi* Lévl. et Vaniot, *Artemisia aurata* Kom., *Artemisia austriaca* Jacq., *Artemisia feddei* Lévl. et Vaniot, *Artemisia keiskeana* Miq., *Artemisia lagocephala* (Fisch. ex Bess.) DC., *Artemisia latifolia* Ledeb., *Artemisia littoricola* Kitam., *Artemisia manshurica* (Kom.) Kom., *Artemisia messerschmidtiana* Bess., *Artemisia selengensis* Turcz. ex Bess., *Artemisia stolonifera* (Maxim.) Kom., *Artemisia terrae-albae* Krasch., *Artemisia umbrosa* (Bess.) Turcz. ex DC., *Aster incisus* Fisch. (syn. *Kalimeris incisa* DC.), *Turczaninowia fastigiata* DC. (syn. *Aster fastigiatus* Fisch.*), Saussurea odontolepis* Sch. Bip. ex Herd., *Saussurea pulchella* Fisch. ex DC., *Saussurea splendida* Kom., *Senecio argunensi*s Turcz., *Chrysanthemum sichotense* (Tzvel.) Worosch. (syn. *Dendranthema sichotense* Tzvel.), *Achirophorus ciliates* (Thunb.) Sch. Bip. (syn. *Hypochoeris ciliata* (Thunb.) Makino), *Trommsdorffia ciliata* (Thunb.) Sojak.

Isolation of essential oils was carried out on the standard procedure on Clevenger apparatus by water distillation.

Obtained essential oils were studied for the cytotoxic activity on *Artemia salina* crustaceans and for antioxidant activity (DPPH).

COMPOSITION OF THE LIPID FRACTION OF *Saposhnikovia divaricata*

B. M. Urbagarova[1,2], V. V. Taraskin[1,2], L. D. Radnaeva[1,2]

1) Baikal Institute of Nature Management SB RAS, Sakhyanovoy 6 str., Ulan-Ude, Russia, 670000
2) Buryat State University, Smolina 24a str., Ulan-Ude, Russia, 670000

The medicinal plant *Saposhnikovia divaricata* (Turcz.) Schischk. [syn. *Ledebouriella divaricata* (Turcz.) Hiroe] (*Apiaceae*) inhabits Mongolia, China, Korea, eastern Siberia (Republic of Buryatia, Zabaikalsky Krai) and the Russian Far East (Sakhalin Oblast, Priamurye, Primorye) and has been used for several thousand years in traditional medicine of China, Japan, and Korea [1]. It possesses a broad spectrum of pharmacological activity including anticarcinogenic and neuroprotective [2–3].

Plants collected in the Republic of Buryatia, Zaibaikalsky Krai, and Mongolia in addition to pharmacy raw material acquired in Sinin (China) were studied. The lipid fraction was obtained via modified Bligh–Dyer extraction [4] followed by acidic methanolysis. The yield was 2.69–17.46% calculated for absolutely dry raw material (adr). The chemical composition of the lipid fraction was studied using an Agilent 7890 GC with a 7000 C triple quadrupole mass spectrometer as the detector.

The lipid fraction of the analyzed samples contained 22 FA, sterols, and polyyne-type compounds. Linoleic (25.32–48.49%), oleic (8.85–39.56%), and palmitic acids (3.90–52–50%) were the principal ones in all samples. The number of unsaturated FA was equal to that of saturated ones. However, the total amount of polyunsaturated (PUFA) and monounsaturated FA (MUFA) in many samples was greater than that of the saturated FA (SFA).

The lipid fraction from roots collected in Mongolia had characteristically high contents (9.84–35.50%) of panaxynol. The FA composition of the Chinese pharmacy material included 14 FA, sterols, and panaxynol, the content of which was 1.23% according to GC-MS data.

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THE STUDYING OF THE QUANTITATIVE CONTENT OF SAIKOSAPONINS IN THE *Bupleurum scorzonerifolium* ROOT OF BURYATIAN AND MONGOLIAN FLORA

Zh. A. Tykheev[1,2], E. P. Dylenova[1,2], V. V. Taraskin[1,2], L. D. Radnaeva[1,2]

1) Baikal Institute of Nature Management SB RAS, Sakhyanovoy 6 str., Ulan-Ude, Russia, 670000, e-mail: gagarin199313@gmail.ru
2) Buryat State University, Smolina 24a str., Ulan-Ude, Russia, 670000

Bupleurum scorzonerifolium Willd. is a perennial herbaceous herb which belongs to *Bupleurum* L. in *Umbelliferae*. Along with Bupleurum chinense DC it is a standard medicinal herb in the Pharmacopoeia of the PRC and it is called Chaihu [1]. Its dried root has been used for more than 2000 years to treat cold and fevers, influenza, inflammation, autoimmune diseases [2]. The unique officinal value of *Bupleurum scorzonerifolium* Willd. results from its complex chemical composition, among saikosaponins, and especially saikosaponin a (SSa) and d (SSd), are the most important and responsible for most of pharmacological properties. Thus, saikosaponin content is one of the most important criteria for determining the quality of *Bupleurum* L. [3].

Roots of *Bupleurum scorzonerifolium* (BS) for research were collected from healthy plants grown in Russia and Mongolia. Chaihu (BSC) was purchased from herbal market in Xining (PRC) and was investigated too (table 1).

Sample preparation for analysis was carried out by method described in the PRC pharmacopeia [1]. The quantitative saikosaponin determination was carried out by HPLC-UV on an Agilent 1200 system with diode array detector (table 1).

TABLE 1. **Herb Samples, Place and Year of Collection, SSa and SSd Content in % of Air-Dried Weight**

№	Place and year of collection	SSa, %	SSd, %
1	BS, Russia, Buryatia, Ivolginsk district, 2014	0.301	0.082
2	BS, Russia, Buryatia, Selenginsk district, 2015	0.395	0.039
3	BS, Mongolia, Khentii aimag, Bayaan Ulaan Uul mauntain neighborhood, 2015	0.410	0.450
4	BSC, PRC, Gansu province, Tanchany, 2014	0.140	0.198

Quantitative content of SSa and SSd in the *Bupleurum scorzonerifolium* roots Buryatian and Mongolian flora was studying for the first time. It was found that the highest content of SSa and SSd was observed in the Mongolian sample.

The total quantitative content of SSa and SSd should be greater than or equal to 0.3% according to the requirements of [1].

Thus, analyzed samples are satisfies to the requirements set by PRC pharmacopoeia in terms of the quantitative content.

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BIOLOGICALLY ACTIVE COMPOUNDS OF *Artemisia frigida* AND *Artemisia jacutica* OF BURYATIAN FLORA

E. P. Dylenova[1,2], S. V. Zhigzhitzhapova[1,2], T. E. Randalova[2], L. D. Radnaeva[1,2]

1) Baikal Institute of Nature Management SB RAS, Sakhyanovoy 6 str., 670000, Ulan-Ude, Russia, e-mail: edylenova@mail.ru
2) Buryat State University, Smolina 24a str., 670000, Ulan-Ude, Russia,

Currently, the chemical composition of *Artemisia* species plants has been actively researched because of the prospects of their use in medicine. The object of this study - *Artemisia frigida* Willd.- is a widely distributed species that has played a significant role in the history of steppe ecosystem vegetation. It is used in folk, Tibetan medicine. We studied the component analysis of terpene compounds of *Artemisia frigida* Willd. and *Artemisia jacutica* Drob. in previous works [1]. *A. jacutica* is an East Siberian endemic that has a limited range. The essential oil of *A. jacutica* contains chamazulene that induces anti-inflammatory, antibacterial and regenerative effects [2]. However, the lipid fraction of these two *Artemisia* species hasn't been studied before.

The objects of this research were the aerial parts of *Artemisia frigida* Willd. and *Artemisia jacutica* Drob. collected in Republic of Buryatia (Russia) in 2016 (flowering period). The lipid fraction was extracted using modified method of Blay-Dier with further acidic methanolysis [3]. Voucher specimens were deposited in the herbarium of Baikal Institute of Nature Management SB RAS. Gas chromatography-mass spectrometry (GC-MS) analysis was carried out to determine the composition of the lipid fraction, using Agilent 6890 Gas Chromatograph equipped with an HP 5973 quadrupole Mass Selective Detector. The lipid fraction was presented by 21 fatty acids, sterols, alkanes and alkenes. The dominant fatty acids in both samples were palmitic (13.37-17.23%), linoleic (13.72-27.56%) and linolenic (13.62-23.31%) acids. Unsaturated acids contained monoenoic, diene and triene acids, including ω3, ω6 fatty acids. The rations of the sum of unsaturated to saturated fatty acids were 44:34 in *Artemisia frigida* Willd. and 42:30 in *Artemisia jacutica* Drob. Fatty acids, especially unsaturated, play an important role in adaptation to low temperature for plants.

Thus, these two species of *Artemisia* are valuable sources of biologically active substances that can be used as efficient plant remedies.

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PHARMACOGNOSTIC ANALYSIS OF *Artemisiae subviscosae herba*

S. Z. Tsybicova[1], T. E. Randalova[1,2], S. V. Zhigzhitzhapova[1,2], L. D. Radnaeva[1,2]

1) Baikal Institute of Nature Management SB RAS, Sakhyanovoy 6 str., 670000, Ulan-Ude, Russia
2) Buryat State University, Smolina 24a str., 670000, Ulan-Ude, Russia

Artemisia subviscosa Turcz. ex Bess. is a subshrub. It grows in the steppes, sandy and rocky hills. *A. subviscosa* is endemic plant of the Baikal region [1]. An early group of scientists studied the composition of the essential oil of *A. subviscosa.* It contains a large amount of terpenoid compounds that not only stimulate the activity of the digestive system, but also has anti-inflammatory, antimicrobial, antiviral, irritating effects.

In this work we present the pharmacognostic analysis of *Artemisiae subviscosae herba* growing in Republic of Buryatia. Raw material was collected in Buryatia, in 2016 (Barguzin region - Ulyun, Yaricta) during budding phase.

The analysis revealed major morphological, anatomical and diagnostic features of *Artemisiae subviscosae herba*, numerical indicators such as humidity, total ash; acid insoluble ash, alcohol soluble extractives, water soluble extractives.

In this plant we found out the presence of flavonoids, saponins, coumarines, tannins, essential oils and fatty acids using standard identity tests.

The essential oil was obtained by hydrodistillation method from the aerial part using Clevenger-type apparatus for 3 hours [2]. The essential oil was analyzed by GC–MS with an Agilent Packard HP 6890N gas chromatograph coupled to an HP MSD 5973 quadrupole mass selective detector. The chemical constituents of the essential oil were identified by comparison of the GC–MS data with those held by the National Institute of Standards and Technology, and by comparisons of their MS and calculated linear retention indices (RI) with values reported in the literature [3].

Essential oils were green and bright yellow colour. Oil yield was 0.3% in terms of the air-dry feed from all aerial part of plant. The oil yield was 0,3% from stems and leaves, from flowers – 0,7%. The oils contained santolina triene (2.5-33%), caryophyllene (10.6%-15.5%), selina-5,11-diene (0.5%-3.0%), germacrene D (2-8%-2.0%), β-selinene (6.3%-9.3%), γ-muurolene (4.3%-7.7%), α-selinene (0.4%-10.0%), aciphyllene (2.5%-8.0%), spathulenol (1.2%-9.0%), caryophylene oxide (1.2%-9.7%) as the major constituents. The oil obtained from stems of *A. subviscosa* contains a large number of santolina triene (33%) and germacrene D (4.6%). The highest content of caryophyllene (15.4%), selina-5,11-diene (3.6%), β-selinene (9.3%), α-selinene (8.6%), aciphyllene (3.1%), caryophyllene oxide (9.7%) detected in leaves, spatulenol (3%) - in flowers.

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CHEMICAL CONSTITUENTS OF NEEDLES OF SIBERIAN PINE *Pinus sibirica*

G. A. Usmanova, E. Kh. Botirov

Surgut State University, Surgut, Russia, e-mail: uga1972@mail.ru

Siberian pine (*Pinus sibirica* Du Tour.) is an evergreen coniferous tree. Grows in the northeast European part of Russia. The drugs from the needles of pine forests possess antimicrobial, antiinflammatory, hemostatic, wound healing, expectorant, diuretic, demulcent, antiscorbutic properties. Pine essential oil is widely used in folk and official medicine as an antiseptic, disinfectant, antiinflammatory, analgesic, tonic.

We studied the components of the hexane and chloroform extracts of dried pine needles. Extraction of raw materials was carried out in Soxhlet apparatus. The crushed plant material was extracted with hexane; the raw material was dried and further extracted with chloroform. The obtained extract was distilled and purified by chromatography on a column of silica gel. Chemical composition of purified extracts was studied by gas-liquid chromatography and chromato-mass-spectrometry.

It is established that the main components of the hexane extract are 1-heptacosanol (6,86%), γ-amorphene (6,12%), γ-muurolene (4,83%), octadecane (3,88%), tetracosyl acetate (2,12%), heptacosane (1,97%), methyl heneicosanoate (1,91%), 1,2,3,4-tetrahydro-1,6-dimethyl-4-(1-methylethyl)naphthalene (1,72%), 1,1,2-trimethyl-3,5-bis(1-methylethyl)-cyclohexane (1,48%), hexadecanoic acid (1,43%), 4,4a,5,6,7,8-hexahydro-4,4a-dimethyl-6-(1-methyl-ethenyl)-2(3H)-naphthalenone (1,39%), β-elemene (1,36 %), 1-octacosanol (1,36%), cholesta-4,6-dien-3-ol (1,34%), 1,2,3,4,4a,5,8,9,12,12a-decahydro-1,4-methanobenzocyclodecene (1,31%), 1,1,7-trimethyl-4-methylundecane-1H-cyclopropa[e]azulene (1,29%), (*Z*) 6-pentadecen-1-ol (1,21%), 5-ethyl-3,4-dihydro-1(2H)-naphtalene (1,16%), 2,2,6-trimethyl-7,9-bis(methylene)-bicyclo[4.3.0]nonan-1-ol (1,10%), androsta-3,5-dien-7-on (1,14%), 2-methylpropyl-hexadecanoate (1,05%) and other minor components.

In the composition of the chloroform extract main components 4,14-retro-retinol (16,64%), ethyl hexadecanoate (11,11%), 6,10,14-trimethyl-2-pentadecanone (7,94%), 10-nonadecanol (6,98 %), ethyl dodecanoate (5,06%), (-)-spathulenol (3,24%), 3,7,11- trimethyl-1-dodecanol (2,21%), ethyl docosanate (1,42%), butyl tetradecyl phthalate (1,28%), ethyl tetradecanoate (1,26%), ethyl heptadecanoate (1,08%), (*Z*)-14-methyl-8-hexadecenal (1,08%), 1,2,3,4-tetrahydro-1,6-dimethyl-4-(1-methylethyl)-naphthalene (1,02%), ethyl octadecanoate (1,02%), ethyl 9-hexadecenoate (0,91%), *Z*-α-bisabolene epoxide (0,82%).

Thus, in the composition of the nonpolar components of the needles of Siberian pine discovered derivatives of diterpenes, sesquiterpenes, tetra- and decahydronaphthaline, steroids, carboxylic acids and their esters, higher alcohols, ketones, alkanes, alkenes and other natural compounds many of which possess significant biological activity.

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ESSENTIAL OIL COMPOSITION AND ANTIMICROBIAL ACTIVITIES OF SOME *Salvia* SPECIES FROM TURKEY

Gökalp İşcan[1], Betül Demirci[1,] Yavuz Bülent Köse[2]

1) Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, 26470, Eskişehir, Turkey, e-mail: giscan@anadolu.edu.tr; gokalpiscan@gmail.com
2) Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Botany, 26470, Eskişehir, Turkey

Salvia (sage) is the largest genus of the *Lamiaceae* family, with nearly 1000 species throughout the world. The genus is widely distributed in Asia, Africa, Europe and South America. With newly described species, 100 *Salvia* species (53 of them are endemic) have been recorded in Turkey. Several species of them are widely used in Anatolia as antiseptics, astringens and spasmolytic. Generally, the leaves of sage consumed as a hot drink in traditional medicine and they are known as “adaçayı”.

In the present study essential oil compositions of *Salvia palestina*, *S. microstegia*, *S. hypargeia*, *S. tomentosa*, *S. blepharochlaena*, *S. virgata*, *S. viridis*, *S. albimaculata*, *S. cryptantha*, *S. frigida* and *S. verticillata* L. subsp. *amasiaca* (Freyn et Bornm.) Bornm that are collected from southern regions of Turkey in the years of 2014 and 2015 were analysed by GC and GC-MS. Detected constituents were mainly germacrene-D, β-caryophyllene, camphor, sabinene, 1,8-cineol and linalool in tested oils.

Additionally antimicrobial properties of the oils were evaluated in consideration of the use as an antiseptic in folk medicine. The oils showed weak to moderate antimicrobial effects between the concentration ranges of 31,25 to 2000 µg/mL against pathogenic bacteria and *Candida* species.

AN ETHNOBOTANICAL REVIEW OF THE GILABURU (*Viburnum opulus* L.) PLANT

Ayhan Altintas

Department of Pharmacognosy, Faculty of Pharmacy, Anadolu University, Eskişehir, Turkey
Yunus Emre Vocational School of Health Services, Anadolu University, Eskişehir, Turkey,
e-mail: anadolu1971@gmail.com

Viburnum opulus L. is a plant belonging to the family Caprifoliaceae. In Turkey, it is mostly grown in the mountainous and marshy parts of Central Anatolia and the Black Sea. Especially in Kayseri and surrounding area its use is widespread. Also in this region it is known as Gilaburu. Gilaburu plant is used as a laxative, antispasmodic, anti-inflammatory, antiallergic, sedative and diuretic in the world.

Due to the particularly effective compound of Gilaburu fruits is said to be an important dietary fruit. Active substances are colorants, tannin and organic acids. It is used for the treatment of kidney stones, bile and liver diseases and stomach pain. Fruit juice is anticancer and antioxidant because of its acids. Due to its antioxidant properties, it has been proven to have anti-aging, anti-mutation, anti-cancer and cholesterol-lowering properties. This plant is also very rich in vitamin C. *Viburnum opulus* L. is among the phytotherapy plants with its natural, easy to use and therapeutic properties.

The study will comprise a review of previously conducted ethnobotanical, chemical, pharmacological studies.

NEW APPROACHES ON THE EXTRACTION, SEPARATION AND ANALYSIS OF LIPID CONTAINING PLANT MATERIALS

Temel Özek

Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, 26470-Eskişehir, Turkey
Anadolu University, Medicinal Plant Drug and Scientific Research Center, 2 6470-Eskişehir, Turkey, e-mail: tozek@anadolu.edu.tr

Extraction involves the separation of medicinally active target compounds of the plant materials by using selective solvents in conventional extraction procedures. However, several extraction techniques can also be applied to medicinal and aromatic plants beside conventional extraction technique. Nowadays, the non-conventional new approaches are more popular since the conventional extraction techniques require more solvent and time to complete overall recovery of the target compounds or compound groups.

The non-conventional techniques generally accepted as more environmental friendly (green technique) due to decreased use of hazardous chemicals, reduced operational time together with better yield and quality of extract.

The qualitative and quantitative studies of target compounds from plant materials generally depend on the selection of proper extraction technique. The selected extraction technique plays a significant and crucial role on the final products. On the other hand, development of modern chromatographic and spectrometric analysis techniques make it easier than before but the successful results exactly depend on the selected extraction technique.

In this context, supercritical CO_2 extraction and fractionation technique and new analysis technique which are called ultra-performance convergence chromatography (UPC^2) using convergence of GC, LC and SFC techniques for separation of compounds in the mixture will be compared with other techniques for target compound separation from lipid containing plant materials. UPC^2 is a holistically design chromatographic system that utilizes liquid CO_2 as a mobile phase to leverage the chromatographic principles and selectivity of normal phase chromatography while providing the easy-of-use of reversed phase LC. Convergence chromatography provides orthogonal and increased separation power compared to LC or GC, to solve separation challenges. This technique provides fast separation and analysis of fat soluble vitamins, triglycerides, fatty acids and so on.

ASSESSMENT OF THREE *Achillea* SPECIES FOR ANTIOXIDANT, ANTIDIABETIC AND ANTICHOLINESTERASE ACTIVITIES

Gülmira Özek

Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy,
26470, Eskişehir, e-mail: gozek@anadolu.edu.tr

In scope of the present work, the potential of three *Achillea* species (Asteraceae) against oxidative damage, neurodegenerative and carbohydrate digestion diseases was investigated.

The essential oils of *Achillea teretifolia* Willd., *A. grandifolia* Friv. and *A. falcata* L. were evaluated for free radical scavenging activity against $DPPH^{\bullet}$ and $ABTS^{\bullet+}$ radicals. The inhibitory potential of the oils against acetylcholinesterase (AChE, from electric eel) was measured with Ellman's method. Antidiabetic effect of the oils was measured *via* inhibiton of α-amylase from porcine pancreas (Type VI-B) using microtiter plate assay based on iodine/potassium method.

Trolox equivalent antioxidant capacity (TEAC) values for *A. teretifolia*, *A. grandifolia* and *A. falcata* oils were determined as 0.52±0.02, 0.62±0.04, 0.25±0.02 mM, respectively. The oil of *A. teretifolia* demonstrated the highest (62.4%) scavenging potential against DPPH radicals, while the oil of *A. falca*ta had weak activity (31.2 %). Anti-AChE activities of the oils were expressed as inhibition percentage: %Inh 74.5±6.0, 67.5±2.3 and 81.4±4.0, respectively. The oil of *A. grandifolia* demonstrated the highest inhibitory potential (IC_{50} 0.20±0.01 mg/mL) against α-amylase.

ASSESSMENT OF *Carduus crispus* ESSENTIAL OILS FOR ANTIOXIDANT, ANTIDIABETIC, ANTIINFLAMMATORY AND ANTIMELANOGENESIS ACTIVITIES

Gulmira Ozek[1*], Sanduin Shatar[2], Altaa Altansetseg[2], S. Yur[3], Kemal Husnu Can Başer[4], Temel Özek[1,3]

1) Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, 26470, Eskisehir, Turkey
2) Institute of Chemistry and Chemical Technology of the Mongolian Academy of Science (MAS), 211051, Ulaanbaatar, Mongolia
3) Anadolu University, Medicinal Plant, Drug andScientific Research Center (AUBIBAM), 26470, Eskisehir, Turkey
4) Department of Pharmacognosy, Faculty of Pharmacy, Near East University, Lefkoşa (Nicosia) N. Cyprus, e-mail: gozek@anadolu.edu.tr

In scope of the present work, the flowers and seeds of *Carduus crispus* (*Asteraceae*) were hydrodistilled to get essential oils. The oils were chromatographically characterized with GC-FID and CG/MS techniques. The oils were found to be predominated with fatty acids. Hexadecanoic (23.3% and 36.5%), tetradecanoic (44.0% and 31.6%) and (*Z*)-9-hexadecenoic (5.1% and 4.8%) acids were found as the main constituents in the flower and seed oils, respectively. The oils were subjected to screening for different biological activities. Free radical scavenging activity of the oils was tested against $DPPH^{\bullet}$ radicals. Potential of the essential oils as inhibitors of lipid peroxidation was measured in linoleic acid/β-carotene system and *via* inhibition of lipoxidase from *Glycine max* (soybean) enzyme. Antidiabetic effect of the oils was investigated *via* inhibition of α-amylase enzyme using I_2/KI based assay. Inhibitory potential of the oils on the production of urea was investigated using xanthine/xanthine oxidase (from bovine milk) test system. Effect of the oils on melanogenesis process was measured *via* inhibition of tyrosinase (from mushroom) enzyme.

The flower and seed oils demonstrated weak free radical scavenging activities. Both of the oils demonstrated strong hypoglycemic effect (57.2% and 90.3%). The oils of *C. crispus* inhibited lipoxygenase with *% Inh.* 26.8 and 55.5. However, the oils found to be inactive against xanthine oxidase. The flower oil demonstrated weak antimelanogenesis activity (*% Inh.* 19.3). The present work is the first comprehensive evaluation of *C. crispus* oils biological potential.

COMPARATIVE STUDY OF FATTY ACIDS IN THE SEED OILS FROM "THREE GLYCYRRHIZA SPECIES" FROM XINJIANG

Qeyser Memtimin Tikin[1,2], Mahinur Bakri[2], Parhat Rozi[2], Aytursun Ablimit[2], Atavulla Tursun[1], Gulshan Abdusadir[1], H. A. Aisa[2*]

1) Hotan Teachers College, Department of Biology-Geography, Hotan, P. R. China
2) The Key Laboratory of Plant Resources and Chemistry in Arid Regions and Key Laboratory of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi, P. R. China

Glycyrrhiza belongs to the Leguminosae family, widely used as herbal folk medicine distributed mainly in Asia, Europe Australia and America..In China cultivated in north regions such as Xinjiang, Gansu, Inner Mongolia and Qinghai There is a good quality and quantity of *Glycyrrhiza* species in Xinjiang Becouse of the special climate.Traditionally,the roots and rhizomes of *Glycyrrhiza* are used in Chinese and Uyghur folk medicine for the treatment of heavy-palpitation,irregular pulse,sore ulcer, swollen sore throat, spleen stomach qi deficiency, peptic ulcer and asthenia.[1] .

Fatty acids are among the important quality markers and it is necessary to determine these qualitatively and quantitatively for the quality control and standardization of herbs. In this study, the composition of oil extracted from seeds of three *Glycyrrhiza* species collected from Xinjiang region of China was analysed by GC- -MS.Quantitative and qualitative difference have been found in the chemical composition of three analysed samples depending on the species.

300 g shade dried seeds were powdered before fatty acids were extracted with 1000 ml n-hexane for 2 h through soxhlet extraction. The solvent was recovered yielding a concentrated extract.Fatty acids were produced from free fatty acids present in seeds oil using BF_3-methanol as derivatizing reagent.The sample was analysed by GC- MS (Agilent Technologies, USA)

There were 20 fatty acids were detected and identified,difference of mainly unsaturated fatty acids in three *Glycyrrhiza* species showed in the table 1.

TABLE 1. **Analysis of the Fatty Acids in the Seed Oils from Three *Glycyrrhiza* Species**

Acid	*Glycyrrhiza glabra* L.	*Glycyrrhiza uralensis* Fish.	*Glycrrhiza inflate* Bat.
Octadecenoic acid	9.98	1.32	0.08
Linoleic acid	46.25	30.18	24.2
Linolenic acid	34.40	43.2	42.14
Eicosatrienoic acid	3.36	24.65	24.26

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CONSTITUENT OF CYTOTOXIC AND ANTIRADICAL ACTIVITY OF ESSENTIAL OIL *Peucedanum litorale*

Zh. B. Iskakova[1], Ye. M. Suleimen[1], R. V. Dudkin[2,3,4], P. G. Gorovoy[2]

1) The Institute of Applied Chemistry, L.N. Gumilyov Eurasian National University, Kazakstan, Astana, Satpayev st, 2, e-mail: zhanariskakova@mail.ru
2) G. B. Elyakov Pacific Institute of Bioorganic Chemistry, Far East Branch, Russian Academy of Sciences
3) Botanical Garden-Institute, Far East Branch, Russian Academy of Sciences
4) Far East Federal University, Russian Federation

Peucedanum litorale Vorosch. & Gorovoj (coastal kitagavia, hayrnik coastal) is a perennial plant of the family *Umbeliferae* (*Apiaceae*).

The aerial part and roots of *P. litorale* were collected at the end of September 2016 in Primorsky Krai, Khasansky district, in the vicinity of the village of Posvet, on the rocks near the sea shore.

Herein, the cytotoxicity, and antiradical activity of essential oil from *P. litorale* growing in the Far East are reported for the first time.

Essential oil was produced from ground air-dried aerial part by steam distillation in Clevenger apparatus for 2 hours using hexane as a trap [1].

Cytotoxic activity of essential oils was determined by the usual method [2] using three parallel tests with 20-40 larvae of *Artemia salina* in each test. The experimental results led to the conclusion that essential oil of *P. litorale* aerial part and roots exhibited at all tested concentrations (10, 5, 1 mg / ml) acute lethal toxicity, i.e., all larvae died (lethality, A, 96%).

Antiradical activity of essential oil was determined by the known colorimetry method for free radicals based on the reaction of DPPH with an antioxidant [3, 4]. The experimental results showed that essential oil from *P. litorale* exhibited weak antiradical activity as compared with butylhydroxyanisole.

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COMPOSITION AND BIOLOGICAL ACTIVITY OF ESSENTIAL OILS FROM KAZAKSTAN AND THE FAR EAST (RUSSIA) PLANTS

Ye. M. Suleimen[1,2], Zh. A. Ibatayev[3], Zh. B. Iskakova[1,4], R. V. Doudkin[5,6,7], P. G. Gorovoi[5], A. B. Myrzagaliyeva[8], T. N. Samarkhanov[8], B. Z. Medeubayeva[8], M. Yu. Ishmuratova[9]

1) The Institute of Applied Chemistry, L.N. Gumilyov Eurasian National University, Kazakstan
2) Nazarbayev University, School Science and Technology, Kazakstan
3) Seifullin Kazak AgroTechnical University
4) Kazak University of Technology and Business
5) G. B. Elyakov Pacific Institute of Bioorganic Chemistry, Far East Branch, Russian Academy of Sciences
6) Botanical Garden-Institute, Far East Branch, Russian Academy of Sciences
7) Far East Federal University, Russian Federation
8) S. Amanzholov East Kazakstan State University
9) E. A. Buketov Karaganda State University

The component composition of a number of plants: *Nepeta denciflora* Kar. & Kir., *Achyrophorus ciliatus* (Thunb.) Sch.Bip., *Aegopodium alpestre* Ledeb, *Angelica anomala* Ave Jall. (*A. jaluana* Nakai), *A. dahurica* Fisch. ex Hoffm. Benth. et Hook. Fil. ex Franch. et Savat, *A. viridiflora* (Turcz.) Benth. ex. maxim, *Artemisia argyi* Levl. et Vaniot, *A. latifolia* Ledeb, *Aster incisus* Fish (=Kalimeris incise DC), *Chrysanthemum sichotense* (Tzvel.) Worosch. (=Dendranthema sichotense Tzvel.), *Cnidium dahuricum* (Jacq.) Turcz, ex Fisch et Mey, *Conioselinum chinense* (L) Britt. Pogg. et Sterns, *Heteropappus* sp., *Hypochoeris ciliata* (Thunb.) Makino (=Achyrophorus ciliates Thunb. Sch. Bip. = Trommsdorffia ciliate Thunb. Soja`k), *Peucedanum cf. P. terebinthaceum* (Fisch ex Trev) Ledeb, *Phlomis maximowiczii* Regel, *Rabdosia excise* (Maxim.) Hara (=*Plectranthus excisus* Maxim), *Saussurea odontolepis* Sch. Bip. ex Herd, *S. splendida* kom., *Seseli seseloides* Turcz Hizoe, *Turczaninowia factigiata* DC (=*Aster fastigiatus* Fisch), *Thymus przewalskii* (Kom.) Nakai, *T. chankoanus* Klok., *Coelopleurum gmelinii* (DC.) Ledeb., collected in the territory of Kazakstan and the Far East (Russia) were investigated by GC/MS method for the first time.

Isolation of essential oils was carried out on the standard procedure on Clevenger apparatus by water distillation.

Obtained essential oils were studied for the cytotoxic activity on *Artemia salina* crustaceans and for antioxidant activity (DPPH).

QUANTITATIVE ANALYSIS OF THE PRESCRIPTION *Kursi wufarikun* ZIYABIT

Salamet Edirs[1,2,3], Ablajan Turak[1,2], Numonov Sodik[1,2], Xuelei Xin[1,2*], Haji Akber Aisa[1,2*]

1) Key Laboratory of Plants Resources and Chemistry of Arid Zone, Xinjiang Technical Institute of Physics and Chemistry, CAS, Urumqi, P. R. China
2) State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, CAS, Urumqi, P. R. China
3) University of Chinese Academy of Sciences, Beijing, P. R. China

The best extract conditions for the prescription *Kursi wufarikun* Ziyabit (KWZ) (root of *G. collinum* and aerial parts of *H. scabrum* were mix with the ratio of 7:3) were found to be ethanol concentration 50%, extraction temperature72°C, solid to solvent ratio 1:20 g/mL, and extraction time 3.0 h using response surface methodology (RSM). Concentrated extractive purified with a column of HPD300 macroreticular resin, and after washed with 3BV of distilled water, then first eluted with 2BV of 30% ethanol, after eluted with 3BV of 70% ethanol. Thereafter, combine the eluted parts of 30% ethanol and 70% ethanol, concentrated and dried under reduced pressure to a constant weight at 45°C.The purified prescription was dissolved in 50% methanol–H_2O and filtered through 0.22 μm nylon membrane microfilters. The chromatographic analysis was achieved using a Waters UPLC with a PDA detector, using an Acquity UPLC BEH Shield RP18 (2.1 × 100 mm, 1.7 μm) column at 35°C. Mobile phases comprised (A) 0.2% formic acid in water and (B) acetonitrile.

The quantitative analysis of the effective part showed that 12 main components has good regression within the test ranges and the total content of them was 11.18%.

TABLE 1. **Retention Time, Regression Equation, Contents and Linear Range of 12 Components**

No.	T_R, min	Component	Regression equation	R^2	Content, %	Linear range, mg/ML
1	2.4	Gallic acid	Y=6649.1X-625.98	0.9999	0.15	10.0–70.0
2	10.5	Catechin	Y=558.67X+3342.2	0.9999	3.63	20.0–1100.0
3	13.0	Chlorogenic acid	Y=4932.2X-11477	1.0000	0.48	57.5–287.0
4	16.8	Epicatechin	Y=708.8X+2911.6	0.9999	0.36	45.0–225.0
5	18.2	Corilagin	Y=3623.1X+1735.8	1.0000	1.97	130.0–650.0
6	40.9	Ellagic acid	Y=21560X-345092	0.9965	0.45	65.0–228.0
7	53.3	Hyperoside	Y=7500.7X+2857.1	1.0000	1.11	55.0–330.0
8	53.9	Rutin	Y=7143.9X+4530.4	0.9999	1.11	57.5–345.0
9	54.8	Isoquercitrin	Y=9655.1X-12230	1.0000	0.87	44.0–308.0
10	59.8	Avicularin	Y=12645X-11462	0.9995	0.22	30.0–150.0
11	63.9	Quercitrin	Y=16511X-20026	0.9998	0.31	30.0–150.0
12	80.9	Quercetin	Y=2568.9X-12928	0.9992	0.51	45.0–225.0

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РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

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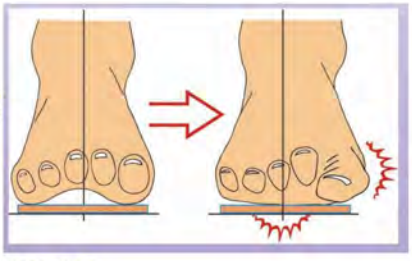

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E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: ЭКСТРАКТА - ИХРВ АН РУз
ГФ - ИП “NOBEL PHARMSANOAT” (РУз)

ЗВЕРОБОЯ ЭКСТРАКТ СУХОЙ

антидепрессантный препарат

Фитопрепарат, применяемый для лечения депрессивных состояний, при беспокойстве и страхе. Активным началом препарата является сумма гиперицинов из зверобоя продырявленного

Рекомендуется для лечения симтоматических и реактивных депрессий, состояниях беспокойства, нарушения сна.

В качестве дополнительного средства при эндогенных депрессиях (особенно в климактерическом периоде), а также при заболеваниях легких, желудка, кишечника, желчного пузыря.

Препарат улучшает настроение, повышает психическую и физическую работоспособность, нормализует сон

Форма выпуска: Капсулы 0,9 мг в блистере №10
Ts 03535440022:2016

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e-mail: plant_inst@icps.org.uz , www.uzicps.uz

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ИП "NOBEL PHARMSANOAT" (РУз)

Сухой экстракт

Tribulus terrestris

Препарат общетонизирующего действия и стимулирующий половую функцию

Сухой экстракт *Tribulus terrestris* – фитопрепарат, проявляющий общеукрепляющее действие и стимулирующий половую функцию.Активными компонентами препарата являются стероидные сапонины фуростанолового типа.

Сухой экстракт Tribulus terrestris используется как средство общетонизирующего действия (для повышения резистентности организма к физическим и психическим нагрузкам, для повышения работоспособности в период интенсивных занятий спортом и увеличения мышечной массы у спортсменов).

Препарат обладает способностью: **у мужчин** - стимулировать выработку тестостерона, увеличивать время эрекции и половое влечение, подвижность сперматозоидов и их количество;**у женщин** - стимулировать выработку эстрогенов, увеличивать либидо, оказывать положительный терапевтический эффект на эндокринную систему и возможные проявления климакса, а также улучшать состояние кожи (за счет повышения синтеза эстрогенов).

Форма выпуска: Таблетки покр. оболочкой по 112,5 мг №30
Ts 03535440023:2016

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Факс: (+99871) 262 73 48;
Тел.: (+99871) 262 59 13, 262 05 48
E-mail: Plant-inst@rambler.ru
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РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ДХО "NIKA PHARM" (РУз)

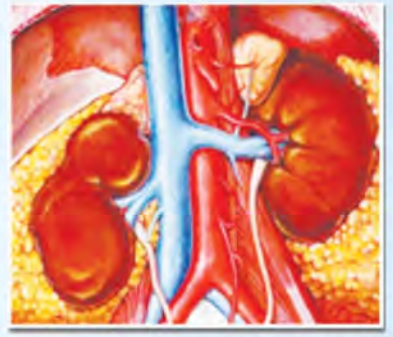
ЦИНАРОЗИД

ГИПОАЗОТЕМИЧЕСКИЙ ФИТОПРЕПАРАТ

Действующее вещество:
лютеолин–7–О–β–D–глюкопиранозид

Ferula varia

Показания к применению:



Хронический гломерулонефрит и хронический пиелонефрит, осложненные хронической почечной недостаточностью с гипертензией;

Вазоренальная гипертензия, осложненная нефросклерозом и хронической почечной недостаточностью;

Общий атеросклероз с поражением сосудов почек с явлениями хронической почечной недостаточности;

Хронические заболевания, приводящие к повышенному катаболизму белка с явлениями гиперазотемии (экстраренальные формы гиперазотемии).

Преимущества:

Цинарозид по своему специфическому гипоазотемическому действию превосходит леспенефрил (UCB, Бельгия). Леспенефрил обладает существенным недостатком – его лекарственная форма в виде спиртовой настойки. Цинарозид исключает этот недостаток, так как его лекарственной формой являются таблетки.

Форма выпуска: таблетки по 50 мг №50
Р. 00880/07/16

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Тел.: 998(71) 262 59 13, 262 05 48
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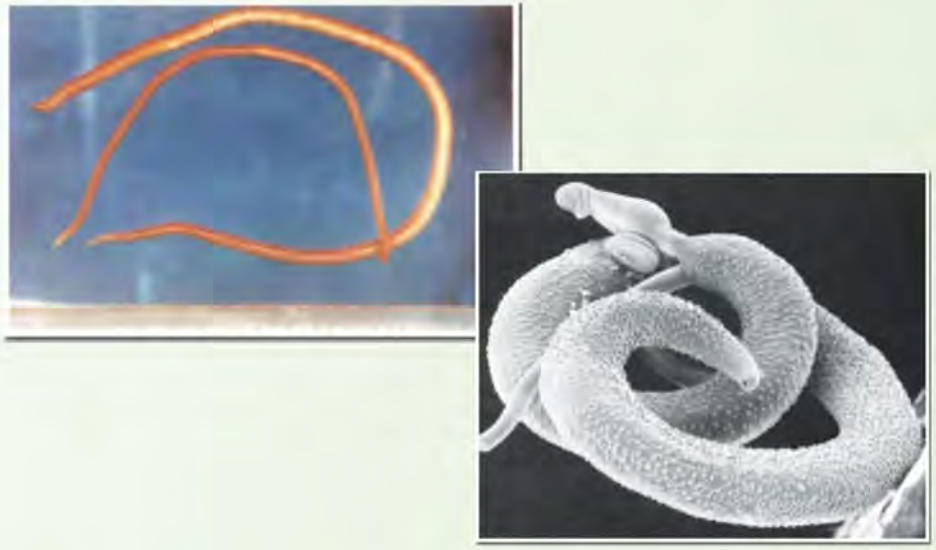
РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ЧНПП "RADIKS" (РУз)

ФЕНАСАЛ

ПРОТИВОГЕЛЬМИНТНОЕ СРЕДСТВО



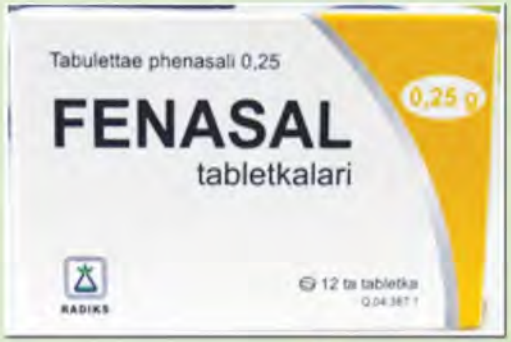
4-Нитро-2,5-дихлорсалициламид (никлозамид)
Идентичен импортному препарату йомезан.

ФАРМАКОЛОГИЧЕСКИЕ СВОЙСТВА:

Антигельминтное средство широкого спектра действия. Высокоэффективен при инвазиях бычьим цепнем, широким лентецом, карликовым цепнем. Фенасал угнетает окислительное фосфорилирование и вызывает паралич ленточных гельминтов, а также снижает их устойчивость к протеолитическим ферментам желудочно-кишечного тракта, что приводит к их разрушению.

ПОКАЗАНИЯ К ПРИМЕНЕНИЮ:

Фенасал является одним из наиболее эффективных лекарственных средств для лечения кишечных цестодозов. Применяют как противоглистное средство при тениаринхозе (заражении бычьим цепнем *Taeniathynchus saginatum*), тениозе (заражении *Taenia solium*), дифиллоботриозе (заражении широким лентецом *Diphyllobothrium latum*) и гименолепидозе (инвазии карликовым цепнем *Hymenolepsis nana*). По современным данным, Фенасал является одним из наилучших противоглистных средств при тениаринхозе.



ФОРМА ВЫПУСКА:

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Факс: (+99871) 262 73 48;
Тел.: (+99871) 262 59 13, 262 05 48

E-mail: Plant-inst@rambler.ru
www.uzicps.uz

COMPONENTS OF *Crambe orientalis* FLOWERS

I. I. Okhunov, U. T. Karimov, S. F. Aripova, O. Abdilalimov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: salima_aripova@mail.ru

In the sum of alkaloids from *Crambe orientalis* L. (*Cruciferae*) flowers the goitrine and a new alkaloid named krambefine were found. On the basis of spectral data the structure of krambefine was established as 1,3-oxazolidin-2,4-dicarboxylic acid dimethyl ether.

TABLE. 1. **GC-MS Analysis of *C. orientalis* Flowers**

№	Compound	Retention time, min	Area, %		
			Fraction A	Fraction B	Fraction C
1	1,3-Dimethylsulfide	4.491	2.13	0.75	–
2	1,3-oxazolidin-2,4-dicarboxylic acid methylesther	6.218			39.18
3	Pyrrolidin-2-on	7.11	2.23	9.98	–
4	5(R)-Methylpyrrolidin-2-on	7.811	6.90	4.93	–
5	Pyperidin-2-on	9.975	–	3.21	
6	Nicotine	13.935	–	–	0.41
7	2,6-Dimethoxiphenol	14.199	3.56	0.63	–
8	Phenylacetic acid amide	16.044	–	3.80	–
9	2-Penthylpyperidine	16.997	8.74	–	–
10	Goitrine (5-vinyl-oxazolidin-2-thion)	24.793	–	–	45.76

The ethanolic extract of *C. orientalis* flowers was diluted by water, acidified with 10% H_2SO_4 to pH 4–5 and treated with extraction benzene (fraction A) and chloroform (fraction B). Acid solution was basified by 25% ammonia solution to pH 10-11, and the sum of alkaloids was isolated into chloroform (fraction C).

Fraction A, B and C were analyzed by GC-MS (see Table).

ADAPTOGENIC SUBSTANCES PHYTOECDYSTEROIDS AND FLAVONOIDS AS THE COMPOUNDS WITH NEPHROPROTECTIVE ACTIVITY

F. R. Egamova, S. M. Yusupova, V. N. Syrov

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: zainab@icps.org.uz

One the most important medicinal problem is the prevention and treatment of kidney disease. Despite of considerable of problem and severity of the prognosis of nephropathy, the range of used domestic nephroprotective medicines is too limited. In this regard, we have evaluated the possibility to use a number of substances of plant origin extracted from local flora.

We have studied ecdysteroids: ecdysteron, turkesteron, ciasteron, 22-acetylciasteron isolated from *Ajuga turkestanica*, as well as flavonoids: cynarozide, lemanin, galangin isolated from *Ferula varia*, *Ammothamnus lehmannii* and *Glycyrrhiza glabra*, respectively. All of these compounds are of special interest because they have the ability to improve the overall non-specific resistance of the organism to many unfavorable factors and at the same time have a certain characteristic only for their specific effect (phytoecdysteroids activate protein synthesis in the organism, flavonoids exhibit tonisation of capillars, antioxidative and anti-inflammatory effects). In tests on rats the renal pathology was induced by subcutaneous administration of nephrotoxic mixture consisting of equal volumes of 0.1% uranil acetate solution and glycerol in a dose of 1 mL/100 g body weight. It was shown that the tested compound (phytoecdysteroids at a dose of 5 mg/kg, flavonoids 50 mg/kg per os) largely prevent increase of end-products of nitrogen metabolism in serum. Under their influence a significant reduction of urea, residual nitrogen and serum creatinine was observed during the whole experiment. It should be note that hyponitrogenic effect of cynarozide was the most pronounced and exceeded the appropriate action of imported drug Lespenephril introduced in a similar manner at a dose of 2.0 mL/kg. Cynarozide decreased the severity of a pathological process in the kidneys, called much earlier restoration in glomerular filtration, recovery of tubular re-absorption, disappearance of proteinuria, normalization of diuresis and daily excretion of the main electrolytes, urea and creatinine, and urinary residue.

Thus, the natural compounds such as phytoecdysteroids and flavonoids have the ability to increase the overall adaptive capacity of the organism, and can also be successfully used at relatively selective destruction of individual organs and systems. Cynarozide currently approved for clinical use in the broad practice of nephrology.

CHEMICAL COMPONENTS OF *Physochlaina alaica* ROOTS

I. I. Ohunov, U.T. Karimov, S. F. Aripova

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: salima_aripova@mail.ru

Low molecular weight metabolites (alkaloids) of the cultivated in Uzbekistan *Physochlaina alaica* E.Korot. kinds (*Solanaceae*) were investigated for the first time. From the alcoholic extract of the roots of *P. alaica* 0.78% sum of alkaloids was obtained, and the five known alkaloids and one new alkaloid 1 have been isolated (Table). The known alkaloids were identified by comparison with authentic samples of the hyoscyamine, hyoscine, 6-oxyhyosciamine, apohyoscine, tropine.

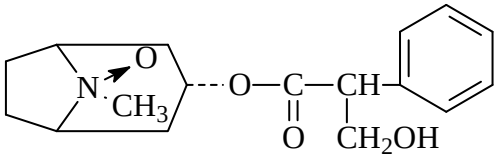
The structure of new alkaloid 1 was elucidated by spectral data (^{1}H NMR and IR) and chemical transformation. Alkaloid 1 was reduced with Zn + HCl.

TABLE 1. **Alkaloids of *Physochlaina alaica***

№	Alkaloid	Formula	mp,° C	$[\alpha]_D$, grad.
1	Hyoscyamine	$C_{17}H_{23}NO_3$	109–110	-22 (EtOH)
2	Hyoscine	$C_{17}H_{21}NO_4$	Oil	-25,6 ($CHCl_3$)
3	6-Oxyhyosciamine	$C_{17}H_{23}NO_4$	61–62	-13,5(MeOH)
4	Apohyoscine	$C_{17}H_{19}NO_3$	79–80	
5	Tropine	$C_8H_{15}NO$	63	

IR spectrum **1**: 710, 755 cm^{-1} (monosubstituted benzene ring); 3375–3410 cm^{-1} (OH); 1730, 1670 cm^{-1} (-O-C=O).

NMR spectrum 1 (δ): 7.203–7.302 (5H, m, Ar); 2.658 (3H, s, N-CH_3).



It was proved by the reduction of **1** with Zn + HCl that alkaloid **1** is *N*-oxide of hyoscyamine.

ISOLATION OF PERSIKANIDIN A FROM THE *Buxus sempervirens*

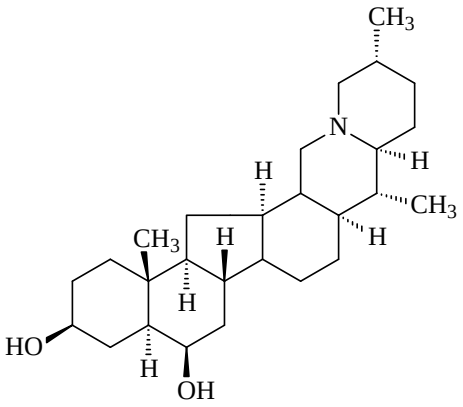
M.A. Eshonov, R. Shakirov

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: mubashshir@inbox.ru

The chloroform fraction (20 g) of total alkaloids of the plant *Buxus sempervirens* [1–3] was eluted by a silica gel column and 80 fractions collected.

From fractions 30–60 after treatment by methanol-acetone (1:1) the base mp 234–239°C (60 mg) was isolated. This base is soluble in chloroform and methanol, worse in acetone. The structure of this alkaloid has been established by X-ray diffraction analysis (XRD). The base was identified as alkaloid persikanidin A, which was isolated before from *Fritillaria persica* [4].

It was isolated from the plant of *Buxus sempervirens* for the first time.



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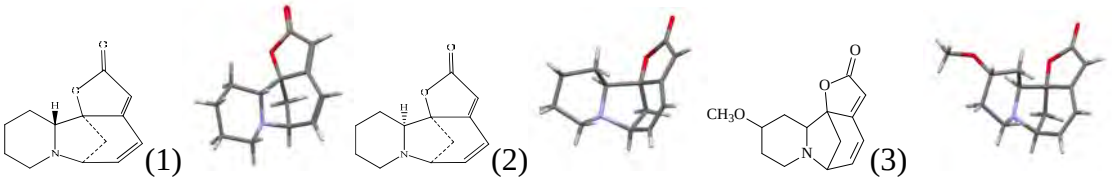
ALKALOIDS OF *Securinega suffruticosa* PALL

U. Kh. Kurbanov

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: utkir.88.88@inbox.ru

Securinega suffruticosa (Pall.) is a shrub first found at Manjuria and Mongolia, and now cultured in several countries. The plant has been used in folk medicine, especially to treat psychic diseases [1]. Securinine is predominated in the alkaloid content of the plant. Securinine used as a drug to treat neurological deceases [2, 3]. It also could be used to treat Alzheimer's diseases [4].

We start to investigate the alkaloid composition of *Securinega suffruticosa* which cultured in Tashkent Botanical garden. The roots, core and leaves of the plant were extracted separately by 80% aqueous ethanol. The sum of alkaloids in roots is 0.428%, leaves 0.27% and core 0.073% of dry plant weight, respectively. It was determined by TLC that the alkaloid amount in each part of the plant is differ, but composition is the same. The Al_2O_3 column separation with benzene-ethylacetate gave individual alkaloids securinine $C_{13}H_{15}NO_2$, mp 143–144°C (1), allosecurinine $C_{13}H_{15}NO_2$, mp 135–138°C (2), securitenine $C_{14}H_{17}NO_3$, mp 126–128°C (3). The structure of these alkaloids were confirmed by X-ray analysis.



(1) (2) (3)

REFERENCES

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LICOCTONINE ALKALOID FROM *Delphinium leptocarpum* NEVSKI

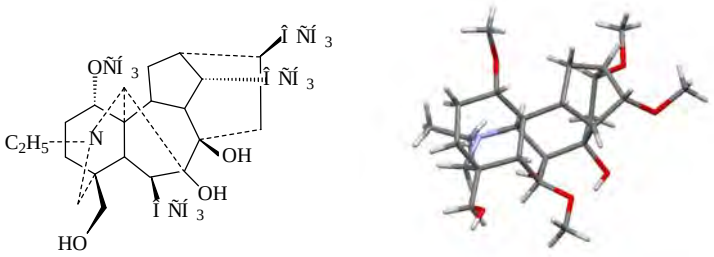
U. Kh. Kurbanov

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: utkir.88.88@inbox.ru

Diterpenoid alkaloids are well known due to their high physiologic activity and complex chemical structure. They consist of 20 carbon and one nitrogen atoms and have basic properties [1]. Diterpenoid alkaloids classification were studied in plant species *Aconitum, Consolida, Delphinium* (*Ranunculaceae* family), *Antragene* (*Antragenaceae*), *Garrya* (*Garryaceae*), and *Inula* (*Compositae*) [2].

This report presents the study of *Delphinium leptocarpum* collected from Boysun Mountains of Surkhandarya region in the flowering season. Aerial parts of the plant were air dried and extracted with two methods by 80% aqueous C_2H_5OH. The first method was extraction of 1.2 kg of dropped plant material material using percalator apparatus. The alkaloids sums were collected by chloroform (1.303 g, 0.11%) and buthanol (13.898 g, 1.156%). The second method was ultrasound extraction of 2 kg of the plant with chloroform (4.035 g, 0.201%) and butanol (26.482 g, 1.33%). The chloroform extraction contains weak (pH 8) and strong (pH 12) basic alkaloids. The weak base alkaloids sum was fractioned by SiO_2 column with chloroform : ethanol solvent system on 70 fractions. Delsoline was separated from 8–10th fractions. Its molecular formula is $C_{25}H_{41}NO_7$, mp 218–220°C. Licoctonine (12 mg) was preparatively separated from 61st fraction with molecular formula $C_{25}H_{41}NO_7$ and mp 120–124°C. The alkaloid crystallized from acetone.

Structure of the alkaloid were established by R-ray analysis.



REFERENCES

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ESSENTIAL OIL AND FATTY ACID COMPOSITIONS OF *Ruta graveolens* FRUITS

D. T. Asilbekova, Kh. M. Bobakulov, D. R. Siddikov, Kh. A. Rakhmatov, N. D. Abdullaev

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: daniya.asilbekova@mail.ru

To continue our study of the lipids and lipophylic compounds isolated from *Ruta graveolens* L. (*Rutaceae* family) [1] essential oil and fatty acids of fruits have been analyzed.

Dried fruits of *R. graveolens* introduced in Uzbekistan were collected during fruiting period and hydro-distilled for 3 h using a Clevenger apparatus to obtain essential oils. The obtained oil was dried over anhydrous sodium sulfate and analyzed by GC/MS techniques on Agilent 5975C inert MSD (USA) equipped with a HP-5 capillary column (30 м × 250 μm × 0.25 μm).

Twenty components accounting for 98.7% among twenty four essential oil constituents of *R. graveolens* were identified. Ketones (92.10%) were the major constituents. The predominant components in its essential oil were 2-undecanone (81.2%), 2-nonanone (6.6%), and 2-tridecanone (2.6%).

The lipids were extracted using Folch method with methanol–chloroform (2:1, v/v), concentrated in vacuum using rotary evaporator at 40°C. The results of TLC analysis have shown triacylglycerides dominating in the lipids composition.

The aliquot of lipids was saponified with 10% KOH in methanol, and fatty acids were partitioned similarly, acidified to pH 2 by diethyl ether, dried and converted to methyl esters using diazomethane. GC analysis of fatty acid methyl esters was performed on Agilent 6890 N GC system using FID and capillary column HP-5 phase. Chromatographic profile of the fatty acids from *R. graveolens* fruit lipids is presented in the table below.

TABLE 1. **Fatty Acid Composition of *Ruta graveolens* Fruits, % GLC**

Saturated acid		Unsaturated acid	
14:0	Trace	16:1ω7	Trace
16:0	5.6	18:2ω6	44.4
18:0	3.2	18:1ω9 + 18:3ω3	45.8
20:0	0.2	20:1ω9	0.8
Total	9.0	Total	91.0

The present work is the first detailed contribution into the chemistry of *R. graveolens* fruit essential oils and lipids.

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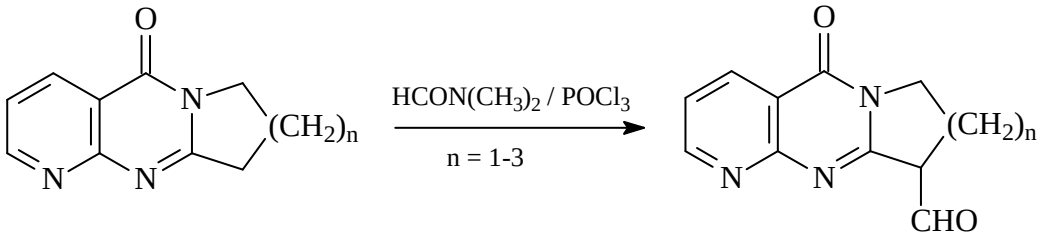
FORMYLATION OF 2,3-TRI(TETRA, PENTHA)METHYLENE-PYRIDO[2,3-d]PYRIMIDIN-4-ONES

Kh. U. Khodjaniyazov

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: hamidkhodjaniyazov@yandex.ru

In continuation of systematic investigation of the synthesis and chemical transformation of 2,3-polymethylenepyrido[2,3-d]pyrimidin-4-ones [1–4], the present work describes formation of aforementioned heterocyclic compounds.

9-Formyl-derivatives were obtained at the reaction of initial compounds with Vilsmeier reagent and subsequent treatment of formed intermediates [5].



Similar proceeding of the reactions to theino[2,3-d]pyrimidinones and quinazolones which are thiophene and benzene analogs of pyrido[2,3-d]pyrimidin-4-ones will be discussed.

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GALACTURONAN OF *Ferula kuhistanica*

M. Kh. Malikova, Kh. Kh. Akhmedova, Kh. A. Rakhmatov, R. K. Rakhmanberdyeva

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: xilola.akhmedova@gmail.com

To study the structure of the main carbohydrate chain of pectin polysaccharides a partial acid hydrolysis based on the stability of the glycoside bonds of different pectin substances (PS) to the hydrolytic action was used. This allows you to choose the conditions for partial depolymerization of pectin polysaccharides of carbohydrate chains.

We selected the conditions for galacturonan of PS isolation from leaves of *F. kuhistanica*. Organic and mineral acid at a temperature from 90 to 100°C were used. The results showed that the highest yield is observed when using trifluoroacetic acid. It should be noted that using of any acid provides the depolymerization that lead to formation of galacturonans PS (DPS) with the same monosaccharide composition - galacturonic acid (Table 1).

TABLE 1. **Yield and Physic-Chemical Characteristics of Galacturonans DPS (1-3)**

Conditions of partial hydrolysis	Yield, %	$[\alpha]_D$ (*c* 1.0; H_2O)	MM, Da
2 h, 140 mL 1N H_2SO_4, 90°C (DPS – 1)	41	+208	21000
2 h, 140 mL 1N H_2SO_4, 100°C (DPS – 2)	30	+192	18500
2 h, 140 mL 1N CF_3COOH, 100°C (DPS – 3)	49	+200	23500

Dedicated DPS have high positive specific rotation compared to the pectin polysaccharides (+165°). This is due to the fact that with no uronide material to some extent reduces the specific rotation of pectins, i. e. specific rotation in proportion quantity uronide material. IR spectra contains main characteristic absorption bands for PS, especially the triplet 910, 870, 815 cm^{-1} revealing the presence of α-1,4-glycosidic linkages between residues of *D*-galacturonic acid.

RELAXANT ACTIVITY OF THE DITERPENOID ALKALOID KARAKOLINE AND ITS DERIVATIVE 14-*O*-ACETYLKARAKOLINE

Yu. T. Mirzaeva[1], P. B. Usmanov[1], Z. Ch. Abraeva[2]

1) Acad. A. S. Sadykov Institute of the Bioorganic Chemistry, Academy of Sciences of the Republic Uzbekistan
2) Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan

Diterpenoid alkaloid karakoline isolated from the plant *Aconitum karakolicum R.* posses curare-like action and caused muscle relaxation similarly to nondepolarizing miorelaxant agents. Recently we found that 14-*O*-acetylkarakoline (14-*O*-AK), a derivative of karakoline, more potently than karakolne relaxed rat aorta, precontracted by different constrictors. To further characterize relaxant activity of 14-*O*-AK its effect on rat aorta contraction induced by high KCl was compared with that of karakoline. These studies were conducted on aortic rings preparation isolated from white rat (200–250 g) and mounted in a 5-mL tissue bath perfused with Krebs' physiological solution aerated with 95% O_2-5% CO_2. The contractile activity of aortic rings was recorded under isometric conditions using Grass FT03 force-displacement transducer and chart recorder (Endim 621.02).

In preliminary experiments karakoline and 14-*O*-AK in wide range of concentration had no effect on basal tone of aortic ring preparation. However, when aortic rings were previously precontracted with 50 mM KCl these alkaloids caused significant and a concentration-dependent relaxation. In these conditions the relaxant effect of 14-*O*-AK first occurred at 1 μM and maximal inhibition of KCl-induced contraction by 96.4 ±4.1 %, of control, attained at a 35 μM. In contrast to the 14-*O*-AK, the relaxant effect of karakoline was first observed only at concentration of 50 μM and maximal inhibition of KCl-induced contraction by 34.2 ± 4.1% obtained at a 200 μM. These results shows that 14-*O*-AK more markedly than karakoline inhibited KCl-induced contraction of rat aortic rings, indicating that 14-O-AK possess more pronounced relaxant activity. Considering, that aortic rings contraction, induced by high KCl is due mainly to the activation of L-type voltage-dependent Ca^{2+}-channels, it is reasonable to assume that the relaxant effect of 14-*O*-AK and karakoline could be attributed to inhibition of extracellular Ca^{2+} entry into smooth muscle cells. These results suggest that the relaxant effect of 14-*O*-AK and karakoline in the rat aorta precontracted with high KCl is mainly due to Ca^{2+} channel blockage and resulted reduction concentration of Ca^{2+} ions in smooth muscle cells. The more potent relaxant activity of 14-*O*-AK, apparently is due to the presence in his structure of acetyl group at carbon atom C14, instead of hydroxyl group of karakoline.

In conclusion, the present study provides experimental evidence for a key mechanism by which 14-*O*-AK and karakoline relaxes the rat aorta, which increases the understanding as to how karakoline and other related diterpenoid alkaloids can mediate relaxation in vitro. The findings of the present study strongly suggest that the differential relaxant activity of 14-*O*-AK and karakoline probably reflect intrinsic structural differences between these two alkaloids.

COMPOSITION OF *Camelus dromedarius* HUMP FAT

Sh. K. Khidoyatova, U. M. Azizov, N. T. Ul′chenko, S. D. Gusakova

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: s.gusakova2004@mail.ru

The composition of Egyptian humped camel *Camelus dromedarius* is well known [1]. We have investigated a composition of a hump fat of arauna elite Kazakhstan kind of *C. dromedarius* derived from the interbreeding of hybrid “Kurt” camels with a Turkmen argana kind.

The sample of a fresh fat was 8.1% humidity, mp 28.2–31.3°C, solidification temperature 28.5–32.4°C, index of refraction n_D^{40} 1.4473, acid number of 10.1 mg KOH, saponification number 199.3 mg KOH, unsaponified substances 3.5%.

Fatty acid composition of fat is determined by GLC on an Agilent Technologies 6890N chromatograph with a flame ionization detector, capillary column HP-5 (30 m × 0.32 mm, the stationary phase thickness 0.25 mm), carrier gas helium, temperature programming from 150°C to 270°C. Compositions of fatty acids are presented in the Table.

TABLE 1.. **Fatty Acid Composition of Hump Fat of *C. dromedarius***

Fatty acids														
12:0	14:1	14:0	15:0	16:1	16:0	17:1	17:0	18:2	18:1	18:0	20:1	20:0	$\sum_{saturated}$	$\sum_{unsaturaed}$
0.33	0.13	7.62	1.31	3.07	35.3	0.40	1.25	2.04	27.16	20.84	0.31	0.24	66.89	33.11

The obtained results shown, that the fatty acids are represented by 13 components with the prevalence of 16:0, 18:1 and 18:0.

In UV-spectrum (C_6H_6, λ_{max} nm) of the fat and ME fatty acids an intensive absorption maximum was observed at 222 ± 2 nm and a weak maximum at 265 ± 2, possibly due to the presence of oxoacids [2].

In compare to the Egyptian humped camel *C. dromedarius*, the hump fat of the Kazakhstan camel had higher n_D^{40}, more unsaponified substances, and higher degree of saturation. 20:0 *и* 20:1 acids were found in the composition of fatty acids for a first time.

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UTILIZATION OF PLANT RAW MATERIAL WITH BIOFUEL OBTAINING

Sh. U. Yuldashev, M. A. Mamatkhanova, G. B. Sotimov, I. B. Payziev

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: yyy.2014@mail.ru

Medicinal plants contain very low amounts of biologically active substances, mainly 0.1–5% [1]. That's why 85–90% of the initial plant raw material, such as ground stems, leaves or roots put into waste after processing of plants on pharmaceutical enterprises. Besides, the concomitants and impurities accumulate during an extract separation, sedimentation, and purification.

Plant lignocellulose biomass is attractive to depolymerization and microbiological bioconversion with obtaining a fuel and other valuable chemical products due to a big mass, low price and high carbohydrate content (60–70%) that is close to one of the cereals [2].

The batch manufacture of cytisine with an annual processing of tens tons of *Thermopsis alterniflora* is organized in the Institute of the Chemistry of Plant Substances. We have investigated the possibility to produce a liquid (bioethanol) and gaseous (biogas) biofuel from the plant wastes after cytisine isolation.

A preliminary treatment of the plant mass and identification of the obtained products was made as described in [3, 4]. Plastic containers of 5 L were used as a methane fermentation reactor. Volume of biogas was evaluated with graduated water gas-holder.

Fermented KPS manure was used as a source of the methane-producing bacteria. Preliminary evaluation has shown that the yield of ethanol and furfurol was 9.6 and 8.2% of the absolutely dry biomass of the cake, accordingly. Wastes remaining after ethanol production were subjected to the anaerobic methanol fermentation. At that, the biogas yield was 300 m^2, and biofertilizer - 100 kg converting to a ton of absolutely dry organic substances of the wastes.

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INVOLVEMENT OF NITRIC OXIDE IN NEGATIVE INOTROPIC EFFECT OF 4′,5-DIHYDROXY-3,6,7-TRIMETHOXYFLAVON IN RAT CARDIAC MUSCLE

S. S. Khushmatov[1], K. R. Baratov[1], O. Z. Toshmatov[2], K. A. Eshbakova[2]

1) Institute of the Bioorganic Chemistry, Academy of Sciences, 100125, Tashkent, Mirzo Ulugbek str., 83, Republic of Uzbekistan, e-mail: Khushmatov_Sh.S@bk.ru
2) Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan

The objective of the present work was to investigate the effects and underlying mechanisms of 4′,5-dihydroxy-3,6,7-trimethoxyflavon on the isolated papillary muscles.

Isometric tension forces were recorded using a force transducer (Type F30/Model D-79232; HSE, Germany). In the experiments, modified physiological Krebs–Henseleit solution containing (in mM): 118 NaCl; 4.7 KCl; 2.5 $CaCl_2$; 1.2 $MgSO_4$; 1.1 KH_2PO_4; 5.5 glucose and 25 $NaHCO_3$; pH 7.4 was used. This Krebs–Henseleit solution was continuously bubbled with 95% O_2 and 5% CO_2 and kept at a temperature of +36 ± 0.5°C by means of water heating system controlled by temperature controller U8 (Bulgaria).

In the experiments, the 4′,5-dihydroxy-3,6,7-trimethoxyflavon (4–10 μmol·L^{-1}) showed dose–dependent positive inotropic effects in rat papillary muscle contractility. In addition, the positive inotropic effect of 4′,5-dihydroxy-3,6,7-trimethoxyflavon was almost completely disappeared in the presence of inhibitor of potential–dependent $Ca^{2+}{}_L$–channel nifedipine (0.01 μmol·L^{-1}) and β-adrenoreceptor inhibitor (±)-propranolol hydrochloride (10 μmol·L^{-1}) under incubation conditions. And 4',5-dihydroxy-3,6,7-trimethoxyflavon (15–50 micromol/L) induced a concentration–dependent decrease of the contractile force of the rat papillary muscle ($p < 0.05$). Pre-treatment with L–NAME (100 micromol/L), an inhibitor of NO–synthase, attenuated the effect of 4,5-dihydroxy-3,6,7-trimethoxyflavon in the isolated rat papillary muscles ($p<0.05$).

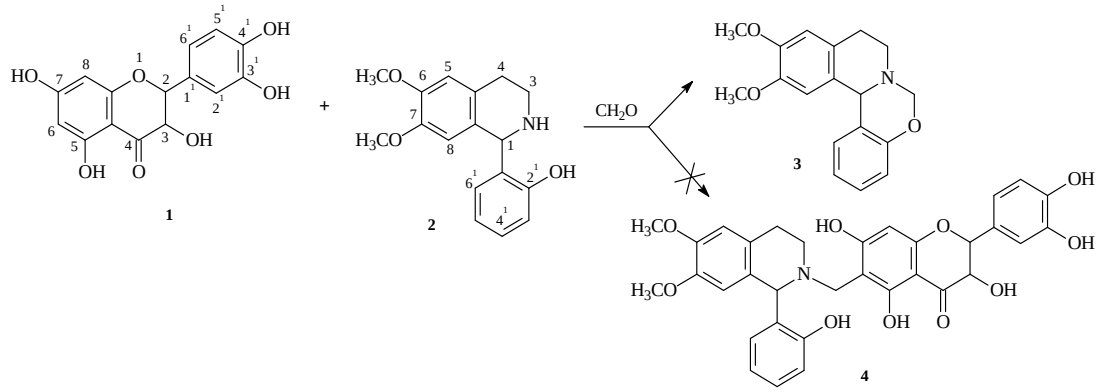
In conclusion, the present study demonstrates that 4',5-dihydroxy-3,6,7-trimethoxyflavon has showed a positive inotropic effect on rat papillary muscles that can be explained with the increase of $[cAMP]_{in}$ and may depend on increase of $[Ca^{2+}]_{in}$. And 4',5-dihydroxy-3,6,7-trimethoxyflavon (10–50 micromol/L) may induce a negative inotropic effect in rat cardiac muscles and this effect at least partly be mediated by NO/cGMP pathway.

THE FEATURES OF DIHYDROQUERCETIN INTERACTION TO 1-(2′-HYDROXYPHENYL)-6,7-DIMETHOXY-1,2,3,4-TETRAISOQUINOLINE

Sh. N. Zhurakulov, V. I. Vinogradova

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: j.sherzod.78@mail.ru

In order to create new biologically active substances we have synthesized a dihydroquercetin (DHQ) conjugates (**1**) with a number of 1-(aryl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolines [1]. We didn't observe the formation of dihydroquercetin DHQ and isoquinoline conjugates during interaction of DHQ to 1-(2′-hydroxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline. The reaction was made in isopropanol medium at 20–25°C in DHQ–isoquinoline–formalin ratio 1:1:1. Dihydroquercetin is not entered into reaction. The main product (86%) was lactam **3**.



1 **2** **3** **4**

The structure of the obtained substance was approved by IR, NMR ^{1}H and mass-spectra.

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CYCLIC ALCOHOL AND FLAVONE FROM *Alhagi canescens*

S. Z. Nishanbaev, Kh. M. Bobakulov, I. D. Sham′anov, N. D. Abdullaev

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: sabir78@rambler.ru

Two individual substances **1** and **2** were isolated by a column chromatography from the ethylacetate fraction of alcohol extract of *Alhagi canescens* (Regel) B. Keller & Shap. aerial part. The plant was collected in flowering time (July 2014) on Togay village outskirts, Uzbekistan district, Fergana region, Republic of Uzbekistan.

Substance 1. Whitish amorphous powder, $C_7H_{14}O_6$, mp 188–190°C, no UV absorbance, IR-spectrum (KBr, ν, cm^{-1}): absorbance bands of hydroxyl groups (3403–3317), aliphatic C–C bonds (2952–2834), and C–O bonds (1127–1104).

^{1}H NMR (400 MHz, $(CD_3)_2CO$–D_2O (2:1), δ, ppm, J/Hz): 3.93 (2H, m, H-3, 4), 3.74 (1H, dd, J = 9.8, 2.3, H-5), 3.70 (1H, dd, J = 9.7, 2.4, H-2), 3.60 (1H, t, J = 9.7, H-1), 3.54 (3H, s, OCH_3), 3.27 (1H, t, J = 9.8, H-6).

^{13}C NMR (100 MHz, $(CD_3)_2CO$–D_2O (2:1), δ, ppm): 83.80 (C-6), 73.17 (C-4), 72.59 (C-2), 72.27 (C-5), 71.57 (C-1), 70.94 (C-3), 60.44 (OCH_3).

Careful analysis of ^{1}H and ^{13}C NMR spectra, comparison of chemical shifts of protons and carbon atoms, and spin-spin coupling constant values allowed to identify the substance **1** as 6-methoxy-cyclohexan-1,2,3,4,5-pentaol (*D*-pinitol) [1].

Substance 2. Yellow amorphous powder, $C_{19}H_{18}O_8$, mp 187–188°C. UV (C_2H_5OH, λ_{max} nm): 258, 271, 353. IR (KBr, ν, cm^{-1}): 3349 (OH), 2940, 2835 (OCH_3), 1658 (C=O, γ-pyrone), 1603–1514 (aromatic C=C bonds), 1489, 1459, 1430, 1357, 1289, 1273, 1248, 1205, 1166, 1132, 1098, 1066, 1030.

^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.91 (1H, br.s, H-8), 6.97 (1H, d, J = 8.4, H-5′), 7.64 (1H, dd, J = 8.4, 2.1, H-6′), 7.68 (1H, d, J = 2.1, H-2′) 9.95 (1H, br.s, 4′-OH), 12.64 (1H, s, 5-OH), 3.74 (3H, s, 7-OCH_3), 3.82 (3H, s, 3′-OCH_3), 3.88 (3H, s, 6-OCH_3), 3.92 (3H, s, 3-OCH_3).

^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 178.19 (C-4), 158.62 (C-7), 155.74 (C-2), 151.71 (C-9), 151.64 (C-5), 149.90 (C-4′), 147.48 (C-3′), 137.72 (C-3), 131.58 (C-6), 122.31 (C-6′), 120.71 (C-1′), 115.63 (C-5′), 112.05 (C-2′), 105.55 (C-10), 91.41 (C-8), 60.03 (7-OCH_3), 59.67 (3′-OCH_3), 56.47 (3-OCH_3), 55.78 (6-OCH_3).

Substance **2** was identified as chrysosplenetin (3,6,7,3′-tetramethoxy-5,4′-dihydroxyflavone) basing on the spectral data and their comparison to literature [2].

These substances were isolated from aerial part of *Alhagi canescens* (Regel) B. Keller & Shap for the first time.

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MAJOR ALKALOIDS OF *Catharanthus roseus*

Sh. M. Adizov[1], A. A. Mamadrahimov[2], B. Tashkhodjaev[1], P. Kh.Yuldashev[1]

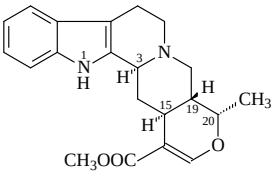
1) Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: adizovsh@gmail.com
2) Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan 83, M. Ulugbek str.,100125, Tashkent, fax: (99871) 262 70 63

Catharanthus roseus, formerly *Vinca rosea* is a member of the *Apocynaceae* family. At present *C. roseus* is only natural source of drugs such as vinblastine (vincaleucoblastine) and vincristine (leurocristine). They have been successfully used in chemotherapy in the treatment of cancers lymphoblastic leukemia (lymphoblastic leukemia), neuroblastoma (neuroblastoma) and breast carcinoma (breast cancer). About 130 alkaloids can be found in *C. roseus*. However, only few (~11) of this high number of chemical entities are frequently analyzed and even fewer (~8) are commercially available (companies Sigma-Aldrich, Gedeon Richter Ltd. and etc.) [1]. For this reason *C. roseus* is being cultivated and studied for it's numerous alkaloids constituents.

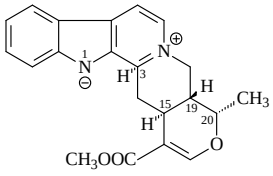
Previously, *C. roseus* has been studied for it's alkaloids content among plants grown in the conditions of Central Asia (at the Institute of Botany, Academy of Sciences of Uzbekistan), and was found that the plant contains alkaloids that amounted to 0.5% by dry weight, and of which a major indole alkaloid ajmalicine was (10%) [2]. In the present work *C. roseus* grown by authors at air temperature in the garden of the Institute of the Chemistry of Plant Substances.

HPLC-ESI-MS/MS analysis of the roots and the aerial parts of *C. roseus* conducted on the water-methanol extract, the following alkaloids were found: ajmalicine, ajmalicine isomer serpentine, serpentine isomer vindolinine, 19*S*-vindolinine, tabersonine and katarantine.

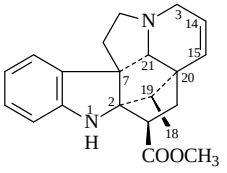
Conditions of separation of mixed alkaloids by HPLC correspond to those described in [2].



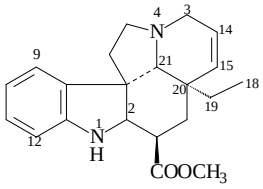
ajmalicine

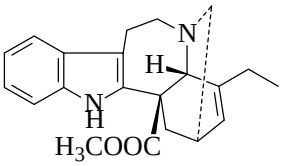


serpentine



vindolinine





tabersoninecatharantine

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LIPIDS OF THE INTRODUCED AMARANTH OF “HELIOS” KIND

Sh. K. Khidoyatova[1], N. K. Yuldasheva[1], N. T. Ul′chenko[1], S. D.Gusakova[1], Sh. Sh. Sagdullaev[1], K. A. Tokhtakhunov[2], M. M. Muminov[3]

1) Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan Tashkent, Republic of Uzbekistan, e-mail: s.gusakova2004@mail.ru
2) Tashkent State Technical University
3) Andijan State University

Plants of the *Amaranthus* genus are well known as fodder, vegetable, and industrial crops. Grain lipids of a number of amaranth species have been studied, but the data are limited on the differences between different kinds of the plant. A high variability of lipids under the influence of climatic, agronomic conditions and the introduction has been established [1]. We investigated the lipids of the introduced in Uzbekistan amaranth of the "Helios" kind. The samples were a grain (I), pressing oil (II) and oil cake (III). The humidity of I was 11.5%, III – 9.5%. Lipids from the samples I and III were extracted with benzene (boiling point 72-76°C) in a Soxhlet apparatus. Lipids yielded from I (dry substance) - 6.8% (extraction oil, sample IV), from III – 4.2%. According to CC, squalene content in II was 5.4%. 7.9% of unsaponifiable substances were yielded from the sample II that was constituted by 68.35% squalene and 0.16 mg% of carotenoids.

Fatty acids I, II, III, and IV were analyzed as their methyl esters using GC on an Agilent 6890 N apparatus with a capillary column HP-5 (length 30 m × 0.32 mm, thickness of stationary phase 0.25 μm), helium as a carrier gas, temperature programmed from 150°C to 270°C. Results of the analysis are shown in the Table.

TABLE.1. **Fatty-Acid Composition of Amaranth of “Helios” kind**

Lipids	Fatty acids									
	14:0	16:0	18:0	18:1	18:3	18:2	20:0	22:0	∑ saturated	∑ unsaturated
II	-	20,60	3.34	31.17	1.39	42.80	0.70	-	24.64	75.36
III	0.23	19.53	3.18	29.79	1.66	44.68	0.67	0.26	23.87	76.13
IV	-	17.46	4.30	35.88		41.38	0.98	-	22.74	77.26

In contrast to this kind of amaranth growing in Russia [2], the introduced kind had fewer oils (7.5 vs 8.5%), fewer contents of squalene in the lipids (5.4 vs 8.5%) and unsaponifiable substances (7.9 vs 11.8%), but the total content of unsaturated fatty acids was higher.

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IRIDOIDS EFFECT ON THE ACUTE ALCOHOL INTOXICATION IN THE EXPERIMENT

A. Nabiev, A. A. Azamatov, I. D. Bobaev

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: akademic1986@list.ru

Iridoids are widespread in *Scrophulariaceae*, *Plantaginaceae*, *Lamiaceae* and some other families of plants. Iridoid-containing plants are used in medicine in gastrointestinal disorders, for better digestion and appetite improvement (1).

Iridoids possess hepatoprotective properties and influences positively on the liver functions (2).

We have isolated iridoid glycosides lamalbid, barlerin and florigidoside C (5-deoxysesamoside) from a methanol extract of *Eremostachus baissunensis* M.Pop. (*Lamiaceae*) collected in vegetation period. They were identified by their UV-, IR-, ^{1}H- and ^{13}C-NMR spectra (3).

It is known that the ethanol detoxification is occurring due to the activity of enzymatic system of hepatocytes. Taking into consideration this fact, we investigated the effects of the iridoid sum on the ethanol detoxification.

The investigated substances were introduced at the doses of 10–50 mg/kg per os in 30 minutes prior the ethanol introduction at a dose of 4.2 mg/kg i.p. Only ethanol was introduced to the control group, and the duration of sleeping in this group was taken as 100%. Detoxification degree was determined by the duration of mice sleeping after ethanol introduction. In our experiments the commercial drug Alcoreliz at a dose of 200 mg/kg decreased the sleeping for 64%, and the iridoids sum – for 57.2% (3).

Apparently, the shortening of sleep duration under AAI is caused by the activation of detoxification function of liver attributed to iridoids presence.

Therefore, the iridoids of *Eremostachus baissunensis* possess antialcohol activity lower than that of Alcoreliz preparation.

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ANTITOXIC ACTION OF *N*-(3,4-DIMETOXYBENZYL)CYTISINE HYDROCHLORIDE IN ACUTE ALCOHOL INTOXICATION

A. A. Azamatov, A. Nabiev, Sh. B. Rakhimov, F. M. Tursunkhodjaeva

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: ftm40438@gmail.com

Acute alcohol intoxication (AAI) causes more 60% of the lethal outcomes of all intoxications. AAI treatment includes a total detoxication, breath recovery, pharmacological correction of CNS, hemodynamic disorders and acidosis.

Earlier we have reported on antitoxic action of cytisine alkaloid and four its derivatives (1). At present work we have continue our investigation of cytisine derivatives in order to search an effective antidote. We investigated the effects of *N*-(3,4-dimethoxybenzyl)cytisine hydrochloride and its combination with succinasol on the duration of narcotic sleep caused by intraperitoneal injection of 25% ethanol solution (6 mg/kg). Succinasol, a commercial drug containing succinic acid, has been used as a control. The investigated substances introduced *per os* for 30 minutes prior to ethanol injection.

Results have shown that *N*-(3,4-dimethoxybenzyl)cytisine hydrochloride at a dose of 5 mg/kg reduces the time of mice sleeping in AAI on 49%, succinasol at a dose of 100 mg/kg – on 48%, and cytisine at a dose of 2 mg/kg – on 35%. A combination of *N*-(3,4-dimethoxybenzyl)cytisine hydrochloride (10 mg/kg) with succinasol (100 mg/kg) reduces the sleeping time on 73%.

Therefore, we have shown that the cytisine derivatives of this range are the promising agents in AAI antidotes searching.

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PECTIN POLYSACCHARIDES *Silybum marianum* AND *Arctium leiosporum*

K. S. Zhauynbaeva

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail:Klara-68@rambler.ru

Natural polysaccharide pectin - a unique biopolymer, it is one of the basic building material of the cell walls of higher plants it has a wide range of functional properties. When combined with water and some other substances it manifests itself as a thickening agent, gelling agents, stabilizer, emulsifier agent, binding metal cations.

Plants of the genus Silybum marianum and Arctium leiosporum are rich sources of bioactive substances with a wide range of pharmacological properties. Accordingly, the carbohydrates were first studied from aboveground plant parts.

Dedicated pectin substances (PS) determined by the method of [1] and their content was 5 and 3.8 %, respectively.

PS are free-flowing powder, completely soluble in water cotnositelnoy viscosity η_{rel} = 8.7 and 3.4 (c 1% ; H_2 O) and MM 40 and 13 kDa, respectively. Monosaccharide composition represented galacturonic acid, rhamnose, arabinose, glucose, galactose.

Quantitative characteristics of PV according to titrimetric analysis correspond to : COP - free carboxyl groups- 12.5 and 11.2% , Ke - esterified carboxyl groups, 17.4 and 9.0 %. The degree of esterification of 58.1 and 55.5%, respectively.

Thus, pectin *Silybum marianum* and *Arctium leiosporum* are high esterificated .

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IMPROVING OF BAKING TECHNOLOGY UNDER THE INFLUENCE OF FOOD PLANT ADDITIVE

T. D. Kasimova[1], D. Sh. Gafurov [2]

1) Acad.S.Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan Tashken
2) Scientific – manufacturing Centre "Donmahsulotlari" Limited Company

Increasing of the food quality of bakery products by use of new plant materials are the most prospective direction of bakery industry nowadays.

Choosing optimal dose of added products, mode of dough production, technological stage addition of products, and also optimal parameters of technological process are the most important for achievement of high quality of products.

The influence of carbohydrate – arabinogalactan isolated from the aerial part of plant *Ferula kuchistanica* on the bread quality has been investigated. It was determined that the addition of arabinogalactan in the dough positively influences on the biochemical, colloid and microbiologic processes of dough preparation, namely: increases initial acidity and porosity, decreases pH. Process of dough fermentation proceeds more actively and gluten become stronger. This capability of arabinogalactan is predetermine its using at the treatment of the flour with weak quality. Results of the test of bakery are presented at this table 1.

TABLE 1. **Influence of Arabinogalactan at the Flour Quality**

Characteristics	Control	Dose of arabinogalactan, % from flour quantity		
		2.0%	5.0%	7.0%
Color	Light -yellow	Light -yellow	Yellow	Yellow-brown
Taste	Attributable of this kind of products, without extraneous taste			
Odor	Attributable of this kind of products			
Form	Good	Good	Good	Satisfactory
Crumb constitution	Baked thoroughly (well) don't moisturizing to the touch			
Moisture, %	43	43.6	43.4	43.7
Acidity, pH	3.4	3.45	3.47	3.5
Porosity , %	76	77	77.5	77.1

So, the moisture of these products was the same as in the control. We observed the decrease of bread porosity in the experiment in comparison with the control however this parameter determined only structured-mechanical properties of crumb and these dates satisfied to the requirements of standard. Increased acidity insignificantly influenced at the taste of product and didn't make it worse. The value of acidity of crumb is considered within the requirements.

The data in Table 1 showed that addition of arabinogalactan led to improve of bread quality. The bread volume is increased and its shape improved in comparison to bread without additives.

At the results of this work it was established the suitability of arabinogalactan to improve the stability of bread to variations in fermentation time and temperature.

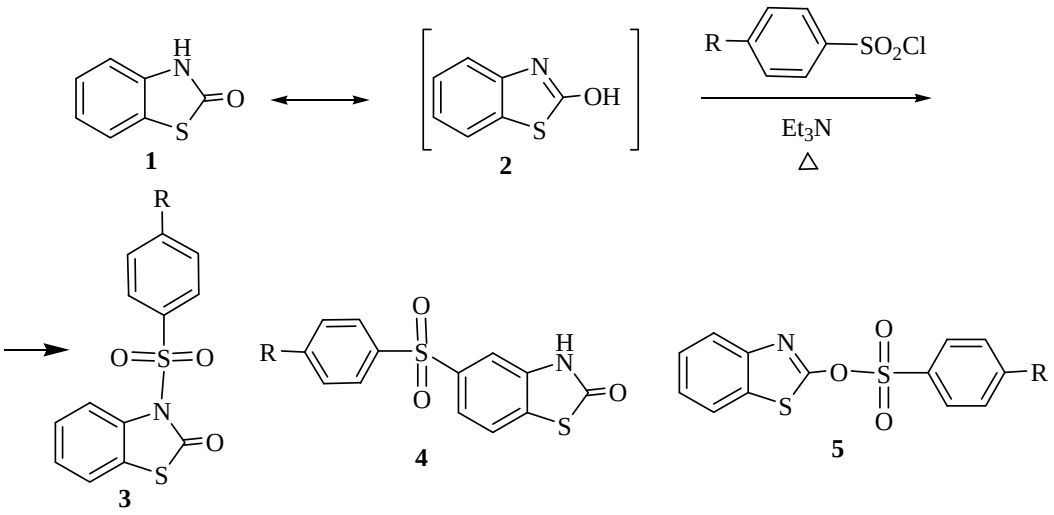
NOVEL *N*-ARYLSULPHOAMIDES IN THE BENZOTHIAZOLINE SERIES

M. I. Olimova, B. Zh. Elmuradov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: b_elmuradov@mail.ru

Benzothiazolines are a large and interesting class among the bicyclic heterocyclic compounds. These heterocycles have plural reactivity, and among the derivatives of them there are many effective drugs for agriculture and medicine. Together with it introduction into benzothiazoline molecules sulphoamide moieties is very important, because arylsulphoamides are simple synthones for further modification and possess different biological activity.

In this work we studied arylsulphonation of benzothiazolin-2-thione (**1**) by p-substituted arylsulphochlorides. It is important to note that arylsulphonation of benzothiazolines goes in the different direction: due to tautomeric presence of the enol form (2-hydroxy-benzothiazoline, **2**) there is possibility of 3-(*N*-arylsulphonyl)-benzothiazolin-2-thione (**3**), 5-arylsuphonyl-benzothiazolin-2-thione (**4**) or 2-(*O*-arylsuphonyl)-benzothiazoline (**5**) formation:



Formation of isomers **3-5** depends on the reaction condition and reagents ratio. We carried out reaction in benzene in the presence of triethylamine and 3-(*N*-arylsulphonyl)-benzothiazolin-2-thiones (**3**) have been synthesized in good yields. Formation of compounds **4** and **5** was not observed. The structures of synthesized compounds were confirmed by spectral methods.

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CHEMICAL COMPONENTS OF *Pulicaria salviifolia*

Sh. O. Melieva, K. A. Eshbakova

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: shohista_m2008@mail.ru

Pulicaria salviifolia refers to one of the richest plant terpenoids genus *Pulicaria* (fam. *Asteraceae*). Species of the genus occur in Eurasia and Africa, mainly concentrated in the Mediterranean. The genus includes 63 species of *Pulicaria*. In Uzbekistan grows 16 species of this genus. *P. salviifolia* is an endemic plant in Uzbekistan.

In folk medicine the plant is actively used to treat various diseases of the gastrointestinal tract, diarrhea, dysentery, constipation, chronic colitis. Decoctions and infusions administered orally to improve the work of the stomach and normalization of acid-base balance. *P. salviifolia* has long been used in folk medicine as a natural remedy against mosquitoes, flies and fleas, in addition as a diuretic.

According to the literature of the active substances in the aboveground part contains psyllium alkaloids, polyacetylene compounds, ascorbic acid, tannins, organic acids, rubber, saponins, essential oils, coumarins, flavonoids, polyacetylene compounds. The roots are found psyllium rubber and polyacetylene compounds.

We have studied flavonoids, terpenoids and coumarins of the aerial part of *Pulicaria salviifolia,* collected Jizzakh region. Raw material extracted with chloroform, ethyl acetate and 70% ethanol. Column chromatography of the chloroform amount allocated following known substances bornyl acetate (**1**), 2-(1,1-dimethylethyl)-1,4-dimethoxy-benzene (**2**), 2,6-octadiene-1-ol, 3,7-dimethyl-acetate (**3**), octatriakontanol 1- (**4**), salvin (**5**), salvinin (**6**), β-stigmasterol (**7**).

Known compounds (**1–4**) were determined by gas chromatography-mass spectral analysis, the compounds (**5–7**) identified by direct comparison of the spectral data (UV, IR, ^{1}H and ^{13}C NMR) with those reported in literature.

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THE METABOLIC ACTIVITY OF IRIDOIDS AND IRIDOID EXTRACTS FROM THE LOCAL FLORA IN THE INFLAMMATION

N. V. Tursunova, F. R. Egamova, N. Z. Mamadalieva, N. H. Yuldasheva, L. T. Zahidova, S. M. Yusupova, V. N. Ahmedov, Z. A. Khushbaktova, V. N. Syrov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: natalya-tursunova@mail.ru

Iridoids are the chemical plant compounds which exhibit diverse biological activity (hepatoprotective, antioxidant, hypoglycemic etc.) in mammals and human. We examined the ability of some isoprenoids to affect on the development of inflammatory edema and metabolic changes induced by formalin in albino mice. The experiments were performed in animals of both sexes weighing 22–25 g. They were administered aqueous solutions of iridoids flomozide A, lamiide, catalposide, harpagide and iridoid extracts from *Phlomis thapsoides, Leonurus panzerioides, Leonurus turkestanicus, Ajuga turkestanica* at a dose of 50 mg/kg orally. Exudative inflammation was induced by an injection of 2.5% formalin solution into the muscle of the right back paw on the 3rd day of the experiment. After appearance of edema (on the next day after injection) the animals were decapitated under light ether anesthesia, both hind legs cut off and difference between the ratio of the legs mass in the control group with inflammation and groups of mice treated by test compounds on a background of inflammation was measured. Simultaneously, glycogen content, the total protein, malonic dialdehyde in the liver tissue and malonic dialdehyde and alanine aminotransferase in the serum was determined. The experimental results showed that catalposide, lamiide and flomozide A demonstrated certain anti-inflammatory effect among individual iridoids (the percentage of reduction of edema was respectively 19.1, 18.5 and 15.3). The immediate impact of the other samples in the inflammation was weaker (11.5-14.0%). At the same time, the metabolic activity of the test substances was more pronounced in these conditions. Thus, the content of glycogen in the liver tissue of the animals received lamiide under inflammation was 1904.1 mg%, which was on 79.7% higher than the indicate in the control group (1060.0 mg%). Effect of harpagide, catalposide and flomozide A was lower. Among test extracts also *P. thapsoides* extract had the ability to save of glycogen content (+30.6%). All compounds are markedly increased the content of total protein in the liver tissue (catalposide, lamiide, harpagide, extracts from *P. thapsoides* and *A. turkestanica* were more active). Antioxidant effect of all individual compounds and extracts from *P. thapsoides* and *A. turkestanica* was quite pronounced (decrease of malondialdehyde accumulation in these groups in comparison to control animals was on 18,0-38,9% in the serum and 17,0–34,1% less in the liver tissue). The compounds also have contributed to a decrease the alanine aminotransferase activity in serum, indicating about inhibition of the liver cytolytic process in the inflammation.

Thus, these data suggest that iridoid glycosides flomozide A, lamiide, catalposide and harpagide and iridoid extracts from the local plants *P. thapsoides* and *A. turkestanica* manifest metabolic and moderate anti-inflammatory effects in the experimental model of exudative inflammation.

DEVELOPMENT OF TECHNOLOGY CAPSULE DOSAGE FORM OF «RAVONOL»

N. E. Mamatmusaeva, Sh. M. Turaboev , N. S. Beknazarova, S. D. Mahmudov, N. N. Abrekova, B. T. Sagdullaev

Institute of Bioorganic Chemistry of the Academy of Sciences of Uzbekistan, Tashkent, 100125, Mirzo Ulugbek, 83

At present, it is important to provide the population of Uzbekistan with quality, safe and effective drugs.

It is known that the variation in metabolism of the stomach and the intestine of humans causes a disturbance of normal intestinal activity, whereby there is a delay of the chair. The reason for this may be poor nutrition, low physical activity, emotional and physical stress, which lead to various diseases, such as constipation. Development of technologies and their implementation to production of biological active supplements and medicines based on natural bioactive compounds has an important in medicine. Dry extract from the pulp of a plum *Prunus domestica L.* was obtained. The aim of our research was the choice of a capsule dosage form and development an optimal technology of the dosage form.

Dry extract obtained from plum had hygroscopic property and therefore obtaining direct dosage form is very difficult. To reduce the hygroscopicity of the dry extract, an aerosil, as a moisture repellent material and also calcium stearate, as anti-friction material in different ratios were selected.

Based on the research the optimal composition for the capsule form was chosen:

Dry extract "Ravonol" – 450 mg

Calcium stearate – 4.0 mg

Aerosil – 6.0 mg

Based on the selected formulation, following technology of capsule mass was developed: extract was dried at 105°C (till moisture content 4.5%), finely milled to a state of dispersion powder. In the made extract added aerosil, which was conducted through a sieve with holes 0.2–0.3 mm, then the mixture was mixed for 30 minutes in the multifunctional mixer HD-100. To the mass also added calcium stearate (0.2–0.3 mm) and mixed for 7 minutes to obtain is homogeneous.

As the positive results of experiments received a lot of pre-packaged in 460 mg capsules in the № 0. Dosage capsule masses was performed by disk method on capsule machine brand “Capsula Filling Mashine NJP200”. Capsules that meets the requirements according to qualitative and quantitative parameters packed up to 10 pieces in a planimetric on the cell the blister machine which brand.

On the basis of the optimal composition for the capsule dosage form has been selected and developed its technology.

SYNTHESIS OF NEW DERIVATIVES OF 2-METHOXYBENZONYL-2-DEOXY-α-ECDYSONE

I. D. Bobaev, U. Yu. Yusupova, M. M. Mahmudova, D. A. Usmanov, N. Sh. Ramazonov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan Tashkent, e-mail: bobaev-isom@mail.ru

Various derivatives of ecdysteroids attract attention of researchers due to the possibility to use them in pharmacology.

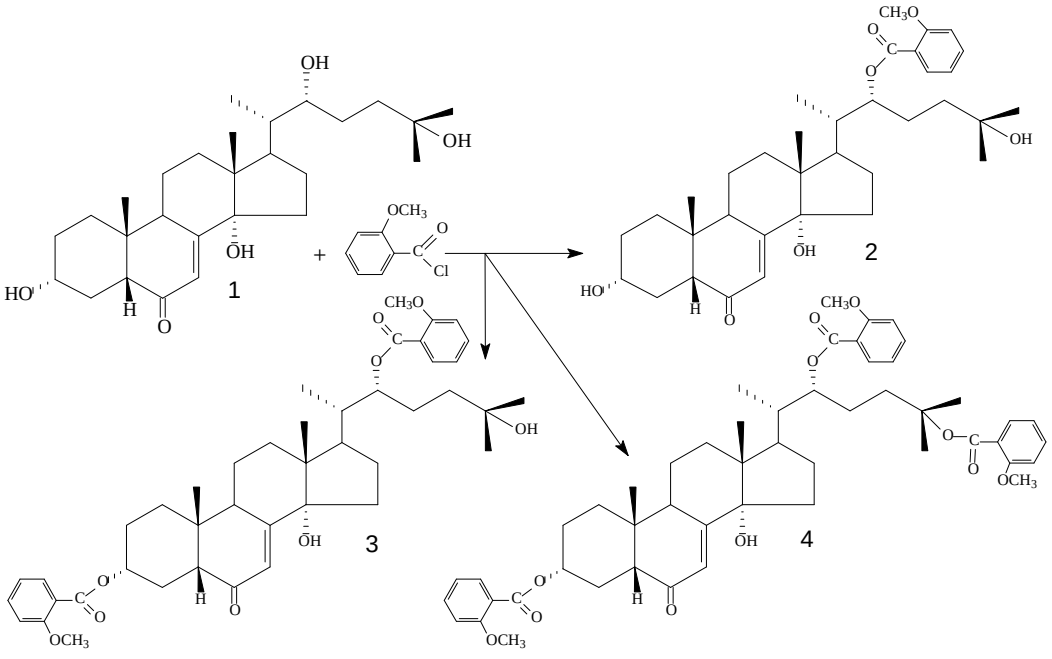
The great interest among the natural conjugates represent ecdysteroids derivatives of carboxylic acids, namely 2-, 3-, 20-, 22-, 25-, or benzoates occurring in plants.

To evaluate differences in the reactivity of hydroxyl groups the speed of their acetylation has been investigated in various derivatives of 2-deoxy-α-ecdysone. 22-O-hydroxyl groups of 2-deoxy-α-ecdysone acetylated most quickly due to the relatively uncomplicated axial conformation. In turn, C_{22}-OH is more reactive capable than C_3-OH.

2-Deoxy-α-ecdysone contains four hydroxyl groups; reactivity of secondary groups in acetylation reactions decreases in the following order: $C_{22} > C_3 > C_{25}$.

In the synthesis of derivatives of 2-deoxy-α-ecdysone o-methoxybenzoyl derivatives the acetylation reaction was performed under the influence of o-methoxybenzoic acid chloranhydride.

Synthesis carried out according to the scheme:



Column chromatography succeeded in separating the mixture into individual components: 3-O-(methoxybenzonyl)-2-deoxyecdysone (2) (8.9%), 3,22-O-di-(methoxybenzonyl)-2-deoxy-α-ecdysone (3) (27.3%), 3,22,25-O-tri-(o-methoxybenz-onyl)-2-deoxy-α-ecdysone (4) (11.6%).

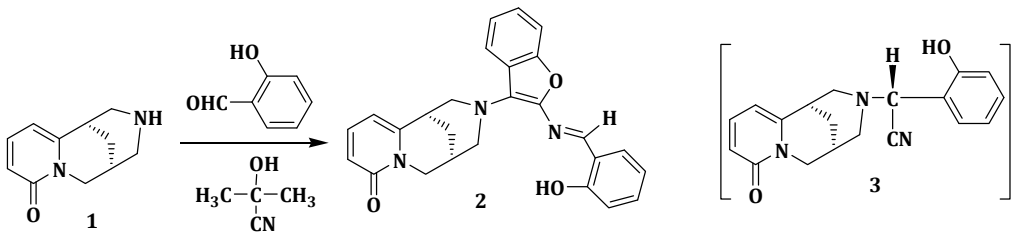
ANOMALOUS REACTION OF CYTISINE WITH SALICYLIC ALDEHYDE IN THE PRESENCE OF ACETONE CYANOHYDRINE

D. S. Ismailova, B. Zh. Elmuradov, U. S. Makhmudov, B. Tashkhodjaev

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: b_elmuradov@mail.ru

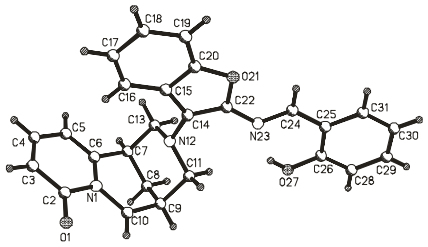
Alkaloid cytisine and its derivatives have different pharmacological activities [1]. Moreover, this alkaloid contains some reactive centers, which can react with electrophilic and nucleophilic reagents [2].

With purpose synthesis of the novel α-aminonitryles of cytisine (**3**) in this work we studied interaction of cytisine (**1**) with salicylic aldehyde in the presence of acetone cyanohydrine. In this reaction we observed anomalous interaction and polycyclic compound – benzofurane cycle consisting cytisine (**2**) has been synthesized as *E*-isomer in good (70%) yield. No compound **3** is formed:



Single crystals of the compound were grown from solution of methanol by slow evaporation of the solvent at room temperature.

The unit cell parameters of the crystals are determined and refined with CCD Xcalibur Ruby diffractometer (Oxford Diffraction) using CuKα-radiation, graphite monochromator (T = 293 K). The three-dimensional set of reflections received at the appropriate diffractometer. The amendment was introduced to the absorption by Multi-scan. A three-dimensional data set of reflections was obtained on the same diffractometer. Absorption corrections were applied using a semi-empirical method in the SADABS program.



Reaction course and mechanism of the interaction will be discussed in our next works.

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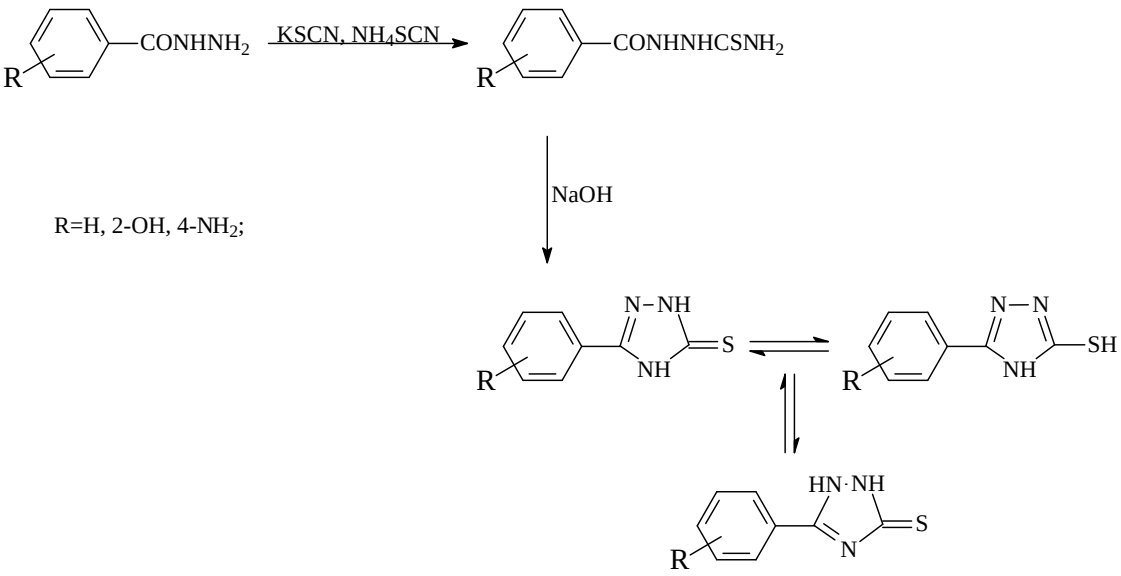
SIMPLE AND EFFECTIVE SYNTHESIS OF 1,2,4-TRIAZOLE-3-THIONES

A. A. Ziyaev, U. S. Makhmudov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: aziyaev64@mail.ru

1,2,4-Triazole having three nitrogen atoms in its molecule, very interesting representative of the five-membered heterocycles, is a component of several widely used remedies in agriculture and medicine (fluconazole, propikanazol, thiotriazoline etc.). Along with the practical significance, 1,2,4-triazole and sulfur derivative 1,2,4-triazole-3-thione have several nucleophylic centers (exocyclic sulfur and nitrogen endocyclic atoms) in the molecule giving opportunities for synthesis the novel compounds with many types of potential biological activity. To study systematically the various chemical transformations we synthesized several 5-aryl-1,2,4-triazole-3-thiones from the corresponding arylthiosemicarbazides by their subsequent cyclization to aryltriazolthiones in alkali solutions:



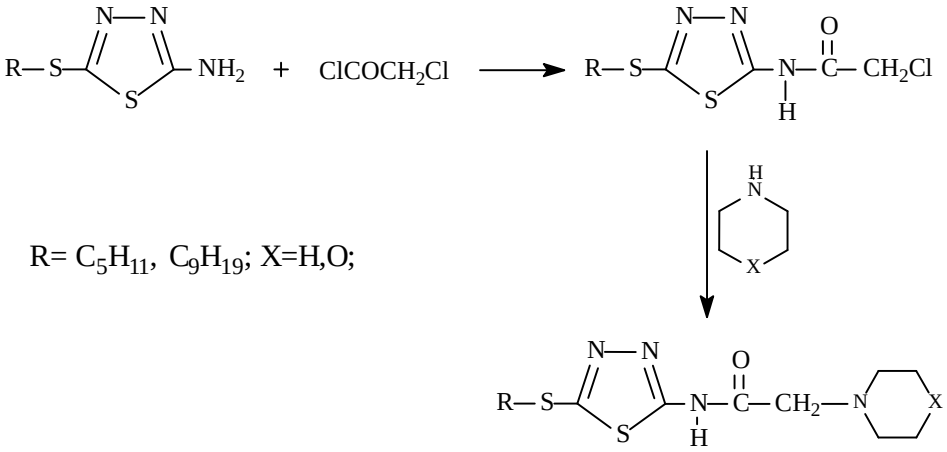
The higher yields of arylthiosemicarbazides were obtained at the reaction with ammonium thiocyanate than with potassium thiocyanate. Also the optimal conditions during heterocyclization of arylthiosemicarbazides in alkaline environment, such as temperature, concentration of alkali solution and etc. were identified. Physic-chemical characteristics of the 5-aryl-1,2,4-triazole-3-thiones were investigated and their structures were confirmed by X-ray analysis.

SYNTHESIS AND AMINATION OF 2-ALKYLTHIO-5-CHLOROACETYL-AMINO-1,3,4-THIADIAZOLES

T. T. Toshmurodov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: ttt1609@mail.ru

Earlier we have reported on the synthesis of 2-alkylthio-5-amino-1,3,4-thiadiazoles and their reactions with chloroacetylchloride, and obtaining of 2-alkylthio-5-chloroacetylamino-1,3,4-thiadiazoles [1, 2]. In continuation of chemical transformations of thiadiazolethiones we are interested in an investigation of the thiadiazole cycle fragments and secondary amines. We carried out reactions of 2-alkylthio-5-chloroacetylamino-1,3,4-thiadiazoles (alkyl = amyl, nonyl) with hetero-cyclic amines (piperidine, morpholine). The optimal reaction conditions were found by varying a time, solvent, temperature and reagents ratio, namely absolute benzene medium, boiling for 12–15 hours, and reagents ratio 1:2 (chloroacetylaminothidiazole:amine), where excess of amine was HCl acceptor:



In this work we obtained novel 2-alkylthio-5-piperidinoacetylamino-1,3,4-thiadiazoles and 2-alkylthio-5-morpholinoacetylamino-1,3,4-thiadiazoles. The structures of the obtained substances were confirmed by IR and ^{1}H NMR spectra.

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SYNTHESIS ON THE BASE OF TRIACANTINE

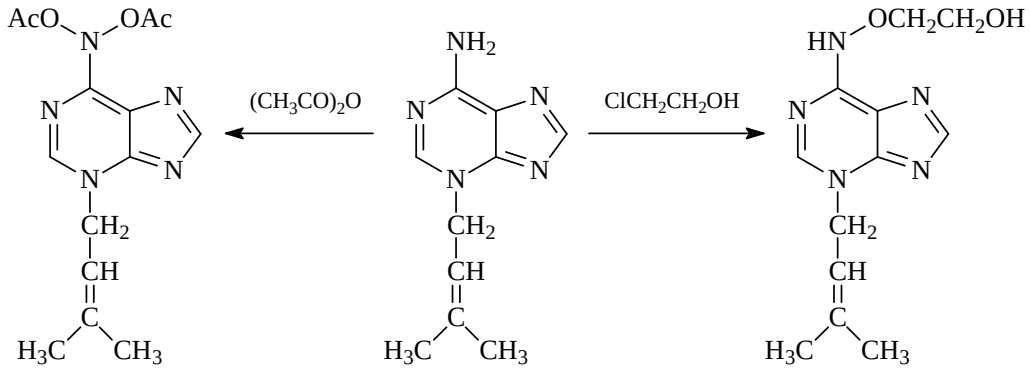
Sh. B. Rakhimov, V. I. Vinogradova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: rshukhrat@mail.ru

Triacantine (**1**) isolated from *Gleditschia triacanthos* L. (*Leguminosae*) has antispasmolic effect on smooth muscle organs, dilates blood vessels, stimulates respiratory center and lowers blood pressure. Young leaves of *G. triacanthos* contain triacantine up to 1%, flowers - up to 0.3%. In other organs content of alkaloids is minor.

In order to find new pharmacologically active substances we carried out acetylation of triacantine with acetic anhydride, and obtained *N*-diacetyltriacantine (**2**).

Alkylation of triacantine with ethylene *mono*-chlorohydrine gave *mono*-hydroxyethyltriacantine (**3**).



2 **1** **3**

The structure of the obtained compounds was confirmed by ^{1}H NMR spectrum.

INFLUENCE OF PROLONGED ADMINISTRATION OF DONAXINE ON PHYSICAL AND PSYCHOEMOTIONAL STATE OF WHITE MICE

Yu. R. Mirzaev, Z. I. Sanoev

Acad.S.Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: ZafarSano19@mail.ru

Previously, we have informed about the pharmacological properties of the alkaloid donaxine isolated from aerial parts of giant reed (*Arundo donax*, Graminea fam.) growing in Uzbekistan. It was shown that donaxine is structurally related to neurotrope compound serotonine and it revealed aphrodisiac property. By pharmacologic width this compound up to 2 times surpasses the known aphrodisiac "Yohimbine". Donaxine is protected by a patent of Uzbekistan. Presented data regarding the study of the influence donaxine on the physical and psycho-emotional state of young growing white mice for 105 days administration at doses of 10 and 50 mg/kg, that corresponds to 2 and 10 "therapeutic dose" in this report. During this period the value of of body weight gain, locomotor activity (by I.P.Lapin et al., 1991), the behavior of mice in the "open field" test, the donaxine influence on anxiety feeling by Kilfoil (et al., 1991) method, as well as its influence on amphetamine (5 mg/kg, s/c) motor activity were measured. Besides, it was studied the influence of donaxine on cataleptogenic effect of haloperidole (0.3 mg/kg, s/c).

The study had showed that weight gain of the mice in the control and experimental groups of mice in all the measurements was practically the same. With regard to motor activity it was observed that in all tests mice under both donaxine doses at 21 and 41st days of administration have manifested a clear trend in the gain of locomotor activity as compared to the intact control mice. In the test an "open field" in an experiment conducted at the 15 and 48th days, it was observed that the mice under donaxine showed more pronounced locomotor activity and examined more number of minks from 2 to 3 times. In the anxiety test by Kilfoil method donaxine at 7 and 38th days of experiment in both doses provided anxiolytic action, expressed in preference light camera and more frequent enters into the cameras. In experiments with haloperidol donaxine at mentioned doses has shortened the duration of catalepsy for 2 times (28 and 55th days). Donaxine in dose of 10 mg/kg at 61th administration day has showed a tendency to increase locomotor activity caused by amphetamine.

Thus, chronic administration of donaxine at small and moderate doses (10 and 50 mg/kg per os), during 105 days didn’t reveal any toxic action, moreover, the alkaloid at less dose, have led to activation of the physical and psychoemotional state of white mice.

EXTRACTION OF GLYCYRRHIZIC ACID USING ULTRASONIC RADIATION

A. M. Khvan, Sh. A. Otaeva, A. Sh. Abdurazakov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: asqar2606@mail.ru

Licorice (*Glycyrrhiza glabla* L.) is known as a medicinal plant since ancient times. In the East medicine decoctions of licorice root used as a painkiller, in wound healing, febrifuge, pulmonary tuberculosis, ulcers and many other diseases. The interest of chemists and physicians to this plant remains steadily high at present. The main component of licorice root is glycyrrhizic acid (GA) and the whole broad spectrum of physiological activity of the plant is attributed to it. The content of the GA in the plant is 25–40% depending on the place of growth. This plant is widespread in the countries of Asia, and South-East Asia. The biological reserve of licorice in the Republic of Uzbekistan is 12.5% of the total reserves in the Confederation of Independent States (CIS) countries. The plants grow in the flood plains of the rivers Syr-Darya, Amu-Darya, Chirchik, Zarafshan, Angren.

Methods of GA isolation from the licorice root are diverse and constantly improving. The use of the ultrasonic radiation is known in the technology of the plant raw materials conversion. The application of ultrasonic radiation accelerates the extraction process, and provides a more complete extraction of the active ingredients. It is clear that in each case the determination of the optimal process conditions is necessary for the achievement of maximum beneficial effect.

In this paper the optimization of the extraction process by an ultrasonic radiation method to increase the yield of glycyrrhizic acid has been performed. The device «BANDELIN SONOREX» (Germany) with the characteristics U230 V ~ 50/60Hz; I 0.4A; P 80/320W; f 35 kHz was used. The process module in all the experiments was 1:10. The extraction process was carried out in the water-alcohol solution. The influence of the licorice root particles, temperature, alcohol concentration, and duration of extraction was researched.

The optimal conditions for extraction of the glycyrrhizic acid from licorice root with use of ultrasonic radiation were established. The essential increase of the glycyrrhizic acid yield in the extract has been achieved.

DEVELOPMENT OF MEDAMINE SUSPENSION TECHNOLOGY

T. Sadikov, A. Sh. Abdurazakov, Z. T. Sadikov, R. K. Karimov, Sh. Sh. Sagdullaev

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: asqar2606@mail.ru

Scientists of the Institute of Chemistry of Plant Substances the Academy of Sciences of Uzbekistan jointly with E.I. Martsinovskii Institute of Medical Parasitology and Tropical Medicine introduced into medical practice anthelmintic drug medamine.

Currently, the drug is used with great success in medical parasitology.

T.e widespread helminth infections bringing great economic losses to livestock. We have conducted extensive research to find new anthelmintic drugs.

Biological research has shown that preparation of Medamine as a suspension provides the best results.

Proceeding from this we have developed laboratory methods for obtaining 2.5% and 10% Medamine suspension.

The main task in the preparation of high-quality suspension preparation is to achieve a high degree of dispersion, which has a positive effect on the pharmacological effect and the stability of the resulting form of the drug.

We have prepared aqueous suspension form of the drug for easy per oral use in animal.

Carried experiments showed that the optimal composition is the use of excipients such as sodium salt of CMC, xanthan, sodium benzoate, glycerol, proteoglycan and etc.

We have developed a spectrophotometric method for the quantitative determination of Medamine in suspension.

Thus, the creation of the new high effective formulations of Medamine as 2.5% and 10% suspensions.

EKDINOX, AN ANTHELMINTIC COMPOSITION

A. M. Khvan, A. G. Eshimbetov, A. Sh. Abdurazakov

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: asqar2606@mail.ru

The problem of the development of effective low-toxic anthelmintics can be solved by creating compositions of substances. For reduction of side effects of the known drug Azinox, which has a high hepatotoxicity, we proposed the composition of Azinox with hepatoprotector Ekdisten (Ekdinox). According to the pharmacological research, Ekdinox retains not only severity of the Azinox antiparasitic activity, but even improves it, that gives an opportunity significantly reduce the effective dose of azinox drug.

In this work, the Ekdinox has been investigated by IR spectroscopy and thermal analysis to determine the nature of interaction between components of the composition and the thermal effects of the composition in comparison with the initial components at the thermal impact.

The detailed analysis of the IR spectra of the Azinox, Ekdisten and five Ekdinox samples with the different ratios of the initial components carried out. The presence of the absorption bands in the region 3200–3500 cm^{-1} in the IR spectrum of the Ekdisten, and the lack of them in the IR spectrum of the Azinox allows analyze the comparative changes of this band in the composition. The probable conjugate structure and possible intra- and intermolecular hydrogen bonds in the Ekdisten molecule and in the Ekdinox conjugate suggested. The data of the IR spectroscopic analysis shows that Ekdinox is the conjugate stabilized by intermolecular hydrogen bonds involving OH-groups of Ekdisten and C = O groups of the Azinox. Thus, Azinox presence in the system leads to destruction of the intramolecular hydrogen bonds of the Ekdisten and part of the hydroxyl groups in the Ekdinox conjugate is free.

Comparative data of the thermal analysis indicate that Ekdinox conjugate is characterized with endo- and exothermic effects different from the thermal characteristics of the initial components. This obviously testifies the formation of sufficiently stable conjugate Ekdinox.

DEVELOPMENT OF THE SUSPENSION FORM OF ANTHELMINTIC DRUGS FENASAL AND AZINOX USED IN VETERINARY

R. K. Karimov, G. V. Zukhurova, A. Sh. Abdurazakov, T. Sadikov

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan Tashkent,
e-mail: asqar2606@mail.ru

Suspensions of drugs are widely used, especially in veterinary. Widespread of suspensions is due to several advantages of them over other dosage forms: a pronounced pharmacological effect as compared to tablets and powders; prolonged action of suspensions for parenteral administration, when compared with the solutions for injection; possibility of masking the unpleasant taste of the drug, which is convenient for use.

The main objective in improving suspension technology is to increase the degree of dispersion of suspensions and, as a consequence, increase the pharmacological effect, as well as increased stability of the resulting suspensions. Water-suspension formulations of anthelmintic drugs are especially important. They are suitable for use in animal husbandry.

We have been studied suspensions by using of glycerol, esaflor, xanthan-gum, sodium CMC, pectin, ABSK, gelatin, azinox, and fenasal.

Glycerol and esaflor are the most acceptable for azinox suspension, and glycerin and xanthan-gum for fenasal.

We investigated different recipes and chosen the optimal conditions for obtaining the suspension. Samples of products were provided for toxicological tests.

The suspensions are stable for 2h and the main component is consisted not less than 2.5%.

Primary biological tests showed that the suspensions of azinox and fenasal have positive results with more than 95% effectiveness.

Thus, new preparative forms of fenasal (2.5%) and azinox (2.5%) created.

DETERMINATION OF THE MASS FRACTION OF IMIDACLOPRID IN THE DALUCHO FORMULATION

R. K. Karimov[1], G. V. Zukhurova[1], Z. Muftakhutdinov[2], A. Sh. Abdurazakov[1], Sh. Sh. Sagdullaev[1]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: asqar2606@mail.ru
2) JV "Electrokhimzavod", Navoi City

The drug Dalucho as 70% wettable powder used for cotton seed treatment against root rot.

The active ingredient of the drug imidacloprid is a technical 1-(6-chloro-3-pyridylmethyl)-N-nitroimidazolidin-2-ylidenamine.

The analysis method based on the separation of imidacloprid and other components of the drug by reverse phase HPLC registration with a UV detector at a wavelength of 260 nm.

Mass fraction of imidaclopride was determined by an external standard.

Terms of calibration and measurement are following:

Column oven temperature, °C:	40
Volumetric flow rate of an eluent, cm^3/min	2.0
Wave length of detector, nm	260
Eluent system: water-buffer solution-acetonitril, cm^3	100
Injected sample volume, µL	5
Retention time, min	2.5
The chromatogram recording time, min	10

The arithmetic value of two parallel definitions are taken as an analysis result which permissible differences should not exceed 1% between them at a confidence level P = 0.95.

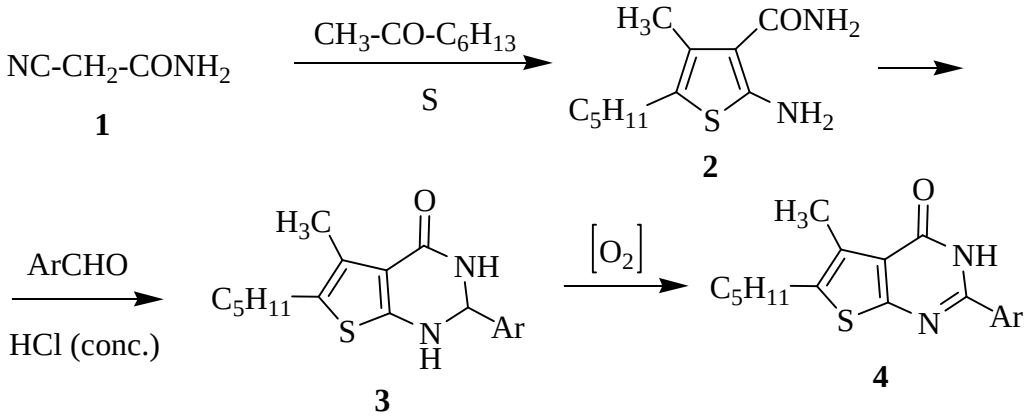
ONE-POT MULTICOMPONENT SYNTHESIS OF 2-ARYL-4,5-DIALKYLTHIENO[2,3-D]PYRIMIDIN-4-ONES

D. Kh. Akramov, B. Zh. Elmuradov

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: b_elmuradov@mail.ru

Thieno[2,3-d]pyrimidin-4-ones are well known heterocyclic compounds. These compounds have plural reactivity due to ambifunctional fragments [1]. At once there are some effective biological active compounds among the thieno[2,3-d]pyrimidin-4-ones which are recommended for agriculture and medicine [2].

Continuing our investigations, in the present work we synthesized 4-methyl-5-pentyl-2-amino-3-carboxylic acid amide (**2**) by cyclization of cyanoacetic acid amide (**1**) and methylhexyl ketone in the presence of sulphur:



The synthesized amide (**2**) is useful synthone for the synthesis of many substituted bicyclic thieno[2,3-d]pyrimidin-4-ones.

We studied one-pot multicomponent synthesis of 5-methyl-6-pentyl-2-aryl-1,2-dihidrothieno[2,3-d]pyrimidin-4-ones (**3**) and its oxidation product – 5-methyl-6-pentyl-2-arylthieno[2,3-d]pyrimidin-4-ones (**4**). Reactions carried out by refluxing of equimolar amounts of reagents (**2**:ArCHO – 1:1) in the presence of concentrated HCl for 4 hours and corresponding compounds have been synthesized in 50–65% yields.

The structure of the obtained compounds was confirmed by instrumental methods of research.

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SYNTHESIS AND SEARCH OF HERBICIDES IN THE SERIES OF XYLIDINE DERIVATIVES

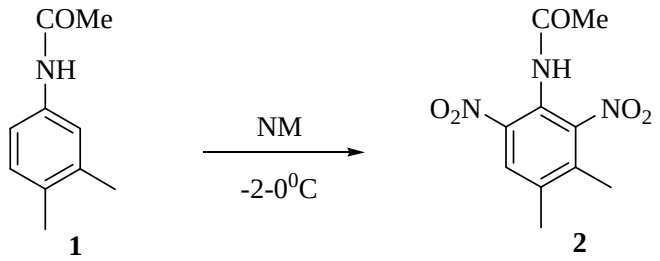
U. B. Mamarozikov, N. K. Khidyrova, O. Vlasova, B. Zh. Elmuradov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: b_elmuradov@mail.ru

Nowadays agriculture of the republic is rapidly developing. There are not only progress in the field of agriculture but also has problems of plant protection from pests and weeds.

Organic synthesis department of the Institute of the Chemistry of Plant Substances actively takes part in the creation of the plant protection products. The studies of the biological activity of the isolated and synthesized compounds are held in the different conditions: laboratory, vegetation and industrial environments with purpose subsequent their introduction into agricultural practice in Uzbekistan.

Recently, for creation of the novel and perspective herbicide in xylidine series (analogues of the Stomp – herbicide) we carried out interaction of *N*-acetyl xylidine-3,4 (**1**) and nitrating mixture (NM, HNO_3–H_2SO_4, 1:1). Nitration carried out at –2–0°C (ice bath) for 15–20 minutes and it was observed the formation of reddish-yellow nitro compound – 2,6-dinitro-*N*-acetylxylidine-3,4 (**2**) in high yield (89%). The reaction goes on the following scheme:



1 **2**

It also revealed the formation of mono-nitro product, but in low yields (3–5%).

Structure of the synthesized 2,6-dinitro-*N*-acetylxylidine-3,4 was confirmed by spectral methods and physic-chemical data (R = 0.75 in the benzene : methanol - 3: 1 solvent system, melting point 160–162°C).

Herbicidal activity of the obtained compound **2** was studied at the Laboratory of Phytotoxicology of the Institute. According to the preliminary results, compound has a moderate herbicidal activity in 0.1% concentration.

Now we are carried out synthesis of *N*-acetyl (or alkyl) xylidines and their mono- and dinitroproducts, which are may be potential biological active compounds. Investigation in this field will be continued.

SELECTIVE ACETYLATION OF BENZIMIDAZOLYL-2-THIOCARBOXYLIC ACID ANYLIDE

U. M. Yakubov[1], N. B. Pirnazarova[2], B. Zh. Elmurodov[1]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, *e-mail:* b_elmuradov@mail.ru
2) Qarshi State University, Qarshi, Uzbekistan

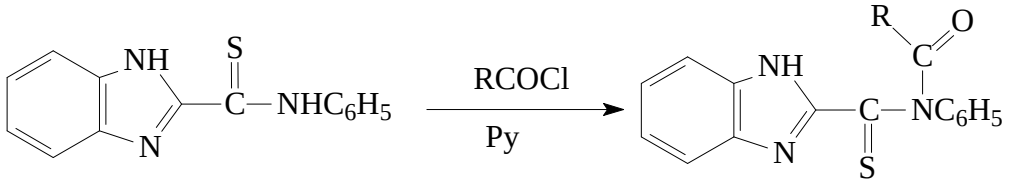
Many drugs (dibazol, medamin, albendazole) found for use in medical practice [1] and in agriculture (olgin, benomyl) in a series of benzimidazole derivatives.

In the literature the reactions (alkylation, carboxyalkylation, acylation) of these compounds at nitrogen atom (or nitrogen atoms), and at aromatic ring were reported.

Furthermore, these compounds are also interesting of a chemical point of view, since there are some reactive centers in their molecule (nitrogen atoms - N-1, N-3, aromatic ring, etc.). The presence of C=S group in position 2, exocyclic amide group to give possibility on currying out reaction with electrophilic and nucleophilic reagents, which in these cases reaction goes in different direction.

Earlier we have studied the reaction of the quinazolone-4-yl-2-thiocarboxylic acid anilide with organic acid chlorides [2].

In this work, we have studied the reaction of benzimidazolyl-2-thiocarboxylic acid anilide with acetyl and benzoyl chloride in the presence of pyridine. The result revealed that the reaction occurs on the exocyclic NH group of thioamide fragment. Apparently, this is due to the direction of the reaction "*hard*" of the acetyl and benzoyl chloride molecules, which attack to exocyclic nitrogen atom, which is a "hard" center of the molecule. The data are in good agreement with of “Hard and soft acids and bases” theory (HSAB).



1 R=CH_3, C_6H_5 **2,3**

Structures of the synthesized compounds were confirmed by IR- and ^{1}H NMR-spectroscopy.

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ULTRASOUND EXTRACTION OF *Alcea* PLANTS

M. J. Rakhmatova[1], B. D. Rakhmonov[2], N. K. Khidirova[1]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: nhidirova@yandex.ru
2) National University of Uzbekistan, Chemical Faculty

Flowers of *Alcea* (*Malvaceae* family) are attractive to investigators due to the rich content on biologically active substances. The analysis of literature showed that chemical composition of *Alcea* roots and flowers is not sufficiently investigated. Furthermore, neutral substances of *Alcea nudiflora* and *Alcea rosea* leaves are not studied. They contain high active polyprenols, sterols, α-tocopherols and etc. [1].

We have isolated extractive substances and sum of neutral compounds of *Alcea* leaves from Namangan and Tashkent regions. Their quantitative and qualitative polyprenol composition was studied by HPTLC and HPLC methods [2].

It was determined 18 unknown terpenoids in *A.rosea* which are differ from that of *A. nudiflora* [3].

Infusion at usual condition and extraction under action of ultra-sound of the sum of neutral substances of *Alcea nudiflora* and *Alcea rosea* leaves were isolated to improve of polyprenol isolation methods. Using of ultra-sound method yielded to increasing of the sum of extractive substances for 19.69% and 31.0%, polyprenols for 26.2% and 19.7%, respectively. The reaction time shortened more than 10–12 times.

Thus, the ultra sound extraction method is more effective to isolate plant polyprenols.

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GROWTH-REGULATORY AND INHIBITORY ACTIVITY OF THE NOVEL QUINAZOLINE THIOAMIDES

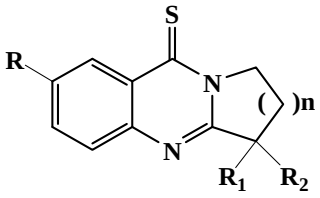
A. O. Nasrullaev, B. Zh. Elmuradov, R. P. Zakirova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: ranozakirova@mail.ru

Studies of the chemical regulation of growth and development of plants is becoming more important practical value as expanding the use of growth regulators in agriculture, new physiological agent with previously unknown spectrum of action.

Currently, it attaches great importance to the development of scientific bases of producing physiologically active substances for agricultural production. The solution of this problem is associated with the identification of the relationship of structure and biological activity of organic compounds. The analysis of this communication allows for planning the synthesis of compounds with the desired properties, which is an important problem of modern organic chemistry.

We studied the growth-regulatory and inhibitory properties of newly synthesized quinazolinethioamides. The evaluation of tested compounds activity was performed by standard methods in bioassays on the seeds of wheat *Moskwich* variety. Seeds were soaked in 0.1%, 0.01% and 0.001% solutions of the compounds for 8 hours, and laid in the Petri dish. Control seeds were soaked in water with a reference drug *Novosil* at a concentration of 0.001%. Experiment was repeated three times.



The maximum growth inhibition was observed for seed treated by compounds NAO-9 and NAO-10 in the 0.01% concentration. Root growth in these cases was by 21.8% and 23.1% lower than the control, and the stem - 15.1% and 22.4%. 0.0001% NAO-15 reduced seedling root growth up to 19.1%, of the stem - 25.6% with respect to control.

Substances under ciphers NAO-30, NAO-40, NAO-42, NAO-65, NAO-77 and NAO-78 showed growth-stimulating activity. The greatest effect of the compounds possessed NAO-30 at a concentration of 0.001% and the NAO-40 in a concentration of 0.0001%.

Compound NAO-40 with a slight inhibitory effects on the first two concentrations on the root and stem growth, however, greatly stimulated the growth of the stem in the processing and concentration of 0.0001% and growth was higher by 13.9% stem, root by 8.1% compared to the control.

ALLOCATION OF GLYCOSIDES IN AERIAL PART OF *Astragalus orbiculatus* PLANT

M. A. Agzamova, I. M. Isaev, R. P. Zakirova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: agzamova_manzura@mail.ru

Plants of genus *Astragalus* (*Leguminosae*) produce cycloartan type methylsteroides. *Astragalus orbiculatus Ledeb.* is a perennial herbaceous plant. It is propagated in Western Siberia and the countries of the Central Asia. Roots of the plant are not rich in cycloartan triterpenoides, whereas in an aerial part of the plant they differ with a noticeable diversity of structures. Among 12 genins and glycosides of cycloartane type isolated from the plant cycloorbicosides A and G were the prevalent compounds. The lanostane type compounds, orbigenin D and orbicoside D, were isolated and described from plant of *Astragalus genus* for the first time.

Earlier the influence of cycloorbicoside G and cyclosiversioside A on metabolic processes in a myocardium of rats has been studied.

In the present research, anatomic-morphological constitution of aerial part of plant *Astragalus orbiculatus* Ledeb was investigated to reveal the sites of accumulation of cycloartane glycosides.

For morphological descriptions of parts of the plant stem leaves were taken from a center stage of propagules. Fixation made in 70% ethanol. Epidermis studied on paradermic and cross sections. Cross sections made through the middle of leaf. Each tissue and epidermis was described according method of Zakharevich S.F. Drugs were prepared by a manual mean, coloration made with methylene blue, with the subsequent sticking up by glycerol-gelatine. Biological microscope was used. Microphotographs made using digital cameras Samsung ES70 and Canon A2300.

The constitution of leaves, petiole of leaves and a caulis of plant *Astragalus orbiculatus* was studied and described. By microscopic examinations it was revealed that bondsare distributed in tissues irregularly. In leaves, inclusions of cycloartane glycosides were found in cells of palisade and a spongy parenchyma, in petiole of leaf, in cells of cortex parenchyma. In tissues of a primary caulis the glycosides are localized in cells of outer 3–4 layers of a primary bark, in tissues of a propagule of II order they are not found.

The description of the constitution of aerial part of the plant will be used for raw materials standardizing.

ENVIRONMENTAL FRIENDLY PREPARATIONS FOR THE PROTECTION OF PLANTS AGAINST SPIDER MITES

O. A. Vlasova, R. P. Zakirova, N. N. Kuchkarova, B. A. Urakov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: ranozakirova@mail.ru

Widespread using of synthetic insecticides and acaricidosis caused problems in plant protection organization and especially the adaptation of herbivore pests to pesticides, disbalance and interactions of living organisms in agrocenosis.

Increased interest to the biologically active substances, first of all, is explained with pressing need to find satisfactory in relation to environmentally friendly for replacing traditional pesticides, which used for controlling harmful pests.

The spider mite is found in all cotton-growing areas of Uzbekistan and is considered one of the major cotton pests.

In the greenhouse conditions, we have researched the toxicity of the aqueous plant extract under the code TN against spider mite *Tetranychus urticae* Koch.

Calculation of biological effectiveness in the experiments was carried out according to the formula of Abbot, which is related to the control.

The experiments were conducted in the greenhouse of the Uzbek Research Institute of breeding, seed production and agricultural technology for the cultivation of cotton line 179 against spider mites. The researching results on the test of plant extract TN on acaricidal activity shown in Table.

TABLE 1. **Acaricidal Activity of Plant Extract TN in Greenhouse Conditions on Cotton**

Variant	Concentration	Average number of spider mite on the leaf			Biological efficacy, %	
		before treatment	after treatment			
			3	7	3	7
Control	–	24	32	43	–	–
Standard entomayt	1.5 l/ha	18	6	0	75	100
TN	5%	38	6	0	88.1	100

Test results have showed that TN extract may be used as an acaricide by spraying of sheet surface plants by 5% aqueous solution against spider mites under greenhouse conditions.

Importantly to notice, that TN drug in 5% concentration is more effective than Entomayt - standard.

POLYPRENOLS OF *Ficus conica*

N. M. Mamatkulova, O. Nigmatullaev, N. K. Khidirova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: nodira66@yandex.ru

Recently the interest to plant polyprenols is increased, and several biologic additives are produced on their base [1, 2]. The polyprenols quantity depended of the variety of *Ficus conica* (Moraceae family) which produced in India and consisted 0.02–0.05% of dry weight of the plant [3]. The aim of our work was to investigate polyprenols of *Ficus conica* of Samarkand and Surkhandarya which is endemic for these regions.

The dried leaves of of two types of these plants collected at maturity period were powdered and extracted four times with 96% aqueous ethanol by infusion method. The sum of extractive substances from Samarkand *F.conica* leaves were isolated with 7.84% (I) yield, while from Surkhandarya – 6.28% (II). Polyprenols fraction were isolated from the sum of extractive substances using column chromotography with *n*-hexane–ethyl ether solvent system by increasing of polarity. A total of 150 fractions were isolated from each plant. Fractions of 50–60 contain polyprenols with 1.22% (I) and 0.98% (II) yields to dry weight of the plant, respectively. The homological composition of polyrenols determined by HPLC were as follows: 3.6% (n=10), 52.4% (n=11), and 43.8% (n=12) for (I), and 9.6% (n=10), 47.8% (n=11), and 42.6% (n=12) for (II).

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STUDY OF PROTECTIVE ACTION OF UCHKUN AGAINST STRESS FACTORS

R. P. Zakirova, N. K. Khidirova, N. M. Mamatkulova, Kh. U. Khodjaniyazov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: ranozakirova@mail.ru

Currently, topical approach in the protection of plants from the effects of adverse conditions and diseases in the modern world practice is the use of preparetions on the basis of secondary plant compounds. Biostimulators activate vital processes in plants, increases resistance to disease and stress.

Plant growth regulator "Uchkun" was created in ICPS AS RUz, stimulates the growth and development of cotton, corn, cereals and other crops [1, 2].

The aim of this work was to study the effect of seed treatment formulation to cotton resistance to infection by the fungus *Fusarium oxysporum* and to salt stress in laboratory conditions.

Seeds of cotton variety C-6524 were treated with 0.001% solution of Uchkun within 6 hours to determine the effect of the preparation on the degree of contamination of sprouts phytopathogen and introduced into Petri dishes on a double layer of filter paper. Control seeds were soaked in water. Preparation "Vitovaks" was used as a reference. Infecting the plants was carried out with a spore suspension of pure culture of *F.oxysporum*, which was obtained by flushing them with sterile distilled water. Counting the number of healthy and diseased plants is carried out at 5-7 days. Salt stress was created by the introduction of 0.75% NaCl solution. Data were processed by mathematical analysis of variance on a computer program Original Pro.

Significant differences in the intensity of the disease symptoms in the control and test plants were observed. The number of infected plants in the experimental version using Uchkun, was lower than the control by 13.4% and amounted to 34.2% and was almost at the level of the reference index to 36.5%.

Seed treatment enhanced the seed germination under saline conditions by 16.2% relative to the control, as well as the accelerated growth of the shoots. The experiments showed the length of the stem and root shoots obtained after treatment with Uchkun exceeded control plants, respectively, 26.3% and 23.5%, and were at the standard level.

Thus, studies have shown that Uchkun reduces the extent of damage of plants by the phytopathogen and contributes to the development of shoots in saline conditions.

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SOME RESEARCH RESULTS AND PROSPECTS OF ALKALOID-CONTAINING PLANTS OF THE CENTRAL ASIA

A. M. Nigmatullaev, K. Tayzhanov, N. I. Mukarramov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan

It is known that alkaloid-carrying plants are sources of high-effective drug compounds.

The first list of alkaloid-bearing plants were given in the works of G. L. Lazurevskiy and A. S. Sadykov (1947), P.S. Massagetova (1932), and Sokolov (1946), which were the results of both the preliminary and deep chemical research. The works devoted to the study of alkaloid-bearing plants of certain regions (Adylov, Atayev, Kholodkovs, Tayzhanov, Gubanov, Kudryashov, Alimbaeva, Arbaeva et al.) appeared later.

I.A. Gubanov (1960) summarized the alkaloid-containing plants of Central Asia. By his estimation, 3500 plants were collected from different regions, 1231 species of them contain alkaloids. Flora of Jungar Alatau and Tien Shan is most studied, 1732 species of plants have been analyzed (Gubanov, 1959, Tayzhanov et al., 1981, Nigmatullaev, Tayzhanov, 1981).

The ICPS AS RUz annually organized expedition to study the flora of Central Asia for alkaloid-containing plants. As a result of research more than 4200 species of plants were investigated (Yunusov, 1981, Aripov, 1993).

During this time, more than 300 species of plants were subjected to deep chemical studies at ICPS AS RUz and more than 1200 alkaloids were investigated, near 600 new alkaloids were related to quinoline, isoquinoline, indole, Amaryllidaceae, steroid, quinozolone, sulfur-containing, diterpene and other classes.

On the basis of the obtained results more than 20 drugs were developed, one of them is allapinine (lappaconitine hydrobromide) which is produced at the Pilot manufacture of the Institute and distributed in Uzbekistan and abroad, as well as more than 120 bioreagents for biomedical research.

It should be noted that not all regions of Central Asia adequately studied in relation to the alkaloid-containing plants. Flora of Pamir, Kopetdag, Kugitang, remnant of the mountains of the desert of Kyzyl Kum and Karakum, Karatau (Syrdarinsky), the Ferghana Valley with its flanking ridges, syrts of Tien Shan were not investigated fully. There are no data on the Aral Sea deserts, the Trans-Caspian and Central Karakum, Moiynkum, Betbakdale, Big Badger and Balkhash-Alakul deserts and others.

PHISICOCHEMICAL PARAMETERS AND FATTY-ACID COMPOSITION OF QUALITY SEEDS OILS OF THE PUMKIN, COMMON FLAX, RAPE, AND SAFFLOWER

N. K. Yuldasheva, N. T. Ul′chenko, R. P. Pirmamedova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: rim.pirmamedova@yandex.ru

The seeds of the pumkin "Spanish" (elite) and the "Palov-Kadu-268" (super-elite) kinds, common flax "Bakhmal-2" and "Bahorikor", rape "Inna" and safflower "Sahro malikasi" (super-elite), "Milutinsky-114" (elite), "Nadir", and "Gallaorol" (super-elite) were investigated.

The content of the oil in the seeds was determined in a Soxhlet apparatus. Lipid extraction was carried out with petrol (b.p. 72–80°C) for 15–18 hours. Hydrolysis of oil, release of fatty acids, their methylation was carried out according to conventional technique [1].

Gas chromatography (GC) of methyl esters and their identification was performed according to [2].

The analysis results showed that the oil content of dry substance of pumpkin seeds in the "Spanish" kind was 36%, and in the "Palov-Kadu-268" -37.2%. In the "Spanish" the content of 18:2 was 48.16%, 18:1+18:3 – 27.86%, unsaturated fatty acids – 76.02%. In the "Palov-Kadu-268" contents of 18:2 – 55.53%, 18:1+18:3 – 29.40%, unsaturated fatty acids – 84.93%.

Oil content in the dry substance of the seeds of the common flax "Bahorikor" achieved 40.6%, and in the "Bakhmal-2" – 41.9%. In "Bahorikor" and "Bakhmal-2" the content of 18:2 was 14.81 and 13.83%, accordingly.The content of unsaturated FA in the "Bahorikor" was 87.37%, and in the "Bakhmal-2" - 86.74%. The content of 18:1+18:3 in both varieties was the same - more than 72%.

Oil content in the dry substance of rape seed variety "Inna" was 47.97%, 18:2 - 18.27%, 18:1+18:3 – 70.32%. The highest safflower seed oil content was observed in "Nadir" kind - 30.6%, the lowest - in "Sahro malikasi" – 26.3%. The maximum amount of 18:2 was observed in "Nadir" – 79.36 %, the lowest - in "Sahro malikasi" – 75.21%. The highest content of oleic acid was observed in "Sahro malikasi" -13.62%, the lowest - in "Milutinsky-114" -11.16%.

The results are of great practical importance for the seed breeding and selection of pumkin, common flax, rape, and safflower.

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COMPONENTS OF *Artemisia persica* GROWING IN UZBEKISTAN

I. D. Sham′yanov[1], R. F. Mukhamatkhanova[1], Kh. M. Bobakulov[1], H. A. Aisa[2], Sh. Sh. Sagdullaev[1], N. D. Abdullaev[1]

1) Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant-inst@rambler.ru
2) Key Laboratory of Plant Resources in Arid Regions, Xinjiang Technical Institute of Physics and Chemistry, CAS, 830011, Urumqi, P. R. China

Artemisia persica Boiss. is a subshrub up to 95 cm growing in Central Asia on stony, gravelly, fine soil-debris slopes, scree, rocks, pebbles in the river valleys, juniper, from the foothills to the upper mountain ridges.

In folk medicine this herb is used as a tonic, antifebrile and anthelmintic remedy.

Previously the essential oils of *Artemisia persica* obtained by hydrodistillation were investigated.

However, the prolonged heating of the plant raw material up to 100°C in the essential oil distillation procedure destroys some natural substances. The main way of artifacts generation is attributed to the hydrolysis of unstable esters. Accordingly, now it is recommended to compare the composition of the essential oil derived from hydro- and steam distillation with the composition of an extract prepared using cold nonpolar solvents (benzene or hexane).

In this regard, this report presents the results of gas chromatography-mass spectral analysis of volatile compounds of hexane and benzene extracts successively obtained from the aerial part of *Artemisia persica* collected in the flowering period in Uzbekistan, in the spurs of the Kurama Range.

In the hexane extract the following compounds were founded (RI, %): (**1**) α-pinene (933, 1.50), (**2**) camphene (948, 0.46), (**3**) (+)-sabinene (978, 0.39), (**4**) 3-carene (1012, 0.79), (**5**) *p*-cumol (1028, 0.59), (**6**) 1,8-cineol (1034, 11.12), (**7**) *trans*-sabinene hydrate (1072, 0.47), (**8**) 1,1-diethoxyhexane (1094, 0.34), (**9**) chrysanthone (1122, 0.60), (**10**) dehydrosabinaketone (1127, 0.47), (**11**) α-campholenaldehyde (1131, 0.77), (**12**) (-)-*trans*-pinocarveol (1146, 1.72), (**13**) *l*-camphor (1151, 36.57), (**14**) (-)-pinocarvone (1169, 1.64), (**15**) (-)-borneol (1174, 14.23), (**16**) *p*-cymen-8-ol (1190, 0.88), (**17**) (-)-myrtenol (1204, 2.05), (**18**) carvacrol methyl ether (1249, 1.10), (**19**) (-)-bornyl acetate (1291, 5.75).

In the benzene extract the following compounds were founded: (**1**) α-pinene (933, 0.59), (**2**) camphene (948, 1.04), (**4**) 3-carene (1012, 0.59), (**6**) 1,8-cineol (1034, 19.59), (**20**) β-thujone (1110, 1.11), (**13**) l-camphor (1151, 45.90), (**15**) (-)-borneol (1174, 12.01), (**19**) (-)-bornyl acetate (1291, 4.26).

In essential oil obtained by hydrodistillation 67 compounds were found, the main ones being (RI, %): (**1**) α-pinene (933, 0.41), (**21**) α-phellandrene (1005, 0.30), (**22**) *n*-cymene (1015, 1.93), (**6**) 1,8-cineol (1034, 2.89), (**23**) artemisia ketone (1048, 14.65), (**24**) α-thujone (1107, 3.72), (**25**) β-thujone (1117, 26.78), (**13**) camphor (1151, 16.61), (**15**) borneol (1174, 3.12), (**26**) piperithone ((1233, 7.26), (**19**) *l*- bornyl acetate (1291, 2.86).

A comparison of the results presented above showed that the greatest amount of volatile compounds are found in the essential oil obtained by the hydrodistillation method in comparison with the method of extraction by nonpolar solvents at room temperature. Probably, the increase of some components in the component composition is associated with the destruction of labile compounds with increasing temperature.

ARTEMISIA JUNCEA VOLATILE COMPONENTS COMPOSITION DEPENDING ON THE ISOLATION METHOD

B. S. Okhundedaev[1], H. M. Bobakulov[1], R. F. Mukhamatkhanova[1], I. D. Shamyanov[1], H. A. Aisa[2], Sh. S. Sagdullaev[1], N. D. Abdullayev[1]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant-inst@rambler.ru
2) Key Laboratory of Plant Resources in Arid Regions, Xinjiang Technical Institute of Physics and Chemistry, CAS, 830011, Urumqi, P. R. China

Artemisia juncea Kar et Kir. (*Asteraceae*) - wormwood sagebrush - a long half-shrub up to 60 cm high, growing in Kazakhstan and Central Asia, including Uzbekistan.

This report presents the results of chromatography-mass spectral analysis of hexane and benzene extracts obtained successively from the aerial part of *Artemisia juncea*, as well as the results of analysis of essential oils obtained by steam and hydrodistillation methods.

In the hexane extract 19 compounds (98.3%) were identified, and 10 compounds (99.7%) were identified in the benzene extract obtained successively after extraction with hexane. Identified components in these extracts are the following (RI): α-thujene (929), α-pinene (936), camphene (952), (+)-sabinene (974), β-pinene (979), α-terpinene (1016), *p*-cymene (1018), *p*-cumol (1024), 1,8-cineole (1029), γ-terpinene (1057), *cis*-4-thujanol (1067), α-thujone (1107), β- thujone (1117), *cis*-sabinol (1140), camphor (1142), α- pinocarvone (1160), *endo*-borneol (1165), 4-terpineol (1176), isoascaridol (1308).

In the essential oil obtained by hydrodistillation, 34 compounds (99.5%) were identified, and 41 (96.5%) obtained by steam distillation. In addition to the above-mentioned basic components obtained during extraction, the following monoterpenoids (RI,%) were detected in essential oils: *cis*-salvene (845, 0.1), tricyclene (925, 0.1), β-myrcene (991, 0.1), α-phellandrene (1005, 0.1), terpinolene (1088, 0.1), α-campholenal (1125, 0.2), 4-acethyl-1-methylcyclohexene (1132, 0.1), *cis*-pinocamphone (1173, 0.2), α-terpineol (1190, 0.2), myrtenal (1193, 0.2), *cis*-carveol (1229, 0.2), cuminyl aldehyde (1239, 0.1), *d*-carvone (1245, 0.6), *cis*-chrysanthenyl acetate (1262, 0.2), bornyl acetate (1285, 0.6), *trans*-sabinyl acetate (1294, 1.0), terpinen-4-acetate (1301, 0.1), δ-terpinyl acetate (1315, 0.1), *trans*-carvyl acetate (1337, 0.1), α-terpinyl acetate (1350, 0.1), *trans*-geranyl acetate (1382, 0.1), 1,3,4-eugenol methyl ether (1407, 0.4), spathulenol (1576, 0.2).

Comparative analysis shows that the component composition of essential oils obtained by steam and hydrodistillation is qualitatively and quantitatively different from the composition of extracts obtained at room temperature.

This is apparently due to the influence of high temperature under steam and hydrodistillation conditions, which causes the destruction of some thermolabile monoterpenoids, for example, such as isoscaridol, 1,8-cineol and others.

USING OF ULTRASONIC WAVES AS PREPARATORY TECHNICS FOR STRENGTHENING ENHANCEMENT OF GROWTH, DEVELOPMENT AND QUALITY OF THE INDUSTRIAL CROPS SEEDS

Sh. H. Rakhimova

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: shahnoza2380@mail.ru

Seeds of high germinating ability are needed for obtaining of a good harvest. For this aim, the seeds before planting were soaked and sterilized to kill harmful microorganisms. Used methods of preparatory treatment has some shortcomings, the main from there is a long time of soak process and impossibility of separation of germinating seeds from unable to germination seeds before their germination. Thus, the improvement and further development of preparatory treatment methods is actual and prospective. Ultrasonic treatment is the used methods for seeds preparatory treatment, but the mechanism of ultrasonic waves influence on the seeds still not studied.

For this study, we have used seeds of industrial crops: wheat, maize, cotton and triticale. Ultrasonic treatment was carried out at the Sonorex RC514, ultrasonic frequency 35 kHz (35000 vibrations per a second) during 10 min. The seeds of the industrial crops were placed into moist medium in the thermostat at 24°C. On the 4^{th} day we measured the length of roots and stems of germinating seeds. As a result, we determined that the preparatory ultrasonic treatment promoted increase of length of roots for 10% and length of stems for 15% in compare to the control seeds.

Experimental investigations carried out at the experiment station determined that the ultrasonic treatment always has a positive influence at the process of seed germination and increase the harvest. The harvests of some industrial crops increased on 20–40% in the average.

Thus, ultrasonic wave application for preparatory treatment of seeds is the most effective methods directed at the enhancement and further development of effective technology for preparatory treatment of seeds to intensify the process of seed germination.

SECONDARY METABOLITES OF *Rudbeckia fulgida*

D. E. Dusmatova, Kh. M. Bobakulov, Kh. A. Rakhmatov, R. F. Mukhamatkhanova, I. D. Sham′yanov, N. D. Abdullaev

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: plant-inst@rambler.ru

Rudbeckia fulgida Aiton. (*Asteraceae*), rudbeckia shiny is a plant of 1.8 m height. It is origin from North America. Currently, it is cultivated in the botanical gardens in Uzbekistan and recommended for floriculture.

This report presents the results of GC-MS analyzes of hexane and benzene extracts obtained from aerial parts of *Rudbeckia fulgida* collected on the experimental field of the Institute during the flowering period.

The hexane extracts of leaves have identified the following components (RI, %): *p*-xylene (867, 5.94), 5,6,7,7a – tetrahydro – 4,4,7a – trimethyl-2(4H)–benzofuranone (1538, 4.58), of flowers - *m*-xylene (853, 5.94), *o*-xylene (875, 5.94), 2-pentylfuran (993, 0.43), β-elemene (1397, 1.17), β-copaene (1424, 3.63), *trans*-α-bergamotene (1437, 6.83), ε-muurolene (1458, 0.98), (-)–germacrene D (1485, 26.12), γ-cadinene (1507, 1.35), (-)-β-sesquiphellandrene (1521, 0.73), kaur-16-ene (1979, 36.48), of the **buds** - *p*-xylene (867, 0.28), *o*-xylene (875, 1.23), 2-pentylfuran (993, 0.35), *trans*-deca-hydronaphthalene (1057, 0,29), *cis*–decahydronaphthalene (1102, 0.53), *L*-α-bornyl acetate (1292, 0.36), (-)-β-cubebene (1398, 0.14), *trans*-β-caryophyllene (1430, 0.49), α-bergamotene (1443, 5.34), γ-cadinene (1524, 0.82), caryophyllene oxide (1577, 3.74).

Unidentified components of the leaves (RI (%): 1556 (11.17), 1581 (7.09), 1612 (23.17), 1646 (12.97), 1681 (16.75) foot up to 71.15%, of the flowers (1458 (2.62), 1821 (6.51)) – 9.13%, of the buds (1480 (2.62), 1545 (2.76), 1558 (2.03), 1607 (8.65), 1614 (7.92), 1638 (6.88), 1650 (3.66), 1684 (12.45), 1726 (27.87), 1925 (8.99)) – 83.83%.

The benzene extracts of the leaves have identified the following components: eucalyptol (1034, 4.56), α-thujone (1110, 0.60), camphor (1150, 0.82), dodecane (1200, 1.14), 1,3,5-triethylbenzene (1226, 0.89), β-bourbonene (1391, 0.96), tetradecane (1400, 1.93), salvial-4(14)-en-1-one (1586, 2.07), dibutyl phthalate (1931, 9.62), of flowers - eucalyptol (1034, 1.24), (+)-camphor (1150, 0.59), dodecane (1200, 0.97), 1,3,5-triethylbenzene (1226, 0.67), tridecane (1300, 0.59), tetradecane (1400, 3.21), salvial-4(14)-en-1-one (1589, 6.17), (-)-alloaromadendrene (1618, 1.72), of the buds - eucalyptol (1034, 0.90), tridecane (1300, 0.21), (+)-cycloisosativene (1374, 1.15), tetradecane (1400, 1.13), 2-(2-methyl-2-vinylcyclopropyl)furan (1617, 0.87), 1-methyl-2-methylene-3,5-divinylcyclohexane (1672, 21.57), ledane (1785, 1.13), dibutyl phthalate (1936, 6.30).

Unidentified components of the leaves (RI (%): 1582 (3.00), 1606 (3.60), 1624 (4.86), 1641 (4.30), 1671 (54.08), 1802 (3.99)) reached to 73.83%, of the flowers (1526 (2.85), 1601 (3.13), 1625 (8.14), 1641 (3.81), 1673 (36.58), 1773 (4.23), 1940 (6.62), 1977 (8.16)) – 72.81%, of the buds (1552 (2.38), 1578 (4.64), 1588 (3.91), 1606 (7.80), 1625 (5.11), 1640 (5.25), 1718 (2.47), 1742 (3.09), 1754 (10.18), 1813 (6.78), 1840 (5.31)) – 56.92%. All compounds above were identified in the aerial part of *Rudbeckia fulgida* for the first time.

VOLATILE COMPOUNDS OF CULTIVATED *Inula caspica*

D. E. Dusmatova, Kh. M. Bobakulov, Kh. A. Rakhmatov, R. F. Mukhamatkhanova, I. D. Sham′yanov, N. D. Abdullaev

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: plant-inst@rambler.ru

Inula caspica Blum ex Ledeb (*Asteraceae*) is a plant of 65 cm height growing in the Central Asia, including Uzbekistan. The plant produces the bioactive sesquiterpene lactones. In folk medicine an infusion is used as an expectorant. Sesquiterpenoids sum exhibited antibacterial activity [1].

This report presents the results of GC-MS analyses of hexane and benzene extracts obtained from aerial parts of *Inula caspica* cultivated on an experimental field of the Institute.

The extracts were analyzed with an Agilent 7890A GC gas chromatography equipped with Agilent 5975C inert MSD quadrupol-mass spectrometer as detector. Separation of the components mixture made on a quartz capillary column HP-5MS (30 m × 250 μm × 0.25 μm) grafted in the temperature range: 50°C (2 min) – 10°C / min to 200°C (6 min) – 15°C / min, to 290°C (15 min). The volume of the sample was 1 μl (hexane, benzene), the mobile phase flow rate of 1.3 ml/min. The components were identified by retention times and mass spectra using W8N05ST.L and NIST08 library.

The hexane extracts of the leaves have identified the following components (RI, %): dodecane (1200, 1.46), tetradecane (1400, 0.83), (R)-dihydroactinidiolide (1535, 2.09), (-)-caryophyllene oxide (1577, 12.61); of the flowers - *o*-xylene (862, 11.51), 2-nonanone (1095, 3.87), dodecane (1200, 0.30), 2-undecanone (1297, 0.68), (-)-germacrene D (1484, 2.20), 4-hydroxy-3,5-dimethoxy-benzaldehyde (1697, 4.29); of the buds - *o*-xylene (862, 2.88), 2-nonanone (1097, 1.37), 3-allyl-2-methoxyphenol (1372, 1.58), (-)-germacrene D (1486, 1.05), isoalantolactone (1925, 46.10). Unidentified components of the leaves (RI (%): 1202 (3.67), 1627 (3.75), 1634 (5.98), 1672 (6.68), 1688 (9.12), 1746 (4.31), 1810 (8.26), 1889 (12.54)) foot up to 54.31%, of the flowers (1651 (3.44), 1673 (4.56), 1710 (14.46), 1772 (8.33), 1805 (22.35), 1843 (8.08), 1941 (3.80)) – 65.02%, of the buds (1680 (9.72), 1784 (8.88), 1824 (14.11)) – 32.71%.

The benzene extracts of the leaves have identified the following components (RI, %): eucalyptol (1034, 6.74), 1,2-diethylbenzene (1054, 1.30), α-thujone (1110, 2.20), β-thujone (1121, 0.62), camphor (1150, 2.02), dodecane (1200, 1.25), 1,3,5-triethylbenzene (1226, 1.28), tetradecane (1400, 3.01), (R)-dihydroactinidiolide (1534, 2.77), hexadecane (1600, 2.41)., of the flowers - α-pinene (935, 1,51), eucalyptol (1034, 18.74), camphor (1151, 2.36), 4-hydroxy-3,5-dimethoxy-benzaldehyde (1697, 56.04). Unidentified components of the leaves (RI (%): 1060 (2.23), 1491 (2.29), 1671 (2.54), 1766 (3.97), 1802 (22.37), 1826 (4.95), 1881 (17.53), 1928 (7.26)) foot up to 63.14%, of the flowers (1741 (2.63), 1932 (14.46)) – 17.09%.

The above compounds were identified in the aerial part of *Inula caspica* for the first time.

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HAEMOSTATIC ACTION OF FLAVONOID SUM FROM PLANT *Polygonum aviculare*

N. A. Yunushodjaeva

Tashkent Pharmaceutical Institute, Health Ministry, Republic of Uzbekistan

Some herbs such as: leaf of *Urtic*a, herbs of *Achillea* and *Persicaria hydropiper*, crust of *Viburmum*, flowers of *Arnica*, herb of *Persicaria maculosa*, crust and fruit of *Berberis* and herb of *Lagochilus inebrians* used as haemostatic remedy at different hemorrhages. Extracts or tinctures of these herbs used orally as herbal medicines.

Plant *Polygonum aviculare* or goose herb is well-known haemostatic remedy. The aim of this investigation was to study of mechanism of haemostatic action of flavonoid sum from plant *Polygonum aviculare*.

Experiment was carried out using white mice and rats of both sexes weighting 20 ± 2 g and 160 ± 20 g, accordingly, and gray rabbits of weight 2.5 ± 0.2 kg. Influence of flavonoid sum at the process of blood coagulation has studied by method of thromboelastogram recording and vascular-platelet hemostasis by evaluation of haemorrhage time and quantity of blood loss, capillary permeability, quantity and functional activities of platelets (adhesion, aggregation, clot retraction).

Results of investigations shown that haemostatic action of *Polygonum aviculare* depend from presence of flavonoids. From thromboelastogram we can see that the maximal haemostatic effect at the intravenous injections of flavonoid sum from plant *Polygonum aviculare* at a dose of 1 mg/kg in the rabbit appeared in 30 min. So, the time reaction, R, reflecting the speed of thromboplastin formation decreased from 45 ± 4.0 to 10 ± 1.0 min, or for 4.5 times: index K, the time of clot formation, decreased from 27 ± 1.7 to 7 ± 0.6 min, or for 3.9 times. At that, hypercoagulation index C_i increased for 3.4 times. Study of flavonoid sum influence on the vascular-platelet hemostasis shown that the drug at a dose of 1mg/kg increased resistance of capillaries of mouse on 53%, that is close to the action of rutin and vitamin P at the doses of 3 and 5 mg/kg (40–47%). The flavonoid sum from *Polygonum aviculare* at the doses of 2 and 4 mg/kg at the intraperitoneal injection to rats decreased time of haemorrhage and quantity of blood loss in 60 minute for 2-4 times. Research of quantity of platelets and their functional activities in rabbit showed that tincture of *Polygonum aviculare* increases quantity of platelets from 400 ± 14 to 800 ± 20*109/l, or on 100% in 60 min. The time of clot retraction decreased from 13 ± 0.8% to 7 ± 0.6 % (42%). Platelets adhesion increased from 20 ± 1.0% to 38 ± 4.0% (90%), and spontaneous aggregation increased from 25 ± 1.4 to 44 ± 2.6% (76%). Thus, the sum of flavonoids from *Polygonum aviculare* influences at I and II phases of blood coagulation – thromboplastine generation, increases thrombin activity and possibly influences at the anticoagulants. Maximal action time started in 30 min, duration of action was more 2 hours. The mechanism of action of plant *Polygonum aviculare* tincture is attributed to their influence at the vascular-platelet haemostasis.

LIPIDS OF KERNELS OF SOME PLANTS FRUITS

N. K. Yuldasheva[1], N. T. Ul′chenko[1], G. Pardaev[2], R. Normachmatov[2], A. N. Aripov, A. I. Glushenkova[1]

1) Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail**:** nigorayuldasheva@rambler.ru
2) Institute of Economic and Service of Samarkand

At the present study for the first time results of analysis of polar lipids of kernels of fruits of the *Pistacia vera* sort "*Nastoyashchii*" collected in the Samarkand region, of the walnut sort "*Yubileinyi*" growing in the Surchandar'ya region, and the almond sort "*Dessertnyi*" growing in the Namangan region are presented.

Neutral lipids (NL) were isolated by benzene ($t_{boil.}$ 72–80°C) in the Soxhlet apparatus, the obtained cake dried and the sum of polar lipids (PL) isolated using mixture of chloroform-methanol (2:1).

Polar lipids separated by CC on the silica gel on NL, glycolipids (GL) and phospholipids (PhL), successively using chloroform, acetone and methanol. The yields of lipids presented in the Table 1.

TABLE 1. **Content NL and PL of Kernels of Fruits of Pistacia (I), Walnut (II) and Almond (III), % of Mass**

Lipids	I	II	III
Neutral	53.71	67.07	56.23
Glycolipids	0.24	0.23	0.10
Phospholipids	0.37	0.55	0.47

From the Table 1 we can see that GL predominated in kernels of fruits of walnut and pistacia, and the yield of PhL from walnut and almond was the highest. The composition of polar lipids was established by analytic TLC on the silica gel using known systems of solvents and specific developers [1].

Principal components of GL of all samples were sterilglycosides, monogalactosildiacylglycerides and digalactosildiacylglycerides were minor components. Phosphotidilcholins are predominated in phospholipids of kernels of fruits of almond and walnut, and in the phospholipids of pistacia phosphotidilinosites and phosphotidilcholines presented almost equally.

In the composition of phospholipids of all kernels phosphotidilethanolamines presented in the trace quantity.

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LIPIDS OF *Stachys lanata* SEEDS

Sh. K. Khidoyatova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: shaxnoza_karimova_80@mail.ru

Stachys lanata Jacq., a perennial ornamental herb (*Lamiaceae* family) grows in the Europe, Caucasia, and Iran. It is a stranger species in Uzbekistan.

We have investigated lipids from the seeds of this plant collected in the Tashkent oblast in 2015.

Free lipids (FrL) were isolated from the seeds by infusion with benzene yielding 22.15% moist weight of seeds. 1.18% fixed lipids (FL) were isolated from the reminder with chloroform-methanol mixture. FrL extract subjected to CC on silica gel to afford neutral lipids (NL), glycolipids (GL) and phospholipids (PhL), 0.4; 0.62 and 0.16%, accordingly.

Lipids have subjected to TLC with silufol and silicagel in the known solvent systems, and NL, GL, and PhL identified with specific reagents and compared to known substances and the literature.

Triacylglycerols, esters of fatty acids (FA), free FA, hydrocarbons, phytosterols and chlorophylls found in NL composition of *S. lanata*. GL contained sterol glycoside esters, sterol glycosides, cerebrosides, digalactosyldiacylglicerols. PhL contained much phosphatydilinositols, and fewer phosphatidylethanolamines and phosphatidylcholines.

Free lipids of *S. lanata* had an oscillation band in IR-spectrum at 1960 cm^{-1} attributed to allenefroup of laballene fatty acid that is distinctive of *Stachys* genus of *Lamiaceae* [1].

Fatty acids were isolated from FL with an alkaline hydrolysis. Then they were treated with diazomethane to afford methyl esters, and the composition and content was determined by GC. The results represented in the table below:

TABLE 1. **Fatty-Acid Composition of *Stachys lanata* Seed Lipids, GC, % of mass**

Fatty acids	16:0	18:0	18:1	18:2	18:3	$\sum_{sat.}$	$\sum_{unsat.}$
Free lipids	5.00	2.30	21.13	70.70	0.87	7.30	92.70

Therefore, FA of *Stachys lanata* seeds contained 22.15% lipids enriched with ω-6 linoleic acid.

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OIL OF SEEDS OF *Salvia hispanica* CULTIVATED IN UZBEKISTAN

N. K. Yuldasheva[1], N. T. Ul′chenko[1], S. D.Gusakova[1], K. A. Tokhtakhunov[2], M. M. Muminov[3]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: s.gusakova2004@mail.ru
2) Tashkent State Technical University
3) Andijan State University

Salvia hispanica of *Lamiaceae* family (chia) is known as a rich source of a protein, food fibers, and ω-3 linoleic acid. *S. hispanica* seeds contain a mixture of phenolic antioxidants that makes the chia oil more tolerant to oxidation in compare to a flax oil. In the USA, Canada and other countries *S. hispanica* seeds used in a production of food additives, candies, and babies nutrition products [1].

It is known, that the *S. hispanica* seeds composition depends on their color (black or white), location and period of collection.

We have investigated black seeds of cultivated in Uzbekistan *S. hispanica* collected in 2015. Moisture of seeds (I) was 5.7%. The oil was extracted from grounded seeds with benzene ($t_{boil.}$72–76°C) in the Soxhlet apparatus. Oil yield (on dry mass) was 34.8%. Fatty acids were isolated by alkaline hydrolysis and then were transformed into methyl esters (ME) with diazomethane.

ME of fatty acids was analyzed by GC on a Chrom-5 device with plasma-ionization detector, steel column (2.5 m × 4 mm) filled with Chromaton-N-AW with 15% Reoplex-400, temperature 192°C, N_2 as a carrier gas. Results represented in the table below.

TABLE 1. **Fatty-Acid Composition of Seed Oil of *S. hispanica*, GC, % of mass**

Oil	Fatty acids*									
	16:0	16:1	18:0	18:1	18:2	18:3	20:0	20:1	$\sum_{sat.}$	$\sum_{unsat.}$
	7.87	0,08	3.23	7.46	18.09	62.45	0.36	0.20	11.72	88.28

*Content of the rest acids: 14:0-0.06%; 22:0-0.1%; 24:0-0.1%

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INTRODUCTION EXPERIENCE OF *Onopordum acanthium* AND *O. olgae* IN TASHKENT

B. A. Nigmatullaev

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan

Onopordum acanthium and *O. olgae* are biennial herbaceous prickly plants to 150–200 cm tall with spindly, branched root of the *Asteraceae* family. This plant is often confused with the thistle, which it resembles only its flowers but not the stems, not leaves and its curative effect.

They grow in the European part of Russia, Baltic region, Northern part of Central Asia and the Caucasus. They are growing like weeds near roads and housing in Uzbekistan, mainly distributed in Tashkent, Samarkand and Surhandarya regions and Karakalpakstan. It is a common weed in cultivated areas.

Flower baskets and leafy shoots of plants used in folk medicine for the treatment of malignant tumors and purulent wounds. Thistle preparations exhibit low toxicity. They possess cardiotonic effect, increases the strength of cardiac contractions, narrow peripheral blood vessels, increases blood pressure, have hemostatic and bactericidal action.

Seeds contain fatty oil (30–35%) and alkaloids (0.1%); alkaloids found in the leaves (0.05%) and sesquiterpene lactone arkciopicrin.

Planting in the ground carried out in early August (01.08.). Seedlings appeared in 15 days after sowing in mid-August. Dirt germination was for *Onopordum acanthium* 82%, and 25% for *O. olgae*.

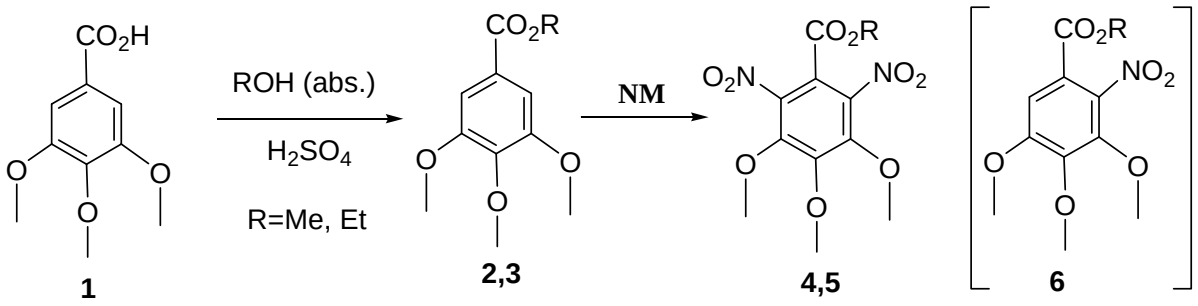
Cotyledon leaves are egg-shaped, 1.5 cm length, 1 cm width. The first pair of true leaves began to appear on the 20th day after germination. In beginning of October, there were three pairs of true leaves. The length of these leaves was 1–2 cm, width 0.8 cm. The leaves remain green until the spring. Re-growth of overwintered plants began in spring 2016 in late March, and in early April began to grow rapidly, and in the end of May reached their height up to 180 cm, length of the sheet was 15 to 35 cm, width 15-20, and the petiole length 5–15 cm depending on the position on the stem. Budding of plants observed by us in April, flowering – in May, fruits in May-June. The seeds are ripe. Thus, *Onopordum acanthium* and *O.olgae* in culture (Tashkent) passes the full cycle of development.

TARGETED SYNTHESIS OF THE DERIVATIVES OF TRIMETHOXYBENZOIC ACID

M. I. Olimova, R. Ya. Okmanov, B. Zh. Elmuradov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: b_elmuradov@mail.ru

3,4,5-Trimethoxybenzoic acid (TBA, **1**) and its derivatives are a good synthons for introduction of TBA residue into molecules of organic compounds. There are preparations which possess high pharmacological activity [1]. With purpose to obtain TBA derivatives we carried out synthesis of some derivatives of **1** – methyl and ethyl esters of TBA (**2**, **3**) and dinitro-products (**4**, **5**):



Etherification was carried out with absolute methanol and ethanol in the presence of sulphuric acid, nitration of the obtained esters was conducted with nitrating mixture (**NM**, mixture of nitric and sulphuric acids); wherein the dinitro- derivatives (**4**, **5**) were synthesized in good (60-65%) yields. Formation of mono-nitro products was not (**6**) observed. Structure of the TBA methyl ester (**4**) is shown in Fig. 1.

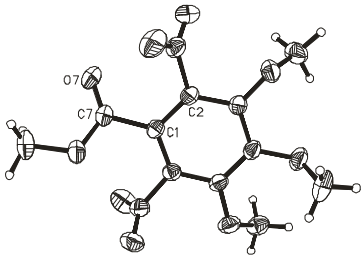


Fig. 1.

XRD results showed that the unit cell in the crystals of 2,6-dinitro-3,4,5-trimethoxybenzoic acid methyl ester (**4**) in an independent part contains 1 and 2 molecules, respectively. Location of nitro and methoxy groups relative to the aromatic ring in the studied crystal structure is the same. As seen from the figure, the nitro group at positions C2 and C6 are not involved in conjugation of p-electrons of aromatic ring.

Structure of the synthesized compounds was confirmed by physical methods of research (mass-, IR-, ^{1}H NMR, X-ray).

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CHARACTERIZATION OF THE PROTEINS OF VALNUT, ALMOND AND PISTACHIO CULTIVATED IN UZBEKISTAN

Sh. Kh. Rakhimova[1], L. G.Mezhlumyan[1], Sh. Sh. Sagdullaev[1], R. Normakhmatov[2], G. Pardaev[2]

1) Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: shahnoza2380@mail.ru.
2) Samarkand Institute of Economy and Service

Nuts are promising plant source of a wide range of biologically active additives production. Lipids and proteins are main components of nut kernels. The aim of this work was the investigation of the chemical composition and nutrition value of nut kernels.

We investigated the walnut ("Yubileyniy" kind, Surkhandariya oblast), almond ("Desertniy" kind, Namangan oblast), and pistachio ("Nastoyashiy", Kattakurgan oblast).

Main physical characteristic represented in Table 1.

Table 1**. Main Parameters of Average Mass, Kernel Content and Moisture**

No.	Kind of nut	Average mass, g	Kernel content, %	Moisture, %
1	Walnut "Yubileyniy"	13.85	44.63	3.67
2	Almond "Desertniy"	1.42	53.4	3.58
3	Pistachio "Nastoyashiy"	0.93	44.7	6.94

Moisture content was determined by the product sample drying in a drying oven at (105 ± 2)° C till reaching a constant mass.

Crude protein (mass fraction) was determined by Kalkar method spectrophotometrically, and by Kjeldahl method calculating the total nitrogen concentration, and its multiplication on the recalculation coefficient: 5.30 for walnut and pistachio; and 5.18 for almond [1].

It was established that the walnut kernels contain 22.7% protein, almond – 22.95%, and pistachio – 27.01% [2].

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PROTEOLYTIC ENZYME INHIBITORS APPLICATION IN MEDICINE

L. G. Mezhlumyan

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail:mezhlumyan1952@mail.ru

Proteolytic enzyme inhibitors widely used in medicine in acute inflammatory states such as septic shock or pancreatitis. Mechanism of the interaction attributed to inhibition the overactive proteolytic enzymes occurring in inflamed tissues, as well as at intensive cell divisions in tumors. A number of proteolytic enzyme inhibitors used in a treatment of neoplastic transformations. Proteolytic system activation is a general link in neoplastic transformation development (Ogloblina O.G. and Aref'eva T.I., 1994; Ferreras M. et al., 2000, DeClerckeY.et al., 2004). Invasive growth is possibly connected to the malignant cells ability to synthesize cysteine, serine and aspartyl proteinases (Levicar N. et al., 2003). It was established that different inhibitors limited a proteolytic activity and inhibited the invasion and metastasis (Turk B. et al., 2002; SeverN. Et al., 2003).

We investigated the grain of local wheat kinds: Chillaki, Ravi, and Oq Marvarid. Bifunctional inhibitors of trypsin and subtilysin were isolated from these kinds of wheat, their molecular masses, amino-acid composition, and inhibitory activity determined. The obtained proteins were given to the Laboratory of Molecular Genetics to determine their cytotoxicity on HeLa, HEp-2, HBL-100, and hepatocytes. The proteinase inhibitor from Oq Marvarid was the most promising and shown the selective cytotoxicity on HeLa cells. It was non-cytotoxic for non-malignant liver cells - hepatocytes.

EFFECTS OF *Scutellaria iskanderi* L. TINCTURE ON THE CENTRAL NERVOUS SYSTEM OF MICE

A. N. Nabiev, N. A. Yunuskhodjaeva

Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan,
e-mail: yunusxodjaeva-n@ mail.ru

Tincture of the plant *Scutellaria iscanderi* L., Labiatae family, used for heart diseases treatment in the Chinese folk medicine (Bazaron, Aseeva, 1984; Minaev, 1991; Corr et al, 2003). *Scutellaria baicalensis* roots tincture in Russia applied to relieve stress, neurosis and reduce high blood pressure. *Scutellaria* plants are widespread in Uzbekistan and now are active investigated. *S. iscanderi* L. is an endemic species growing in Uzbekistan. In the present study, the tincture of *S. iscanderi* L. effects on the function of the central nervous system of mice is investigated. The tincture prepared in accordance with the State Pharmacopeia X1 with 70° ethanol in a ratio of 1 part of ethanol per 5 parts of the herb.

Pharmacological research of dealcoholized tincture of *S.iscanderi* with a method of Lapin showed that it reduces the motor activity of mice from 30 to 50% at doses of 0.2 and 0.4 ml, respectively. This effect prolonged from one to five hours. The depressing effect of the motherwort tincture in these conditions was 20-32%, and its development differed from that for *S. iscanderi* and prolonged for 2-3 hours. A combination of sodium ethaminal and *S. iscanderi* tincture on the hypnotic effect showed that the test mice treated with an *S. iscanderi* solution at a dose of 0.2 and 0.4 ml per a mouse were in the lateral position for up to 127 minutes (5 of 5) and 205 minutes (5 of 5), i.e. for 2 and 4 times greater, respectively, than that in the control group, in which the average sleep duration was 56 minutes. It seems, the tincture may act on the stem of the brain structures of mice. Study of the anticonvulsant action of *S. iscanderi* tincture on the model of pentylenetetrazole convulsions demonstrated that the oral administration of the test solution prevents the convulsions in 60% and death in 80% mice. A similar effect is observed in strychnine convulsions.

Conclusion. *S. iscanderi* solution depresses the motor activity of mice, enhances the soporific effect of stem drug ethaminal sodium and prevailed the effects of motherwort. *S. iscanderi* solution antagonizes to a convulsive action of pentylenetetrazole and strychnine.

ACYCLIC ALCOHOL FROM THE AERIAL PART OF *Seseli korovinii*

E. Kh. Khalilova[1], N. Yu. Beshko[2]

1) Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: elik_ch@rambler.ru
2) Institute of Botany and Zoology of the Academy of Science of the Republic of Uzbekistan

Plants of *Apiaceae* family are widespread in the Uzbek flora; the *Seseli* genus is considered the promising in every respect. In spite of many chemical investigations of the chemical composition of *Seseli* genus, there are some species not investigated in chemical and biological aspects, in particular, *Seseli korovinii* Schishk. We have investigated earlier the volatile compounds of the aerial part of *S. korovinii* by chromato-mass-spectral analysis. Continue the phytochemical investigation of *S. korovinii*, we successively extracted the aerial part with hexane, benzene (to remove the hydrophobic compounds), and 96% ethanol. From the alcohol extract we have isolated a crystalline substance $C_6H_{14}O_6$, mp 168^oC, which was identified as six-atom acyclic alcohol mannitol widely used in medicine as a diuretic, and in pharmaceutical (an additive) and food industry (a sweetener). Mannitol was isolated from *S. korovinii* for the first time. *S. korovinii* is a promising source of the biologically active acyclic alcohol.

BIOLODICAL ACTIVITY OF THE SOLUBLE PROTEIN FRACTIONS ISOLATED FROM THE MAIZE AND WHEAT GRAIN

N. V. Korablyova, Sh. Kh. Rakhimova, L. G. Mezhlumyan, V. N. Syrov

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: korablyovan@ mail.ru, shahnoza2380@mail.ru

The soluble fraction of proteins was isolated from wheat and maize grain using a buffer containing 0.8 M NaCl, 10 mM K_2HPO_4, and 1mM EDTA. Further purification of the soluble fraction was performed using 50 mM Tris-HCl. By electrophoresis with 15% SDS we found that the fraction consists of 12 protein components with molecular weights of 6–98 kDa. The amino acid ratio in this fraction was dominated by asparagine, arginine, glutamine and leucine.

In the experiments on biological activity, it was determined the effect of the soluble fraction on some parameters of lipid and carbohydrate metabolism in rats. Male rats weighing 180–200 g were used in the experiments. The substances were administered orally at a dose of 10 mg/kg. A total cholesterol, triglycerides, glucose and total lipids were determined in the rat serum, glycogen content in the liver.

The results showed that the soluble fractions of wheat and corn grain have a certain cholesterol-lowering and hypoglycemic effects. Thus, in rats receiving the soluble fraction of proteins isolated from the corn, serum cholesterol content was 32.6% less than in the control, the effect of the soluble fraction isolated from the wheat was18.8%. Serum triglyceride levels were also significantly lower than the control values, for the soluble protein fraction of maize 28.6%, and for that of wheat 13.2%. The total lipids were reduced by 49.9% when the soluble protein fraction of maize applied, and by 11.1% – for the one of wheat. Use of the soluble proteins fractions of maize and wheat in the experimental conditions contributed a noticeable decrease in blood glucose levels: 56.2% and 43.6%, respectively. It was noted the glycogen-preserved effect in the rat liver. When administered the soluble protein fractions of maize and wheat, the glycogen contents in rats were 92.6% and 79% higher than in the control animals, respectively.

Thus, the soluble protein fraction has hypoglycemic and hypocholesterolemic effects.

FLAVONES OF AERIAL PART OF *Scutellaria cordifrons*

B. S. Ohundedaev[1], R. A. Husainova[2]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: boxundedayev@mail.ru
2) Tashkent Pharmaceutical Institute, Oybek st., 45, Tashkent, 100015,
the Republic of Uzbekistan

Genus of *Scutellaria* L. (*Lamiaceae* family) in the Flora of Central Asia presents 120 species, of which 32 species are grown in Uzbekistan [1, 2].

Plants of the genus *Scutellaria* L. are used in traditional medicine in nausea, dyspepsia, gastrointestinal disorders, hypertension, ascites, malaria, bleeding, acute respiratory infections, heart disease, rheumatism, headache, and respiratory diseases. In scientific medicine they are used for atherosclerosis, insomnia and nervousness combined with high blood pressure, heart rhythm disorders, and inflammation of the heart muscle [3, 4].

Nowadays only roots of *Scutellaria cordifrons* Juz. grow in Uzbekistan are used in medicine. It was shown that they contain the aglycone and glycosylated flavonoids [5], and the aerial part of the plant has not been explored.

We have continued the study of the phenolic compounds composition from aerial parts of this plant species.

The dried and crushed aerial parts of the plant *Scutellaria cordifrons* collected in the flowering phase of Tashkent region, were extracted with 70% aqueous alcohol, after removing alcohol aqueous of residue was treated sequentially with chloroform, ethyl acetate, and *n*-buthanol. The ethyl acetate fraction was chromatographed on a column with silica gel (150/300 mesh) and several fractions each contains a variety of polyphenols received. Then these fractions were re-chromatographed on a column with the adsorbent Sephadex LH-20. As a result, two flavonoids isolated and identified by a direct comparison of UV- and IR-spectra with those of standard samples. They were identified as 5,7,3′,4′-tetrahydroxyflavon (luteolin) (1) and 5,6,7-trihydroxyflavon (baicalein) (2).

These flavonoids were isolated from this plant species for the first time.

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PHENOLIC COMPOUNDS FROM AERIAL PARTS OF *Polygonum coriarium*

S. Z. Nishanbaev, Kh. M. Bobakulov, I. D. Sham′anov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: sabir78@rambler.ru

We have continued study of the chemical composition of phenolic compounds from aerial parts of *Polygonum coriarium* Grig.

The dried and grinded aerial parts of the plants collected in the phase of flowering in the Pskem river ravine of the Tashkent region, were extracted with 70% aqueous alcohol, and after removal alcohol the aqueous residue was sequentially treated with chloroform, ethyl acetate and *n*-butanol. The ethyl acetate fraction was chromatographed on a column with silica gel (50/300 mesh), and several fractions containing various phenolic compounds obtained. Then, these fractions were subjected to re-chromatography on a column with Sephadex LH-20. As a result, two phenolic compounds **1** and **2** were isolated.

Compound 1. Amorphous white powder, $C_9H_8O_2$, mp 131–133°C. UV-spectrum (C_2H_5OH, λ_{max}, nm): 215, 270. IR-spectrum (KBr, ν, cm^{-1}): 2920–2650 (hydroxyl groups), 1683 (–C=O), 1630 (C=C), 1608, 1594 (benzene ring). ^{1}H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 6.41 (1H, d, J = 16.0, H-8), 7.33 (3H, m, H-3, 4, 5), 7.51 (2H, m, H-2, 6), 7.61 (1H, d, J = 16.0, H-7). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 119.44 (C-8), 129.30 (C-2, 6), 130.11 (C-3, 5), 13152 (C-4), 135.90 (C-1), 146.45 (C-7), 170.47 (C-9).

On the basis of UV, IR, NMR spectra data, as well as comparing the physical-chemical constants with described in the literature [1] the compound **1** was identified as cinnamic acid.

Compound 2. White crystalline powder with a reddish tinge, $C_{10}H_8O_4$, mp 204–206°C. In the UV spectrum of compound has absorption maxima at 256, 300, 315, and 340 nm. In the IR spectrum (cm^{-1}) absorption bands at 3300–3350 (OH), 2930, 2845 (-OCH_3), 1708 (>C=O), 1612 (C=C) were observed. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.82 (3H, s, OCH_3), 6.22 (1H, d, J = 9.4, H-3), 6.78 (1H, s, H-8), 7.22 (1H, s, H-5), 7.91 (1H, d, J = 9.4, H-4), 10.29 (br.s, OH). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 55.99 (CH_3), 102.74 (C-8), 109.58 (C-5), 110.51 (C-10), 111.67 (C-3), 144.44 (C-4), 145.21 (C-6), 149.47 (C-9), 151.09 (C-7), 160.61 (C-2).

On the basis of the spectral data analysis and comparison with those described in the literature the compound **2** was identified as 7-hydroxy-6-methoxycoumarin (scopoletin) [2].

These biologically active phenolic compounds were isolated from the aerial parts of the *Polygonum coriarium* Grig. for the first time.

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INVESTIGATION OF DEUTERIUM EXCHANGE OF α-METHYLENE GROUP PROTONS OF MACKINAZOLINONE BY ^{13}C NMR SPECTROSCOPY

M. G. Levkovich, B. Zh. Elmuradov, Kh. M. Shakhidoyatov, N. D.Abdullaev

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: b_elmuradov@mail.ru

By ^{13}C NMR spectroscopy methods an exchange kinetics of the hydrogen atoms of the mackinazolinone α-methylene groups on deuterium in CD_3OD have been studied. It was revealed additional details of the process kinetics. In particular, it succeeded in isolating two occurring at different rates exchange process. In the first stage takes place replacement of the first methylene group proton, and in the second stage - the second proton. The second process is a delay relative to the first stage.

In [1, 2] it has been described rather unusual chemical process, an exchange in the CD_3COOD and CD_3OD; in this case takes place exchange of the α-methylene group protons of mackinazolinone and its analogues on the deuterium atoms.

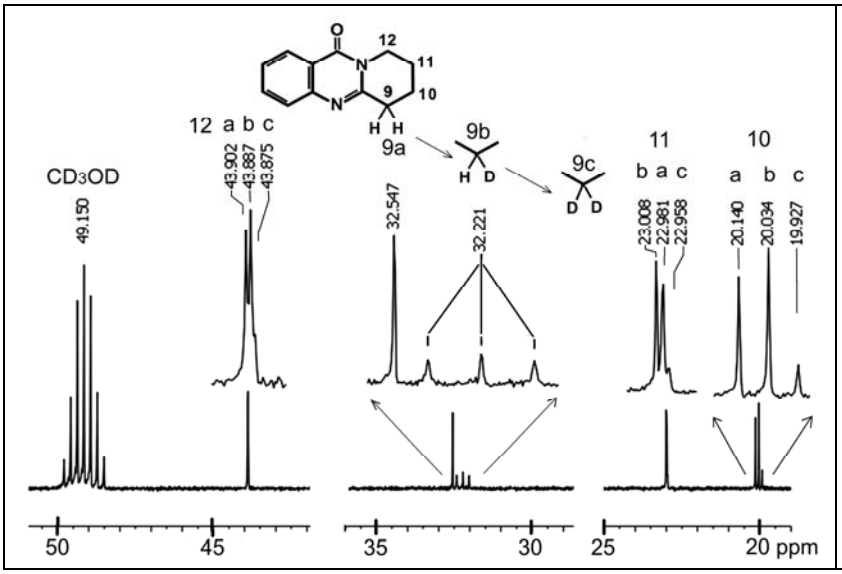

Fig. 1. ^{13}C NMR-spectrum of the aliphatic part mackinazolinone in CD_3OD in partial (42%) the exchange of H-9 methylene protons on deuterium atoms.

Deuterium exchange time in the graph is equal to 186 days.

In order for the registration of the ^{13}C NMR spectrum proved significantly lower than the observed kinetic processes, the slowest process of deuterium exchange of mackinazolinone has been chosen: it is dissolution in the pure CD_3OD [1, 2]. Deuterium exchange process was monitored for 6 months according to the ^{13}C NMR and ^{1}H NMR signals of the H-9 methylene group. The integrated intensity of the H-9 signal during this period declined from 100 to 58%.

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EVALUATION OF AGGREGANT PROPERTIES OF STACHYDRINE ALKALOID

V. N. Axmedov, R. A.Botirov, Z. A. Khushbaktova, A. Z. Sadykov, Sh. Sh. Sagdullaev

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: vokhidzhon.akhmedov.1984@mail.ru

The Central Asian flora is rich of wild medicinal plants, one of them is *Capparis spinosa* (caper), Capparidaceae, growing in Zhizzakh, Tashkent and other regions of Uzbekistan. This plant contains alkaloids such as stahydrine, choline, and flavonoids.

The relatively few publications on the stahydrine influence on blood clotting were issued before so we started work on a more detailed study of its effect on blood clotting and overall pharmacological properties.

Acute toxicity study was performed on white mice of both sexes weighing 18–21 g. The investigated stahydrine bases were administered intravenously at doses of 250, 500 and 1000 mg/kg. After a single administration of substances the animal state was monitored hourly during the day of administration, three times per a day for 2–3 days and once per a day in the subsequent 14 days of the experiment. It was not noted any changes in behavior, the state of mucous membranes, breathing, heart rate, motor activity, and the death of the mice. As a dose of 1000 mg kg refers to the group of non-toxic compounds, we not considered testing of higher doses of drugs as necessary. Due to the absence of dead animals, the LD_{50} calculations were proved impossible.

The Institute is working on the creation and development of an industrial technology of stahydrine. Preliminary studies have shown that technological sample of stahydrine for its purity and acute toxicity corresponds to the chemical sample.

The influence of stahydrine on the blood clotting was investigated *in vitro* and *in vivo*. Experiments were carried out on rabbits and rats. The whole blood clotting time was examined by Lee and White method, blood tolerance to heparin - by Sirman, re-calcification time was determined by the method of plasma Bergergof and Roka micromethod, thrombin time, prothrombin time - by Quick.

Studies have shown that intravenous administration of the stahydrine technological sample to rabbits (2.8–3.2 kg) at a dose of 10 mg/kg (control group of animals was injected in equivolume amount of solvent) increases the whole blood clotting for 22, 5% (by the method of Lee and White). In addition to the clotting time shortening in the whole blood, there was a decrease of plasma re-calcification time by 20.8%. There was a reduction of thrombin and prothrombin time, increasing of plasma tolerance to heparin on 15.6%.

Thus, the preliminary results indicate that stahydrine is low toxic compound and promotes the process of blood coagulation.

EVALUATION OF ANTI-AGGREGATIVE PROPERTIES OF *Aesculus hippocastanum* SEED SKIN EXTRACT

V. N. Axmedov, I. D. Bobaev, Z. A. Khushbaktova, V. N. Syrov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: vokhidzhon.akhmedov.1984@mail.ru

Horse chestnut (*Aesculus hippocastanum*) is a large deciduous tree with opposite leaves and with large seeds 3–4 cm in diameter. Extract from ripe seed skin of horse chestnut contains coumarin glycosides (esculine, fraxin), flavonoids (quercetin, kaempferol), triterpene saponins (escine), as well as vitamins E and B, and triterpene glycoside escine widely used in Russia as a venotonic remedy with expressed capillary protective and anti-exudative activity (Mashkovskii M.D., 2008). Coumarin glycoside esculin stimulates antithrombotic activity in the serum, increases the production of white flowers clustered in the erect pyramidal brush. Fruits are shiny brown spherical thorny boxes antithrombin in the reticuloendothelial system.

Skin of horse chestnut seeds was extracted with MeOH, and the concentrated extract was diluted with an equal volume of water. After evaporation of the aqueous portion in vacuo, the dry aqueous extract was obtained. Escine was determined by TLC.

Effect of this extract on the blood clotting system in rabbits was investigated by intravenous administration of the drug at a dose of 50 mg/kg. Blood was taken in one hour after injection and whole blood clotting time were measured by the method of Lee and White. The whole blood clotting time in rabbits increased for 26%. Determination of the extract effect on the blood coagulation system of rabbits was carried out colorimetrically in vitro. In these experiments, we also observed an increase in the whole blood clotting time by 33%. It has been determined a re-calcification time of plasma by the Bergergof-Roka method. Plasma recalcification time was increased in these animals compared to the original on 35%. The results obtained by the Sirman method showed the prolongation of thrombin time by 23.0%.

Thus, a dry aqueous extract of the skin of horse chestnut seeds has an antithrombotic effect on the blood coagulation system: increases the clotting of whole blood *in vitro* and *in vivo*, as well as lengthens the re-calcification time of plasma.

SECONDARY METABOLITES OF THE AERIAL PARTS OF *Crocus korolkowii*

B. S. Ohundedayev[1], Kh. M. Bobakulov[1], A. V. Makhmudov[2], S. Z. Nishanbayev[1], I. D. Shamyanov[1]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: boxundedayev@mail.ru
2) Institute of the Gene Pool of Plants and Animals, Academy of Sciences of the Republic of Uzbekistan, 100053, Tashkent, str.Bogishamol, 232, e-mail: azizbek.mahmudov@inbox.ru

Crocuses are one of the most beautiful early-flowering plants. From the point of view of medicine, crocus (saffron) possesses antioxidant, anti-aging, tonic, blood purifier, moisturizing, whitening properties.

In flora of Uzbekistan are growing two species of crocus: *Crocus alatavicus* and *Crocus korolkowii*.

Crocus korolkowii Regel & Maw (*Iridaceae*), crocus (saffron), is one of the representatives of mountain and foothill grasslands of Central Asia. It is insufficiently studied decorative species, and bee plant belongs to a group of obligate ephemeroids.

For phytochemical studies *Crocus korolkowii* was collected in the Tashkent Botanical Garden in flowering stage, in first decade of March. To isolate the secondary metabolites the aerial part was extracted with hexane and benzene.

By chromatography-mass-spectral analysis of hexane extract the following components were identified: (name of the substance, the retention time in minutes; the content % (retention index)): α-isophoron 8.541, 2.39 (1129), 2,6,6-trimethyl-1,3-cyclohexadiene-1-carbaldenyde 9.727, 11.35 (1206), (+)-car-2-en-4-one 10.059, 4.00 (1229), 3,5,5-trimethyl-4-hydroxy-1-cyclohexanone-2-ene 11.443, 7.07 (1325).

In the benzene extract: γ-hydroxybutyrolactone 5.165, 0.12 (923), *n*-undecane 8.098, 0.34 (1100), pelargonaldehyde 8.203, 0.57 (1107), α-isophoron 8.504, 0.83 (1126), 2,2,6-trimethyl -1,4-cyclohexanedion 9.236, 0.37 (1174), *n*-tridecane 11.074, 1.16 (1299) 4-hydroxy-3,5,5-trimethy-1-2-cyclohexen-1-one 11.394, 2.36 (1322), α-tetradecene 12.341, 0.44 (1389), *n*-tetradecane 12.445, 1.04 (1398), *n*-pentadecane 13.767, 4.02 (1492), α-hexadecene 14.972, 0.56 (1576), *n*-hexadecane 15.071, 1.46 (1533), *n*-tridecane 15.710, 0.37 (1626), *n*-tetracontane 16.448, 1.08 (1675), α-octadecen 17.856, 1.88 (1762), palmitic acid methyl ester 20.647, 3.62 (1904), dibutyl phthalate 21.453, 7.38 (1931).

These compounds were identified in the aerial parts of the *Crocus korolkowii* Regel & Maw. for the first time.

EFFECTS OF GLYCYRRHIZIC ACID AND ITS AGLYCONE ON THE ARTIFICIAL BILAYER MEMBRANE

D. D. Fayziev, Kh. A. Yuldashev, D. N. Dalimov, B. N. Babaev, R. Z. Sabirov

Institute of Bioorganic Chemistry of the Academy of Sciences of Uzbekistan,
Mirzo Ulugbek Str., 83, Uzbekistan, Tashkent, 100125, e-mal: diyor09@mail.ru

Natural compounds which are capable of self-organization and recognition of other particles and molecules are the subject of long-term investigations by chemists for modeling various biochemical processes. Glycyrrhizic acid (GA) is one of these compounds that is capable of self-organization and formation of supramolecular structures. Despite the great interest in the study of various properties of GA and its aglycone, glycyrrhetic acid, little information about the interaction of these terpenoids with membranes is available in literature, although it is known that the packaging of the molecule in the crystal structures packaging of lipid molecules in natural and model membranes.

With this regard, we aimed to evaluate the ability of GA to form bilayer-like structures in the conditions in which natural lipids form them spontaneously. Attempts to form bilayer lipid membranes (BLM) from pure GA were unsuccessful, and we were able to detect bilayer-like structures with measurable capacity in none of the 10 experiments. In order to enhance the degree of ionisation and thus, the amphiphylic properties of the molecule, we employed a monoammonium salt of GA.

As a control, we used asolectin (soybean phospholipids), which formed stable BLM with a capacity of app. 150 pF, and the experiments lasted for 600 seconds (n = 5). BLM consisting of equal amounts of GA and asolectin (1:1, wt:wt) with a capacity of 150 pF was successfully formed, however, the life-time of BLM was significantly reduced to 274 ± 33 seconds (n = 7) without change in the membrane conductance. Reducing the concentration of GA in above-mentioned experimental conditions to 10% did not affect the conductance of BLM. In this case, the life-time of the membrane containing 33.3% GA was 428 ± 7 seconds (n = 3), and at a lower concentration of GA membranes remained stable throughout the experiment (600 s).

Studying the effects of GA on BLM at the concentration of 1, 10 and 100 μM, we found that GA does not affect the conductance and stability of artificial BLM. In contrast to GA, its aglycone, glycyrrhetic acid, at a concentration of 100 μM and introduction into the both sides (cis/trans) resulted in increased membrane permeability. The ionic membrane current was rising in a stepwise manner, which indicates a possible formation of ion channels. However, at lower concentrations (1 and 10 μM) and when administered only to the *trans*-side (100 uM) glycyrrhetic acid also had no effect on the conductance of BLM and its stability.

In conclusion, we have shown that GA as a pure compound is not capable to form bilayer-like structures similar to the BLM. Introduction of GA into the membrane-forming solution does not affect on the conductance of artificial BLM, but at the concentration of more than 25% it reduces the membrane life-time. Glycyrrhetic acid dose-dependently affected on the membranes formed by asolectin and exhibited activity similar to the formation of ion channels.

EXTRACTION OF FLAVONOIDS FROM GRASS *Bidentis tripartite* L.

T. A. Hajibaev

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: hajibaev84@mail.ru

Bidentis tripartite L. (*Asteraceae*) is the wild and cultivated annual herbaceous plant, grows near streams, in gardens, in the swamps, near the rivers and spread almost everywhere.

In traditional medicine used as an anti-allergic and anti-inflammatory remedy in the form of infusion.

Bur beggar-ticks contain flavonoids, such as luteolin, isokoreopsin, flavanomarein, luteolin, cynarozide, sulfuretin, sulfurein, maritemitin, maritimein and others. The content of the sum of flavonoids is about 1.5%.

In the experimental-technological laboratory of the Institute of Plant Chemistry of the Academy of Sciences of Uzbekistan a technology for producing a new drug - dry extract of *Bidentis tripartite* developed.

Pharmacological studies have demonstrated that flavonoids of *Bidentis tripartite* L. show antihistamine and antiallergic activity.

The flavonoids of *Bidentis tripartite* growing in Uzbekistan not been completely studied. However, it is known from the literature that most of the flavonoids are practically insoluble in water.

To develop the production technology of the sum of flavonoids the cycle was examined by stages. For this purpose, it has been studied the extraction stage the aerial part *Bidentis tripartite* L. harvested in the Tashkent region. As a result of the experiments it was found that the highest yield of flavonoids is observed at the six-fold extraction of the raw material with a particle size of 2–6 mm in 70% ethanol at room temperature.

SELECTION OF THE FILLERS FOR CUCUMAZIM TABLETS

M. A. Azizova[1], Sh. Sh. Sagdullaev[1], Kh. K. Dzhalilov[2], L. G. Mezlumyan[1]

1) Acad.S.Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: azizova.pharmi@mail.ru
2) Head Department on the Quality Control of Drugs and Medical Equipment,
Public Health Ministry RUz

In our preliminary experiments, we used 14 compositions of a compressible mass. We have studied their technological, physical and mechanical properties of tablets prepared from them. We have used sucrose, dextrose, maltodextrin, lactose, MCC "Introcell", sorbitol, fructose and other substances in various combinations as fillers.

Since Cucumazim is easily soluble in water, the purified water, 95, 70 and 40% ethyl alcohol, 1 and 3% starch paste have been chosen as a granulating liquid phase.

Technological characteristics of the four experimental compositions of Cucumazim 0.005 g tablets prepared by wet granulation showed satisfactory results. The correctness of the technology choice in the laboratory series of Cucumazim tablets production confirmed by analytical data on the quality of the finished product and its stability under specified conditions and shelf-life.

The final selection of the optimal recipe composition will be made on the basis of further biopharmaceutical research.

INVESTIGATION OF COTTON CELLULOSE AND ITS PRODUCTS USING CUSTOMS CHEMICAL EXAMINATION

K. M. Karimkulov, N. K. Djuraeva, I. R. Askarov

Higher Military Customs Institute, State Customs Committee of the RUz,
Tashkent Medical Academy, Andijan State University

More than half of a century scientists interests are not abating, even amplified to the molecular and sub-molecular levels of cellulose structures. Cotton fiber is used as an important feedstock in manufacture of cellulose and its derivatives. In this regard, to determine the package of goods of cotton fiber and its products, according to the commodity nomenclature of Foreign economic activity, the relationship between structure and mechanical properties of cotton cellulose has been studied. First of all, we studied the elementary units of cellulose, the structure of macromolecules and molecular weight. It is known that the reactivity of cellulose is attributed to the presence of hydrogen bonds between the macromolecules, since the penetration of chemicals is very difficult. For this reason, almost all chemical reactions take place in a heterogeneous environment. Despite these tough conditions, the yield of the desired product don't reach to100%.

Chemical purification of cotton cellulose. The chemical properties of cotton cellulose were studied. After separating the cellulose from 5 varieties of cotton fibers in conditions of natural biosynthesis its molecular weight, structure and other features were studied. To avoid impurities from cotton fiber (lignin, fats and resins, etc.), gem cellulose components were removed. 50 g sample of cotton fiber were selected. Mechanical impurities like sand, stone, etc. separated, passed through the mesh, washed 2–3 times with hot water. Mass was placed in a 3 L flask with 1% solution of sodium hydroxide and boiled for 4–5 h until becoming brown. After cooling, the mass was washed 4–5 times with a solution of 1% sodium hydroxide. Pulp was bleached by 1 liter of 0.2% activated chlorine sodium hypochlorite. After drying the pulp at 50–700°C in the final stage in the 1050S, the yield of cellulose was 84–85%.

The yield of pure cellulose was:

For first grade cotton – 85%; for the fourth grade cotton – 81%;

For the second grade cotton – 84%; for fifth grade cotton – 80%;

For the third grade cotton – 83%.

Determining the amount of fat waxy substances. To determine the amount of fat in the composition of the cellulose 5g cotton resin was washed with dichloroethane and poured 1.5–2% of the volume of the total desiccator dichloroethane placed together with filter paper. Solution was heated in water bath for 5–6 h. Grease and tar was distilled into another flask. Residue of the solvent was distilled. The precipitate was dried at 100°C. The amount of fat and tar were determined by the following formula:

$x = \frac{a - б}{c}$ 100, where a – the mass of the flask together with fat and tar, in grams, b – weight of empty flask in grams, c – the mass of the sample, in grams.

The studied samples contained 0.05% grease and resin.

EFFECT OF THE CENTRAL ASIAN TORTOISE′S EMBRYONIC EXTRACT ON THE TORTOISE′S BLOOD LYMPHOCYTES

N. Tagayalieva, R. Yakubova, M. Fomina, E. Nazirova

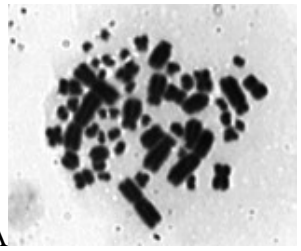
Institute of Bioorganic Chemistry, Uzbekistan Academy of Sciences,
83, M. Ulugbek str., Tashkent

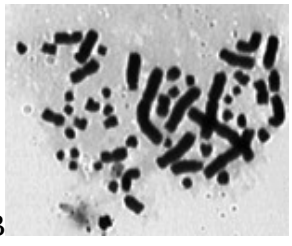
Inhabiting the earth for almost 250 million years, a tortoise is an extraordinary animal with the lowest levels of DNA substitution among the amniotes, the highest proportion of CG islands and their asymmetric distribution between gene sites typical of the mammals. Its ability to survive in freezing of 50% of body fluid, 2-month anoxia and ultrahigh doses of radiation is amazing. Previously, we demonstrated blast transformation activity of tortoise′s total embryonic extract (TTEE) in human peripheral blood lymphocytes, and its mitogenic and protective effect on the tortoise's bone marrow cells.

The work was initiated to study TTEE mitogenic effect on the tortoise′s peripheral blood lymphocytes.

The tortoise′s blood was sampled by a sterile syringe soaked with heparin. To culture lymphocytes, the modified method of Moorhead et al. adapted for tortoise's cells was used. 0.8–1 mL of the tortoise′s whole blood were added to cell culture medium containing RPMI-1640 medium with glutamine, 10% of autologous serum, gentamicin/flukonazol and 20–200 μg/mL of TTEE. 40–200 μg/mL of phytohemaglutinin (PHA) were used as a positive control solution. The cell culture was incubated at 24°C, that is a tortoise′s physiological temperature, with gentle gently shaking twice a day to avoid excessive agglutination of blood cells. Culture of the tortoise′s lymphocytes was terminated on the 4^{th}, 5^{th}, 6^{th} and 7^{th} day. One and a half hour prior to fixation the culture medium was added with colchicine. The hypotony achieved, Carnoy fixative was used to fix the cells. The cells were pipetted on the microscopic slides were used to be Giemsa stained and to microscopically determine optimum culture time and TTEE concentration by mitotic index (the proportion of cells dividing at a given time).

The mitotic index was found maximum when the tortoise′s lymphocytes were cultured for 5–6 days in the medium containing 150–200 μg/mL of TTEE. PHA was active at the concentration of 200 μg/mL within the same time periods.





Metaphase chromosomes from blood of male (A) and female (B) Central Asian tortoise (*Testudo horsfieldii*)

Thus, the Central Asian tortoise′s total embryonic extract produces mitogenic effect on the peripheral blood lymphocytes of the tortoise in the doses of 150–200 μg/mL.

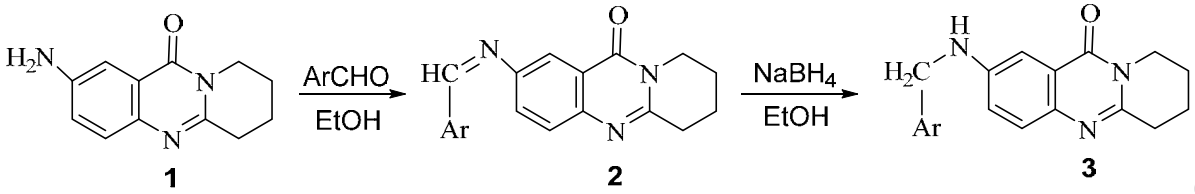
TARGETED SYNTHESIS OF 6-ARYLAMINOMACKINOZOLINONES

R. R. Nuritdinova[1], B. B. Zhurayev[1], B. Zh. Elmuradov[2*], Kh. S. Tadjimukhamedov[1]

1) Mirzo-Ulugbek National University of Uzbekistan, Chemical Faculty, Tashkent 100195, Uzbekistan
2) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: b_elmuradov@mail.ru

Tricyclic quinazoline alkaloid – mackinazolinone is widely distributed in nature. Most often it occurs in the plant of *Mackinlaya* sp. [1, 2]. Chemical modification of tricyclic quinazoline alkaloids and their derivatives may open very interesting direction in the field of fundamental science as well as for development efficient preparations for agriculture and medicine [3]. There are in molecule of mackinazolinone some reactive centers: activated methylene group (α-carbon atom), C=N bond, carbonyl C=O group and benzene ring. These centers can react with different electrophilic and nucleophilic reagents to give new derivatives with various activities.

The object of this work is 6-substituted mackinazolinones. It should be noted that the 6-amino derivative in reactions with aromatic aldehydes, depending on the reaction conditions to form a different products on both centers - an amino- and α-methylene group:



1 **2** **3**

6-Aminomackinazolinone (**1**) was synthesized by reduction of 6-nitromackinazolinone with $SnCl_2$ in the presence of concentrated HCl. The obtained compound **1** reacts with aromatic aldehydes to give corresponding Schiff's bases (**2**), which can smoothly reduced at 0°C to 6-(*N*-alkylated)-aminomackinazolinones (**3**) in good yields. Nowadays investigations in this field are continued. The structure of the obtained compounds was confirmed by physical methods of research.

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3. Nasrullayev A.O., Tosheva N.A., Elmuradov B.Zh., Eshmuratova A.A., Azimova Sh.S. *Journal of Basic and Applied Research*, 2016, Vol.2, No.4, 470-475.

STUDY OF FRUIT *Ziziphus jujube* MILL. DEVELOPMENT AND TECHNOLOGY OF DRY EXTRACT

D. Mirakilova, N. Esonova, U. Azizov

A. Sultanov Uzbek Scientific Research Chemical-Pharmaceutical Institute (UzKFITI) of AK Uzpharmsanoat, Uzbekistan, Tashkent, 100125, Durmon Yuli, 40, e-mail: uzkfiti_uzb@umail.uz

Jujube is one of the unique and forward-looking plants growing in Uzbekistan in terms of implementation on the basis of the technologies of new products from them. This work is aimed on studying the fruit jujube, the composition of BGH based on them, to find the optimal conditions of extraction of water-soluble polysaccharides (VRPS) and obtaining a dry extract.

As a raw material to produce a dry extract ripe fruit jujube were used, collected in 2014 in Bagat district of Khorezm region.

In the first phase of our research we studied anatomical properties of jujube fruits. It was found that the raw material is a solid, cleaned of sepals and peduncle fruit spherical or oblong drupe, fruit length up to 5 cm, 5–7 cm diameter. The color of the fruit is brown or reddish-brown. Smell is absent. It consists of a fleshy fruit, nutritional, powdery pulp and concluded in its cavity fruitlets - nuts oblong. The walls of the dried fruits are of hard brittle, outer surface shiny, less dull, more or less wrinkled. Flesh color is pale green, the taste - sweet, slightly astringent. Contents VRPS to absolutely dry raw material is not less than 1.5% total ash and moisture content of not more than 10%, the content of impurities (mineral and organic) is not more than 1%.

Next, we investigated ways of VRPS extraction from jujube fruits. We studied the influence of various factors on the extraction process: such as the degree of grinding of raw materials, dependence of the VRPS of temperature and time, the nature of the extractant, the impact of hydronic.

In order to select the optimal conditions, we carried out experiments with a feed having a different degree of grinding - less than 2 cm; 2.0–3.5 cm and 3.5 cm.

Also on vegetable raw material extraction rate is greatly influenced by the temperature factor, so the effect of temperature on the yield was studied in VRPS intervals 30-400S, 50-600S, and 90-1000S 70-800S.

To select the raw hydro-extraction were carried out in a ratio of 1:10, 1:20, 1:30, 1:40 and 1:50.

It was also studied the influence of time on the extraction process. Timed operation studied at intervals of 30 to 150 minutes.

Thus, it was found that the main factors affecting the extraction process are: the degree of grinding – 2–3.5 cm, extraction temperature – 70-800S, hydronic – 1: 30, extraction time – 120 minutes.

In the above conditions, the technology of the dry extract from stems of stem-rose and turned out samples submitted for pharmacological studies of antihypertensive activity.

TECHNOLOGY OF NEW DRUGS ON THE BASIS OF ROOTS OF HOLLYHOCK PINK

D. Mirakilova

A. Sultanov Uzbek Scientific Research Chemical-Pharmaceutical Institute (UzKFITI) of AK Uzpharmsanoat, Uzbekistan, Tashkent, 100125, Durmon Yuli, 40, e-mail: uzkfiti_uzb@umail.uz

Essential drugs for the treatment of upper respiratory tract infections are herbal preparations because of their safety, effectiveness and mild.

Among the variety of cough medicines a combination of drugs that will ensure more effective therapy due to multi-directional action components occupy a special place. As an effective expectorant and antitussive use such medicinal plants as licorice root, grass of *Thermopsis*, mint leaves, althea root, root-stem roses, the rhizome of turmeric, plantain leaves, rose hips, and others.

Previously, we developed and introduced into medical practice tablets of Altseum and Glitsirozin based on the roots of stem-rose.

In order to find formulations that provide high efficiency of the drug continue our research to develop technologies capsules or syrups based on the roots of the stem-rose.

In this report the results to obtain new expectorants capsules and syrup based on a combination of the above herbs.

For expectorant syrup standardized and meet the requirements of the relevant specification above herbs they have been used. Preparation of extracts from these plants was carried out by extracting of grinded plant raw material with water at a ratio of plant material: water 1:20 at a temperature of 700°C for 1.5 hours. To this extract sugar syrup is added in a ratio of 1:1, sodium benzoate in an amount of 1% by weight of the syrup and the alcohol 96% (to 10%). The technique of standardization syrup from which 1 mL of the preparation should contain 0.01 g and 0.05 g polysaccharides glycyrrhizic acid.

We also technology for producing encapsulated formulation expectorant and anti-inflammatory drug glitsirozin has been developed consisting of a mixture of dry extracts of the roots of the stem-rose pink and licorice.

Detected of glitsirozin substance granulation mode and select the optimum particle size distribution for capsules. Composition of fractions and the basic technological properties of the substance determined. The kinetics of moisture sorption of glitsirozin granules in hard gelatin capsules at different values of relative humidity and storage of capsules of glitsirozin suggested at a relative humidity no higher than 59.2%.

Technological properties, such as mass of capsules, flowability, bulk density, compressibility, compressibility, elasticity, strength, plasticity, determining a number of technological parameters such as the rate of formation of granules, pressure, pressing speed were studied.

Both drugs are currently in clinical trials.

STEROIDS FROM *Pulicaria uliginosa*

B. J. Komilov, K.A. Eshbakova

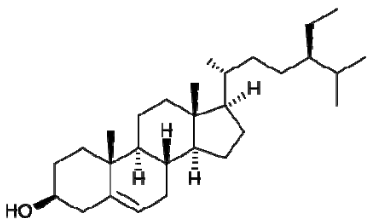
Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: e_komila@yahoo.com

Continuation of chemical research on the aerial parts of *Pulicaria uliginosa* collected during the flowering period in Namangan region of Uzbekistan. From the alcoholic extract by column chromatography on silicagel eluting with hexane–ethyl acetate three steroids were isolated were isolated.

One of them was identical to β-sitosterol (**1**), the second isolated compound were identical to β-stigmasterol (**2**) and the third compound was identical to stigmasterol 3-*O*-β-*D*-glucoside (**3**).

Identification of β-sitosterol, β-stigmasterol and stigmasterol 3-*O*-β-*D*-glucoside have been established on the basis of their physical and chemical properties and the analysis of their spectral data IR, ^{1}H, ^{13}C NMR, DEPT, HMBC, COSY and compared with literature data.

Stigmasterol 3-*O*-β-*D*-glucoside has been isolated from *Pulicaria uliginosa* for the first time.



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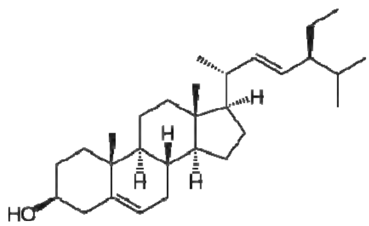

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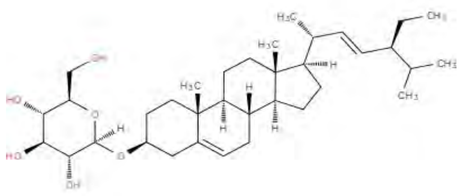


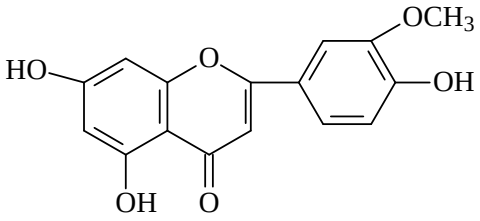
3

AGLYCON FLAVONS FROM *Dracocephalum komarovii*

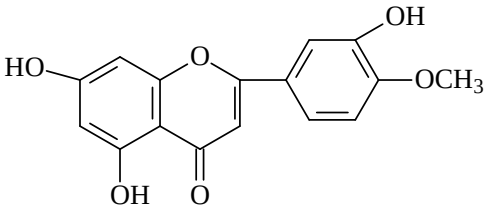
Z. O. Toshmatov[1,2], K. A. Eshbakova[1,3], H. A. Aisa[1]

1) Key Laboratory of Plant Resources in Arid Regions, Xinjiang Technical Institute of Physics and Chemistry, CAS, Urumqi, 830011, P. R. China, E-mail: haji@ms.xjb.ac.cn
2) PhD student of Chinese Academy of Sciences CAS-TWAS president fellowship 2014, Beijing, P. R. China, e-mail: zokir_06@mail.ru
3) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: e_komila@yahoo.com

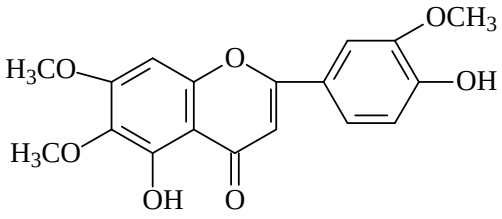
In continuation of our research, the aerial part of *Dracocephalum komarovii* was collected in blossoming period around of Tashkent (Uzbekistan). From ethylatcetate fraction by chromatography over a column with silica gel the gradient elution by hexane and hexane–ethyl acetate (9:1, 4:1, 2:1) was carried out, each fraction is further separated on a Sephadex LH-20 and HPLC, and four compounds (**1**–**4**) of flavon nature were isolated. The structures of isolated compounds were established on the basis of their physical and chemical properties, IR, UV, PMR, ^{13}C NMR, HSQC, HMBC and DEPT spectral data analysis. As a result the compounds were identified with chrysoeriol (**1**), cirsilineol (**2**), diosmetin (**3**) and luteolin (**4**).



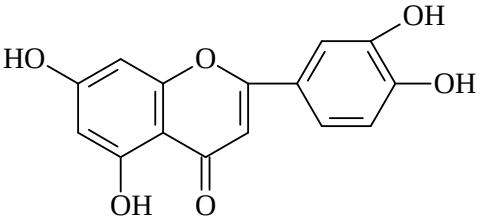
Chrysoeriol



Diosmetin



Cirsilineol



Luteolin

All compounds are known as new for this plant, and cirsilineol is new for the this genus.

COUMARIN GLYCOSIDES FROM *Fraxinus syriaca*

H. Sh. Kamoldinov[1,2], K. A. Eshbakova[1,3], H. A. Aisa[1,2]

1) Key Laboratory of Plant Resources in Arid Regions, Xinjiang Technical Institute of Physics and Chemistry, CAS, Urumqi 830011, China, e-mail: haji@ms.xjb.ac.cn
2) PhD student of Chinese Academy of Sciences CAS-TWAS president fellowship 2014, Beijing, P. R. China, e-mail: zokir_06@mail.ru
3) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: e_komila@yahoo.com

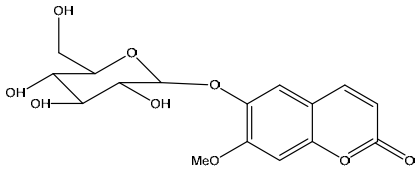
Fraxinus syriaca Boiss is large tree with thick brown-gray cylindrical branches, with the usual light, small lenticels, a height of 10 to 15 meters, grows in floodplain forests and mountains of Central Asia. Branch and leaves may be a source of esculin, a main component of the drug "eskuvit" used in scientific medicine in various bleedings, hemorrhoids, varicose veins and fraxinol. They have antispasmodic properties. The leaves in the experiment show antibacterial, antiprotista, and phytoncidic activity.

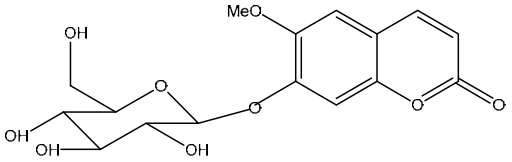
We have investigated the aerial parts of *F. syriaca* collected in the Surkhandarya region of Uzbekistan. Air-dried ground plant material (1000 g) was extracted at room temperature by EtOH (70%, 6 × 5 L). The combined extracts were distilled under vacuum. The extract was condensed, the residue (120 g) diluted with H_2O (1:1). The diluted solution was processed successively with hydrocarbons, $CHCl_3$, EtOAc, and BuOH. BuOH fraction (27 g) was subjected to chromatography on a column (130 × 2.5 cm) with silica gel using a gradient of solvents chloroform and chloroform - methanol. By elution with a mixture of chloroform methanol (8:1) 0.11 g magnolioside (**1**) was isolated. Further elution of the column with chloroform–methanol (7:1) gave pure fraxetin-7-*O*-β-*D*-glucopyranoside 0.25 g (**2**).

Structure of the isolated compounds have been established on the basis of their physical and chemical properties and the analysis of their IR, UV, ^1H, ^{13}C NMR, HSQC, HMBC spectral data analyses.

Magnolioside (1), $C_{16}H_{18}O_9$, mp 227°C.

Fraxetin-7-*O*-β-*D*-glucopy ranoside (2), $C_{16}H_{18}0_{10}$, mp 164–166°C.





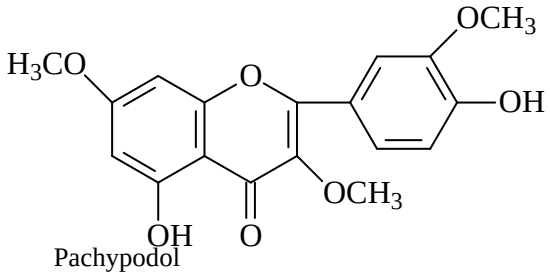
Magnolioside and fraxetin-7-*O*-β-*D*-glucopyranoside from *Fraxinus syriaca* were isolated for the first time.

FLAVONOIDS FROM *Dracocephalum komarovii*

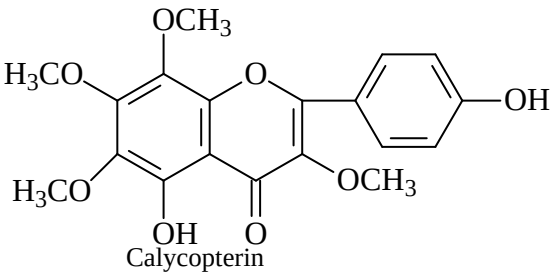
Z. O. Toshmatov[1,2], K. A. Eshbakova[1,3], H. A. Aisa[1]

1) Key Laboratory of Plant Resources in Arid Regions, Xinjiang Technical Institute of Physics and Chemistry, CAS, Urumqi 830011, China, E-mail: haji@ms.xjb.ac.cn
2) PhD student of Chinese Academy of Sciences CAS-TWAS president fellowship 2014, Beijing, P. R. China, e-mail: zokir_06@mail.ru
3) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: e_komila@yahoo.com

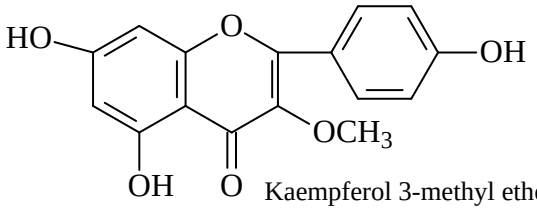
We have investigated the aerial part of *Dracocephalum komarovii* (2000 g) collected in blossoming period around of Tashkent (Uzbekistan), extracted with 70% alcohol in room temperature. The combined alcohol extract was condensed in vacuo and subjected to chromatography over a column with silica gel by gradient elution with hexane and hexane–ethyl acetate (16:1, 12:1, 9:1, 4:1, 2:1). Each fraction was further separated on a Sephadex LH-20 and HPLC to afford compounds **1** (8 mg), **2** (118 mg), **3** (51 mg), **4** (127 mg), **5** (11.4 mg), **6** (21 mg), **7** (38 mg), **8** (0.51 g), **9** (2.78 g), and **10** (17 mg). The structures of isolated compounds were established on the basis of their physical and chemical properties, IR, UV, PMR, ^{13}C NMR, HSQC, HMBC and DEPT spectral data, and also TLC analysis. As a result the compounds were identified as pachypodol (**1**), calycopterin (**2**), kaempferol 3-methyl ether (**3**).



Pachypodol



Calycopterin



Kaempferol 3-methyl ether

Pachypodol and calycopterin were isolated from *Dracocephalum komarovii*, and kaempferol 3-methyl ether from genus *Dracocephalum* for the first time.

SYNTHESIS OF OPTICAL ACTIVE ISOMER – SYTOPHILURE – AGGREGETION PHEROMONE OF RICE (*Sitophilus oryzae* (L.)), GRAINARY (*S. granarius* (L.), AND MAIZE (*S. zeamais* Motsch) WEEVILS

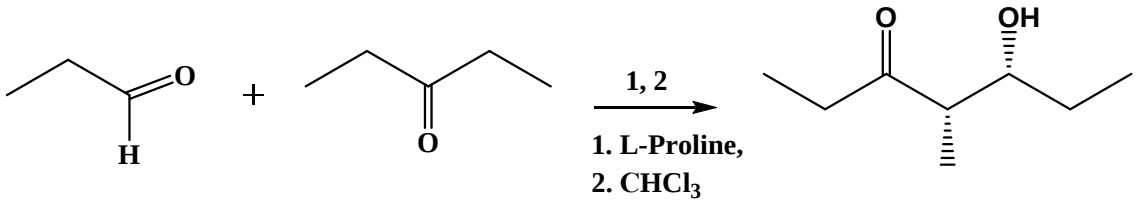
G. S. Shakirzyanova[1], B. N. Babaev[1], B. Zh. Elmuradov[2], V. S. Abdukakharov[1]

1) Institute of Bioorganic Chemistry AS RUz, Tashkent, Uzbekistan
2) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan

Organocatalysis is a perspective sphere of synthetic organic chemistry and bioorganic chemistry. The aldol reaction is widely regarded to be one of the most important carbon-carbon bond-forming utilized in organic synthesis. Catalytic enantioselective carbon-carbon bond-forming represents important problem into synthesis of biologically active substances. The chiral amino acid catalysts has widely usage for most powerful enantioselective reactions [1, 2].

(4*S*,5*S*)-(+)-4-methyl-5-hydroxyheptan-3-one, Sitophilure, an aggregation pheromone of rice (*Sitophilus oryzae* (L.)), grainary (*S. granarius* (L.) and maize (*S. zeamais* Motsch) weevils, one of the main pests insects of stored products in Uzbekistan, have been received by conditions of asymmetric synthesis by using of *L*-proline.

The stereo-specific reaction between 3-pentanone and propionaldehyde in the presence of *L*-proline has been conducted in conditions of aldol reaction. The structure-functional activity of *L*-proline improves catalytic possibilities of asymmetric aldol synthesis in anhydrous solvents.



It has been found that more suitable solvent for such reaction was chloroform. *L*-proline is insoluble in chloroform but it dissolves in water very well and could be extracted from water.

Heterogeneous compounds were mixed at room temperature during of 32 hours. Mixture were treated by saturated NH_4Cl, extracted by ethyl acetate and dehydrated by $MgSO_4$. The crude reaction mixture was purified by flash column chromatography (hexane, ether). HPLC analysis using (ChiralPak® AS – Amylose tris [(*S*)-α-methylbenzylcarbamate], 98% MeCN – 2% *i*-PrOH, t_R(major)=7.998 VP, t_R(minor) = 7.072 VV; S:R - 57.0722:28.0855, t_R(major) = 8.007 VP, t_R(minor) = 7.025 VV; S^*:R^*-43.4765:30.0490 (74%).

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ASSESSMENT OF SAFETY DURING STORAGE AND EFFICIENCY OF VITAMINIZED ALOE SYRUP

Sh. T. Khojiakbarova, U. M. Azizov

A. Sultanov Uzbek Scientific Research Chemical - Pharmaceutical Institute

Aloe arborescent (Latin *Aloe arborescens*, also known as century plant) is a kind of Aloe plants of family *Asphodeliaceae*. Average percent composition of natural chemical elements of Aloe arborescent per 100 g, namely: about 7% of proteins, 2% of lipids, 22% of waste products (including all various mineral elements of plant), 70% of carbohydrates (which are the part of numerous types of complex and simple glycides), and insignificant quantitative portion of vitamins (free aminoacids and other organic natural molecules with various chemical properties). It is the portion of active substances, biologically active and the distinctive feature of Aloe species.

Preconditions for this are theoretical developments on extraction of some labile biologically active substances, and also inclusion to ND of modern methods for standardization, which allow determine substances in the process of production and in finished products.

The purpose of present researches is the assessment of safety, in process of storing and effectiveness of vitaminized aloe syrup. Vitaminized syrup was prepared by mixing sugar solution with aloe extract.

The composition in grams:

aloe extract – 1.0, ascorbic acid – 3.0, sugar syrup 64% –145.0 (sugar – 96.0, purified water – 54.0). Total mass – 154.0 g.

In selection of syrup′s base, firstly, the influence of sugars origin on safety of anthracene derivatives in process of storing syrups was evaluated. With this purpose syrups on fructose and sucrose with content of anthracene derivatives of 0.15% were prepared. Samples were kept at room temperature. The obtained results are given in figure 1.

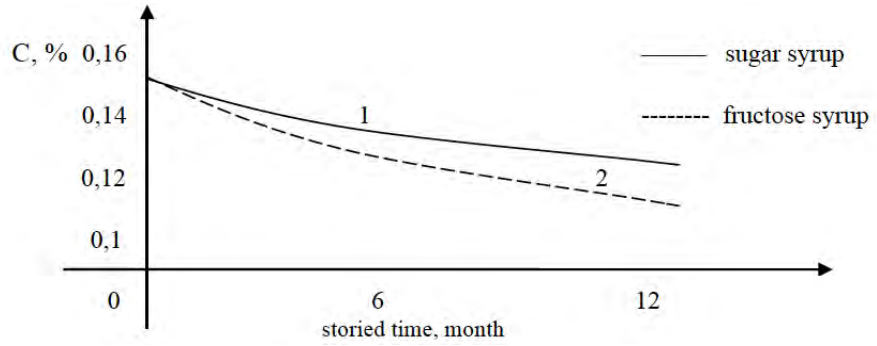


Fig. 1. Nature of influence on stability in storing process of vitaminized syrup of aloe.

As it can be seen from data on Fig. 1, the higher stabilizing effect in relation to the complex anthracene derivatives of aloe during 1 year of storage shows the sucrose, and also more economically available auxiliary substances.

On the basis of conducted researches we suggested the optimal composition of syrup, containing anthracene derivatives of aloe.

Vitaminized aloe syrup requirements of SanPC 2.3.2 1078-01 for BAS to food were worked out.

STUDY OF DIURETIC ACTIVITY OF “UROSTIM” SUBSTANCE

U. M. Azizov, H. U. Aliyev, U. A. Khadjieva, O. I. Khudoiberdiev

A. Sultanov Uzbek Scientific Research Chemical-Pharmaceutical Institute, Tashkent, Republic of Uzbekistan

Currently used synthetic diuretic drugs sold in the pharmacy network in Uzbekistan are mainly imported and expensive.

Based on previous studies, in UzKFITI the combined diuretic drug, consisting of a mixture of dry extracts of 8 herbs: herb of yantak, grass of ervy woolly, herb of horsetail herb Tribulus, yarrow herb, cucumber seeds, corn silk and licorice roots created. To study the chemical composition of the investigated drug (the substance "Urostim") the amounts of basic groups of biologically active substances, organic acids, flavonoids and tannins were determined.

Definition of diuretic activity and the optimal dose of the substance "Urostim" were carried out as described in V. Gatsura. 54 white rats of both sexes, weighing 180–195 g were administered a drug infusion (1:10) once orally at a dose of 150 mg/kg. Control animals received distilled water in an appropriate amount. As comparison, multi-drug "diuretic collection No.2» consisting of a mixture of 40% of bearberry leaf, fruit of juniper 40%, licorice root 20% as a tincture prepared according SP XI, which is orally administered once at a dose of 15 mL/kg. After drug administration urine was collected in metabolic chambers for 24 hours. The data are given in the table:

Input drugs	Number of animals	Dose of Administered drugs	Volume of urine before drug administration, ml	Volume of urine after administration of drugs per a day		Diuretic effect, %
				ml	%	
Control group	6	H_2O 4 ml/100 g of weight	–	5.15±0.65	100	–
Substance "Urostim"	6	150 mg/kg	5.15±0.65	9.89±0.41	185	86
Diuretic collection No.2	6	15 mL/kg	5.35±0.56	7.19±0.65	158	58

As can be seen from Table, drug "Urostim" at a dose of 150 mg/kg increases diuresis for 86% relatively to control, and for 28% in compare to the reference preparation diuretic collection No.2.

TECHNOLOGY OF "ANTIDIABETOL" SUBSTANCE

U. M. Azizov, U. A. Khadjieva, M. I. Abdullaev, D. U. Madjitova

A. Sultanov Uzbek Scientific Research Chemical-Pharmaceutical Institute, Tashkent, Republic of Uzbekistan, e-mail: uzkfiti_uzb@umail.uz

Diabetes mellitus is included in the list of major diseases that cause death in third place after cardiovascular diseases and cancer.

As synthetic drugs and 150 plant species have hypoglycemic activity known in the literature.

Creation of medicines on their basis is an actual task, especially in Uzbekistan, where the scientific and material resources for their research are available.

In UzKFITI, basing on a study of glucose-lowering activity of dry extracts the following 8 local medicinal plants: the tubers of Jerusalem artichoke, herbs yantak false, grass Ajuga turkestanica, the leaves of nettle, burdock root, chicory roots of the ordinary, the roots of licorice, rose hips, a new hyperglycemic drug "Antidiabetol" was created.

For obtaining of a dry extract of "Antidiabetol" preparation the plant material was ground and sieved for leaves and grass of size 7 mm, tubers, roots up of size 5 mm, and 0.5 mm for fruits.

Dry "Antidiabetol" drug extract obtained by extracting three times of the mixture of the crushed material (tubers of Jerusalem artichoke – 7.0 g, burdock root – 6.0 g, chicory root of the ordinary – 6.0 g, grass of yantak false – 5.5 g, leaves nettle – 7.0 g, rose hips – 7.5 g, roots of Ajuga turkestanica – 5.5 g, licorice root – 5.5 g) by hot water (70–80°C) in ratio 1:30 (first extraction), 1:15 (second extraction), 1:7 (third extraction) for 2 hours. The resulting aqueous extracts were combined and concentrated by distilling off water at a temperature of 70°C under vacuum. The resulting thick extract is dried in a vacuum oven at 600°C to constant weight. The dry extract yield was 16.2 g (32.4%). Dry "Antidiabetol" extract product is a brown powder with a sweet taste and characteristic smell.

The chemical composition of prepared dry extract "Antidiabetol" on the contents of the main groups of biologically active substances: flavonoids, tannins, organic acids and inulin was investigated. Content of flavonoids, tannins, organic acids were identified in dry extracts according to methods described in GF XI. The content of flavonoids was 1.95%, organic acids – 5.3%, tannins – 6.1%, and inulin – 34%.

Experimental batches of the drug substance Antidiabetol were tried and tested, and laboratory production schedules developed.

ANTIBACTERIAL EFFECTS AND TOXICOLOGICAL\ PROPERTIES OF CARBOXYMETHYLCELLULOSE DERIVATIVES CONTAINING GUANIDINE

O. R. Akhmedov, Sh. A. Shomurotov, N.T. Muydinov, A.S. Turaev

Institute of Bioorganic Chemistry of the Uzbek Academy of Sciences, M. Ulugbek st., 83, Tashkent 100125 (Uzbekistan), e-mail: Oliy86@bk.ru

One of the major challenges of modern chemistry, biology, and medicine is the development of new antibacterial compounds possessing wide range of antibacterial effects with minimal amount of side effects. In recent years, there is a great development in the research aimed at obtaining new antibacterial polymers.

It is known that polymeric guanidine derivatives possess a wide range of antibacterial effects, are non-toxic, and do not possess cumulative properties.

Based on the aforementioned, we have obtained derivatives of carboxymethylcellulose containing a guanidine group in the structure. A compound of guanidine fragment with the macromolecule occurs through amine connection. Obtaining guanidine containing derivatives of carboxymethylcellulose, include the following steps: periodate oxidation of the carboxymethylcellulose, the condensation reaction of the oxidized polymer with guanidine and reduction -C=N- linkage via $NaBH_4$. Optimal conditions for the reaction (temperature, time, ratio of the reacting components, and the pH) were identified.

Structure and composition of the obtained compounds were studied by the method of IR-spectroscopy, elemental (nitrogen), and X-ray analysis.

In order to study the antibacterial effects of obtained compounds, they were tested against gram (+) and gram (–) microorganisms. It was found that guanidine derivatives containing carboxymethylcellulose possess antimicrobial effects at a concentration of 50 ug/mL against *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogenes*, *Streptococcus faecalis*, and *Klebsiella*. Moreover, it was found that the antibacterial effect of guanidin carboxymethylcellulose has a dose dependent character, with increasing concentration of the test drug to 75–100 ug/mL bacteriostatic effect begins to grow.

Conducted pharmacological studies have shown that the guanidine derivatives containing carboxymethylcellulose are classified as low-toxic substances (LD_{50} = 1780 mg/кg), do not have a cumulative effect (K = 0.9) and do not have local irritating effect at a concentration of 0.5–5.0%.

Thus, based on the held biomedical research it can be concluded that the guanidine containing carboxymethylcellulose derivatives can find use as inner and outer antibacterial compounds in the future.

NATURAL PLANT COMPOUNDS AS PLANT PROTECTION REMEDIES AGAINST PHYTOPATOGENES AND ARTHROPOD PESTS

Z. Tilyabaev, Kh. Kh. Kushiev, D. N. Dalimov

A. S. Sadykov Institute of Bioorganic Chemistry of AS RUz, 100125 Tashkent, Mirzo Ulugbek str., 83, fax: (99871) 262 70 63, e-mail: tilyabaevzaid@mail.ru
Gulistan State University, 120100, Gulistan, Microdistrict-4, e-mail: hkushiev@yandex.ru

Recent research showed that the preparations against agricultural crop pests developed on the base of various compounds that performed different functions in biological systems. There is information about pronounced insecticidal activity of compounds isolated from 28 plant families represented by alkaloids, terpenoids, glycosides, etc. The first alkaloids tested as insecticides were nicotine and anabasine isolated from *Anabasis aphylla* L.

In current communication there have been reported the results of monitoring and search for the effective insecticides of plant origin and their chemical modifications against crop pests. There have been also outlined the results on insecticidal activity of such alkaloids as anabasine, piperidine, lupinine, epilupinine, cytisine, salsolidine as well as glyzirrhizic acid from *Glycyrrhiza glabra* L., peptides from the seeds of *Nigella sativa*, melon (*Cucumus melo* L.) seeds, fig (*Ficus carica*) latex, and cotton (*Gossypium*) leaves.

Insecto-acaricidal activity of compounds was discovered against *Schizaphis gramina* Rond., *Musca domestica* L., *Galleriae mellonella* L., *Partacella Sp, Sitatroga cerealella* O., *Agrotis segetum* Schiff, *Spodoptera exiqua* Hon, *Helicoverpa armigera* Hbn., *Puccinia recondita* Rob, and *Leptinotarsa decemlineata*.

The activity of alkaloids against the pests studied was found to decrease as their molecular hydrophobicity increases. The modification of alkaloid structure enhances their activity; however, they become toxic for warm-blooded organisms. For the phosphororganic derivatives of lupinine, in contrast to their epilupinine analogs, their high toxicity was detected. *N*-[β-(diethoxyphosphinyl)-mercaptoethyl]anabasine, in terms of its activity against *Schizaphis gramina* Rond., is very similar to that of well-known Rogor. The combined mixtures of preparations based on lupinine and piperidine enhance the toxic effect of carbophos (against spider mite) and dorsan against caterpillars of *Agrotis segetum* Schiff. The modification of salsolidine structure enhanced its action against *Aphis craccivora* Koch and caterpillars of *Agrotis segetum* Schiff in mixtures with phosalone and pyrethroids such as decis, sumi-alpha and furi. DKM-1 preparation developed on the basis of glyzirrhizic acid effectively suppressed the growth of *Puccinia recondita* Rob. A wide-ranged insecticidal activity was discovered for the peptides isolated from melon seeds. They were found to be toxic for *Leptinotarsa decemlineata*, *Agrotis segetum* Schiff and *Helicoverpa armigera* Hbn. A diverse phytopatogeneous activity was discovered for the peptides isolated from seeds of *Nigella sativa* and cotton (*Gossypium*) leaves.

ALKYLATED DERIVATIVES OF 5-MERCAPTO-3-PHENYL-1,3,4-THIADIAZOLE-2-THIONE

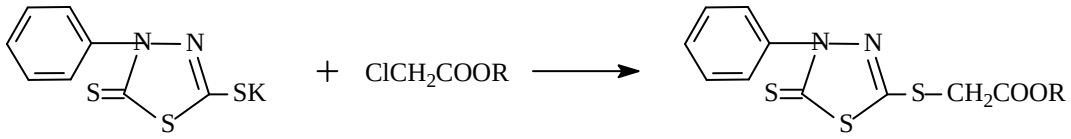
B. N. Babaev[1], A. A. Ziyaev[2]

1) A. S. Sadykov Institute of Bioorganic Chemistry, Uzbek Academy of Sciences, 100170, Tashkent , Mirzo Ulugbek st., 83, e-mail: bahrom-nur@rambler.ru
2) S.Yu. Yunusov Institute of Plant Chemistry, Uzbek Academy of Sciences , Tashkent, 100170, Mirzo Ulugbek st., 77, e-mail: aziyaev64@mail.ru

Nowadays 1,3,4-thiadiazole derivatives have received significant attention and have been increasingly investigated due to their diverse range of biological properties. They exhibit, for example, antimicrobial, antimycobacterial, anticancer, antiinflammatory, carbonic anhydrase-inhibiting effect, antianxiety, antidepressant, antioxidant and other properties [1, 2].

In the molecule of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione several centers with lone pairs of electrons present, which allow various chemical modifications of them them. The presence of pharmacophore groups in the structure of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione-nitrogen and sulfur ring atoms, as well as phenolic and two sulfur atoms of the cycle is likely allows to synthesize its derivatives with a wide spectrum of biological activity.

Based on the above, to search for new derivatives of thiadiazoles alkylation of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2-thione chloroacetic acid alkyl esters studied:



R=CH_3, C_2H_5, i-C_3H_7, C_4H_9, C_5H_{11}, $CH_2C_6H_5$:

The reaction takes place at the boiling point solvents (acetone, ethanol) in the presence of potash to give the 2-alkylthio-5-mercapto-3-phenyl-1,3,4-thiadiazole in high yields (85–93%). The resulting compounds are crystalline materials which are soluble in most organic solvents. The IR spectra absorption bands observed are characteristic for C = O group at 1740–1720 cm^{-1}, that confirms, along with X-ray analysis, the structure of the synthesized compounds.

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QUALITATIVE AND QUANTITATIVE DETERMINATION OF FLAVONOIDS IN MEDICINAL PLANT *Scutellaria iscanderi* L., BY THE METHOD OF CHROMATO-MASS-SPECTROMETRY

P. L. Ismailova, M. G. Ismailova, N. A. Abzalova

A. S. Sultanov Uzbek Research Chemical-Pharmaceutical Institute

One of the most important classes of active compounds, containing in medicinal plant raw material are flavonoids having wide spectrum of biological action and antioxidant activity. Currently, for identification and quantitative determination of flavonoids in medicinal agents are widely used combined methods of analysis including different versions of chromatographic separation of the studied components having considerably greater sensitivity and selectivity.

The objective of this work is qualitative and quantitative analysis of flavonoids in tincture and different organs of medicinal plant *Scutellaria iscanderi* L. applying chromato-mass-spectrometric method. Analysis method is based on combination of two independent methods, HPLC and mass-spectrometry. The first method helps to separate mixtures into the components, the second one – identification and quantitative analysis. To study component composition the substances were analyzed by HPLC method. Separation was carried out in HPLC (Agilent Technologies -1260, USA) column with reverse phase 2.1 × 150 mm (3.5 μ) Eclipse XDB. It was used the mixture of eluents A-0.05% buffer solution of formic acid with water, B-acetonitril and C-isopropanol with gradient 0-min 18% B+ 2%C, 15-min 72% B+8% C, 18-min 18% +2% C. Speed rate -0.25ml/min. By the method of ESI-mass-spectrometry (electrospray) were obtained mass-spectra of substances using mass-spectrometer 6420 Triple Quad LC/MS. Registration of mass-spectra of the samples were conducted by negative ionization. The following parameters of mass-spectrometer were chosen: scanning range of 100–2200 *m/z*, consumption of gas dehydrator 3 L/min, gas temperature 300°C, gas pressure in needle sprayer 20 psi, evaporator temperature 300°C, voltage in capillary 4000 V. The sample for analysis was prepared by extraction of 1 g of plant raw material in 5 mL of 80% methyl alcohol. Concentration of FSS standard for comparison is of 1 mg/g. Analysis results are presented in table.

No.	Sample	Luteolin	Apigenin	Quercetin
1	Aerial part	0.04375 mg/g	0.05122 mg/g	0.00770 mg/g
2	Leaves	0.09928 mg/g	0.17269 mg/g	0.05261 mg/g
3	Tincture	0.09631mg/ml	0.19321 mg/ml	0.01288 mg/ml

Thus, applying HPLC-mass spectroscopy flavonoid amount in the composition of tincture of *Scutellaria iscanderi* L. plant was determined.

STUDY OF THE TECHNOLOGY OF PURIFICATION OF TOTAL ALKALOIDS FROM *Nitraria sibirica* PALL WITH MACROPOROUS RESIN

Chimengul Turghun, Mahinur Bakri, Haji Akber Aisa

Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Science, 830011, Urumqi, P. R. Cnina

Nitraria sibirica Pall. (NSP) belonging to the *Zygophyllacea* family is one of the dominant species in Xinjiang, China, which plays a key role in improving the ecological environment due to its superior tolerance to severe drought and high salinity. As a traditional Uyghur herb, the fruits and leaves of NSP were used to treat hypertension, menstrual disorders and gastroenterities [1, 2]. Up to date, only a few phytochemical investigations of NSP have been reported [3, 4]. To optimize the purification technology of total alkaloid purification from the *Nitraria sibirica* leaf, the HPD-100, HPD-101, HPD-300, HPD-450, HPD-500, HPD-600, HPD-750, AB-8 eight kinds of resin were screened out to research its effects on the alkaloids of static, dynamic adsorption. Results indicated that the adsorption and resolution effects of HPD-450 resin on *N. sibirica.* Leaf′s total alkaloids were the best, the dynamic of adsorption tests proved that the optimum process conditions were: the sample liquid concentration 0.884 mg/mL sample solution pH 4, solution treatment capacity was 5BV, flow rate 2BV/h, washing with 5BV water, 30%, 50%, 70% ethanol was used as eluent, eluent volume was 5BV. After purification, the total alkaloid content increased from 0.58 % to 5.67%.

Conclusion. HPD-450 macroporous resin can effectively purify total alkaloids from the leaves of white thorn leaves, and the process is stable.

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POLYVINYLCHLORIDE AS A MATRIX FOR OBTAINING THE RESINS

M. M. Karimov[1], M. Q. Rustamov[1], M. B. Kayumov[1], N. R. Mukhamedov[2], Sh. Ya. Mirzaahmedov[2]

National University of Uzbekistan named after Mirzo Ulugbek
State Enterprise "Educational-Experimental Centre for High Technologies"

There are numerous academic investigations on the base of polyvinylchloride (PVC), starting from implementation of improvement its low thermal stability which induces the process of dehydrochlorination up to chemical alteration in order to obtain materials for certain applications. For instance, references of many works contain data on enhancing its low mechanical properties by addition inorganic plasticizers. In addition, the influence of many organic stabilizers for decreasing probable degradation of the matrix PVC during exploitation the products on its base were investigated [1].

As one more new direction may consider recent progress in surface modification of PVC films. Surface modification of polymer films became bright field of investigations due to emerging many new abilities giving special properties to polymer materials and items on the its base which stimulated appearance several innovation technologies. Except environmental factors, such as pressure, pH and temperature, contacts between various materials to a considerable degree controlled by surface interaction, notably their hydrophilic nature, topography and chemical content.

Chemistry in wide comprehension in these investigations was essentially directed to modification this polymer material by chemical reactions for expansion its range of application. By many researchers these tertiary and allyl atoms of chlorine at the normal and secondary combination with different content of double carbon-carbon bonds were exposed to many chemical modifications. The chemical modifications were undertaken not only for determining usual chemical regularity, but for improving properties of PVC too, in certain fields of application. Leading and attractive applications particularly were formulated in the chemical modification field of PVC in a direction of obtaining various ion-exchange materials (fibers, films, grains), ion selective electron membranes, membrane sensors and items for biomedical equipments.

Physical and mechanical properties of PVC and chemical resistance in various environments, also presence in its structure chemical active chlorine permits easy obtain ion-exchange materials on its base. As modifier reactants were selected substances containing various functional groups in their structure. Structure of the obtained resins was proved by IR-spectroscopy and potentiometry.

It was established that improvement of hydrophobicity of the solvent in a number of water, water-alcohol, water-glycerine positively influences to reaction yield and leads to enhancing static exchange volume of the obtained products. Influence of the temperature had an extreme character. Increasing of the temperature up to 140–145°C led to sharp acceleration of polymer destruction and degradation of its physical and mechanical properties.

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OIL CAKE OF SESAMUM

M. B. Davlyatova[2], A. I. Glushenkova[1], Sh. Sh. Sagdullaev[1]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan
2) Bukhara Engineer Technological Institute

Sesamum indicum is the only representative of the family *Pedaliaceae*.

Oil cake is widely used as the addition in the baking, salads, sauces and so an. It attributed to a great quantity of vitamin-mineral composition, calcium (to 1/76%), phosphorus (1.43%), protein (to 33%) and fat.

We investigated yield of neutral lipids (NL) (contained in the oil) and polar lipids (PL) of the sesamum oil cake and fatty acid composition of NL. Neutral lipids were extracted three times by hexan with intensive mix on the magnetic mixer. Then from unfatty material polar lipids were isolated by mixture of chloroform methanol (2:1) (Folch method).Then from PL glycolipids (GL) and phospholipids (PhL) were isolated using column chromatography, yields of NL made up 34.4%, GL-0.74%, Phl – 0.23% from the mass of oil cake. The principal components of NL were triacylglycerols, in the GL-sterylglycosides (main component) and their ethers, monogalactozil- and digalactozildiacylglycerides. Phospholipids enriched by phosphatidilcholines, and as minor components were phosphatidilethanolamines and phosphatidilinosites.

For the establishment of fatty acid composition of the neutral lipids, they were hydrolyzed by KOH. The obtained fatty acids were processed by diazomethan to obtain their methyl ethers for the analysis on an GC Aligent 6890 with flame – ionization detector using capillary column (30 m × 0.32 mm) with hard phase HP-5, carrier gas helium, temperature of programming 150–270°C (Table 1).

TABLE 1. **Fatty Acid Composition of NL, % of Mass**

Fatty acid	Neutral lipids
16:0	8.27
18:0	5.79
18:1	44.46
18:2	40.54
20:0	0.67
20:1	0.27
$\Sigma_{\text{saturated acids}}$	14.73
$\Sigma_{\text{unsaturated acids}}$	85.27

As seen from Table1, NL contains more 85% unsaturated fatty acids, among them 40% is essential linoleic acid.

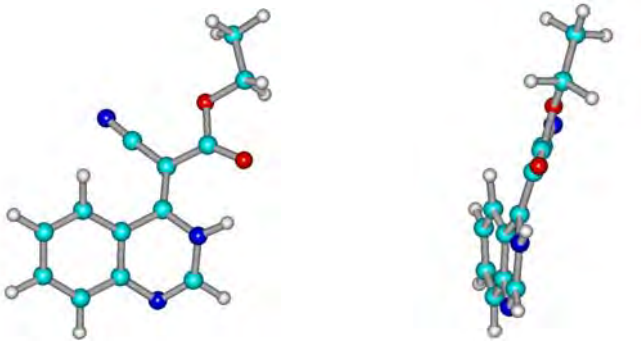
STUDY OF THE TAUTOMERY OF 2-SUBSTITUTED QUINAZOLINES WITH RESIDUES OF CH-COMPOUNDS AT C-4

M. Tulyasheva, B. F. Rasulev

Tashkent Pharmaceutical Institute, Ministry of Health, Republic of Uzbekistan,
Bd.45, Oybek str., 100015, Tashkent, Uzbekistan, e-mail: tulyasheva2012@yahoo.com

In this study investigations devoted to tautomeric transformations of 2-substituted-3,4-dihydroquinazoline-4-ylidencyanoacetic and malonic esters by computational methods have presented.

Quantum-chemical calculations were conducted using semiempirical methods of PM3 and AM1. Investigations revealed 4 tautomeric forms in these compounds, and they changed character in dependence of nature on substituents of 2 and 4 positions.



Front view Side view

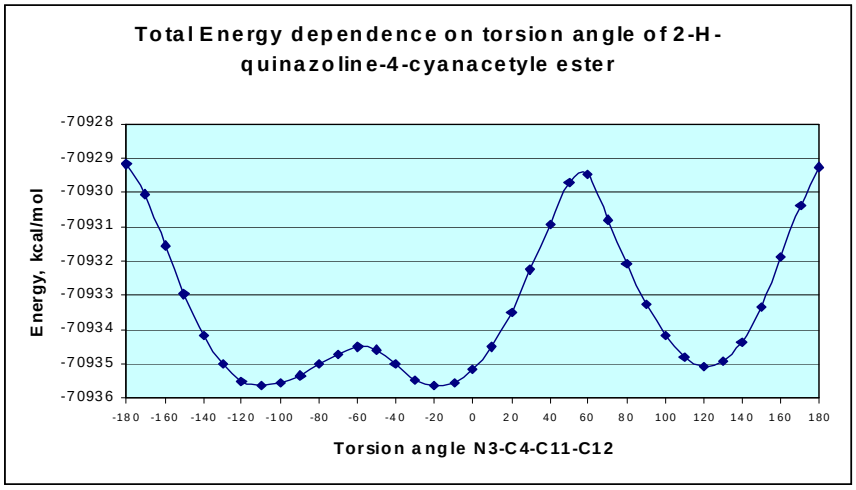


Fig. 1. Heat of Formation energy dependence on torsion angle of 2-H-quinazoline-4-cyanacetyle ester

By the experimental data (^{1}H NMR spectroscopy) we have observed as tautomeric form B, as tautomeric forms A and C, apparently in equal quantities.

The hydrogen bond interactions between the carbonyl group and the NH of the quinazoline ring add extra stability to the isolated products. These hydrogen bond interactions were identified from the ^{1}H NMR spectra and the computational studies, which show a bond distance of about 2.03 and 2.08 Å, respectively.

TO THE PROBLEM OF OBTAINING PUREES FROM ROOT AND TUBER CROPS

S. Sh. Abdullaeva, H. S. Nurmuhamedov, A. Sh. Abdullaev

Tashkent Chemical Technological Institute, 100011, Tashkent, Republic of Uzbekistan,
e-mail: sadshon1975@yandex.ru

Nowadays, the food industry needs food powders and semi-products from vegetable raw materials which can be widely used as filling agents and the flavoring additives; dyes of foodstuff; raw materials for various concentrates, medical and other drinks of different function; additives at preparation of baby food; initial basis of various medical and preventive medicines; components for instant garnishes.

Creation of modern highly effective technologies with the minimum losses of raw materials and high quality of finished goods is an actual task of food industry of any country. Now there is some lag of the industrial enterprises for processing of agricultural raw materials from the level of research and development. The majority of the existing technologies are equipped with power-intensive facilities that not always allows receive the products meeting the high requirements. The developed technology for receiving fine food purees from a root - tuber crops is based on the method of instant pressure release which serves for cleaning and preparation of puree, and also on fractionation of solid non-uniform systems in a three-phase fluidized layer where process of washing of the cleared tubers in parallel proceeds.

It is known that cleaning of root crops is made for removal invaluable in the food relation (thin skin) of parts of raw materials and according to drop of toxicity of a target product. The dominating part of harmful substances (herbicides, fungicides, salts of mineral fertilizers) in tubers of root crops during maturing accumulates in the cover. Besides, the substances promoting darkening of the cleared tubers are also concentrated near a thin skin.

For cleaning of a thin skin the root - and tuber crops with impurity of z = 3–15 of % come to the device of steam thermal processing which is based on the principle of instant pressure release. Pressure of sharp steam chosen depending on a version and initial moistness of raw materials. This method provides full cleaning and simultaneous removal with a thin skin of tubers the stuck soil and other mechanical impurities. Duration of steam thermal processing and its temperature established from their grade, size and kinds of tubers.

Further the purified material from the device of steam thermal processing moves for division into fractions in the device of a liquid fluidized layer. There is a cleaning of the stuck pieces of a thin skin and simultaneous washing of crude pulp with a mode.

Then, in the knife disk device, the tubers crush on pieces of 50 × 50 × 50 mm in size.

Further cubes of tubers move in the device of steam thermal processing for receiving puree by method of instant pressure release. It was revealed, that this puree, unlike the puree received by a traditional method, is partially dried and contains less moisture.

In the conclusion, it should be note that the above technology of receiving puree from a root – and tuber crops directed to development of products of healthy food from local vegetable raw materials.

PEDILININE, A NEW ALKALOID FROM *Haplophyllum pedicellatum*

Kh. A. Rasulova, M. A. Eshonov

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: khalida.rasulova@gmail.com

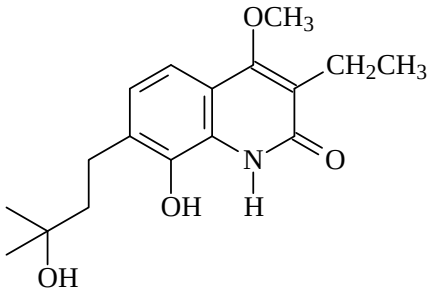
Haplophyllum is one of the richest for alkaloids kinds – *Rutaceae*. Until now, 27 plants of *Haplophyllum* have been investigated on alkaloids in the world, including 20 ones in laboratory of alkaloids chemistry. In result from plants of this sort there were isolated more than 90 quinoline bases, from them about 75, including 53 new, were found in the Central Asian types of Haplophyllum.

According to pharmacological studies, alkaloids of *Haplophyllum* showed sedative action on the central nervous system and no toxicity. Along with analgesic, anticonvulsive, sedative effects, some preparations demonstrated estrogen activity.

The study of quinoline compounds from plant sources is of huge importance because of their high physiological activity.

We have investigated alkaloids from the roots of *H. pedicellatum*, collected in Babatag of Uzbekistan. The roots of plant were extracted with MeOH. From methanolic extracts 0.65% total alkaloids were obtained. By column chromatography of total alkaloids were isolated known alkaloids evoxine, skimmianine, haplamine, glycoperine, as well as a new base with m.p. 201°C, which was named pedilinine.

The structure of pedilinine (1) was established on the basis of spectral data and was confirmed by direct comparison with a product found from folifinine.



Thus, pedilinine is a new alkaloid isolated from the plant.

ALKALOIDS OF ORGANS OF PLANTS *Haplophyllum ferganicum*

D. R. Kodirova, Kh. A. Rasulova, P. H. Ganiev

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: khalida.rasulova@gmail.com

Plants genus *Haplophyllum* have long been known for its medicinal properties. Infusions of several plants are widely used in national medicine as an anesthetic for toothache, thoracic and gastric diseases, externally for skin diseases, as a sedative with increased nervous excitability and nervous heartbeat.

Studied plant *Haplophyllum* ferganicum on the alkaloid content collected in the vicinity of Sadkok Namangan region. Leaves, stems, flowers and seeds individually extracted with 80% ethanol in Ultrawave bath. The evaporated extract is divided into 2 parts. 1 part of the extract divided into basic and neutral fractions. The amount of each individual plant alkaloids allocated treatment in the same method of extracts. Results are shown in the Table.

TABLE 1. **The Contents of Total Alkaloids in Haplophyllum Ferganicum Organs**

Organs of plants	Plant Weight (g)	The contents of alkaloids, % weight of air-dry feed
Leaves	295	0.83
Stems	211	0.41
Seeds and flowers	136	1.1

As seen from the data given in the richest table the content of alkaloids are seeds and flowers (1.1%) of the plant. Leaves contain less alkaloid (0.83%). The lowest content of alkaloids was observed in the stems (0.41%) of the studied plants. Almost valuable drug evoksin was isolated as the main alkaloid from the plant.

Part 2 of the extract divided by the solubility in organic solvents. Are obtained gasoline, chloroform, ethyl acetate and the alcohol part. In the separation on a silica gel column of the identified gasoline skimmianin, evoksin, haplamin, flindersin and metilevoksin.

STUDYING OF DOSES OF PREPARATIONS К-19 FOR APPLICATION AS RADIOSENSITIZING ON MICE WITH TUMOUR THE SARCOMA 180

Sh. N. Ibragimov, N. A. Agzamova, H. Kholturaeva, Z. M. Enikeeva

National Scientific Center of Oncology at the Ministry of Health of RUz, 383, str. Farobiy, City Tashkent, Uzbekistan

At last time formed representation that for increase effect of ionizing radiation by the most perspective direction application of chemotherapeutic preparations possessing radiosensitizer properties simultaneously with radial therapy [Gladilina I.A., 2011] is represented.

For the purpose of working out of less toxic radiosensitizer are studying of new antitumor preparation К-19 obtained based on colchamine, as agent to increase action of an irradiation.

Irradiated tumors of animals on instrument "THERATRON" with power 112 Gr/min., source of Co^{60} at total single dose of equal 6, 4,5 and 3 Gr, and also at repeated irradiation - at dose of 1,5 Gr for 4 time, or 1 Gr for 3 time, protecting animals lead plates with special aperture.

Determined antitumor activity at single introduction of preparation together with an irradiation on animals with tumour the Sarcoma 180 at late period after inoculation tumours.

The optimum mode of application К-19 together with an irradiation on animals with tumours were found (were found doses, time of introduction till an irradiation, of equal 16–24 hours) at 1-fold introduction.

In comparison with an irradiation 6, 4,5 and 3 Gr at action that obtained the effect of growth inhibition of tumours in 80, 66 and 35 % (on volume of tumours) accordingly.

Were introduction К-19 at dose 80 mg/kg till an irradiation of 6 Gr its action are increased by 20 %, at the same dose to an irradiation of 4,5 Gr its action increases by 34 %, and introduced into the same dose to an irradiation 3 Gr its action increased by 60 %.

К-19 at dose of 52 mg/kg are increased by irradiation action 4,5 Gr by 25 %, entered into the same dose to an irradiation 3 Gr its action increased by 42 %.

Application of preparation during 16 hours till an irradiation in higher dose promotes don`t only more considerable potentiation of its action (on 34-60 %), but also to decrease in adventitious influence of an irradiation both on weight of spleen, and on quantity of leukocytes.

The biological action of К-19, an irradiation strengthening action, it has shown, that in particular, in an inhibition of synthesis of nucleonic acids, infringement of reparation of DNA, activity suppression topoisomerase, updating mitotic cycle, as leads to occurrence in this preparation expressed antitumor and radiosensitizer activity.

HPLC METHOD DEVELOPMENT FOR DETERMINATION OF THE SUCCINATE OF MORPHINE AND MORPHINE-BSA CONJUGATE

A. D. Abidova, S. A. Sasmakov, D. R. Mansurov, E. G. Yusupova, G. A. Piyakina, Sh. S. Azimova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,e-mail: sasmakov@web.de

The morphine-BSA (Bovine Serum Albumin) conjugate is used to determine the long-lasting anti-morphine response in the diagnostic test kits. The conjugate is synthesized from morphine succinate. It is necessary to determine the reaction conditions and product standardization.

A sensitive and rapid reverse phase HPLC method is developed for the simultaneous determination of the succinate of morphineand morphine-BSA conjugate. The reaction mixture, succinateof the morphine and morphine-BSAconjugatewere chromatographed on aZorbax-Eclipse XDB-C18reversed-phase column (3.0 × 150 mm, particle size 3.5 μm). The mobile phase was Acetonitrile-Water, 5 to 95 (v/v) in 0–15 min. Detection was at 280 nm. The total elution time was shorter than 15 min. The optimized method was validated (linearity- $r>0.999$), and acceptable for analyzingof succinate of the morphine and morphine-BSAconjugate.

The developed method may be useful to control of reaction process, and to investigate of purity and the stability of morphine conjugate.

USE OF *Pichia pastoris* EXPRESSION SYSTEM FOR OBTAINING OF RECOMBINANT PROTEINS

O. N. Ashirov, Sh. Sh. Xasanov, J. M. Abdurahmanov, S. A. Sasmakov, Sh. S. Azimova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: sasmakov@web.de

*Pichiapastoris*is a methylotrophic yeast, successfullyused for production of a wide variety of recombinant proteins. As a eukaryote, *Pichiapastoris*has many of the advantages of higher eukaryotic expression systems such as protein processing, protein folding and posttranslational modification, while being as easy to manipulate as *E. coli* or *Saccharomyces cerevisiae*. These features make *Pichia*very useful as a protein expression system.

For obtaining of recombinant plasmids encoding “target protein - GFP” we have used the plasmid DNAs which designed for heterologous intracellular- pPIC3.5and secretedpPIC9-expression in *Pichiapastoris*.In constructed vectors,the target DNA sequence is located strong after the *AOX1* (gene is responsible for the vast majority of alcohol oxidase activity in the cell) promoter that encodes a secretion signal. Expression of the *AOX1* gene (GFP gene) is tightly regulated and induced by methanol to high levels. In methanol-grown shake-flask cultures, this level is typically about 5 percent of total soluble protein.

Theobtained recombinant plasmids pPIC3.5-TP and pPIC9-TP are giving a possibility forhigh level producing of green fluorescent protein (GFP).

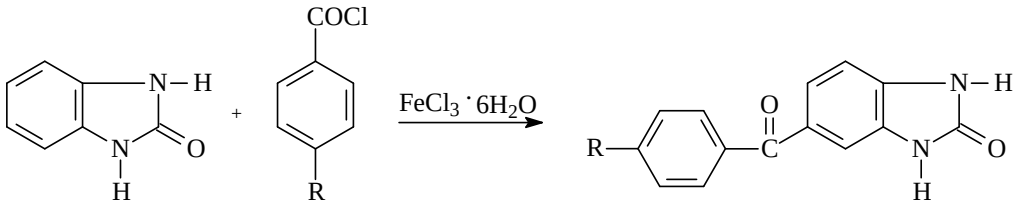
CATALYTIC ACYLATION OF THE BENZIMIDAZOLE-2-ONE AROMATIC ACID CHLORIDES

Y. R. Takhirov, D. A. Dushamov, Z. M. Ataullayev, R. Sh. Kuryazov

Urgench State University Named after Al-Khorezmi Faculty of Natural Sciences, Urgench, Uzbekistan, e-mail: yuldash_78@mail.ru

We have previously demonstrated the possibility of acylation benzothiazolin-2-ones [1,2] benzimidazolin-2-ones [3] aromatic acid chlorides using small amounts of catalyst in nitrobenzene. However, these reactions are carried out at a temperature 200–210°C nitrobenzene and distillation is very difficult, resulting in oxidation products. Therefore, it seemed interesting to carry out these reactions in the absence of a solvent and to compare the data obtained.

Reactions benzimidazolin-2-one (**1**) aromatic acid chlorides (**2–6**) in the presence of $1 \cdot 10^{-2}$ moles $FeCl_3 \cdot 6H_2O$ conducted without a solvent at a temperature 150–160°C. The reactions were synthesized corresponding 5 (6)-aroilbenzimidazolin-2-ones.



1 **2-6** **7-11**

2,7 R=H, **3,8** R=CH_3, **4,9** R=OCH_3, **5,10** R=Br, **6,11** R=NO_2;

The optimal conditions for the acylation reaction and identify the use of small amounts of catalyst. According to our study, the reactions carried out with a molar ratio of reagents 1:2-6:$FeCl_3 \cdot 6H_2O$ =1:1,5:$1 \cdot 10^{-2}$ to proceed without a solvent at a lower temperature (150–160°C). According to this method yields compounds **7–11** higher than conducted using nitrobenzene.

The structure of the synthesized compounds is proved by IR-spectroscopy, mass-spectrometry. Temperature melting compounds **7–11** are identical with those given in the literature [3], but obtained by other methods.

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DESIGNING OF RECOMBINANT PLASMID DNA pBacPAK8-TP, ENCODING TARGET PROTEINS IN BACULOVIRUSES

J. M. Abdurahmanov, Sh. Sh. Xasanov, O. N. Ashirov, N. A. Tosheva, A. A. Eshmuratova, S. A. Sasmakov, Sh. S. Azimova

Acad. S. Yu.Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: sasmakov@web.de

The recombinant plasmid containing DNA sequence of “target protein” was designed. The recombinant plasmid DNA is created on the basis of vector pBacPAK8, which designed for expression of recombinant proteins in baculoviruses system. It is contained the following elements (genes): Polh – strong late promoter for controlling of expression of foreign genes in nuclear polyhedrosis viruses and ampicillin resistance gene for selection in *E. coli.* For cloning of recombinant plasmid DNA accordance with the physical map of the vector pBacPAK8, and “target gene” were digested by *EcoRI* and *NotI*. As a result, the pBacPAK8/*EcoRI/NotI* linear fragment of vector and an insert (target gene) with complementary "sticky" ends were obtained. After ligation in molar ratio of 1:10 (vector:insert) using the T4 DNA-ligase, the ligate was transformed into *E. coli* NEB-5α.

Identification of the recombinant clones was carried out using PCR and restriction analysis.

This plasmid DNA may be used for expression of recombinant proteins in baculoviruses expression system.

DETERMINATION OF HIGH-LEVEL PRODUCING SILKWORM LARVAE KINDS OF RECOMBINANT PROTEINS

N. A. Tosheva, A. A. Eshmuratova, J. M. Abdurahmanov, S. A. Sasmakov, G. A. Piyakina, Sh. S. Azimova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: sasmakov@web.de

Heterologous gene expression in baculovirus system offers several advantages such as correct post-translational modifications and high yields of biologically active proteins. The expression system is based on the replacement of a strong, very late, non-essential for virus replication, viral gene, termed polh - polyhedrin, with a gene of interest. The insertion of foreign DNA at the polyhedrin locus within the viral genome results in incorporation of the foreign DNA into progeny virus particles and subsequent high-level expression of the recombinant protein within eukaryotic insect cell lines. More recently, an increasing number of investigators use *Bombyx mori* nucleopolyhedrovirus (BmNPV) in baculovirus expression system. BmNPV, especially infected silkworm larvae, is used for large-scale production of recombinant proteins. The key advantage of this recombinant protein manufacture platform is a low manufacturing cost for producing a broad range of protein-based prophylactic and therapeutic means.

In this regard, relevant is the determination of sorts of silkworm larvae synthesizing the target protein with high-yield. For this purpose, we have infected with recombinant baculovirus rBm-GFP, the domestic silkworms larvae Guzal and Orzu. The intensity of expression of recombinant GFP protein was determined by fluorescence microscopy, SDS-PAGE and immunoblotting.

The results showed that the silkworm larvae Guzal is the most suitable for obtaining of large amount of recombinant GFP in a baculovirus expression system.

SYNTHETIC OLIGONUCLEOTIDES FOR THE DETERMINATION OF HCV RNA IN HUMAN BLOOD BY PCR

S. A. Ikramov, A. A. Mahnyov, O. B. Alimuhamedova, J. M. Abdurahmanov, S. A. Sasmakov, D. R. Mansurov, E. G. Yusuova, Sh. S. Azimova

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: genlab_icps@yahoo.com

Hepatitis C virus (HCV) is an RNA-containing virus with positive strand, which appears itself as an agent leading to a serious chronic disease impairs the patient's quality of life. Viral Hepatitis C has six genotypes,the genomes of these genotypes are highly heterogeneous. Advanced methods of diagnosis of the virus HCV is a PCR analysis.

In our case, on the base of the nucleotide sequence of the genome of viral hepatitis C have been designed primer pairs: ACF91-ACR93; HCV-F - HCV-R; HC1313 - HC1314. Then, primers size of 20–26 base pairswere synthesized at DNA - synthesizer ASM-800 and purified by polyacrylamide gel electrophoresis.

PCR results were analyzed by gel electrophoresis. The analysis found that a clear positive result given the primers HCV-F and HCV-R.

On the base of these primers, we can construct the PCR test-system for analysis of HCVvirus.

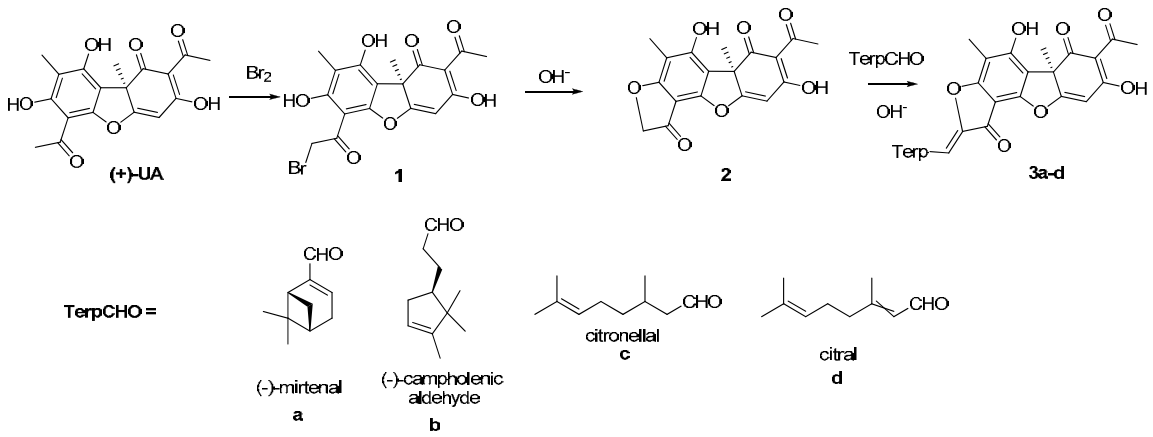
SYNTHESIS AND BIOLOGICAL ACTIVITY OF TERPENOPHENOLS DERIVED FROM USNIC ACID

O. A. Luzina[1], A. S. Filimonov[1,2], A. L. Zakharenko[3], O. I. Lavrik[3], N. F. Salakhutdinov[1,2]

1) Novosibirsk Institute of Organic Chemistry. N. N. Vorozhtsov, 630090, Russia, Novosibirsk, 9-Prospect Academician Lavrentiev St.
2) Novosibirsk State University 630090, Russia, Novosibirsk, 2 Pirogova Str.
3) Institute of Chemical Biology and Fundamental Medicine, (ICBFM SB RAS) 630090, Russia, Novosibirsk, 8-Lavrentiev Avenue

Natural meroterpenoids (including terpenophenols) - an important class of natural compounds [1]. Among them there are agents with outstanding biological activity (eg cannabinoids). Methods of terpenophenols isolation from natural sources are often time-consuming and inefficient. Therefore the development of approaches to the synthesis of biologically active terpenophenols and identify opportunities of their application in pharmacology is a promising area of investigation. Furthermore, synthetic conjugates of phenolic compounds with terpenes usually have low toxicity and multitarget mechanism of action. Usnic acid (UA) is a common secondary lichen metabolite; it has a broad spectrum of biological activity [2]. However, appreciable toxicity prevents its widespread use for therapeutic purposes. The synthesis of new derivatives on the basis of usnic acid, in particular compounds that combine fragments usnic acid and a physiologically active natural substance monoterpenoids, can reduce toxicity and modify the biological activity.

On the basis of (+)-usnic acid we obtained a number of compounds **3a–d** which are conjugates of natural phenol and linear or cyclic terpenic aldehydes - citral, citronellal, (–)-mirtenal and (–)-kampholenic aldehyde.



Screening of their inhibitory activity with respect to human reparative enzyme Tdp1 showed that active concentrations reduced with increasing of the terpene moiety mobility (IC_{50} 15 μM for **3a**, 1.5 μM for **3b**, 0.17 μM for **3c**). Thus, compound **3c** is effective inhibitor of Tdp1 and has significant potential as candidate drug for anti-cancer therapy.

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WATER-SOLUBLE POLYMERS AS MODIFIER OF NAPHTHALIC ANHYDRIDE BASED SEED PROTECTANTS

Yu. Ya. Spiridonov[1], S. S. Khalikov[2], O. Yu. Selyutina[3], N. E. Polyakov[3]

1) All-Russian Research Institute of Phytopathology, Moscow region, Bolshie Vyazemy, Russia, e-mail: spiridonov@vniif.ru
2) Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences, Moscow, Russia, e-mail: salavatkhalikov@mail.ru
3) Voevodsky Institute of Chemical Kinetics and Combustion of Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia, e-mail: polyakov@kinetics.nsc.ru

Improving farming is achieved through rational implementation in production of a number of necessary measures, including the solution of the problem of protection of cultural plants from the herbicide applied during the growth of the previous culture. The modern approach how to eliminate the negative impact of herbicide residues is application the antidotes [1].

Development of protectants based on known antidote - naphthalic anhydride (NA) with a complex action, including antidotal activity against herbicide metsulfuron-methyl, is described in [2]. To modify the properties of NA, in particular, to improve its water solubility, the inclusion complexes with water soluble polysaccharides (arabinogalactan (AG), sodium carboxymethylcellulose (Na-CMC)) and oligosaccharides (glycyrrhizic acid (GA) and its sodium salt) have been prepared using mechanochemical techniques [3].

The report will highlight the methods of synthesis and evaluation of physicochemical properties of the compositions, as well as the results of biological testing of these compositions on the antidotal activity. We analyzed the dynamics of penetration of the compositions in wheat and barley seeds, and suggested the possible mechanisms of penetration in the processed vegetable objects. It was demonstrated the possibility of increasing the solubility of the NA in the complexes with polysaccharides by dozens of times, as well as strengthening its penetration in wheat and barley. The greatest effect on the permeability of NA (10 times) showed polysaccharide arabinogalactan.

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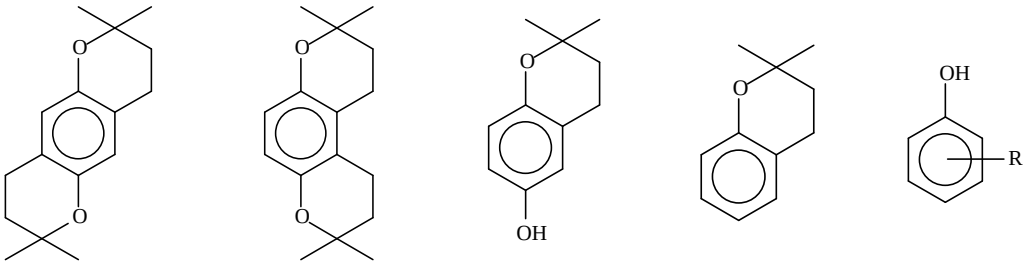
FEATURES OF ALKYLATION OF PHENOLS WITH PRENOL

I. V. Fedorova[1], I. Yu. Chukicheva[1], A. A. Korolyova[1], S. S. Klepikova[2], A. V. Kutchin[1]

1) Institute of Chemistry, Komi Science Centre, 167982 Russia, Republic of Komi, Syktyvkar, Pervomaiskaya st.,48
2) Syktyvkar State University Pitirim Sorokin, 167000 Russia, Republic of Komi, Syktyvkar, October prospect, 55

Natural terpenophenols have a wide range of biological activity. In particular, they benzopyran derivative chromanes (tocopherols, cannabinoids, flavonoids, coumarins, anthocyanins, etc.) have a vitamin, antioxidant activity and have influence on the central nervous system [1–6]. It causes interest to the synthesis of similar compounds.



1 **2** **3** **4** **5**

Alkylation of hydroquinone and phenol with prenol (natural allyl alcohol containing one double bond) has studied. The main products of interaction of hydroquinone and prenol by reagent method in the presence of $(i\text{-PrO})_3Al$ at 120°C and 160°C were the esters of the chromane-type **1**, **2** and **3** with a total yield of 83 and 87% respectively. Reagent method is based on the use of aluminum isopropoxide as a substrate for alkylation, who is also a catalyst. It should be noted that at using of catalytic amounts of $(i\text{-PrO})_3Al$ the **1**–**3** chromanes have not formed. In this case, *ortho*-prenylhydroquinone as the major product, have isolated with yield of 65%. Alkylation of phenol with prenol at presence of equimolar amount of $(PhO)_3Al$ at 120°C and 160°C the chromane **4** (43–56%) have isolated as the main product. Catalytic alkylation of phenol with prenol in the presence of $(PhO)_3Al$ at the same temperatures has led to the formation *ortho*- and *para*-C-alkylation products **5** with total yield of 61–74%. In this reaction the chromanes have not formed.

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STUDY CHEMICAL TRANSFORMATIONS IN ADSORBENT REFINING BY HEAT TREATMENT

A. V. Protopopov, S. A. Bobrovskaya, A. V. Voroshilova, S. A. Betsina, O. V. Myasnikova, T. A. Fominih

Polzunov Altai State Technical University, Russia, 656038, Barnaul, Lenin avenue, 46;
e-mail: a_protopopov@mail.ru

Waste adsorbents are bentonite exposed to extraction with diethyl ether in order to separate the adsorbed oil. The separated oil contains the main part of a group of higher fatty acids and esters thereof. To study the interaction of the polymerization process carried out the oil isolated in one experiment with sulfur and carbamide in the second at 130°C for 15 minutes. For comparison transformations taking place was held control experiment with the original oil in similar conditions.

Research on the solubility in carbon tetrachloride, ethyl acetate and acetone showed high solubility of the starting oil in all three solvents. The oil was subjected to thermal stresses, in these solvents dissolve less, and after reaction with carbamide or sulfur solubility is drastically lowered, and in the case of reaction with carbamide in a greater degree.

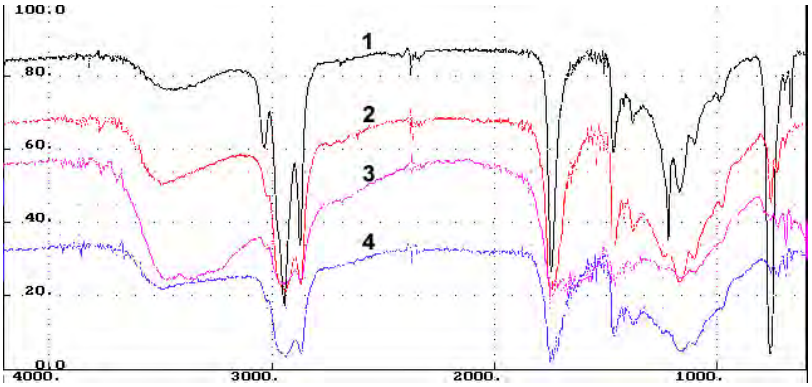

Fig. 1. The IR spectra of the starting oil (1), oil, heat treated (2), after reaction with carbamide (3), after reaction with sulfur (4).

To study the possible chemical reactions during thermal exposure resulting products were analyzed by IR spectroscopy.

After the heat treatment the oil intensity band at the IR spectrum is practically not changed compared to the original oil. Substantial chemical transformations while occurs. Reducing the solubility can be proved oil thickening due to evaporation of volatile components.

After the heat treatment in the presence of sulfur is observed decrease in the intensity of the absorption bands responsible for the fluctuations of unsaturated carbon bonds. This indicates occurring crosslinking reactions and condensation of unsaturated fatty acids. When interacting with carbamide IR spectra observed almost complete disappearance of the absorption band, responsible for the vibrations of unsaturated carbon bonds, and the appearance of absorption bands, amino group responsible for absorption. Consequently, carbamide during thermal exposure is reacted with higher fatty acids forming part of the oil, to form a three-dimensional mesh structure.

Studies have shown the ability to produce composite materials by condensation of higher fatty acid residue in the fat and oil refining adsorbents.

A NEW SPIRO COMPOUND FROM *Caragana acanthophylla*

L. Mahsut[1,2], L. Pan[2], M. Imerhasan[1*], K. A. Eshbakova[3], X. G. Jia[2]

1) College of Chemistry and Chemical Engineering, Xinjiang University, Urumqi, 830046, P. R. China, e-mail: imerhasan@yahoo.com
2) Xinjiang Institute of Chinese Traditional Medical and Ethical Materia Medica, Urumqi, 830002, P. R. China
3) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: komila@yahoo.com

Caragana acanthophylla Kom. is a kind of Uyghur′s traditional herbal medicine, long been used in folk of Xinjiang China. The ethanol extract from the aerial parts of *Caragana acanthophylla* let to the isolation of one new spiro compound: 1-carbonyl-3-methoxy 2,4-diene-spiro-[5,9]-14,15-dihydroxy naphthalene (compound **1**), and four known compounds **2–5**. They are calycosin (compound **2**), psoracinol (compound **3**), octadecyl caffeate (compound **4**), (–)-syringaresinol (compound **5**). Compounds **2–5** were isolated from *Caragana acanthophylla* for the first time. The molecule structures of the isolated compounds **1–5** is determined on basis of ^{1}H NMR, ^{13}C NMR, 2D NMR and Mass spectrum.

The air-dried and powdered aerial parts of *Caragana acanthophylla* were extracted three times with boiling 80% ethanol. The extract was then condensed and successively partitioned with petroleum ether, dichloromethane, ethyl acetate and n-butyl alcohol. The dichloromethane fraction was repeatedly chromatographed over silica gel column, Sephadex LH-20 and finally purified by recrystallization. Finally compound **1–5** were isolated. We used ^{1}H NMR, ^{13}C NMR and mass spectra in addition to comparison with literature data to identify the isolated compounds.

Materials. The plant material was collected from Urumqi, Xinjiang, People's Republic of China, on 20 May, 2014. The specimen was identified by Dr. Guoping Wang, Xinjiang Institute of Chinese Traditional Medical and Ethical Materia Medica.

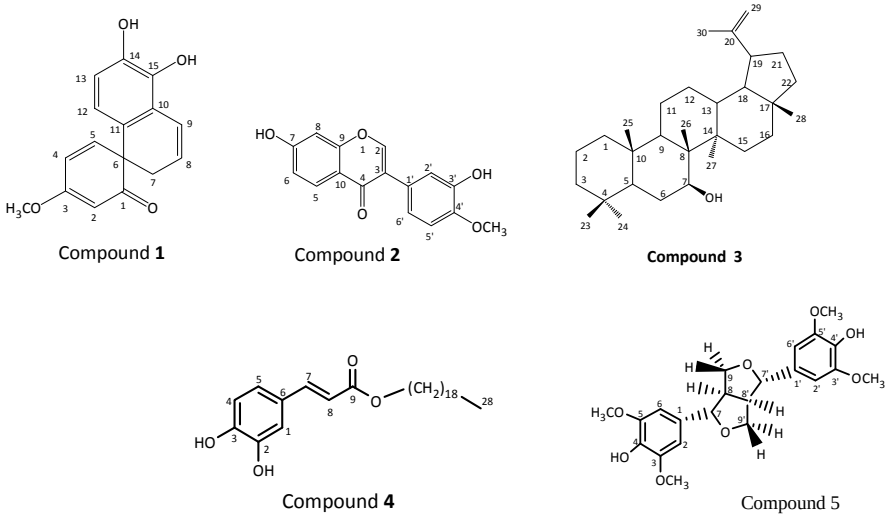

Fig. 1. **Structures of compounds 1–5 isolated from ethanol extract of *Caragana acanthophylla***

PLANTS OF THE GENUS MAGNOLIA INTRODUCED IN ADJARA (GEORGIA) AS POTENTIAL SOURCES OF BIOLOGICALLY ACTIVE ALKALOIDS

N. S. Vachnadze, L. G. Kintsurashvili, T. Sh. Suladze, V. Y. Vachnadze

TSMU Iovel Kutateladze Institute of Pharmacochemistry, Sarajishvili st. 36, Tbilisi, Georgia

Alkaloids have been studied in *Magnolia* species, introduced in Adjara as plant resources of biologically active substances with potential medicinal application: *Magnolia grandiflora* L., *M. delavayi* Franch, *M. virginiana* L., deciduous: *M. acuminata* L., *M. cambellii* Hook. et Thoms., *M. denudata* Desr. D.C., *M. liliflora* Desr, *M. kobus*, M. l*oebneri* Kache, *M. obovata* Thunb., *M. Kobus* f. borealis Sarg., *M. salicifolia* Maxim., M. sinensis (Rehd. et Wils.) Staf, *M. soulangeana* Soul.-Bod, *M. stellata* (Siebi et Zucc) Maxim., (дерево и кустарник) *M. glauka*, *M. officinalis* L., *M. tripetala* L, *M. wantsonii* Hook, deciduous shrub *M. coco* D. C. [1].

In folk medicine Magnolia species find extensive use in treatment of various diseases. The research goal was obtaining total alkaloids from the barks and leaves of *Magnolia* species. Phytochemical investigations of *Magnolia* species have shown that they mainly contain aporphine alkaloids: liriodenine, lanuginosine, d-isolaurenine, remerine, kaaverine, magnoflorine etc.

Leaves and barks contain different alkaloids. The leaves contain: d-isolaurenine, lanuginosine and liriodenine, while the bark alkaloids are – remerine, lanuginosine, liriodenine, kaaverine, *d*-kaaverine, magnoflorine.

Identification of isolated alkaloids was carried out based on their physical-chemical properties and spectroscopy data.

Cytotoxic activity of total alkaloids obtained from *Magnolia* species was studied at the Laboratory LASEVE, University of Quebec at Chicoutimi, Department of Fundamental Sciences, Chicoutimi Quebec, Canada.

The cytotoxic activity of alkaloids was assessed using the resazurin reduction test. Cytotoxisity was evaluated on human lung carcinomma (A-549), human collon adenocarcinoma (DLD-1) and human normal fibroblasts (WS-1) cell lines obtained from the American Type Culture Collection (ATCC). Cytotoxic activity of total alkaloids was expressed at the concentration inhibits cell growth by 50% (IC_{50}). Etoposit was used as positive control.

The examined components total alkaloids of *Magnolia glauca* (barc) have shown strong cytotoxic activity against DLD-1 (6,6 ± 0,6) and WS-1 (7,2 ± 0,9), but moderate activity against A-549 (29,4 ± 1,0). Although total alkaloids of Magnolia officinalis was moderately active against all cell lines.

FATTY ACID COMPOSITION OF FRUITS OF *Viburnum opulus* L. GROWING IN GEORGIA

D. S. Lagazidze[1], M. K. Orjonikidze[1], G. V.Tsagareishvili[1], J. N. Aneli[1], R. A. Abramovich[2], S. V. Goryainov[2]

1) Tbilisi State Medical Universitry I. Kutateladze Institute of Pharmacochemistry, 36 P. Sarajishvili str., 0159, Tbilisi, Georgia
2) Peoples′ Friendship University of Russia, Miklukho-Maklaya str., bldg.. 8/2, 117198, Moscow, Russia

Cranberry is one of the valuable medicinal plants. It is widely spread at Tsiv-Gombori ridge (Eastern Georgia), but a chemical composition of the Georgian phenotype is less studied.

We have studied fatty oil obtained by extraction of air-dried fruits in Soxhlet extractor; hexane was used as extraction agent. The oil yield was 11–13% (absolutely dry fruits). Physical and chemical parameters determined by the standard methods were the following: density 0.913 g/cm^3; refractive index – 1.4715, an acid number 1.72 mg KOH/g; an iodine number 33,03% I_2; peroxide value – 1,01% . The fatty acid composition of the oil determined according to GOST 31 663-2012. Methyl esters of fatty oils were obtained by interesterification with acetyl chloride (CH_3COCl).

The specimens were analyzed by gas chromatography on Agilent 7890A, equipped with a flame ionization detector; capillary column Agilent CP-Sil 88 CB, 0.22 mm × 50 m, the carrier gas – helium, carrier gas rate – 1.5 mL/min. Chromatograph operating conditions: injector temperature 250°C, the initial chromatograph oven temperature – 150°C, then heating at with a rate of 4°C /min up to 220°C. Volume of the injected specimen – 1 mL. Fatty acids identification was carried out by comparing the retention times of peaks in the chromatograms of the test specimens with the peaks in the chromatogram of the standard 37 Supelco FAMES mix (Sigma–Aldrich, Germany) obtained under the same chromatographic conditions. The presence of the following fatty acids was found.

TABLE 1. **Fatty Acid Composition of *Viburnum opulus* L. Fruit Oil (n = 3)**

Fatty acid name	Fatty acid index	Fatty acid content (% of total acids)
Lauric	12:0	0.17
Myristic	14:0	0.14
Palmitic	16:0	2.59
Hexadecanoic	16:1	0.09
Palmitoleic	16:1 9 cis	0.08
Stearic	18:0	0.79
Oleic	18:1 9 cis	56.47
Iso-octadecadienic	18:2 i	0.03
Linolic	18:2	38.78
α-linolenic	18:3 ω-3G	0.45
Arachic	20:0	0.06
Gondoinic	20:1	0.34

The main oil components of the studied fruit specimens of Cranberry Tree (*Viburnum opulu*s L.) growing in Georgia, are unsaturated fatty acids (95%), oleic and linoleic acids. The other fatty acids are present in insignificant amounts.

BIOLOGICALLY ACTIVE COMPONENTS OF FLOWERS OF *Crocus adami* J.

A. Sh. Aliyeva, E. N. Novruzov

Institute of Botany of NANA, Baku, Badamdar Highway, 40 AZ1073
E-mail: eldar_novruzov@yahoo.co.uk

Continuing the study of biologically active components of the family *Jridaceae* Juss., studied the qualitative composition and quantitative content of anthocyanins, flavonoids and carotenoids Crocus Adami J., collected in the vicinity of the village Bichenek (NAR). It was found that depending on the height above sea equation flavonols vary within 540.1% 760.3 mg anthocyanins – 317.5–535.4% mg carotenoids 28.3–39.4%. The largest number of test substances accumulate in the middle mountain belt (1670 m above sea level).

Chromatographic analysis of the alcoholic extract of fresh flowers showed the presence of 5 anthocyanins, 6 flavonoids, 7 carotenoids. It was found that the height of the terrain and habitat conditions do not affect the qualitative composition of the pigments.

By combined method of column and paper chromatography of alcoholic extracts of flowers, isolated in the individual form anthocyanin 4, 5 flavonoids and 6carotenoids. On a base of results of chemical, spectral and chromatographic analyzes of anthocyanins identified as cyanidin-3-glucoside, cyanidin 3,5-glucoside, flavonoids - quercetin, izoramnetin, kaempferol, rutin, izoramnetin-3,7 glucoside, carotenoids, α, β carotene, lycopene, zeaxanthin, neo-β-carotene, krotsetin. Content krotsetina privails over other carotenoids.

DEVELOPMENT OF COMPLEX VEGETABLE-FATTY SYSTEM WITH BALANCED FATTY-ACID STRUCTURE

N. R. Djuraeva, I. B. Isabaev

Bukhara Engineering-Technological institute, K. Murtazaev Street, 15,
Bukhara, Uzbekistan

One of the major directions of development of new kinds of fatty products is possibility of formation functional properties in fatty products for the account of application of traditional and nonconventional components. Creation of the vegetable-fatty systems balanced on fatty-acid structure and enriched with essential and minor components is preferable. As vegetative fraction of system it is expediently to use non-defatted high-oil vegetative raw materials.

The most significant and perspective is the germinal product of wheat (Triticum vulgare, Triticum durum) which oil differs by equation of fatty-acid structure on parity to poly-saturated fatty acids of the class ω6 and ω3. Triacylglycerides of the wheaten germ contain in a significant amount ω3 which practically is absent in many widespread vegetable oils and fats. By development of vegetable-fatty compositions we use non-defatted flour from the germinal product of wheat. For emulsion fatty products has been determined maximal admissible dose of non-defatted flour from the germinal product of wheat at 10% to the receipt quantity of raw materials and it was shown that its further increase leads to deterioration of organoleptic and physical and chemical indicators, and also to reduction of periods of storage of the product under the influence of water fraction. However such dosage does not provide the recommended parity of fat acids in compositions.

Considerable interest represents waterless fatty compositions with use of palm-oil, the mutton fat, creamy melted butter, and also their mixes with vegetable oils as sunflower, soya and olive. As samples of comparison were used fatty product and non-defatted flour from the germinal product of wheat.

It is determined that these compositions are not balanced and differ with raised maintenance of saturated fatty acids and lowered maintenance of poly-saturated fatty acids. Though correlation of fat acids in fatty fraction changes to the best, however it is not enough for reception of functional composite mixes. As to a parity ω6 to ω3 in mixes with creamy melted butter and the mutton fat, seeming at first sight admissible for dietetic therapy, so against a background of obvious deficiency of poly-saturated fatty acids it has no essential physiological value.

Full replacement of hard fats with liquid vegetable oils is not possible because of sedimentation of parts of the flour component. In this connection 30–50% of hard fats replaced with vegetable oils.As a result fatty fractions of all offered compositions were characterized by optimum correlation of poly-saturated fatty acids of the class ω6 and ω3 and sufficiently corresponded to demanded correlation of saturated fatty acids : mono-saturated fatty acids : poly-saturated fatty acids. And, dynamics of changes of this data in process of increase of the share of non-defatted flour from the germinal product of wheat in compositions testifies to an essential role of the latter in optimization of fatty-acid structure at sharing with fats and vegetable oils. Variants from 70% non-defatted flour from the germinal product of wheat were differed with most balanced fatty-acid structure.

As perspective raw materials for composites also could be used the amaranth (Amaranthus) which oil is characterized by presence of squalen and vitamin E in rare, especially active tocotrienoic form. These complex systems can be used as functional additives at the production of bakery and flour confectionery products, and also at the production of semi-finished products for the “atola” type products.

ANALYSIS OF CHEMICAL COMPOSITION ON UYGHUR TRADITIONAL PATENT MEDICINE – QIZIL GULKANT

Abulizi Yimiti, **Mehrigul Abdulahat**

College of Chemistry and Chemical Engineering, Xinjiang University,
830046, Urumqi, P. R. China

Qizil Gul（Rosa rugosa）kant is a preparation of the traditional Uighur medicine. In this papers produced by four different manufacturers Qizil gulkant as raw material to extract (reflux extraction, Soxhlet extraction, drying incineration) the major and trace elements, total flavonoids, saponins, alkaloids and determine those content. There were differences in the content of each composition from different manufacturers of the Qizil gulkant. The recoveries (n = 9) of total flavones and total saponins from four samples were 96.1–108.2% and 88.7–95.7%, respectively. The relative standard deviations (RSD)were less than 10%.

The chemical components composition of volatile oil from four kinds of Qizil Gulkant samples were compare and analyzed. The volatile oil from different samples was extracted by organic solvent extraction methods and identified by GC/MS. Seventy-five compounds were isolated and sixty-two compounds were identified. Among them, twelve in common components for four kinds of samples. Aliphatic compounds were more than other compounds in the volatile oil, and representing 69.04–81.3% of the total peak area. Followed by the aromatic compounds, and which representing 17.43–29.36% of the total peak area. While, the types and representing of terpenoids were less. Because of the Qizil Gulkant′s raw materials were from different areas and different manufacturers, there are differences in the constituents and contents of volatile oils.

Uyghur traditional patent medicine research shed light on the pharmacological action essence of chemical composition. This study expected to play the role of physical plaster roses sugar and Exploitation of experimental data and analytical methods.

APPLICATION OF NATURAL COMPOUNDS FOR THE CREATION OF INNOVATIVE ANTHELMINTIC DRUGS

I. A. Arkhipov[1], S. S. Khalikov[2], Yu. S. Chistyachenko[3], A. V. Dushkin[3], A. I. Varlamova[1], M. B. Musaev[1]

1) All-Russian Research Institute of Fundamental and Applied Parasitology Animal and Plant RAS, 28, B. Cheremushkinskaya str., Moscow, Russia
2) Institute of Organoelement Compounds RAS, 28, Vavilova str., Moscow, Russia, e-mail: salavatkhalikov@mail.ru
3) Institute of Solid State Chemistry and Mechanochemistry Siberian Brunch of RAS, 18, Kutateladze str., Novosibirsk, Russia

Creating drugs based on using natural compounds as auxiliaries can in some cases effectively address targeted delivery of substances to biological targets because of their structural similarity. It should also be borne in mind that the use of well-known and used in practice anthelmintic substances and the latest achievements in supramolecular chemistry is one of the most efficient, effective and promising areas of modern biotechnology. This significantly reduces implementation time of new drugs in the practice of veterinary medicine and addressed topical issues of import substitution.

Our research on the development of medicines for veterinary use by mechano-chemical modification of substances known anthelmintic substances, water-soluble polymers in order to increase their effectiveness and range of action allow you to create and offer to the practical application of innovative anthelmintics, retain high activity while reducing the active ingredient application rate (up to 10 times or more).

This report will be presented data on solid-phase synthesis by joint mechanical treatment of anthelmintic drugs on the basis of benzimidazole derivatives (carbendazim, albendazole, fenbendazole, triclabendazole) and natural substances (polysaccharides, saponins, etc.). It will be presented the data analysis of the physico-chemical properties of the solid dispersions and the possibility of obtaining supramolecular complexes such as "guest-host". Promising to get innovative products is confirmed by the data obtained in laboratory models and experimental animals in tests of their anthelmintic activity.

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NEW COUMARIN DERIVATIVES FROM ROOTS OF *Heracleum pastinacifolium*

G. K. Gasumova[1], S. V. Serkerov[2]

1) Ganja State University, Heydar Aliyev Avenue 159, Ganja AZ-2000;
e-mail: gultakin@mail.ru
2) Institute of Botany, Azerbaijan National Academy of Sciences, Badamdarave, 40,
Baku AZ1073, e-mail: s.serkerov@mail.ru

Plants belonging to the *Heracleum* genus contain a various biologically active coumarinderiveatives. Published data indicate that in the *Apiaceae* family plantsrepresentative of which is *Heracleum pastinacifolium* contains a significant amount of coumarin derivativeshaving practical value.

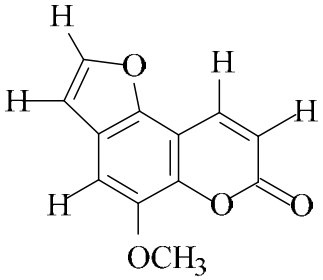
Anticarcinogenicactivity of a small number of coumarins such as peucedanin, prangenin, xanthotoxin, isopimpinellin, isoimperatorin, oxypeucedanin hydrate, marmesin, heraclenolandostolindicatesprospects of research on the isolation and study of plant substances.

From the roots of *Heracleum pastinacifolium* has been isolated two new furocoumarins: $C_{12}H_8O_4$, mp 172–174°C (1) and $C_{17}H_{16}O_7$, mp 151–153°C.

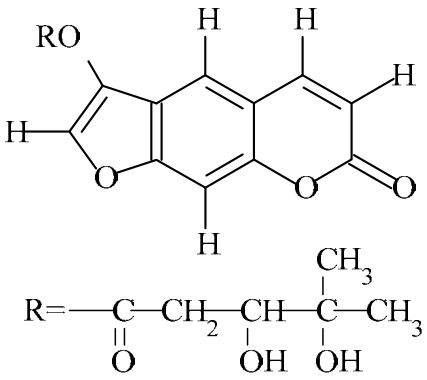
Substance 1. IR (ν, cm^{-1}): 1730, 1630, 1600. ^{1}H NMR (δ, ppm, J/Hz): 4.0 (3H, s), 6.35 (1H, d, J = 9.9), 7.10 (1H, s), 7.16 (1H, d, J = 2.3), 7.94 (1H, d, J = 2.3), 7.98 (1H, d, J = 9.9).

Substance 2. IR (ν, cm^{-1}) 3550, 3300, 1740, 1630. ^{1}H NMR (δ, ppm, J/Hz): 1.10 (3H, s), 1.20 (3H, s), 3.90 (1H, t, J = 9.65), 4.35 (2H, d, J = 9.65), 6.28 (1H, d, J = 10.0), 7.0 (1H, s), 7.10 (1H, s), 7.80 (1H, s)

Based on the data obtained at the interpretation of IR-, ^{1}H NMR, ^{13}C NMR, and ^{13}C Dept 135 and Dept 90 spectra of the studied compounds the structures of **1** and **2** has been established as, respectively:



(1)



(2)

LIPIDS OF SEEDS OF PULMONARIA OBSCURA – THE PERSPECTIVE VEGETABLE SOURCE OF POLYUNSATURATED FATTY ACIDS

S. G. Yunusova[1], N. I. Fedorov[2], M. S. Yunusov[1]

1) Ufa Institute of Chemistry of the Russian Academy of Sciences
2) Ufa Institute of Biology of the Russian Academy of Sciences,
450054, Ufa, pr. October, 71, e-mail: msyunusov@anrb.ru

Throughout works on searching of perspective vegetable sources of lipids with ω-3, ω-6 as polyunsaturated fatty acids, studied lipids of seeds of a plant of *Pulmonaria obscura* Dumort. (family *Boraginaceae* Juss.) growing in the territory of Russia in the Republic of Bashkortostan. Information about lipids of seeds of this plant in literature is absent.

The genus *Pulmonaria* – falls into to family the *Boraginaceae* Juss. The scientific name of a sort came from the Latin word pulmo – a lung, in the territory of Russia three types of Pulmonaria grow. The Pulmonaria is most widespread not clear meets almost across all territory of the European part of the country from the western borders to the Urals. The plant is widely applied in traditional medicine, a good melliferous herb, leaves are used for preparation of salads.

Neutral lipids are isolated (NL, 35% of weight of air dry seeds), polar lipids (PL, 0.6%), including gliko-(GL, 0.4%) and phospholipids (PhL, 0.2%).

Using various methods (thin-layer chromatography, preparative thin-layer chromatography, specific reactions, physicochemical methods of the analysis, chemical reactions) isolated, determine the content and the identified the composition of the NL. Neutral lipids contained (in % relative to the Σ NL): esters of cyclic alcohols (steroids) – 0.5; triacylglycerides (TAG) – 94.6; the free fatty acids (FFA) – 1.4; diacylglycerides (DAG) – 2.0; sterols – 1.2; monoacylglycerides (MAG) – 0.3.

Using a method of gas-liquid chromatography the composition of the fatty acids (FA) of common NL and all acylcontaining classes of lipids is established.

Fatty acids of common NL were presented: saturateds: 16:0 (the main) – 7.5% and 18:0 –- 1.9%; monounsaturated 18:1 – 14.6%; essential polyunsaturated fatty acids (PUFA) – 72.2% among which identified: ω - 6 – 57.5% (α-linoleic – 32.9% and γ-linolenic – 24.6%); ω-3 – to 15% (α-linolenic 11.0% and stearidonic – 4.0%); the total of high molecular weight FA made about 3% (20:0, 20:1, 22:0, 24:0).

Composition of FA of the main class NL – TAG was almost identical to composition of Σ NL.

According to results of research , considering the high content of neutral lipids (oil) and essential polyunsaturated fatty acids, collateral presence at their composition of high quantities of ω-3 and ω-6 of acids, seeds of *Pulmonaria obscura* Dumort. can be a potential an additional source of PUFA and a plant perspective for an introduction.

RESEARCH OF INFLUENCE OF VITAMINS ON FORMATION OF QUALITY OF FAT-SOLUBLE PRODUCTS

B. S. Nuritdinov, K. H. Majidov

Bukhara Engineering-technological Institute, 200100, K. Murtazaev street, 15, Bukhara

Fat-soluble vitamins and provitamins are entered into food and cosmetic products mainly in the form of oil solutions. Tocopherols (T) and carotenoids (C) are stable at storage in the oil form and are well acquired by an organism. Scientific work is directed on reception of preparations of tocopherols from wheat germs. Wheat germs used as raw materials. Raw materials stored in the dried up form, crushed directly ahead of use. Oil content was defined by the method of exhaustive extraction with chloroform at room temperature. Thus from raw materials are taken triglycerides and carotenoids, but not carotenoids so their maintenance is not reflected in general oil content. At maintenance definition of tocopherols and carotenoids the joint hinge of raw materials extracted with ethanol during 15 mines at boiling temperature of extraction mixes, in the filtered extracts tocopherols defined on Emery-Angel method with use of α-tocopherol as the standard, carotenoids - on absorption at length of a wave of 440 nanometers. The maintenance of carotenoids is expressed in recalculation on β-carotin. In preliminary researches it is determined that ethanol extraction of carotenoids from raw materials is a little more effective, than extraction with chloroform or hexane.

TABLE 1. **The raw materials had low oil content and the low maintenance of carotenoids**

Raw materials	Oil content, % to CV	The maintenance, mg/g CV		Parity T:C
		tocopherols (T)	carotenoids (C)	
Wheat germs	11.68	8.08	0.024	337

The positive factor for reception of tocopherols preparations is high parity of T:C. The developed technology of reception of water-soluble preparations of carotenoids is used as the base technology. The scheme includes three-stage preprocessing of raw materials for the purpose of its enrichment with easy-extractable carotenoids, alcohol extraction of carotenoids from the enriched raw materials and sorption of carotenoids on a water-soluble sorbent (pectin). The yield of carotenoids is made about 60 % to the maintenance in raw materials, by concentration - from 25 to 100 mg/g of a sorbent. Tocopherols are well dissolved in ethanol and are easily taken from vegetative raw materials so its preprocessing is not required. Process of reception of water-soluble tocopherols preparations is reduced to two basic stages: to reception of alcohol extract of tocopherols and their sorption on hydrophilic sorbent.

STUDYING OF QUALITY AND FOOD VALUE OF SOME FOODSTUFF

N. N. Sabirova, N. R. Djuraeva, I. B. Isabaev, K. H. Majidov

Bukhara Engineering-Technological Institute, 200100, K. Murtazaev street, 15, Bukhara

Scientific work is directed on development of combination of receipt ingredients and functional additives with use of compounding of bakery products; in particular, national small loafs from wheat flour and composite mixes. In creation of mixes were used compositions from the flour of first grade wheaten, grain crops nonconventional for bakery, secondary products of flour-milling and canning manufactures, powder of herbs. Preparation of raw materials for manufacture of small loafs made according to the "Collection of technological instructions for manufacture and bakery products". In the process of preparation to the batch pressed yeast planted in water in the ratio 1:3 and received barmy suspension. At application of dry yeast they were also planted in a small amount of water for the purpose of reception of suspension of homogeneous consistence. At application of peas it was preliminary crushed to the powder-like conditions. Remained receipt quantity of the flour, salt solution and water loaded to leavened dough in dough-mixing machine of mark NFJ-50, and the dough mixed up in 10 minutes before formation of homogeneous mass without lumps and traces of unmixed mass. The dough put on fermentation within 40–60 minutes at temperature 29–31°C before achievement of the determined final acidity. The fermented dough was cut on pieces of the demanded weight. Workpiece of dough stacked in oiled shape. Dough proof carried out in proof cases at temperature 35–40°C and relative humidity of air of 65–75% or in the conditions of baking shop. The end of proof was determined in organoleptic way. Approximated duration of proof was 40–45 minutes. Baking of dough workpiece carried out in stove of mark NFX-32 during 25–30 minutes at temperature of the baking chamber 230–250°C. By experimental researches is offered new assortment of a small loaf "Soglik" from wheat flour and composite mix. Approximated yield of product at humidity of the flour of 14.5% for small loaf "Soglik" with weight 0.200 kg is 131.0–133.5%. The new compounding of the small loaf essentially differs from well-known structures. In recommended compounding the special attention is given on use of composite mixes as pea and oat floors, wheaten bran and lactoserum. By experimental researches proved positive influence of functional components of composite mixes on formation of consumer advantages, physiological value and safety of bakery products.

CHEMICAL COMPONENTS OF *Marrubium anisodon*

A. A. Ibragimov[1], P. K. Igamberdieva[2], O. M. Nazarov[1], N. Yusupova[1]

1) Fergana State University
2) Fergana branch of Tashkent Medical Academy

Marrubium anisodon C.Koch.(*M. alternides* Rech. Fill.) is a plant of *Lamiaceae* (*Labiatae*) of family, perennial herb. Hoarhound (eng.), "Шандра очереднозубая" (Rus.) or "Қатортишли девортагиўт" (Uzb.) grows in the most parts of the World, including Central Asia. Botanists describe it as an undesirable plant, which grows in stony slopes, herb-grassland steppes, and also in urban area: along the fence, brooks, at landfills, everywhere.

According to the literature sources it contains amino alcohol choline, alkaloid stachydrine, vitamin C, summary fractions of flavonoids, anthocyanes, essential oils.

There is information about using the extracts of aerial part of the plant in folk medicine for treatment of throat and respiratory tract by way of rinsing the throat and oral cavity. Tincture prepared from this plant has a sedative, hypotensive and hemostatic properties.

Two above mentioned factors, namely: wide range of its growing and its health-giving properties for a human attracted us to make detailed analysis of chemical components of Marrubium anisodon along with other plants of Fergana region.

7.4 kg of raw material *Marrubium anisodon* were extracted with 96% ethanol. Then we got 545 g (7.3%) of unrefined mixture of extracted substancies, which was fractioned to acid, phenol, alkaloid and neutral fractions. The alkaloid fraction (7.1 g of mixture bases 0.09% of raw material weight) was chromatographed on the silica gel column.

We used distilled dissolvents: heptane, acetone, benzol, dichloroethane, alchohol. We extracted the agent with melting temperature 225–226°C (acetone–ethanol) identified with stachydrine from the last dichlorethane-alcohol effluents.

The fraction of neutral agents was separated on the column of aluminium oxide, eluated with CCl_4–$CHCl_3$, 4:1 mixture.

Further we continued the eluation adding 1/20 part of ethanol, and we combined related fractions. At standing of condensed colorless crystals of substance №1 fall in the shape of needles well dissoluble in CCl_4, hard dissoluble by other dissolvents.

We extracted insignificant quantity of the agent №2. We described these compounds in spectral way. Agent №1: M^+346, structure $C_{20}H_{26}O_5$; Agent №2: M^+360, structure $C_{20}H_{24}O_6$. Absorption bands O–H (3466 cm^{-1}), C–H (2939–2871), C=O (1741 are at infrared specter № 1, which corresponds to lacton and to ester carbonil). The band related to furane cycle is detected in the range of 1505 cm^{-1}.

The band related to furane is detected at ultraviolet specter shot in alcohol at 214 nm (lg ε 3.71). Mass-spectrometric fragmentation № 1 and 2 is related to peregrinin and marrubin in the structure of which furane cycle is contained. Thus, on provisional information, we extracted neutral agents peregrinin and marrubin, besides of alkaloid staxidrine.

EVALUATION OF POTENTIAL ANTICANCER ACTIVITY OF *Nerıum oleander* AGAINST DIFFERENT LEUKEMIC CELL LINES

Ahmet Beyatli[1], Mediha Suleymanoglu[1], Bashak Varol[2], Serap Erdem Kuruca[1]

1) Istanbul University, Istanbul Faculty of Medicine, Physiology Department, Istanbul, Turkey
2) Istanbul University, Istanbul Faculty of Medicine, Department of Biophysics, Istanbul, Turkey

Medicinal plants are still considered an important source of new anti-cancer agents. The main objective of this study was to evaluate the effects and the mechanism of cell death of different extracts obtained from leaves of *Nerium oleander* against the K562 (chronic myelogenous leukemia) and P3HR-1 (Burkitt's lymphoma) cell lines. Three extracts of *N. oleander* including the ethanol, methanol and acetone extracts were examined. The cytotoxicity of extracts were evaluated by the MTT assay (3-(4,5- dimetylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) in K562 and P3HR-1 cells and the molecular mechanisms by western blot analysis. Further, the DNA fragmentation was accomplished using diphenylamine assay. The results showed that the extracts have different cytotoxic degree on cells but it were generally in a dose dependent manner. Our results suggest that *N. oleander* need for further cytotoxic and phytochemical research to approve activity against cancer cells.

PHASE TRANSFORMATIONS OF LIPID SYSTEM ON INFLUENCE OF MEMBRANE ACTIVE DITERPENOIDS

P. G. Kosimbetov[1], K. R. Allambergenova[1], A. P. Matekeeva[1], T. F. Aripov[2]

1) Karakalpak State University, 1, Chardjou Abdirov Street, 230100, Nukus, Uzbekistan
2) Institute of Bioorganic Chemistry, Academy of Science of the Republic of Uzbekistan, 83, Mirzo Ulugbek Street, 100170, Tashkent, Uzbekistan

Among the natural compounds diterpenoids have vast practical importance [1]. The main pharmacologically active component of *Lagochilus* genus plants is labdane series diterpeniods: lagochiline and its derivatives, which have hemostatic properties [2].

Aim of the research is study of phase transformations of lipid system which formed from dimirystoilphosphatidylcholine (DMPC) on influence of lagochiline and its some derivatives with the ascertaining purpose of the theoretical aspects of molecular mechanisms of their hemostatic action on blood coagulation system.

Decreasing of a value of the total enthalpy of phase transformation process of DMPC in case of its interaction with membrane active molecules characterizes an excluding of some parts of lipid system at the expense of initial structure destroying of lipid membrane by penetrating of guest molecules into bilayer. In our experiments increasing of concentration of 3,18-*O*-izopropylidenlagochiline (IPL) and 3,18-*O*-ethylidenlagochiline (EL) relatively to concentration of lipid led to consistently decreasing of the total enthalpy value of lipid phase transformation process. In case of the main component lagochiline and comparative preparation lagoden the similar result did not observe. Dependence of changing of values of the total enthalpy of lipid melting process ($\Delta H/\Delta H_0$), temperature of the main phase transformation (T_P) and melting process cooperation ($1/2\Delta T_P$) on diterpenoids concentration is presented in Table 1.

TABLE 1. **Dependence of Changing of the Thermodynamic Parameters of Lipid Phase Transformation Process on Concentration of the Studied Diterpenoids**

Samples	Relation of concentration	Thermodynamic parameters of the process		
		$\Delta H/\Delta H_0$	T_P	$1/2\Delta T_P$
DMPC	control	1.00	24.3	0.6
IPL:DMPC	1:50	0.97	23.9	1.3
IPL:DMPC	1:35	0.88	23.4	1.6
IPL:DMPC	1:20	0.59	22.6	1.8
EL:DMPC	1:50	0.98	24.0	0.9
EL:DMPC	1:35	0.91	23.6	1.2
EL:DMPC	1:20	0.76	23.0	1.5

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DEPENDENCE OF LIPID MELTING PROCESS ON pH VALUE IN THE PRESENCE OF 3,18-*O*-IZOPROPYLIDENLAGOCHILINE

K. R. Allambergenova[1], P. G. Kosimbetov[1], A. P. Matekeeva[1], T. F. Aripov[2]

1) Karakalpak State University, 1, Chardjou Abdirov Street, 230100, Nukus, Uzbekistan
2) Institute of Bioorganic Chemistry, Academy of Science of the Republic of Uzbekistan, 83, Mirzo Ulugbek Street, 100170, Tashkent, Uzbekistan

Modulating action of 3,18-*O*-izopropylidenlagochiline (IPL) molecules on blood coagulation system was determined by the research of their hemostatic activity, which connecting with membrane activity in lipid bilayers [1].

Aim of the research is study of interaction of IPL molecules with lipids which formed from dimirystoilphosphatidylcholine (DMPC) by the microcalorimetric method for ascertain of the diterpeniod penetrating into bilayer membrane in different values pH. Choice of DMPC as lipid system is connected with that it is the main structure forming component of biological membranes of platelets and tissue endothelial cells which contacting with blood in different values pH [2].

The correlative transformation of the main phase transformation temperature of DMPC was observed in melting thermogramm in case of introduction of IPL molecules into lipid bilayers which formed from DMPC during different values pH starting 5 in the direction to 10 (Fig. 1). Maximal value of the main phase transformation temperature of DMPC in the presence of IPL molecules is detected on pH value 7.5. It testifies that optimal interaction of IPL molecules with DMPC lipid bilayers takes place exactly on this value pH that conforming to biological solutions in cells.

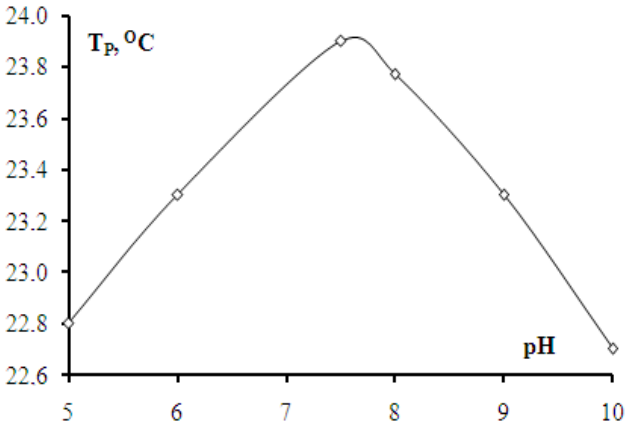

Fig. 1. Dependence of DMPC melting temperature (T_P) on different values pH in the presence of IPL molecules.

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STUDY OF THE CATION-ANION SELECTIVITY OF LIPID BILAYERS MODIFIED BY LAGOCHILINE DERIVATIVES

A. P. Matekeeva[1], K. R. Allambergenova[1], P. G. Kosimbetov[1], T. F. Aripov[2]

1) Karakalpak State University, 1, Chardjou Abdirov Street, 230100, Nukus, Uzbekistan
2) Institute of Bioorganic Chemistry, Academy of Science of the Republic of Uzbekistan, 83, Mirzo Ulugbek Street, 100170, Tashkent, Uzbekistan

Study of the cation-anion selectivity of bilayer lipid membranes (BLM) modified by 3,18-*O*-izopropylidenlagochiline (IPL) and 3,18-*O*-ethylidenlagochiline (EL) molecules was presented that membranes most selectively for bivalent cations. In case monovalent cations these diterpenoids did not have selectivity.

Bi-ionic systems are fruitful in comparative analyses of the selectivity of modified membranes for different cations [1]. Experiments were performed in two stages. In the first, the relative permeability of BLM for Ca^{2+} and monovalent cations (such as K^{+} and Na^{+}) was examined. During the second stage, the bilayer permeability for Ca^{2+} was compared with that for other divalent cations.

In the presence of a 3-fold transmembrane NaCl and KCl gradient (50 mM/150 mM; *cis*/*trans*) membrane permeability modified by these diterpenoids was not observed. Cation-anion selectivity BLM modified by IPL and EL molecules was observed when bilayer was separated by bivalent electrolytes. Typically voltage-current relationships of BLM modified by IPL and EL molecules are presented on Fig. 1. The positive value of zero current membrane potentials indicates that cations pass through diterpenoid-modified BLM better than anions.

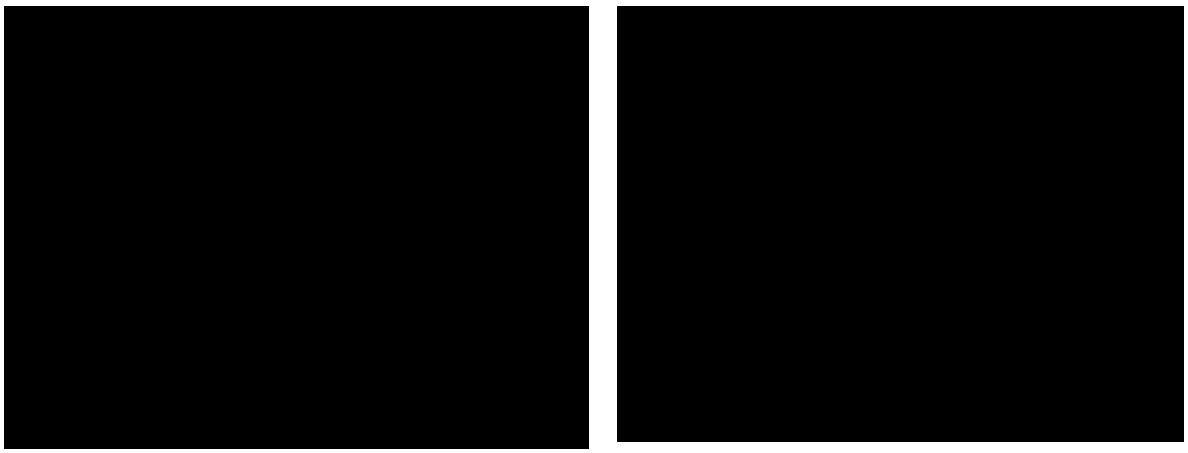

Fig. 1. Representative voltage-current curves of modified BLM at asymmetrical ionic conditions: (A) a gradient of $CaCl_2$ (5 mM/15 mM; cis/trans) in the absence of 150 mM NaCl at both sides on bilayer membranes modified by IPL and EL molecules, and (B) a gradient of $CaCl_2$ (5 mM/15 mM; cis/trans) in the presence of 150 mM NaCl at both sides on bilayer membranes modified by IPL and EL molecules.

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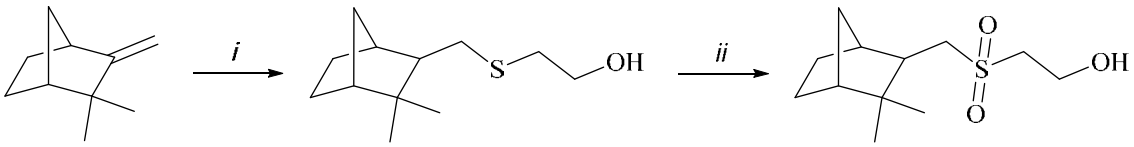
RESEARCH IN THE MOLECULAR MECHANISM OF HEMOCOAGULANT ACTIVITY OF CAMPHENE SULFONE

L. E. Nikitina[1], S. V. Kiselev[1], A. V. Bodrov[1], V. A. Startseva[1], V. V. Klochkov[2], L. F. Galiullina[2], O. V. Aganova[2], A. V. Khaliullina[1,2], Z. R. Azizova[1], A. A. Rakhmatullina[1,3]

1) Kazan State Medical University, 420012, Kazan, ul. Butlerova, 49, Russian Federation
2) Kazan (Volga Region) Federal University, 420008, Kazan, ul. Kremlevskaya, 18, Russian Federation
3) Republican Hemotransfusion Center of Tatarstan Ministry of Health, 420140, Kazan, pr. Pobedy, 85, Russian Federation

It has been shown that the synthesized camphene sulfone (see Scheme 1), in contrast to acetylsalicylic acid and clopidogrel, completely inhibits the activation of platelets induced by adrenaline and arachidonic acid, and reduces the effect of ADP, collagen and ristocetin. Detailed NMR studies and molecular dynamic simulations using model SDS membranes indicates that the bicyclic fragment of sulfone is embedded inside the SDS micelle, whereas the $-SO_2(CH_2)_2OH$ fragment of sulfone is located on the outer part of the micelle and is accessible by solvent.



Scheme 1. Reagents and conditions: (i) $HSCH_2CH_2OH$, $BF_3 \cdot Et_2O$, Et_2O, rt; (ii) H_2O_2/AcOH.

It has been demonstrated that the hemocoagulant activity of sulfone is due to its ability to inhibit platelet activation and suppress the catalytic activity of phospholipid surface which is involved in the formation of coagulation clotting factor complexes. Taking into account the low toxicity of thioterpenoids, the obtained compound can be considered as a potential drug for the treatment and prevention of thrombophilia, and as a stabilizer of blood preparation in transfusiology [1, 2].

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STUDY THE COMPOSITION OF ESSENTIAL OILS OF *Achillea millefolium* L. BY GC-MS

A. N. Muhamadiev, N. T. Fazlieva, N. Q. Muhamadiev, Sh. M. Sayitkulov

Samarkand State University, Uzbekistan, e-mail: m_nurali@mail.ru

Studying volatile substances in ether-oilseed plants is of great practical importance, since these substances are in the form of so-called essential oils are widely used in medicine as an aromatherapy agent, as a flavoring for foods, as fragrant substances in perfumes and cosmetics, as fragrant compounds in household chemistry. In connection with this studying the composition of essential oils extracted from plants is important.

The purpose of this work is GC-MS study of the chemical composition of essential oil extracted from Achillea millefolium L., grown in Uzbekistan.

Aerial part of Achillea millefolium L. was collected in the territory of Urgut district of Samarkand region in July 2016. To extract the essential oil the crushed aerial parts of the plant (500 g) has been subjected to hydrodistillation for 3–4 hours. After the extraction the oil was collected in glass vials and dried over anhydrous Na_2SO_4. After appropriate purification and drying the oil has the following physicochemical characteristics: density – 0.922 ± 0.005, g/mL; refractive index – 1.493 ± 0.004; acid number – 1.42 ± 0.02, essential number – 19.63 ± 0.02.

GC-MS analysis of the essential oil of anise was performed using silica capillary column 25 m long and with 0.25 mm inner diameter and the stationary phase film thickness 0.25 micrometers. Qualitative analysis of the essential oil components was carried out on the retention parameters and comparing the mass spectra with the data of the library of mass spectral data Wiley275 and directories, and quantitative analysis - by internal normalization. The analysis time – 50 minutes.

By the GC-MS method the following components from the oil composition of *Achillea millefolium* L. were found: α-pinene (6.38), camphene (2.07), sabinene (16.74), β-pinene (6.44), myrcene (0.78), *p*-cymene (1.08), limonene (1.31), 1,8-cineole (12.92), γ-terpinene (1.12), α-thujone (1.03), thujanol (0.57), methanol (1.11), borneol (12.28), terpinine-4-ol (6.08), α-terpineol (1.11), α-thujenal (0.18), dodecane (0.21), *trans*-carveol (0.46), cyclohexene (0.14), bornyl acetate (8.06), azulen (0.88), β-caryophyllene (2.27), germacrene D (1.62), γ-cadinene (0.87), α-cadinol (0.92), chamazulene (5.31), myristic acid (0.24), pentadecanoic acid (0.51).

Thus, the main components of the ether oil are α-pinene (6.38), sabinene (16.74), β-pinene (6.44), 1,8-cineole (12.92), borneol (12.28), terpinine-4-ol (6.08), bornyl acetate (8.06), chamazulene (5.31).

The work was carried out in the grant frame A-12-25.

OPTIMIZING THE EXTRACTION CONDITION OF ESSENTIAL OILS BY FULL-FACTOR PLANNING THE EXPERIMENT

N. Q. Muhamadiev, B. K. Nayimova, A. N. Muhamadiev, A. Sh. Saidov, K. F. Khalilov

Samarkand State University, Uzbekistan, e-mail: m_nurali@mail.ru

The essential oils of medicinal plants have a broad spectrum of biological activity (antimicrobial, antiviral, antifungal), their qualitative and quantitative composition depends on many factors: the difference in chemotypes and growing conditions, storage technology, etc.

In this regard, the need for the development of rapid and effective methods of extraction and determination of the qualitative and quantitative composition of the essential oils in the plant material, and phytopreparation is an actual task.

The purpose of this work – optimizing the conditions for the extraction of essential oils by full-factor planning the experiment.

The extraction process of ether oils by microwave and thermic heating has been optimized by grinding level of the plant (L.: d = 1–3 mm), the process temperature (t, °C = 120–260) and mixing rate (ϑ_{mixing}= 30 × 80 rotation /min), as well as duration of the process (τ = 20 × 200 min). For this, a plan for the experiment was made on the basis of the method of full-factor planning the experiment. The oil composition has been studied by GC-MS.

The results of extraction of essential oils and their physico-chemical characteristics are shown in Table 1.

TABLE 1. **Physicochemical Properties of Essential Oils of *Pimpinella anisum* L. Depending on the Heating Method (n = 5)**

Index	Method for heating the raw material	
	Microwave	Thermic
Duration of the process, min	30 ± 3	175 ± 5
Oil output, % on a.s.s.	2.52 ± 0.12	2.11 ± 0.11
Density c^{20}, г/cm^3	0.983 ± 0.005	0.978 ± 0.004
Refractive index,	1.556 ± 0.004	1.548 ± 0.004
Acid number, mg KOH/g	0.42 ± 0.03	0.38 ± 0.03
Ether number, mg KOH/g	105.4 ± 2.5	107.3 ± 2.4

Indicators of the important advantages of using microwave heating: reduction in distillation time of essential oils from raw materials by ~ 6 times and increase its output by 16%. Physicochemical parameters, as well as qualitative and quantitative composition of obtained essential oils do not have significant differences.

On the basis of a set model were identified the best conditions for the extraction of essential oils from the aerial parts of the plant *Pimpinella anisum* L .: d = 1–2 mm; t °C = 160–165°C; ϑ_{mixing} = 48–60 rotation/min; τ = 12–15 min

The work was carried out in the grant frame A-12-25.

SYNTHESIS OF AMINO ACIDS

G. S. Simonyan

Yerevan State University

Reaction of diethylamine (DEA) with *N*-[(trihydroxymethyl)methyl]amid of acrylic acid (TA) was studied in water. DEA (Aldrich), TA (Aldrich) were been used without further purification. All samples were prepared on distilled water.

Mixture of equal molar quantity of DEA and TA weremaintained at 293 K in water till end of reaction. The reaction yield is 97 %.

CH_2=CHCONH-CH(CH_2OH)$_3$ +(C_2H_5)$_2$NH→(C_2H_5)$_2$NCH_2–CH_2CONH-CH(CH_2OH)$_3$

Product of reaction: *N*-[(trihydroxyoxymethyl)methyl]amide of 3-diethylamino propanoic acid was separated from water by lyophilozation and dried at room temperature. The reactionproduct is white powdery substance. It is soluble in water, DMF, DMSO, FA and 1,4-dioxane [1].

Hydrolysis of *N*-[(trihydroxyoxymethyl)methyl]amide of 3-diethylamino propanoic acid was carried out at 80°C:

(C_2H_5)$_2$NCH_2–CH_2CONH-CH(CH_2OH)$_3$+H_2O→
(C_2H_5)$_2$NCH_2–CH_2COOH+NH_2-CH(CH_2OH)$_3$

3-Diethylamino propanoic acid and tris(hydroxymethyl)aminomethane were obtained. The reaction yield is 95%.

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STUDY OF THE CHEMICAL COMPOSITION OF THE ABOVE-GROUND PARTS OF *Hippophae rhamnoides* AND THE SUBSTANCE OBTAINED ON ITS BASIS

A. Sh. Aituarova, A. I. Zhusupova, G. E. Zhusupova

Al-Farabi Kazakh National University, 71 al-Farabi Ave., Almaty, 050040, Republic of Kazakhstan

In order to provide the pharmaceutical industry of the Republic of Kazakhstan with medicinal products of its own origin great attention is given to chemical and biological study of wild medicinal plants. The possibility for application of the latter in medicine is induced by its environmental friendliness, breadth of plant growth area, therapeutic efficacy and biological safety of medicinal forms produced on their basis.

The object of our study is the sea buckthorn (*Hippophae rhamnoides*), the perennial plant of Elaeagnaceae family, collected in Tyulkubas district of the Southern Kazakhstan region. *Hippophae rhamnoides* was chosen as the object of our study due to the rich biochemical composition of its above-ground parts.

The sea buckthorn is a hardy plant, resistant to drought and cold, and might be useful for melioration. It contains almost all fat-soluble and water-soluble vitamins, minerals, flavonoids, tannins, polysaccharides, and other biologically active compounds (BAC), essential for the human organism. The stems and leaves of this plant are not studied well, unlike the fruits.

Macroscopic and microscopic analysis of stems and leaves was conducted. Content of radionuclides was revealed: Cs-137 is less than 3.0 Bq/kg at acceptable content of 400 Bq/kg, Sr-90 is less than 3.0 Bq/kg at acceptable content of 200 Bq/kg). The absence of heavy metals (Pb, Cd, Cu, As, Hg) was established.

Microbiological purity of samples was defined (1 g of raw material is allowed to have not more than 10^7 of bacteria, 10^5 of yeasts and molds (in total) and not more than 100 *Escherichia coli*).

According to conventional techniques of the State Pharmacopoeia of the Republic of Kazakhstan (2008, 2009) for the above-ground parts of *Hippophae rhamnoides* its quantitative indicators were determined, as: moisture, ash content (total ash, ash insoluble in 10% HCl, sulphated ash) and extractives.

An optimal technology for isolation of corresponding substances from the leaves and stems of *Hippophae rhamnoides* plants was developed; their quality indicators were identified as shown below.

Chemical and chromatographic methods of analysis were applied for phytochemical analysis of the major classes of biologically active compounds in the above-ground parts of *Hippophae rhamnoides* plants and extracted substances.

Comparative analysis of the quantitative content of amino and fatty acids was conducted in the substances and initial plant samples by means of gas chromatography.

The content of the relevant macro- and microelements was determined by means of atomic absorption spectroscopy.

The data obtained revealed the high quality of the raw material, collected in the Southern Kazakhstan region, as well as rich biochemical composition, facilitating its further introduction into the State Pharmacopoeia of the Republic of Kazakhstan.

AMINO ACID AND FATTY ACID CONTENTS OF *Atraphaxis pungens*

A. K. Umbetova, G. Sh. Burasheva

Kazakh National University al-Farabi, Kazakhstan, Almaty, 050040

Atraphaxis pungens is a wild plant family *Polyganaceae.* The chemical composition of the polyphenolic compounds of the Kazakhstan species of the *Atraphaxis* genus described in V. B. Omurkamzinova.

The study of acid complex is limited data on the composition of phenol carbonic acids, information on amino- and fatty-acid composition of Kazakhstan species of the *Atraphaxis* genus is missing.

Fatty acid methyl esters were analyzed in a Chrom-42 chromatograph using Celite 545 adsorbent on Chromosorb WAW (He carrier gas, flame ionization detector, carrier gas flow rate 30 mL/min, detector temperature 188°C, and over temperature 230°C). The acids were methylated by NaOMe at 60–70°C.

The composition of amino acids was established using an amino acid analyzer (He carrier gas, flame ionization detector 300°C, and condenser temperature 250°C on Chromosorb WAW). Samples were hydrolyzed in HCl (5.7N) for 24 h in sealed ampuls at 110°C.

The study revealed that *Atraphaxis pungens* contains 20 amino acids and eight known fatty acids that differ in their quantitative contents. The major amino acids were glutamic asid

SULPHOMETHYLATION OF LIGNOCELLULOSIC MATERIALS – RICE STRAW AND RICE HUSK

Z. K. Djumanova, P. G. Kosimbetov, A. P. Matekeeva

Karakalpak State University, 1, Chardjou Abdirov Street, 230100, Nukus, Uzbekistan

One of the lesser-known areas of chemical modifications of technical lignins and lignocellulosic materials is their introduction in their structure of the macromolecule functional groups which give them solubility. Sulfoalkyle groups together with such as the ionogenic groups and carboxymethyl groups and attached phosphomethyl groups lignine ability to dissolve in water or aqueous – alkaline medium.

Previously to increase the solubility of the drug was conducted sulphomethylation dioksanlignin cotton stalks and hydrolytic lignin. In this paper we present the results sulphomethylation of lignocellulosic materials – rice husk and rice straw with sodium bisulfite and 40 percent formalin solution, at temperature 90°C. As a result of modifications could introduce into lignocellulosic materials sulfur 0.5–2.0 percent (Table 1).

TABLE 1. **Sulphomethylation of Lignocellulosic Materials, in Percent**

№	Sample of lignocellulosic materials	Output sulphomethylation lignocellulosic materials	S	Komarovs Lignin	
				before the reaction	after the reaction
1.	Rice straw	120	1.0	21.4	18.8
2.	Rice husk	116	2.0	27.2	17.3

Date in table 1, shows, that the highest content of sulfur found in the rice husk sulphomethylated than straw. Decrease Komarovs lignin content in these samples may be indicative of a dissolution of the lignin sulphomethylation process.

The IR-spectra of the samples of sulfomethylated lignocellulosic materials have absorption bands characteristic (cm^{-1}): -OH (3430–3440), benzene rings substituent (1510, 1610) and C-S bond (R-SO-R) (1034, 1109).

Thus, a new method of chemical modification of lignocellulosic material in sulphomethylated derivatives was proposed. In this case, may occur simultaneously processes of the destruction of the structure of lignin in the plant and sulfoalkylation for free and liberated, as far as the process flow, the hydroxyl groups of lignin.

REACTION ABILITY OF THE DIMER COMPOUNDS OF LIGNINS

Z. K. Djumanova, P. G. Kosimbetov, A. P. Matekeeva

Karakalpak State University, 1, Chardjou Abdirov Street, 230100, Nukus, Uzbekistan

For information on centers of editorial activity the electronic structure of the dimeric compounds of lignins was calculated by quantum-chemical method. Electronic structure of the predecessors of lignin is described by point charge on the atoms. Differences in values of the dipole moment of these compounds indicate uneven charge distribution in the molecule. The electronic structure of the molecules describe by point charge on the atoms. Availability of electrons at the immediate pair of oxygen atom OH-group leads to the formation of structures in all three significant negative charge.

The molecule siringylpropanic ether *p*-oxyphenilpropan significant negative charge is concentrated in all of the oxygen atoms. This may indicate that the investigated molecule can participate in editorial substitution or elimination. The calculation showed, that the atoms C2, C6 siringylpropanic level, and atoms C8, C9, C10, C12 *p*-oxyphenilpropanic link molecules may be the center of electrophilic substitution.

The dimer molecule veratrilrpopanic and vanilic acid significant negative charge is concentrated in all of the oxygen atoms in the C6, C11 and Cγ volumes. This means that the atoms marked can be the center of electrophylic substitution. The calculations showed, that the molecules of this type of basic reaction centers are oxygen-containing groups – OCH_3 and COOH.

Quantum-chemical calculations of the electronic pinorezinola connection structure containing cyclic C-C and C-O-C bond showed that the negative charge is concentrated in all of the oxygen atoms, as well as C1, C2, C3, C6, C7, C8, C11 and C12 volumes of the benzene ring symmetrical building a pinorezinole molecule. The most reactive sites in the molecule are also oxygenate a group –OH, OCH_3 and oxygen ring C-O-C bond which can be centers electrophylic substitution.

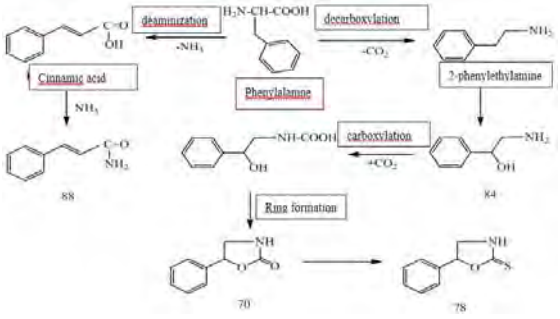
Thus, for multifunctional dimer precursors of lignin is characterized by multicenter chemical activity. The logical consequence of this is the absence, in contrast to cellulose, the uniformity of the primary microstrectures, which determines the heterogeneneity of the discorder ana lignin at the molecular level.

POSSIBLE SCHEME OF BIOGENESIS MIGNONETTE ALKALOIDS

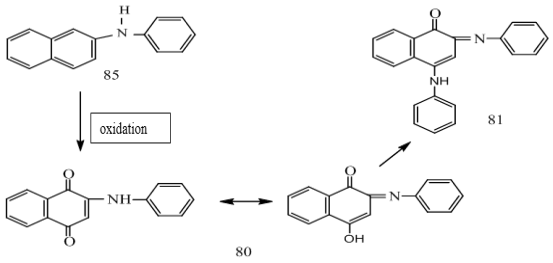
M. M. Tadjibaev, E. X. Botirov

Andijan Medical Institute

It is supposed that alkaloids are final products of protein metabolism in plants, and in connection with that as predecessors of most alkaloids are considered amino acids. To this sign alkaloids unite in lysine groups, ornithine and proline, tryptophan, phenylala - nine and tyrosine, histidine, etc. Phenilalanine and tyrosine are initial connection in biosynthesis of isoquinoline alkaloids. Reactions decarboxylation and deaminization are the main ways of catabolism of proteinogenous amino acids. Initial connection in biosynthesis of mignonette alkaloids, apparently, is phenylalanine which as a result of decarboxylation reaction forms 2-phenyletilamine whereas deaminization of phenylalanine leads to formation of cinnamon acid. Cinnamon acid, certainly, is the predecessor of amid of cinnamon acid allocated by us from R. lureola. Oxidation 2-feniletilamina in vivo results last leads to 1-phenyl-2-aminoetanol (29), as a result carboxylation and the subsequent ring formation forms mignonette (14) (scheme 16). It is necessary to notice that intermediate biosynthesis compound 1-phenyl-2-aminoetanol (29) it is allocated by us from mignonette that the biosynthesis scheme is an additional proof offered.



Scheme of biogenesis of resedine, 1-phenyl-2-aminoetanol and amid ofcinnamicacid.



Scheme of biogenesis of lutine and lutinine.

As stated above, we allocated also phenyl-β-naphtilamine (85), lutine (80) and lutinine (81). from mignonette. While it is not clear, what connection is the predecessor of these nitrogen containing compounds, but the analysis and comparison of structures of these connections allows drawing some conclusions concerning their Lutine, is probably formed from phenylalanine as a result of fermentative oxidations in vivo. Further interaction of tautomer enol forms of lutine with aniline leads to biosynthesis of lutinine.

In actual practice reactions, certainly, they proceed with the assistance of enzymes and with a great number of intermediate stages.

THE STUDY OF BIOACTIVE COMPONENTS OF AERIAL PARTS OF KAZAKHSTAN LOOK ORIGANUM VULGARE

S. A. Uzakbay, Z. B. Halmenova, A. K. Umbetova

Faculty of Chemistry and Chemical Technology, Al-Farabi Kazakh National University, Almaty, Kazakhstan

The genus origanum of the largest in the family *Lamiaceae*, has long been used in medical practice.

The object of our study is the aboveground part *Origanum vulgare*. The plant is harvested in the flowering period in 2015 in the Almaty region.

By conventional methods of the State Pharmacopoeia of Kazakhstan and the Pharmacopoeia of the USSR were identified indicators of high quality of raw material: moisture (4.9%) and total ash (7.68%), ash insoluble in 10% hydrochloric acid (7.83), sulfate ash (1.69%).

Qualitative and quantitative content of basic groups of biologically active components amino acids (9.24%), polyphenols (3.41%), tannins (17.2%), flavonoids (1.53%), carbohydrates (0.4%), alkaloids (1.67%).

By atomic absorption spectroscopy were determined the mineral composition of the aerial parts of the plant *Origanum vulgare*. According to the quantitative content of micro elements in the form of plant dominates - iron, and of macronutrients - potassium.

The essential oils with steam distillation using a GC-MS method extracted from the aerial parts of *Origanum vulgare*. Fifty compounds were identified. The yield of essential oil of oregano whole herb was 0.9%. Also, were identified 43 volatile component, among which the main components are docosene-1 (69.85%), β-sitosterol (5.26%), nonadecane (2.59%), heptacosane (2.47%), 1-hexadecene (1.35%), hexadecyl ester (1.31%), 5-α-cholesta-8-en-3-ol (1.12%).

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A STUDY OF THE MAIN GROUPS OF BIOLOGICALLY ACTIVE COMPOUNDS OF THE AERIAL PARTS OF *Satureja amani* PLANTS OF KAZAKHSTAN SPECIES

A. N. Nurtazina, A. K. Umbetova, Z. B. Halmenova

Al-Farabi Kazakh National University, Faculty of Chemistry and Chemical Engineering, Kazakhstan, Almaty, 050040, fax: +7(727) 377 33 44, e-mail: alusha_93@mail.ru

Lamiaceae Lindle families consists of 200 sorts and 3500 species and occupies the 13th place by the variety of species and the 3rd place by the distribution on the Earth.

The object of our research is the aerial part of *Satureja* plant genus. This plant was prepared during blossoming at the Institute of Phytointroduction and Botany at the Ministry of science and education of the Republic of Kazakhstan.

The *Satureja* plants are known to be a source of obtaining essential oil. According to V. A. Krastelevsky, an yield of essential oil from dry grass reaches 0.37%; from fresh it reaches 0.1%. The quality of oil to a significant eztent depends on the vegetation stage. The composition of oil contains has resulted in founding: 30–42% of a karvakrol, to 20% of a tsimol and 40% of terpenes.

Phytochemical research alkaloids, glycosides, organic acids, iridoida, carbonic acids, flavonoids, tannins, phytoncides, saponina and some other Biologically Active Substance.

The most optimal extract both for leaves and for stalks is 50% ethyl alcohol. Based on the obtained data. The technological schemes of obtaining substances have been made.

Early we investigated amino-, acid-fatty and vitamin of *S. amani* plants. 3 types of vitamins, 8 fatty acids and 20 free amino acids have been identified. The ointment based on Vaselinum. Its pharmaceutical properties were not studied. Further it is planned to obtain tinctures in different ratios and to obtain drug.

The volatile oils constitutes were extracted from the aerial part of a *Satureja amani* plant by water steam distillation. They were analyzed by GC-MS method. Eighty three compounds were separated. Their relative contents were determined by area normalization in which 83 volatiles were identified. Active principles of the Kazakh traditional plant medicine that are responsible for the activity were determined. The major volatile constituents are hexacosane (16.52%), tricosane (13.12%) and heneicosane, 11-decyl- (7.94%). They have antihypernociception, anti-inflammatory, antimicrobial, antibacterial and analgesic activities respectively.

Satureja has a stimulant, carminative, astringent, diaphoretic, antibacterial, antifungal, antiparasitic, antiviral, expectorant, antioxidant and analgesic properties. It is used in the treatment of diseases of the cardiovascular, digestive and nervous systems. *Satureja* species stimulates appetite, improves digestion, helps to cure flatulence, diabetes, headaches, tones, increases appetite.

SUSPENSION AND MONOAPPARAT OBTAINING TECHNOLOGY OF CARBOXYMETHYLCELLULOSE BASED ON MICROCRYSTALLINE AND POWDER CELLULOSE

Sh. A. Yuldoshov, A. I. Shukurov, A. A. Sarymsakov

Scientific Research Center of Polymer Chemistry and Physics at the NUU, Tashkent, 100128, A. Kadiri 7b str, e-mail: sherzodbek_y@mail.ru

Microcrystalline cellulose (MCC) and powder cellulose (PC) has significantly difference i.e. structure, properties, morphology from traditional celluloses. Because of sharply rising of modified cellulose compounds application, we have investigated probability of synthesis condition of carboxymethyl cellulose (CMC) from MCC and PC with a high quality index.

The aim of this study was to investigate the obtaining conditions of water-soluble Na-CMC from MCC and PC by suspension and monoapparat technology.

It was determined the optimal conditions for obtaining of CMC from MCC and PC by suspension and monoapparat technology.

Suspension technology of CMC synthesis based on providing the alkaline treatment and etherification reaction in organic solvent condition such as benzene, toluene, acetone, dioxane, isopropanol, xylene, aliphatic primary and secondary alcohols that allows increasing the utilization ratio of the alkylating agent to 90%.

Feature of monoapparat obtaining technology of CMC is in alkaline treatment process used the calculated amount of sodium hydroxide solution.

Advantages of monoapparat technology are single stage of mercerization, production equipment design, lower energy and material spending, consequently, low production costs.

The obtained data shows that the effective degree of substitution (DS) of CMC obtained from MCC and PC at the expense of 0.9–1.1 mol of alkylating agent to 1 mol elementary unit of cellulose, depending on its degree of polymerization and degree of dispersion, obtained by suspension and monoapparat technology are achieved at DS = 0.38–0.42 and DS = 0.45–0.52 respectively. Thus, in similar samples of CMC obtained from cotton cellulose effective DS, which favor to completely dissolution in water achieved at flow rate of monochlorine acetate acid 1.8–2.0 moles per unit of cellulose chain obtained by suspension and monoapparat technology at DS = 0.55–0.60 and DS = 0.63–0.65, respectively.

FLAVONOIDS FROM THE AERIAL PART OF *Scutellaria adenostegia*

A. M. Karimov[1], T. N. Slobodyanyuk[2], E. Kh. Botirov[2]

1) Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan
2) Surgut State University, Russia, e-mail: botirov-nepi@mail.ru

Thirty two *Scutellaria* species grow in Uzbekistan and are used in folk medicine to treat epilepsy, allergies, neurosis, hypertonia, and other diseases. Pharmacological studies confirmed that extracts and individual flavonoids of *Scutellaria* plants possessed antitumor, antiviral, hepatoprotective, antioxidant, antiinflammatory, anticonvulsive, and antibacterial properties.

We studied flavonoids of *S. adenostegia* aerial parts, growing in the vicinity of Turakurgan, Republic of Uzbekistan, in order to discover new sources of biologically active flavonoids. Chromatography over a column of silica gel of the EtOAc fraction of the EtOH extract of the aerial parts afforded flavonoid 1, $C_{21}H_{20}O_{10}$, mp 276–278°C, (+)ESI-MS *m/z* 433 $[M + H]^+$, λ_{max} 279, 350 (sh); the *n*-BuOH fraction, flavonoid 2, $C_{21}H_{20}O_{11}$, mp 288–289°C; (+)ESI-MS *m/z* 449 $[M + H]^+$, λ_{max} 277,5, 307, 328 (sh), 364 (sh) nm.

^{1}H NMR spectrum of flavonoid 1 (DMSO-d_6, δ, ppm, J/Hz): 3.07–3.48 (4H, m, H-2″–H-5″), 3.65 (2H, m, 2H-6″), 4.61 (1H, t, J = 5.8, 6″-OH), 4.90 (1H, d, J = 7.4, H-1″), 6.62 (1H, s, H-3), 6.98 (1H, s, H-6), 7.56 (3H, m, H-3′, 4′, 5′), 8.08 (2H, dd, J = 2.1 and 8.2, H-2′, 6′), 8.64 (1H, br.s, 8-OH), 12.19 (1H, s, 5-OH). ^{13}C NMR spectrum (DMSO-d_6, δ, ppm): 182.61 (C-4), 163.48 (C-2), 152.38 (C-5), 151.49 (C-7), 144.44 (C-9), 132.20 (C-4′), 130.83 (C-1′), 129.20 (C-3′, 5′), 127.06 (C-8), 126.53 (C-2′, 6′), 104.97 (C-3), 105.38 (C-10), 101.21 (C-1″), 98.78 (C-6), 77.30 (C-5″), 75.74 (C-3″), 73.22 (C-2″), 69.69 (C-4″), 60.65 (C-6″).

Enzymatic hydrolysis of flavonoid 1 with β-glucosidase produced *D*-glucose and norwogonin (5,7,8-trihydroxyflavone). Thus, flavonoid 1 is norwogonin 7-*O*-β-*D*-Glucopyranoside. From *S. adenostegia* this compound isolated for the first time.

^{1}H NMR spectrum of flavonoid 2 (DMSO-d_6, δ, ppm, J/Hz): 3.08–3.47 (4H, m, H-2″–H-5″), 3.66 (1H, dd, J = 5.3 and 11.1, H-6″), 3.69 (1H, m, H-6″), 4.88 (1H, d, J = 7.3, H-1″),6.58 (1H, s, H-3), 6.79 (1H, s, H-6), 6.,89 (2H, d, J = 8.8, H-3′, 5′), 7.94 (2H, d, J = 8.9, H-2′, 6′), 8.64 (1H, br.s, 8-OH), 10.36 (1H, br.s, 4′-OH), 12.33 (1H, s, 5-OH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 182.40 (C-4), 164.04 (C-2), 161.33 (C-4′), 152.34 (C-5), 151.21 (C-7), 144.32 (C-9), 128.64 (C-2′, 6′), 126.96 (C-8), 121.28 (C-1′), 116.03 (C-3′, 5′), 105.13 (C-10), 102.66 (C-3), 101.25 (C-1″), 98.63 (C-6), 77.30 (C-5″), 75.75 (C-3″), 73.23 (C-2″), 69.70 (C-4″), 60.67 (C-6″).

The mass-fragmentation suggests that the flavonoid 2 is a glycoside of isoscutellarein (the presence of the ion $[Y_0]^+$ *m/z* 287 – [aglycone + H – hexose]$^+$). Enzymatic hydrolysis of flavonoid with в-glucosidase produced *D*-glucose and isoscutellarein (5,7,8,4′-tetrahydroxyflavone).

Based on the above data the flavonoid 2 identified as isoscutellarein 7-*O*-β-*D*-glucopyranoside. Isoscutellarein 7-*O*-β-*D*-glucopyranoside from plants of the genus *Scutellaria* isolated for the first time.

OBTAINING OF FIREPROOF, FIRE-RETARDANT WOOD CHIPBOARD BY USING OF CARBOXYMETHYLCELLULOSE

Sh. A. Yuldoshov, A. I. Shukurov, A. A. Sarymsakov

Scientific Research Center of Polymer Chemistry and Physics at the NUU, Tashkent, 100128, A. Kadiri 7b str, e-mail: sherzodbek_y@mail.ru

Nowadays, most of converted timber and wood chipboard bring to our Republic by import. The major part of these imported materials classified as flammable and fire-hazardous.

The aim of this work was to investigate of obtaining condition of fireproof, fire-retardant, high quality wood chipboard by using of carboxymethylcellulose samples.

The goal is achieved by adjusting the particle size distribution of wood chips, selection of effective local fire-retardant agents, establishment of their content in pulp in the manufacture of chipboard retardant, the definition of the optimal composition of the flame-retardant particleboard.

It was found that the wood chips used in the manufacture of granulometric composition has the following characteristics – 8.12 mm – 53%, 4.7 mm – 32%, 3.2 mm – 5%.

Particleboard production technology is based on a mixture of chopped wood or sawdust with a binder - urea-formaldehyde resin and hardener - ammonium chloride, water-repellent additives, followed by the formation of "carpet" and pressing.

To reduce the flammability index of wood particleboard was added different types and quantities of flame retardant agents.

Woodchips treated with orthophosphoric acid then neutralized by ammonium hydrate that made fire-retardant agent - ammonium dihydrophosphate in the structure of wood. The obtained product was dried at the temperature 85–90°C to 4–6% moisture.

The dried product mixed with binder and pressed on a hydraulic press at temperature 170–180°C.

To increase fire resistance and physical-mechanical properties of particleboard we were studied the process of addition of carboxymethyl cellulose (CMC) and microcrystalline cellulose (MCC) in the content of chipboard.

Adding of Na-CMC solution to the composition promotes a uniform distribution of flame retardant agent in pulp and improve its thermal stability, and MCC increase the chipboard density by filling of the pulp pores, thereby reducing oxygen in the pores of chipboard.

It was determined that increase in the amount of MCC in 1% of CMC solution fire-retardant properties of obtained chipboard samples increases sharply and reaches a weight loss of 0.6% when burning.

BIODEGRADABLE, BACTERICIDAL MEDICAL FILM BASED ON SODIUM CARBOXYMETHYLCELLULOSE CONTAINED SILVER NANOPARTICLES

Kh. E. Yunusov, A. A. Sarimsakov, S. Sh. Rashidova

The Scientific Research Centre of Polymer Chemistry and Physics under National University of Uzbekistan, 100128, 7 "b" A. Kadyri street, Tashkent,
e-mail: carbon@uzsci.net, haydar-yunusov@rambler.ru

Silver nanoparticles have an extremely large specific surface area, increasing the surface area bring to increases of contact with bacteria, viruses and fungi. Significantly increase is occurred bactericidal activity, even in decreasing the concentration of silver at hundreds times. However, decreasing in size of silver until nanoparticles, substantially increase the speed their agglomeration by increasing the surface energy.

The aim of this work is making bactericidal medical film based on Na – carboxymethylcellulose, contained stabilized silver nanoparticles and the study their structures and properties.

We have studied the conditions and the exchange of sodium cations with silver cations in solutions of Na-CMC. It was experimentally determined that when Na-CMC with DS – 0,65, 0.69, 0.85 by exchange with 0,35; 0,4 and 0,5 mol % ions of Na^+ to ions Ag^+ formed Ag^+CMC^- like stable form of hydrogel which is bad soluble in water, in difference to alkali metal salts of Na-CMC that apparently, explained carboxyl groups of Na-CMC ability to forms complexion with ions silver.

Determined, optimal conditions of formation of hydrogels Ag^+CMC^-, from water-soluble CMC fractions with different DS and DP. By the photoirradiation hydrogels was define the conditions of formation of silver nanoparticles with different shapes and sizes.

Synthesized stable nanoparticles by photochemical method could be explained by the Mott-Gurney theory.

Based on the results of investigations has chosen following conditions of formation homogeneous silver nanoparticles in size: Time of UV - irradiation 30 minutes; content of the CMC in hydrogel 0.08 mol; content of $AgNO_3$ in hydrogel 0,003 mol. Spherical silver nanoparticles with size 5–35 nm were formed in the selected conditions.

Bactericidal and bacteriostatic activities of synthesized film, containing silver ions and nanoparticles were investigated on strains *Staphylococcus epidermidis* and *Candida albicans.*

High bactericidal activity of film contained 5–35 nm spherical silver nanoparticles compared to silver ions was determined, against of pathogenic test bacterium *Staphylococcus epidermidis* and *Candida albicans.* Actually, the high bactericidal activity of this samples can be explained by small size of silver nanoparticle, high surface and can entering easily of in nucleus of microbe.

By the changing the proportions of components and conditions of reaction, have shown, the possibility of formation of stabilized silver nanoparticles from spherical until rod-like structure.

Obtained covering agents like film contained, stabilized silver nanoparticles can be used in medicine as a bactericidal drug to cure the burns and wounds.

THE NEW FORM OF BIOSOLUBLE EYE MEDICINAL FILMS WITH ANTIVIRAL ACTIVITY

Kh. M. Djuraeva, Yu. B. Li, A. A. Sarymsakov

The Scientific Research Centre of Polymer Chemistry and Physics under National University of Uzbekistan, 7 "b" A.Kadyri street, Tashkent, Uzbekistan 100128, e-mail: carbon@uzsci.net

Among widespread diseases of eyes the special place is taken away to diseases of a virus aetiology. Virus keratitis last years is the most widespread type of diseases of the eyes which untimely treatment leads to sight loss.

Among the known medical products intended for treatment virus keratitis there are drops, ointments which basically are directed for treatment of symptoms of diseases, but didn′t instead of suppression of reproduction of the virus. There is a unique preparation in the form of eye drops for direct treatment of virus diseases of an eyes - ophtalmopheron. Among known eye medicinal films (EMF) there are no preparations of the diseases of an eyes of a virus aetiology directed for treatment. Considering the above-stated elaboration of highly effective ophthalmologic preparations in the form of EMF the virus diseases of an eyes intended for treatment is an actual problem of chemistry of high-molecular compounds and pharmacology.

The research purpose is consists in obtain of new generation EMF intended for treatment virus keratitis an eye on the basis of a biodegradable substrate from cleared Na-CMC and substances antiviral a preparation of a wide spectrum of action «SelAgrip».

As a polymeric substrate film – forming material have been used high purity samples Na-CMC, by the various DP and FS, expose to swelling, dissolution and biodegradation with designated speed, and in quality antiviral a preparation – a substance "SelAgrip" allowed to manufacture and wide of application in conformity T.Ph.A – 42 Uzb – 1554 – 2010.

For obtain EMF prepared 2 % s' water solution high purity Na-CMC. Solution mixed on a mechanical mixer before full dissolution Na-CMC. Then a solution centrifuge at 3500 rev/min, several times for removal of insoluble fraction Na-CMC. After centrifuge in solution Na-CMC added plasticizer glycerine and mixed within 15–20 minutes.

In parallel prepared 4 % s' water solution of a preparation "SelAgrip". Solution of a preparation "SelAgrip". Solution mixed 20-30 minutes before full dissolution of a substance and centrifuge at 3000 rev/min. solutions Na-CMC and "SelAgrip" mixed at various of correlations. Films EMF cast on fat-free glass plates by means of the laboratory stand.

By change of a relations of components of a mix are created antiviral EMF containing 0.1-1.5 % of the active beginning inductor interferon with antiviral activity "SelAgrip".

On the base of experimental researches following optimum characteristics antiviral EMF are founded: the size of films on length 7–9 mm, width 3,5–4,5 mm, a thickness 25–40 microns, breaking strength 2,5–3,5 kgf/mm^2, explosive lengthening 8,6–9,4 %, time of full dissolution in water 0,4–1,4 h, pH 1 %-s' solution 6,8–7,8, the substance content in EMF- 0,8 - 1,2 %. Thus, received EMF represent the transparent, slightly yellowish films possessing by antiviral activity which didn't negative influenced on sight.

On the basis of medicobiological tests their high activity under the relation of viruses of a herpes of eyes is shown. Medicobiological tests EMF "GlazAvir" persists.

PREPARATION OF AMIDES OF HETEROCYCLIC ACIDS

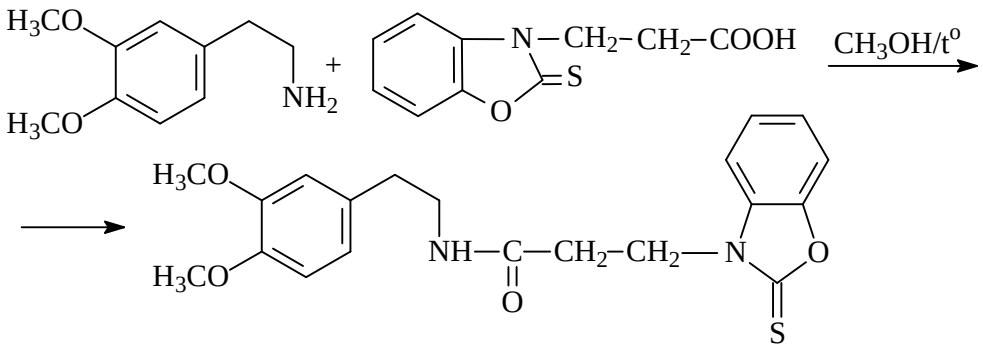
A. B. Yusupov[1], M. Alimova[1], A. T. Ayupova, V. I. Vinogradova[2]

1) Samarkand State University, Uzbekistan. e-mail: ayusupov.chem@gmail.com
2) S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan

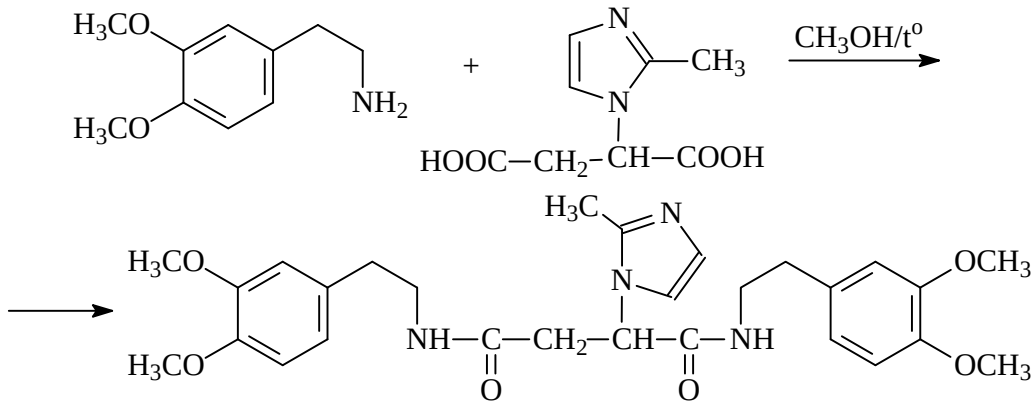
A compound having the isoquinoline cycle and imidazole, benzoxazole and other heterocycles, that is a combination of a single molecule of two or three heterocyclic systems enhances the pharmacological influence substances. We have tried to develop methods of synthesis of such substances. In their synthesis the starting substances are readily converted to the heterocyclic compound as pyridine, pyrrole, quinoline, isoquinoline and others.

Among these derivatives, there are the cycles containing pyridine, imidazole, 2-thioxobenzoxazole. Studying synthesis and pharmacological activity of imidazole and 2-thioxobenzoxazole containing derivatives of isoquinoline signifies the actuality of this research work. With this purpose, we conducted the synthesis of homoveratrylamine with dibasic imidazole containing acid and a monobasic 2-thioxobenzoxazole acid. The first step of the synthesis we have obtained amides of acids. Below a synthesis scheme is presented:

Preparation of amide of monobasic acid:



Preparation of amide of dibasic acid:



Identity and purity of the obtained compounds were examined by TLC on silicagel with different solvents. Their structure was confirmed by IR- and NMR spectra.

ISOLATION AND CHARACTERIZATION OF COTTON SEED PHOSPHOLIPASE D FROM THE NEW COTTON CULTIVAR C-7300

Sh. R. Mad′yarov[1], V. V. Uzbekov[1], O. N. Veshkurova[1], R. A. Yuldasheva[2], I. G. Amanturdiev[2], Sh. E. Namazov[2], Sh. I. Salikhov[1]

1) Institute of Bioorganic Chemistry, Uzbekistan Academy of Sciences
2) Cotton Breeding, Seed Production and Cotton Cultivation Agrotechnologies Research Institute, Ministry of Agriculture and Water Resources of Uzbekistan, Tashkent, Uzbekistan, e-mail: shuhm@yandex.ru

Cotton seeds are a valuable source of feed protein but their wide application for cattle breeding and especially for poultry breeding is limited due to presence of gossypol - specific polyphenolic cotton component which has negative effects on growth and reproductive power of farm livestock. Moreover gossypol is a cellular, vascular and nervous toxin and is capable to be cumulated in tissues.

Natural gossypol represents a mixture of optical isomers (so called (+) and (–) enantiomers) which demonstrate different biological activity and toxicity to nonruminant animals. It is determined that (–)-gossypol is more toxic for warm-blooded animals in comparison to (+)-gossypol. Preliminary experiments showed that cottonseeds which contain high level of (+)-gossypol could be used for broiler chicken feeding whereas (–)-gossypol cotton seeds bring to stop of their growth. This is the basis for use of cotton seed adapted cultivars with high content of (+)-gossypol for poultry breeding.

Adapted cultivars C-7300 with relative content of (+)-gossypol in seeds 94% and higher was created at Cotton Breeding, Seed Production and Cultivation Agrotechnologies Research Institute of the Ministry of Agriculture and Water Resources of Uzbekistan. At present the cultivars has passed procedures of grade testing and certification. Total nitrogen, protein composition, oil amount and residual amounts of gossypol were determined to evaluate nutrient value of oil cake produced from these seeds.

Partially purified preparation of phospholipase D (PLD) from seeds of this cultivar is isolated in the work in previously described conditions. PLD which preserves a part of activity in oil cake (till 30%) is a lipolytic enzyme which hydrolyses feeding diet phospholipids till important metabolites: alcoholic bases (choline, ethanolamine, inositol, serine, etc.) and phosphatidic acid – an important bioregulator of membrane enzymes and intracellular signaling.

Cotton seed flour was extracted by tenfold volume of Tris buffer with pH 9.0 during 3 hours at 4–6°C. After 20 min centrifugation at 6000 rpm the supernatant was precipitated by 2 volumes of cooled to –15°C acetone at 15 min agitation and was centrifuged at 3000 rpm during 5 min. The precipitate was dissolved in minimal volume of deionized water. After centrifugation at 6000 rpm the supernatant was subjected to secondary precipitation as described above. The obtained solution was lyophilized. Activity of this preparation (0.18 mkM/min/mg) almost did not differ from earlier isolated preparations from 108-F and Tashkent-1cotton seeds, pH_{opt} = 5.6, temperature optimum is 32°C (at activation by ether), $[S]_{opt}$ = 2–5 mM and $[Ca^{2+}]_{opt}$ = 50 mM.

This preparation can be multiply used after its stabilization by one of available method.

Highly purified preparations obtained on the basis of partially purified preparation can be used for structural-functional studies of biological membranes and membrane enzymes.

As can be seen from the above PLD activity can be considered as one more test for nutrition value of cotton seeds and other plant components of feeding diet. This PLD preparation can be also used as present-day preparation instead of preparations from 108-F and Tashkent-1 cotton seeds cultivars which are not used at present.

GLOBALWARMING, INSECTS RESOURCES AND HIGH TECHNOLOGIES

Sh. R. Madyarov[1,2], A. Sh. Khamraev[2]

1) Academy of Sciences of the Republic of Uzbekistan, Institute of Bioorganic Chemistry
2) Institute of the Gene Pool of Plants and Animals, e-mail: shuhm@yandex.ru

Class of insects (*Insecta*) is the most numerous among zoogenous living organisms containing about 2 million of species. These animals have multibillion tons of annual reproduction.

Insects historically originated in the same epoch as plants. Both plants and insects survived difficult periods of sharp climate changes and are safely existed and developed in present-day world being accumulated not less defense mechanisms of survival, metabolic path ways and especially diversity in morphological architecture than plants have.

Unfortunately pharmaceutical industry still is mainly based on pharmaceuticals from plants, on synthetic preparations but preparations from insects and other animals are very seldom, often they represent products of alternative medicine. Last years world warming is progressively felt due to greenhouse effect. This promotes high development of all flesh including insects which have a real danger for national economy and all mankind.

These animals apart from several dozens of insect species are not used industrially. Even such historically biotechnological originated industries as sericulture and apiculture exist only for production of such main products as silk and honey with co-products. But other the part of bioorganic materials in these industries practically is not used. Last decades biotechnological goods become reality due to intensively developed non-textile direction in science and technology of sericulture. This increases cost effectiveness and employment in the branch.

Precise study of physiological, biochemical and biophysical processes in insects on molecular level can lead to heuristic discoveries of rational ways of bioresourcesuse for progressive achievements in bio-nanotechnology and present day pharmaceutical industry.

The data of nutritive value of protein, carbohydrate and lipid isolates, stimulating and biological activity of pupae, fibroin and sericinhydrolyzates, isolated enzymes, inhibitors and methods of sericulture and silk technology wastes utilization are represented in the study.

From the other hand the integrated study of such most important biopolymers as fibroin, sericin and chitin their biosynthesis, biotransformation, obtaining of their different derivatives and composites as well as their physical forming will give not only new biomedical and biotechnological materials but will lead to creation such high-tech processes as widespread in wild-life 3D printing, space biotechnology, self-assembling, refolding, tuning of biomolecules,integrated biotransformation, nano-packaging, programmed regulation of drugs activity etc.Different pharmaceutical products are proposed at present for health support. Among them arerefined pharmaceutical forms of active substances or their incompletely studied mixtures,biologically active additives with not scientifically reasonable composition as well as complex mixtures of natural components in alternative medicine with long courses of use. The new effective pharmaceuticals, realPaul Ehrlich’s “magic bullets” will replace there with use of last achievement in metabolomics, with strict consideration of natural chelating properties of bioregulators on membrane level and based on the detail studied pharmacokinetics data, on biocompatible nano-dosage, on organ targeted specific effect of action and on other achievements of modern medicine, pharmacology and biotechnology.

Bio- and nano-technological approaches and methods developed in last decades for well studied mulberry silkworm will be significantly useful in complete study of renewable organic raw material of numerous insects.

THE STUDY OF ANTIOXIDANT ACTIVITY OF ECDYSTERONE INCLUSION COMPLEXES WITH α-, β- AND γ-CYCLODEXTRINS

P. K. Kudabaeva, B. S. Temirgaziev, A. T. Kazbekova, A. Sh. Atanbaev, G. Habdolda, B. I. Tuleuov, S. M. Adekenov

International Research and Production Holding "Phytochemistry", 100009, Karaganda, Kazakhstan, M.Gazaliev Str.4, fax: 8 (7212) 433 127, e-mail: phyto_pio@mail.ru

It is known that supramolecular nanoencapsulation of pharmaceutical preparations by cyclodextrins (CD) allows to obtain the solid dosage forms from liquids, and also increases the solubility and improves bioavailability [1].

In this regard, the aim of this paper is to study the antioxidant (AOA) activity *in vitro* from synthesized ecdysterone inclusion complexes with α-, β- and γ-cyclodextrins.

In vitro experiments have been carried out by relevant procedures. Determination of iron-reducing capacity (Ferric Reducing Antioxidant Power assay) satisfies the following scheme: to 0.1 mL of investigated substance in range concentrations of 0.1 mg/mL phosphate buffer of 0.25 ml is added (0.2 M, pH 6,6) and 0.25 mL of 1% solution of hexacyanoferrate (III) potassium. The reaction mixture has been incubated for 25 minutes at temperature of 50°C, the reaction has been stopped by adding 0.25 mL of 10% trichloroacetic acid solution.

The mixture was centrifuged for 10 minutes (3000 r/min). Top coating in the volume of 0.5 mL has been mixed with 0.5 mL of distilled water and 0.1 mL of 0.1% $FeCl_3$. Absorbance measurement is made at λ = 700 nm.

The obtained data reflected in the table, which shows the concentration dependence indexes of optical density for studied objects and the standard - ascorbic acid (AA).

Sample	0,25 mg/mL	0,5 mg/mL	0,75 mg/mL	1 mg/mL
α-	0.0173± 0.0059	0.0300± 0.0010	0.0483± 0.0049	0.0603±0.0015
β-	0.0307± 0.0012	0.0387±0.0015	0.0490± 0.0052	0.04967± 0.0015
γ-	0.0657± 0.0025	0.0680± 0.0017	0.0743± 0.0051	0.0840±0.0036
AA	0.9490±0.0213	1.2693±0.0021	1.4227±0.0220	1.8077±0.0038

Thus, it has been found that the antioxidant property among the three objects mostly expressed for ecdysterone complex with γ-cyclodextrin.

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ISOLATION OF ECDYSTERONE SUBSTANCE *Silene wolgensis* (HORNEM.) BESS.)

A. M. Kozhanova, E. A. Bayzhigit, G. S. Agitaeva, B. S. Temirgaziev, A. N. Zhabayeva, B. I. Tuleuov, S. M. Adekenov

International Research and Production Holding "Phytochemistry", Republic of Kazakhstan, Karaganda, 100009, Gazaliyev Str., 4, fax: (87212) 433 127, e-mail: phyto_pio@mail.ru

It is known that currently ecdysteroids are found in more than 126 species of the genus *Silene* (*Silene* L. *Caryophyllaceae* Juss) clove, and so many ecdysteroid containing species have not been identified none of the other families [1, 2].

Silene species are characterized by high quantity of ecdysteroids: 1–3%, especially in reproductive parts of some species, up to 7% of ecdysterone (20E) [3].

In this regard, in order to develop optimal this article describes the conditions for isolation of substance 20E from Kazakhstani type of *Silene wolgensis* (Hornem) Bess with its content of 1.76%, based on dry weight, have been studied the effect of a number of technological factors (concentration of selective extraction agents, temperature, extraction multiplicity and time) on a quantitative isolation of 20E from the aerial parts of studied plant raw material. On the basis of obtained data it is established that the maximum output of 20E from *Silene wolgensis* raw material is achieved within 3 hours after extraction agents boiling under the following process parameters: extraction agent - 96 % ethanol, fineness of raw material - 7 mm, extraction temperature of – 70°C, the raw material and extracting agent ratio (1:10), the multiplicity of extraction - 4. As a result of conducted study the technological scheme of 20E substance production is optimesed, the basic stages of the process are determined and experimental-industrial regulations of its isolation from *Silene wolgensis* are developed.

Thus, there are effective, non-expensive in terms of hardware performance isolation of 20E conditions, using the extraction agent according to GMP requirements of industrially significant raw material of the Republic of Kazakhstan - *Silene wolgensis*.

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SCREENING OF FLORA OF KAZAKHSTAN TO REVEAL NEW PLANTS SPECIES – SUPERPRODUCERS OF PHARMACOLOGICALLY ACTIVE STEROID COMPOUNDS

A. M. Kozhanova, P. K. Kudabayeva, G. S. Agitayeva, E. A. Bayzhigit, A. Sh. Atanbayev, G. Habdolda, B. I. Tuleuov, S. M. Adekenov

International Research and Production Holding "Phytochemistry", Republic of Kazakhstan, Karaganda, 100009, Gazaliyev Str., 4, fax: (87212) 433 127, e-mail: phyto_pio@mail.ru

As a result of multi-year researches of N. K. Abubakirov, Z. Saatov, U. A. Baltayev et al. scientific school the number of new sources of ecdysterone from the genera *Silene* L. and *Dianthus* L. (family *Caryophyllaceae* Juss. (Clove)) is proposed. A great quantity of ecdysteroids have been isolated from these genera.

In this context, continuing the research in this area, we have involved new plants for screening that representing previously unexplored type of data of perspective ecdysteroid containing species of a studied flora.

All the representatives of *Caryophyllaceae* Juss family have been collected: *Dianthus superbus* L. and *Silene repens* Patrin. - in the mountains of Saur, near Churchutsu village in East Kazakhstan region, *Silene media* (Litv.) Kleopow - in Zaisan basin, in Kulundzhun neighborhoods in East Kazakhstan region and *Arenaria potaninii* Schischk. - near Zaisan village, Zhemeney river in East Kazakhstan region. Objects of research are aerial parts of plant raw material have been collected in 2016 at flowering stage.

The quantitative content of ecdysterone in ethanol extracts of studied plants is determined by reverse-phase high performance liquid chromatography (HPLC).

Extracts samples	Quantitative content of ecdysterone by HPLC, %
Ethanol extract of *Dianthus superbus* L.	Not detected
Ethanol extract of *Silene repens* Patrin.	0,61
Ethanol extract of *Silene media* (Litv.) Kleopow	0,53
Ethanol extract of *Arenaria potaninii* Schischk.	0,04

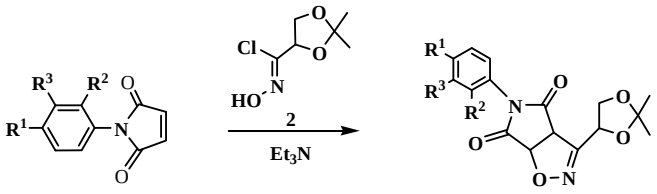
Thus, analysis fully confirmed the preliminary paper and thin layer chromatography on the presence and absence of ecdysterone substance in studied plant species, according to data obtained by HPLC. The high content of ecdysterone in the extracts has been found in creeping campion (*Silene repens* Patrin) 0,61% and intermediate campion (*Silene media* (Litv.) Kleopow 0,53%, which further allows to recommend them as a promising source of ecdysterone - the substance of actoprotector drugs.

SYNTHESIS AND *in vitro* ANTICANCER AND LEUKOCYTE COMMON ANTIGEN ACTIVITY OF DIOXO-PYRROLINO-[3′,4′-*D*]ISOXAZOLE DERIVATIVES CONTAINING (1′,2′-*O*-ISOPROPYLIDENEDIOXYETHYL)

M. Imerhasan*, S. Helil, T. Muhammed

College of Chemistry and Chemical Engineering, Xinjiang University, 830046, Urumqi, P. R. China, e-mail: imerhasan@yahoo.com

Fifteen 3-(1′,2′-*O*-isopropylidenedioxyethyl)-5-aryl-3a,6a-dihydro-4,6-dioxo-pyrrolino[3′,4′-*d*]isoxazole derivatives were synthesized by 1,3-dipolar cycloaddition reaction of *N*-arylmaleimid derivedes and the nitrile oxide *in situ* generated from the 2,3-*O*-isopropylidenedioxyethyl-*D*-glycerohydroximoyl chloride in the presence of triethylamine. The structures of the target compuonds were characterized by elemental analysis, UV, IR and ^{1}H NMR. The initial activity of the screening, some compounds show varying degrees of anti-cancer, anti-inflammatory and immune disease activity in some extent. The compounds **3a–3o** showed Cdc25A phosphatase inhibitory activity of 56.99%~99.94%, at the test concentration of 20 мg·mL^{-1}, and among them **3f, 3h, 3i, 3m, 3o** were not inhibition activity, The rest of the compounds inhibition rate is still 66.85–99.84%, even at the concentration as low as 5 μg·mL^{-1}, it deserves future study. At the test concentration of 20 μg·mL^{-1}, inhibition activity of 63.08–89.26% against leukocyte common antigen (LCA) CD45 protein tyrosine phosphatase A except for compound **3i**, and have great application in the treatment of cancers, Inflammatory and immune diseases.



	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o
R^1:	H	CH_3	OCH_3	Cl	Br	F	H	CO_2H	H	H	H	NO_2	H	H	H
R^2:	H	H	H	H	H	H	Br	H	CH_3	NO_2	H	H	Cl	H	CO_2H
R^3:	H	H	H	H	H	H	H	H	H	H	CH_3	H	H	Cl	H

Scheme 1 Synthetic route of 3a-3o

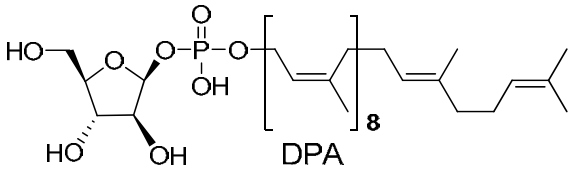
*****Project supported by the National Natural Science Foundation of China (No 21462043, 21062019)

SYNTHESIS AND ANTITUBERCULOSIS ACTIVITY OF SOME PHOSPHORUS CONTAINING GLYCOLIPIDS OF GLUCURONIC ACID, GLUCOSE AND GLUCOSAMINE

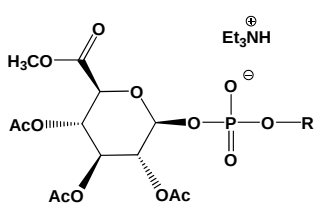
O. V. Andreeva, R. R. Sharipova, E. S. Izmestev, B. F. Garifullin, V. E. Kataev

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center, Russian Academy of Sciences, Arbuzov str. 8, Kazan, 420088 Russian Federation, e-mail: ovandreeva76@mail.ru

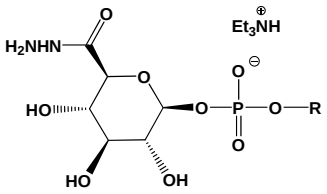
It is known that decaprenolphosphoarabinose (DPA) is used in the mycobacterial cell wall biosinthesis as the source of the *D*-arabinose. Some its mimetics have been synthesized to evaluate their ability to inhibit the in vitro growth of *M. tuberculosis*.



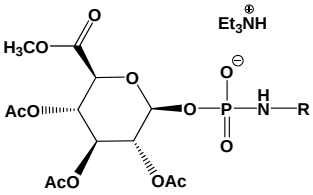
In this report we present the synthesis of previously unknown DPA mimetics that are the phosphorus containig glycolipids of *D*-glucuronic acid, *D*-glucose and *D*-glucosamine **1**–**7**.



1, 2



3,4



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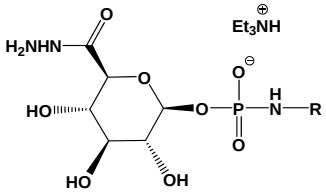

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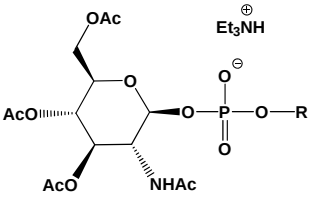

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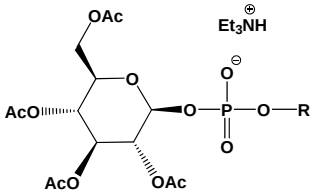
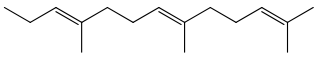


8, 9

1, 3 R = C_7H_{15}

2, 4 R =



5, 6 R = $C_{11}H_{23}$

7, 8 R = $C_{16}H_{33}$

9 R = $C_{10}H_{21}$

The evaluation of the antituberculosis activity of the glycolipids obtained has shown that they are about 3 times more active than known mimetics on the basis of arabinofuranose.

This study was performed under financial support of the Russian Science Foundation (grant № 14-50-00014).

SEPARATION AND PURIFICATION OF POLYPHENOLIC BIOACTIVE COMPOUNDS FROM ROSE USING CROSSLINKED POLYMERS

Turghun Muhammad*, Memetimin Mahmut

College of Chemistry & Chemical Engineering, Xinjiang University,
Xinjiang Key laboratory of Oil and Gas Fine Chemicals, Urumqi 830046, P. R. China

Polyphenols are a group of chemical substances found in plants, characterized by the presence of more than one phenol unit or building block per molecule. The best described property of polyphenolics is the antioxidant ability to scavenge free radicals produced by cells metabolism or in response to external factors [1]. It is very appealing to scientists to elaborate a reliable method for the determination of the total content of polyphenolic antioxidants. In order to increase medicinal value of the roses and pomegranate flowers and several new solid-phase adsorption materials were synthesized and packed into the SPE cartridges for separation and purification plant polyphenols. We provide technical support for application of polyphenols separation and enrichment.

Using 1,2-phenylene diacrylate monomer as functional monomer, and divinylbenzene as cross linking agent, molecularly imprinted polymers specific for o-Diphenol was synthesized; in the same way, using itaconic acid, methacrylic acid, acrylamide and styrene as functional monomers, ethylene glycoldimethacrylate as cross linking agent, crosslinked polymers were synthesized then packed into SPE cartridges. The maximum binding capacity and the best loading conditions were optimised by breakthrough experiment, when the sample loaded at the concentration of 1.0 g • 1L, in pH = 2 buffer solution on the cartridge, the maximum adsorption capacity of o-Diphenol was up to 41.6mg • 1g; Itaconic acid cross-link polymer after optimized preparation conditions showed surprisingly high binding capacity and their value is 49.5 mg • 1g.

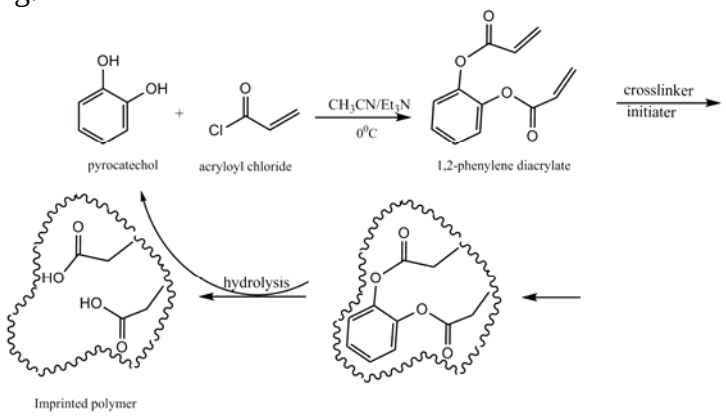


Fig. 1-1. The preparation of molecular imprinted polymer.

Acknowledgment. This work was supported by the National Natural Science Foundation of China (21565025).

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MODIFICATION OF ANTHRACYCLINE ANTIBIOTICS BY SESQUITERPENE LACTONES TO SIDE EFFECTS PREVENTION

M. E. Neganova, A. V. Semakov, L. V. Anikina, E. F. Shevtsova, S. A. Pukhov, S. G. Klochkov

Institute of Physiologically Active Compounds of Russian Academy of Sciences, 142432, Russia, Moscow region, Chernogolovka, IPAC RAS, e-mail: neganova83@mail.ru

One of the important directions of chemotherapy of oncological diseases is the use of various antitumor antibiotics. It is possible to isolate among other a special group of antitumor antibiotics that have high antimitotic activity and are widely used in medical practice - anthracycline antitumor. Alongside with their numerous advantages, they have a lot of serious lacks - first of all their high and irreversible cumulative dose-dependent cardiotoxicity, which is caused by free radical damage to myocardial cell membranes.

To reduce toxicity to healthy cells, anthracycline antitumor antibiotics were modified by natural pharmacophores - sesquiterpene lactones from plants of the *Asteraceae* family, capable of influencing the key moments of toxicity formation, in particular oxidative stress. A series of conjugates of known anthracycline antitumor antibiotics - daunorubicin, doxorubicin - and natural and modified sesquiterpene lactones were synthesized and studies of their biological activity were carried out.

At the initial stage, the effect of test compounds on the survival of different human tumor cells was studied to compare the level of activity with the initial anthracyclines. It was shown that all test substances demonstrate high cytotoxic activity. For some conjugates, cytotoxic activity is significantly higher than of the initial antibiotics.

The next step was to study the effect of anthracyclines and their derivatives on the process of lipid peroxidation of rat brain homogenate to detect antioxidant activity. As expected, unlike the scaffold antibiotics, which do not have antioxidant activity, some conjugates effectively suppressed the process of lipid peroxidation.

Thus, modification of anthracycline antibiotic by sesquiterpene lactones can act as a basis for the development of effective antitumor agents with reduced toxicity in relation to healthy cells.

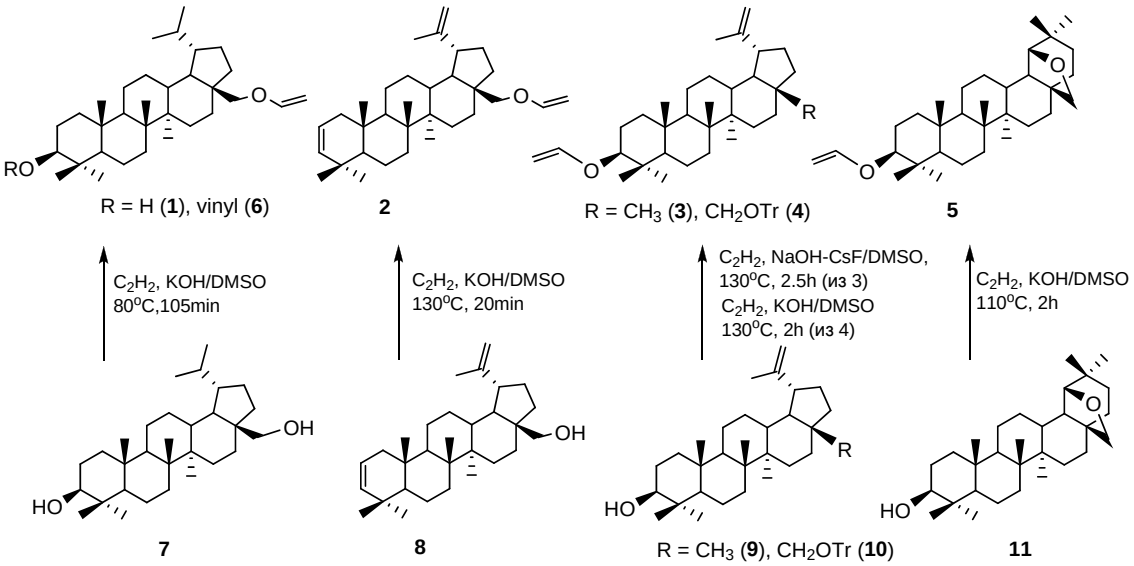
This work was supported by RFBR (project 15-03-03940).

SYNTHESIS OF *O*-VINYL ETHERS OF LUPANE TRITERPHENOIDS – POTENTIAL MONOMERS IN POLYMERIZATION REACTIONS

N. G. Komissarova, A. V. Orlov, O. V. Shitikova, M. S. Yunusov

Ufa Institute of Chemistry, Russian Academy of Sciences,
450054, Ufa, Prosp. Oktyabrya, 71, e-mail: ngkom@anrb.ru

Interest in polymers based on natural compounds is due to the possibility of creating biocompatible and biodegradable polymer materials for various purposes, polymer drugs and target carriers of drugs [1]. One of the classes of secondary metabolites that are promising for the development of such polymeric structures are pentacyclic trperenoids of the lupane series [2]. Earlier, we developed a method for the *O*-vinylation of betulin with acetylene in a superbasic medium [3, 4]. Now we report on the synthesis of new mono- (1) - (5) and divinyl (6) ethers of lupane triterpenoids - potential monomers in reactions of cationic and radical co- and RAFT-polymerization, as well as polyacetalisation. *O*-Vinylation of the diol (7) and alcohols (8)-(11) with acetylene took place in the superbasic medium KOH/NaOH-CsF - DMS, with the formation of the goal compounds with a yield of 52–78%.



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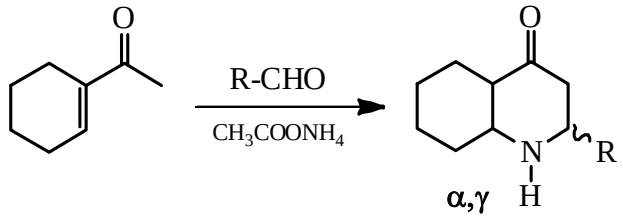
SYNTHESISOF ANALOGUESOF NATURAL DECAHYDROQUINOLINEALKALOIDS

O. T. Zhilkibayev

Al-Farabi Kazakh National University, 050040, Almaty, Al-Farabiavenue 71,
e-mail: zhilkibaevoral@mail.ru

Decahydroquinoline frame is the basis of a number of natural alkaloids(lepadine, pumiliotoxine, castonospermine, nitramine, etc), and dimethoxyphenyl groups have their own pharmacological potential (include in composition of many natural compounds and drugs). The union of these fragments in one molecule led to the effective physiologically active compounds with a wide range of biological effects.The combination of decahydroquinoline frame and dimethoxyphenylethyl group in the synthesized compounds in one molecule makes their close structural analogues of such natural alkaloids and antispasmodics as laminarine, salsolidine, no-Spa, and etc. Analysis of the literature shows that the number of works devoted to the description of the synthesis of decahydroquinoline is limited and mostly described the synthesis of alkylsubstituted derivatives, but their phenylsubstituted derivatives have not been studied.

For the purpose of obtaining physiologically active substances with specified properties carried out the synthesis of 2-dimethoxyphenyldecahydroquinoline-4-ones with various provisions of the methoxyl groups at the phenyl ring. Decahydroquinolines are obtained by one-step method: condensation acetylcyclohexanone with the corresponding dimethoxybenzaldehyde in absolute ethanol in the presence of ammonium acetate. As a result of the reaction a mixture of the two isomers of 2-dimethoxyphenyldecahydroquinaline-4-ones (γ-,α-) are formed.



R
2′,3′-$(OCH_3)_2C_6H_4$-;
2′,4′-$(OCH_3)_2C_6H_4$-;
2′,5′-$(OCH_3)_2C_6H_4$-.
3′,4′-$(OCH_3)_2C_6H_4$-;
3′,5′-$(OCH_3)_2C_6H_4$-;

The stereoisomers were separated into individual forms. The isomers of γ-aminoketones with an equatorial orientation of dimethoxyphenyl groups dominate in a mixture. The structure of the individual stereoisomers is determined on the basis of IR, ^{1}H and ^{13}C NMR spectroscopy.

It is found that all synthesized compounds have a wide range of biological effects. Their antiarrhythmic and spasmolytic activity was studied. The number of compounds simultaneously possessing antiarrhythmic and spasmolytic activity was discovered. By index of antiarrhythmic activity some compounds have lower toxicity and higher activity in comparison with all standard drugs (procainamide, quinidine, lidocaine, verapamil). Spasmolytic activity of derivatives of decahydroquinoline exceeds papaverinein 2–5 times and have similarities with SPE at low toxicity.

These findings expand a view about biological activity of derivatives of decahydroquinolineand open up new prospects.

ESSENTIAL OIL COMPOSITION AND MORPHOLOGICAL, ANATOMICAL CHARACTERISTICS OF *Stachys megalodonta* HAUSSKN.& BORNM. EX P.H. DAVIS SUBSP. *Mardinensis* R. BHATTACHARJEE ENDEMIC IN TURKEY

M. Kurkcuoglu[1], S. Kucuk[2*], M. Kursat[3], K. H. C. Baser[4]

1) Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy,
2) 26470, Eskisehir, Turkey
2) Anadolu University, Faculty of Pharmacy, Pharmaceutical Botany,
26470, Eskisehir, Turkey
3) Bitlis Eren University, Faculty of Science and Arts, Department of Biology, Bitlis, Turkey
4) Near East University, Faculty of Pharmacy, Department of Pharmacognosy, Near East Boulevard, ZIP: 99138, Nicosia, N. Cyprus, e-mail salan@anadolu.edu.tr

Stachys L. (Delicay) (*Lamiaceae*) is presented in Turkey by 89 species. 46 species are endemic in Turkey. *Stachys megalodonta* Hausskn. & Bornm. ex P. H. Davis subsp. *mardinensis* R. Bhattacharjee is locally known as “gevrek delicay”. They are aromatic perennial subshrubs used as spices or herbal teas in traditional Turkish medicine.

The aerial parts *S. megalodonta* subsp. *mardinensis* of (*Lamiaceae*) was water distilled for 3 h using a Clevenger-type apparatus. The essential oil was analyzed by GC-FID and GC-MS, simultaneously. The main constituents were identified as α-pinene (17.7%), germacrene D (7.2%), 1,8-cineole (6.1 %), β-caryophyllene (4.8%), limonene (3.1%), camphene (3.1%) and camphor (2.9%) for *S. megalodonta* subsp. *mardinensis*. It′s morphological, morphometric and anatomical properties are described in the present study. Data obtained after investigations were compared with those in the Davis′s “Flora of Turkey”. Morphological and anatomical results are supported by photographs and illustrations.

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VOLATILE COMPOUNDS OF *Tripleurospermum pichleri* (BOISS.) BORNM. AND *Tripleurospermum rosellum* var. *album* E. HOSSAIN FROM TURKEY

Mine Kurkcuoglu[1]*, Huseyin Inceer[2], K. Husnu Can Baser[3]

1) Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, 26470, Eskisehir, Turkey.
2) Karadeniz Technical University, Faculty of Sciences and Arts, Department of Biology, TR-61080 Trabzon, Turkey,
3) Near East University, Faculty of Pharmacy, Department of Pharmacognosy, Near East Boulevard, ZIP: 99138, Nicosia/TRNC, Mersin 10, Turkey,
e-mail: mkurkcuo@anadolu.edu.tr

The genus *Tripleurospermum* Schultz Bip. is represented in Turkey by 31 taxa, 15 being endemic in Turkey.

Microdistilled essential oils of the dried flowers of two endemic species *Tripleurospermum pichleri* and *Tripleurospermum rosellum* var. *album* were analyzed by GC-FID and GC/MS. The oils were characterized by the occurrence of matricaria esters as main constituents.

The oil of *T. pichleri* contained (2*Z*,8*Z*)-matricaria ester (64.9%), (2*E*,8*Z*)-matricaria ester (12.3%), 8*Z*-2,3-dihydromatricaria ester (6.8%) and (2*E*,8*E*)-matricaria ester (3.3%) as main constituents. The oil of *T. rosellum* var. *album* was characterized by the occurrence of (2*E*, 8*Z*)-matricaria ester (39.2%), (2*E*,8*E*)-matricaria ester (32.8%), β-sesquiphellandrene (11.0%), 8*Z*-2,3-dihydromatricaria ester (4.4%) and (2*Z*,8*Z*)-matricaria ester (3.8%) as major components.

To the best of our knowledge, this is the first report on the GC and GC/MS determination of the essential oil composition of the *Tripleurospermum* species studied.

Acknowledgment. The authors acknowledge the Scientific and Technological Research Council of Turkey (TUBITAK, Project No. 106T162) for financial support.

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PIPERIDINE ADAMANTANECARBOXYLATES

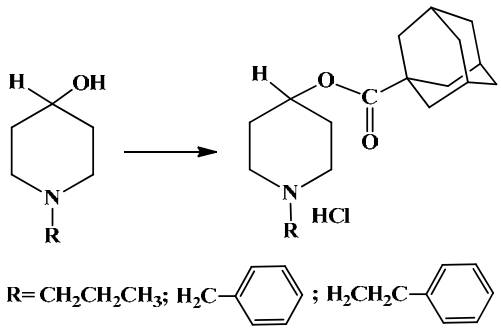
F. M. Sadyrbayeva[1], D. A. Sultanova[1], U. B. Issayeva[2], G. S. Akhmetova[2], V. K. Yu[1,2], K. D. Praliyev[2]

1) Kazakh-British Technical University
2) Institute of Chemical Sciences named after A. B. Bekturov, Almaty, Kazakhstan, e-mail: farikaznu@mail.ru

The cyclic system of adamantane has unique properties such as bulkiness, symmetry, and high lipophilicity. Due to these properties, adamantane derivatives can easily permeate through biological membranes, adsorb on the cells and cause biological effect. The search for the novel drugs in the adamantane family is of current interest [1].

The high biopotential and technological availability of piperidine derivatives [2] are unquestionable, and the current research aims at making the synthetic "assembly" of piperidine fragments and adamantane into new molecular systems possessing potential biological activity.

Acylation of [1-propyl-, 1-benzyl-, 1-(2-phenylethyl-)]-4-hydroxypiperidines using chloroacetic anhydride of adamantanecarboxylic acid is carried out in chloroform and twofold excess of acylating agent is added during more than 24 hours.



Synthesized esters of adamantanecarboxylic acid with the yield of 55–70% are white-coloured crystal substances. The ultrasound activation of acylation has resulted in the reaction time reduction up to 2–3,5 h and in the yield increase up to 80-90 %.

The structure of synthesized hydrochlorides of piperidine adamantanecarboxylates was figured out on the basis of NMR and IR spectroscopy results.

The authors thank the Ministry of Education and Science of the Republic of Kazakhstan for financial support (0251/ STP).

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PHYSICOCHEMICAL CHARACTERISTICS OF SERICIN EXTRACTED BY WATER AND ALKALINE SOLUTIONS

Z. U. Sherova, A. B. Ishmatov, Z. K. Mukhidinov

V. I. Nikitin Chemistry Institute of the Republic of Tajikistan Academy of Sciences
299/2 Ainy str., Dushanbe 734063, Tajikistan, e-mail: ishmat_0405@mail.ru

More than 150 tons of silk waste is produced annually at the coconut-processing factories of the Republic of Tajikistan, which are cocoons that are unreadable, unwoven coconut wool and pupae.

Utilization of this waste is of great economic importance for the economy of Tajikistan, since for each kilogram of silk produced, raw materials account for more than 1 kg various wastes. The shell of defective cocoons and fibrous waste of cocooning are valuable textile and biological raw materials with up to 30% of adhesive sericin suitable for technical, sanitary, medical, cosmetic and other purposes.

The aim of this work was the utilization of silk waste from the cocoon-winding factories of the Republic of Tajikistan, by extracting sericin under mild conditions with an optimal yield and preserving its initial (adhesive) properties for further use in the above mentioned purposes.

Extraction of sericin from silk waste was carried out in alkaline and aqueous solutions after removal of fat and wax substances. Physicochemical characteristics of extracted sericin were studied. The resulting powder was soft, silky and a homogeneous consistency with a dark brown color. According to the results, when extracting sericin by an alkaline method, the density of the solution was 0.965 g/ml, while extracting sericin with an aqueous solution formed a density of 0.986 g/mL. The yield of sericin powder was 12.16% for the alkaline extraction method and 2.41% for the aqueous extraction method.

IR spectroscopic analysis of extracts of sericin, obtained by two various method, was performed on a FT IR spectrophotometer (FT-IR Spectrum 65 (Perkin Elmer)) using the attenuated total reflection (ATR). It was shown that silk wast traetment with alkaline solution leads to decrease in the protein fraction of the в-sheet conformation, and the appearance of the peak at 1664 cm^{-1}, is referred to as α-helix and disordered structures.

ABOUT PSYCHOSTIMULATING ACTIVITY OF FURANOQUINOLINE ALKALOID OF SKIMMIANINE

Yu. R. Mirzaev, Z. I. Sanoev, Kh. A. Rasulova

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

Previously conducted in the Department of Pharmacology and Toxicology of ICPS studies have revealed psychotropic agents of different chemical classes of plants origin, including furanoquinoline alkaloids from the Haplophyllum perforatum. It was stated that skimmianine is main alkaloid in aerial part of plant and reach 70% of sum. Alkaloids of Haplophyllum including skimmianine were recognized as sedative or antipsychotic compounds. However, in the psychiatric practice any preparation were not included. Attention is drawn to the fact these alkaloids were studied in high doses 10–100 mg/kg. In our studies it was noted, that skimmianine in doses 0.1–1.0 mg/kg per os activated of mice behavior. Detailed studies have showed, that skimmianine activated locomotor activity of mice in experiments, as by Lapin method, so by Hall. Alkaloid decreased intensity of Haloperidol catalepsy, in some degree increased intensity of amphetamine locomotor action, improved the “search activity” of mice in the test of “Open fild” by Hall method. Besides, the compound increased the duration of mice forced swimming in experiments by Porsolt. Skimmianine have revealed expressed anxiolytic action in experiments by Kilfoil. Presented results of conducted experiments evidenced about psychostimulating activity of skimmianine used in small doses reaching 1/500 – 1/5000 of LD_{50}. Skimmianine would be accepted as natural plant antidepressant. Among known antidepressants representatives with furanoquinoline structure were not revealed. The Institute intended to defense skimmianine by patent in quality of potential antidepressant preparation.

SYNTHESIS AND CRYSTAL STRUCTURES OF 2-ALKYLTIO-5-ACETAMIDO- AND -CHLOROACETAMIDO-1,3,4-TIADIAZOLES

T. T. Toshmurodov, U. S. Makhmudov, A. A. Ziyaev, B. Zh. Elmuradov

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

The presence in the molecule of 5-amino-1,3,4-thiadiazoline-2-thione of pharmacophore sulfur and nitrogen containing fragments makes it one of the widely studied five-membered heterocycle, which is of great interest for researchers in the field of chemical transformations. Among the derivatives of this class, many types of biological activity are described, such as pharmacological, pesticidal, etc. [1]. In addition, aminothiazolinthiones can exhibit multiple reactivity due to the presence of a functional amino group in the position fifth, a sulfur atom and nitrogen in the ambibunctional thioamide system NH-C=S.

In this work we report a synthesis of new 2-alkylthio-5-acetamido- and chloroacetamido-1,3,4-thiadiazoles **1**–**4** (**1**, R=Ac, R_1=Et; **2**, R=Ac, R_1=Pr; **3**, R=$ClCH_2CO$, R_1=Et; **4**, R=$ClCH_2CO$, R_1=Pr) by the reaction of 2-alkylthio-5-amino-1,3,4-thiadiazoles with acetyl and chloroacetyl chlorides in benzene. In this case, the most optimal synthesis conditions (ratio of reagents, temperature, solvent, etc.) are established. The spatial structures of synthesized compounds **1-4**, whose crystals were grown from methanole, were further investigated.

Molecular structures **1**, **2**, **3** and **4** contain flat aromatic thiadiazole nucleus and mobile thioethyl and thiopropyl fragments at position C2, with an accuracy of ± 0.004, ± 0.010, ± 0.005 and ± 0.007 Å, respectively, whose location relative to the thiadiazole nucleus is approximately similar (The value of the torsion angle S1-C2-S6-C7 178.1, -109.1, 168.6 and 167.5^0 for **1**, **2**, **3** and **4**, respectively). The acetamide and chloroacetamide fragments are located at small angles with respect to the thiadiazole ring - 3.2, 5.1, 11.7 and 11.6^0 for **1**, **2**, **3** and **4**, respectively.

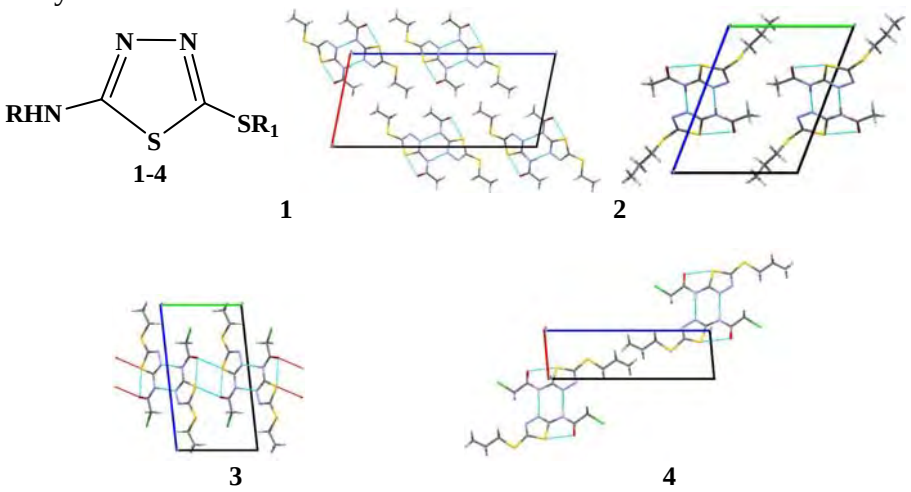

Fig. 1. Packing of molecules in the crystals of **1**–**4**

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SYNTHESIS OF PHOSPHORYLATED DERIVATIVES OF ALKALOIDS, THEIR STRUCTURE, BIOLOGICAL ACTIVITY AND PERSPECTIVES OF PRACTICAL APPLICATION

M. B. Gafurov, Z. Tilyabaev, D. N. Dalimov, A. A. Abduvakhabov

A. S. Sadykov Institute of Bioorganic Chemistry of Academy of Sciences
of the Republic of Uzbekistan, 100125, Tashkent, Uzbekistan,
Mirzo Ulugbek str., 83, e-mail: mahmudgafuov@mail.ru

Intensive research on the synthesis of organophosphorous compounds has started after establishing that their biological action is based on their ability to irreversibly inhibit the enzymatic activity of acetylcholinesterase hydrolyzing a neurotransmitter.

The possibility to enhance the anticholinesterase effect by modifying organophosphorous compounds with natural compounds such as alkaloids became a new era in their research, which had been initiated by academicians A. S. Sadykov and A. A. Abduvakhabov.

This research includes the aspects of synthetic routs development, reactivity of organophosphorous derivatives of alkaloids, and establishment of their structures using modern analytical techniques.

The application of phosphorylated alkaloids in the reactions with cholinesterases has allowed examining the effect of their conformations on the sensitivity of enzymes of different biological origin.

Authors have reviewed the literature information including their own research data on pharmaco-toxicological properties of chemically modified alkaloids and their application as plant protectors and synergists of industrial insecticides, as protectors against highly toxic compounds, anti-arrhythmic and anti-cancer preparations and as extractants of noble metals.

Thus, it can be seen that there are unlimited possibilities associated with chemical modification of alkaloids and search of promising physiologically active compounds on their basis.

POLYSACCHARIDES OF *Scutellaria adenostagia*

A. A. Siddikova, R. K. Rakhmanberdyeva

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: rkrahman@rambler.ru

Scutellaria L. is a genus of plants of the family *Lamiaceae* includes about 350 species widespread in subtropical and tropical regions, including Europe, North America and East Asia [1, 2]. In Uzbekistan, 32 species of *Scutellaria* L. grow which are used in folk medicine for the treatment of epilepsy, allergy, neurosis, hypertension and other diseases [2, 3].

This work is devoted to the study of the carbohydrate complex of the aerial part of *S. adenostagia* collected in the Namangan region of the Turakurgan region during flowering.

The carbohydrate complex was isolated according to a known method [1]. Isolated alcohol-soluble sugars (ASS), water-soluble polysaccharides (WSPS), pectin substances (PS) and hemicelluloses (HMC). ASS according to PC data consists only of glucose. The monosaccharide composition of the isolated polysaccharides was determined by complete acid hydrolysis followed by GC analysis.

The results of the study showed that in the aerial part of the plant, WSPS (13%) accumulate more and their monosaccharide composition is represented by galactose (14.4%), arabinose (31.0%), glucose (5.6%), mannose (35%), xylose (4.4%) and rhamnose (0.4%).

The WSPS is a light-brown colored amorphous powder completely dissolved in water. A homogeneous polysaccharide-glucoarabinogalactan (GAG) with MM of 15 kDa consisting of glucose (5.6%), arabinose (27.2%) and galactose (55%) was obtained by fractional precipitation of WSPS. In the IR spectrum of GAG, absorption bands characteristic of polysaccharides were observed. It should be noted that in the spectrum there are absorption bands related to acetyl groups (1742, 1250 cm^{-1}). Therefore, GAG is a naturally acetylated polysaccharide.

PS are a beige powder, soluble in water with the formation of viscous solutions – η_{rel}. 3.12 (*c* 1%; H_2O), monosaccharide composition of PS includes neutral and acidic monosaccharides.

HMC-brown amorphous powder, completely soluble in alkali, the main monosaccharide is xylose, and also insignificant amounts of glucose and galactose. Consequently, the GMC refers to xylans.

Thus, the presence in the aerial part of *S. adenostagia* of alcohol-soluble sugars, water-soluble polysaccharides, pectin substances and hemicelluloses has been established. The WSPS contains a naturally acetylated glucoarabinogalactan.

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SUPRAMOLECULAR COMPLEXES OF SOME FLAVONOIDS WITH GLYCYRRHIZIC ACID AND ITS SALTS

U. D. Matchanov, R. S. Esanov[1], A. G. Eshimbetov[2], A. D. Matchanov[1]

National University of Uzbekistan 1) Institute of Bioorganic Chemistry
2) Institute of Chemistry of Plant Substances

The chemical transformation of accessible and easily isolated natural compounds in search of biologically active substances has become an independent scientific direction of bioorganic chemistry. The most attention is attractedto natural biologically active flavonoids, in particular quercetin and rutin, which exhibit antioxidant properties.

Flavonoids are a group of phenolic compounds that are contained in virtually all plant species. The most rich in these substances are leaves, flowers, as well as stems and bark of plants (they can contain up to 3% of flavonoids).

But most of them are poorly soluble in water, because of which their biological activity is limited. To improve the solubility, various methods are used, the preparation of salts, chemical modification, and the preparation of complex compounds with polymeric carriers and natural low-molecular terpenoids.

One such compound is glycyrrhizic acid (HA) and its salts. Due to their chemical structure, they exhibit unique properties, like solubilization. HA is found in licorice root as mixed salts. The content of HA in the roots and rhizomes ranges from 2 to 24%.

The aim of this work is to obtain supramolecular complexes of some flavonoids with HA and its salts, study of physic-chemical and spectral characteristics.

HA and its salts wereisolatedfrom the root of licorice (*Glycyrrhiza glabra*), and purified by a previously known method. Flavonoids were obtained by extraction of the flowers of Japanese sophora, and purified by the methods of re-crystallization, and column chromatography.

Based on the isolated substances, supramolecular complexes were obtained in various molar ratios. The physic-chemical and spectral characteristics of the compounds were studied. The structure of the obtained supramolecular complex compounds was characterized by a comparative study of the IR and UV spectra of the starting compounds with the spectra of the obtained supramolecular complexes.

In all the compounds obtained, a characteristic mixing of the band of the valence vibrations of the C = O group into a high-frequency region relative to the original ones is observed, which indicates the hydrogen bonds that form between complex-forming components.

Thus, supramolecular complexes of flavonoids with HA and its salts have been obtained, physicochemical properties and IR and UV spectral characteristics have been studied.

EFFECT OF PLANT TERPENOIDS, KARATAVIC AND GALBANIC ACIDS ON THE REGULATORY VOLUME DECREASE IN RAT THYMOCYTES

S. I. Rustamova[1], R. Sh. Kurbannazarova[1], P. G. Merzlyak[1], Z. A. Khushbaktova[2], V. N. Syrov[2], M. P. Yuldashev[2], B. A. Tashmukhamedov[1], R. Z. Sabirov[1]

1) A. S. Sadykov Institute of Bioorganic Chemistry of Academy of Sciences of the Republic of Uzbekistan, 100125, Tashkent, Uzbekistan, Mirzo Ulugbek str., 83
2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: sarvinoz711@inbox.ru

Among natural compounds, terpenes and terpenoids are one of the most common groups of substances that have a greate structural diversity and a very wide range of biological activity. Thus, galbanoic acid was shown to have an anticoagulant activity, to inhibit acetylcholinesterase and P-glycoprotein, and to suppresse the grows of cancer cells. Biological effects of the karatavic acid remain poorly investigated at present.

Here, we studied the dose-dependent effects of the two plant terpenoids, karatavic and galbanic acids, on the regulation of thymocyte cell volume under hypoosmotic stress.

In control isotonic medium (normal Ringer′s solution), the thymocyte volume remained at a constant level for app. 20 minutes. When placed in the hypoosmotic environment, the thymocytes first swelled rapidly and then restored their volume to a level close to the initial level within 20–30 minutes. When the cells were incubated for 15 minutes in a hypoosmotic environment, the regulatory volume decrease (RVD) averaged at 79.0 ± 3.2 % (n = 19). We recorded the volume regulation curves upon addition of the karatavic acid into the incubation medium at concentrations of 1–150 μM. At small doses in the range of 1–10 μM, a small but statistically significant improvement in the cells ability to restore their volume could be observed. That is, the drug at a low dose is not an inhibitor, but an activator of the thymocyte mechanism of regulation of the cell volume. We observed this phenomenon for the first time and believe that it deserves close attention. A further increase in the drug concentration led to a gradual suppression of the regulation of the thymocyte volume. This portion of the dose-dependence curve was well described by the Hill equation with a half-maximal inhibition (IC_{50}) at 33.1 ± 1.6 μM and Hill coefficient of 2.6 ± 0.3.

In our further experiments, we investigated the regulation of thymocyte volume when introducing galbanic acid at concentrations of 10–100 μM. Over the entire range of concentrations studied, we observed a smooth dose-dependent suppression of the ability of thymocytes to regulate their volume under hypoosmotic stress conditions. No activation of RVD process was observed with this drug. The dose response curve was well described by Hill equation with a half-maximal inhibition (IC_{50}) at 20.6 ± 0.7 μM and Hill coefficient of 2.7 ± 0.2.

In both cases, the Hill coefficient for terpenoids was close to 3, which on the one hand indicates a positive cooperativity of the inhibition process, and on the other hand may indicate that RVD inhibition requires binding of several molecules to one of the three principal components of the cell volume regulation machinery of thymocytes: the calcium entry. Ca^{2+}-activated potassium conductance and volume-regulated anion conductance. We shall elucidate this mechanism in our further studies using electrophysiological techniques.

TOTAL LIPIDS OF C*ynara scolymus* L. LEAVES

T. A. Mirrakhimova[1], L .G. Mejlumyan[2], G. M. Ismoilova[1]

1) The Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan,
e-mail: Mtanzila_1986@mail.ru, +998946158624
2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan

Lipids perform the important functions in live organisms and their cells, and involved in various metabolic processes. They are structural and functional part of cells membranes, participate in energy exchange, etc. In this connection, the content various lipids, their structures in the plant and an extract of this plant have the important therapeutic value, and should be investigated.

The purpose of the present research was studying of the total lipids of artichoke *Cynara scolymus* L. leaves, grown up in Uzbekistan.

Methods. Extragent – chloroform–methanol mix (2:1, v/v), leaves of an artichoke, washing of an extract for removal nonlipid components was spent 0.5% by water solution $CaCl_2$.

Results. For total lipids extraction 15.548 g of the crushed air-dried raw materials was used. The extraction spent triple (200 mL, 150 mL, 60 mL), then the extract released from nonlipid components. Extract was transferred to preliminary weighed dry flask after washing. Flask contents evaporated on the rotor evaporator to dryness dry and weighed. The rest of an extract of the total lipids was 0.8496. In a percentage dryness the yield of total lipids was 5.46%. Loss of weight of raw material at drying was 8.87%. Total lipids were divided with a column chromatography on neutral lipids, with chloroform, glycolipids – with acetone and phospholipids with methanol. The received fractions dried up on the rotor evaporator to dryness and weighed (Table 1).

TABLE 1. **Structure of the Total Lipids of Leaves of *Cynara scolymus* L.**

№	Groups of lipids	From a lump lipids, g	From a lump lipids, %	From weight of raw materials, %
1	Neutral lipids	0.0764	56.6	3.09
2	Glycolipides	0.0496	36.8	2.01
3	Phospholipids	0.0089	6.6	0.36
4	Total sum	0.1349	100	5.46

Conclusions. The total sum of lipids was obtained with yield of 5.46%. Also it was established that the total lipids are presented by neutral lipids and glycolipids.

VALUATION OF ANTIHYPOXIC ACTIVITY OF PROANTHOCYANIDINS FROM *Polygonum coriarium*

D. A. Narbutaeva, R. Kh. Shakhidoatov, V. N. Syrov, Z. A. Khushbaktova

Acad. S.Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

The antihypoxic activity of proanthocyanidincatacin isolated from *Polygonum coriarium* Craig.evaluated. The study of antihypoxic activity of catacin carried out in hypoxic, normobaric, hypobaric and tissue hypoxia conditions in mice (weight 20–22 g). Preliminary introduction of the catacin preparation and the reference preparation Mildronate from JSC «Grindeks» (Latvia) for 60 min to mice at a dose of 100 mg/kg *per os* prior to their placement in the chamber (hypoxic, normobaric hypoxia) promoted 80% increase of survival of the experimental animals. With increasing the dose of test substances to 150 mg/kg their antihypoxic effect increased and was 84% and 82%, accordingly. In tissue hypoxia caused by sodium nitroprusside (at a dose of 20 mg/kg), catacin and mildronate also increased the life expectancy of animals by 86% and 80%.

The obtained data were a base for conducting a study of catacinin experimental pulmonary edema, which was reproduced by a single intraperitoneal injection of 1.5% thiourea, since in this pathology an important link in pathogenesis require urgent pharmacotherapy is increased hypoxia and activation of lipid peroxidation. Catacinwas introduced in 2 hours after hypoxia and during further 3 days (100 mg/kg). In the control group 30% animals died, in the groups receiving catacin and mildronate all animals remained alive. The severity of pulmonary edema in rats treated with catacin and mildronate was 10.6 and 12.8%, in control – 35%. It was noted, that in pathology catacin promoted an increase in the serum content of PVK, and a decrease in the level of MK (by 31.5 and 27.5%), while under the action of mildronate these changes were 30.6 and 18.3%. In control animals the content of PVK decreased by 29.3, and the level of MK increased by 46.4%. The revealed changes in the content of PVK and MC resulted in an increase in the value of ORP MK / PVK by 7.9 and 3.4 mV, accordingly.

It is obvious that during hypoxia the rat mitochondria under the influence of catacin continue to function normally without increasing its activity and absorbing oxygen, but by preserving the functional state with reducing the sensitivity threshold of cytochrome oxidase. Due to the above, breath remains aerobic with significant reduction of the partial pressure of oxygen, and the mechanisms of mitochondrial membranesdamagenot activated.

SYNTHES OF GOSSYPOL SHIFF'S DERIVATIVES AND DEVELOPMENT OF METHOD FOR FAST DETERMINATION OF THE YIELD OF REACTION BY LC-MS

J. B. Tursunkulov[1], A. A. Mamadrahimov[2], S. A. Maulyanov[1], B. T. Ibragimov[2]

1) Uzbekistan National University
2) Institute of Bioorganic Chemistry

Nowadays, many works have been done to modify gossypol in order to obtain substances with an activity greater than that of the original gossypol. This confirmed by studies of gossypol, which made it possible to obtain effective medicines on its basis.

Gossypol has a high virucidal activity against a number of viruses. In this work, the reaction of gossypol with isoniazid has been studied which possess antiviral, antituberculosis activity for the production of drugs based on gossypol. It is known that isoniazid is used as a medicine for the treatment of all types of tuberculosis.

Based on the above, a new Schiff base of gossypol was synthesized using isoniazid as amino compound.

The reactions were carried out in homogeneous conditions by mixing equimolar aceton solutions of gossypol and isoniazid (1:2) at 70°C for 7 hours. The precipitate was filtered and re-crystallized from a mixture of benzene and acetone (1:1).

To identify the obtained Schiff base of gossypol with isoniazid, chromatographic analysis was carried out using a sensitive and selective high performance liquid chromatography - mass spectrometry (HPLC-MS) method. Both liquid chromatography and MS conditions were optimized. The developed method was successfully used for the determination of Shiff 's bases of gossypol.

The MS was operated in negative mode with data collected from 1–10 min. Initially, full scan Q1 mass spectra was acquired over the range of *m/z* 50–1500 then SIM mode was applied for qualitative analyses of Shiff's base of gossypol. The SIM mode was more sensitive in comparison with full scan mode in selection of ions. In our research, the SIM mode also successfully applied in defining parent ion of Shiff's base of gossypol with isoniazid 755 [M – H] from other concomitant ions having the same *m/z* present.

The developed method proved the suitability of liquid chromatography-tandem mass spectrometry for the confirmation of the presence and quantity content of Shiff′s base in reaction mixture.

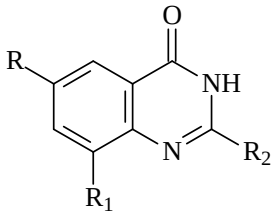
FUNGICIDAL AND BACTERICIDAL ACTIVITY OF QUINAZOLINE AND BENZIMIDAZOLE DERIVATIVES

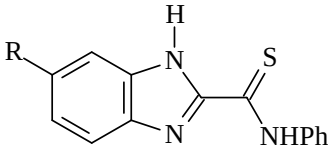
R. P. Zakirova[1], U. M. Yakubov[1], N. B. Pirnazarova[2], B. Zh. Elmuradov[1]

1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz
2) Qarshi State University, Qarshi, Uzbekistan

The use of plant protection products is an integral element of modern technology, which ensures the preservation of the harvest from phytopathogens. At prolonged use of fungicides, especially with a single mechanism of action, resistant forms of disease arise that require the use of new drugs. To search for biologically active substances, it is necessary to establish a connection between the structure of synthesized molecules and their biological effect. Therefore, studies of the connection "structure-activity" of heterocyclic compounds are certainly relevant.

The aim of this work is the synthesis of thioamides of the benzimidazoline and quinazoline series of compounds **1–5** and the establishment of their antimicrobial activity against fungus *Fusarium oxisporum* Schrf. *Vasinfectum Bilai* and bacteria *Xanthomonas malvacearum*:





1, R= R_1=R_2= CH_3; **2**, R= Cl; **3**, R= H; **4**, R= NO_2
5, R=R_1=H; R_2= C(S)NHPh

Biotests to determine the activity of compounds were carried out using the paper disc method. Phytopathogens are cultivated on a medium of potato broth with the addition of 20 g of sucrose and 20 g of agar-agar per 1 L. The spore material was applied to the surface of the culture medium with a glass spatula, after which paper discs wetted in 0.5% solutions of the test compounds were placed on the surface. Petri dishes were placed in a thermostat and cultivated at a temperature of 26–27°C. After 2–5 days, measurements were made of the zone of growth retardation of microorganisms. Studies have shown that the compounds showed no fungicidal activity with respect to the culture of the fungus *Fusarium oxisporum*.

Biotests on the bactericidal activity type on the *Xanthomonas malvacearum* culture showed that the compounds **2**, **3** and **4** have weak activity. The maximal zone of absence of growth was for compound 2–5 mm, slightly less this indicator was for compound **3** and **5** – 3 mm. In the standard using Bronopol, the zone of lack of growth was – 17 mm.

Thus, it was found that the synthesized compounds **2**, **3**, **5** show a weak antibacterial effect with respect to *Xanthomonas malvacearum*.

SYNTHESIS AND BIOLOGICAL ACTIVITIES OF 22,25-*O*-DIACETATE-20-HYDROXYECDYSONE

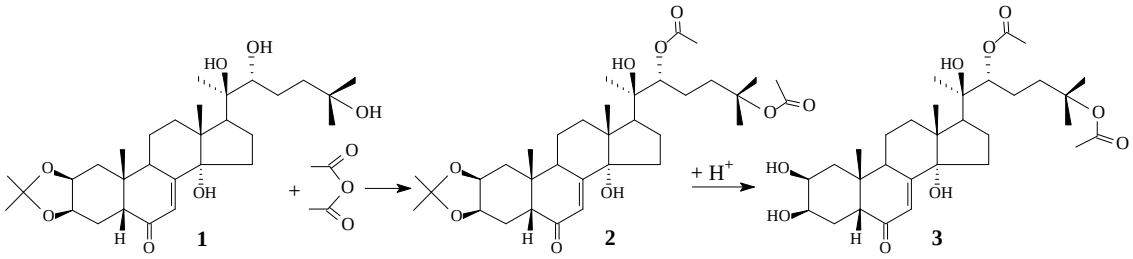
I. D. Bobaev[1], A. N. Blinnikov[2], I. V. Zavarzin[2], Kh. M. Bobakulov[1], N. Sh. Ramazonov[1], N. Kh. Yuldasheva[1], Z. A. Khushbactova[1], V. N. Syrov[1]

1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: bobaev-isom@mail.ru
2) N. D. Zelinsky Institute of Organic Chemistry RAS, Moscow

Nowadays, the promising direction of using natural compounds is the modification of the structure of secondary plant metabolites, leading to previously unknown derivatives. The purpose of such transformations is to enhance the biological effect of natural compounds and to search for new types of activity. One of the promising directions for the transformation of ecdysteroids is the use of the acylation reaction.

We have obtained 2,3-*O*-monoacetonide-20-hydroxyecdysone, 20,22-*O*-monoacetonide-20-hydroxyecdysone and 2,3,20,22-*O*-diacetonide-20-hydroxyecdysone by a known method.

Based on the interaction of 2,3-*O*-monoacetonide-20-hydroxyecdysone (**1**) with acetic anhydride, the derivatives 2,3-*O*-monoacetonide-22,25-*O*-diacetate-20-hydroxyecdysone (**2**) and 22,25-di-*O*-acetate-20-hydroxyecdysone (**3**).



Their structure was established by the analysis of the spectra of ^{1}H, ^{13}C NMR and 2D experiments. Studies of the biological activity of 22,25-di-*O*-acetate-20-hydroxyecdysone (**3**) showed their hypoglycemic effect (Table 1).

TABLE 1. **Hypoglycemic Activity of 20-Hydroxyecdysone and 22,25-di-*O*-Acetate-20-hydroxyecdysone in Experiments on Intact Rats (M ± m, n = 6)**

Group	Blood glucose level, mM/l		Effect in %
	Initial	After 3 hours	
Control	3.73±0.16	3.63± 0.14	↓2.7
20-Hydroxyecdysone	3.85±0.12	3.22±0.18*	↓16.4
22,25-di-O-acetate-20-hydroxyecdysone	4.16±0.15	2.90±0.26*	↓30.3

*Authentically to the original level ($p < 0.05$).

It has been established that the introduction of the acyl group at C-22 and C-25 into the 20-hydroxyecdysone molecule leads to an increase in the sugar-reducing effect.

EFFECT OF POLYSACCHARIDS ON THE SYSTEM OF HEMOSTASIS IN PATHOLOGIES OF THE BLOOD COAGULATION SYSTEM

L. I. Shevchenko[1], Kh. Ya. Karimov[1], R. K. Rakhmanberdieva[2], O. B. Shadibekova[1], T. R. Alimov[1]

1) Scientific Research Institute of Hematology and Blood Transfusion MH RUz, Tashkent, altirar@rambler.ru
2) Acad. S.Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

Nowadays, despite the long progress in pharmacology and hematology, the problem of blood coagulation system diseases remains one of the important tasks of medicine. Many pathological conditions, including poisoning, lead to violations of the hemostatic system, often ending with a fatal outcome. The development of the means that can prevent the development of these conditions is of great importance. In accordance with this, a water-soluble polysaccharide (WSP) of *Cardariarepens* is of interest, which affects haemostasis in disorders of blood coagulation [3, 10]. WSP is an amorphous powder consisting of rhamnose, arabinose, xylose, glucose, galactose in a ratio of 1.5: 13.3: 1.0: 1.0: 21.0, respectively, and galacturonic and glucuronic acids.

The purposeof this work was to characterize the action of water-soluble polysaccharide (WSP) of *Cardariarepens*on the hemostasis system inheliotrine intoxication.

The experimentswere performed on 30 rats weighing 180–220 g.The experimental model of acute intoxication with heliotrine(HI)was reproduced by single injection to rats subcutaneously asublethal dose of heliotrine, prepared at the rate of 40 mg per 100 g of body weight.Changes in hemostatic parameters were studied: activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), plasma fibrinogen (PF), XIIa-dependent fibrinolysis, platelet adhesion, platelet aggregation (PA) with adenosine diphosphate (ADP).

Coagulation hemostasis parameters were studied on the «Humaclot Junior»coagulometer (HUMAN, Germany), and platelet hemostasis on an«Biola» aggregation analyzer (Biola, Russia) using the «Renam» test systems (Russia). In animals after the introduction of WSP with HI, an increase in APTT was detected, which indicates the anticoagulant properties of the polysaccharide. The time of XIIa-dependent fibrinolysis decreased by 1.5 times. The content of PF increased by 2.3 times.

Thus, the administration of WSP resulted in a positive effect on hemostasis in heliotrine intoxication, a correction of XIIa-dependent fibrinolysis with more active recovery of platelet hemostasis parameters such as adhesion and platelet aggregation, which in turn is likely to contribute to the prevention of thrombosis development and microthrombosis in severe pathological conditions, accompanied by damage of liver function.

THE VOLATILES OF THE SEEDS OF JAPANESE PADOGA TREE (*Sophora japonica* L.)

V. N. Khusinov[1], Kh. M. Bobakulov[2], V. N. Abdullabekova[1]

1) Tashkent Pharmaceutical Institute; st.Oybek, 45, Tashkent, 100015, Uzbekistan
2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

Japanese padoga L. is a tree with the height from 15 to 20–30 m from the family of *Fabaceae*. Japanese padoga is very wide-spread in Uzbekistan as a decorative and honey hood plant.

Materilas and method of investigation the fruits of *Japanese padoga* grow in Tashkent were takenas the object. The seeds were unpeeled. After that, the seeds were dried and crushed during a day. From 10.0 g of crushed seeds were obtained hexane and benzene extracts by using ultrasound extraction. Analysis of obtaining extractions was carried outon gas chromatography mass-spectrometry Agilent 7890A GC/5975C inert MSD. Identification of compounds was done by comparing mass-specters with the data base of Wiley and National Institute of Standards and Technology (NIST) libraries (W8N05ST.L and NIST08.L)

The compounds of hexane extraction were determined by using chromate-mass-spectrum: (name, contents, (%) (index retention)): octane 4.47 (800), ethylcyclohexane, 0.71 (831), α-pinene, 26.97 (931), camphene, 0.99 (968), β-pinene, 7.22 (974), 3-karen, 5.43 (1011), *p*-cymene, 0.59 (1021), cymene, 2.04 (1028), eucalyptol, 17.23 (1035), α-vinyl-α-valerolactone, 3.85 (1049), α-thujone, 1.78 (1105), β-thujone, 1.36 (1116), α-isophoron, 0.54 (1099), camphor, 4.50 (1143).

In benzene extraction were identified: α-pinene, 12.93 (931), eucalyptol, 9.45 (1021), γ-terpinen, 2.68 (1022), *n*-undecane, 2.81 (1100), camphor, 2.49 (1143), dodecane, 4.00 (1200), tetradecane, 2.94 (1400), di-*iso*-butyl-phtalate, 29.66 (1889), *n*-nonadecane, 2.63 (1900).

For the first time the volatiles of seeds of Japanese padoga tree growing in Uzbekistanwere studied in this work. Analysis of conducting investigations indicated that the compounds which found out in extractions had terpenoid character.

ESSENTIAL OIL AND FATTY ACID COMPOSITIONS OF *Ferula prangifolia* KOROVIN FRUITS GROWING IN UZBEKISTAN

Kh. M. Bobakulov[1], D. R. Siddikov[1], G. Ozek[2], T. Ozek[2,3], K. H. C. Baser[4], D. T. Asilbekova[1], Sh. Sh. Sagdullaev[1]

1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz
2) Anadolu University, Department of Pharmacognosy, Faculty of Pharmacy, 26470, Eskisehir, Turkey
3) Medicinal Plants, Drugs and Scientific Research Center (AUBIBAM), Anadolu University, 26470, Eskisehir, Turkey
4) Near East University, Faculty of Pharmacy, Department of Pharmacognosy, Lefkosia (Nicosia) N. Cyprus

The genus of *Ferula* is represented in the flora of Uzbekistan by 45 species, eight of which are endemic species. The fruits of endemic *Ferula prangifolia* Korovin species were collected in 2013 at the stage of ripening in Chakak area of Tashkent region (Uzbekistan). The fruits were hydrodistilled to obtain essential oil in 0.7% yield and extracted by Folch method to obtain fatty oil. Chemical compositions of the oils were analyzed by GC-FID and GC-MS techniques. Eighty one individual compounds were characterized representing 96.96% of the total essential oil. The major constituents were sesquiterpene hydrocarbons and their oxygenated derivatives with α-cadinol, δ-cadinene, τ-muurolol, spathulenol, β-elemene, bicyclogermacrene, α-muurolene and γ-cadinene as the main components.

The fatty oil (yield 12.9% on dry weight) extracted with chloroform–methanol (2:1, v/v) contained unsaponifiable matters (14.8 mg/g). The major compounds of the fruit fatty oil were triglycerides (95%). The fatty acid composition of the fatty oil studied was found as follow: 12:0–0.1, 14:0–0.6, 15:0–0.2, 16:0–7.9, 17:0-tr., 18:0–2.9, 20:0– 0.7, 16:1ω7–0.7, 18:2ω6–47.1, sum of 18:1ω12 and 18:1ω9–39.3 and 20:1ω11–0.5. Hence, unsaturated fatty acids (87.6%) predominate in fatty oils. The present work is the first study on *F. prangifolia* fruit essential oil and fatty acid compositions.

HEPATOPROTECTIVE ACTIVITY OF AN IRIDOID FROM *Phlomis severtzovii* IN THE EXPERIMENT

A. A. Azamatov, A. N. Nabiev, I. D. Bobaev

Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: akademic1986@list.ru

It was established that some iridoids possess hepatoprotective properties [1].

We have isolated a known iridoid 6-β-hydroxyipolmide [2] from a butanol extract of the aerial part of *Phlomis severtzovii* (*Lamiaceae*) collected in vegetation period.

It is known that the ethanol detoxification is occurring due to the activity of the enzymatic system of hepatocytes. Taking into consideration this fact, we investigated the effects of the iridoid on the ethanol detoxification.

The investigated substances were introduced at the doses of 10–25 mg/kg *per os* in 30 minutes prior the ethanol introduction at a subtoxic dose of 4.2 mg/kg i.p. Only ethanol was introduced to the control group, and the duration of sleeping in this group was taken as 100%. Detoxification degree was determined by the duration of mice sleeping after ethanol introduction. In our experiments the commercial drug Succinasol at a dose of 100 mg/kg decreased the sleeping for 52%; the iridoid – for 49% at a dose of 25 mg/kg, and for 33% at a dose of 10 mg/kg. The results demonstrated that 6-β-hydroxyipolmide iridoid is equal to Succinasol in antitoxic action. Succinasol contains a succinic acid and participates in biochemical processes activated the detoxic properties of the liver. It was established earlier, that iridoids destroy free radicals formation, control cholesterol, increase the energy and immunity, decrease inflammation, and support the healthy activity of heart and brain [3].

Therefore, the iridoid of *Phlomis severtzovii* possesses antialcohol activity equal to those of Succinasol preparation.

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EFFECTS OF SOME ALKALOIDS ISLATED FROM THE CENTRAL ASIAN PLANTS ON ANIMAL MODEL OF ACUTE ALCOHOL INTOXICATION

A. A. Azamatov, F. M. Tursunkhodjaeva, J. Rejepov

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: akademic1986@list.ru

Aim of investigation was the study of effects of some alkaloids isolated from the Central Asian plants on animal model of acute alcohol intoxication in order to find a promising antidote.

The investigated substances were injected to rats and mice *s.c.* at the doses of 4.5 mg/kg and 6.0 mg/kg accordingly in 30 minutes before *i.p.* injection of 25% ethanol solution. The effects of the investigated substances on the duration of sleep caused by ethanol were observed. Each experiment was repeated six times. Caffeine and cytisine alkaloids have been used as a standard.

Acute alcohol intoxication (AAI) causes more 60% of lethal outcomes connected to different intoxications (1). Lethal single dose of ethanol is 4–12 g per kg of body weight. AAI therapy measures include total detoxication, recovery of pulmonary ventilation, and correction of central nervous system and haemodynamic disorders and acidosis.

Caffeine has been used as a common standard. This alkaloid is included to the conventional scheme of AAI treatment. Cytisine stimulates *N*-cholinoreceptors of vegetative ganglia, adrenal glands and sino-carotide zone.

In our experiments we investigated effects of lappaconitine, *N*-desacetyllappaconitine (*N*-DAL) and four derivatives of cytisine on AAI model. Lappaconitine, *N*-DAL and cytisine drug substances were manufactured in the Institute of the Chemistry of Plant Substances. Three cytisine derivatives have been obtained by chemical modification of cytosine by a group of Dr. Valentina Vinogradova, Laboratory of Alkaloids Chemistry, ICPS (2). It was found that amongst the investigated alkaloids *N*-methylcytisine exceeded both caffeine and cytisine for 1.2 and 2.85 times, accordingly. In general, the investigated substances were arranged by their activity as follow: *N*-methylcytisine

Thus, our investigation has demonstrated that *N*-methylcytisine is a promising agent in treatment of acute alcohol intoxication.

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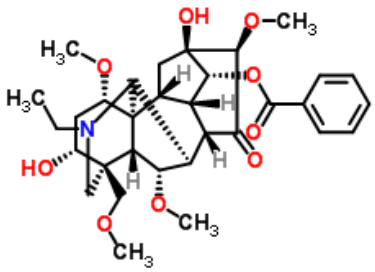
ON PHARMACOLOGY OF PYROACONITINE

F. N. Dzakhangirov, M. N. Sultankhodjaev, F. M. Tursunkhodjaeva, V. F. Tukhtasheva, A. A. Azamatov

Acad. S.Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: akademic1986@list.ru

Pyroaconitin is a product of pyrolysis of the neurotoxic alkaloid aconitine. Cash and Dunstan (1901) described it for a first time as a compound similar to aconitine, but less toxic. In the Alkaloids Chemistry Laboratory an individual pyroaconitine was isolated and chemically characterized (M.Sultankhodjaev).



Being injected intravenously to white mice pyroaconitine causes adynamia, exophthalm, short-term respiratory acceleration of followed by respiratory depression, decreased muscle tone, and death in asphyxia. Symptoms of poisoning characteristic to aconitine are absent. LD_{50} is 2.5 mg/kg (LD_{50} of aconitine is 0.12 mg/kg). In anesthetized rats (sodium ethanamine 40 mg/kg i.p.) pyroaconitine at the doses of 0.5–1.5 mg/kg (i.v.) does not significantly affects on the heart rate and RR intervals, prolongs PQ, QRS intervals, widens the P tooth, increases the amplitude and rounds

R tooth. The drug in doses of 0.05–1 mg/kg (i.v.) has a pronounced antiarrhythmic, anti-fibrillar and antitoxic effect in cardiac arrhythmias caused by aconitine. ED_{50} of the antiarrhythmic action is 0.1 mg/kg. Preliminary intraperitoneal administration to mice of pyroaconitine prevents the development of symptoms of neurointoxication, heart fibrillation and death of animals poisoned by intravenous injection of a lethal dose of aconitine (0.2 mg/kg). ED_{50} of antifibrillatory action is 0.5 mg/kg. (i.p.) Pyroaconitine in the concentration of 0.1-0.5% causes the anesthesia of rabbit eye for of 55–110 minutes. By activity and duration of action pyroaconitine surpasses cocaine, but concedes to the latter in the rate of anesthesia.

Thus, pyroaconitine has the pharmacological properties qualitatively different than aconitine.

STUDY OF GENERAL TOXICITY OF FERULEN

J. Rejepov, F. N. Dzhakhangirov, V. F. Tukhtasheva, A. A. Azamatov

Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: akademic1986@list.ru

Ferulen is a natural mixture of esters of sesquiterpene alcohols obtained from the root of Ferula tenuisecta Korov.

Systemic toxicity of the drug was evaluated on white mice and rats in intragastrinal application.

The results of the conducted researches established that Ferulen belongs to the category of low-toxic substances by its parameters of acute toxicity in the oral application. The species and sex sensitivity to the drug is not expressed. It doesn't cumulate in the body of experimental animals. Prolonged use of the drug for 4 months has well tolerated by experimental rats without hematological, biochemical, weight gain, histomorphology of internal bodies and brain side effects. It was observed a weight loss of androgen-dependent organs related to the specific activity of the drug.

STUDY OF THE SPECIFIC TOXICITY OF FERULEN

J. Rejepov, F. N. Dzhakhangirov, V. F. Tukhtasheva, A. A. Azamatov

Acad. S.Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: akademic1986@list.ru

Evaluation of specific toxicity of Ferulen was carried out according to methodical instructions on evaluation of allergenic properties (1988), immune system (1984, 2000) and mutagenicity (1991).

In the test of anaphylaxis and active cutaneous anaphylaxis on guinea pigs it was established that the drug has no allergenic effects. In the experiments on the CBA mice ferulen in doses of 10-25-50 mg/kg stimulated the reaction of delayed-type hypersensitivity and increased the phagocytic activity of macrophages on a dose-dependent manner. The assessment of mutagenic activity of the drug using chromosomal aberrations in bone marrow cells and the dominant lethal mutations methods shown the absence of mutagenic effects.

ANATOMICAL STRUCTURE OF VEGETATIVE ORGANS OF *Crambe kotschyana* BOISS. (FAM. *Brassicaceae*)

G. M. Duschanova[1], I. I. Okhunov[2], U. T. Karimov[2], S. F. Aripova[2]

1) Institute of Genetic Pool of Plant and Animals, AS RUz,
2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: salima_aripova@mail.ru

C. kotschyana Boiss. is a perennial endemic forage plant, reaching 2.5 meters in height. Pharmacological studies conducted in the Department of Pharmacology and Toxicology of the ICPS AS RUz on the model of experimental thyreotoxicosis in rats studied and determined the antithyroid activity of the sum of alkaloids of this plant. This was a base for development a medicinal product for use in endocrinological practice in the treatment of patients with thyreotoxicosis. Anatomical structure of its vegetative organs, which is necessary for the development of the Pharmacopeial article on medicinal raw materials – the grass of *C. kotschyana* was investigated.

The method of anatomical study. Simultaneously with the morphological description, the aerial plant organs in ethanol (70%) were fixed for anatomical study. The epidermis was studied in the paradermal and transverse sections. Each tissue described by S.F. Zakharevich method. Transverse sections were made through the middle of the leaf, the flower stem, the pedicel and the base of the petiole and stem. Preparations prepared by hand were stained with methylene blue, safranin, followed by sealing in glycerine gelatin. Microphotographs are made with a computer microphotoset with a digital camera (Canon A123).

Thus, in *Crambe kotschyana* a sheet of dorsiventral type of structure, palisadic and spongy parenchyma is chlorophylliferous and in the cells there are idioblasts. The main vein and petiole leaf is parenchymal, in the margins and corners under the epidermis are located lamellar groups of cells of the collenchyma. Stem, flower spike and pedicel type of the structure. In the central cylinder there are numerous conducting beams - large and small. Conductive beams are closed, collateral, more sclerific. Large conductive bundles include 2-3 bundles (main vein, leaf petiole) and 7–8 bundles (stem), single bundles relatively small. Such a structure of beams is characteristic for a given genus and family.

GIBBERELLINE A3 FROM THE MICROSCOPIC FUNGI *Trichodesma harzianum*

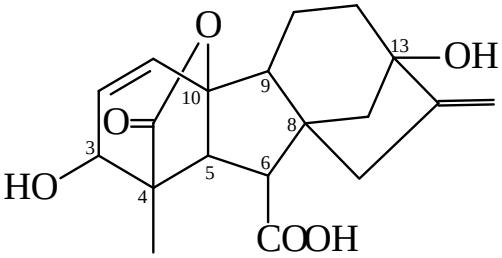
L. S. Kamalov, K. K. Turgunov, S. F. Aripova

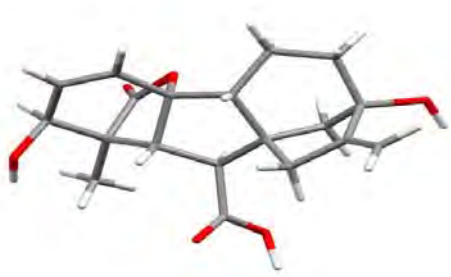
Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: salima_aripova@mail.ru

Microscopic fungus *Trichodesmaharzianum* is a mushroom-saprophyte called "green mold", one of the most important in the soil. This fungus is an antagonist, one of the universal and effective agents of the biological regulation of wilt diseases and root rot of many cultures. A number of mechanisms make it possible to suppress the development of causative agents of seed, root and soil infections, as well as diseases of fruits and leaves. The fungus easily penetrates the sclerotia of the fungus-phytopathogen and slowly dissolves its cells from the inside. It is used as a fungicide.

We first isolated from the ethyl acetate fraction of the biomass of the fungus *T. harzianum* crystalline compound 1 with m.p. 158–160°C. To establish structure 1, a single crystal was obtained, which was transferred to the X-ray diffraction pattern.

The results of RSA showed that the isolated substance 1 is a known compound - gibberellic acid (gibberellin A3). The configurations of the chiral centers in the molecule have the values: 3*S*, 4*S*, 5*R*, 6*S*, 8*S*, 9*R*, 10*R* and 13*S*. In the literature (bank CCDC) there are data on the crystal structure of this molecule [1].





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Gibberellin A3 isolated from the fungus *T. harzianum*for the first time.

PROCESS OF DRYING OF WATER EXTRACT FROM *Bidens tripartite*

T. A. Hajibaev, R. M. Khalilov

Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: hajibaev84@mail.ru

Immunostimulating drug "Immunocor" was created by the scientists from the Institute of the Chemistry of Plant Substances of the Academy of Sciences Republic of Uzbekistan and Immunology Scientific Center of the Ministry of Health of Republic of Uzbekistan on the basis of polysaccharides of tripartite tickseed *Bidens tripartite* L. (*Asteraceae*).

On the purpose of developing the technology of obtaining the Immunocor substance, various methods of drying the water extract from the tickseed grass have been studied.

The extracts were dried in the dryers "ShCB-45K" and "IKS-2M", were obtained in the form of a solid mass. The dried extract was ground in a mill, the obtained dry extracts were hygroscopic.

When using the spray dryer "Anhydro-2", an extract was obtained in the form of powder substance.

To study the effect of drying regimes on the quality of the obtained product, the following parameters were investigated:

concentration of the solution (10, 15, 20, 25, 30%);

supplying rate of the solution (2, 4, 6 L/h);

temperature of the drying agent at the inlet (140, 150, 160, 170, 180, 190°C)

outlet (70, 75, 80, 85, 90, 95, 100, 110°C) into the dryer;

Supplying pressure of the solution to the drying chamber (0.05; 0.1; 0.15; 0.2 MPa).

As a result, it was determined that the optimal solution is a concentration of 10–15%.

The best speed of the solution was a rate of 4 L/h. At a speed of 2 L/h, the heat of the drying agent was used ineffectively, and at the rate of 6 L/h the solution partially adhered to the walls of the dryer.

The optimum temperature of the drying agent at the inlet is chosen: 180 ± 10°C. At lower temperatures, the obtained powder was wet, and at 200°C or higher, the carbohydrates of the extract were burnt, so that the color of the product became dark.

The temperature of the processed drying agent at the outlet was chosen to be 85 ± 5°C, at the temperature of 80°C and below, the powder turned out to be wet, and at 90°C and higher, the obtained product began to burn and acquire a brown color, and also adhere to the walls of the dryer.

The optimal pressure of the supplied solution was 0.15 MPa. At the pressure of 0.05 and 0.1 MPa, the solution was poorly sprayed inside the dryer, and the resulting product was wet. At the pressure of 0.2 MPa, the solution adhered to the upper wall of the dryer.

DETERMINATION OF CHIMGANIN IN THE SUBSTANCE OF ESTERS FROM THE AERIAL PARTS OF *Ferula angrenii* BY HPLC METHOD

M. A. Mamatkhanova, R. M. Khalilov, A. U. Mamatkhanov

Acad. S.Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

The technology for obtained of substances of estrogens preparation on the based of the esters of terpenoid alcohols from the aerial parts of *Ferula angrenii* was developed. From the literature date is known, that the roots of *Ferula angrenii* contain esters such as chimgin, isochimgin, ferolin, chimganidin, chimganin. It is also known that chimganin show the most pronounced estrogenic activity. To this aim, we decided that the standardisation of substances of esters obtained from the aerial parts of *Ferula angrenii* should be conducted in reference to chimganin.

The determination of the presence of chimganin in the substance was carried by the high performance liquid chromatography (HPLC) method. The standard sample of chimganin with appropriate purity was used, the instrument calibrated was conducted according to the standard.

As a result of the investigation, the presence of chimganin in the substance obtained from the aerial parts of *Ferula angrenii* was established, which indicates the presence of chimganin in aerial part of this plant.

COLLOIDAL-CHEMICAL CHARACTERISTICS OF THE PRODUCTS OF BIOSYNTHESIS OF *Bacillus subtilis* sp. BS-26 STRAIN

A. E. Kurbanbaeva[1], G. I. Dlumaniyazova[2], U. K. Akhmedov[1]

1) Institute of the General and Inorganic Chemistry, Academy Science Republic of Uzbekistan
2) Institute of Microbiology, Academy Science Republic of Uzbekistan

Nowadays, a great attention of researchers is attracted to surfactants of natural origin - biogenic surfactants (bio-surfactants) due to role that surfactants perform in life of the cell, their meaning in interaction of microorganisms with the environment. The practical meaning of microbial surfactants due to their ability significantly reduce the surface and interfacial tension of water solutions and emulsify and demulsify of various substances.

Although microbial surfactants are relatively new product of biotechnology they are widely used in the processes of cleaning soil and water from oil, in the oil producing, mining, chemical, pharmaceutical agricultural and food industries and other.

Action of microbial surfactants are associated with the processes of absorption, desorption and solublization of organic substances.

In this work, we selected strain of *Bacillus subtilis* sp. BS-26 that was characterized by the highest synthesis of surfactants and investigated their colloidal-chemical properties.

The ability to synthesize of bio-surfactants was assessed by the following indicators: surface tension (δ) of cell-free culture liquid, surfactants conditional concentration, which was determined for express quantitative assessment of bio-surfactants in the culture liquid.

Qualitative analysis and preparative isolation of lipids were carried out by the method of thin-layered chromatography (TLC) in the system for elution - chlorophorm: methanol: acetone: acetic acid (90:10:1:1)

Acidic-basic properties of water solutions bio-surfactants were regulated by the addition of ammonium carbonate and 0.1N hydrochloric acid. pH was measured by ionomer EV-74.

The dependence of the water solutions bio-surfactants from concentration was varied exponentially, and when concentration reached 0.04-0.05% the surface tension has minimum values (pH 5.2, δ 31.5), which indicated at the formation of saturated layer surfactants at the interphase boundary liquid–air.

The values of the critical micelle concentration were determined graphically. The critical micelle concentration and minimum surface tension (δ_{min}) depends on two factors: surfactants concentration and pH.

To explain the established dependencies we carried out potentiometric titration of water solutions surfactants containing a carboxyl group with a solution of sodium hydroxide. It was established that with a potentiometric titration of water solutions surfactants there is a jump in the region pH 7.1–9.3 with an equivalence point at the pH 8.3 that coincides with a jump in the dependence of critical micelle concentration from pH 7.2 of bio-surfactants.

TECHNOLOGY AND STANDARDIZATION OF CAPSULATED FORM OF IMMUNOMODULATING COMPLEX ON THE BASIS OF PLANT RAW MATERIAL

M. A. Akbaraliev[1], T. F. Ibragimov[2,3], M. G. Ismailova[1]

1) Tashkent Pharmaceutical Institute, 45-Oybek street, Tashkent, 100015, Uzbekistan,
fax: (99871) 256 45 04, e-mail: mirzokhid.akbaraliev@mail.ru
2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: itf-tim@mail.ru
3) FV - Nobel Pharmsanoat, 5A, Karasu buyi street, Tashkent, 100050, Uzbekistan,
fax: (99871) 265 91 99, e-mail: timur@nobel.uz

Nowadays, drugs based on medicinal plants attracted a great attention due to their purposeful action and low toxicity.

Previously, we have obtained a complex of plant-based immunomodulating agents based on standardized extracts from plant matter: birch (*Betula pendula*), Radiola (*Rhodiola rosea*) and Echinacea (*Echinacea purpurea*)

Extracts from birch ordinary have long been used in folk medicine for many ailments, as well as antiviral, antimicrobial and immunomodulating.

Rodiola rosea: the plant is traditionally used in folk medicine as a means to increase immunity, adaptive properties of the organism, enhance physical and mental activity, regulate metabolic processes, as anti-inflammatory, antipyretic and antiallergic agent.

Echinacea purpurea has a bacteriostatic, fungicidal, virosostatic and anti-inflammatory effect, suppresses the formation of hyaluronidase, enhances deicopoiesis, is a potent activator of macrophages, granulocytes and lymphocytes (especially T-lymphocytes), increasing the body's defenses, immunity and thus refers to plant stimulants or modulators of the immune system.

To improve the bioavailability and the process of encapsulation, we selected the auxiliary substances, namely microcrystalline cellulose, aerosil and calcium stearate. The selected technological formula made it possible to obtain a quality encapsulated form of the complex preparation in the process.

The obtained capsules were subjected to tests: appearance, identification, moisture content, mass uniformity, average weight (± 10%), disintegration time (not more than 30 min), dissolution (not less than 80%), quantitative content of flavonoids (± 10%) and microbiological purity.

As a result of our work, we obtained capsules of immunomodulating action based on a complex of plant substances that meet all the requirements of international pharmacopoeias.

STANDARTIZATION OF SUM OF IMMUNOMODULATING AGENTS BASED ON MEDICAL PLANT

M. A. Akbaraliev[1], T. F. Ibragimov[2,3], M. G. Ismailova[1]

1) Tashkent Pharmaceutical Institute, 45-Oybek street, Tashkent, 100015, Uzbekistan, fax: (99871) 256 45 04, e-mail: mirzokhid.akbaraliev@mail.ru
2) 2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, fax: (99871) 262 73 48, e-mail: itf-tim@mail.ru
3) FV - Nobel Pharmsanoat, 5A, Karasu buyi street, Tashkent, 100050, Uzbekistan, fax: (99871) 265 91 99, e-mail: timur@nobel.uz

Currently, the pharmaceutical industry focuses on natural compounds, as their biological effect is due to direct-aimed action, and should also be noted a synergistic effect, which in turn is caused by the influence of the total components.

Our research is aimed to obtaining of immunomodulating drug based on a complex of standardized dry extracts from plants: birch (*Betula pendula*), Rodiola (*Rhodiola rosea*) and Echinacea (*Echinacea purpurea*). The technology of extracting active components was designed in such way as to extract the main components of medicinal plants as much as possible.

The obtained dry extracts were successfully standardized in accordance with international pharmacopoeias.

Dry extract of birch: standardization was carried out on the sum of triterpenoids. The main parameters: content of active components (Assay), appearance, identification, loss on drying, ash content.

Dry extract of rodiola: standardization was carried out on the sum of flavonoids. The main parameters: content of active components (Assay), appearance, identification, loss on drying, ash content.

Dry extract of echinacea: standardization was carried out on caftaric acid and cichoric acid. The main parameters: the content of active components (Assay), appearance, identification, loss on drying, ash content.

Based on the abovementioned extracts, we obtained a complex of sums of extracts from the abovementioned plants, which meets all the requirements of international pharmacopoeias.

The resulting complex is the subject of further research.

ON MANUFACTUREOF PLATYPHYLLINE HYDROTARTRATE FROM THE AERIAL PARTS OF *Senecio platyphyllus*

R. A. Botirov, D. K. Mutalova, Z. Ch. Abraeva, V. I. Vinogradova, A. Z. Sadykov, Sh.Sh. Sagdullaev

Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: botiroovr@mail.ru

Platyphyllinehydrotartrate is well known medicinal preparation used over the world. It is used as an imported spasmolytic drug in the Republic of Uzbekistan. The needs of our republic are 5–6 kg of pharmacopeial substance per a year.

We developed the technology for manufacture of platyphyllinehydrotartrate from the aerial part of *Senecio platyphyllus* by water-alcohol extraction. We have used the aerial parts of *Senecio platyphyllus* grown in PRC and Republic of Georgia to obtain the stable samples of the drug. The platyphyllinehydrotartrate yield was 0.1–0.2% of air dried plant mass. Preliminary calculation shown, that the manufacture of platyphyllinehydrotartrate drug substance from the imported plant raw material is more profitable than the import of the ready pharmacopeial substance.

Now we are working under the preparation of the scientific-technical documents for the registration of the preparation in the Republic of Uzbekistan.

EXTRACTION OF *Chamomille officinalis* FLOWERS BY A LIQUID CARBON DIOXIDE IN SUPERCRITICAL CONDITIONS

A. I. Sanoev[1], O. T. Juraev[1], D. K. Mutalova[1], Haji Akber Aisa[2], Zhao Bo[2], M. A. Mamatkhanova[1], Sh. Sh. Sagdullaev[1]

1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz
2) Xingiang Technical Institute for Physics and Chemistry, AS PRC, Xingiang, P. R. China

Chamomille officinalis is one of the most popular plants used in medicine. The therapeutic effect of this plant is conditioned by a complex of biologically active substances contain if the flowers. Main of them is volatile and thermolabile substances.

We used the method for extraction in supercritical conditions by a liquid carbon dioxide in order to isolate the complex of biologically active substances from the raw material, extracts, sub-products etc. without heat treatment. 0.5 kg of crushed chamomile flowers (1–5 mm) were placed in the extraction device (supercritical extraction device Deyang Strong Tech, Ltd, China), and extracted by carbon dioxide at 18–20 MPa and 30°C for 90 minutes. The yield of biologically active substances was 0.35% of air dried mass of the raw material. The chemical composition of the extract is investigated.

CHROMATO-SPECTROPHOTOMETRIC METHOD OF QUANTITATIVE DETERMINATION OF ACONITINE IN THE TUBERS OF *Aconitum soongoricum*

D. K. Mutalova, O. T. Juraev, A. Z. Sadikov, Sh. Sh. Sagdullaev

Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

Alkaloid aconitine is widely used in medicine experimental practice to create various models of cardiac pathology in laboratory animals in the study and search of new drugs for the treatment of heart diseases [1]. The anti-inflammatory homeopathic drug Aflubin [2], based on aconitine (Medis, Germany) is also known. The main source for the industrial production of aconitine are some of the most widespread plant species of aconite, including the tubers of the *Aconitum soongoricum* which growing in some districts of Central Asia.

The quantitative determination of aconitine in raw materials was developed, which includes the obtaining the sum of alkaloids, separating on a chromatographic plate and determination of aconitine in the eluate by spectrophotometric method [3]. To avoid the accompanying substances, the amount of alkaloids was chromatographed on a fixed layer of silica gel TLC Silica gel 60 F 254 in the system of the solvents: toluol–diethylacetate–diethylamine (70:20:10). Elution was carried out with 95% ethyl alcohol, and eluent was dried. The dry residue is quantitatively dissolved in alcohol and measured on a spectrophotometer in cuvettes with a layer thickness of 10 mm at a wavelength of 230 ± 2 nm, using 95% ethyl alcohol as the reference solution. In parallel, the optical density of the alcohol solution of the standard aconitine sample is measured. The aconitine content in terms of absolutely dry matter in the feed is calculated by the formula:

$$x = \frac{D \cdot m_0 \cdot C_0 \cdot 100}{D_0 \cdot m(100 - W)}$$

where: D_0 – optical density of the solution of the standard aconitine sample; D – optical density of the test solution; m_0 – mass of a standard sample of aconitine, in grams; m – mass of raw materials, in grams; W – loss in mass when dried, in percent; C_0 – quantitative content of aconitine in a standard sample, in percent.

The developed method was tested on samples of raw materials with a rich content of aconitine. The relative error of the method was 0.9%.

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A NOVEL CYCLOARTANE GLYCOSIDE FROM *Astragalus mucidus*

T. Kh. Naubeev[1], A. A. Janibekov[2], K. Dzh. Kucherbaev[3]

1) Karakalpak State University named after Berdakh, Nukus, 700742, Ch. Abdirov st., 1, e-mail: timan05@mail.ru
2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz
3) South Kazakhstan State Pharmaceutical Academy, Laboratory of Medicinal Plants, 160019, Shimkent, Republic of Kazakhstan, e-mail: kkjamal@mail.ru

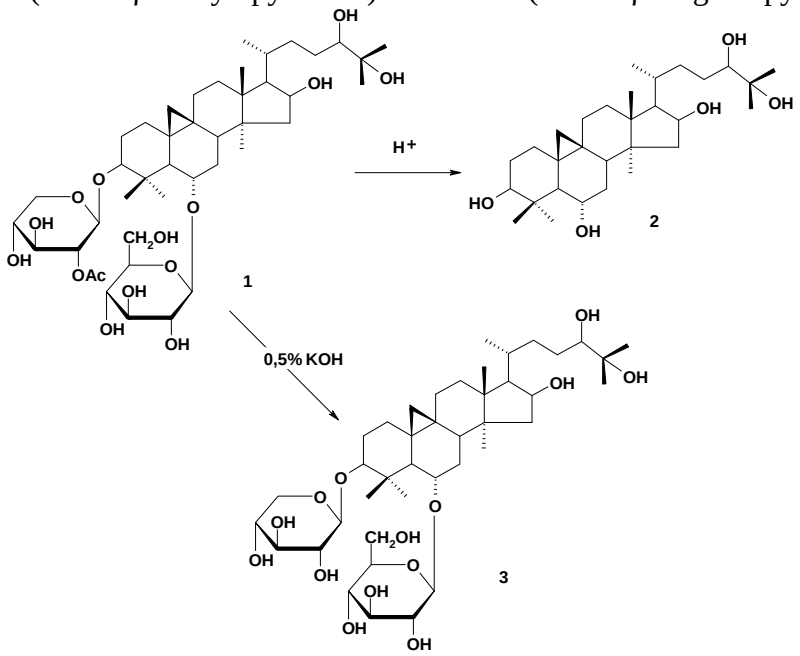
Continuing our chemical investigations of isoprenoids from *Astragalus* (*Leguminosae*) plants and study of their chemical transformation [1] we have isolated a novel triterpenoidal glycoside, cycloascidoside I (1), from the aerial parts of *Astragalus mucidus* Bunge.

The singlet signal observed in ^{1}H NMR spectra at δ 2.05 corresponding to the three proton units and the signals of carbon atoms observed in ^{13}C NMR spectra at δ 21.73 and 170.56 indicate of the presence of one acetyl group in molecule of the glycoside.

Alkaline hydrolysis of cycloascidoside I (**1**) gave a glycoside **3** identified as cycloascidoside A (**3**) [1].

Acidic hydrolysis of cycloascidoside I (**1**) gave a genin **2** identified as cycloasgenin C [2].

In ^{1}H NMR spectrum the anomeric protons of sugar part of the novel glycoside (**1**) resonate at δ 4.80 (H-1 of β-*D*-xylopyranose) and δ 4.96 (H-1 of β-*D*-glucopyranose).



Thus, the abovementioned experimental data allow to conclude that the isolated novel cycloartane glycoside, cycloascidoside I has the chemical structure 3-*O*-β-*D*-(2-OAc)-xylopyranoside, 6-*O*-β-*D*-glucopyranoside of 24*R*-cycloartane-3β,6α,16β,24,25-pentaol.

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CYCLOARTANE TRITERPENE GLYCOSIDE CYCLOMACROSIDE E FROM *Astragalus harpilobus*

A. A. Janibekov[1], N. Z. Mamadalieva[1], T. H. Naubeev[2]

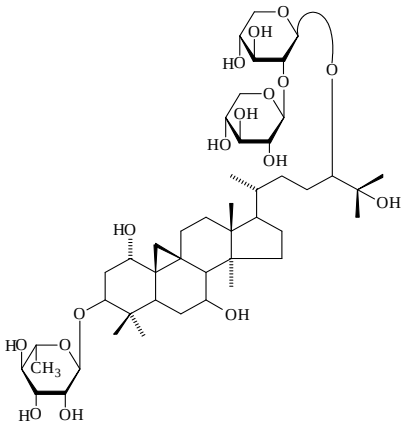
1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz
2) Berdakh Karakalpak State University

Astragalus L. is one of the largest genuses of the family *Leguminosae*.Genus *Astragalus* is widely distributed throughout the temperate and arid regions and has been estimated to contain 2000–3000 species.

We continued our ongoing phytochemical studies of the isoprenoidsfrom the plant species *Astragalus*, such as *Astragalus harpilobus*. This species has not been studied before. Aerial parts of *A. harpilobus* were collected from the Republic of Karakalpakstan on September 2013.

Dried aerial parts (0.7 kg) of *A. harpilobus* was extracted with methanol (5 × 4 L) at the room temperature. The extract was then concentrated under reduced pressure to give residues which constituted the crude extract. To crude extract added water and successively extracted with chloroform and then with *n*-butanol. After evaporation of the solvents in vacuo, 39.5 g of dried butanol extract was obtained. Further the butanol extract was applied on a silica gel column. The column was eluated using the solvent system chloroform–methanol–water (70:23:3) and isolated unknown triterpene. Study of the chemical structure of unknown triterpenewas investigated using 1 D and 2 D NMR and ^{13}C NMR.

On the basis of ^{1}H NMR, ^{13}C NMR, DEPT, COSY, HSQC and HMBC data the isolated compound was identified as known cycloartane glycosidecyclomacroside E, which has the structure 3-*O*-α-*L*-rhamnopyranoside,24-*O*-[(β-*D*-xylopyranosyl)(1→2)-β-*D*-xylopyranoside] -24*R*-cycloartan-1α,3β,7β,24,25-pentaol. This compound previously had been isolated from *Astragalus macropus* Bunge. We identified cyclomacroside E from A. *harpilobus* for the first time.



GC-QTOF-MS ANALYSIS OF ESSENTIAL OIL FROM FENNEL AND IT′S ANTIBACTERIAL ACTIVITY

Jumai Maitusong[1,2,3], Mahinur Bakri[1], Maitinuer Maiwulanjiang[1], H. A. Aisa[1*]

1) The Key Laboratory of Plant Resources and Chemistry in Arid Regions and Key Laboratory of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi, P. R. China
2) University of Chinese Academy of Sciences, Beijing, P. R. China
3) College of Xinjiang Uyghur Medicine, Hotan, P. R. China

Foeniculum vulgare Mill. Commonly known as fennel, belongs to the *Umbelliefare* family, widely used as vegetables, food spices and herbal folk medicine. According to the Chinese Pharmacopoeia, the dried ripe fruits of fennel could dispel coldand, relieving pain [1]. It is also used in Uyghur folk medicine for the treatment of cough, asthma, digestive disorders, diuresis, and improving acuity of vision [2].

Literature reports it have several effects such as gastrointestinal functional regulation, choleretic effecanti-mutagenic action, gonadotripic effect, liver protective effect, diuretic effect and treatment of infantile diarrheaeffect [3].

The fennel seeds used in this study were collected from Hotan Xinjiang. 80 g of herb sample was soaked in water for 12 h, beforeextracted by hydro-distillation method for 8 h using an essential oil extractor.The composition of essential oil was analysed by GC-QTOF MS (Agilent Technologies,USA) Retention indices were calculated by using the retention times of C_7–C_{40} *n*-alkanes that were injected at the same chromatographic conditions. The individual peaks were identified by comparing their mass spectra with the MS library (NIST 14), as well as comparing of the retention indices of elution peaks with literature data.

Moreover antibacterial activity of the essential oil was determined againstfive species of bacteria and two species of fungi. The density of inoculated bacteria was 10^6 cfu/mL, the fungal density was 10^5cfu/mL, each inoculum was inoculated with 100 ul. The essential oil samples were diluted with petroleum ether to 1:1 (v/v).

The percentage value of oil extraction yield was 3.2%, 101 components were detected and 53 of them were identified account for 99.6% of the total oil, out of which, anethole was the major compound with 55.44%, followed by estragole 22.04%.

The antibacterial test results showed that this oil was active against *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Bacillus subtilis*, *Candida albicans*, *Aspergillus niger*.

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CHEMICAL CONSTITUENTS OF *Limonium gmelinii*

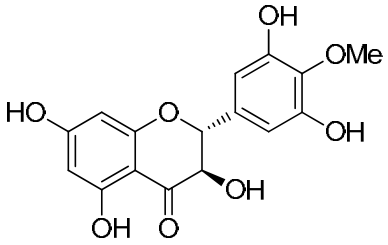
Amanguli Tuohongerbieke[2,3], Haji Akber Aisa[2], Gulnar Sabir[1*]

1) Xinjiang Inistitute of Chinese Material Medica and Ethnomedicine, 830002, Urimqi, P. R. China
2) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
3) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China

Plants of *Limonium* genus are exceedingly hardy, grow on saline soils, belong to halophytes, and can regulate the content of sodium and calcium salts in soils.

The most common species is *Limonium gmelinii*, the roots of which are used in folk medicine as an astringent and for acute gastro-intestinal diseases and diseases of the upper respiratory tracts [1].

In this study an attempt has been made to investigate the chemical constituents of ethyl acetate extraction of the roots of *Limonium gmelinii* growing in Xinjiang, China. The ethyl acetate extraction was chromatograghed on a silica gel column to divide into several fractions by gradient elution using chloroform/methanol. These fractions were further chromatograghed subsequently with silica gel, sephadex LH-20 and ODS column to obtain two compounds. Their structures were confirmed to be (2*R*,3*R*)-2-(3,5-dihydroxy-4-methoxyphenyl)-3,5,7-trihydroxychroman-4-one (**1**) [2], and 2-(3,5-dihydroxy-4-methoxyphenyl)-3,5,7-trihydroxychroman-4-one (**2**) by NMR and mass data.



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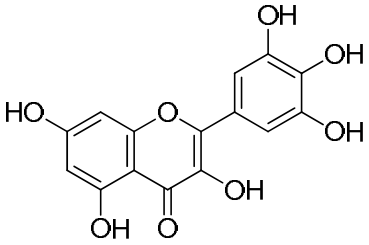

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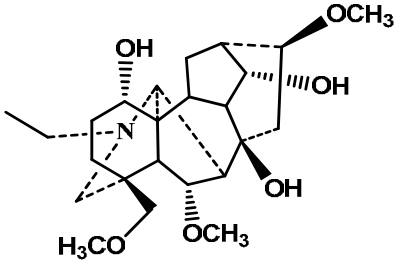
ISOLATION AND IDENTIFICATION OF DITERPENOID ALKALOIDSFROM *Aconitum sinchiangense* W. T. Wang

Ahmatbeck Samanbay[1,2], Bo Zhao[2], Haji Akber Aisa[2*]

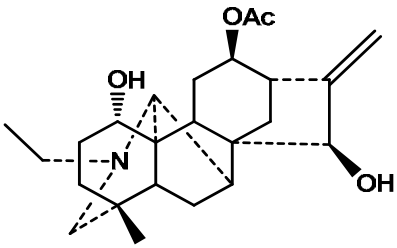
1) Xinjiang Medical University, Xinyi Road 393, 830011, Urumqi, Xinjiang, P. R. China
2) Key Laboratory of Plants Resources and Chemistry of Arid Zone, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi, Xinjiang, P. R. China, e-mail: haji@ms.xjb.ac.cn

Aconitum sinchiangense W. T. Wang belongs to the *Aconitum* genus of *Ranunculaceae* familyis mainlydistributed in the southern slope of the Tianshan Mountainsof Xinjiang, China. No phytochemical study on this plant had been reported. Diterpenoid alkaloids are the main active ingredients of *Aconitum* which have showed anti-inflammatory, analgesic, anesthetic, anti-arrhythmic, cardiac and anti-tumor activities.

During our phytochemical investigation on *A.sinchiangense*, twoditerpenoid alkaloids: neoline [1] (1) and 12-acetyl-12-epi-mapelline [2] (2) were isolated from the whole herb. Their structures were established on the basis of spectroscopic analyses, including HR-ESI-MS and 1D and 2D NMR. All the two compounds were isolated for the first time from this plant.



neoline



12-acetyl-12-epi-mapelline

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OPTIMIZATION OF MOLDING PROCESSING METHOD OF TRADITIONAL UYGHUR MEDICINE FORMULA *Ela* TABLETS

Ayinuer Reheman[1,2,3], Jian Jun Xu[1], H. A. Aisa[1*]

1) The Key Laboratory of Plant Resources and Chemistry in Arid Regions and Key Laboratory of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi, P. R. China
2) University of the Chinese Academy of Sciences, 100039, Beijing, P. R. China
3) Institute of Xinjiang Traditional Uyghur Medicine, Urumqi, Xinjiang, P. R. China

Central Asian traditional Uyghur medicine (TUM) belongs to the family of unani medical systems derived from the Greco-Arabic tradition [1], it has a unique theoretical system. *Ela* is a Traditional Uyghur Medicine that has the function of impotence and aphrodisiac, and can treat the erectile dysfunction [2].

In this study, we optimize the molding condition of uyghur medicine formula *Ela* for improving more comprehensive active compounds, more balanced proportion of natural PDE5 inhibition composition supplement tablets with *Ela* formula which have complementary PDE5 inhibition ingredients.we use the wet granulation tablet method, single factor and orthogonal experiment to selecting the best molding process of *Ela* tablets. The proportion of the extract and the incipient is 35–65%, the microcrystalline cellulose (MCC) and the lactose as the filler (accounting for 44% of the amount of powder), the cross-linked polyvinylpyrrolidone (PVPP) and the low-substituted hydroxypropyl cellulose (L-HPC) are disintegrating agent (internal and external addition) accounting for 20% of the binder, the adhesive is polyvinylpyrrolidone 5% PVP-K30 ethanol solution, the lubricant is magnesium stearate (1%). The disintegration time is 8.34 minutes, tableting pressure 10.4 kg/mm, moisture content of 5.16% [3].

Through molding process optimization, we have successfully produced complex tablets with higher bioavailability, its triangle appearance, piece weight variation, hardness, friability, disintegration and other related to tablets indicators have reached the appropriate quality requirements.

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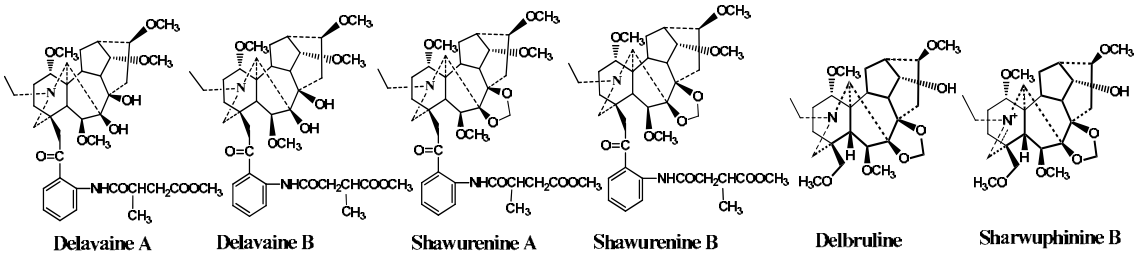
DITERPENOID ALKALOIDS FROM *Delphinium pseudoaemulans* C. Y. Yang

W. J. Xue[1,2], B. Zhao[1], G. A. Zou[1], H. A. Aisa[1*]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, Urumqi 830011, Xinjiang, P. R. China, e-mail: haji@ms.xjb.ac.cn
2) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China

Diterpenoid alkaloids are a large group of structurally complex natural products displaying a wide range of interesting chemical properties and biological activities. The plants of the genus *Delphinium* are the main source of diterpenoid alkaloids and have many activities which have been used as traditional folk medicines for the treatment of postoperative pain, inflammation, cough, rheumatism and neuralgia [1].

Delphinium pseudoaemulans C. Y. Yangis only distributed in Xinjiang Province of China. No phytochemical study on this plant has been reported to date. In the course of our studies, sixditerpenoid alkaloids, delavaine A (**1**), delavanie B (**2**) [2], shawurenine A (**3**), shawurenine B (**4**) [3], delbruline (**5**) [4], sharwuphinine B (**6**) [5], were isolated from the aerial parts of *D. pseudoaemulans*. Their structures were elucidated by MS, 1D and 2D NMR techniques. All of the three compounds were isolated from this plantfor the first time.



Acknowledgements. This work was supported by the Projects of International Science &Technology Cooperation of the Xinjiang Uygur Autonomous Region (Grant No. 20166014), andthe Central Asian Drug Discovery & Development Centre of Chinese Academy of Sciences.

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TWO FLAVONOIDS FROM *Nitraria sibirica*

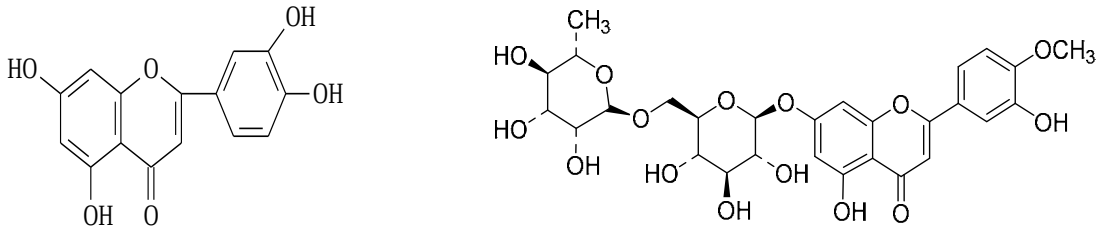
Chimengul Turghun[1], Mahinur Bakri[2], K. A. Eshbakova[2,3], H. A. Aisa[1*2*]

1) University of Chinese Academy of Sciences, Beijing, P. R. China
2) The Key Laboratory of Plant Resources and Chemistry in Arid Regions and Key Laboratory of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi, P. R. China
3) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

Nitraria sibirica Pall (*Nitrariaceae*) is spread through the Middle East, Central Asia, and widely distributed in Xinjiang Uyghur Autonomous Region and north part of China′s desert region, and maintains a balance in the desert ecosystem. They got special physiological properties of droughtand salt-resistances that prevent soil desertification and alleviate the degree of soil salinity–alkalinity [1].

As a kind of traditional Uyghur medicine, fruits and leaves of *N. sibirica* was used in the treatment of hypertension, menstrual disorders, gastroenteritis It is found in many traditional prescriptions with high pharmaceutical efficiency. The main chemical constituents of *N. sibirica* are flavonoids, alkaloids, a variety of mineral elements, amino acids, pigments, unsaturated fatty acids, volatile oils and so on [2].

In our present study, flavonoid luteolin [3] and diosmin [4] were isolated from the leaves of *N. sibirica* and purified by silicagel, Sephadex LH-20 column chromatographied. Their structures were elucidated by MS and NMR spectrum. These two compounds were isolated from this plant for the first time.



1 **2**

Fig. 1. Structure of compounds 1–2.

Acknowledgment. This work was supported by the West Light Foundation of Chinese Academy of Sciences (No. XBBS201312).

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CHEMAL CONSTITUENTS OF *Achillea millefolium* L.

Hongliang Li[1,2], Jun Li[1], H. A. Aisa[1]*

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
2) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China

Achillea millefolium L. (English name: yarrow), has played an important role for a long time as a drug in traditional and modern medical practice [1]. Its anti-inflammatory properties have been investigated and its methanolic extract has been reported to exhibite a significant cytotoxicity against cultured human tumor cell lines MCF7WT *in vitro* [2].

In this phytochemical investigation, the whole herb of yarrow was extracted with 95% EtOH. The extract was suspended in aqueous and extracted with ethyl acetate. Then the ethyl acetate extract was chromatographed on a silica gel column eluted with a gradient of solvent system of petroleum ether/ethyl acetate. Two compounds were isolated by crystallization from fractions, and their structures were determined to be β-sitosterol (**1**) [3] and centaureidin (**2**) [4] with the spectral investigations (1D NMR: ^{1}H, ^{13}C, 2D NMR: HMBC, HMQC, COSY) and comparison with the previous literatures.

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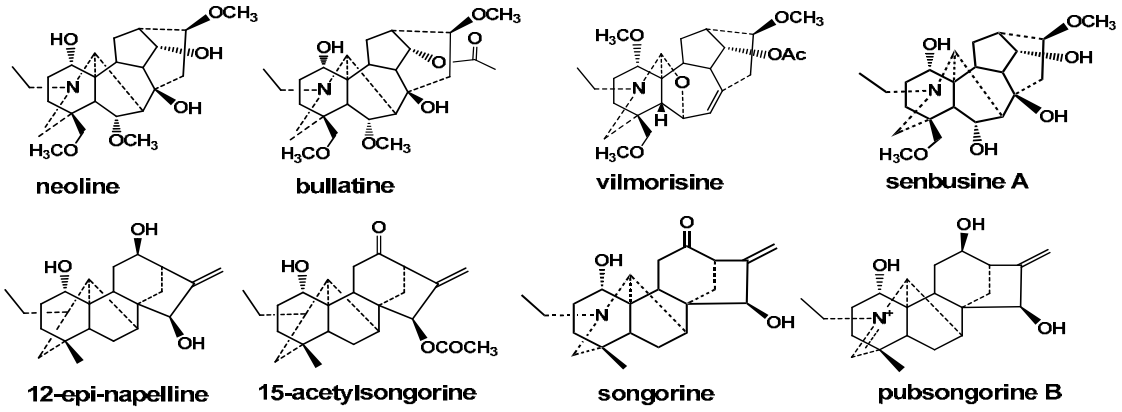
STUDY ON THE DITERPENOID ALKALOIDS CONSTITUENTS FROM *Aconitum smirnovii*

B. Zhao, H. A. Aisa

State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China, e-mail: haji@ms.xjb.ac.cn

The genus *Aconitum* belongs to the*Ranunculaceae* family, comprising of approximately 400 species, is distributed in the temperate regions of the northern hemisphere region, such as Asia, Europe and North America. Many species of this genus have been widely used in folk medicine as an anesthetic, analgesic, anti-inflammatory, sedative and to treatment of rheumatism and toothache [1].

Aconitum smirnovii Steinbis an endemic species to the Central Asia, but no phytochemical study on this plant had been reported [2]. During our investigation of the diterpenoid alkaloids composition from this plant, eight C_{19}-diterpenoid alkaloids: neoline (**1**), bullatine (**2**), vilmorisine (**3**), senbusine A (**4**), 12-*epi*-napelline (**5**), 15-acetylsongorine (**6**), songorine (**7**) and pubsongorine B (**8**), were isolated from thewhole herb of *A. smirnovii*. All the compounds were isolated from this plant for the first time.



Acknowledgment. This work was supported by the Projects of the West Light Foundation of Chinese Academy of Sciences (No. 2015-XBQN-B-14) and the International Science &Technology Cooperation of the Xinjiang Uygur Autonomous Region (Grant No. 20166014) and the Central Asian Drug Discovery & Development Centre of Chinese Academy of Sciences.

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CHEMICAL COMPONENTS FROM *Hyssopus serashanicum* COLLECTED IN TAJIKSITAN

Omina Shomirzoeva[1,2], Sodik Numonov[1], Haji Abker Aisa[1]*

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
2) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China

The plants of genus *Hyssopus* have been used for the treatment of skin disease, liver disease, menstrual disorders, as expectorant and cough suppressant for common cold and central nervous system disease in medicinal practice [1].

Hyssopus seravshanicus (*Lamiaceae*), a perennial, branched, semi-shrub growing in sunny habitats, mainly in depleted pastures on limestone, is a widespread species in Mediterranean region like the northwestern part of Tajikistan, Uzbekistan and Afghanistan. [2]. It has been used in traditional medicine for a long time as a, antispasmodic, stomachic, antifungal and expectorant properties. A literature survey revealed that so far very little phytochemical work has been carried out on *Hyssopus seravshanicus*. The plant is aromatic and a few studies have reported several biologically active constituents especially main compound from essential oil [2, 3].

In this work, we obtained two phenylpropanoids from *H. seravshanicus* by all kinds of isolation techniques such as solvent extraction, silica gel chromatography, sephadex LH-20 chromatography and preparative HPLC. Their structures were successfully identified to be 1-hydroxyl-2-*O*-β-*D*-glucopyranosyl-4-allylbenzene [4] and demethyleugenol-β-*D*-glucopyranoside [5] on the basis of 1D, 2D NMR and mass spectroscopic data. These two compounds are structure isomers, and were isolated from the genus *Hyssopus* for the first time.

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CHEMICAL CONSTITUENTS FROM THE SEEDS OF *Lepidium sativum*

Aida Kaiyrkulova[1,2], Jun Li[1], Haji Akber Aisa[1*]

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
2) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China

Lepidium sativum L., also known as garden cress, is a valuable food and medicinal plant belonging to the family of *Brassicaceae*, that is widely cultivated in China, Europe, Eastern Asia, and India [1]. It has been reported that seeds of *L. sativum* possess various therapeutic properties such as antioxidant, antimicrobial, anti-inflammatory, hypoglycemic, anti-hypertensive, anticancer activities and efficacy in gastrointestinal diseases. The seeds are also used for the treatment of diabetes, high blood pressure, respiratory disturbances, rapid fracture healing, hypercholesterolemia and anaemia [2–6].

Dried powdered seeds was extracted with EtOH (95%) at room temperature. The combined extract was evaporated *in vacuo*. The condensed residue was worked up sequentially with petroleum ether, EtOAc, and *n*-BuOH. The ethyl acetate fraction was chromatographed over a column of silica gel and Sephadex LH-20 successively. Structures of isolated compounds were established on the basis of their physical and chemical properties and the analysis of their spectral data by MS, ^{1}H, ^{13}C and 2D NMR and the isolated compounds were identified as (*E*)-methyl 3-(4-hydroxy-3,5-dimethoxyphenyl) acrylate (**1**) [7] and 4-hydroxy-3-methoxybenzoic acid (**2**) [8] (Fig. 1). These two compounds were reported from *L. sativum* L. for the first time.

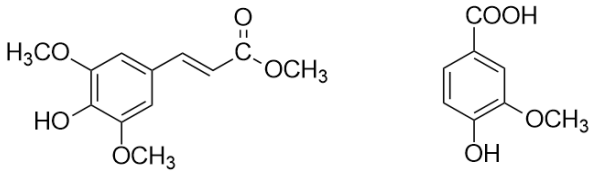

Fig. 1. Structures of compounds 1–2.

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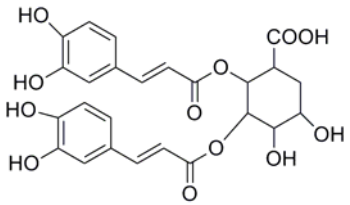
EVALUATION OF CAFFEOYLQUINIC ACID EFFECT ON MELANIN CONTENT IN MURINE B16 CELL AND MOLECULAR MECHANISM OF 1, 5-DICAFFEOYOL-QUINIC ACID PROMOTE MELANIN SYNTHESIS

Nuramina Mamat[1,2], H. A. Aisa[1*]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, 830011, Urumqi, Xinjiang, P. R. China
2) University of the Chinese Academy of Sciences, 100039, Beijing, P. R. China

Caffeoylquinic acid (CQA) is widespread phenylpropanoids found in most plants. It is produced by condensation of quinine and one or more caffeic acids by esterification [1]. According to the number or the position of caffeoyl groups, CQA are classified into various derivatives, such as Mono-CQA, di-CQA, tri-CQA. CQA derivatives have a variety of bioactivities such as antioxidant, antibacterial, anticancer, antihistamic and et [2].

In this study we first measure the 9 kind of dissimilar caffeoylquinic acid (3-CQA; 4-CQA; 5-CQA; 3,4-diCQA; 3,5-diCQA; 4,5-diCQA; 1,3-diCQA; 1,5-diCQA; 1,3,5-triCQA) effect on melanin synthesis in B16 cell. We found that 1,5-diCQA, 3,5-diCQA and 3-CQA significantly increase the melanin content and TYR (tyrosinase) activity in B16 cell and 1,5-diCQA has the highest activity.



Secondly we investigate molecular mechanism of 1,5-diCQA (Fig.1) promoted melanin synthesis using western blot analysis. Our result shows that expressions of TYR, TRP1 (tyrosinase-related protein1), TRP2 (tyrosinase-related protein2) and MITF (microphthalmia-associated transcription factor) were up-regulated after treated B16 cell with 1,5-diCQA. It was also found that 1,5-diCQA promotes the phosphorylation of Akt, p38 and Erk, which was involved in MAPK signal pathway. cAMP level and phosphorylation of CREB was also significantly increase. These results suggested that 1, 5-diCQA mediated the acceleration of melanin synthesis by MAPK and PKA signal pathways.

Acknowledgment. This work was supported by the Funds for the Xinjiang Key Research and Development Program (2016B03038-3).

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A NOVEL CHALCONE DERIVATIVES-PMPP ENHANCES MELANOGENESIS

Yin Li[1,2], Niu Chao[1], H. A. Aisa[1,2]

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Urumqi, 830011, Xinjiang, P. R. China
2) University of the Chinese Academy of Sciences, 100039, Beijing, P. R. China

Kaliziri [*Vernohia anthelmintica* (L.) Willd.] is a kind of traditional Uyghur medicinal plant growing only in the high altitude localities of southern Xinjiang and limited regions of Pakistan and India. Its fruits extract is vastly used for treating vitiligo and as one of the most popular Uyghur medicines. Some significant chalcone compounds are isolated from the plant and it is suggested that they play an important role in vitiligo treatment. Recently, a new series of chalcone derivatives were designed and synthesized by our research group. In consideration of the generally low cytotoxicities of these compounds, we tested all of the derivatives in B16 melanoma cells, and identified 1-(4-((3-phenylisoxazol-5-yl)methoxy)phenyl)-3-phenylprop-2-en-1-one (PMPP) (Fig. 1) is one of the most promising candidate compound with activating effect on melanin synthesis and tyrosinase activity better than the positive control 8-methoxypsoralen (8-MOP).

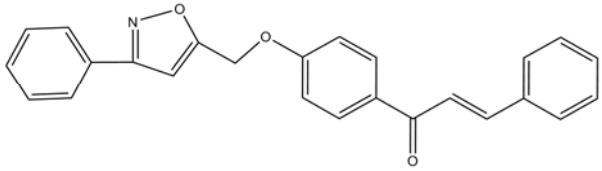


Fig. 1. **Chemical structure of PMPP.**

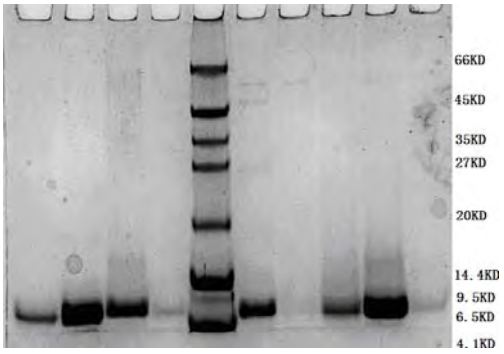
Acknowledgment. This work was supported by the Funds for the Xinjiang Key Research and Development Program (2016B03038-3).

ISOLATION AND CHARACTERIZATION OF ANTIMICROBIAL PEPTIDES FROM *Cuminum cyminum* L.

Y. Mijiti[1,2], Yang Jian[1,2], P. Rouzi[1,2], A. Wali[1,2], A. Yili[1*], H. A. Aisa[1*]

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
2) University of Chinese Academy of Sciences, 100039, Beijing
e-mail: abu@ms.xjb.ac.cn,haji@ms.xjb.ac.cn

Cuminum cyminum L. commonly known as traditional dish and favorite food in northwest China for country. It is a popular spice used many food and Traditional Uyghur medicine preparations. Here we isolated more than 5 new antimicrobial peptides from *Cuminum cyminum* L. seeds by 50% ethanol, C18 reverse phase column chromatography for the first time. Then the isolated fraction was purified using FPLC-ion exchange chromatography and characterized by HPLC. The peptides components and molecular weights were determined as 3333.52, 4550.82, 6587.89, 7786.13, 9766.79 Da by mass spectrometry. Here we are going to isolate and prepare the bioactive polypeptides by function oriented isolation method and mainly evaluation of peptides fraction. Those which have evaluated a high degree of activity against the bacteria strains and fungi activities peptides were tested against three strains of *Candida albicans*, E. coli and Staphylococcus aurous. In addition, we hope to establish a reasonable budget and realistic peptides fraction preparation methods.



Mass spectrometry analysis of antimicrobial active fractions proved presence of low molecular peptides.

Acknowledgment. Thanks for financial support to the project of“Supporting Xinjiang 201491160” and 2014 "the light of the western" talent training plan; thank the Training Project of Xinjiang Autonomous Region for Technological Innovation of Youth Talents for financial support.

OPTIMIZATION OF EXTRACTION AND MEMBRANE SEPARATION TECHNOLOGY FOR ANTIBACTERIAL POLYPEPTIDES FROM BOVINE BONE MARROW

P. Rouzi[1,3], A. Waili[1,3] , A. Abduwali[1,3], Y. Mijiti[1,3], A. Yili[1,2*]

1,2) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
3) University of Chinese Academy of Sciences, 100039, Beijing,
e-mail: abu@ms.xjb.ac.cn

The separation and concentration of water extract polypeptides from bovine bone marrow were studied systematically by ultrafiltration membrane separation equipment. The fractional membrance separation and purification craft process, sequence of operation and the chief craft parameterses had been done. With the protein quality, extraction rate, molecular weight, antibacterial activity as evaluation indexes, the ultrafiltration membranes used molecular weight 10KD, 3 KD and 1 KD, it was separated them into 6 Molecular parts and related indicators were measured. The content of protein in different molecular weight segments was in the following order: 1 KD>3 KD>10KD, and the 10 KD retained membrane could effectively separate protein and polypeptide parts. Conclusion: Ultrafiltration can be effectively separated proteins and peptides from different molecular weights, able to meet product quality requirements, and provide the basis for subsequent industrial production.

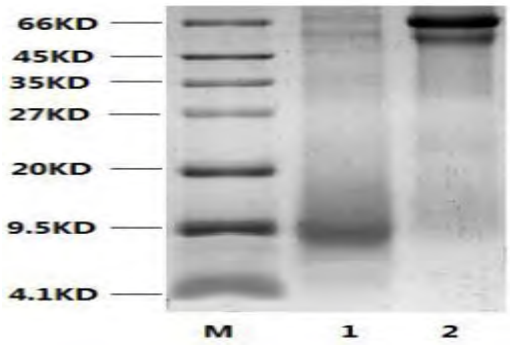


Fig. 1. 10% SDS-PAGE of the protein fraction

Acknowledgment. Thanks for financial support to the project of Xinjiang Autonomous Region for Technological Innovation of Youth Talents and the Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

STUDY ON THE METHOD OF CONTINUOUS EXTRACTION OF PROTEIN FROM SEEDS OF *Glycyrrhiza uralensis*

P. Rouzi[1,3], Q. Memtimim Tikin[4,1] A. Waili[1,3], Y. Mijiti[1,3], A. Yili[1,2*]

1,2) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
3) University of Chinese Academy of Sciences, 100039, Beijing
4) Biologe-Geography Department, Hotan teacher′s college of Xinjiang Uygur Autonomous Region, 848000, Hotan, Xinjiang, P. R. China, e-mail: abu@ms.xjb.ac.cn

Licorice is one of the most commonly used Chinese herbal medicine, Chinese medicine it derived from *Glycyrrhiza uralensis*, *Glycyrrhiza inflata*, *Glycyrrhiza glabra*, the main producing areas are Xinjiang, Inner Mongolia, Gansu and arid area of northwest china, although the "Chinese Pharmacopoeia" contained 3 varieties of licorices, wild and cultivated *Glycyrrhiza uralensis* become the main variety in the current market circulation. In this paper, seeds of *Glycyrrhiza uralensis were used as study subject*, the suitable extraction methods to determine protein of seeds were selected, and its molecular weights were analyzed. The protein quality and content was taken as the index, Firstly, the seed defatted powder was extracted with 50% ethanol, followed by extraction with PBS + precipitation with ammonium sulfate (30, 50, 70%), and finally precipitated with 5% acetic acid + acetone. The results showed that the protein content of 5% acetic acid + acetone precipitation was higher than that of other two methods, and the content of 50% site protein in PBS+ ammonium sulfate fractionation precipitation was the highest. Conclusion, all three methods can extract protein and polypeptide of liquorice's seeds, which provides the basis for further research and development of active components of *Glycyrrhiza uralensis*.

TABLE 1. **Comparison of Extraction Methods (100 g)**

project	fraction	protein quality	protein content	extraction yield
PBS+ Ammonium sulphate(2)	30%	2.47g	36%	2.05%
	50%	0.93g	83.08%	0.7%
	70%	0.54g	30.66%	0.38%
	total	3.94g		0.45%
5%acetic acid+atceton(3)		5.90g	38.75%	4.91%
total		13.9g		11.5%

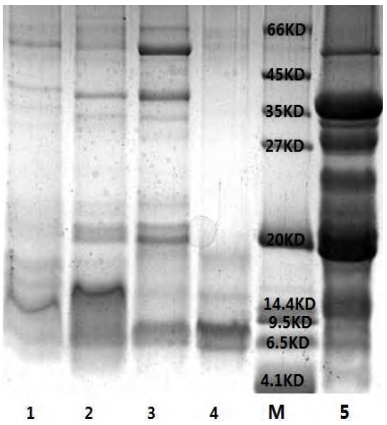


Fig. 1. 12% SDS-PAGE of the protein fraction

In Fig. 1: 1.50% ethanol extraction fraction; 2.30% Ammonium sulphate part; 3.50% Ammonium sulphate part; 4. 70% Ammonium sulphate part; M: Marker5. 5% acetic acid + atceton fraction.

STUDY ON THE TECHNOLOGY OF ULTRAFILTRATION MEMBRANE SEPARATION IN PREPARATION OF WHEY PROTEIN AND LACTOSE

P. Rouzi[1,2], A. Waili[1,2], A. Abduwali[1,2], Y. Mijiti[1,2], A. Yili[1*]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi, Xinjiang, P. R. China
2) University of Chinese Academy of Sciences, 100039, Beijing, P. R. China,
e-mail:abu@ms.xjb.ac.cn

Donkey milk, because of its chemical composition and human milk is closer to the dairy, food industry and nutrition community widespread concern. Xinjiang is China′s largest number of donkey raising provinces. Therefore, several donkey breeding bases and companies have been established with the development of donkey milk as the main product. Can be related products (milk powder, cheese, candy, etc.), by-products, whey further recovery and utilization is still in a blank state. A whey is a yellow-green solution containing lactose, protein, minerals and fat. The biggest feature is the large volume and the presence of a wide range of nutrients in the milk, nutrition whey in raw milk accounted for more than half.Allegedly, donkey milk can be used to treat asthma, bronchitis, diabetes, ulcers, gastritis and other diseases, some women can even rely on donkey milk to relieve menopausal discomfort.In many areas of Xinjiang, there are many people drinking donkey milk to treat tuberculosis and gastric ulcer and other diseases. Whey protein has certain functional properties and biological activity. In this paper, the byproduct - donkey whey liquid as the test material, to explore its protein and lactose preparation methods and process conditions. With the extraction rate and content of protein and lactose as indexes,The protein and lactose were prepared by the method of concentration + dialysis, ammonium sulfate fractionation and ultrafiltration membrane separation and concentration system.The results showed that 10KD ultrafiltration membrane can effectively isolate protein and lactose, the protein content can reach 61%, lactose content of 74%.Compared with the existing process, the utility model has the advantages of less pollution, lower energy consumption and higher yield, and the process has good development prospects for the recovery and utilization of whey.

TABLE 1.**Comparison of Three Method**

No	project	Protein content (%)	Lactose content (%)
1	After dialysis	51	31
	non-dialysis	40	48
2	30%	11	18
	50%	36	11
	70%	42	10
3	10KD retention fluid	61	18
	10KD permeation fluid	15	74

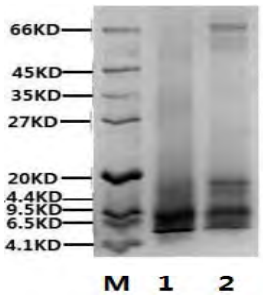


Fig. 1. 12% SDS-PAGE of 1

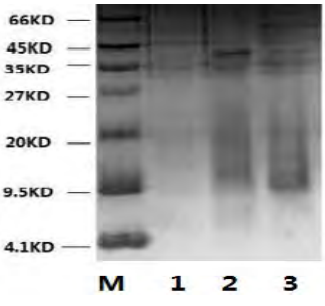


Fig. 2. 12% SDS-PAGE of 2

In Fig. 1: 1: protein of after dialysis; 2. protein of non-dialysis; In Fig. 2: 1,2,3 are 30%, 50%, 70% ammonium sulfate precipitation fraction.

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COMPARISON STUDY ON METHODS OF EXTRACTION ACTIVE PROTEIN AND PEPTIDE FROM BOVINE BONE MARROW

P. Rouzi[1,3], A. Waili[1,3] , Y. Mijiti[1,3], A. Yili[1,2]

1,2) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
3) University of Chinese Academy of Sciences, 100039, Beijing, e-mail:bu@ms.xjb.ac.cn

Bovine Bone marrow is a kind of traditional nutrition and healthy food in China. Marrow extract is rich in protein, Ka, P, Fe, Zn, Cu, chondroitin, lecithin and other nutrients, it has good healthy function for children and adults. According to traditional Chinese medicine, bovine bone marrow tastes sweet, warm in nature, enrich blood and benefit essence, quench thirst, hemostasis, arrest leucorrhoea. Indications are lack of essenceand blood, consumptive disease, weakness and thin, diabetes, hematemesis, hematofecia, metrorrhagia and metrostaxis. Uygur medicine didn′t include bone marrow as singleingredient drug, but commonly used in the internal medicine and surgicalprescription, the functions are relieve swelling and pain, malacia etc. In this paper, bovine bone marrow was used as the test material, and the effect of different extraction methods on the extraction rate of bovine bone marrow protein and peptide were screened, and the best extraction methods were determined. There were 9 kinds of methods were used, such as water-extraction, NaCl (0.5%, 1%, 1.5%), PBS, Tris-HCl and so on, content of protein, extraction rate, antibacterial activity and some other items were used as the index of investigations. The results showed that the extraction effect of water extraction, Tris-HCl and NaCl was obviously better than other methods, and the processes was simple, fast and low cost, which was suitable for industrial production. The results of the comprehensive analysis show that, Tris-HCl used as a extraction solution, its parts can separate the polypeptide section with 30% of ammonium sulfate precipitation, and 0.5% of NaCl extracts can also isolated polypeptide part, it will provide the basis for the further development and application use on bovine bone marrow polypeptide purification.

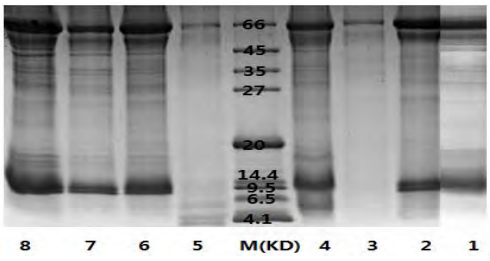

Fig. 1. 10% SDS-PAGE of the protein fraction.

Acknowledgment. Thanks for financial support to the project of Xinjiang Autonomous Region for Technological Innovation of Youth Talents and the Central Asian Drug Discovery and Development Center of Chinese Academy of Sciences.

ISOLATION, PURIFICATION AND MONOSACCHARIDE COMPOSITION ANALYSIS OF POLYSACCHARIDES FROM *Fritillaria pallidiflora* SCHRENK

A. Abuduwaili[1,3], P. Rouzi[1,3], A. Waili[1,3], Y. Mijiti[1,3], A. Yili[1,2]

1, 2) The Key Laboratory of Plant Resources and Chemistry of Arid Zone and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics
Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
3) University of Chinese Academy of Sciences, 100039, Beijing, e-mail:abu@ms.xjb.ac.cn

Fritillaria pallidiflora Schrenk, belongs to the *Fritillaria* genus of *Liliaceae* family. The dried bulbs of this plant used as one of the important source of Fritillaria pallidiflora for antiasthmatic, anti-tussive and expectorant agents in traditional Chinese medicine. Polysaccharide was known as exhibiting anticancer, antimicrobial, anti-inflammatory activities and improving human immune system, has a wide application in the medicine, cosmetics and food industry. The isolation and structure identification of polysaccharides from *F. pallidiflora* still at an initial stage. Polysaccharides were isolated from the *Fritillaria pallidiflora* Schrenk (FPS) through Successive cold water and hot water extraction, ethanol precipitation, deproteinized by Savage method, dialyzed against water and lyophilized, named FPSP-C and FPSP-H. FPSP-C was fractionated by DEAE-52 anion exchange chromatography and Sephadex G-100 gel filtration chromatography, which obtained the neutral sugar FPSP-C-N. The purity was identified by ultraviolet spectrum. The monosaccharide composition which characterized by GC Chromatography showed that FPSP-C-N was a heteropolysaccharide, mainly composed of glucose, mannose, galactose and arabinose with a molar ratio of 10:2.3:2:1, also have some, xylose, and rhamnose.

TABLE1. **Polysaccharides Yield and Sugar, Protein Content of Extracts**

Extract	Yield, %	Neutral sugar, %	Protein content, %
FPSP-C	3.04	16.5	15.05
FPSP-H	4.26	49.86	5.47

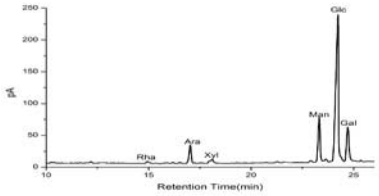

Fig. 1. GC Chromatography of FPSP-C-N.

Acknowledgment. Financial support of this research was provided by the Program for the National Natural Science Foundation of China (No. U1403201).

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STUDY ON PREPARATION OF CHICKPEA (*Cicera rietinum* L.) SPROUTS PROTEIN HYDROLYSATES AND ITS ANTIBACTERIAL ACTIVITIES

A. Wali[1,2], A. Yili[1*], P. Rouzi[1,2], Y. Mijiti[1,2]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics and Chemistry, Academy of Sciences of the People′s Republic of China, 830011, Urumqi, Xinjiang, Beijing South Road 40-1, P. R. China, e-mail: abu@ms.xjb.ac.cn
2) University of Chinese Academy of Science, 100039, Beijing, P. R. China

Dry chickpeas (*Cicer arietinum* L.) were purchased from Mori (China). Samples were manually cleaned from impurities. And the cleaned seeds were used for the sprouting experiment. Chickpea sprouts protein extracts (CSPEs) were hydrolyzed by proteases preparations from plant (Papain), animal (Trypsin) and fungal (Alcalase and Neutral Proteases) sources. In experiments Neutral Proteases fraction (NPF), Alcalase fraction (AF), Trypsin fraction (TF) and Papain fraction (PF) were tested in vitro for antibacterial activity against *St.epidermidis* and *E.coli* et al 5 different bacteria′s. Table 1 showed that NPF have better activity for *St. epidermidis* (15 mm), *E.coli* (15 mm) and PF have better activity for *C. albicans* (15 mm). Moreover, the high molecular weight protein band could not be observed in Papain and Alcalase (Fig. 1). This hydrolysates have the highest DH, thus the large MW was hydrolyzed into small peptides.

TABLE 1. **Antimicrobial Activity *in vitro* of Peptide Fractions (NPF, AF, TF and PF) from Cicer *arietinum* L. Sprouts Protein Hydrolysate**

No.	Bacteria	CSPEs	NPF	AF	TF	PF
1	*St.epidermidis*	12±0.2	**15±03**	10±0.1	10±0.1	10±0.1
2	*E.coli*	12±0.2	**15±0.3**	10±0.1	10±0.1	10±0.1
3	*Klebsiella*	7.0±0.1	12±0.2	**12±0.2**	**10±0.1**	7.0±0.1
4	*C.albicans*	10±0.1	10±0.1	10±0.1	1.0±0.1	**15±0.3**
5	*Sal.typhimurium*	10±0.1	14±0.2	**12±0.2**	7.0±0.1	7.0±0.1

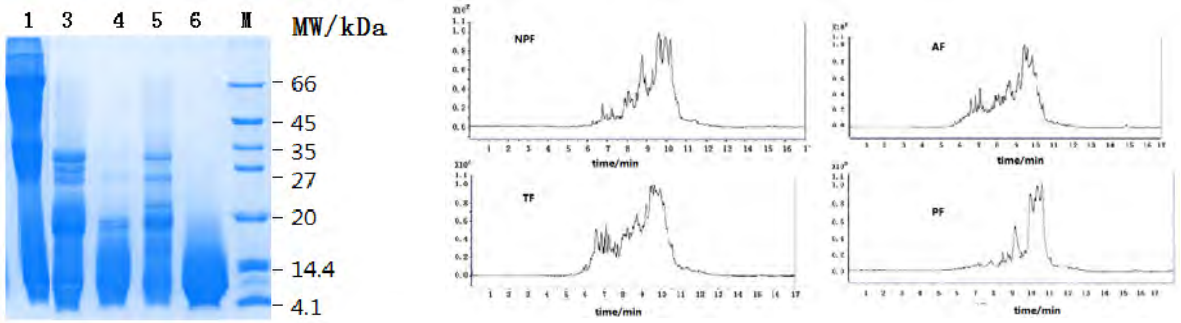


Fig. 1. A: Gel electrophoresis in 15% PAAG: line M: marker proteins. line 1: Chickpea sprouts protein extracts (CSPEs); line 3: Neutral Proteases fraction (NPF); line 4: Alcalase fraction (AF); line 5: Trypsin fraction (TF); line 6: Papain fraction (PF). B: LC/MS diagram of four different enzyme fraction.

Acknowledgment. Thanks for financial support to the project of“Supporting Xinjiang 201491160” and 2014 "the light of the western" talent training plan; thank the Training Project of Xinjiang Autonomous Region for Technological Innovation of Youth Talents for financial support.

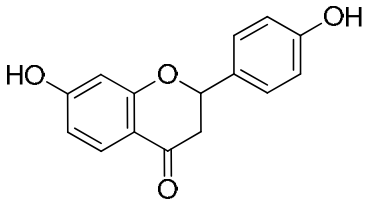
CHEMICAL CONSTITUENTS OF THE *Euphorbia alatavica* BOISS

Nurmuhammat Kehrimen[1,2], Rushangul Rouzimat[2], Jie Gao[2], H. A. Aisa[2*]

1) Xinjiang Medical University, Xinyi Road 393, Urumqi, 830011, Xinjiang, P. R. China
2) Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, Urumqi 830011, Xinjiang, P. R. China, e-mail: haji@ms.xjb.ac.cn

Euphorbia is a large genus consisting of more than 2000 species widely distributed in the world, of which about 200 species distributed in Central Asia and China. Many species of the *Euphorbia* genus have been used as the main component in the traditional Uighur folk medicines for the treatment of abdominal pain, abdominal distention, skin disease, and paralysis.

Euphorbia alatavica Boiss, belonging to the *Euphorbia* genus, is a perennial herb widely distributed in the Xinjiang Uighur Autonomous Region of China and Central Asia. To the best of our knowledge, there is no phytochemical study report on this plant. The air-dried whole plant of *E. alatavica* (10 kg) was extracted with methanol. One alkaloid named as Naringenin (**1**) [2], and one flavonoid identified as 8-hydroxy-3-methoxy-5*H*-pyrido [2, 1-c] pyrazin-5-one (**2**) [3] were isolated from the methanol fraction of *E. alatavica*. Structures of isolated compounds have been established on the basis of their spectral data as UV, ^{1}H, ^{13}C and 2D NMR. These compounds have been isolated from *E.alatavica* for the first time and chemical structure as follow:



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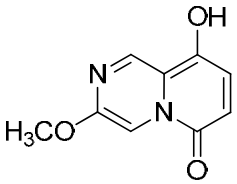

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Acknowledgment. The investigation was funded by International Cooperation and Exchange of the National Natural Science Foundation of China (No. 31110103908) and Central Asia Drug Discovery and Development Centre of Chinese Academy of Sciences.

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DITERPENE CONSTITUENTS OF *Euphorbia glomerulans*

Aobulikasimu Hasan[1,2], Jie Gao[1], H. A. Aisa[1*]

1) The Key Laboratory of Plant Resources and Chemistry of Arid Zone, and State Key Laboratory Basis of Xinjiang Indigenous Medicinal Plants Resource Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, 830011, Urumqi, P. R. China
2) University of Chinese Academy of Sciences, Beijing 100039, P. R. China,
e-mail: haji@ms.xjb.ac.cn

Diterpenes occurring in plants of the *Euphorbia* genus (*Euphorbiaceae*) are of considerable interest in natural product drug discovery because of their wide range of biological activities and structural diversity. *Euphorbia glomerulans* Prokh. Consp. Syst. Tithym. As. Med. is mainly distributed in Xinjiang of China and Central Asia. The chemical constituents of this plant, especially diterpenoids, have not been reported.

The whole plant of *E. glomerulans* (4.7 kg) was extracted with acetone at room temperature, and the extract (358 g) was suspended in CH_3CN and partitioned with cyclohexane to yield the CH_3CN soluble extract (105 g), which was further separated by repeated column chromatography and semi-preparative HPLC to obtain four jatrophane-type diterpenoids (Fig. 1), 3β,7β,8α,15β-tetraacetoxy-5α-benzoyloxyjatropha-6(17),11*E*-dien-9,14-dione (**1**) [1], 3β,8α,15β-triacetoxy-5α,7β-dibenzoyloxyjatropha-6(17),11*E*-dien-9,14-dione (**2**) [1], 5α,7β,8α,9α,15β-pentaacetoxy-3β-benzoyloxyjatropha-6(17),11*E*-dien-14-one (**3**) [2], and 3β,7β,8α,9α,15β-pentaacetoxy-5α-benzoyloxyjatropha-6(17),11*E*-dien-14-one (**4**) [2]. These compounds were isolated from this plant for the first time. Their structures were identified by MS and NMR spectroscopic data.

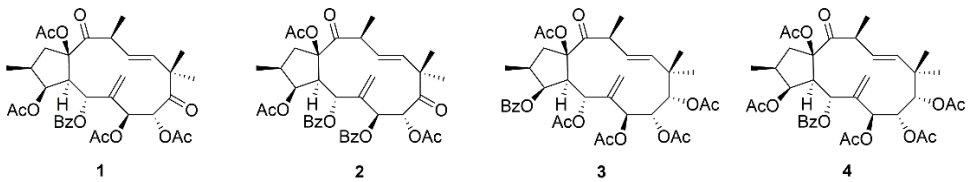

Fig. 1. Diterpenes isolated from *Euphorbia glomerulans.*

Acknowledgment. This work was supported by the Projects of National Natural Science Foundation of China (Grant No. 21572263) and the Central Asian Drug Discovery & Development Centre of Chinese Academy of Sciences.

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ULTRASOUND-ASSISTED EXTRACTION OF PROTEINS FROM SHEEP ABOMASUM BY RESPONSE SURFACE METHODOLOGY

Bing Liu[1,2], A. Yili[1], A. Aisa[1]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi Xinjiang, P. R. China
2) University of Chinese Academy of Sciences, 100039, Beijing
e-mail: abu@ms.xjb.ac.cn, haji@ms.xjb.ac.cn

Sheep abomasum (SA) is the fourth stomach of sheep and rich in proteins. Every year the sheep meat processing industries consistently generate large amounts of by-products, including SA. In past decades, the mainly application of SA is the extraction of chymosin for cheese manufacturing[1]. However, with the significantly development of substitutes, including plant and microbial sources substitutes, sheep rennet only covers little part of the world demand for cheese making, more and more SA are not utilized sufficiently. The purpose of the current work was to extract protein from SA as much as possible using ultrasound-assisted extraction method (UAE). Response surface methodology (RSM) was applied to optimize the UAE extraction parameters. The results showed that under the optimum conditions of ultrasonic time 29 min, ultrasonic power 400 W, ratio of liquid to solid 25 (mL/g), pH = 10, the water-soluble protein contents of SA was 321 mg/g dry SA. Compare to conventional extraction method (CEM), the water-soluble protein contents of SA was significantly increased from 216 to 321 mg/g dry SA, and the extraction time was decreased from 240 to 29 min. Conclusion: ultrasound-assisted extraction of proteins from sheep abomasum by response surface methodology can be effectively applied to extract protein from SA in industrial production.

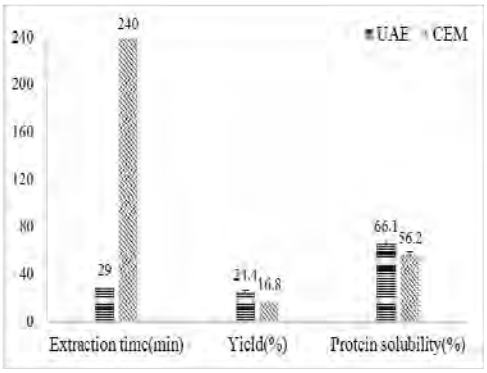

Fig. 1. Comparison study on the method of UAE and CEM.

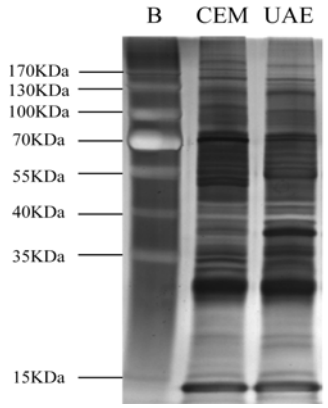

Fig. 2. Gel-electrophoresis of protein from SA obtained by CEM and UAE in PAAG (12%).

Acknowledgment. Thank for the Central Asia Drug Research and Development Center of the Chinese Academy of Sciences and the Training Project of Xinjiang Autonomous Region for Technological Innovation of Youth Talents for financial support.

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A PHARMACEUTICAL EXTRACTIONS FROM *Lamb fourth* STOMACH

Bing Liu[1,2], A. Yili[1], A. Aisa[1]

1) Key Laboratory of Plant Resources and Chemistry in Arid Regions, Xinjiang Technical Institute of Physics & Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi, Xinjiang, P. R. China
2) University of Chinese Academy of Sciences, 100039, Beijing,
e-mail: abu@ms.xjb.ac.cn, haji@ms.xjb.ac.cn

Lamb fourth stomach (LFS) is traditionally food and medicine homologous raw materials in china and rich in nutrients, including protein, fat, carbohydrates, vitamin B_1, vitamin B_2, calcium, and other mineral elements [1]. However, the mainly application of the LFS is the extraction of chymosin for the production of cheese [2, even though it has lots of other active ingredients. Hence, efficiently utilize LFS as the production of pharmaceutical raw materials is significant. In this paper, the goal of the present work was to look for a fast and effective method to extract and prepare pharmaceutical extractions with high activity of chymosin and pepsin, high values of yield and protein concentration. Eight fractions of pharmaceutical extractions were extracted and prepared from the defatted LFS by different processing method. Compared to the conventional extraction methods, pharmaceutical extractions were prepared with new method showed the highest activity of pepsin and chymosin, up 25182 Ru/g and 3796.4 u/g respectively, and improved the extraction yield from 2.4% to 5.2%, protein yields up 64.3%. Therefore, the pharmaceutical extractions from Lamb fourth stomach can be regarded as one of the valuably potential pharmaceutical raw materials, and could be applied for valuable food additives and pharmaceutical products.

Acknowledgment. Thank for the Central Asia Drug Research and Development Center of the Chinese Academy of Sciences and the Training Project of Xinjiang Autonomous Region for Technological Innovation of Youth Talents for financial support.

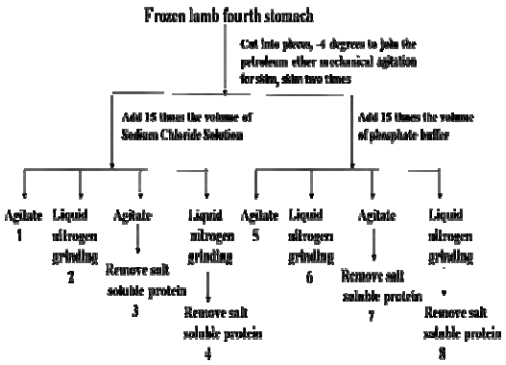

Fig. 1. Experimental flow chart.

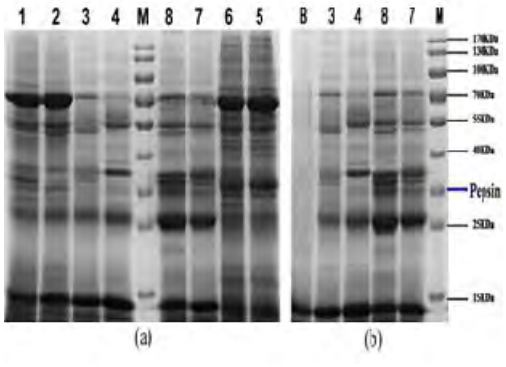

Fig. 2. Gel-electrophoresis of protein fraction from LFS in PAAG (12%)

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DITERPENOIDS AND FLAVONOIDS OF *Pulicaria gnaphalodes*

K. A. Eshbakova[1,2*], B. D. Komilov[1], Sh. O. Melieva[1], Kh. Hasanova[2], H. A. Aisa[2,3*]

1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: e_komila@yahoo.com
2) Key Laboratory of Plant Resources and Chemistry of Arid Zone, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi, Xinjiang, P. R. China, e-mail: haji@ms.xjb.ac.cn;
3) Key Laboratory of Xinjiang Indigenous Medicinal Plant Resources Utilization, Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing South Road 40-1, 830011, Urumqi, P. R. China

Plant *Pulicaria gnaphalodes* (*Asteraceae* family) is widespread in Central Asia. It is used as an antifungal agent in folk medicine. Earlier, we extracted and identified 25 compounds of diterpenoid, coumarinic, sterol and phenolic nature from the aboveground part of the plant collected in the Tashkent region (Uzbekistan) [1–4].

Continuing to study the chemical composition, the aerial part of *Pulicaria gnaphalodes* was extracted by chloroform and n-butanol, and fractions were subjected to a column chromatographywith a gradient system of hexane: ethyl acetate (10: 1-1: 1), chloroform:methanol (20: 1-1: 1) and methanol:water (6: 4) with Slegagel and Sephadex LH 20adsorbents.We have isolated 1-6 compounds of diterpenoid and flavonoid nature:salvin (1), salvinin (2), kasticin (3), salvifolin (4), quercetin-3-*o*-β-*d*-galacturonide (5), quercetin-3-*o*-β-*d*-glucuronide (6).

The chemical structures of the isolated compounds were established on the basis of the spectral data of ^{1}H, ^{13}C NMR and 2D experiments, and by comparison with those in the literature.

Compounds 1, 2 were isolated for the first time from the plant *Pulicaria gnaphalodes*, and the compounds 4, 5, 6 from the genus *Pulicaria*.

The antioxidant property of the compound 5 on ABTS (2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonicacid) diammoniumsalt) had been studied. An antioxidant, vitamin C (IC_{50} = 5.34 ± 0.42) was chosen as the control. The compound 5 showed high effect with a value of IC_{50} 4.80 ± 0.22 μg/mL.

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CARBOHYDRATES, LIPIDS AND PROTEINS OF AMARANTH CULTIVATED IN UZBEKISTAN

N. K. Yuldasheva[1], M. X. Malikova[1], S. D. Gusakova[1], R. K. Rakhmanberdyeva[1], Sh. K. Khidoyatova[1], L. G. Mejlumyan[1], K. A. Tokhtakhunov[2], M. M. Muminov[3]

1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: s.gusakova2004@mail.ru, rakhmanberdieva@mail.ru
2) Tashkent State Technical University
3) Andijan State University

The most promising types of non-traditional raw materials include the plant amaranth, which has a specific chemical composition. In the last decade amaranth has been cultivated and intensively studied as a source of high-lysin protein, valuable pectin polysaccharides, physiologically active oil. In 2013, experts from the Tashkent State Technical University and the Center for the Introduction of Innovative Technologies (Andijan) started work on introduction of foreign amaranth sorts on soils with low bonitet (including saline soils) and its usage as a crop for a second seeding after harvesting cereals. The aim of this work is to study the carbohydrates and proteins of seeds, and the carbohydrates and lipids aerial part of the universal (both grain and fodder) "Kharkivsky-1" amaranth sort grown in Uzbekistan.

From the seeds and aerial part alcohol-soluble sugars (ASS), water-soluble polysaccharides (WSPS), pectic substances (PS), hemicelluloses (HMC) and then fiber were isolated (Table 1).

TABLE 1. **Carbohydrate Complex of Seeds and the Aerial Part of Amaranth (% from mass)**

Sample	ASS	WSPS	PS	HMC	Fiber
Seeds	3.0–4.0	55.6	4.1	2.8	7.0
Leaves + stems	2.3–4.0	15.8	3.6	7.5	27.0

The data from Table 1 demonstrate that the dominant polysaccharides are WSPS in the seeds, while WSPS and fiber in the aerial part.

Lipids of the amaranths air-dry aerial part of the 60-day stage vegetation of 2016 season were studied. The total lipids content was 2.72% on dry substance. In unsaponifiable substances of the lipids, 0.04% of squalene, 0.01 mg % tocopherols and 0.04% phytosterols were found. The content of the sum of glycolipids, phospholipids and pigments was 1.1%. Fatty acids of amaranth's aerial part contains 12 components with the predominance of unsaturated acids 18:1, 18:2 ω6 and 18:3 ω3. It should be noted, that the presence of minorities of high molecular saturated acids in FA mixture is 20:0–26:0.

The seeds were chopped to powder and defatted. Total protein was isolated from the acetone powder using alkaline extraction, centrifugation, precipitation with ammonium sulfate, dialysis in running water and lyophilization of the protein solution. It was found that amaranth seeds contained 22.5% of proteins. The amaranth protein of is characterized by a high content of glutelin (68%) and albumin (46%) fractions.

LIPIDS OF *Zizyphus jujuba* FRUITS

M. B. Davlyatova, Sh. Sh. Sagdullaev, F. I. Inoyatova, A. I. Glushenkova

Acad. S. Yu. Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan,
e-mail: mavlyuda.davlyatova@mail.ru

The plant *Zizyphus jujuba* (Unabi ordinary) belongs to the family *Pamnuceae*. It is widely used in folk medicine, perfumery, food and canning industry [1]. Carbohydrates, fats and vitamins are found in fresh fruits [2].

We studied the composition of fatty acids of common lipids extracted from the air-dried flesh of unabi fruit by five-fold infusion with a mixture of chloroform and methanol (2:1) at room temperature. The extract was treated with 0.05% aqueous solution of $CaCl_2$ to remove non-lipid components. The lipid yield was determined gravimetrically after removal of the solvent, followed by drying the lipids in a vacuum drying oven at 60°C. It was 0.89% of the pulp weight. To isolate fatty acids, the lipids were hydrolyzed [3], and then they were methylated with freshly prepared diazomethane [4]. The composition of the fatty acid methyl esters obtained was determined by gas chromatography on an Agilent 6890N instrument with a flame ionization detector and identified by retention time in comparison with model samples [5] (Table 1).

TABLE 1.**The Composition of Fatty Acids of Total Lipids of Flesh of Fruits of *Zizyphus jujuba*, % GC by weight**

Fatty acid	Total lipids
Capric (10:0)	0.18
Lauric (12:0)	1.35
Myristic (14:0)	1.86
Myristoleic (14:1)	5.73
Pentadecanoic (15:0)	0.38
Palmitic (16:0)	18.80
Palmitoleic (16:1)	49.02
Margaric (17:0)	0.65
Stearic (18:0)	2.72
Oleic (18:1)	10.76
Linoleic (18:2)	5.09
Arachic (20:0)	0.94
Gadoleic (20:1)	0.15
Behenic (22:0)	1.40
Lignoceric (24:0)	0.80

It can be seen (Table 1) that the main saturated acids are palmitic (16:0) and stearic (18:0). From unsaturated acids, it should be noted a high percentage (49.1%) of palmitoleic acid (16:1), which has antitumor and antimicrobial effects and the presence of oleic acid (18:1) – 10.76%.

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ECOLOGICALLY SAFE TECHNOLOGY FOR MANUFACTURE OF ACONITINE ALKALOID OF HIGH PURITY FROM *Aconitum soongoricum* TUBERS

O. T. Juraev, D. K. Mutalova, A. Z. Sadykov, Sh. Sh. Sagdullaev

Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

Aconitine is widely used in medical experimental practice for obtaining models of heart pathology in laboratory animals and searching for new drugs for the treatment of cardiovascular diseases [1]. Homeopathic medicine "AFLUBIN" based on aconitine of high purity (MEDICE Arzneimittel Petter GmbH, Germany) also known for its anti-inflammatory properties.

Companies in different countries produce alkaloid aconitine ("Sigma-Aldrich", Germany, "Merck", France, etc.) of different purity (70–98%) [2].

According to the technology developed by us earlier, our Institute produces aconitine bioreagent with purity not less than 96% [3].

Recent times, the need for a high pure aconitine has increased. MEDICE Arzneimittel Petter GmbH, Germany expressed its readiness to sign a long-term contract (for the next 5–10 years) for the purchase of aconitine alkaloid with purity more than 98.5%.

We have developed a new technology for the production of aconitine alkaloid of high purity (99.0–100.0%) from *Aconitum soongoricum* tubers eliminating the use of some solvents such as chloroform and diethyl ether. According to this method, the plant raw material is extracted with a 75–85% solution of ethanol, thickened, and an aqueous residue obtained. Purification of the main product from the concomitant alkaloids (karakoline, songorine, mesaconitine, 3-dihydroxyaconitine, 15-dihydroxyaconitine, napelline, etc.) and non-alkaloid impurities starts after alkaloids precipitation from the aqueous residue (mainly non-alkaloid impurities and some concomitant alkaloids) and processing the sum of alkaloids with alcohol (all concomitant alkaloids except 3-dihydroxyaconitine and 15-dihydroxyaconitine not precipitated). Technical aconitine can easily be purified from 3-dihydroxyaconitine and 15-dihydroxyaconitine by column chromatography using alumina with Brockman activity I as the sorbent. An elution system was anhydrous chloroform. The polarity of the eluent was adjusted by the addition of ethanol. The product of high purity (99.0–100.0%) was obtained by recrystallization of the final product from methanol.

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SYNTHESIS AND X-RAY ANALYSIS OF α-AMINONITRILES

M. T. Meylieva[1], A. A. Kodirov[1], N. I. Mukarramov[2], K. Turgunov[2]

1) Karshi State University, Karshi, Republic of Uzbekistan
2) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz

The use of chemical plant protectors is one of the most important agro-industrial methods for increasing the yield of agricultural crops. Their use, including plant growth regulators, contributes to the increasing of plant resistance to disease and unfavorable conditions, early ripening of the crop, increased yield and the production of a higher-grade product. One of the promising classes of compounds, α-aminonitriles – the nitriles of vital α-amino acids can be classified as plant growth stimulants [1–3].

Along with this, α-aminonitriles have several reaction centers in their molecule (nitrile, amino and activated methylene groups, as well as β-carbon atoms, which can undergo various chemical transformations) [4].

To study the stereochemistry of α-aminonitriles by X-rays we synthesized *N*,*N*′-bis-(α-cyanisopropyl) ethylenediamine.

X-ray diffraction analysis shows that the asymmetric part of the crystalline cell consists of one molecule of α-aminonitrile. The length of bonds between atoms corresponds to statistical values.

Analysis of intermolecular interactions shows the formation of symmetric hydrogen bonds in NH ... NC functional groups in the crystals.

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RATIONAL USE OF LOCAL RAW MATERIAL RESOURCES IN TECHNOLOGY OF COSMETIC GELS

G. M. Khakberdiyeva, Ya. K. Nazirov, A. T. Sharipov

Tashkent Pharmaceutical Institute, Republic of Uzbekistan, Tashkent,
Mirabad district, Oybek St., 45

In recent years, the condition of the atmosphere and the hydrosphere from where come to an organism various including chemical compounds, harmful to the person, worsenedconsiderably. We developed compositions of cosmetic gel of immunosupressored action considered these features.

Drug under the conditional name Onbiks-2 is synthesized under the leadership of professor N. I. Baram by scientists of Laboratory of Polyphenols of Institute of Bioorganic Chemistry,Academy of science of the Republic of Uzbekistan, and it was offered for development of technology of receiving cosmetic gel of immunosupressored action to use in plastic surgery. Taking into account physical and chemical properties of substance, the optimal structure including meeting the requirements of auxiliary carriers was developed. In optimization of the structure, we were guided by the following properties inherent in cosmetic. For the prevention of a casting-off of a donor skin it is necessary to consider all factors which promote the correct implantation of alien skin, first of all the picked-up composition and a way of putting cosmetic. The following carriers for the offered cosmetic (table 1) which were in turn used in development of five structures of carriers were chosen and designated on the maintenance of each series on the quantitative content of the local collagen received by our scientists under the leadership of the honored worker of science of the Republic of Uzbekistan, professor S. N. Aminov.

TABLE 1. **The Colloids Used as a Part of Cosmetic Gels**

Natural colloids	Amylum	Cellulose
Tragacanth	Vegetable starch	Methyl cellulose
Alginates	Animal starch	cellulose glicollic acid
Collagen	Dextran	Ethylcellulose

Designating value of albuminous colloids it should be noted their efficiency in respect of construction them from amino-acid chains of various length and, depending on a way of processing, they may contain also free amino acids; thus, they can quite be compared to albuminoushydrolysates that undoubtedly accelerates their absorbability. Derivative cellulose mainly carry out a role of stabilizers of gels. The kind of Amylum causes augmentation, or decrease of viscosity of the offered gels as after surgical intervention, use of gels of smaller viscosity follows and in process of rising of an angenesis the augmentation of viscosity of gels is accepted and effective. The drug Onbiks-2 was administered in structure gels in the form of 2% a leg of aqueous solution and homogenized in five series of carriers by conditionally designated Roman digits. When studying quality indicators of the developed structures by the following criteria: appearance, tiksotropical properties of viscosity and parameters of a point of a current, character of a syneresis, pH, loss of weight by the most optimum counted a basis at number IV which contains 2% solutions of collagen T, solution of Amylum, solution of sodium of carboxymethylcellulose and Glycerinum in the ratio 2:4:1:3. Researches on studying of quantitative content of the main active ingredient at a development stage.

CRYSTAL STRUCTURE OF THE(2-OXO-1,3-BENZOXAZOL-3(2*H*)-YL)ACETIC ACID

J. M. Ashurov[1], N. J. Obidova[1], H. B. Abdireymov[2], B. T. Ibragimov[1]

1) Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, M. Ulugbek Str. 83, Tashkent 700125
2) Karakalpak State University, Nukus str. Abdirova 1, Karakalpakstan 742012

Benzoxazolone derivatives show biological activity in many fields. (2-Oxo-1,3-benzoxazol-3(2*H*)-yl)acetic acidis a member of a biologically active class of compounds. Here we report the structure of the compound (2-oxo-1,3-benzoxazol-3(2*H*)-yl)acetic acid (**I**). Its molecular structure in the crystal has been determined by X-ray diffraction. Molecules of **I** (Fig. 1) show two relevant intramoleculardegrees of freedom, namely the relative orientation of thesubstituent at N with respect to the benzoxazolone plane andthe conformation within the carboxylic acid moiety. Theseparameters can be associated with the torsion angles C6–N1–C8–C9, θ_1 and N1–C8–C9–O3, θ_2. Molecules of **I** consists of an essentially rigid benzoxazolon system. Both the benzene ring (C1–C6) and the fivemembered heterocycle (C1, O1, C7, N1, C6) are each planar within error and almost coplanar with each other, with a dihedral angle of 0.36 (3)°. Both substituents are slightly displaced from the least-squares plane through the heterocycle, with distances of 0.0122 (5) Å for the carbonyl oxygen atom O2 and 0.0396 (6) Å for C8 associated with the acetyl group. Two torsional degrees of freedom are required to describe the overall non-planar molecule: the heterocycle and the acetyl group are almost perpendicular, with C6–N1–C8–C9 of –91.82 (6)°, and the conformation within the acetyl moiety can be described by N1–C8–C9–O3 with –10.57 (8)°.

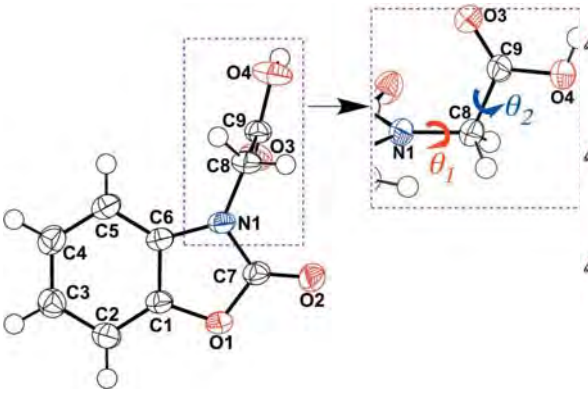

Fig. 1. Molecules of I.

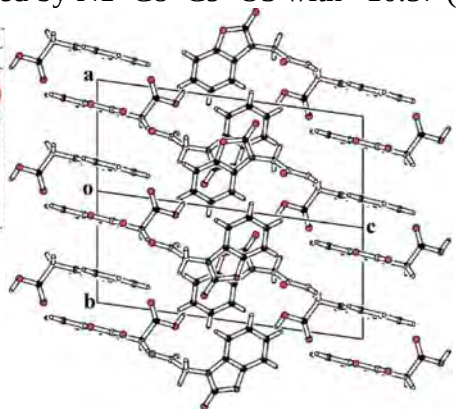

Fig. 2 Packing in crystals of I.

Packing of **I** (Fig. 2)in the crystal is dominated by two kinds of interaction: 1) Moderately strong classical O–H···O hydrogen bonds between the carboxylic acid and the keto function of a neighbouring molecule with a donor·acceptor distance of 2.6177 (9) Å link the molecules into chains in the [010] direction. 2) Dipole–dipole interactions play an important role.

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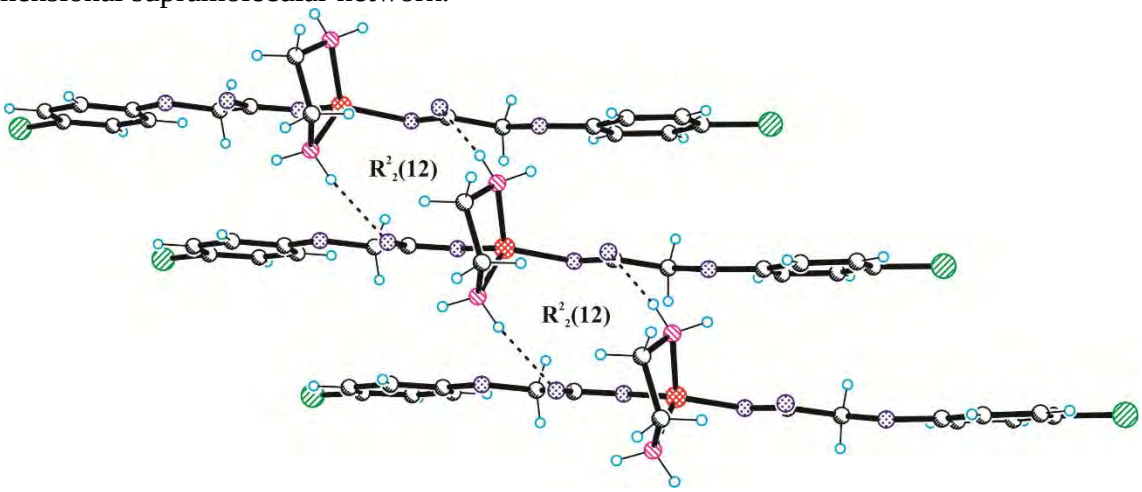
SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF THE MIXED LIGAND COMPLEX BIS((P-CHLOROPHENOXY)ACETATO-O)-(ETHYLENEDIAMINE-K^2N,N')-ZINC(II)

J. M. Ashurov

Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, M. Ulugbek, Str. 83, Tashkent 700125, Uzbekistan

Phenoxyacetic acid and its derivatives are biologically active compounds which are widely used as herbicides and plant growth substances. The interaction of metal ions with *p*-chlorophenoxyacetic acid (*p*CPA) results in theformation of complexes in which it demonstrates monodentate, bidentate and tridentate. *p*CPA also can show bridging and catena forming properties. Here, we report the synthesis and structure of the title compound $[Zn(C_8H_7ClO_3)_2(C_2H_8N_2)]$. The mononuclear title complex, $[Zn(C_8H_7ClO_3)_2(C_2H_8N_2)]$, was obtained by the reaction of zinc (II) acetate dihydratewith *p*CPA and ethylenediamine in a mixture of water and ethanol solution. The Zn (II) atom has a tetrahedral coordination, involving two carboxylate O atoms of two monodentate *p*CPA ligands and two N atoms of one bidentateethylenediamine molecules. The pCPA ligands are asymmetrically coordinated to the Zn atom with two different C–O distances of 1.967 (3) and 1.978 (3) Å. The dihedral angles between the N1/Zn/N2 plane and the O/Zn/O′ planes are 87.61(7)°. The interplanar angles between the acetate and *p*-chlorophenoxy planes in the two independent ligands are 5.51 and 5.98°. In the crystal, molecules are linked by N–H···O hydrogen bonds, forming chains propagating along [100], which are linked by C–H···O hydrogen bonds, forming a sheet structure. Two N–H···O hydrogen bonds between the NH_2 group and carbonyl oxygen atoms from neighbouring molecules make antiparallel C(6) chains that are interwoven into subsequent $R^2_2(12)$ rings.The molecules are further linked by C–H···π stacking of the benzene rings and methylene groups (pCPA) and Cl···Cl interactions, generating a three-dimensional supramolecular network.



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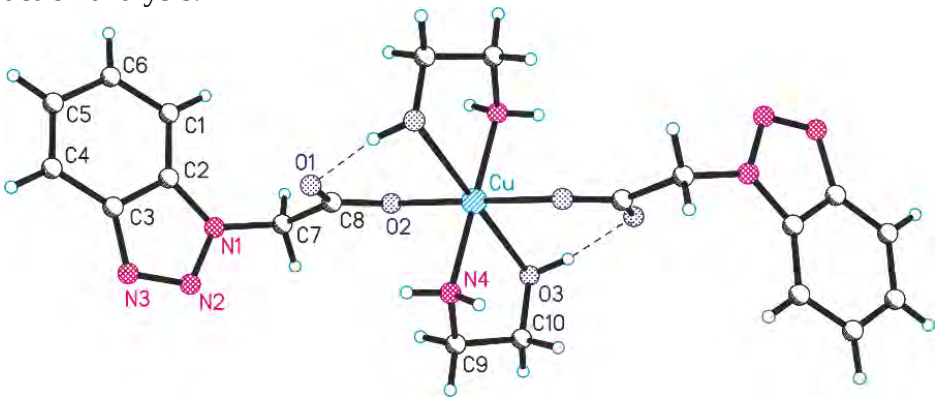
HETEROLIGAND COPPER(II) COMPLEXES WITH 2-(1H-BENZOTRIAZOL-1-YL)ACETIC ACID AND MONOETHANOLAMINE: SYNTHESES AND CRYSTAL STRUCTURES

G. K. Alieva[1], J. M. Ashurov[1], H. B. Abdireymov[2], B. T. Ibragimov[1]

1) Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, M. Ulugbek Str. 83, Tashkent 700125
2) Karakalpak State University, Nukus str. Abdirova 1, Karakalpakstan 742012

Benzotriazol derivatives exhibit a good degree of analgesic, diuretic, anti-inflammatory, antiviral and antihypertensive activities.Heteroligand complexes of a series of metals with benzotriazol derivatives were also studied and characterized.

The study of systems containing a metal, a complexone, and an additional ligand is an important scientific practical problem, because mixed complex formation increases the biological activity of the metal ion. Monoethanolamine (MEA) containing nitrogen and oxygen atoms was chosen as an additional ligand. In this work, heteroligand complexes of the composition $[Cu(BTA)_2(MEA)_2]$ (**I**), (BTA = (1H-benzotriazole-1-yl)acetic acid) were synthesized for the first time, and their molecular and crystal structures were determined by X-ray diffraction analysis.



The asymmetric part of the crystal of **I** contains one BTA anion coordinated to the metal through the carboxyl O atom and one MEA molecule chelating the metal by two heteroatoms (O, N). The Cu atoms in **I** occur in special positions at inversion centers. In complex **I**, the Cu–O(2) and Cu–N(4) bond lengths are 2.030 (3) and 1.981(3) Å, respectively, the length of the Cu–O(3) axial bond is 2.492(3) Å. The apical Cu–O bond distance is the longest (2.492(3) Å) due to the Jahn Teller effect.

In the crystal of **I**, an intramolecular hydrogen bond is present between the H atoms of the O(3) MEA molecule and the O(1) atom of the carboxyl group.The intermolecular hydrogen bond N(4)– H(4A) Å · O(2) (O · O3.048(4) Å) is formed in complex **I** between the O(2) atoms of the carboxyl group and the amino groups of MEA. The eight membered pseudo heterocycles with the graph setS(8) is formed in the structure due to this hydrogen bond.

This work was supported by the Academy of Sciences of Uzbekistan, project no. BA-FA-F7-004.

COMPLEXES ON THE BASE OF NATURAL COMPOUNDS – DERIVATIVES OF BENZOIC ACID

A. B. Ibragimov

Institute of General and Inorganic Chemistry of Uzbekistan Academy of Sciences,
M.Ulugbek Str.,77a

Some simplest derivatives of benzoic acid are occurred naturally and demonstrate wide spectrum of biological action. *P*-aminobenzoic acid (vitamin B_{10} or H_1) and *p*-hydroxybenzoic acid (PHBA), which possess weak antimicrobial and growth stimulating action are such compounds. Ethanolamines are also characterized by analogical types of the bioactivity. In order to enhance bioactivity of these compounds due to their synergism, one has to synthesize substances containing both components. Therefore we prepared organic salt and metal (coordination) complex on the base of these natural compounds and monoethanolamine (MEA).

The structures of vitamin B_{10} salt with MEA (**1**) and a mixed-ligand complex of Cd with PHBA and MEA (**2**) are shown in Figs. 1 and 2.

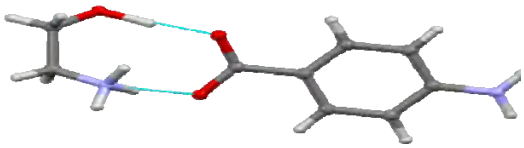


Fig. 1.

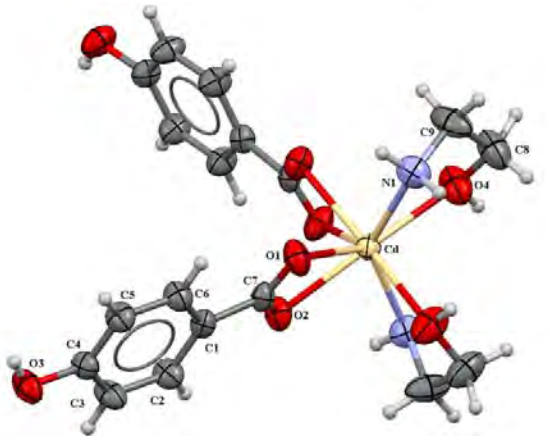


Fig. 2.

There are one molecule of vitamin B_{10} and one molecule of MEA in the asymmetric part of the orthorhombic unit cell of the compound **1**. The nitrogen atom of the MEA molecule is protonated owing to transferring of the vitamin B_{10} molecule into a benzoate form. The 1:1 supramolecular complex is formed due to a generation of the two intermolecular H-bonds between carboxylate group of the vitamin B_{10} molecule and amino- and hydroxyl-groups of the MEA molecule. These H-bonds may be identified by synthon $R_2^2(8)$, which serves for molecular recognition of the components in the supramolular association.

In the mixed-ligand complex Cd-ions coordinate 2 MEA and 2 PHBA molecules. Metal ion is located on an inversion center. Each ligand is coordinated by bidentate mode. The PHBA molecules are in a benzoate form in order to compensate of the metal ion charge.

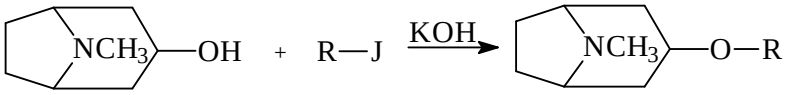
SYNTHESIS OF *O*-ALKYL DERIVATIVES OF TROPINE

I. I. Okhunov, Sh. Zhurakulov, U. T. Karimov, N. I. Mukarramov

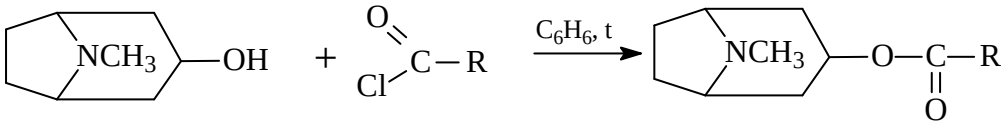
Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, e-mail: salima_aripova@mail.ru

Interest to research of tropane alkaloids is due to the fact that the many compounds of this class have valuable pharmacological properties and are still used in medicine.

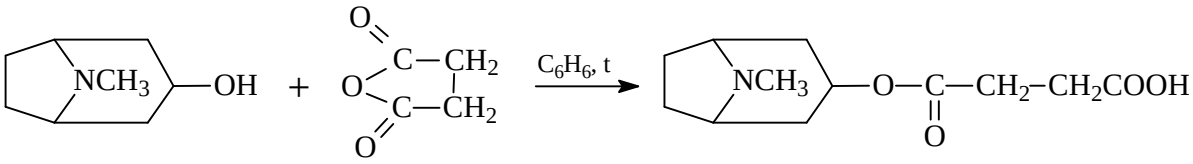
It is known that tropane alkaloids from the plants of *Convolvulaceae* family possess high physiological activity and some of them are used in medicine. So, the alkaloids of the tropines, atropine, scopolamine, hyoscyamine, which possess cholinolytic and spasmolytic properties, are used in neurology, surgery and in the treatment of eye diseases. In-depth pharmacological studies of tropane alkaloids have shown that they have a pronounced m-cholinolotic effect. In order to obtain highly pharmacologically active derivatives of the alkaloid tropine, several alkyl halide reactions were carried out.



R= $-C_4H_9$; $-C_6H_{13}$; $-C_7H_{15}$; $-(CH_3)CHCH_2$; $-C_4H_9CH_2$;



R= $-CH_3$; $-C_6H_5$



TECHNOLOGY OF NATURAL POLYMERS OBTAINING FROM WASTE OF SILK PROCESSING

R. Yu. Milusheva, O. B. Avazova, A. T. Abdurasulov, S. Sh. Rashidova

Institute of Polymer Chemistry and Physics, Uzbekistan Academy of Sciences, 100128, Tashkent, Kadiriy str.,7 b, e-mail: carbon@uzsci.net

When developing the technology for extracting valuable components from silk waste, priorities are given to obtaining polymer systems for solving the problems of the agro-industrial complex, creating biologically active materials for agriculture (fish farming, poultry farming), medicine, food industry, and preserving environmental safety.

One of the main types of silk-milling waste in Uzbekistan are the silkworm pupae (about 4 thousand tons), which represent a natural composite of chitin, lipids, protein (up to 50%), syricine and fibroin.

When processing pupae of the silkworm at the initial stage, up to 18–25% of the fat-and-oil substances used for various technical purposes are allocated. A qualitative analysis of the lipid component of pupae showed that the oil contains limiting and unsaturated higher fatty acids, glycerophosphates, monoglycerides, cholesterol. They can be used as substitutes for vegetable oils in the perfumery, paint and varnish, pharmaceutical and other industries for the production of particularly expensive products, thanks to some properties of the lipid complex.

The second stage of processing of pupae of the silkworm is the isolation of the protein, i.e. Deproteination. To prevent denaturation of the protein, the conditions of technological operations are selected: the temperature is not more than 80°C, the composition of the solvents is stepwise for the initial and complete isolation of the protein part by an alkaline solution, coagulation, protein separation conditions (centrifugation – 10.000 rpm). To remove salts and other low-molecular impurities, the protein precipitate is dialyzed. The nitrogen content of the isolated protein varies from 10 to 15%. Analysis of the amino acid composition of proteins isolated from pupae of silkworms showed that they contain essential amino acids: lysine, histidine, threonine, isoleucine and phenylalanine, as well as partially replaceable amino acids: arginine, glycine and tyrosine. On IR spectra, all absorption bands of polypeptides are observed. The protein isolated from pupae of the silkworm contains up to 90% of protein components with a low molecular weight of up to 20 kDa, which will be in demand in the production of feeds for fish and poultry. A protein with a low molecular weight is easily assimilated by living organisms. It was also found that the protein from pupae of silkworms according to the parameters of acute toxicity, belongs to the category of low-toxic substances (Class IV).The third stage of processing is the isolation of chitin (3–4.5%) after the stages of deproteinization and demineralization. The resulting chitin has an average molecular weight of from 100 to 200 kDa. The fourth stage of processing is the production of chitosan of various degrees of deacetylation, which ranges from 70 to 95%, molecular weight up to 150 kDa.

The obtained protein was successfully tested as an active component of fodder for fish farming and poultry farming: fish productivity of up to 20 kg/m3 was achieved, which is much higher than normative indices, and egg production by 25% in comparison with the control. Dedicated according to this technology, the protein has a wide application prospect for breeding fish and poultry.

THE DEVELOPMENT TECHNOLOGY OF CAPSULE ON THE BASIS OF SUBSTANCE GLACEMBRIN

M. I. Madrakhimova, B. A. Abdurakhmanov, G. B. Sotimov

S. Yu. Yunusov Institute of the Chemistry of Plant Substances of AS of RUz,
100170 Uzbekistan, Tashkent, M. Ulugbek str., 77, e-mail: latin06@mail.ru

The active substances for obtaining capsule “Glacembrin” is dry extract that received from plant *Glycyrrhiza glabra* L, family *Fabaceae*.

The researches of technology properties of substance «Glacembrin» show that it doesn′t have positive characteristics of flowability.

For obtaining flowability mass with positive technological parameters is applied method of wet granulation with using excipients: sodium hydrogen carbonate, starch, glucose, sucrose, lactose, microcrystalline cellulose (MCC), methylcellulose (MC), sodium carboxymethylcellulose (Na CMC); Binding: purified water, ethyl alcohol, starch paste, sugar syrup, solutions: carboxymethyl cellulose (CMC), hydroxyethylcellulose (OEC), hydroxypropyl methylcellulose (CMO), polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), polyethylene glycol 400, gelatin; Antifriction: potato starch, talc, polyethylene oxide-4000, aerosil, stearic acid, calcium stearate, magnesium stearate.

After choosing necessary excipients are obtained encapsulated mass with good technological properties.

Based on actual data the capsule «Glacembrin» characterized like hard gelatine capsule. Based on research of technological properties of dry extracts, the chosen excipients to aim for obtain granulate with optimal technological properties and quantity of active substance for dry extract «Glacembrin».

The optimal volume of filled capsule «0» was chosen respectively.

The capsule of «Glacembrin» is obtained of proposed technology by all parameters conform to requirements of GPh IX, issued II.

Thus, the technological properties of the dry extract of glacembrine have been studied and showed that for encapsulation necessary to improvement flowability by previously wet granulation and added disintegrates and antifriction excipients.

CHEMICAL MODIFICATION OF PEAT BY THE METHOD OF ESTERIFICATION

M. V. Efanov, M. P. Sartakov

LLC “MIP “Ugra-Biotechnology”,
628011, Russia, Khanty-Mansiysk, Studencheskaya street, 27

It is known that the process of acetylation of cellulose-containing materials can be used to obtain the thermoplastic esters for use as environmentally friendly bio-resistant and hydrophobic binder materials. Mechanochemical activation method plant material for chemical modification is the most promising in the light of economy and ecology [1]. However, works on the systematic study of the process of acetylation (esterification) of peat in various environments literature.

The developed method of esterification of peat consists of two phases, alkaline pretreatment and acetylation [2]. Alkali activated peat mass of 2.0 g was placed in a round bottom flask 100 mL capacity, provided with reflux condenser and placed in a heating mantle heated to 100 0C. The reaction mixture was added acetic anhydride (1 mol Ac_2O on 1 mole of Oh-groups of the peat) and kept it at 100°C for 2–8 h. At the end of the reaction, the resulting product was precipitated with water and washed the residue from acetic acid to neutral medium. The product was dried to constant weight in a desiccator. The solubility of the products acetylation of peat was determined in acetone, and the contents of the linked acetyl groups after saponification alcoholic solution of alkali with the subsequent return of the conductometric titration of the resulting acetic acid [3].

The influence of duration mechanochemical acetylation activated in the presence of NaOH peat on the properties of the obtained products. It is shown that the peat milling in a planetary mill AGO-3 in the presence of NaOH increases its reactivity towards esterification, and particularly to the formation of a partially soluble in acetone products. With increasing duration of acetylation is an increase in the content of the linked acetyl groups in the resulting product from 12 to 18 % and their solubility in acetone. It is established that with increase of the duration of the process of acetylation of peat from 2 to 8 h increases the degree of conversion of his groups from 48 to 73 %.

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EXTRACTION AND STUDYING OF HUMIC ACIDS OF SOME BROWN AND COALS OF TAJIKISTAN

Zh. Oliftayeva, M. Umarkhon, S. V. Aliyeva, Sh. Kh. Khalikov

National University, Khorog State University, Tajikistan, 734025, Dushanbe, Rudaki Ave., 17, e-mail: Xalikov1941@mail.ru

Research of humic acids (H.a.) it is connected with their to rich composition, complex structure and high biological activity.

Object of our research became, successfully developed pools of stone and brown coal as "Shurob", "Fon-Jagnob", "Ziddi", "Sayyod", "Nazar-Aylok", "Kurtekin".

Release of humic acids was the purpose of the real work (H.a.) from brown and coals of the called fields, definition of cindery elements of coals and H.a., and also studying of structural and group structure of these connections. The initial stage of this work consisted in definition of humidity, an ashcontent, bitumens. Then carried out extraction H.a. and definition of element composition of ashes of coals and H.a., the main components of ashes of examinees of coals are 21 macro and microelements: Ti, Ni, B, Mo, Zn, Co, Na, Ca, Al, Mn, Sn, Mg, Fe, Pb, Si, Cr, Cu, V, P, Ag which K maintenance fluctuates 0.00086 (Pb) to 27.10% (Si).

These elements in the course of extraction H.a. in the alkaline environment from coal partially pass in the connected look into composition of extract. H.a., allocated from coal samples with water and alkaline extraction with the subsequent their sedimentation in acidic environment [1], and also a by dimetilsulfoksid (DMS) method in the option changed by us. An exit H.a. the coals extracted from samples, fluctuates from 9% to 23% (Table 1). Researches by means of IK – nuclear magnetic resonance ^{13}C of spectroscopy have shown to polyfunctionality allocated H.a.. A research by means of the TSK-method showed the komplementarno-connected high-molecular particles with low-molecular connections, forming irregular a structure with transition from friable structure to more a decent form.

TABLE 1. **Content of Excipients and Humic Acids in Samples of the Called Fields of Coals**

Names fields coal		Contents, %					
		Humidity	Ash-content	Bitumens	*exit of humic acids	**exit of humic acids	ash-content of humic acids
1	Shurob	7.2–11.59	10.01–13.36	11.1–14.70	22.66		2.43–5.94
2	Fon-Jagnob	19.8	2.28	18.18	15.4	19.90	0.8
3	Ziddi	5–19.92	2.18–8.96	7.14	16.5		4.37
4	Nazar-Aylok	2.65	2.6–3.55	2.04–5.54	9.54		0.26
5	Sayyod	6.92	16.4–32.11	15.21	16.6	17.50	0.04
6	Kurtekin	2.2–9.83	3.0–4.5	3.0–3.62	13.19		0.25

*It is received by a pyrophosphatic method; **it is received by a dimetisulfoksidny method.

SYNTHESIS AND HERBICIDE ACTIVITIES OF HETEROCYCLIC THIOAMIDES

U. M. Yakubov[1], R. P.Zakirova[1], D. A. Nasimova[2], N. B. Pirnazarova[2], B. Zh. Elmuradov[1]

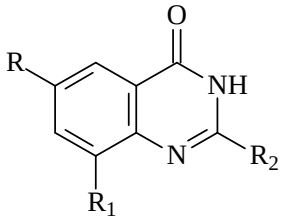
1) Acad. S. Yu.Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: plant_inst@icps.org.uz
2) Qarshi State University, Qarshi,Uzbekistan

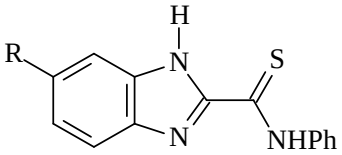
Plant protection using chemicals is very important for the increasing the efficiency of agricultural activities. Herbicides are widely used in the agro-industrial complex. In this regard, the search for new biologically active compounds that can increase the yield of crops is an important and urgent task of the organic synthesis.

Investigation of the herbicidal activity of the heterocyclic thioamides was carried out in laboratory conditions on sprouts of wheat and cucumbers. Control seeds were soaked in water, samples in 0.5% and 0.05% concentration of the test compounds for 18 hours. After the plug, the seeds were spread on filter paper in Petri dishes, moistened with an equal amount of water, and germinated for 5 days at the temperature 20–22°C in a thermostat. Then the germination parameters of the seeds were examined, and the length of the roots of the seedlings and the height of the stem part of the plants were measured.

The results of the initial tests showed that the compounds in 0.5% concentration showed herbicidal activity and completely suppressed the development of the seeds of both cultures.

Inconcentration 0.05%the compounds **1**and **2** showed greater activity on wheat. They reduced seed germination on 50%. Compounds **3–5** reduced germination on 40%. The greatest suppression of sprout growth was observedin compounds **1**, **3**, and **5**. The length of the roots in these variants was below control by 60%, the stem by 50%:





1, R= R_1=R_2= CH_3; **2**, R= Cl; **3**, R= H; **4**, R= NO_2
5, R=R_1=H; R_2= C(S)NHPh

In the culture of cucumbers, the lowest germination was observed when the compound **4** was exposed to 0.05% concentration, on third day only 30% of the seeds went up, on fifth day – 69%. On the growth of sprouts the greatest activity was exerted compound **1** in the same concentration. The length of the root was below the control by 42%, the stem by 29%.

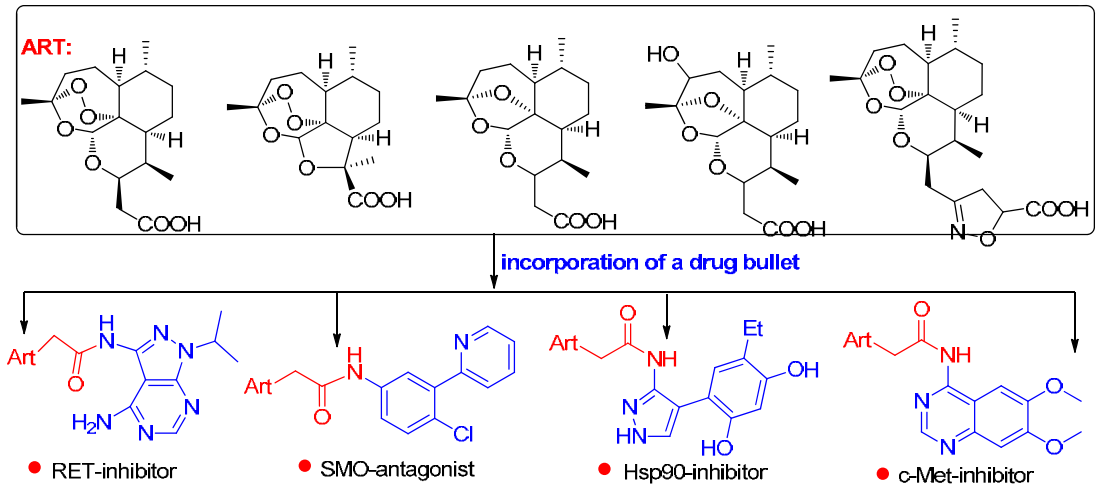
Thus, the obtained results prove the perspectives of creating herbicide preparations based on the thioamide compounds.

ANTICANCER DRUG DISCOVERY BASED ON NATURAL PRODUCTS

Gang Liu, Ao Zhang

CAS Key Laboratory of Receptor Research, and Synthetic Organic and Medicinal Chemistry Laboratory (SOMCL), Shanghai Institute of Materia Medica (SIMM), Chinese Academy of Sciences, Shanghai, China 201203; e-mail: aozhang@simm.ac.cn

The natural product artemisinin (Qinghaosu) is a well-known anti-malarial drug, and has been repositioned for the development of novel antitumor agents due to its unique structure and safety profile. Nevertheless, compared to thier potent anti-malarial activity, the majority of reported artemisinin analogues (artemalogues) only displayed limited in vitro and in vivo anticancer potency. In addition, the precise anticancer mechanism of these artemalogues) are also poorly understood. Therefore, chemical modification on artemisinin is highly needed both for the development of more potent anticancer artemalogues and for the understanding of the mode of actions. To generate structurally more diverse artemalogues, we conducted an alternative medicinal chemistry campaign by different targeted drug bullets, thus affording a series of structurally novel targeted artemalogues. Several compounds demonstrated superior *in vitro* antiproliferative effects against cancer cell lines with further developmental potentials.



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Liu G.; et al.: *RSC Adv.* **2016**, *6*, 98975-98984
Liu G.; et al.: *Eur. J. Med. Chem.* **2015,** *103*: 17-28

Publications

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ИП "NOBEL PHARMSANOAT" (РУз)

ЦИТИЗИН

ДЫХАТЕЛЬНЫЙ АНАЛЕПТИК - ОСНОВА ПРЕПАРАТОВ ОТ КУРЕНИЯ

Thermopsis alterniflora

Действующее вещество:
Алкалоид цитизин, получаемый из травы дикорастущего растения *Thermopsis alterniflora* (термопсис очередноцветковый).

Показания к применению:
Цитизин применяют для получения «Цититона» – стимулятора дыхания и кровообращения (0,15% раствор Цитизина для инъекций). Применяют Цититон в случае рефлекторных остановок дыхания при операциях и травмах, в случае ослабления дыхательной и сердечно-сосудистой деятельности, при различных интоксикациях и инфекционных заболеваниях, при угнетении дыхания, кровообращения и в послеоперационном периоде, асфиксии новорожденных.

Применение препарата предписано при рефлекторной респираторной блокаде. Повышающее кровяное давление действие Цититона позволяет использовать его при шоковых и коллаптических состояниях; при респираторной и циркуляторной депрессии больных с инфекционными заболеваниями.

Цитизин является также активной субстанцией известного препарата Табекс (Болгария), обладающего холиномиметическим действием. Препарат Табекс применяется при хроническом никотинизме (табачной зависимости) – для отвыкания от курения.

Преимущества: При рефлекторных остановках дыхания (при операции, травмах и т.д.).
Цитизин может быть использован как дыхательный аналептик: в связи с процессорным эффектом может применяться при шоковых и коллаптоидных состояниях, при угнетении дыхания и кровообращения у больных.

Форма выпуска:
таблетки "Никотинабс" по 1,5 мг, №100;
инъекционный раствор "Цититон" - ампулы по 1 мл, 0,15%
Р. 09/158/3

Ташкент 100170, ул. Мирзо Улугбека, 77.
Факс: (+99871) 262 73 48;
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E-mail: Plant-inst@rambler.ru
www.uzicps.uz

РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ИП "NOBEL PHARMSANOAT" (РУз)

АЛЬБЕНДАЗОЛ

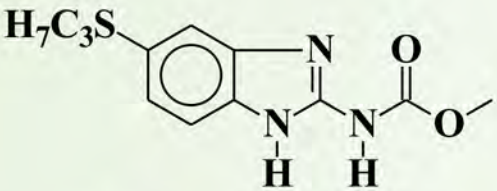
АНТИГЕЛЬМИНТНОЕ И ПРОТИВОПРОТОЗОЙНОЕ СРЕДСТВО

Нейроцистицеркоз, вызванный личиночной формой свиного цепня (***Taenia solium***).

Эхинококкоз печени, легких, брюшины, вызванный личиночной формой собачьего ленточного червя (***Echinococcus granulosus***). Используется в качестве вспомогательного средства при хирургическом лечении эхонококкозных кист.

Нематодозы: аскаридоз, трихоцефалез, анкилостомидоз, энтеробиоз, стронгилоидоз, некатороз; описторхоз, лямблиоз, микроспоридиоз, токсокароз.

Смешанные гельминтозы: капилляроз, гнатостомоз, трихиноз, гименолепидоз, тениоз, клонорхоз, кожные мигрирующие личинки, лямблиоз у детей.



2-Метоксикарбониламино-5-
-пропилтио-1***H***-бензимидозол

Препарат превосходит по эффективности декарис, вермокс, пирантел и др. Особенно эффективен Альбендазол в отношении личиночных форм цестод Echinococcus granulosus, Taenia solium и нематод Strongyloides stercolatis. Преимущества в сравнении с препаратами аналогичного действия заключаются в разовом назначении Альбендазола при трихоцефалезе и анкилостомидозах, более высоком паразитоцидном действии и в простой схеме лечения.

В качестве вспомогательного средства при хирургическом лечении эхонококкозных кист. Нематодозы: аскаридоз, трихоцефалез, анкилостомидоз, энтеробиоз, стронгилоидоз, некатороз; описторхоз, лямблиоз, микроспоридиоз, токсокароз. Смешанные гельминтозы: капилляроз, гнатостомоз, трихиноз, гименолепидоз, тениоз, клонорхоз, кожные мигрирующие личинки, лямблиоз у детей.

Противопоказания: Гиперчувствительность к Альбендазолу, беременность, период лактации, детский возраст (до 6 лет - безопасность не определена) с осторожностью. Угнетение костномозгового кроветворения, печеночная недостаточность, цирроз печени, патология сетчатки глаза.

Форма выпуска: Таблетки по 200 мг и 400 мг, №6 и №3.
Р. 08.10.2013

Ташкент, 100170, ул. Мирзо Улугбека, 77.
Факс: (+99871) 262 73 48;
Тел.: (+99871) 262 59 13, 262 05 48

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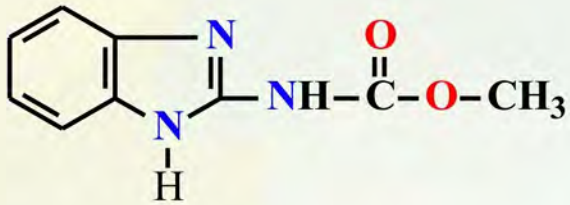
РАЗРАБОТЧИК ПРЕПАРАТА: ИНСТИТУТ ХИМИИ РАСТИТЕЛЬНЫХ ВЕЩЕСТВ ИМ. АКАД. С.Ю. ЮНУСОВА АН РУз (ИХРВ АН РУз)

ПРОИЗВОДИТЕЛИ: СУБСТАНЦИИ - ИХРВ АН РУз
ГЛФ - ЧНПП "RADIKS" (РУз)

МЕДАМИН

АНТИГЕЛЬМИНТНОЕ СРЕДСТВО

Действующее вещество:
2-Метоксикарбониламинобензимидазол



Медамин

Фармакологические свойства: Противогельминтный препарат, обладает активностью в отношении кишечных нематод. Проникает через оболочку гельминта и парализует его мускулатуру, в результате чего гельминт теряет способность фиксироваться в просвете кишечника. По противоглистному действию Медамин близок к мебендазолу.

Показания к применению: Медамин эффективен в отношении различных кишечных нематод. Применяется при лечении аскаридоза, трихоцефалеза, энтеробиоза, анкилостомидоза, стронгилоидоза.

Преимущества:
Медамин заменяет импортные препараты вермокс, карбендазим и декарис.

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DEVELOPMENT OF BIOADDITIVES BASED ON CAMEL MILK FOR PREVENTION AND THERAPY OF IRON-DEFICIENCY ANEMIA

O. Kh. Saitmuratova[1,2], N. J. Sagdiyev[1], Yo. U. Zokirov[2]

1) Acad. A.S.Sadykov Institute of Bioorganic Chemistry, e-mail: info@biochem.uz
2) Tashkent Pediatric-Medical Institute

There are some high efficiently iron containing preparations for the treatment of anemia. They are (Kobavit, Ferrum-Lek, Tardiferon and others) organic complex compounds and efficient enough. However, they possess side effects such as explicit allergic reactions, sickness, dizziness etc. Besides, these preparations are quite expensive and imported into our republic. A number of authors suggest that consumption of insufficient food containing bioavailabile iron and/or iron inflowing promoters as well as transport proteins and possibly ascorbic acid cause anemia. Authors recommend enriching the food consumption with bioavailable iron.

In this regard, search and development of anti-anemic food additives from local natural raw materials containing iron is one of actual problems. Milk and dairy products relate to those products. Camel milk exceeds dairy products of cattle, mare and others by contents of iron. It stimulates defensive power of the body for a long time and applied for treatment of not only anemia but also tuberculosis, chronic gastritis, colitis and a number of other diseases.

At the Institute of Bioorganic chemistry of Sciences Academy of Uzbekistan biologically active additives (BAA) on the basis of camel milk and dairy products (Ver-Mol-1 and Ver-Mol-2) have been developed. The chemical compositions (amino acids, carbohydrates, microelements) of the produced bioadditives have been studied.

It was determined that BAA contains all essential amino acids and significant quantity of iron and zinc which are easily digested/assimilated. Pharmacological investigations demonstrated that anti-anemic activity of BAA exceeds “Tardiferon” (product from Switzerland).

Thus, development of BAA (Ver-Mol-1 and Ver-Mol-2) based on camel milk will allow providing all region of Uzbekistan, first of all maternity hospitals with valuable products for the prevention of iron-deficiency anemia.

PHARMACOCORRECTION OF METABOLIC DISORDERS UNDER STRESS AND HEPATITIS IN RATS WITH ALLOXAN DIABETES BY FLAVONOID DRUGS

N. H. Yuldasheva

Acad. S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
Academy of Sciences of the Republic of Uzbekistan, Tashkent, e-mail: zainab@icps.org.uz

One of the main trends in modern regenerative medicine is the elaboration of effective pharmacological agents from plant material for the correction of disturbed adaptive processes of the organism under the influence of various unfavorable factors. In this context, the aim of our work was to determine the potential relationship identified earlier adaptogenic action of flavonoids with the appearance of their characteristic hepatoprotective activity. Experiments were carried out on the male rats weighing 150–180 g at their immobilization in the supine position during 16 hours. It was shown that the preventive introduction of the flavonoid sums from *Thermopsis alterniflora* (contains apigenin, formononetin, luteolin and others.) and *Vexibia alopecuroides* (contains glabrol, veksibidin, ammotamnidin et al.) at a dose of 50 mg/kg orally prevented increase of adrenal mass, as well as involution of the thymus and spleen under stress condition. The drugs prevented the gastric mucosa destructions, normalized the parameters of carbohydrate, lipid and protein metabolism in liver, inhibited the processes of free-radical oxidation and reduced the activity of antioxidant enzymes. These positive changes was more pronounced if the flavonoid sums were administered to the rats with developing paracethamol, heliotrine or carbon tetrachloride hepatitis on the background alloxan diabetes (we used animals with blood glucose levels of 200–250 mg%). The drugs not only significantly lowered blood glucose levels (on 30–40%, $p<0.05$), but also normalized the morphologically functional state of adrenal, thymicolymphatic system as well as metabolic and functional state of the liver. It was established the increase of glycogen stores, catalase and superoxide dismutase activity, significant reduce of the malondialdehyde and fatty degeneration rate, improve protein synthesis processes. Also there was the increase of bile excretion, the bile acids synthesis, cholesterol excretion and the hepatic metabolism of bilirubin level recovery.

Thus, the flavoniod sums from *T. alterniflora* and *V. alopecuroides* not only increase the resistance of the animal to long-term immobilization of rats in an uncomfortable position and different hepatitis on the background of alloxan, but also have a therapeutic effect to the liver in these conditions. The preparations on the base of flavonoids from these plants may be useful in protection of organism from the adverse effects of stress and disturbance of hepatobiliar system in hepatitis and diabetes.

EFFECTS OF EXOGENOUS ABSCISIC ACID ON *L*-PROLINE CONTENT IN COTTON SEEDLINGS WITH DIFFERENT RESISTANCE TO SALINITY

К. М. Kuldosheva, S. B. Navruzov, Z. Golubenko, N. A. Abdurashidova, A. A. Akhunov

Acad. A. S. Sadykov Institute of Bioorganic Chemistry, e-mail: info@biochem.uz

Salinity is one of the common adverse environmental conditions. Osmotic stress caused by high levels of NaCl leads to disruption in water balance, reduce a turgor pressure, the closing of stomata, inhibition of photosynthesis, and ultimately to the destruction of the membranes and the death of the organism. Under the influence of "salt shock" the formation of reactive oxygen species increases that leads to activation of antioxidant enzymes. In addition, the increase in the abscisic acid (ABA) content is one of the central aspects of plant response to the salt impact. Moreover, ABA increases the synthesis of low molecular weight antioxidant compounds such as proline.

The aim: study of the exogenous ABA effect on accumulation of L-proline in leaves of two cotton cultivars differing by their resistance to salinity.

TABLE 1. **Exogenous ABA effect on accumulation of L-proline in leaves of Gulistan and C-4727 cotton cultivars (n = 3; m ± M)**

Sample	The amount of proline, mkg/mL			
	Guliston		C-4727	
	1 h	24 h	1 h	24 h
Control	163.2 ± 1.2	162.9 ± 1.9	62.9 ± 1.3	67.8 ± 1.7
1 % NaCl	177.2 ± 1.8	158.5 ± 1.6	91.4 ± 2.1	56.5 ± 1.4
ABA	195.8 ± 1.1	135.2 ± 2.4	93.3 ± 1.6	60.6 ± 0.8
1 % NaCl + ABA	265.8 ± 1.5	116.6 ± 0.9	83.2 ± 1.7	63.9 ± 1.6

Given data are statistically different ($P < 0.05$)

Obtained results showed that in the first hours of stress the exogenous ABA increased the synthesis of *L*-proline in Gulistan and C-4727 cultivars up to 62.8% and 32.3%, respectively. After 24 h of salt stress in both cotton cultivars leaves the *L*-proline amount was lower compared to control. ABA could possibly increase the activity of antioxidant enzymes.

Thus, exogenous ABA increased accumulation of *L*-proline in Gulistan cultivar resistant to salinity, while the reverse was observed in C-4727.

Proline accumulation facilitates the "osmotic adaptability" that leads to decreasing of the internal osmotic potential and possibly contributes to salt tolerance.

MODERN CONDITION OF COTTON FIBER AND ITS PRODUCTION CLASSIFICATION

K. M. Karimkulov, N. K. Djuraeva

1) The Higher Military Customs Institute, State Customs Committee of the RUz, Tashkent
2) Tashkent Medical Academy, e-mail: Kurbonkul@inbox.lv

The value of cotton fiber production in the Republic of Uzbekistan occupies fifth-sixth place in the world production of cotton fiber and second place on its export. Cotton fiber is the main strategic goods of the Republic. Cotton production provides the cotton filament, waste cotton plant, waste of textile industry, cotton lint, cotton, cotton wool and many other wastes. The problems appear at the export of these mentioned products on classification of goods, on the goods nomenclature of Foreign Economic Activity of the Republic Uzbekistan.

World cotton industry developed more than two ages in the manner of independent national industry often on local rules and trade procedures, units of the measurement and internal standard quality. The size of the stacks and their density differed in miscellaneous countries. China releases stacks both on 80 kg, and 225 kg. The rate of the weight in South Asia are on stacks 170 kg, 400 pounds - in West Africa, 480 pounds of the stack are accepted in USA, 227 kilos stacks in Australia and 720 pounds of the stack in Egypt. The standards of quality are differ in many countries, including universal cotton standards and multiple national standards, supported national organization in many cottons-sow countries. Some countries have qualitative parameters, founded on numeral, which unite the color, texture and litter in one category, others use the letters. In some countries qualitative standards are differentiated on sorts, in the other countries distinguish the cotton and saw topple degenerate**.** The different standards quality do not find the concordant correlation, allowing produce the exact comparison of different sorts of cotton and its production.

As a result of complex study of physic-chemical and mechanical characteristic of goods filament was proved by us need to its classification of cotton filament and its products on Goods nomenclature of foreign economic activity. Herewith necessary to come from such parameter, as length filament, mass share vice and rubbish admixtures, linear density, moisture, factor to maturity, molecular mass, viscosity solution and etc. In requirement of international standard as main parameter of cotton fiber is accepted its length. In other words, there is practicability and need to provide in correspondence to with requirements of international standard applicable in practice state standards and standard specifications on cotton filament and its different marketable products. We designed methods of the determination of the new goods codes for cotton filament and its product on the base of their chemical composition, legally protecting economic interests of the Republic.

For the first time different kinds of cotton filament were investigate, but cellulose is chosen on the known method. Leaving the cellulose from miscellaneous sort filament was studied.

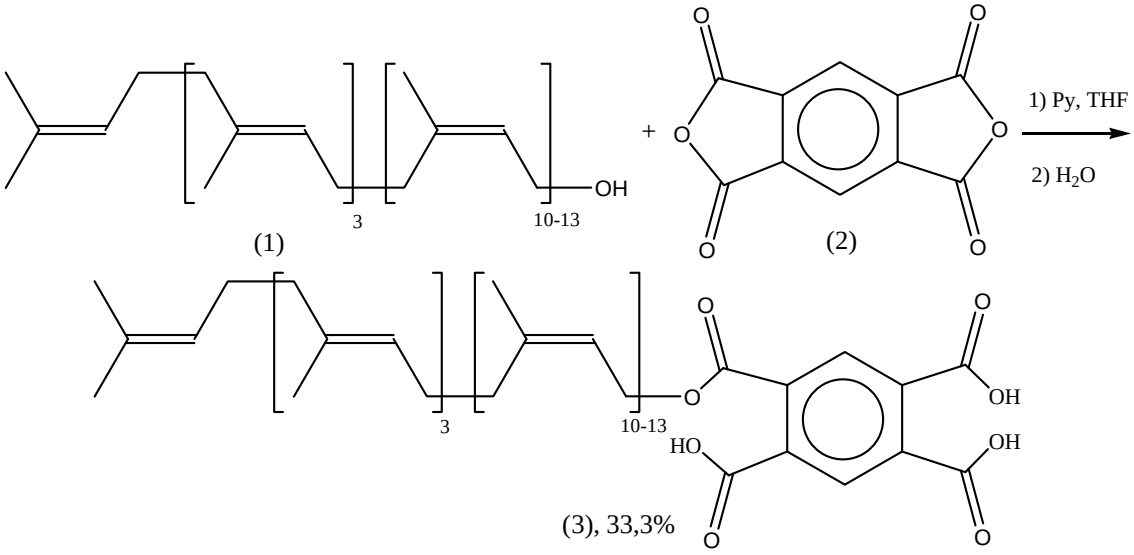
So, we consider reasonable to take the length of a filament as a main criterion in classification of cotton filament in Goods nomenclature of foreign economic activity, and include additional code numbers 10 and 11 into the subheading 5201000100.

ETHERIFICATION OF POLYPRENOLS BY PYROMELLITIC DIANHYDRIDE

F. T. Mukasheva[1], V. V.Veselovskiy[2], G. A. Atazhanova[1], S. M. Adekenov[1]

1) JSC "International research and production holding "Phytochemistry", Republic of Kazakhstan, Karaganda, 100009, M. Gazaliyev str. 4, fax: +7 (7212) 43 31 27, e-mail: phyto_pio@mail.ru
2) N. D. Zelinsky Institute of Organic Chemistry RAS, Moscow, Leninsky Prospect str. 47, Moscow, tel. +7 499 137 29 44

In recent years, polyprenols and their derivatives draw the attention of researchers in the capacity of potential sources of new medicaments with immunomodulatory, antiviral, hepatoprotective and wound healing activity. We synthesized the new derivative (3) of the present line based on the Siberian fir (*Abies sibirica* Ledeb.) polyprenols (1) - the mixture of homologs containing from 14 to 18 isoprene units.



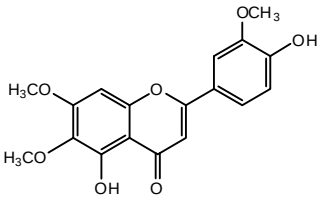
Monoether of pyromellitic acid (3) was obtained by processing of polyprenols (1) in argon atmosphere by pyromellitic dianhydride (2) in tetrahydrofuran solution in the presence of pyridine as an acylation catalyst, and by further hydrolysis of the reaction. The reaction path control was conducted by thin-layer chromatography method. The reaction mixture was extracted by methyl tertiary butyl ether, the extract was dried above anhydrous Na_2SO_4, was concentrated in vacuum and the residue was chromatographed on silica gel. The obtained polyprenilpyromellitate (3) is straw-colored amorphous powder, the yield is 33.3%. Its structure was determined on the basis of ^{1}H NMR and IR-spectroscopy data.

SYNTHESIS OF 2-(AZIDOALKOXY CHALCONE)CIRSILINEOL

G. M. Baisarov[1], G. K. Mukusheva[1], L. K. Salkeyeva[2], S. M. Adekenov[1]

1) JSC "International research and production holding "Phytochemistry",
Republic of Kazakhstan, Karaganda, 100009, M. Gazaliyev str. 4,
fax:+7(7212)433127, e-mail: phyto_pio@mail.ru
2) E. A. Buketov Karaganda State University, Republicof Kazakhstan,
Karaganda, 100000, Universitetskaya str., 28, e-mail: lsalkeeva@mail.ru

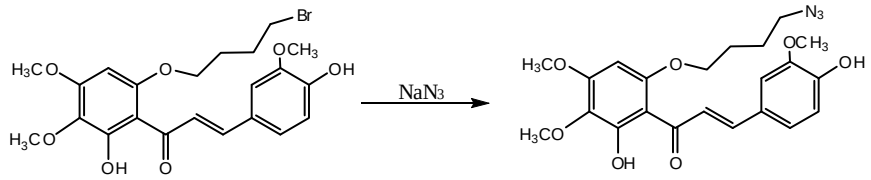
Flavonoid cirsilineol (**1**), isolated from *Artemisia glabella* Kar. et. Kir, is a potential source for the synthesis of biolologically active compounds, which is determined bysignificant antioxidative and hepatoprotective activities [1].



(1)

When cirsilineol molecule interacts with 1,4-dibrombutanin acetone with the presence of potassium carbonate, 2-(azydoalkoxy)chalcone of cirsilineol (2) is obtained. The reaction proceeds according to the scheme of Michael retro-reaction – *O*-alkylationwith formation of this derivative (2)with the yieldof 60.6%.

An azidation reaction with sodium azide under warming in DMF was performed based onmolecule (2), as a result a new derivative (*E*)-1-[6-(4-azidebutoxy)-2-hydroxy-3,4-dimethoxy-phenyl]-3-(4-hydroxy-3-methoxyphenyl) prop-2-en-1-one (3) with the yield of 35.6% was obtained.



(2) (3)

Composition and structure of these compounds are verified by ^{1}H NMR, ^{13}C, IR- and UV-spectrums data.

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NEW DERIVATIVES OF ARTEMIZETINE FLAVONOID

R. Zh. Khassenova, G. K. Mukusheva, S. M. Adekenov

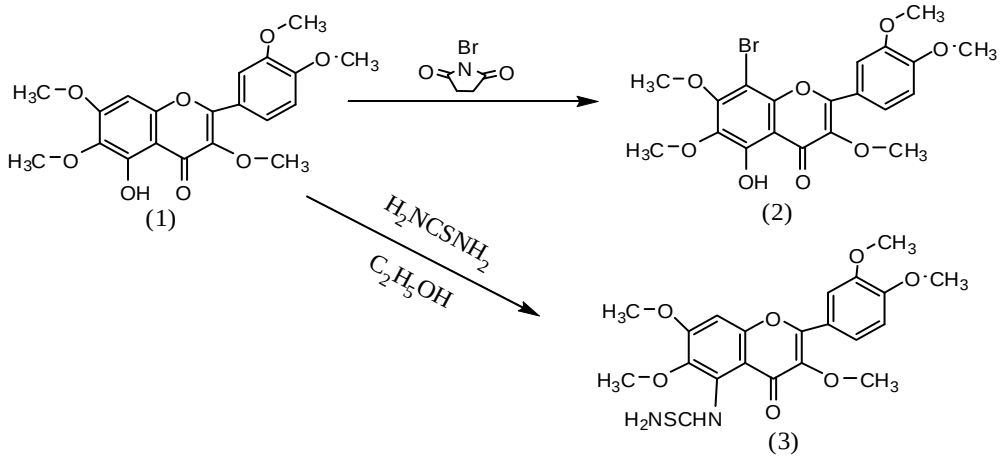
JSC "International research and production holding "Phytochemistry",
Republic of Kazakhstan, Karaganda, 100009, M. Gazaliyev str. 4,
fax:+7 (7212) 43 31 27, e-mail: phyto_pio@mail.ru

High interest in research of natural flavonoids and their different modifications is conditioned by the significant role of these compounds for living processes of plant and animal organisms, wide range of their physiological activity and low toxicity.

In order to extend biological activity of natural polyphenols, we conducted chemical modification of methoxylated flavonoid – artemizetin (1), isolated from *Ajania fruticulosa* (Ledeb.) Poljak [1].

Bromination reaction based on artemizetine molecule with *N*-bromosuccinimide in dioxane under the temperature of 50–60°C was conducted, as a result artemizetine monobromide (2) was obtained with the yield of 46.7%.

New derivative – 5-artemizetinedehydroxythiocarbamide (3) was synthesized through artemizetine and thiocarbamide interaction, with the yield of 31%.



Composition and structure of synthesized compounds are verified by IR, UV, ^{1}H NMR and ^{13}C spectroscopy data.

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QUALITY DETERMINATION OF ANTIHELMINTIC MEDICINES BY PHYSICAL AND CHEMICAL METHODS OF ANALYSIS

Z. T. Sadikov, L. T. Pulatova

Higher Military Customs Institute of SCC of RUz, Tashkent, e-mail: zsadikovs@mail.ru

The present stage of development of foreign economic activity in the Republic of Uzbekistan is connected with a basic change of the forms and methods applied in this sphere for decades of prior development.

In the course of implementation of market transformations our country has faced the avalanche flood of the consumer market counterfeited and illegal products.

The fact that the bulk of consumers first of all gives preference to price product characteristics is the cornerstone of a problem and in much smaller degree is guided by the trademark symbolizing its quality and reliability. Therefore cases when counterfeit products hold a dominant position in the market are frequent, forcing out legal goods.

It is possible to include medicines to number of such goods. Production and sale of counterfeits were purchased by global nature. According to many foreign specialists, the main part of counterfeited medicines gets on the world market from India and China.

As practice shows, the medicines most often forged are taped in the course of control of their quality on compliance to demands of normative documents on an indicator "Authenticity".

The greatest use for establishment of authenticity has a range of photometric methods and a thin-layer chromatography. The TLC method is the simply and available from the point of view of analysis cost. At the same time, this method allows carry out the semi-quantitative and quantitative analysis that is especially important at identification of the forged medicine containing active ingredients in the quantities which aren't corresponding specified on a label.

The IR and UV-range photometry methods are also of great importance at detection of the forged medicines. Use of a ready collection of ranges considerably simplifies such analysis.

Therefore, an actual task is development of techniques of a snap analysis of antihelmintic medicines by TLC, IR methods and photometry in UV range using the equipment of a domestic production, allowing tap the forged medicines.

As a result of complex research of physical and chemical properties of antihelmintic drugs Vermoxum, Zentel, Albendazol of foreign production as defined quality indicators of these drugs. By means of above-mentioned methods of the analysis it was proved that qualities of domestic antihelmintic medicines are much higher, than similar medicines of a foreign parentage.

APPLICATION OF PLANT MATERIALS AS A FUNCLIONAL INGREDIENT OF BAKERY PRODUCTS

G. Z. Dzhakhangirova, P. M. Tursunkhodzhaev

Chemical-Technological Institute, 32, Navoi Str., Tashkent,
e-mail: djaxangirova77@mail.ru

Nowadays, a new trend has developed in the field of nutrition creating a science-based approach to nutrification of socially important basic foods, such as bread and bakery products, essential and minor substances to the recommended adequate intake level. Modern methods for the preparation of bread include both conventional technologies and the use of various additives, including products of fruit, berries, and vegetable processing. The introduction of these product additives to the formulation allow solving a number of technological challenges: improving consumer product advantages, increase its biological value, intensification of pastry formation process, expanding the range of "healthy eating" food sector, the main raw material savings. We investigated the chemical composition of the fruit and vegetable powder semi-products made from apples, beets, carrots, pumpkin and red pepper. The developed technology of bakery products preparation with these additives contributes to the enrichment of products with dietary fibers, vitamins, minerals, improves their quality indicators, which are important from the consumer point of view, as well as increases the output of products and extend their freshness. A toxicological assessment of the products with investigated herbal supplements after intragastrical introduction to the laboratory animals to determine their effect on the functional characteristics of the internal organs and major blood biochemical parameters in rats was carried out. The introduction of fruit and vegetable additives in the diet of rodents do not adversely impact on the clinical and behavioral reactions. The greatest weight gain was observed in rodent experimental groups. Although no difference in body weight observed in experimental animals prior to the experiment, at the end of the experiment it was on average 9.2% ($P < 0.03$), and feed costs per 100 g of body weight decreased for 16.7 ... 27.1% ($P < 0.05$) relatively to a reference sample. The consumption of water per 100 g of body weight of rats was higher in the control group, and by the end of the experiment, it was by an average of 2.6% greater than the same meaning in the animals of experimental groups. Pathological studies revealed no visible changes of internal organs of the experimental groups of rats in compare to the control group. The content of sulfhydryl groups, the activity of cholinesterase and catalase in whole blood in animals of experimental groups was not significantly different from that of the control group throughout the experiment (45 days). The results of clinical trials have confirmed a positive physiological effect of fruit and vegetable supplements as a functional ingredient in the recipe for the bakery filling human diets with natural bioactive nutrients such as β-carotene, bioflavonoids, and dietary fibers. The use of natural raw materials in the technology of bread making will also reduce the use of non-alimentary additives, and, therefore, increase the level of food safety and physiological effects of their use in the diet.

STUDY OF THE AMOUNT OF FLAVONOIDS SEEDLINGS IN COTTON

M. A. Mamasolieva, N. R. Khashimova, A.A Akhunov

Institute of Bioorganic Chemistry of the Academy of Sciences of Uzbekistan, 83 M.Ulughbek Str, Tashkent, Uzbekistan, 100125, e-mail: malika8582@mail.ru

In literature there is a lot of information about bioflavonoids that play important role in the process of oxidation and reduction in plants. They are consist of a large group of polyphenolic compounds having a benzo-γ-pyrone structure and are ubiquitously present in plants. Flavonoids synthesized by phenylpropanoid pathway. Available reports tend to show that secondary metabolites of phenolic nature including flavonoids are responsible for the variety of pharmacological activities. Flavonoids are hydroxylated phenolic substances and are known to be synthesized by plants in response to microbial infection. Their activities are structure dependent. The chemical nature of flavonoids depends on their structural class, degree of hydroxylation, other substitutions and conjugations, and degree of polymerization. Bioflavonoids stimulate respiration of tissue; they take part in a protection of plant tissues from ultraviolet and visible radiation rays and also have antihypoxic property. Also, flavonoids are involved in the synthesis of a phytohormone auxin, which is stimulating the growth and development of plants, activates defense mechanisms against bacterial and viral pathogens, cleaves the free radicals that are formed under unfavorable environmental effects. The mechanism of action of flavonoids is closely linked with the activity of the enzyme phenylalanine ammonia-lyase (PAL), which is also involved in the synthesis of salicylic acid and auxin. From the foregoing, there is a correlation between the activation of PAL and the amount of flavonoids. To study this relationship it was determined number of flavonoids in roots, stems, leaves of seedlings resistant to wilt cotton varieties Namangan-77. In order to select an analytical wavelength previously UV spectra of extracts and standard samples of quercetin and rutin in the individual state and with the addition of aluminum chloride which forms a complex with the test compounds were obtained. Spectrophotometric method was used to determine the amount of flavonoids based on the standard quercetin and rutin. Experiments were carried out in 5 replicates. The average values of flavonoids based on the quercetin amounted in roots 0.117 mg/ml, in stems 0.115 mg/ml, in leaves of 0.199 mg/ml. In comparison to rutin the average values of flavonoids amounted in roots 0.0342 mg/ml, in stems 0.0332 mg/ml, and in leaves 0.0729 mg/ml.

Results of the work showed high content of total flavonoids in leaves and roots of the seedlings. The correctness of determining was monitored by the method of standard addition. A relative standard deviation does not exceed 0.04.

The PAL activity in the leaves was 38.57 pKat/g, in hypocotyls - 10.26 pKat/g, and in roots - 18.06 pKat/g of fresh wt. There was a significant correlation in the leaves between PAL activity and amounts of flavonoids ($r = 0.525$, $p < 0.01$).Where PAL activity was absent there was no accumulation of flavonoids, with the concentration of flavonoids actually dropping.

STUDY OF HYDROLYSIS KINETICS OF DICHLORALKYLAMINE EPHEDRINE AND PSEUDOEPHEDRINE BY PMR SPECTROSCOPY

N. U. Yusupov[1], H. R. Tukhtaev[2], Y. I. Oshepkova[1], V. G. Kartcev

1) LTDSC «MED STANDART», e-mail: info@medstandart.uz
2) Tashkent Pharmaceutical Institute of the Republic of Uzbekistan, e-mail: pharmi@bcc.com.uz

It was studied the hydrolytic conversions of N-β-dichlorethyl derivatives of ephedrine and pseudoephedrine. Hydrolysis kinetics was studied in an alkaline medium, ether: buffer solution (buffer solution of Na_3PO_4 + D_2O, pH = 9.0) at 25°C, using H^1 and ^{13}C - spectroscopy. The concentration of the starting alkylating compounds and their hydrolysis products in the organic phase after separation was determined in a thin layer of silica gel and identified in a mass spectrometer. For the assessment of the reactivity of the alkylating agents effective rate constant (Kh, s-1), calculated on the initial sections of kinetic curves (Figure 1) was taken was taken:

I - N-β-dichlorethyl derivatives, II - N-β-dichlorethiyl derivatives of ephedrine of pseudoephedrine

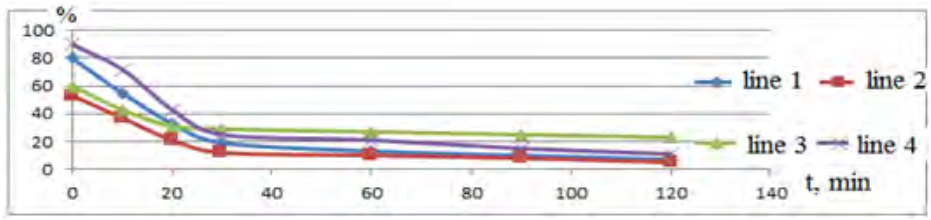

Fig. 1. Comparative kinetics of hydrolysis of N-β-dichlorethyil derivatives of ephedrine and pseudoephedrine: 1 - N-β-dichlorethyl derivatives of ephedrine; 2 - N-β-dichloroethyl pseudoephedrine-derivative; 3 - N-β-chlorethyl derivatives of ephedrine; 4 - N-β-chloro-ethyl derivative of pseudoephedrine

As it can be seen in Fig. 1, the hydrolysis of N-β-dichlorethyl derivative of pseudoephedrine (2.4) occurs in ~ 2.5 times faster than derivative of its diastereoisomer corresponding to the values of constants: II - Kh = 4.0 s-1; I - Kh = 1.75 s-1.

The study of the mass spectra allowed establish the molecular weight and fragmentation paths of intermediate and finish products of the hydrolysis reaction. Given the hydrolysis reaction rates for the compound I - N-β-dichlorethyl derivatives of ephedrine was used NMR method ^{13}C, and for compound II - N-β-dichlorethyl derivatives of pseudoephedrine was used PMR spectroscopy in ^1H nuclei. For both compounds cis- and trans-isomers of intermediate alkylating products were ascertained: I - *cis*; II- *trans*.

PHYSIC-CHEMICAL CONSTANTS AND EXCRETION OF H^3-THYMIDINE N-(β CHLORETHYL)-PIPERIDINE DERIVATIVES, PERHYDROAZEPINE AND DECAHYDROCHINOLINE FROM ANIMAL BODY

I. A. Khodjaeva[1], H. R. Tuxtaev[1], N. U. Yusupov[2], Y. I. Oshepkova[2], V. G. Karcev

1) Tashkent Pharmaceutical Institute of the Republic of Uzbekistan,
e-mail: pharmi@bcc.com.uz
2) LTD «MEDSTANDART», e-mail:info@medstandart.uz

To determine the effect of modifying factors on biokinetic cellular processes the biological activity in the same doses of 20 mg/kg, LD_{50} - total toxicity, PT (%) - percentage of tumor growth inhibition (S-180), RG (%) - relative renewal of life for generalized leukemia (La) /compared with physic-chemical properties /Kd (%) - partition coefficient in the lipophilic medium, pharmacokinetic parameters /P∞ (%) - asymptotic amount of excreted mark in urine, $t_{1/2}$ (h) - the period of half-life from the animal body / and excretion of H^3-thymidine from animal body, alkylators of "direct action» - N- (β-chlorethyl) - derivatives of heterocyclic amines piperidine (I), perhydroazepine (II) and decahydrochinoline (III) were studied.

TABLE 1. **Pharmacokinetic parameters of N-(β-chlorethyl) derivatives of piperidine (I), perhydroazepine (II) and decahydroquinoline (III)**

Parameter	I	II	III
Dose (mg / kg)	20	20	20
$\mathbf{K_d}$ (%)	0.40	0.15	0.21
$\mathbf{P_\infty}$(intact)	71	58	64
$\mathbf{P_\infty}$ (tumor)	59	46	53
$\mathbf{t_{1/2}}$(intact)	56	27	41
$\mathbf{t_{1/2}}$(tumor)	23	26	21
LD_{50}	50	37	80
PG (La)	105	115	110
PT (S-180)	70	80	60
Excretion of H^3- thymidine (P, %)	7.0	11.0	2.7

Comparison of given in Table 1 quantitative assessments shows that excretion rate of the mark and total amount of the excreted in urine radioactive material are naturally increased with increasing of lipophilicity of the compound. Furthermore, the more anti-tumor activity of the compound, and the greater amount of H3-thymidine is excreted in urine. Apparently, alkylating compound with a higher antitumor activity more strongly hinders the process of H3-thymidine incorporation into DNA, and therefore free of H3-thymidine is excreted in the urine in increasing numbers.

EVALUATION OF ANTIOXIDANT AND ANTIMICROBIAL ACTIVITIES OF *Rubus sanctus* EXTRACTS

Ali Sen[1], Sibel Dösler[2], Ahmet Dogan[3], Leyla Bitis[1]

1) Marmara University, Faculty of Pharmacy, Department of Pharmacognosy, 34668, Haydarpaşa, İstanbul, Turkey
2) Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, 34116, Beyazıt, İstanbul, Turkey
3) Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, 34668, Haydarpaşa, İstanbul, Turkey, e-mail: ali.sen@marmara.edu.tr

In this study, antioxidant and antimicrobial activities of aqueous ethanol extracts obtained from leaves (RSL), stem (RSS), and roots (RSR) of *Rubus sanctus* Schreber were evaluated using different antioxidant tests, including DPPH and ABTS methods. Total phenolic and total flavonoid contents of the extracts were estimated by Folin-ciocalteu reagent and aluminum chloride ($AlCl_3$) methods, respectively. Antimicrobial acitivity was carried out using Clinical and Laboratory Standards Institute (CLSI) broth micro-dilution (BMD) methods against seven bacteria (*Staphylococcus aureus* ATCC 29213, *Staphylococcus epidermidis* ATCC 12828, *Enterococcus faecalis* ATCC 29212, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 4352, *Proteus mirabilis* ATCC 14153) and one fungi (*Candida albicans* ATCC 10231).

Aqueous ethanol extracts showed 50% inhibition of DPPH radical in the concentration range of 5.13-26.27 µg/mL, in which RSR and RSL extracts demonstrated the strongest activities with the IC_{50} values of 5.13 and 6.11 µg/mL, respectively. Similarly, RSR and RSL extracts showed the most potent ABTS scavenging activities with IC_{50} values of 2.45 µg/mL and 4.74 µg/mL, respectively, whereas RSS has the lowest IC_{50} values (10.50 µg/mL). Total phenol content was expressed as gallic acid equivalent (GAE) and it was the highest in RSR (250.4 mg GAE/ g extract), followed by RSL (220.9 mg GAE/ g extract), finally RSS (110.1 mg GAE/ g extract) with the lowest phenolic content. Total flavonoid contents of extracts expressed as catechin equivalents (CE), varied from 94.55 to 176.3 mg CE/g extract. The RSR showed the highest amount of flavonoid contents followed by RSL and RSS. In the present study, total phenolic and flavonoid content were found reasonably correlated with IC_{50} of DPPH (r^2 = 0.81 and 0.86, respectively) and ABTS (r^2 = 0.82 and 0.88, respectively). This results were in agreement with previous reports showing that the phenolic compounds contribute significantly to the antioxidant activity.

RSR, RSL, and RSS showed strong antifungal activity against *Candida albicans* with MIC values of 5, 10 ve 39 µg/mL, respectively. RSL and RSR showed potent antimicrobial activity against *Enterococcus faecalis* with MIC values of 39 and 78 µg/mL, while RSS exhibited moderate activity against same bacteria with MIC value of 625 µg/mL. RSL only demonstrated weak antibacterial activity against *Staphylococcus aureus* with MIC value of 1250 µg/mL. None of extracts showed activity against the gram-negative bacteria.

As a result, RSL and RSR extracts could serve as potential sources in the discovery of new natural antimicrobial and antioxidant agents.

In vitro ANTIMICROBIAL POTENTIAL OF VARIOUS EXTRACTS FROM ENDEMIC *Stachys subnuda* AERIAL PARTS

Ali Şen[1], Sibel Döşler[2], Ahmet Doğan[3], Leyla Bitiş[1]

1) Marmara University, Faculty of Pharmacy, Department of Pharmacognosy, 34668, Haydarpaşa, İstanbul, Turkey
2) Istanbul University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, 34116, Beyazıt, İstanbul, Turkey
3) Marmara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, 34668, Haydarpaşa, İstanbul, Turkey, e-mail: leylabitis@marmara.edu.tr

The genus *Stachys* consists of nearly 300 species throughout the world. Turkey is one of the richest countries for *Stachys* diversity and it is represented by 83 species with a level of 48% endemism in Turkey. *Stachys* species are widely used in folk medicine and they are known as sedative, antispasmodic, diuretic, emmenagogue, stomachic, digestive, carminative, tonic and throat pain reliever. Several *Stachys* species have also been reported for uses on genital tumors, sclerosis of the spleen, inflammatory tumors and cancerous ulcers (1). Secondary metabolites that are found in these species are generally flavonoid glycosides, iridoids, diterpenes and essential oils (2).

In this study, Antimicrobial activities of methanol extract (SSM) of *S. subnuda* aerial parts and also hexane (SSH), chloroform (SSC), ethyl acetate (SSE), aqueous methanol fractions of its were investigated against *Staphylococcus aureus* ATCC 29213, *Staphylococcus epidermidis* ATCC 12828, *Enterococcus faecalis* ATCC 29212, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 4352, *Proteus mirabilis* ATCC 14153, *Candida albicans* ATCC 10231 by micro-dilution methods according to National Committee for Clinical Laboratory Standards procedures.

SSH and SSC showed high antifungal activity against same fungus with MIC values of 39 and 78 µg/mL, respectively, while SSM exhibited moderate activity against *Candida albicans* with MIC value of 625 µg/mL. SSK and SSM demonstrated moderate and weak activity against *Staphylococcus aureus* with MIC values of 312.5 and 1250 µg/mL, respectively. Only SSC showed moderate antibacterial activity against *Enterococcus faecalis* with MIC value of 625 µg/mL, whereas only SSM showed weak activity against *Staphylococcus epidermidis* with MIC value of 1250 µg/mL.

SSH and SSC extracts could act as alternative sources for the development of new antimicrobial agents. Therefore, there is a need to isolate compounds that are responsible for antimicrobial activities of SSH and SSC extracts of *S. subnuda*.

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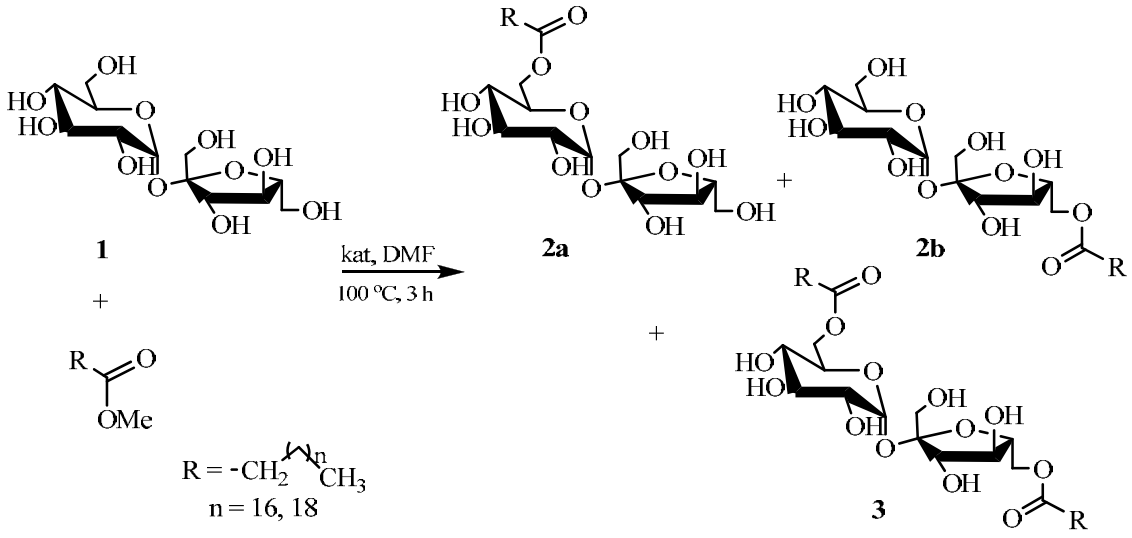
SYNTHESIS OF SUCROSE FATTY ACID MONOESTERS

L. I. Vlasova[1], S. S. Faizullina[2], O. S. Kukovinets[2], V. A. Dokichev[1,3]

1) Ufa Institute of Chemistry of the Russian Academy of Sciences,
71 prospect Oktyabrya, 450054, Ufa, Russian Federation
2) Bashkir State University, 32 Validy Street, 450076, Ufa, Russian Federation
3) Ufa State Aviation Technical University, 12 K. Marx Street, 450008, Ufa,
Russian Federation, e-mail:_dokichev@anrb.ru

Sucrose fatty acid monoesters are producing from renewable, inexpensive, and readily available resources. They are widely used in food, cosmetics, and pharmaceuticals as nonionic surfactants. These esters are completely biodegradable, harmless to the environment, nontoxic, compatible with skin. Therefore, synthesis of long-chain fatty acid sucrose monoesters is an actual problem and the search for optimal conditions represents undoubted practical interest.

Herein, we wish to report a method of preparing mono- and diesters of sucrose based on the reaction of transesterification of sucrose **1** with methyloleate, methylpalmitate and methylstearate using of various catalysts (Li_2CO_3, Na_2CO_3, K_2CO_3, Cs_2CO_3, CsF CH_3ONa,) at 100 ^oC in dimethylformamide (DMF) as solvent. Sucrose monoesters **2a,b** yield reaches 40% and 15% sucrose diesters **3**, respectively.



A series of mono- and diesters of sucrose containing higher fatty acids representing interest as surfactants with antibacterial properties has obtained.

This work was financial supported by the Russian Science Foundation (Grant №14-33-00022)

PHYTOCHEMICAL RESEARCH OF *Limonium leptophyllum* PLANTS AND ITS ISOLATED SUBSTANCE

A. A. Kalabaeva, M. K. Assemova, F. Shaheen, G. E. Zhusupova, M. Iqbal Choudhary

Al-Farabi Kazakh National University, Al-Farabi 71, Almaty, Kazakhstan
e-mail: aizhan.06@mail.ru

Finding a new sources of vegetable raw materials is an important task for the development of the pharmaceutical industry of the Republic of Kazakhstan. The object of our study is the aboveground part of the *Limonium leptophylluim* plant, that was collected in September 2016 in Almaty region during the period of their flowering. Drying and grinding to 3 mm steps were in part of preparation procedure. Quality analysis of raw materials for carried out in accordance with the requirements of the State Pharmacopoeia of the Republic of Kazakhstan (2009). The obtained results (moisture content - 9.59%, total ash - 10.84%, ash insoluble in 10% HCl - 0.02%, sulfate ash - 10.79%) indicate the purity of the samples. Indicators "Microbiological purity", "Heavy metals" and "Radionuclides" set for the aboveground part of the *Limonium leptophylluim* plant are in accordance with acceptable standards for their medicinal plants. Pesticides and mycotoxins are not found. Amino acids, fatty acids, and trace elements compositions were set for the tested plants. The content of essential aminoacids and polyenes are dominant. Selection procedure was done to find the most optimal extraction, 50% ethanol was used as a solvent at a ratio 6:1. 200 g of the dried extract was dissolved in 350 ml MEOH: H2O (70%: 30%) solvent system. The multiple exhaustive extraction with solvents of different polarities were applied to obtain hexane, dichloromethane, ethyl acetate, butanol and aqueous fractions. They were concentrated and analyzed by thin layer chromatography (TLC). The selected dichloromethane fraction was studied by column chromatography on the silica gel with a column height 65 cm and internal diameter 5 cm. The separation was carried out by the gradient elution from hexane with a nonpolar solvent followed by increase in the polarity of the solvent system hexane:ethyl acetate:methanol. The 202 fractions were collected totally, which were analyzed by TLC. The identical R_f in fractions were pooled and then subjected to repeated chromatographical analyses. Two individual substances are identified and isolated by complex physical and chemical constants as quercetin and apigenin. The chemical and biological study of the aerial parts of the plant species *Limonium leptophylluim* continues.

ANTIBACTERIAL ACTIVITY OF ETHANOLIC EXTRACT FROM *Kochia prostrata*

G. A. Seitimova[1], A. M. Alzhanbayeva[1], B. K. Yeskaliyeva[1], G. Sh. Burasheva[1], Sezer Okay[2]

1) Al-Farabi Kazakh National University, Faculty of Chemistry and Chemical Technology, Almaty, Kazakhstan
2) Cankiri Karatekin University, Faculty of Science, Department of Biology, Cankiri, Turkey, e-mail: balakyz@mail.ru

Kochia is found in arid areas, deserts, and costal and saline habitats of Central Asia, North and South Africa, Europe, Russia. There are 10 species of the plant genus *Kochia*; 9 of these are indigenous to Kazakhstan. The genus *Kochia* has been used in traditional Chinese medicine to treat diuresis and skin diseases. It has also been used for the treatment of pain in micturition, rubella, eczema and cutaneous pruritus in traditional Chinese preparations. The cardiotonic and diuretic activities of the plant have already been reported.

Air-dried and finely powdered aerial parts of the plant *Kochia prostrata*, which belonging to the halophytes were collected from saline soils at South Kazakhstan region, were exhaustively extracted by maceration for 72 hrs. at room temperature with ethanol (80%) till complete exhaustion.

The ethanolic extract was tested *in vitro* for its antibacterial activity. The disk diffusion method was used to determine the inhibition zones of the ethanolic extract from *Kochia prostrata*. It was screened against *Klebsiella pneumoniae, Enterococcus faecalis, Pseudomonas aeruginosa, Methicillin-resistant Staphylococcus aureus* (MRSA) and *Escherichia coli*. In the disk diffusion assay, the maximal inhibition zones ranged between 8 and 9 mm, which indicate that extract of *Kochia prostrata* showed significant activity against the tested bacterial species.

Moreover, the results obtained give a scientific support and confirm the traditional medicinal use of *Kochia prostrata* in skin diseases.

ANTIINFLAMMATORY EFFECTS IN ROS OF EXTRACTS FROM *Verbascum marschallianum*

M. M. Nykmukanova[1], B. K. Yeskaliyeva[1], G. Sh. Burasheva[1], M. I. Choudhary[2]

1) Al-Farabi Kazakh National University, Almaty, Kazakhstan, e-mail: balakyz@mail.ru
2) H.E.J. Research Institute of Chemistry, University of Karachi, Karachi-75270, Pakistan

The genus *Verbascum* (mulleins) comprises of probably about 360 species of plants in the *Scrophulariaceae* family. From antiquity *Verbascum marschallianum* has been used as a medicinal herb, it contains diverse polysaccharides, iridoid glycosides, flavonoids, saponins, volatile oils and phenylentanoids. Mulleins have been used in the traditional folk medicine for centuries, for treatment of a wide range of human ailments, inter alia bronchitis, tuberculosis, asthma, and different inflammations. Despite all applications the knowledge of the metabolites, accumulated in different mullein species, is still limited and based mainly on determination of the major compounds.

The aim of the study was to screen the antiinflammatory activity and phytochemical analysis of various extracts of *Verbascum marschallianum*, *Scrophulariaceae* family. The antiinflammatory activity of various extracts from V. *marschallianum* was determined with Oxidative Burst Assay using Chemiluminescence Technique. The results provide evidence that the extracts of V. *marschallianum* contained glycosides, flavonoids, saponins and phenolic compounds which may be responsible for the substantial antiinflammatory activity. The ethanolic (IC_{50} = 25.3 ± 1.6), ethyl acetate (IC_{50} = 16.7 ± 5.1) and dichlormethane (IC_{50} =20.3 ± 2.9) extracts showed moderately antiinflammatory activity. But hexane and *n*-butanol extracts are inactive. Standard used for the assay is Ibuprofen IC_{50} = 11.2 ± 1.9

The ethyl acetate extract was directly injected for chromatographic analysis. Then the major compound – luteolin was obtained by a recycling preparative HPLC system (LC-908W), using a ODS M-80 column with water:methanol 90:10 isocratic elution. Luteolin was obtained with a purity degree of > 97% (yellow powder) and its structural identity was confirmed by comparison of analytical data (1D and 2D NMR, IR, UV and mass-spectrometry).

The luteolin was screening to inhibition of antiinflammatory activity and showed good antiinflammatory activity (IC_{50} = 8.2 ± 1.6) against the standard inhibitor Ibuprofen.

The study ascertains the value of plants used in medicine, which could be of considerable interest to the development of new drugs, to supports there is scientific basis of their utilization in traditional medicinal for for inflammatory diseases.

STUDY ELEMENT-ORGANIC FRACTION OF EXTRACT *Saussurea controversa* DC

E. Yu. Avdeeva, E. A. Krasnov, E. E. Shults, Y. E. Reshetov

Siberian State Medical University, 2 Moskovsky trakt, Tomsk, 634055, Russia,
e-mail: elenaavdeev@yandex.ru

Among the 115 species of the genus Saussurea that grow in Russia, most are poorly understood, despite their potential for use in medicine. So Saussurea controversa DC (*Asteraceae*) extract, which has immunomodulatory activity [1] is very promising for the treatment of necrotic lesions, in particular osteomyelitis [2]. Considerable interest for research is the element-organic fraction obtained from an aqueous ethanolic extract *S.controversa* high yield [3].

The aim of the work was to study the composition of the element-organic fraction from *S.controversa* extract exhibiting immunomodulatory activity.

Inorganic components investigated neutron activation method. The sample was prepared by ashing fraction in a muffle furnace at a temperature 450–500°C. The resulting sample (ash content of 35%) was found 31 element, with a predominant content (g / kg) Ca (138.8), Si (1.02), K (1.01), Na (0.216), Fe (0.05), Mg (0.043), Cu (0.003), Zn and Mn (at 0.002).

For the study of organic component fraction was dissolved in acidified water under heating (80°C) and extracted with butanol. After evaporation obtained light yellow powder was soluble in ethanol, wherein not detected proteins, amino acids and carbohydrates. The electronic spectrum showed a maximum at 287 nm and an additional peak in alkaline medium at 428 nm. The IR (KBr), ν, $см^{-1}$: 1592, 1538 (aromatic ring); 1642 (CO - - H); 1749 (C=O); 3076, 3108, 3447 (OH); 1124 (OH); 842 (p-substitution in the aromatic nucleus). ^{1}H NMR (300 MHz, CD_3OD): δ 1.5(2H,m), 1.8(2H,m), 2.3(1H,t), 3.57(2H,t), 4.41(2H,t), 6,86(1H,d,2), 7,44(1H,d,2). ^{13}C NMR (75.47 MHz, CD_3OD): δ 19.96, 31.37, 62.59, 67.86, 120.05, 120.16, 120.22, 155.76,161.58,182.26. Thus, the organic component is a hydroxylated aromatic structure with a carboxyl group on which the inorganic component may form a salt.

The presence of macro- and micronutrients in combination with biologically active substances in fraction S.controversa can cause a number of effects: immunomodulatory (zinc) and regenerating bone (calcium).

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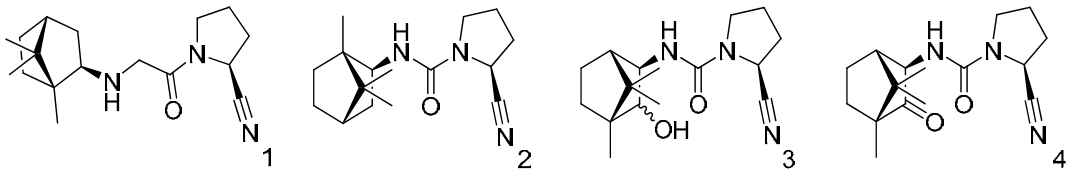
SYNTHESIS OF NEW CAMPHOR BASED ANTIDIABETIC COMPOUNDS

S. O. Kuranov[1], O. A. Luzina[1], M. V. Khvostov[1], N. F. Salakhutdinov[1,2]

1) N.N. Vorozhtsov Novosibirsk Institute of Organic Chemistry. 9 Lavrentiev Avenue, Novosibirsk, 630090, Russia
2) Novosibirsk State University, 2 Pirogova Str., Novosibirsk, 630090, Russia
e-mail: s.o.kuranov@chemomsu.ru

Type 2 diabetes mellitus is a metabolic disease characterized by impaired control over the blood glucose level. The worldwide trend of diabetes is currently taking a form of epidemic; according to the World Health Organization, the number of cases will have exceeded 350 million by 2030. Glucagon-like peptide-1 (GLP-1) plays an important role in glucose homeostasis because it triggers insulin release by pancreatic β-cells. A very short lifetime in the organism is a characteristic feature of GLP-1, since it is very rapidly degraded due to the dipeptidyl peptidase 4 (DPP-4) enzyme. For this reason, drugs inhibiting the DPP-4 enzyme are used to treat diabetes.

We have synthesized the series of substrate-like compounds 1-4 having a (S)-N-acetylpyrrolidine-2-carbonitrile and modified bornyl fragment as substituent. Bornyl amines were obtained from (+) -1 and (-) -camphor 2. Bornyl hydroxyamine 3 and ketoamine 4 were prepared via camphorquinone.



To access the in vivo efficacy of obtained compounds, ability to inhibit glucose excursion after oral glucose load in oral glucose tolerance test (OGTT) in mice was carried out. Compound 1 has shown the ability to reduce blood glucose compared to control group.

TABLE 1. **Blood Glucose level in OGTT, mmol/l**

Time, min	0	30	60	90
Vildagliptin	3,22±0,15	9,60±0,93[#]	7,50±0,63[#]	6,03±0,48
1	3,37±0,24	12,58±0,73[#]	9,18±0,79	6,65±0,28
Control group	3,17±0,25	16,03±0,71	11,67±0,91	7,93±0,72

The administered compound dose was 10 mg/kg orally.
The administered glucose were 2,5 g/kg orally.
[#] $p<0,05$ against control.

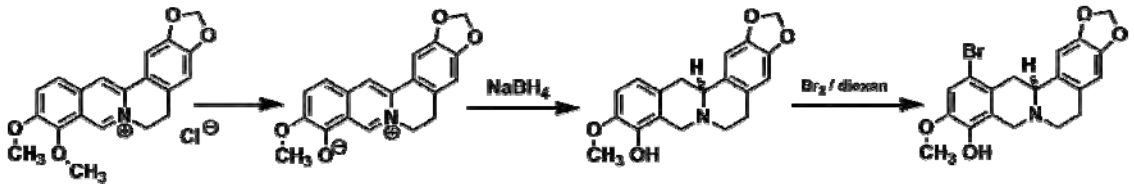
SYNTHESIS OF TETRAHYDROBERBERINE 9-*O*-SULFONATES

I. V. Nechepurenko, E. D. Shirokova, N. I. Komarova, N. F. Salakhutdinov

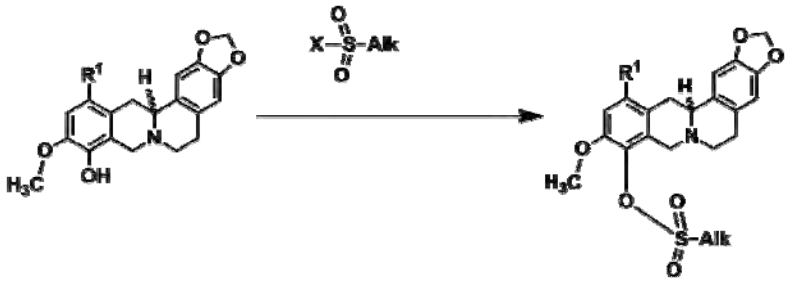
N. N. Vorozhtzov Novosibirsk Institute of Organic Chemistry of the Siberian Branch of Russian Academy of Sciences, 630090, ave. Lavrentyeva, 9, Novosibirsk, Russia, e-mail: niv@nioch.nsc.ru

The main criterion in the prevention of cardiovascular diseases is a decrease of total cholesterol level in blood. Statins are currently used for this purpose; they are effective but have a number of severe side effects. The search for agents with a mechanism of action different from statins is the modern trend in the lipid-lowering drugs development. Such compounds should not inhibit cholesterol biosynthesis, but regulate cholesterol level in a body.

It has been reported that berberine **1**, widespread plant isoquinoline alkaloid, to possess cholesterol-lowering effects, and we used it as a "scaffold" for new derivatives synthesis. The reduced derivatives **2** and **3** were obtained by berberine **1** modification. The reaction between hydroxy- derivatives **2** or **3** and sulfonyl chlorides resulted in the formation of 9-*O*-alkyl- or fluoroaryl- sulfonates **4**, **5**. Hypolipidemic activities of the compounds **4**, **5** are being studied.

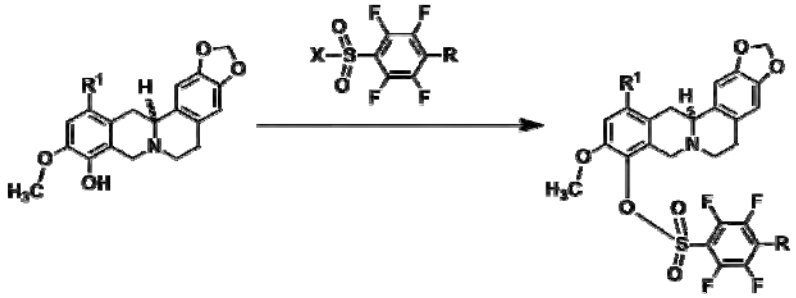


1 **2** **3**



2, 3 **4**

R^1 = H, Br R^1 = H, Br; Alk = Me, Et, n-Pr, n-Bu



2, 3 **5**

R^1 = H, Br R^1 = H, Br; R = H, F, CF_3

SYNTHESIS AND FLOCCULATION PROPERTIES OF CROSSLINKED CATIONIC STARCHES

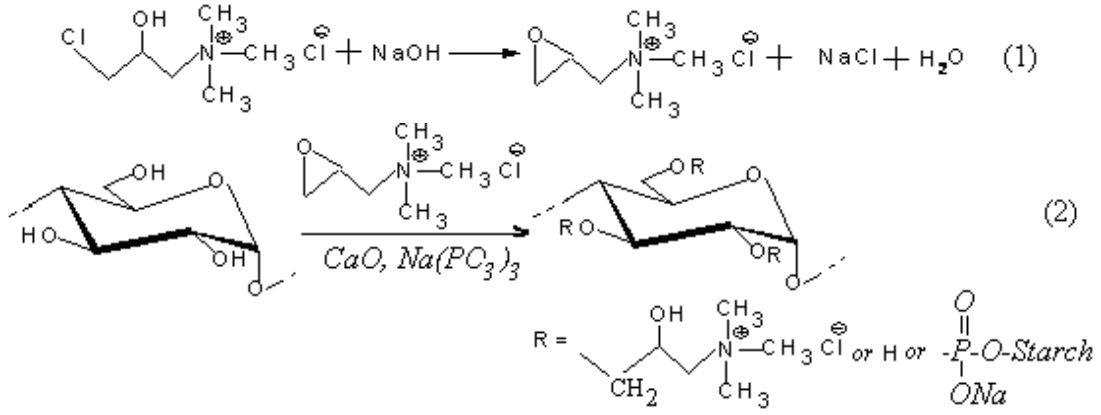
S. M. Butrim, T. D. Bil′dyukevich, N. S. Butrim, T. L. Yurkshtovich

Belarusian State University, Research Institute for Physical Chemical Problems, 220050, Minsk, Belarus, e-mail: butryms@bsu.by

One of the most demanded starch derivatives - cationic starch is synthesized now mainly in water suspension that demands the big expenses for technological equipment of an industrial line and the big expense of water both for carrying out of the reaction, and for the subsequent washing a ready product. «Semi-dry method of cationisation» has a lot of advantages:

- higher efficiency of cationisation reaction and reception possibility cationic starches with higher degree of substitution ($DS_{cat.}$);
- the minimum losses of starch and elimination of problems with sewage, as result of absence of a stage of washing;
- smaller expenses for equipment of a technological line and minimum time of mixing;
- the absence of necessity of use salts and economy of energy as reaction can be spent at a room temperature.

The general scheme of reaction on the developed way can be presented as follows:



The «semi-dry cationisation» of potato starch with use 3-chloro-2-hydroxypropyltrimethylammonium chloride (Quat 188), crosslinker (sodium trimetaphosphate) and catalysts have been studied. It was established, that the content of cationic groups, reaction efficiency and the degree of crosslinking depend on the water content in a mix, reaction time and from molar ratio starch: catalyst : crosslinker: Quat 188.

The synthesised high-substituted crosslinked cationic starches ($DS_{cat.}$> 0.14) keep granular structure and unlike low-substituted that are dispersed in cold water to form a colloidal solution and can to find wider application. The possibility of use of crosslinked cationic starches as effective flocculants which are not conceding by the efficiency widely applied cationic synthetic flocculants on a basis polyacrylamide and its derivatives was shown on modelling systems of the 0.1 % caolin dispersions.

MEDICINAL REMEDIES FROM THE PLANTS OF GEORGIAN FLORA

M. D. Alania, K. G. Shalashvili, T. G. Sagareishvili, N. Sh. Kavtaradze, M. G. Sutiashvili, E. P. Kemertelidze

Tbilisi State Merical University, I.Kutateladze Institute of Pharmacochemistry, P. Sarajishvili str., 36, Tbilisi, 0159, Georgia, e-mail: merialania@yahoo.com

The study of plants of Georgian flora on the content of biologically active compounds revealed that some substances derived from certain species have a high therapeutic activity. On their basis several remedies were created: antiviral ointment “Rhodopes” that contains flavonoids of *Rhorodendron ungernii* Trautv. (RU) leaves; hypoazotemic, hypoglycemic and diuretic tablets “Flaronin”, containing individual flavonoid glycoside robinin from leaves and flowers of *Astragalus falcatus* Lam. (AF); and capsules “Saturin” based on raw extract of *Satureja hortensis* L. (SH) for treatment and prevention of type II diabetes.

The active substance of “Rhodopes” was obtained from the 80 % alcoholic extract of leaves of RU. In this sum less polar flavonoids prevail. The chemical study showed that the main constituents are: flavonols (27 %) - quercetin, quercitrin, isoquercitrin, hyperin, rutin; catechins - (+)-catechin, (–)-epicatechin, (+)-gallocatechin (12%), and leucoanthocyanins (17%) [1].

AF proved to be rich by the content of flavonoid robinin (2.2 %) – the active compound of “Flaronin”. The mother liquor of robinin contains also other flavonoids and cycloartan glycosides. Pharmacological study of dried mother liquor showed the effect similar to “Flaronin”. The major constituents are robinin, kaempferol-7-rhamnoside, nicotiflorin, kaempferol, flavonoid olygosides - falcoside A-E, cyclogaleginoside A and B [1, 2].

Leaves of SH are rich in phenolic compounds (up to 2 %). Six flavonoids and two phenyl-carbonic acids were isolated and identified: apigenin, luteolin, cynarosid, luteolin-7-β-D-glucuronid, scolimosid, isorhoifolin, rosmarinic and chlorogenic acids [1]. The essential oil (EO) with the yield 1 % was obtained by the steam distillation from the air-dried raw material of SH. Main constituents: terpene hydrocarbons – 49.4 %, thymol – 28.25 % and its ether methyl carvacrol – 17.15 % were detected by GLC analysis. HPLC analysis revealed 201.1 mg % amino acids with the high content of proline (76.48 %). According to the data of atomic absorption spectroscopy potassium (5.32 %) prevails other mineral components in dry extract.

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TRANSFORMATION OF NATURE ISOFLAVONES AND THEIR ANALOGUES INTO 6-AZOLYLUMBELLIFERONE DERIVATIVES

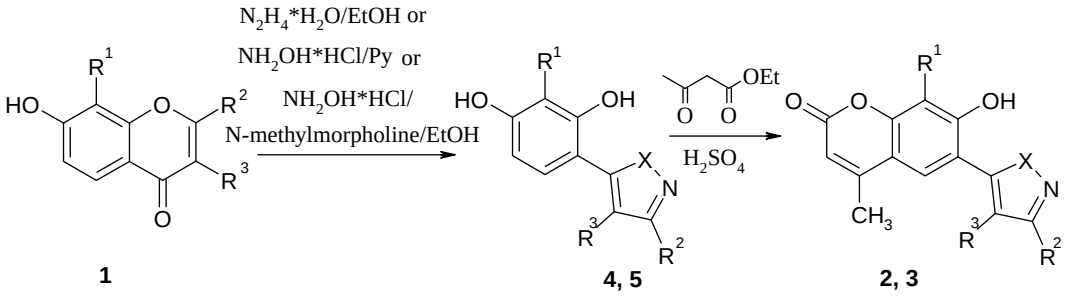
T. V. Shokol, N. G. Gorbulenko, M. S. Frasinyuk, V. P. Khilya

Chemical Department of Kyiv National Taras Shevchenko University, Volodymyrska st., 64/13, Kyiv, Ukraine, e-mail: shokol_tv@univ.kiev.ua

Coumarine and chromone derivatives are natural plant bioregulators. The co-occurrence of formononetin and umbelliferone in *Dalbergia volubilis* is of interest from biogenetic considerations [1] and the transformations of γ- and α-benzopyrones are the subject of research for chemistry of natural and heterocyclic compounds. Pyrazolyl- and isoxazolylcoumarines are known for their interesting spectral-fluorescent properties and were found to induce antibacterial, antimicrobial and anti-inflammatory activities.

The main method for the synthesis of pyrazolyl- and isoxazolylcoumarines is the completion of the azole ring to the coumarine core with 1,3-diketones or enaminoketones via reaction with hydrazine or hydroxylamine [2].

The aim of the present work was to develop an alternative approach to the synthesis of 6-azolylcoumarines via the formation of the coumarine cycle on the base of substituted pyrazoles and isoxazoles. We have transformed natural isoflavones and their analogues **1** into 6-(3(5)-pyrazolyl)- and (5-isoxazolyl)-4-methylumbelliferone derivatives **2, 3** in two stages, i.e. recyclization of the starting chromones **1** under the action of hydrazine hydrate or hydroxylamine hydrochloride into 4-azolyl-1,3-benzenediols **4, 5** followed by condensation with ethyl acetoacetate via the Pechmann reaction [3].



1 **4, 5** **2, 3**

X=NH (**2**, **4**), O (**3**, **5**),
R^1=H, Me; R^2=H, Me, CF_3;
R^3=Ph, 2-$MeOC_6H_4$, 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 4-BrC_6H_4, 4-ClC_6H_4, PhO, 2-$MeOC_6H_4O$, 4-methylthiazol-2-yl

Such approach allows to receive the desired products with various (aryl, aryloxy and hetaryl) substituents on the azole ring and to create combinatory libraries of hetaryl analogues of natural coumarines, which would make them available and expand the scope of their application.

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GENUSES *Angelica* AND *Prangos* – SOURCE OF BIOLOGICALLY ACTIVE COMPOUNDS

I. G. Heydarov, S. V. Serkerov

Institute of Botany, National Academy of Sciences of Azerbaijan
Badamdar highway 40, Baku AZ1073, e-mail: s.serkerov@mail.ru

Representatives of the *Apiaceae* family are characterized by the maintaining of coumarinclass compounds such as osthol, oxypeucedanin, imperatorin, isoimperatorin etc. Dihydrofurocoumarinsmarmesin, deltoin, and furocoumarinsprangeninhydrate, alloimperatorin are meet rare. Some of the abovementioned compounds, for example, osthol contributes to lowering blood pressure, xanthotoxin, psoralenandbergapten have considerable photosensitizing activity, prangenin has some anti-tumor properties. According to the recent year'sdata anticarcinogenic activity detected in peucedanin, prangenin, xantootoxin, isopimpinellin, isoimperatorin, oxypeucedanin hydrate, marmesin, heraclenol and ostol. The last compound also have clearly expressed coronary dilating and pressor properties.

From the roots of *Angelica purpurascens* (Ave-Lall.) Gilli isolated and on the basis of IR-, ^{1}H and ^{13}C NMR, ^{13}C Dept 135 spectra identified: fellopterin, $C_{17}H_{16}O_5$, mp 101.0–102.5°C; xanthotoxin, $C_{12}H_8O_4$, mp 145.0–146.0°C; ostruthol, $C_{21}H_{22}O_7$, mp 137.0–138.0°C; biak-angelicin, $C_{17}H_{18}O_7$, mp 106.5–107.5°C, and from roots of *Prangos biebersteinii* Karjag. – imperatorin, $C_{16}H_{14}O_4$, mp 108.0–109.0°C; osthol, $C_{15}H_{16}O_5$, mp 84.0–85.0°C; isooxypeucedanin, $C_{16}H_{14}O_5$, mp 145.0–146.0°C; pranferol, $C_{16}H_{16}O_5$, mp 109.0–110.0°C; oxypeucedanin hydrate $C_{16}H_{16}O_6$, mp 137.0–138.0°C and bergaptol, $C_{11}H_6O_4$, mp 277.0–280.0°C.

THE *O*-ACYLATION OF 5α-STEROIDAL OXIMES WITH *N*-PROTECTED AMINO ACIDS

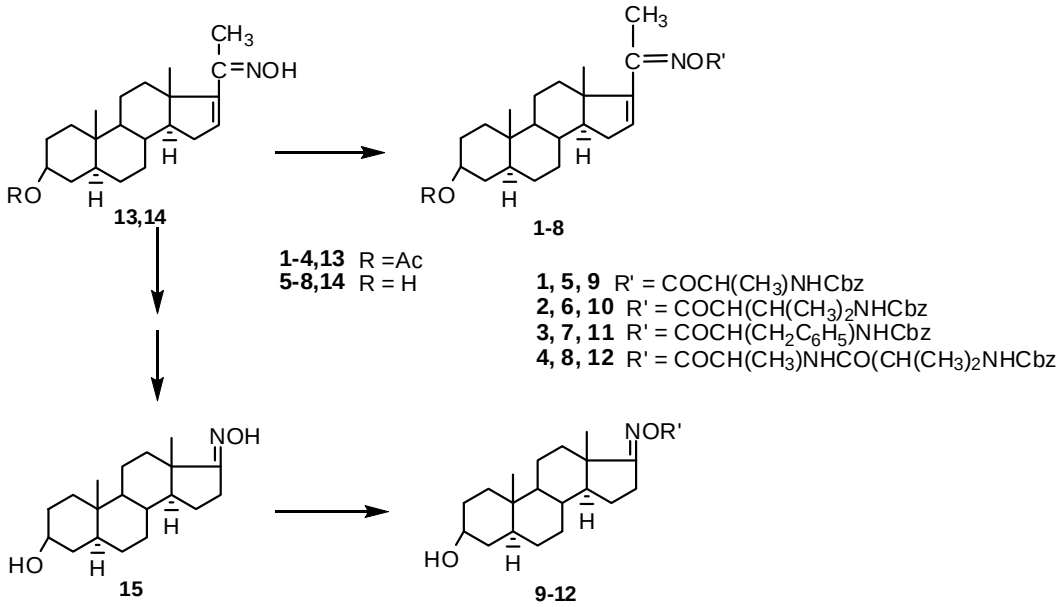
N. N. Barbakadze, N. Sh. Nadaraia, M. L. Kakhabrishvili, E. O. Onashvili

Tbilisi State Medical University Iovel Kutateladze Institute of Pharmacohemistry,
36 P. Sarajishvili str., 0159, Tbilisi, Georgia, e-mail: nana_barbakadze@yahoo.com

Chemical modification of natural compounds of plant origin by introduction of pharmacophore groups is a perspective direction for received of compounds with goal-seeking activities. Tigogenin from plant "*Yucca gloriosa"* (introduced in Georgia), is an available raw material for the synthesis of many interesting steroidal compounds.

In continuation of our extensive research on steroids new 5α-steroidal peptides **1-12** were synthesized. The starting materials – 3β-acetoxy- **13**, 3β-hydroxy-20-hydroximino-5α-pregn-16-ene **14** and 3β-hydroxy-17-hydroximino-5α-androstane **15** were synthesized from 3β-acetoxy-5α-pregn-16-en-20-one. The latest was obtained by splitting of tigogenin.

The *O*-acylation of **13**–**15** with *N*-protected (α-aminoacyl)benztriazoles (*N*-Cbz-*L*-Ala-Bt; *N*-Cbz-*L*-Val-Bt; *N*-Cbz-*L*-Phe-Bt) and N-protected (α-dipeptidoil)benztriazole (*N*-Cbz-*L*-Ala-*L*-Val-Bt) in the presence of Et_3N at 65°C in THF afforded the desired products **1**–**12** in yields of 44–73%.



Despite the fact, that compounds **14**, **15** containing two hydroxyl groups, the *O*-acylations proceeded chemoselectively towards the oxime hydroxyl group.

Our study showed that *N*-acylbenzotriazoles of amino acids are efficient reagents for the preparation of 5α-steroidal peptides **1**–**12**.

The structures of synthesized compounds are proved by ^{1}H, ^{13}C NMR spectral data and elemental analysis.

LIPID COMPOSITION OF SOME GEORGIAN CULTIVATED SPECIES

B. Kikalishvili, Ts. Sulakvelidze, M. Malania, D. Turabelidze

TSMU I.Kutateladze Institute of Pharmacochemistry,
e-mail: bkikalishvili@mail.ru

The aim of present study was the investigation of seed oil from Georgian cultivated species: *Linum usitatissimum* L. *Ruta graveolens* L. *Cucurbita maxima* Duch., for their fatty acid and phospholipid content in order to reveal the prospective raw for food additives and cosmetic preparations.

Identification of free fatty acids was carried out by HPLC analysis on the apparatus PTG-1 with the refractive detector R-401 and μ-bondapak C_{18} reverse phase column. Eluent 1 – methanol-water (1:2); eluent 2 – tetrahydrofuran-acetonitrile-water (5:7:9) + 0.1% acetic acid solution. The results were processed using the "OASIS-74" software. Quantitative determination of phospholipids in polar lipids was determined by spectrophometric assay.

Variations in seed oil content are shown in Table 1.

TABLE 1. **Oil content in the seeds of some Georgian cultivars**

Plant species	Linum usitatissimum	Ruta graveolens	*Cucurbita maxima* Duch
Oil content (%)	32	8	42

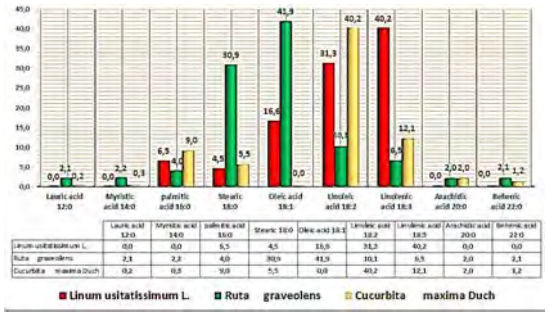


Fig. 1. **Fatty acid composition of Georgian cultivar plants.**

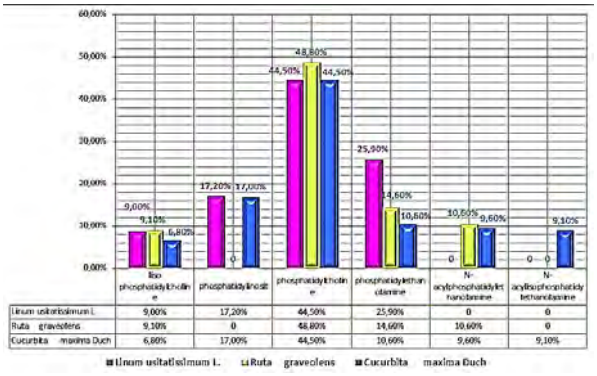


Fig. 2.

The predominant fatty acids were presented by linoleic, oleic, palmitic, and stearic. Among the cultivars significant differences in content of oil were observed for myristic, palmitic, stearic, oleic, and linoleic acids. Low lauric and arachidic acid levels were observed (Fig. 1).

Next phospholipids: lisophosphatidylcholine, phosphatidylinositol, phosphatilcholine, phospha-tidylethanolamine, N-acilisophosphatidylethanolamine, N-acylphosphatidylethanolamine and unidentified compound were isolated and identified from the polar fractions of *Linum usitatissimum* L. *Ruta graveolens*, *Cucurbita maxima* Duch. (Fig. 2).

CELLULOSE ESTER WITH AROMATIC ACID FROM THE FRUIT COAT OATS

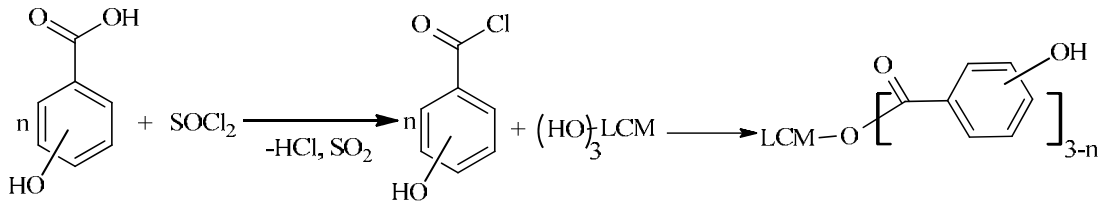
A. V. Protopopov, S. A. Bobrovskaya, A. V. Voroshilova, M. V. Klevtsova

Polzunov Altai State Technical University, Russia, 656038, Barnaul, Lenin avenue, 46,
e-mail: a_protopopov@mail.ru

In this paper we investigate the chemical modification oats shell (ligno-cellulosic material) meta- and ortho-hydroxybenzoic acid in order to obtain products suitable for further processing in various areas of construction, energy industry, in the manufacture of plastics and elastomers, as well as medicine and ecology. The effectiveness of this study lies in the fact that the production of cellulose esters obtained will allow to involve oats processing waste in the production cycle to obtain materials for various purposes.

The acylation is carried out by varying the fusion time within 1.5 hours in the temperature range of 25–55°C. The resulting products were precipitated into toluene and washed with ethanol, then dried to constant weight.

The reaction scheme is represented below:



Analysis of the acylated product by IR - spectroscopy showed the presence of absorption bands in the 3600–3400 cm^{-1} characteristic of the absorption bands of stretching vibrations of OH-groups. By increasing the synthesis temperature is shifted to the absorption band of 3400 cm^{-1} and an increase in the intensity of the absorption bands at 2900 cm^{-1}, characteristic for C-H vibrations in the aromatic ring connection. The absorption band in the region 1730–1750 cm^{-1}, characteristic of the stretching vibrations of CO-groups in the esters, its intensity increases with an increase in the synthesis of time. The presence of absorption bands in the region 1610–1450 cm^{-1}, responsible for the fluctuations of the aromatic ring, is justified by the presence of structural units of residual lignin and acid introduced.

In the course study received the done cellulose esters containing in combined form m-hydroxybenzoic acid with a degree of substitution of from 0.6 do1,5 and *o*-hydroxybenzoic acid with a degree of substitution of from 1 to 2.5. IR spectroscopy confirmed the formation of the ester bond. Thus confirmed the formation of cellulose esters directly from the seedcoat oats in thionyl chloride environment.

KINETICS ACYLATION FRUIT COAT OATS AROMATIC ACIDS

A. V. Protopopov, S. A. Bobrovskaya, A. V. Voroshilova, M. V. Klevtsova

Polzunov Altai State Technical University, Russia, 656038, Barnaul, Lenin avenue, 46,
e-mail: a_protopopov@mail.ru

The processing the kinetic data for the acylation reactions were performed for Yerofeyev-Kolmogorov equation. The proposed reaction conditions, a linear relationship between ln [-ln (1-a)] and on which lnt further determined reaction rate constant (K) using the method Sakovich.

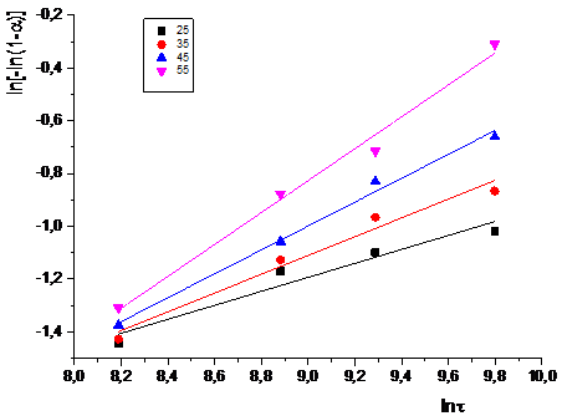


Fig. 1. Kinetic anamorphoses acylation of the LCM o-hydroxy benzoic acid.

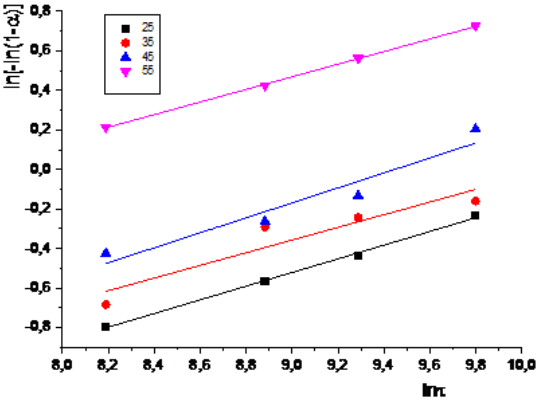


Fig. 2. Kinetic anamorphoses acylation of the LCM m-hydroxy benzoic acid.

The thermodynamic parameters of the reaction acylation hydrolyzed oat shell was determined based on the Eyring equation. To do this, plotted in coordinates ln (Kħ/Tkb) by 1/T, and subsequently calculated the enthalpy and entropy of activation.

TABLE 1. **Reaction Rate Constant**

Aromatic carboxylic acid, which is part of acylated LCM	Reaction rate constant (K), s^{-1} fusion at appropriate temperatures			
	25°C	35°C	45°C	55°C
o-Hydroxy benzoic acid	$3{,}63 \cdot 10^{-7}$	$1{,}95 \cdot 10^{-5}$	$6{,}17 \cdot 10^{-5}$	$1{,}91 \cdot 10^{-4}$
m-Hydroxy benzoic acid	$9{,}47 \cdot 10^{-6}$	$1{,}30 \cdot 10^{-5}$	$2{,}99 \cdot 10^{-5}$	$1{,}71 \cdot 10^{-5}$

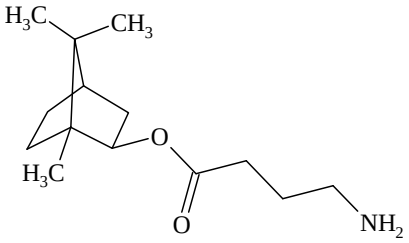
The results presented in the table show that the free energy of activation for the acylation process is not influenced by the substituent at benzene ring of an aromatic carboxylic acid, and its average value $\Delta G^{\neq}$ 110 kJ/mol. However, significant influence substituent benzoic acid ring has on the entropy and enthalpy of activation.

SYNTHESIS AND ANALGESIC ACTIVITY OF NOVEL ESTERS BASED ON BORNEOL AND INHIBITORY AMINO ACIDS

M. V. Nesterkina, I. A. Kravchenko

I. I. Mechnikov ONU, 65026, Odessa, Ukraine, Dvorjanskaya 2,
e-mail: mashaneutron@gmail.com, kravchenko.pharm@gmail.com

The aim of the present study is synthesis of novel esters based on borneol and inhibitory amino acids such as gamma-aminobutyric acid (GABA) and glycine with further investigation of their analgesic activity. Aforementioned esters **I** and **II** were synthesized using DCC/DMAP coupling method.



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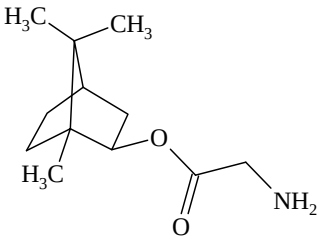


II

In the current research, borneol esters were applied topically in an ointment (2% w/w) using mixture of polyethylene glycol (PEG 1500), polyethylene oxide (PEO 400) and 1,2-propylene glycol in the ratio of 4:2:3 as a base. Antinociceptive effect of esters **I** and **II** was evaluated by models of thermal (hot plate) and chemical stimuli (formalin, capsaicin and AITC) in mice after topical application of the ointment. Analgesic action was comparable with the reference drug benzocaine (BZC) which is a local anesthetic commonly used as a topical pain reliever.

TABLE 1**. Analgesic Activity of Compounds I and II Tested by Thermal- and Chemical-Induced Models of Acute Pain in Mice (2% w/w ointment)**

Compound	Reaction time (in sec)			
	Hot plate	Formalin test	Capsaicin test	AITC test
Control (ointment base)	10.8 ± 0.9	83.3 ± 10.6	47.8 ± 2.8	67.5 ± 3.0
Compound **I**	45.7 ± 2.2	22.7 ± 0.8	12.0 ± 2.6	9.3 ± 1.7
Compound **II**	49.3 ± 0.7	19.3 ± 1.5	14.7 ± 1.2	20.3 ± 1.0
Benzocaine	18.3 ± 0.9	36.3 ± 2.4	28.7 ± 6.6	48.0 ± 2.0

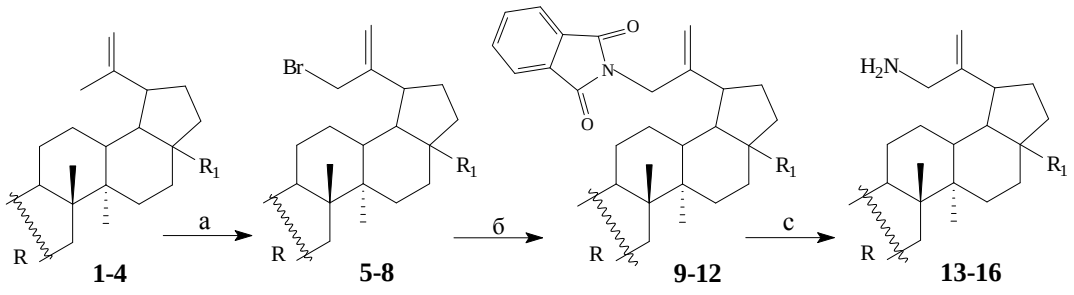
As seen in Table, borneol esters **I** and **II** were found to produce an antinociceptive effect in both thermal- and chemical-induced models of acute pain after their topical application compared with control group of mice. It is noteworthy that studied esters **I** and **II** better attenuated the pain reaction induced by thermal and chemical stimuli in comparison with reference drug BZC as evidenced by reaction time recorded for these compounds.

AMINATION OF BIOLOGICALLY ACTIVE DERIVATIVES OF BETULIN AND BETULONIC ACID

G. F. Krainova, V. V. Grishko

Institute of Technical Chemistry of Ural Branch of the RAS, Academician Korolev St., 3, 614013 Perm, Russian Federation, e-mail: Gulja.perm@mail.ru

To enhance bioavailability of low-molecular triterpenoids by forming noncovalent bonds to natural and synthetic water-soluble polymers (in particular, carboxymethyl cellulose), a possibility to introduce the amine fragment at C-30 position of biologically active derivatives of betulin and betulonic acid opted earlier, incl. diacetate **1**, triazole **2** [1], oxime **3** [2], and 2,3-secolupane diamide **4** [3], for the synthesis of new potential monomers was studied.



1,5,9,13: R= CH_3COO , R_1 = $-CH_2OOCCH_3$; **2,6,10,14:** R= , R_1 = $-OOCCH_3$;

3,7,11,15: R= NC, HO-N=CH , R_1 = $-OOCCH_3$; **4,8,12,16:** R= NC, $H_5C_2COO(CH_2)_2HNOC$, R_1= $-CONH(CH_2)_2OOCC_2H_5$

Reagents and conditions: а) N-Br , DAK, CCl_4 ; б) N , DMSO; с) NH_2NH_2, MeOH

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THE USE OF MEDICINAL VEGETABLE RAW MATERIAL IN THE TOOTH POWDERS RECIPE

P. A. Yavich, L. I. Churadze, M. B. Kakhetelidze, M. A. Gabelaya

TSMU Iovel Kutateladze Institute of Pharmacochemistry, Sarajishvili st. 36, Tbilisi, Georgia, e-mail: mziakakhetelidze@yahoo.com

In recent years due to unwanted side effects, which have the majority of produced tooth pastes, containing substances, that negatively affect both the oral cavity organs and the whole body (sodium lauryl sulfate, triclosan, chlorhexidine, metronidazole, etc.), has renewed interest in the use of dental powders, that previously were one of the most common tools designed for oral hygiene.

The disadvantage of dental powders is on the one hand their relatively high abrading ability, resulting in abrasion of tooth enamel, and disruption of its integrity, on the other hand - the complete absence of any composition of biologically active natural substances.

It is known that during brushing, mastering and absorption of active substances in the oral cavity occurs on average within 30 seconds. It results in recent appearance of assortment of tooth powders, containing in their composition a high percentage of finely chopped parts of medicinal plants (flowers, leaves, stems, etc.). These powders have a rather low rate of flowability that does not allow to use dispensing containers and causes difficulties in their use. One of the means of increasing the flowability index is to mix crushed herbs with fine particulate calcium carbonate with a particle size of about 2–20 microns. Study of quantitative relationship between calcium carbonate and chopped vegetable raw materials has shown that in the optimal variant takes place an increase in the total mass flow index.

When using dental powders containing different chopped vegetable raw materials and calcium carbonate in specific proportions is takes place saturation with oral bioactive components having disinfectant, anti-inflammatory, wound-healing properties. . For example, mint leaves, lemon, mandarin, eucalyptus and bay leaf and others contain a variety of essential oils; smoke tree leaves - tannins; chamomile, sage, nettle - the amount of flavonoids, etc. Regular introducing of biologically active substances, using the tooth powders,into the oral cavity contributes to maintaining normal acid-base balance and preservation of the health of the gums, teeth and other oral cavity organs.

EVALUATION OF THE EFFECTIVENESS OF BIOLOGICALLY ACTIVE PREPARATIONS BASED ON PLANT RAW MATERIALS ON SPRING WHEAT

N. G. Vlasenko, M. T. Egorycheva, M. P. Polovinka

Siberian Researches Institute of Soil Management and Chemicalization of Agriculture of SFSCA RAS, Krasnoobsk, Novosibirsk Region, Russia, e-mail: vlas_nata@ngs.ru

Modern biologically active herbal preparations able to stimulate the immune system of plants, increase resistance to pathogens, to provide growth stimulating effects, thereby ensuring an increase in productivity and quality of grain, as well as establishing the biological balance in agrocenoses and an overall improvement in the ecology.

Compounds of this class include new preparations: Bioclad – on the basis of an extract of the lichen genus *Cladonia* [1]; Bius – on the basis of an extract *Abies sibirica* and of an extract of the lichen genus *Usnea* [2]; Larus – a mixture of larch extract and extract of the lichen genus and of an extract of the lichen genus *Usnea* [3]. The drugs used for the processing wheat seeds before sowing and spraying of wheat plants in the phase of tillering and earing.

Pre-seeding treatment reduced the prevalence of plant root rot in wheat tillering stage on 42.8–68.3%. The density of plants standing in comparison with control increased on 3.8–20.7% at 2–3 leaf stage and on 2.2–21.6 % – in wax ripeness phase. The best on this indicator was Bioclad. The number of stems per plant increased compared to the control on 14.7–19.8%, and total number of productive stems per 1 m^2 – on 10.5–15.7 %, plant survivability increased by 2-2.8 %. High rates in this case ensured by Larus. Productivity increased by 4–11 %.

Reducing the prevalence of plant diseases and the growth promoting action of preparations has led to an increase in grain of productivity relative to control on 14.4–18 % when used in the tillering phase and on 10.4–53.8 % – in earing phase. The maximum additional yield of grain in the first case was obtained from the use of the Bius and Larus, the second - from the Bioclad and the Larus.

The conducted research confirmed the potential use of new preparations of natural origin as for seed treatment and during the growing season as fungicides. Expanding the range of preparations based on natural substances and their inclusion in the technology of cultivation of grain crops after registration will help to solve the problem of ecologization of plant protection.

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THE BIOLOGICALLY ACTIVE COMPOUNDS OF POLYGONATUM GENUS GROWING IN GEORGIA

L. N. Gvazava

Iovel Kutateladze Institute of Pharmacochemistry of TSMU, 36, P. Sarajishvili st., 0159, Tbilisi, e-mail: liligvazava@yahoo.com

During the investigation of *Polygonatun* genus (family *Convallariaceae*), growing in Georgia, it was established the high content of steroids (spirostans and furostans) and phenolics (flavonoids and stilbenes) in some of species, and characterized by a wide spectrum of pharmacological activity: cardiotonic, cytotoxic and antibacterial.

Raw material was collected in May-June in Georgia (Kojori, Saguramo).

Chemical composition of plant *Polygonatum obtusifolium* (C. Koch) appeared to be especially interesting.

Previously, were allocated and described four sapogenins: smilagenin, diosgenin, yamogenin and pennogenin, which were isolated after acid hydrolysis of the raw material.

Herein we communicate result of a structural study of four glycosides from this plant.

The structures of the glycosides were established using chemical transformation and GLC, IR, mass and NMR spectroscopy.

Glycoside **1** is (25*R*)-spirost-5-en-3β,17α-diol 3-*O*-α-*L*-rhamnopyranosyl-(1→2)-β-*D*-glucopyranoside.

Glycoside **2** is 26-*O*- β-*D*- glucopyranosyl-(25*R*)-furost-5-en-3β,17α, 22α,26-tetraol 3-*O*-α-*L*-rhamnopyranosyl- (1→2)-β-*D*-glucopyranoside.

Glycoside **3** is (25*S*)-spirost-5-en-3β-ol 3-*O*-β-*D*-glucopyranosyl-(1→2)-[β-*D*-xylopyranosyl -(1→3)]-β-*D*- glucopyranosyl -(1→4)-β-*D*- galactopyranoside.

Glycoside **4** is 26-*O*-β-*D*-glucopyranosyl-(25*S*)-furost-5-ен-3β,22α,26-triol 3-*O*-β-*D*-glucopyranosyl-(1→2)-[β-*D*-xylopyranosyl-(1→3)]-β-*D*-glucopyranosyl-(1→4)-β-*D*-galactopyranoside.

We have isolated and identified phenolic compounds also - derivatives of quercetin (isoquercitrin, hyperin, rutin) and kaempferol (astragalin, kaempferol-3-*O*-α-*D*-arabinopyranoside).

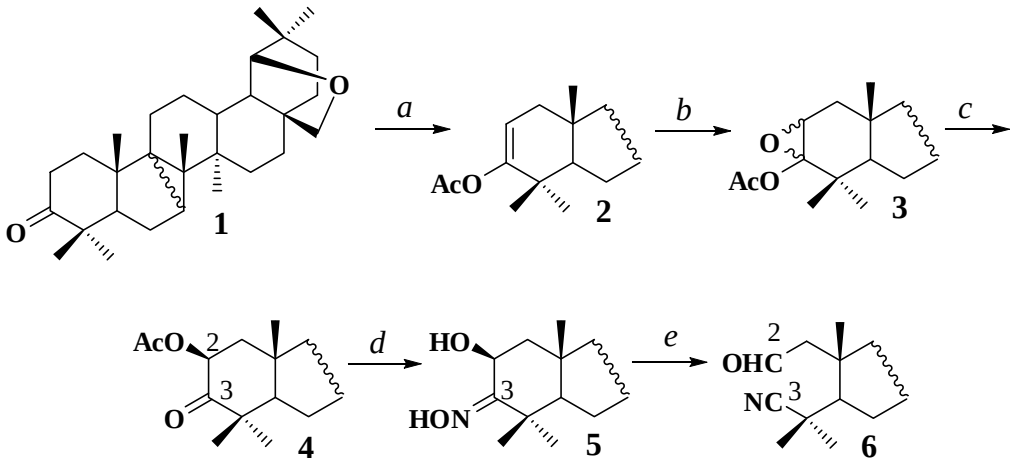
Also have been allocated and identified cis- and trans-forms of stilbenes: *cis*-3,5,3′,5′-tetrahydroxy-4-metoxy-stilbene and *trans*-3,5,3′,5′-tetrahydroxy-4-metoxy-stilbene.

SYNTHESIS OF NEW 2,3-*seco*-18α*H*-OLEANANE ALDEHYDONITRILE

I. A. Tolmacheva, A. V. Nazarov, V. V. Grishko

Institute of Technical Chemistry of Ural Branch of the RAS, 3, Acad. Korolev St., 614013 Perm, Russian Federation, e-mail: tolmair@gmail.com

The Beckmann fragmentation of triterpene 3-hydroxy and 3-oxo-substituted 2-oximes was earlier used in synthesis of 2,3-seco-triterpenoids with 2-nitrile and 3-carbonyl/carboxyl groups [1-3]. We have considered a possibility of obtaining alternative 2,3-seco-triterpene structures of a new type. The 18αH-oleanane 3-oxime **5** (as the regioisomer of 2-oxime [1]) were obtained from 2β-acetoxy-19β,28-epoxyolean-3-one **4** produced as a result of stereoselective thermal rearrangement of diastereomeric epoxides **3** [4]. Oxime **5** undergoes the Beckmann fragmentation to 4-cyano-2-aldehyde **6** with use of tosyl chloride.



(*a*) $CCl_4/H_2SO_4/CH_2=C(CH_3)OCOCH_3$; (*b*) *m*-$ClC_6H_4CO_3H/CH_2Cl_2$;
(*c*) C_6H_6, reflux; (*d*) $NH_2OHxHCl/C_5H_6N$, reflux; (*e*) TsCl/Py/reflux.

This work was financially supported by the Russian Foundation for Basic Research (Grant No. 16-53-00029_Bel_a).

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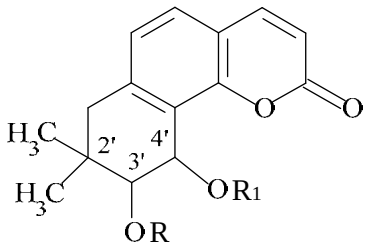
Seseli campestre SOURCE OF ANGULAR PYRANOCOUMARIN DERIVATIVES

N. Kh. Mikailova, S. V. Serkerov

Institute of Botany, National Academy of Sciences of Azerbaijan
Badamdar highway 40, Baku AZ1073, e-mail: s.serkerov@mail.ru

Among the *Apiaceae* family representatives the species of the *Seseli* genus are characterized including linear and angular furocoumarins, also kellactone derivatives.

By chromatography method from the sum of extractives obtained from air-dry roots by acetone extraction, four individual substances were obtained: $C_{14}H_{14}O_4$, mp 190.5–191.5°C (1), $C_{19}H_{20}O_6$, mp 120.0–121.5°C (2), $C_{19}H_{20}O_6$, transparent resin (3), $C_{24}H_{26}O_7$, mp 176.0–177.0°C (4), of which (1) and (4) based on data of IR-, ^{1}H NMR, ^{13}C, ^{13}C Dept 135 and Dept 90 spectra are identified as kellactone and diangelatkellaktone, respectively. Substances 2 and 3 are new, which according to the IR-, ^{1}H NMR, ^{13}C, ^{13}C Dept 90 and Dept 135 spectra have the structure 3′α-angeloiloxy-4′β-oxy-3′,4′-dihydroseselin (2) and 3′α-oxy-4′β-senecioiloxy-3′,4′-dihydroseselin (3). Acetylation of compound (3) and (4) leads to monoacetyl-derivatives: 3′α-angeloiloxy-4′β-acetoxy-3′,4′-dihydroseselin (2a) and a 3′α-acetyloxy-4′β-senecioiloxy-3′,4′-digidroseselina (3a). Structure 2a and 4 are identical to those praeruptorin A and B, respectively, isolated by Chinese scientists T. Liang, W. Yae, O. Li from *Peucedanum praeruptorum* Dunn plants, having activity against the gastric cancer.



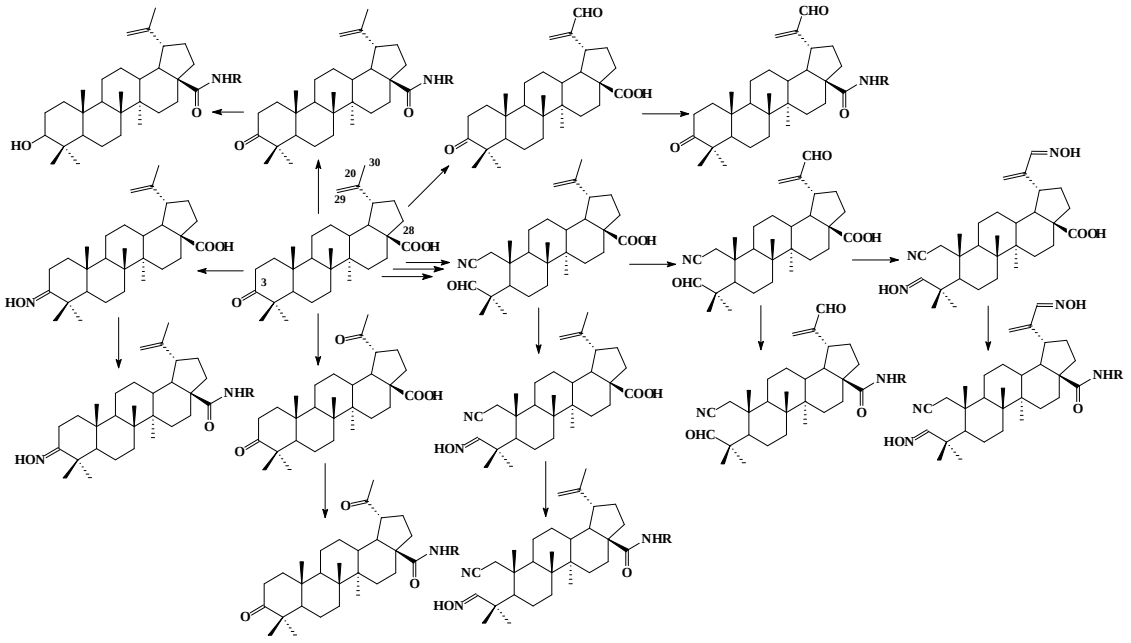
(1) R=R1=OH
(2) R=-αAng; R1=-βOH
(3) R=-αOH; R1=-βSenec
(4) R=R1=Ang
(2a) R= -αAng; R1=-βAc
(3a) R=-αAc; R1=-βSenec

SYNTHESIS AND MODIFICATIONS OF BIOLOGICALLY ACTIVE 2,3-SECOTRITERPENE AMIDS AND CYCLIC ANALOGUES

E. V. Igosheva[1], I. A. Tolmacheva[1], O. V. Savinova[2], E. I. Boreko[2], V. V. Grishko[1]

1) Institute of Technical Chemistry of Ural Branch of the RAS, Perm, Russia
2) The Republican Research and Practical Center for Epidemiology and Microbiology, Minsk, Belarus Republic, e-mail: ekig00@mail.ru

Lupane-type triterpenoids as natural low molecular weight metabolites display multi-purpose biological activity. In most cases, directed chemical transformation of triterpenoids endows them with enhanced target properties, in particular, antiviral, cytotoxic and anti-inflammatory action. At that point, positions C3, C28 and isopropylidene fragment (C20, C30) of triterpene sceleton are the most promising for modifications.



Synthetic transformations of betulonic acid and of its 2,3-secoderivatives result in C28-amide conjugates including C3, C29, C30 functionalized derivatives with inhibitory activity (IC_{50} 10.3–29.5 mg/L) against virus of herpes simplex type 1.

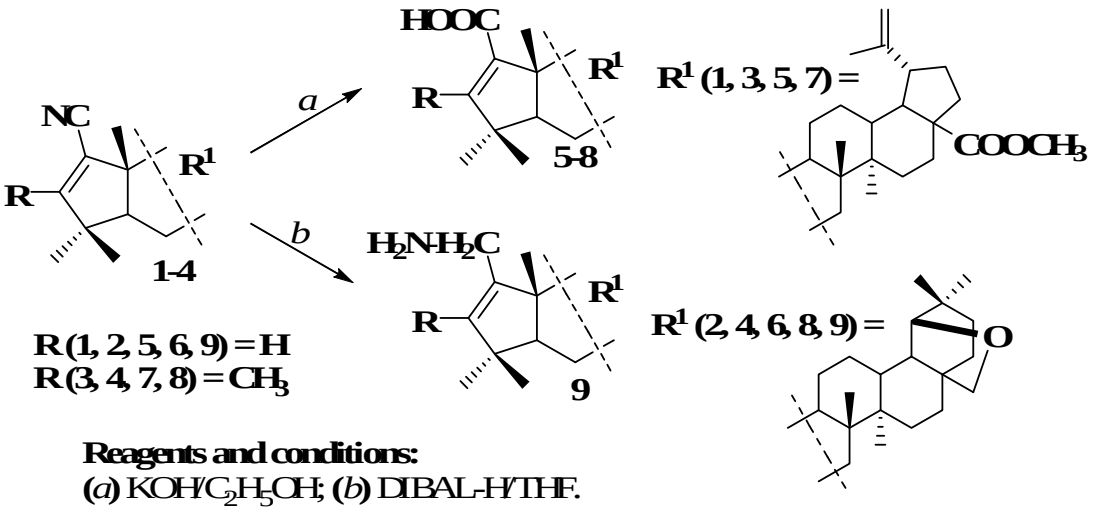
This work was financially supported by the Russian Foundation for Basic Research (Grant No. 16-53-00029 Bel_a) and Government of Perm Region (Project Nr. C-26/056).

SELECTIVE TRANSFORMATIONS OF CYANO GROUP OF TRITERPENE α,β-ALKENE-NITRILES

A. V. Konysheva, I. A. Tolmacheva, V. V. Grishko

Institute of Technical Chemistry of Ural Branch of the Russian Academy of Sciences
Acad. Korolev St. 3, Perm, 614013, Russia, e-mail: Pereslavceva89@mail.ru

The methods for selective transformations of cyano group were developed for lupane and 18αH-oleanane α,β-alkene-nitriles **1**–**4** described previously [1, 2]. It was found that only under conditions of protracted (for 5 days) boiling in alcoholic 15% KOH solution, the nitrile group of alkene-nitriles **1**–**4** was hydrolyzed with subsequent formation of the α,β-unsaturated A-pentacyclic acids **5**–**8**. Only alkennitrile **2** undergoes reductive conversion under the action of the DIBAL-H reagent; at that point, independently on the process conditions (temperature, molar ratio of reagents, solvent), the reaction results in formation of amine **9.**



SCHEME 1.

This work was financially supported by the RFBR Grant № 16-03-00865.

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THE FERULAS OF UZBEKISTAN ARE THE SOURCE OF TERPENIC DERIVATION

O. N. Avalbaev[1], U. Rahmankulov[1], H. U. Usmonjonova[2], A. M. Nigmatullaev[3]

1) Jizzakh State Pedagogigal Institute, e-mail: avalbayev7788@mail.ru
2) Jizzakh State Politechnical Institute
3) Institute of the Chemistry of Plant Substances

During the last 45–50 years structure of plants which can be found in territory of our Republic and its neighbouring countries have been learned by Uzbek scientists including The Institute of the Chemistry of Plant Substances named after Sobir Yunusov.

Inconsequense, different combinations are devided. There are more than terpinoid peculiarities including that only 121 groups and almost 500 types of *Apiaceae* L. family are members of this family.

In this family members of *Ferula, Heracleum Angelica, Prangos, Torilis* groups are perspective.

By learning chemical structure of *Ferula* L. it is defired that 85 types from 106 typs which grow in the Middle Asia and 90 types from 110 types which grow in territory of Previous Union save terpenic derivation.

Some scientists of the institute experimented that almost 90 types of ferul 34 save terpenic derivation and it is defined that 55 types of them save kumarins 34 types of them save essential oil and 18 types of them save seskviterpenic laktons.

It is also defined that from 63 types of ferule which grow in Uzbekistan, 32 of them save 20 of them save complex ethirs and 9 of them save lakton 27 types of ferula which save terpinoids are endemic of Tyanshan. They grow: 8 types of them in desert, 4 types of them in full-desert, 9 types of them in hills 12 types of them in hill-mountain 23 types of them in mountains.

The result of searching shows that monocarps types save lactons much more and policarp types save complicated ethirs and kumarins.

In the result of learning by types of botanics, chemics, pharmaceutists and technologics estrogen peculiar items are disjoined and agitated to medicine. Tefestrol preparation which in gynecology and Panoferol preparation which used in veterinary are created from types of *Ferula tenuisecta, F. kuhistanica*.

FLAVONOIDS OF *Fraxinus excelsior* LEAVES

E. H. Kerimli[1], S. V. Serkerov[2]

1) Azerbaijan Medical University, A. Bakikhanov str. 23, Baku AZ1022, Azerbaijan, e-mail: kelvin83@list.ru
2) Institute of Botany, Azerbaijan National Academy of Sciences, Badamdar ave. 40, Baku AZ1073, e-mail: s.serkerov@mail.ru

Carbohydrates, phenols, coumarins and other compounds belong a diverse group of biologically active substances has been identified from *Fraxinus excelsior* organs according to literature sources.

The leaves of *Fraxinus excelsior* were collected from Guba region the Republic of Azerbaijan in 2012.

Crushed and dried leaves of *Fraxinus excelsior* (750 g) were extracted 3 times 24 hours with 70% EtOH at room temperature. The combined extracts were evaporated under vacuum nearly to the aqueous residue. The aqueous residue was extracted with hexane and hexane phase rejected. The aqueous phase was extracted with $CHCl_3$ and again the aqueous phase was extracted with n-BuOH. BuOH phase was dried by sodium sulfate and evaporated by filtration from filter paper. BuOH residue is dissolved in 40% EtOH by heating and then cooled. As the result of process, yellow color powdery was settled.

Components of total flavonoid compounds were identified by Agilent series 1200 HPLC mass-spectrometry 6538 qTOF (electro spray ionization) interface.

These four compounds were identified:

1. Rutin $C_{27}H_{30}O_{16}$; a) MW = 610.1615; RT = 14,139 min; negatively charged ions: *m/z* 609.154 ($[M - H]^-$); b) MW = 610.1535; RT = 11.986 min; positively charged ions: *m/z* 611.1608 ($[M + H]^+$).

2. Hirsutrin $C_{21}H_{20}O_{12}$; a) MW = 464.106; RT = 18.246 min; negatively charged ions: *m/z* 463,0987 ($[M - H]^-$); в) MW = 464.0951; RT = 18.362 min; positively charged ions: *m/z* 465.1023 ($[M + H]^+$).

3. Nicotiflorin $C_{27}H_{30}O_{15}$; a) MW = 594.167; RT = 23.009 min; negatively charged ions: *m/z* = 593.1598 ($[M - H]^-$); в) MW = 594.1583; RT = 20.994 min; positively charged ions: *m/z* 595.1656 ($[M + H]^+$).

4. Astragalin. $C_{21}H_{20}O_{11}$; MW = 448.1112; RT = 25.717 min; negatively charged ions: *m/z* 447.1039 ($[M - H]^-$);

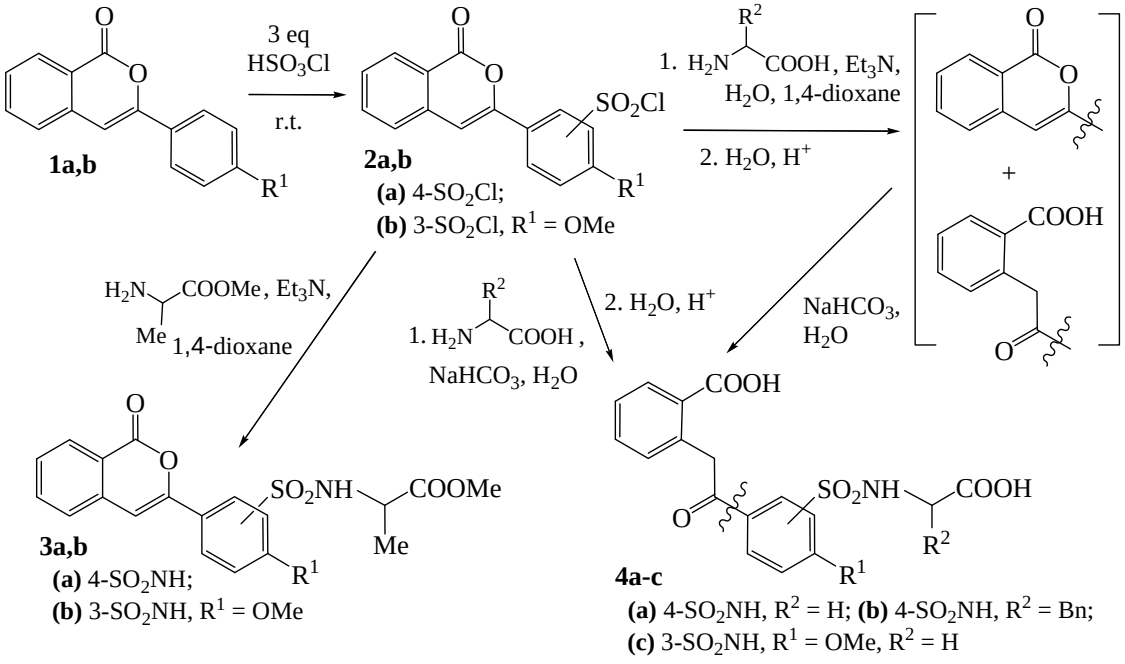
According to received information, in the total flavonoid compounds (TFC) is rutin, 89.733%; hirsutrin 4.473%; nicotiflorin 5.530%; astragalin 0.264%.

3-ARYLISOCOUMARINS AMINO ACID DERIVATIVES WITH SULFONAMIDE GROUP

S. V. Shilin, O. V. Shablykina, A. A. Riabchenko, V. V. Ishchenko, V. P. Khilya

Kyiv National Taras Shevchenko University, Faculty of Chemistry, 12 L. Tolstogo st., Kyiv, 01033, Ukraine, e-mail: varang77@ukr.net

To continue research on new amino acid derivatives of isocoumarins [1] we have studied the possibility of connecting these natural structures through pharmacophore sulfonamide moiety. Strategy of introduction of the sulfonamide group in the 3-arylisocoumarins was developed by us earlier [2]. At the first step isocoumarine sulfochloride was prepared, a second reaction was carried out with an amino acid. The natural 3-phenylisocoumarin **1a** (found in *Homalium laurifolium* [3]) and its synthetic analogue **1b** with activating aromatic substituent electron donating methoxy group were selected to be modified.



Sulfochlorination and subsequent reaction with amino acid ester occur using standard techniques with a good yield. But when free amino acids were used in the reaction, water is necessary for their dissolving, and complete or partial disclosure of isocoumarin cycle under the action of water from the reaction mixture was observed. Such a rapid hydrolysis of the isocoumarin lactone system in such mild conditions isn't typical for these compounds; so it is assumed that modified amino acid compounds have solubility in a basic medium.

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TESTING THE EFFECTIVENESS OF SOFTWOOD WOOD GREENS IN ANIMAL

T. V. Hurshkaynen[1], A. V. Kutchin[1], A. V. Filatov[2]

1) Institute of Chemistry Komi Science Center Ural Division of RAS, 48 Pervomaiskaya Str., Syktyvkar, Russia, 167982
2) Vyatka State agricultural academy, 133 October prospect, Kirov, Russia, 610017, e-mail: hurshkainen@chemi.komisc.ru

At the Institute of Chemistry of Komi Science Centre, research on the emulsion extraction of coniferous wood greenery and release of biologically active components continues. Tests of emulsion extracts show their high efficiency as crop protection agents and feed additives for animals. Physiological studies of coniferous feed additives have carried out, which have shown a stimulating effect of drugs on the body and increased productivity of animals and birds.

Use of feed additive Verva based on abies extract in pig-breeding has a scientific and practical interest. Study on effectiveness of the drug for the productive qualities of pigs during fattening was carried out. Experiments were carried out with 60 pigs of large breed white × landrace in a pig-breeding complex of JSC "Zarechie" (Kirov). To a basic diet of experimental groups consisting of young animals Verva drug was added during 30 days once a day: for the first group the dose was 1 g, for the second - 3 g and for the third - 5 g per one animal. It is shown that use of the drug Verva for the pigs feeding since the first day of fattening during 30 days in a dose of 1 g per animal per day according to comparative properties have a positive impact on the productive qualities of fattening calves.

These studies allow one to make suggestion that the feed additive Verva has cumulative properties and prolonged action, which will allow one to use the drug in small doses over a short period, but at the same time to receive the high weight gain of the animals.

Investigations of the effect of Verva on the reproductive ability and the prevention of postpartum diseases with 40 basic sows were also performed. It was found that the use of the feed additive for sows since 80 days of gestation during 30 days in a dose of 3-5 g has a positive effect on pregnancy, childbirth and post-natal period. The newborn young animals during the early postnatal period have better growth energy and development accompanied with its high safety.

Results of scientific and practical research of the effectiveness of the feed additive Verva allow us to recommend the use of natural active ingredients to enhance nonspecific young resistance and the intensity of pig growth, to increase safety of livestock. The drug can be used in the pig industry, small-scale commercial farms with different technologies of animal rearing, in breeding and farms.

This work is carried out with the financial support of the project 15-15-34-68 of the program of UB RAS.

THE STUDY OF THE CHEMICAL COMPOSITION OF *Halogeton glomeratus* BELONGING TO THE FAMILY *Chenopodiaceae*

A. B. Kudekova, A. K. Umbetova, G. Sh. Burasheva

Kazakh National University al-Farabi, Kazakhstan, Almaty, 050040,
e-mail: aibo_85@mail.ru

More interest is paid to wild plants because of extensive areas of growth that ensures to provide the public health service needs of medicinal raw materials.

The object of our study is *Halogeton glomeratus* – a perennial plant of the family *Chenopodiaceae*. There are few studies from the chemical point of view. It is used to feed the sheep.

According to conventional techniques of the USSR State Pharmacopoeia and the State Pharmacopoeia of the Republic of Kazakhstan for the aerial parts and roots *Halogeton glomeratus* the amounts of high quality of raw materials: moisture, ash (total ash) and the amount of active substances were determined. Standards providing the definition of authenticity, purity, and goodness of raw materials are the main conditions to ensure the quality of herbal raw materials.

Macro- and micronutrients were identified by the method of atomic absorption spectroscopy in the total ash. Chemical and chromatographic methods of analysis were carried out phytochemical analysis of the major classes of biologically active substances in the aboveground parts and roots of *Halogeton glomeratus*.

For quantitative analysis of the main groups and classes of biologically active substances were used all known methods of numerical analysis. Amino acids, fatty acids and a lipophilic part of the aboveground parts and roots of *Halogeton glomeratus* were identified by the method of gas-liquid chromatography and chromato-spectrometry.

For the first time conditional phytopreparation obtained from the aboveground parts of *Halogeton glomeratus* revealed antileishmanial activity.

ALKALOIDS FROM ROOTS OF *Cephalaria tchihatchewii* Boiss IN TCHIHATECH

I. S. Movsumov, E. A. Garayev, T. A. Suleymanov

Azerbaijan Medical University, e-mail: eldargar@mail.ru

Continuing the study of biologically active substances of the members of the fam. Dipsacaceae L., we have studied alkaloids composition of *Cephalaria tchihatchewii* Boiss in Tchihatech from Azerbaijan flora. *C. tchihatchewii* is perennial herb. The raw materials for the study were prepared at the beginning of July in 2015 near the village Mistan of Azerbaijan Republic at an altitude of 2350 m above the sea level.

Earlier from flowers of *C. tchihatchewii* β-sitosterol, free oleanolic acid, luteolin, quercetin, hyperoside, quercimeritrin, synaroside were isolated and identified and after hydrolysis sum of triterpene saponins hederagenin and oleanolic acid were obtained.

With known methods alkaloids sums (about 0.61%) consisting of at least 4 substances with R_f 0.80; 0.50; 0.29 and 0.13 first have been received of plant roots. Solvent system: chloroform-ethanol, 20: 1. Sorbent: Sorbfil, Reagent: Dragendorff solution.

The base substance **1** has been received from petroleum ether by recrystallization of sum. Sunbstance **1** is small needles crystals, the composition is $C_{10}H_9NO_2$, mp 80–81°C, soluble in chloroform, ethanol, hexane, insoluble in water. IR spectra were recorded on a Varian instrument (USA), the melting temperature on the unit "Smp 20 Striart" (UK). On the basis of the physico-chemical properties, spectral and chromatographic data using authentic samples the selected base was identified as gentsianin.

According to literature data gentsianin has the expressed anti-inflammatory, hypothermic and sedative effect and several times as active as sodium salicylate and amidopirina.

Isolation and identification of the other alkaloids roots of *C. tchihatchewii* is being continued.

ESSENTIAL OILS: MODERN TRENDS, PROSPECTS OF STUDY AND APPLICATION

G. A. Atazhanova

JSC “International research and production holding “Phytochemistry”, Republic of Kazakhstan, Karaganda, 100009, M. Gazaliyev str. 4, e-mail: arglabin@phyto.kz

Today the essential oil market is steady and there is a strong demand for the product that is used in the pharmaceutical, food, perfumes and cosmetics industries, and other economic activities. Food industry consumes the largest amount of essential oils – 50% of total production, followed by perfumes (30%), pharmaceuticals (15%), cosmetics (5%) and medical aromatherapy (about 1%).

The essential oil field is considered as one of the most profitable industries. With its unique natural and climatic conditions, the Republic of Kazakhstan could become the largest producer of essential oils and products based on them in the world.

For a number of years, the International research and production holding “Phytochemistry” has been developing a new scientific direction connected with multidimensional study of essential oils from the plant resources of Kazakhstan.

Systematic research of essential oils of more than 170 plant species in the flora of Kazakhstan was conducted for the first time at the laboratory of terpenoids chemistry. Component composition was described, more than 1800 mono- and sesquiterpenoids were identified, the obtaining methods were developed for practically available of them and chemical modifications of their molecules were conducted.

Works on the development of new detergents based on essential oils of *Artemisia glabella*, *Ajania fruticulosa*, *Thymus marschallianus* and citrus peel are also performed, during which their optimal composition was selected and experimental-industrial regulation using environmentally sound natural substances was developed. For example, for the production of toilet soap with bactericidal effect, essential oils obtained by microwave extraction were used. Microwave extraction is considered as established tool of “Green Chemistry”, since its application reduces the duration. In this case, heat carrier and the use of organic solvents are eliminated.

Thus, the production of environmentally sound natural products based on essential oils is potential for the business: because minimum amount of capital is required for the start; the product is demanded, and the competition is minimal; and also there is a domestic raw material base.

2-(4-BROMBUTOXY)-6-HYDROXY-4-METHOXYCHALCONE WITH HEPATOPROTECTIVE ACTIVITY

P. Zh. Zhanymkhanova, G. K. Mukusheva, R. B. Seidakhmetova, S. M. Adekenov

JSC "International Research and Production Holding "Phytochemistry", Republic of Kazakhstan, Karaganda, 100009, Gazaliyev str. 4, e-mail: phyto_pio@mail.ru

Natural compounds, especially flavonoids, due to their structural variety allow to form a range of new medications with wide spectrum of pharmacological activities. Synthesis of compounds, mixed with different functional fragments in one molecule, attracts interest in terms of studying their mutual influence on biological activity and discovers new opportunities for the following targeted chemical modification.

In order to widen the variety of biologically active substances, new pinostrobin halogen derivative 2-(4-brombutoxy)-6-hydroxy-4-methoxychalcone with anti-inflammatory [1] and hepatoprotective activity is obtained.

Interaction of pinostrobin flavanone with dibromoalkane in the acetone with the presence of potassium carbonate is processing in accordance with Michael retro-reaction scheme - *O*-alkylation, the structure of which is confirmed by XRD [2].

For the research of hepatoprotective activity of 2-(4-brombutoxy)-6-hydroxy-4-methoxychalcone, the culture of Hep G2 cells in 96-well plates was used. Cells were cultivated in EMEM medium with addition of 200 mM of L-glutamine, 10% of embryonic bovine serum, 100 Un/ml of penicillin, 100 mkg/ml of streptomycin and 25 mkg/ml of amphotericin B. Cells were incubated under 37 °C in the atmosphere of 5% CO_2. The sample of 2-(4-brombutoxy)-6-hydroxy-4-methoxychalcone was used at the concentration of 3 and 5 mkg/ml. Hepatoprotective preparation "Carsil" was used as comparative preparation. Control groups consisted of cells with analogue concentrations of DMSO and CCl_4. Tetrachloromethane (CCl_4) was used as hepatotoxic agent, which was added to the all wells in 0.5% concentration.

2-(4-brombutoxy)-6-hydroxy-4-methoxychalcone at the concentration of 3 and 5 mkg/ml demonstartes evident hepatoprotective activity in comparison with control and comparative preparation "Carsil".

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QUALITATIVE DETERMINATION OF APIGENIN IN THE RAW MATERIAL OF *Serratula coronata* L.

D. K. Nurkadyrov, P. Zh. Zhanymkhanova, G. K. Mukusheva, S. M. Adekenov

JSC "International Research and Production Holding "Phytochemistry", Republic of Kazakhstan, Karaganda, 100009, Gazaliyev str. 4, e-mail: phyto_pio@mail.ru

Serratula coronata L. is a potential source of ecdysteroids and phenolic compounds [1, 2].

In order to determine qualitative content of apigenin, we conducted comparative study of the extracts of primary and secondary raw materials of *Serratula coronata* L., after the isolation of ecdysteroids. Qualitative and quantitative content of apigenin in ethanolic extracts of *Serratula coronata* L. is conducted through the reverse phase high performance liquid chromatography with high pressure. The results of qualitative content of apigenin in the extracts are provided in the table below.

TABLE 1. **Qualitative content of apigenin in the extracts of *Serratula coronata* L.**

No.	Sample	Qualitative content of apigenin according to HPLC, %
1	*Serratula coronata* L. (raw material, 70% ethanol)	1,8
2	*Serratula coronata* L. (raw material, 96% ethanol)	3,7
3	*Serratula coronata* L. (secondary raw material, 96% ethanol)	2,2

According to the data provided in the Table, high qualitative content of apigenin in 96% ethanolic extract is 3,7%.

As a result, *Serratula coronata* L. is a potential source of such polyphenolic compounds as: apigenin, rutin and quercetin, this allows to use it as a potential source of medicinal raw material for the formation of new medications.

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DEVELOPMENT OF SOFT PHARMACEUTICAL FORM FOR DENTAL DISEASES TREATMENT

A. N. Zhabayeva[1], N. G. Titova[1], Kh. I. Itzhanova[2], S. M. Adekenov[1], K. Altynbekov[3]

1) JSC "International Research and Production Holding"Phytochemistry", Republic of Kazakhstan, Karaganda, 100009, Gazaliyev str. 4, e-mail: phyto_pio@mail.ru
2) "KaragandaPharmaceutical Plant" LLP, Karaganda, 100009, Botanicheskaya str. 10/1, e-mail: kfz@mail.ru
3) Kazakh Medical University named after S.D. Asfendiyarov, Republic of Kazakhstan, Almaty, 050000, Tole bi str. 88, e-mail: info@kaznmu.kz

Herbal medicines are used widely in medical practice for different diseases treatment. Phytopreparations contain biologically active components, which in most cases are non toxic, have no amyctic effect on skin, do not cause allergic response, and the most important thing is that they are active towards the strains of microorganisms and viruses resistant to antibiotics and synthetic medicaments.

Potential sources for obtaining antibacterial, anti-inflammatory and vulnerary medicines are representatives of *Salicaceae* family, in particular, species of poplar (*Populus* L.) genus.

We developed a technology for obtaining antiparadontal medicine - "Topolin 5 % gel, with the extract of Matricaria chamomilla". An optimized content of soft pharmaceutical form is selected.

In the clinic of dental institute of KazNMU named after S.D. Asfendiyarov (Almaty), a clinical testing in the form of application of new phythopreparation "Topolin 5 % gel with the extract of Matricaria chamomilla" was performed. 24 patients were treated in complex therapy of paradontium disease of inflammatory-destructive nature. As a result of performed experimental research, it was established that original content of gel composition provides high adhesion to the mucous surfaces, reliable fixation of medicine ongingivae, contributes for better allocation of active components due to good absorbability.

On the basis of experimental investigation, it was found that new developed pharmaceutical form "Topolin 5 % gel with the extract of Matricaria chamomilla" has antibacterial, antiinflammatory and regenerative activities, also reduces the length of treatment of paradontium disease and mucous surface of oral cavity up to 5–7 days.

GC-MS STUDY OF NONPOLAR CONSTITUENTS FROM *Trifolum pratense* L. AND *Caragana arborscens* Lam.

A. A. Drenin, E. Kh. Botirov

Surgut State University, Russia, e-mail: botirov-nepi@mail.ru

Introduction. Plants of genus *Trifolum* and *Caragana* are members of the family *Fabaceae*, species which are widely distributed in Russia and have medicinal, ornamenttal, industrial and fodder value. To date from various organs *Trifolum pratense* L. flavonoids, isoflavonoids, tannin, essential oils, terpenoids, alcohols, aldehydes, ketones, phenols, phenol carboxylic acids, fatty acids and other compounds have been isolated. From *Caragana arborscens* Lam. isolated flavonoids, fatty acids, tannins, amino acids, minerals and other substances. We have studied the nonpolar components of the aerial part *Trifolum pratense* and leaves of *Caragana arborscens*, growing in the Khanty-Mansi autonomous area.

Materials and Methods. The data for the study of natural nonpolar components of the aerial part *Trifolum pratense* and leaves of *Caragana arborscens* are given. Air-dry chopped raw material was extracted sequentially with hexane and chloroform in a soxhlet apparatus. The extracts were purified on a silica gel column and subjected to GC instrument "Crystal 2000-M." The main components of the mixture were determined by the method of gas chromatography-mass spectrometry apparatus Perkin Elmer Clarus 500. The identification of substances was performed using databases of mass spectra of «NIST-2005".

Results and Discussion. The studies found that the main components of the hexane and chloroform extracts aerial part of *Trifolum pratense* are hexadecane, eicosane, heptacosane, tetracosane, nonacosane, 3,7,11-trimethyl-1-dodecanol, hexadecyloxirane, (E)-2-decenal, 6,10,14-trimethyl-2-pentadecanone, ethyl hexadecanoat, phthalic acid dioctyl ester, phthalic acid diisooctyl ester, cholesta-4,6-dien-3β-ol, phytol, tocopherol.

As part of the hexane and chloroform extracts *Caragana arborscens* found hexadecane, octadecane, 2-methyloctadecane, eicosane, heptacosane, tetracosane, nonacosane, 3,7,11-trimethyl-1-dodecanol, 6,10,14-trimethyl-2-pentadecanone, phthalic acid dioctyl ester, 1-methyl-1-(2-methylpropyl)-2-nonylcyclopropan, phytol.

As part of the studied plants found 2 phthalic acid esters (dioctyl- and diizooktil- ftalats). It has been established that they are synthesized by endophytic microorganisms found in the rhizosphere and protect the plants by synthesizing phthalates with repellent, larvicidal, and insecticidal activity.

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CRYSTAL STRUCTURE OF *N*-ETHYL-*N*-CYTYSINOCARBOTIOAMIDE

K. M. Turdybekov, A. S. Kudusov, D. Zh. Karabekova, E. K. Musenova

E. A. Buketov Karaganda State University, Republic of Kazakhstan, Karaganda, 28, Universitetskaya str., e-mail: xray-phyto@yandex.kz

Previously, *N*-ethyl-*N*-cytisinocarbothioimide (**1**) was synthesized by the interaction of the cytisine alkaloid with ethyl isothiocyanate [1]. In the present work, data are presented for X-ray diffraction analysis of the crystal of molecule **1**, the general form of which is shown in the figure. The configuration of the chiral centers C7 and C9 is correlated with the (–)-cytisine molecule known in the molecule [2].

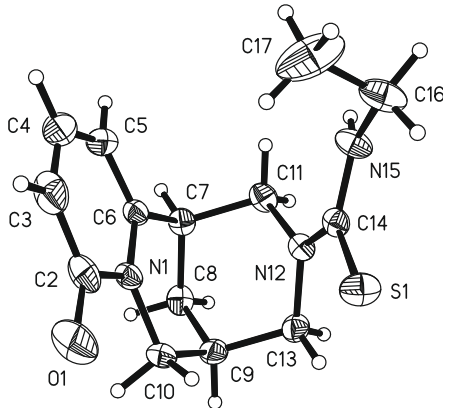

Fig. 1. Structure of the molecule 1.

It has been established that the bond lengths and valence angles in the cytisine backbone of structure 1 are standard. The exception is a certain extension of the C14= S1 (1.693 (2) Å) bond and the shortening of the N12-C14 (1.360 (2) Å) bond [3]. This is explained by the presence of a mesomeric effect due to conjugation between the unshared electron pair of the nitrogen atom N12 and the double bond C14=S1. This effect leads to a change in the coordination of the nitrogen atom N12. For example, in the molecules of N-methylcytisine [2] and N-cytisinyl aldehyde [4], the coordination of the N12 atom is pyramidal (the sum of the valence angles is 335.7°, 334.3 °), whereas in molecule 1, the coordination is plane-trigonal (the sum of the valence angles 359.7°). The dihydropyridine ring is flat with an accuracy of ±0.02 Å, the carbonyl atom O1 is almost in the plane of the atoms of this cycle, the deviation is 0.11 Å. The tetrahydropyridine ring takes the conformation of the distorted 8α-sofa (ΔC_S^8=8.3°) with the exit of the C8 bridge from the middle plane of the remaining atoms (±0.04 Å) of the cycle at 0.73 Å. The piperidine cycle is in the conformation of the distorted chair (ΔC_S^8=2.6°, $\Delta C_2^{7,8}$=0.9°). The thiocarbonyl group is somewhat unfolded with respect to the C11 and C13 atoms (the torsion angle C13N12C14S1 = -12.9 (2)^o).

Molecules **1** in the crystal due to weak hydrogen bonds N15 -H ... O1 (1 + x, y, z) (distances N ... O 2.812(2) Å, H ... O 2.00(2) Å, angle NH ... O 155(2)^o) form chains along the [a, 0, 0] direction.

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BIOACTIVE COMPONENTS OF THE *Eremurus Hissaricus* POLYSACCHARIDE CHARACTERIZATION

S. R. Usmanova, A. Ashurov, A. S. Jonmurodov, Z. K. Muhidinov

V. I. Nikitin Chemistry Institute of the Tajikistan Academy of Sciences
299/2 Ainy str., Dushanbe 734063, Tajikistan Republic, e-mail: zainy@mail.ru

The medicinal plants are rich in carbohydrates, proteins, phenolic compounds, fat-wax substances and microelements, which alone or in combination constitute the beginning of the therapeutic effect of these plants for humans. Extraction of bioactive compounds from plant materials is used in the first step in the preparation of food supplements or dietary supplements, food ingredients, pharmaceuticals and cosmetics.

Recently, a great interest is the study of Eremurus plants from the family of asphodel (*Asphodeloideae*). There are 50 species of Eremurus are known, of which in Tajikistan grows 29.

The biochemical composition of the *E. hissaricus* species in various phases of development (budding, flowering, fruiting, rest and deep peace) were studied, which are most common in the region of the southern slope of the Gissar Range of the Republic of Tajikistan.

The roots of *E. Hissaricus*, grown at the high-altitude biological station Siyakuh of the Institute of Botany, Plant Physiology and Genetics of the Academy of Sciences of the Tajikistan Republic (2200 m above sea level) were used.

Previously, the content of carbohydrates in root tubers of *E. hissaricus* plants was determined. The dynamics of accumulation of polysaccharide in *E. hissaricus* has been established during the annual cycle of development: the maximum accumulation of carbohydrates occurs during the fruiting phase and dormancy and late dormancy periods, the minimum - for the period of recovery from the late dormancy state in winter time and the budding phase. The isolated polysaccharides were consist of β-configurations in the pyranose sugars, belong to glucomannan polysaccharides. This statement is confirmed by stretching narrow peak in 2923.15 cm^{-1} of –CH of ether (methyl or acetyl) group and also by strengthening of main carbohydrate skeleton absorption in the region 1000–1200 cm^{-1} attributed to C–O–C glucosidal stretching vibrations. The peaks observed by FT IR spectra at 1248 cm^{-1} and 1735 cm^{-1} indicate the presence of acetyl groups in the polysaccharide structure.

Analyze of molar mass determined by HP SEC shows presence of high molar mass water soluble and low molar mass acid soluble polysaccharides. However, acid extraction compared with water extraction indicates an appreciable decrease in Mw and Mz as well as viscosity and hydrodynamic radius of macromolecule (Rh(w)).

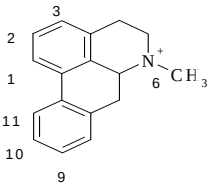
Other valuable components of the study in the roots of *E. Hissaricus* were the fat fraction, phenolic compounds, proteins and nitrogen compounds, which the subjects of future studies.

TECHNIQUE FOR SYNTHESIS OF PHENANTHRIDONE ALKALOIDS FROM HERBAL'S APORPHINE ALKALOIDS: SYNTHESIS OF SECO-GLAUCINE AS A MODEL STUDY

E. V. Vetrova, E. V. Maksimenko, A. V. Lekar, S. N. Borisenko, S. S. Khizrieva, A. F. Bugaeva, N. I. Borisenko

Southern Federal University, Stachky Av. 194/2, Rostov-on-Don, 344090, Russia,
e-mail: boni@ipoc.rsu.ru

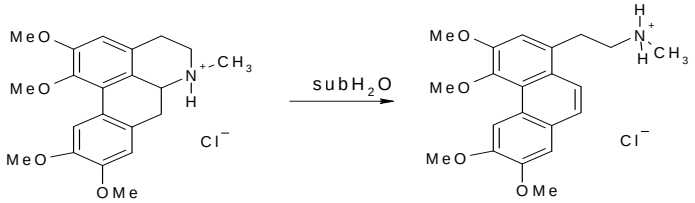
In the present paper, the technique for synthesis of phenanthrene alkaloids from herbal's aporphine [1] alkaloids in subcritical water [3,4] is studied. Phenanthrene derivatives obtained by semi-synthetically from the plant's alkaloids have the more higher value of antioxidant activity and may exhibit new a therapeutic applications the other than the original aporphine substances.



Corydine R_1 =OH; R_2 =OCH_3; R_9 =H; R_{10} =OCH_3; R_{11}=OCH_3
Boldine R_1 = OCH_3; R_2 =OH; R_9 =OH; R_{10} =OCH_3; R_{11}=H
Glaucine R_1 = OCH_3; R_2 =OCH_3; R_9 = OCH_3; R_{10} =OCH_3; R_{11}=H
Talicmedin R_1 = OCH_3; R_2 =OH; R_9 = OCH_3; R_{10} =OCH_3; R_{11}=H

Fig. 1. Typical structure of the aporphine herbal's alkaloids.

The synthesis of the seco-glaucine was selected as a model study. The glaucine is an alkaloid contained in various kinds of plants, such as *Glaucium flavum*, *Glaucium oxylobum*, *Croton lechleri* и *Corydalis yanhusuo*.The technique of synthesis of the phenanthrene seco-glaucine from glaucine using medium of subcritical water (Fig. 2) is studied in the temperature range 100 °C to 250 °C.



glaucine seco-glaucine

Fig.2.

It is shown that the maximum yield of the target phenanthrene's alkaloid (seco-glaucine) is achieved at a temperature of 250 °C in water medium without catalytic additives. The studied technique for synthesis of the phenanthrene's alkaloids makes possible to develop environmentally friendly technologies for the production of new kinds drugs based on the herbal's aporphine's alkaloids which are widely distributed in the plant kingdom.

Acknowledgment. This research was supported by the internal grant of the Southern Federal University (Project No ВнГр-07/2017-04).

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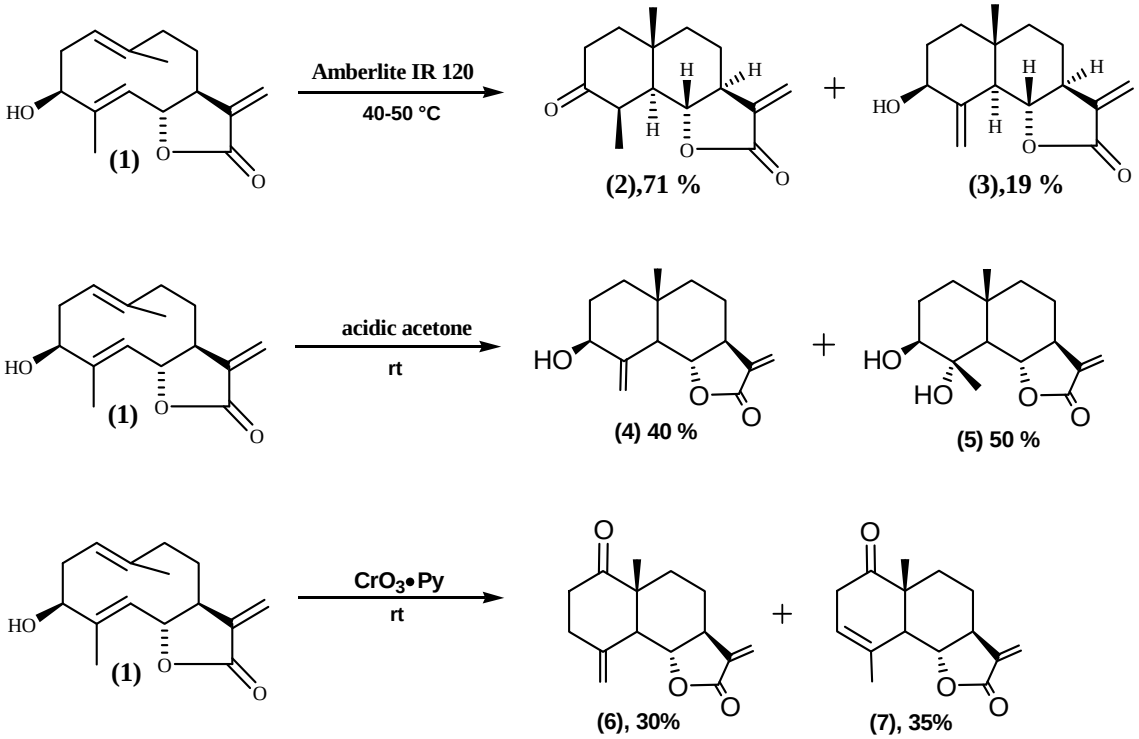
CARBOCYCLIZATION OF (+)-HANPHILLINE

N. Merkhatuly, S. B. Abeuova, A. T. Omarova, D. D. Naushabekova, R. N. Zhorabekov, E. E. Nurgaliyeva

Academician Ye. A. Buketov Karaganda State University, e-mail: merhatuly@ya.ru

Reactions of stereospecific carbocyclization of (+)-hanphilline (1) were investigated and different *trans*-eudesman sesquiterpene γ-lactones were synthesized. The one-step synthetic method of guaianolides on the basis of *E*,*E*-germacranolide (+)-hanphilline (1) was developed. *E*,*E*-Germacranolide (+)-hanphilline was isolated by us from Noble Yarrow (*Achillea nobilis* L.).



The structures of synthesized eudesmanolides (2–7) have been investigated using IR, ^{1}H NMR, mass-spectroscopy and X-Ray analysis.

Developed synthetic methods may be one of the key stages in the strategy for the synthesis of biologically active eudesmane sesquiterpene γ-lactones.

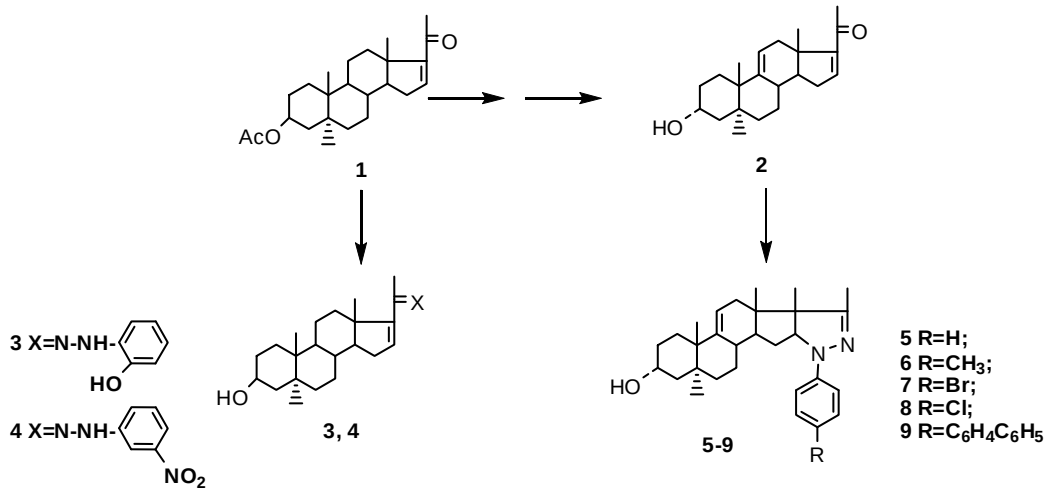
SYNTHESIS OF NEW HYDRAZONE – AND PYRAZOLINE DERIVATIVES OF 5α-STEROIDS

N. Sh. Nadaraia, N. N. Barbakadze, M. L. Kakhabrishvili

Tbilisi State Medical University Iovel Kutateladze Institute of Pharmacohemistry,
36 P. Sarajishvili str., 0159, Tbilisi, Georgia, e-mail: nnadaraia@ymail.com

Elaborate of the synthesis method of steroidal hydrazones and steroidal compounds modified by nitrogen containing five-membered heterocycles are important, because steroidal hydrazones and pyrazolines are characterized with antifungal, antitubercular, anti-inflammatory, anticancer, anticonvulsant, cardiovascular or antidepressant activities. Steroidal pyrazoline have also attracted attention as useful synthons inorganic chemistry and serve as precursors for the preparationof pyrazole derivatives.

In order to synthesis of potential bioactive 5α-steroids we are studied condensation reactions of steroidal α-enones: 3β-acetoxy-5α-pregn-16-en-20-one **1**and 3α-hydroxy-5α-pregn-9(11),16-dien-20-one **2** with some hydrazides and hydrazinesin ethanol with catalytic amount of acetic acid. It was established, that by interaction of ketone **1**with salicyloic- and m-nitrophenylhydrazides hydrazones **3**, **4** were formed. By interaction of ketone **2** with phenylhydrazine, *p*-methyl-, *p*-bromo-, *p*-chloro- and *p*-phenylphenylhydrazines cyclocondensation products - 3α-hydroxy-1′-aryl-3′-methyl-5α-androst-9,(11)-eno[17,16-d]pyrazolines **5**–**9** were confirmed.



This work was supported by Shota Rustaveli National Science Foundation (SRNSF) [No. YS-2016-51, “Potential bioactive steroidal nitrogen-containing compounds”].

BIOCHEMICAL COMPOUNDS IN *Eremurus hissaricus* ROOTS

A. S. Jonmurodov[1], S. R. Usmanova[1], A. Abdullaev[2], B. B. Jumaev[2], E. G. Safarov[2], Z. K. Muhidinov[1]

1) V. I. Nikitin Chemistry Institute of the Tajikistan Academy of Sciences, 299/2 Ainy str. 734063, e-mail: abduvalid@mail.ru
2) Institute of Botany, Plant Physiology and Genetics of the Tajikistan Academy Sciences 73406317, Dushanbe, Karamov str., 27, e-mail: abdumanon@mail.ru

It is well known that Tajikistan is unique natural laboratory, and is one of the richest floristic in the territories of Central Asia, where grows more than 5000 species, only higher spore and seed plants. In this respect, great interest relevant to the study of biochemical compounds of the ephemeroid plants- perennial herbaceous plant with a short growing season, which coincides with the onset of summer. One of ephemeroids is Eremurus. In nature there known 50 species of Eremurus, from these 30 species grows in Central Asia. In this work we study isolation and characterization of biological active compounds (fat and waxes, carbohydrates, phenolic substances and protein) from whole roots of Eremurus Hissaricus (*E.hissaricus*) growing in the southern slopes of the Hissar Ridge, Ziddi village, Tajikistan.

Analysis of the main biological components in whole *E.hissaricus* roots in the budding phase showed that the fat & wax substances make up 4.98%, phenolic compounds 10.79%, proteins and nitrogen compounds 3.37%, water and acid soluble carbohydrates 35.94% and 16.9% comprising of mono-oligosaccharide and polysaccharides respectively. It should be noted that the remaining mass of the cell wall -21.28% manly contain lignin, cellulose and hemicellulose. In the flowering phase, the content of fat fraction and phenolic compounds decreased, while in the fruiting phase those compounds were markedly increased. However, their content was lower than in the budding phase. In the dormancy phase, the content of fat fraction, water-soluble sugars significantly increase in relation to the marked phases of vegetation, the content of phenolic compounds, acidic polysaccharides, oligo- and monosaccharides, and the remaining mass is markedly reduced. The content of proteins and nitrogen compounds remains almost the same. In the phase of a deep dormancy (winter time) content of fat fraction, phenolic compounds and water-soluble sugars increases in relation to other phases, and the content of proteins and nitrous compounds, acidic polysaccharides, oligo- and monosaccharides decreased markedly. Apparently, increase in the content of fatty fraction, phenolic compounds and water-soluble sugars in the roots of *E.hissaricus* plays important role in the period of recovery from the state of winter rest and the phase of the formation of the leaf rosette.

Acknowledgment. The work was supported by International Scientific and Technical center (Project T-2148).

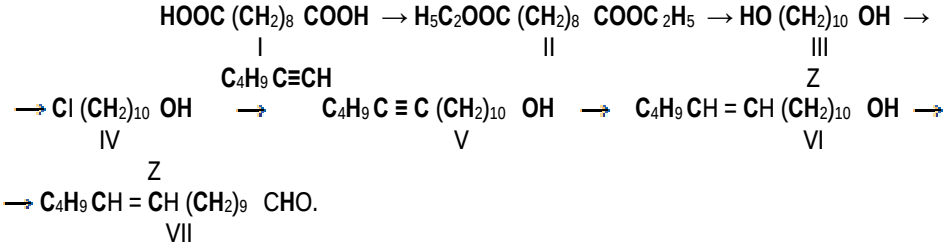
SYNTHESIS AND ATTRACTIVE PROPERTIES OF (Z)-11-HEXADECENAL, THE MAIN COMPONENT OF THE PHEROMONE OF COTTON BOLLWORM (*Heliothis armigera* Hb.)

H. Khaitbaev, B. N. Babaev, Z. Tilyabaev

A. S. Sadykov Institute of Bioorganic Chemistry of AS RUz 100125 Tashkent,
Mirzo Ulugbek str., 83, e-mail: khaitbaev5@ mail.ru

The long-term intensive use of synthetic pesticides has been absolutely prohibited by Stockholm convention accepted in May 23rd, 2001 due to increased number of problems related to the appearance of resistant populations of insect pests. It has been found that many of these preparations besides their toxic effect on humans and usefulness for animals also exhibit carcinogenic effect.

More effective and reliable results of protection against arthropods were achieved by applying the preparations based on secondary metabolites that are involved in the mechanism of arthropod pest communication. Such low molecular bio-regulators include sex pheromones, compounds produced by insects and released into environment for intraspecific communication. Environmental advantages of pheromones are undoubted: their action is highly specific, effective doses are minimal, they are non-toxic and do not produce toxic metabolites. In order to synthesize the pheromone of cotton bollworm we have used so called synthon approach, which involves the development of methods to prepare key and intermediate compounds that can be further transformed to target products. Here we report on synthesis of (Z)-11-hexadecenal, one of the pheromone components of cotton bollworm (*Heliothis armigera Hb.*) obtained by modified acetylene method (I-VII) using hex-1-yne and 10-chloro-decan-1-ol (IV) according to the following scheme:



Using heptan-1-ol as an extractant has allowed to decrease the regeneration of decan-1,10-diol from 17% to 3%, and to increase the yield of 10-chloro-decan-1-ol up to 75%. There has been found a better way to extract the products from the reaction (VII) mixture. In order to minimize losses on stages (VII) and (VI) the filtration through silica gel column has been suggested instead of vacuum fractionation. GLC analysis of reaction products has been conducted on Aniezone L-15% Chromatone N-AW at working temperature of 200–250°C, using He as a gas-carrier at the rate of 30 mL/min in the column of 1m long. The method suggested differs from known ones by a greater availability of the reagents used, simplicity of the experiment conduction and higher yield of target products. Synthesized (Z)-11-hexadecenal has been found to exhibit high attractive properties when tested on fields of different regions of Uzbekistan. Within 10 days there have been trapped more than 200 butterflies, which suggests that there is a critical number of this pest on the cotton fields and protective measures against them are extremely needed.

EFFECT OF TOTAL FLAVONIDS OF TURMERIC (CURCUMA) ON THE INTEGRITY OF RED BLOOD CELLS AND VOLUME REGULATION OF THYMUS LYMPHOCYTES

O. J. Khamidova, R. Sh. Kurbannazarova, D. D. Fayziev, P. G. Merzlyak, B. A. Tashmukhamedov, R. Z. Sabirov

A. S. Sadykov Institute of Bioorganic Chemistry of AS of Uzbekistan, 83 Mirzo Ulugbek Str., 100125, Tashkent, e-mail: rano_1971@mail.ru

A variety of therapeutic effects exerted by flavonoids and the absence of their toxicity for the human body cause an ever increasing scientific interest to this class of substances. Turmeric (local name is zarchava), the rhizome of *Curcuma*, has been widely used since ancient times as a spice, coloring, flavoring, and as a traditional medicine. Although a wide variety of biological effects of extracts and individual components of the turmeric have been described, its effects on the volume-mediated cellular processes remain poorly investigated. In the present work, we employed an ultrasonic-aided extraction with 80% ethanol in order to isolate the total flavonoids from *Curcuma* powder and tested the resulting extract on its effect on the integrity of the human red blood cells (RBC) assessed by hemoglobin release and volume regulation of the rat thymus limphocytes tested using a light transmittance method.

In order to quantify the flavonoid content of the obtained extract, we used a standard $AlCl_3$-based colorimetric assay and quercetin as a standard. We found that the concentration of total flavonoid in our extract was 4.32 ± 0.15 mg/mL in quercetin equivalent.

In our further experiments, we observed a dose-dependent increase in the extracellular hemoglobin content of the human RBCs. At a concentration of 32.8 μg/ml, the extract started to cause lysis of RBCs, and when the concentration was increased up to 200 μg/mL, we observed a 100%-level of hemolysis. The half-maximal hemolytic effect of the extract (IC_{50}) was 100 ± 1 mg/mL.

In the next series of experiments, we tested the effect of the extract on the ability of rat thymocytes to restore their volume after swelling under hypoosmotic stress. In control isotonic medium (normal Ringer's solution), the thymocyte volume remained at a constant level for app. 20 minutes. When cells were placed in the hypoosmotic environment, they first swelled rapidly and then restored their volume to a level close to the initial level within 20–30 minutes. When the cells were incubated for 15 minutes in a hypoosmotic environment, the regulatory volume decrease (RVD) averaged at 76.6 ± 3.4 % (n = 5). When added to the hypoosmotic medium, the turmeric extract completely blocked the recovery phase of the thymocyte volume regulation. Thus, at 43.2 μg/ml concentration, the RVD was suppressed down to 1.75 ± 2.41% (n=5). The effect of the turmeric extract on the thymocyte cell volume regulation was dose dependent exhibiting two phases: first high-affinity phase which was observed at 1–2 μg/mL and second low-affinity phase with a half-maximal effect at 14.8 ± 0.16 μg/mL.

We also tested the turmeric extract on the artificial lipid bilayers but observed no effect at all the tested concentrations.

EFFECT OF GLYCYRRHIZIC ACID AND ITS AGLYCONES ON ERYTHROCYTES AND TYMOCYTES

D. D. Fayziev, O. J. Khamidova, S. I. Rustamova, N. M. Chorieva, R. Sh. Kurbannazarova, P. G. Merzlyak, R. Z. Sabirov

A. S. Sadykov Institute of Bioorganic Chemistry of AS of Uzbekistan, 83 Mirzo Ulugbek Str., 100125, Tashkent, e-mail: diyor09@mail.ru

Licorice (*Glycyrrhiza glabra)* belongs to legumes and contains triterpens, saponins, flavonoids, isoflavonoids, chalcones and other biologically active compounds in their roots. Glycyrrhizic acid is a major component of the licorice root. Although its numerous biological activities are well known, no studies have been performed on the effects of this compound and its aglyconic forms on the volume-dependent cellular processes. The aim of the present study was to investigate the effects of derivatives of glycyrrhizic acid – mono ammonium salt of glycyrrhizic acid (MASGA) and its aglycons, α- and β-glycyrrhetinic acids, on the integrity of human erythrocytes in isotonic condition and on the volume regulation of thymocytes under hypoosmotic stress.

In our experiments, MASGA and α-glycyrrhetinic acid did not cause a release of haemoglobin from human red blood cells in the concentrations range of up to 500 μM. In contrast, β-glycyrrhetinic acid was found to destroy the red blood cells walls and cause haemolysis. The IC_{50} for β-glycyrrhetinic acid to cause haemolysis was 192.2 ± 4.7 μM (n = 6) suggesting that this compound is a moderate hemolytic.

Next, the effects of derivatives of GA on volume regulation of rat thymocytes under hypo osmotic stress conditions (147.1 mOsm/kg H_2O) was studied. In isotonic conditions (290 mOsm/kg H_2O), the volume of thymocytes remained constant for app. 20 min (n = 5). Under hypoosmotic stress conditions, the cellular volume first passively increased and then, during the incubation time of 15 minutes the volume decreased down to the level of 79.3 ± 1.7% (n = 13). This phenomenon is called a regulatory volume decrease, or RVD. When we studied the effect of different concentrations of MASGA on the thymocytes RVD, we observed a two-phase effect. Up to 150 μM concentration the RVD decreased down to a level of 56.1 ± 1.5 % (n = 8), and then, from 200 μM on, the RVD increased to a level of 69.8 ± 2.5% (n = 8). Thus, MASGA exhibits moderate inhibitory effect on RVD at low doses. In contrast, there was no significant effect of α-glycyrrhetinic acid in the doses of up to 200 μM. However, surprisingly, when β-glycyrrhetinic was added into the experimental medium, the cell volume regulation decreased depending on the drug dose, and at 75 μM the cell volume regulation system has been fully blocked (RVD = 1.8 ± 0.7%, n = 5). Eventually, the RVD indicator started to increase beginning from app. 100 μM concentration and at 200 μM concentration it reached 33.9 ± 2.2% (n = 5). Thus, the effect of the β-glycyrrhetinic acid was also bi-phasic, similar to GA, but suppressory capacity was much more profound. The dose-dependency curve of the first phase was fitted to a Hill equation with a half-maximum effect at 26.6 ± 1.2 μM and Hill coefficient of 3.1 ± 0.4 (n = 5). The value of the Hill coefficient would suggest that 3–4 molecules are expected to be bind to a principal component of the thymic RVD machinery in order to block the system.

POLYPHENOL GOSSITAN SHOWS PROTECTIVE EFFECT ON CARDIAC MITOCHONDRIAL FUNCTION IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

M. K. Pozilov, M. I. Asrarov, S. M. Mavlyanov

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, 100125, Tashkent, Mirzo Ulugbek str., 83, e-mail: mamurjon2281@mail.ru

It is known, that at *diabetes mellitus* in damage of the heart muscles it is revealed that mitochondria are markedly damaged. Currently, despite extensive research on the role of cardiac mitochondria in the development of diabetes, their correction with polyphenolic compounds has been studied insufficiently.

Polyphenol gossitan has been isolated from *Gossypium hirsutum L*. revealed a high activity of gossitan against the influenza virus (Salikhov et al., 2012). However, gossitan influence on mitochondrial function is not investigated and, therefore, our aim was to study the effect of gossitan on *mitochondrial* permeability transition pore (mPTP) opening in the *heart mitochondria of* streptozotocin *(STZ)*-induced *diabetic rats.*

Experiments were performed on 30 white mongrel male rats weighing 180–200 g. The animals were divided into three groups: I group - control, II group - animals with *STZ*-diabetes, which once were injected with an *STZ* (50 mg/kg of body weight intraperitoneally in a 0.1 mol/L citrate buffer, pH 4.5), and III group – *STZ*-diabetes + gossitan (*per os* dose of 10 mg/kg of body weight) for 8 days starting from 12th day after administration of *STZ* and reached a predetermined level of hyperglycemia. Blood glucose was determined using glucose oxidase determination set «Glucose - enzymatic-colorimetric test» (Cypress diagnostic, Belgium). Mitochondria isolated from rat hearth by differential centrifugation according to N.A. Palchikova. MPTP condition assessed by the speed of Ca^{2+}-dependent swelling of mitochondria, the mitochondrial suspension recording light scattering at 540 nm.

Ca^{2+} ions are used as an inducer for activation of mPTP permeability at concentration of 20 μM. According to obtained data, at STZ-diabetes, swelling of cardiac mitochondria increases by 86.1 ± 7.1% in comparison with the control. This process can be explained by increase of Ca^{2+} load and lack of membrane stability in cardiac mitochondria. That provides high permeable state of mPTP. At STZ-diabetes, as a result of an eight-day treatment once a day with gossitan (10.0 mg/kg), swelling of mitochondria from heart was significantly inhibited by 51.9±4.8% compared to the control in III group animals. Hence, in STZ-diabetes, the main reason for the discovery of mPTP pores is considered to be the development of oxidative stress, prooxidants, induction of lipid peroxidation, oxidation of mPTP complexes of thiol groups. Due to the strong antiradical properties of polyphenolic compounds, the content of free radicals in the mitochondria can be reduced and the inhibitory property of cyclosporin A with the binding of the domain matrix CyP-D can be regulated.

Thus, the STZ-induced diabetes causes, including the development of mitochondrial dysfunction, manifested opening mPTP. Pharmacotherapy of rats with STZ-induced diabetes by gossitan corrects mitochondrial dysfunction, effectively influencing the state of mPTP.

STATE OF APOPTOSIS OF THYROID CELLS IN OFFSPRING UNDER THE PESTICIDES EXPOSURE ON MOTHER′S ORGANISM

N. B. Zokirova[1], **V. N. Syrov**[2]

1) Tashkent Medical Academy
2) S. Yu. Yunusov Institute of the Chemistry of Plant Substances,
e-mail: plant_inst@icps.org.uz

In physiological conditions, there is a balance between apoptosis and cell proliferation maintaining the tissue homeostasis. Defects in apoptotic mechanisms lead to a various human diseases, including the development of malignancy and cancer process. The significance of apoptosis of endocrine system cells in the mechanism of the toxic effect of pesticides of new generation remains unclear.

The aim of this study was to determine the state of apoptosis in thyroid cells of offspring in prenatal and early postnatal exposure to pesticides.

The experiments were performed on nulliparous white mature female rats, which were divided into 3 groups of 30 animals each. Two groups of animals for 30 days before pregnancy, in the period of pregnancy and lactation daily *per os* received, respectively, pesticides cyhalothrin or fipronil. The third group, which received a sterile saline solution, served as a control. Progeny, obtained from experimental and control females, was examined in dynamics on the 3, 7, 14, 21 and 30 days after birth. Apoptotic cells on thyroid sections were determined using monoclonal rabbit antibodies to caspase-3 and p-53 family proteins (Thermo Scientific, USA). The index of apoptosis per 1000 thyrocytes was counted. All digital data were processed by the method of variation statistics and P values < 0.05 were considered significant.

It has been revealed that both fipronil and cyhalothrin when exposed to the mother's organism cause pronounced induction of apoptosis in the thyroid gland of the offspring. In the thyroid gland of the offspring under the influence of cyhalothrin and fipronil the apoptosis index was 3.5–4 and 4.5–5 times higher, accordingly, than the control group in all periods of the study ($P < 0.05$). Our previous studies have shown that both pesticides in conditions of prenatal and early postnatal exposure cause a slow decrease in the growth and formation of the thyroid gland in the offspring in the form of hypothyroidism. Recent data show that thyroid hormones also have a high anti-apoptotic effect, which opens great prospects for the regulation of apoptosis in various diseases. It possible that the intensity of induction of apoptosis in our experiments is, in a certain extent, determined by the degree of thyroid dysfunction and the weakening of the anti-apoptotic effects of its hormones. Earlier, we also showed that both pesticides in prenatal and early postnatal conditions cause pronounced oxidative stress in offspring. We believe that in the mechanism of induction of cell apoptosis, along with direct toxic effects of drugs, hypothyroidism and oxidative stress observed in offspring played an important role. Induction of cell apoptosis is more pronounced in fipronil exposure compared to cyhalothrin. Thus, disclosure of mechanisms of apoptosis induction under the influence of new generation of pesticides contributes to the development of pathogenetic methods for the prevention and treatment of latent toxic effects in pregnant women and their newborn children.

EFFECT OF GOSSYPOL ON THE REGULATION OF THYMOCYTE CELL VOLUME UNDER HYPOOSMOTIC STRESS

N. M. Choriyeva[1,2], R. Sh. Kurbannazarova[2], P. G. Merzlyak[2], Kh. L. Ziyayev[2], A. M. Ermatov[2], B. A.Tashmukhamedov[1,2], R. Z. Sabirov[1,2]

1) Faculty of Biology and Soil Science, Mirzo Ulugbek National University of Uzbekistan named after, VUZ Gorodok, 100174 Tashkent
2) A. S. Sadykov Institute of Bioorganic Chemistry of Ac.Sci. of Uzbekistan, 83 Mirzo Ulugbek Str., 100125, Tashkent, e-mail: chorgiza85@mail.ru

Gossypol is polyphenolic compound found in the cotton plant (*Gossypium L.*) and other species of the genus *Malvaceae*. It exhibits a wide variety of biological effects, such as anticancer, antiviral activity and effects on the activity of key metabolic enzymes. Recently, a great interest to this relatively old substance is related to its newly found property as a BH3-mimetic, which places gossypol among perspective apoptogenic anticancer agents. Cell volume regulation is deeply involved in the mechanisms of apoptosis and cell proliferation. However, the effects of gossypol on the cell volume-mediated processes are poorly investigated. Therefore, in the present study we concentrated on the effects of this drug on cell volume regulation of rat thymus lymphocytes under the hypoosmotic stress.

In our experiments, in isotonic medium (normal Ringer's solution), the thymocyte volume, assayed by a light transmission method, remained at a constant level for app. 20 min. Upon entering into the hypoosmotic environment, the cells swelled rapidly and then recovered their original volumes within 20-30 minutes. In control conditions without drug, the decrease in the volume of the osmotically swollen thymocyte (called RVD, or regulatory volume decrease) incubated for 15 minutes ranged from 63% to 91% and averaged at 84.02 ± 1.28% (n=5). Such a variation in the reduction in cell volume was possibly due to a different physiological state of the experimental animals in different days of experiments. Gossypol, when added to the hypoosmotic medium, greatly reduced the ability of thymocytes to restore their volume after osmotic swelling. However, such inhibition was observed at relatively low concentrations up to 10 μM. Further increasing the dose of the drug resulted in a restoration of the RVD process and at 100 μM it was 124.0 ± 9.8% (n=5). Thus, the dose-dependent effect of gossypol on the thymocytes volume regulation was bi-phasic with a high-affinity inhibiting phase and low-affinity activation phase. The first phase was well described by a Hill equation. Fitting to this equation yielded the half-maximal effect (IC_{50}) at 2.07±0.30 μM and a Hill coefficient of 2.64 ± 0.62. This value of the Hill coefficient may suggest that binding of app. 2-3 gossypol molecules to a key component of the thymocytes cell volume regulation is necessary for its inhibition. The second (rising) phase of the dose-response curve is difficult to explain. We hypothesize that gossypol may form new pores in the thymocyte plasma membrane. These new pores could be permeable for the intracellular osmolytes (such as KCl, taurine and aminoacids), which may exit from the cells and cause cell shrinkage.

SYNTHESIS OF ESTERS OF MONOCHLORINE ACETIC ACID AND SOME TERPENICAL ALCOHOLS AND PLANT PHENOLS

A. K. Abdushukurov[1], A. U. Choriev[2]

1) National University of Uzbekistan named after Mirzo Ulug'bek, Uzbekistan, Tashkent
2) Karshi State University, Uzbekistan, Karshi, e-mail: azimjon-organik@mail.ru

Chemical modification of natural compounds by different reagents is an important method of obtain new biologically active compounds. Aim of this investigation is obtain of new derivatives of natural compounds - esters of monochloracetic acid. This acid was selected as modified agent due to high biological activity of its derivatives. The active development of chemistry of plant phenols, intensive elaboration of methods of synthesis and investigation of chemical reactions of their derivatives is attributed to the wide range of their useful properties, in particular, antimicrobial, anti-inflammatory and anti-convulsant activity. As objects for synthesis the following natural phenols were choosed: cetyl alchohol, geraniol, mentol, borneol, and plant phenols: evgenol, vinylin and vanilal. These compounds are characterized by different biological activity. Note, that biological affectivity of esters of carbonic acids is higher than activity of initial acids and their salts. Namely, for these compounds it is possible to expect the presence of synergistic effect caused by mutual influence of pharmacophore groups in target esters.

Synthesis of esters based on interaction of corresponding alcohols and phenols with chloracetylchloride in absolute diethyl ether, in the presence of pyridine. The advantages of this method: the simplicity of reaction passing, easy extraction of obtained products, and good reproduction. To solution of 10 mmol of corresponding alcohol or phenol in 50 ml of absolute diethyl ether at 20–23°C 10 mmol of chloracetylchloride and 10 mmol of pyridine were added. Obtained reaction mixture was kept for 23–36 h at 20–23°C. Obtained esters were purified by method of column chromatography on silicagel using hexane as an eluent. Corresponding esters were obtained with yield 90–94%. The structure of synthesized esters have been confirmed by data of elemental analysis, UV- and IR-spectra, and by cryoscopical determination of their molecular masses.

ANTIMICROBIAL EFFECT OF ETHANOLIC EXTRACTS FROM *Cuscuta europeae*

K. A. Kakhorova, Z. S. Khashimova, Sh. M. Miralimova

A. S. Sadykov Institute of Bioorganic Chemistry AS of Uzbekistan,
Tashkent, Uzbekistan, e-mail: ibchem@uzsci.net

Nowadays, many strains of microorganisms have acquired drug resistance, which makes it necessary to search new means with antimicrobial activity for modern medicine.

Currently, a large group of parasitic plants (*Haustorya*) including different species of mistletoe (*Viscus alba* L.) and dodder (*Cuscuta* L.), which contain cytotoxins have attracted the attention of scientists.

Dodder is used as anti-inflammatory, antitumor and anti-infectious agent in medicine of many countries.

Earlier, we have established the cytotoxic activity of water and alcohol extracts of different dodder species grown in the Central Asia on a transplantable cell culture line.

The aim of this work was to study the antimicrobial activity of the alcohol extract of dodder on different strains of microorganisms.

Dodder (*Cuscuta europea*) seeds from plants growing on meadow grasses were used as raw material.

The seeds, ground in a mortar, were treated with 50% ethanol (1:10) constantly stirring at room temperature. Obtained alcohol-water extract used to determine the antimicrobial activity.

The antimicrobial activity was determined as following. 100 μL of a suspension of night-indicator culture cells with 0.5 McPharland haze was added to 10 mL of molten and cooled soft Muller-Hinton agar (0.75% agar), mixed and poured evenly onto pre-prepared plates containing 20 mL of solid Muller-Hinton agar. As the soft agar solidified, a spot (5 μL) of the solution of the being tested antimicrobial substance was applied to its surface. After diffusion of the solution in agar, the cup was placed in a thermostat at 3°C for 24 h, then the presence or absence of growth zones of the indicator culture at the spot deposition site was observed.

In this work, it was established that the dodder extract has antimicrobial activity in relation to the studied test culture. In this case, the most expressed antimicrobial activity of the dodder extract was shown in relation to *S. aureus* at a concentration of 200 μg/mL. On *E. coli* the antimicrobial effect of the extract was insignificant. Thus, the dodder extract has an antimicrobial effect on conditionally pathogenic microorganisms, and its further investigation is promising.

DETERMINATION OF A COUMARIN IN CLOVERS

G. M. Raimova, K. E. Nasirov, J. F. Ziyavitdinov

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan,
e-mail: guli_raimova@mail.ru

Coumarins are natural compounds based on benzo-α-pyrone, a lactone of cis-ortho-oxycinnamic acid. One of the characteristic pharmacological properties of coumarin derivatives is anticoagulant, coronary dilatation, P-blocking and choleretic properties of coumarins are also known.

The aim of the study was an empirical evaluation of existing methods and determination of a coumarin in clover.

Samples of clover harvested during the flowering period were used for the study. The raw material, crushed to a particle size of not more than 2 mm, was extracted in a feed/extract ratio of 1: 100. The most complete extraction of coumarins (in free form and in the form of glycosides) was achieved with ethyl alcohol of different concentrations, both in the cold and under heating. As an extractant, water, ethyl alcohol at concentration of 45–96% was used. Extraction was prepared using a stirring device with a rotating water bath platform.

The completeness and influence of the extraction conditions (extractant, maceration method, time, temperature) was monitored by the HPLC method for the content of coumarins and coumaric acids in the recovered extracts. The analysis was carried out on an Agilent Technologies 1200 chromatography module with a DAD detector and an automatic sampler, an Eclipse XDBC18 chromatographic column of 4.6 × 150 mm, 5 μm. Mobile phase: A - 0.1% phosphoric acid, B - acetonitrile, flow rate - 1 ml/min, gradient, % per a min.: 5% - 3 min, 80% - 18-23 min, 5% -25 min, absorption at 278 nm. The duration of the analysis was 25 minutes. The concentration of the standard sample was 1 mg/ml, the concentration of the test sample is 5 mg/ml. Coumarin was used as a standard sample.

HPLC analysis in extracts from clover revealed coumarin and a component with a retention time of 14.48 min, having a coumarin spectrum. When extracting coumarin from vegetable raw materials, it was found that the use of 45% and 96% as an extractant of ethyl alcohol made it possible to reach the maximum content of coumarin, but when clover was extracted with an aqueous extractant, coumarin was not observed.

The quantitative determination of coumarins in clover is a two-fold extraction with 96% ethyl alcohol for 60 minutes in a boiling water bath under reflux. At the same time, the yield of extractive substances was 36% of the initial mass, with a free coumarin content of 0.64%.

CHARACTERIZATION OF CYNAROSIDE/γ-CYCLODEXTRIN INCLUSION COMPLEX

U. G. Gayibov[1], S. N. Gayibova[1], M. T. Honkeldieva[1], L. Y. Izotova[1], V. N. Syrov[2], S. M. Yusupova[2], T. F. Aripov[1]

1) Institute of BioorganicCchemistry, Academy of Science of Uzbekistan, 100125, Tashkent, M.Ulugbek Str., 83, e-mail: info@biochem.uz
2) Institute of the Chemistry of Plant Substances, Academy of Science of Uzbekistan, 100170, Tashkent, M.Ulugbek Str., 77, e-mail: plant_inst@icps.org.uz

CDs are cyclic oligosaccharides, containing 6 (α-CD), 7 (β-CD) or 8 (γ-CD) α-(1,4)-linked glucose units, formed from enzymatic degradation of starch by bacteria. The most important structural feature of these compounds is their toroidal shape, with hydrophobic interior cavity and hydrophilic shell. They are capable of forming inclusion complexes both in solution and in solid state with a variety of guest molecules, which are placed in their hydrophobic interior cavity. Cyclodextrin molecules are relatively large with a number of hydrogen donors and acceptors and, thus, in general, they do not permeate lipophilic membranes. Cyclodextrins are widely used as "molecular cages" in the agrochemical, pharmaceutical, food and cosmetic industries. Cynaroside (3′,4′,5,7-tetrahydroxyflavone 7-*O*-β-*D*-glucopyranoside, or luteolin 7-*O*-β-*D*-glucopyranoside) is a valuable natural individual active principle and deserves a particular attention due to significant pharmacological effects, considering outcomes of its investigations, as well of hypoazotemic activity. A wide range of reports have been published regarding the encapsulation of natural polyphenolic agents by CDs, for food and drug delivery proposes. In this study we learned the formation of cynaroside/γ-cyclodextrin inclusion complex by powder diffraction (PXRD) and termogravimetry (TG-DSC) techniques. The PXRD results showed variations in the PXRD line patterns of cynaroside, γ-CD and cynaroside. Cynaroside-γ-CD complex exhibited new diffraction lines compared with cynaroside and γ-CD. TG-DSC results showed that the pure cynaroside exhibited an endothermic peak at 241.9°C which represents the melting of flavonoid and is almost in accordance with the literature value (248°C). γ-CD showed an endothermic peak at 305.9°C which may be attributed to a distruction process. The DSC curve of cynaroside-γ-CD shifted endothermic peak to 249.3°C. The new peak may be probably due to the interaction of cynaroside with γ-CD and the formation of inclusion complexes.

ACTION OF EUFORBIN ON THE RAT LIVER MITOCHONDRIA FUNCTIONS

G. T. Abdullaeva, G. V. Abdulhakova, Z. Sh. Ahmedova, N. G. Abdullajanova, M. I. Asrarov

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, 100125, Tashkent, Mirzo Ulugbek str., 83, e-mail: Gulbahor79@ramblerl.ru

The mitochondrion is sensitive target cell organoid to a variety of biologically active compounds. On the basis of modern researches, the development of the pathology and the key of pathological conditions in organism is mitochondrial dysfunctions. In etiology of diseases the correction of mitochondrial dysfunctions using biologically active compounds from local plants is an acute problem of modern biophysics, pharmacology, and experimental and clinical medicine.

Purpose of this work was to study the effect of polyphenol compound euforbin on rat liver mitochondria functional processes and to investigate its pharmacological effect.

There is an increasing evidence for the concept of redox-driven alterations of mitochondrial function, as well as mitochondrial reactive oxygen species generation as a key event for the development of metabolic inflexibility.

The classic inductors like Ca^{2+}-ions, Fe^{2+}/ascorbate and the ATF show the destabilization of the functional activities of mitochondria. Many disorders of mitochondria functional parameters – changing of the conformational status of mPTP, strengthening of lipid peroxidation processes and increasing of MDA concentration, divorcing of oxidation and phosphorylation are observed. In these conditions the dysfunctions of the activity of mitochondria were determined. It was shown that the polyphenol euforbin influenced effectively on the process of oxidation and phosphorylation in the mitochondrion respiratory, suspended the membrane lipids peroxidation, and reduced the level of permeabilization of mPTP. It was determined that the polyphenol euforbin in the range of concentration (1<30 mkM) influence effectively to the rat liver mitochondria dysfunctions and show medicinal properties.

Based on the obtained results, the polyphenol euforbin may be used as a new membrane active and antioxidant, as well as cardio protector agent in medicines.

EFFECT OF OROXYLIN A ON AN OXIDATIVE PHOSPHORYLATION IN THE RAT LIVER MITOCHONDRIA

E. J. Komilov, N. A. Ergashev, M. I. Asrarov, B. J. Komilov

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, 100125, Tashkent, Mirzo Ulugbek str., 83, e-mail: info@biochem.uz

Mitochondria play an important role in energy metabolism in the cell. Under normal conditions the oxidative metabolism of living cells and of certain isolated systems leads to the synthesis of compounds containing high-energy phosphate bonds. These compounds are known to be essential for such functions as growth, muscle contraction, nerve conduction, etc.

It is well known, that many biological active compounds *in vitro* lead to the dissociation of oxidative phosphorylation in intact mitochondria of rat liver. However, in various pathologies, dysfunction of the functional parameters of the mitochondria involved in the regulation of membrane permeability and may be corrected by biologically active compounds. These kind of biological active compounds are polyphenols and flavonoids.

Flavonoids have a very broad spectrum of action on biological objects, demonstrating various biological effects. The effect of flavonoid oroxilin A on respiration and oxidative phosphorylation of mitochondria has been studied.

The effect of oroxilin A on respiration and oxidative phosphorylation of mitochondria show that this flavonoid at the concentration of 10 μM has no effect on the oxidation of succinate in the V_3 and V_4 states, while the values of control of respiration and ADP/O decreased by 4.95% ($P > 0.05$) and 5.95% ($P < 0.01$) compared with the control. However, in 20 μM of the concentrations of oroxilin A resulted some reduction in V_3 state by 5.75% ($P > 0.05$), the V_4 state increased by 9.97% ($P > 0.05$). At the same time, the coefficients of control of respiration and ADP/O was 12.4% ($P > 0.05$) and 4.76% ($P < 0.05$). During the action of oroxilin A at concentrations of 40 and 50 μM on the respiration of the mitochondria the V_3 state was no significant decrease in comparison with the control. In the same concentration of oroxilin A the state V_4 increased by 65.1% ($P < 0.001$) and 87.5% ($P < 0.001$), respectively. At the same concentrations, a decrease in the control of respiration coefficient by 39.2% ($P < 0.001$) and 48.8% ($P < 0.001$) was observed and the ADP/O indication also decreased by 21.4% ($P < 0.001$) and 26.2% ($P < 0.001$), respectively, with respect to control.

Thus, the obtained data show that oroxilin A effectively influences to parameters of respiration and oxidative phosphorylation of rat liver mitochondria and leads to the dissociation of oxidative phosphorylation.

INVESTIGATION OF NEFROPROTECTOR EFFECTS OF THE DRY EXTRACT OF "CICHORIUM INTYBUS"

Z. U. Usmanova

Tashkent Pharmaceutical Institute, Tashkent, Republic of Uzbekistan,
e-mail: fzt70@mail.ru

To correct the negative effect and eliminating the toxic action on kidney in using several drugs it is necessary to include the nefroprotecting facilities. Some plants including "Cichorium intybus" have properties which are similar to nefroprotectiveg properties such as absence of nefrotoxicity, existence of anti-oxidating and antiphlogistic activity.

Aim of the project. Analyzing the nefroprotective properties of the dry extract of the "Cichorium intybus".

Materials and methods. The nefroprotective action was investigated on rats weighed 160–220 g with deep poisoning by dichloride of mercury. The animals were divided into three groups and had the same conditions of vivarium, including the nutrition. The experimental pathology was caused by intra-abdominal implementing of the sublimate (2.0 mg/kg). The analyzing drugs were implementing *per os* 7 days before implementing of the sublimate and after on the background of caused intoxication basing on the set doses (50mg/kg). The animals were decapitated on the 6^{th} day after sublimate injection. The control animals were implemented by the same dose of solvent. The efficiency of the nefroprotective action were marked by normalization of the indicators of functional renal condition. The condition of urea in blood was measured by ureatic method, creatinine - by method of Yaffe with proper equipment of "Laheme". The static cultivation were held by the criteria of Student.

According to the results, the implementing of sublimate caused the serious toxic damage of kidney with expressing hyperazotemia. The concentration of creatinine and urea decreased significantly in the process of experimental pathology in the group that got 50 mg/kg of dry extract of "Cichorium intybus" beforehand. If the level of urea in the control group were equal to 41 ± 9.33 g/l the concentration of urea in experimental group was from 30 ± 65.5 to 214 ± 20.1 g/l. The drug increases the urination for 18%. So, if on the control the quantity of urine was 5.0 ml, after implementing the drug this indicator increased to 5.9 mL.

Thus, the dry extract of the "Cichorium intybus" in a dose of 50 mg/kg decreases the level of urea and creatinine in blood, caused by toxic implementing of sublimate. The drug shows protecting properties during the toxic nephropathy.

THE EFFECT OF DIABENIT GLYCOINUVIT AND STEVIL 50 ON LIPID METABOLISM IN ALLOXAN DIABETES

Z. T. Fayzieva, E. S. Bagdasarova, R. T. Tulyaganov

Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan, e-mail: fzt70@mail.ru

The aim of the study was to evaluate some parameters of lipid metabolism in rats with alloxan diabetes treated with diabenite glycoinovit and stevil 50.

The subject of the study was the substance of diabenite glycoinovit and stevil 50. The effect of diabenite glycoinuvite and stevil 50 on the community lipids were studied in 72 mature male rats weighing 170–190 years under conditions of alloxan diabetes. With a one-time intravenous injection of a diabetic dose of alloxan was 150 mg/kg.

In experimental animals, diabenitis and glycoinovitone were administered internally at 50 and 100 mg/kg, and stevil 50 to 100 and 500 mg/kg as an aqueous solution for comparison, a-lipoic acid was used at a dose of 20 mg/kg. The content of total lipid was determined by conventional biochemical methods.

The results of the experiments revealed a significant increase in the level of total lipids in the blood serum of rats with alloxan diabetes from 9.6 ± 0.1 g/L to 17.4 ± 0.4 g/L. The pharmacotherapy by a-LC significantly reduced the level of total lipids in 1.66 times and has made 10.3 + 0.15 g/L having approached them to value of intact rats. With diabenite at doses of 50 and 100 mg/kg the content of total lipids decreased by 1.89 and 1.91 times with respect to the untreated group of 9.2 + 0.3 g/L, respectively. In contrast to diabenite, the effects of stevil 50 were less pronounced. Such a high level of total lipids in rats with alloxan diabetes with the use of stevil 50 at doses of 100 and 500 mg / kg decreased in 1.38 and 1.26 times and was, respectively, 12.6 ± 0.1 g/L and 13.8 ± 0.2 g/L, slightly higher than that of intact rats.

Glycoinuvite at doses of 50 and 100 mg/kg caused a significant decrease in high values of total lipids and 1.51 and 1.55 times, respectively. The value of total lipids was 11.5 ± 0.3 g/L or 11.2 ± 0.4 g/L.

Hence, the new compounds used markedly reduce the level of total lipids in blood serum of rats with alloxan diabetes. In this respect, diabenite is not inferior to a-LC. At the same time, it was of interest to study which specific lipids the new compound influenced on. The pharmacotherapy of alloxan diabetes with diabenite reliably reduced the high level of total cholesterol in serum in 1.81 and 1.89 times in doses of 50 and 100 mg/kg and a-LC in 2.2 times.

There was also a decrease in the level of triglycerides and B-lipoproteins in the blood. The effect of stevyl 50 and glycoinuvite was somewhat weaker.

Thus, diabenite by its hypolipidemic hypocholesteronemic and hypotriglyceridemic effects is not inferior to a-LK and recommended for correction of lipid metabolism disorders in diabetes mellitus.

THE IFLUENCE OF DRY EXTRACT OF "CICHORIUM INTYBUS"

Z. U. Usmanova

The Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan, e-mail: fzt70@mail.ru

The aim of the project: To study the effect of dry extract of "Cichorium intybus" on a diabetes caused by experimental way on rats in compare to Gluher's drugs.

The materials and methods: The diabetes of rats was caused by implementing the diabetes into rats (dosage: 150 mg/kg). Than, during the next 14 days rats were cured by implementing the "Cichorium intybus" and 100 mg of the Gluher drugs. The biochemical indicadors were recorded.

The result of the project: According to the results it was identified that the dosage of glucose in blood of rats rised four times and was equal to 27.3 ± 1.14 mol/l. The dosage of glucogen in liver decreased 2.5 times and became equal to 1.9 ± 0.15 g%. Moreover, it was explored that the general dosage of cholesterol, the activity of AlT and AcT was fixed.

Because of dry extract (100 mg/kg per day) till the 14-th day the dosage of glucose in blood decreased to 48%. Futhermore, It was found that the dosage of glucogen I liver rised significantly. For instance, glucogen in the liver of rats after recieving the dry extract of "Cichorium intybus" and Gluher drugs became equal 6±0.32 and 5.1±0.29% which is triple and twice bigger than control group indicators.

Cholesterol, ALT and AST parametres of animals treated with drugs decreased significantly else to normal. The experiment was continued on several rats and till the 28-th day the biochemical indicators were checked second time.

The second record shows that the dosage of glucose in blood of cured rats decreased till 6.1 ± 0.63 and 6.6 ± 0.64 mol/l. To compare the control group rats cuped the dosage of glucose at the level of 7.8 ± 0.63mol/l.

The amount of glucogen from the second record were equal to 4.6 ± 0.42%, 5.3 ± 0.42 g/% in typical group of rats that were cured by dry extract of "Cichorium intybus" and Gluher drugs.

The other biochemical indicators decreased significantly and stopped at stable physiological level.

Overall, dry extract of "Cichorium intybus" have a positive influence on diabetes and stabilizes the biochemical indicators, normalizes metabolism.

Sum up: According to the experiment dry extract of "Cichorium intybus" can be used as hypoglycemic drug to cure the 2-nd type of diabetes.

DEVELOPMENT OF THE LC-MS METHOD IN THE ANALYSIS OF "INTRALIN" MEDICINAL PREPARATION

A. A. Mamadrahimov[1], L. A.Makhmudova[2], R. A.Khusainova

1) The Tashkent Pharmaceutical Institute, Tashkent, 100147, Uzbekistan
2) Institute of Bioorganic Chemistry, Uzbek Academy of Sciences, Tashkent, 100125, Uzbekistan

In the pharmaceutical industry, drugs from the cephalosporin group have recently been widely produced. One of the widely available preparations in our republic is "Intralin", which containing cefazolin, a powder for the preparation of a solution for injections. The purpose of our research is to develop a methodology for the qualitative detection and quantification of cefazolin in the medicinal preparation "Intralin", by LC-MS.

Qualitative and quantitative determination of cefazolin content in the preparation "Intralin" was carried out by HPLC-MS.

HPLC-MS with a triple quadrupole Triple Quad QQQ Agilent Technologies (USA) was used in the work. Chromatographic conditions were selected as follows: mobile phase: 5 min. H_2O is 100% for isocratic elution and acetonitrile/water in a ratio of up to 80% of organic solvent in gradient elution. The column temperature was set at 20 °C.

The ionization was carried out with electrospray (ESI), the gas flow rate of the desiccant (nitrogen) was 10 ml/min at a temperature of 300°C, the gas pressure on the 20 psi spray nozzle, the strain of the fragmentator, respectively, for cefazolin 100 V, the capillary voltage was 4000 V.

Analyses were conducted in both single ion mode (Single IonMode-SIM) and full-scan (Full scan mode) mode for the development of a method for the determination of cefazolin. For SIM, the regimes were applied for qualitative and quantitative analysis using target ions m/z 455 for cefazolin in positive ion monitoring.

The following ion peaks are observed in the mass spectrum of the preparation:

The ion with *m/z* 455.2 corresponds to the mass ion M^+/.The ion with *m/z* 377.2 is formed as a result of the rupture from the molecular ion of carbon (IV) oxide and hydrogen sulfide with *m/z* 77. The ion with *m/z* 355 is formed by the ejection from the molecular ion of the fragment with *m/z* .99 which corresponds to the methylthiadiazole ion.

The content of cefazolin (X) in the preparation, in μg/mg, was calculated by the formula:

$$X = \frac{S \times M_0 \times 25 \times P \times 100}{S_0 \times 25 \times M \times (100 - W)} = \frac{S \times M_0 \times P \times 100}{S_0 \times M \times (100 - W)}$$

In general, the results obtained suggest that the method developed by us is easy and convenient to use for the qualitative and quantitative determination of cefazolin in intralin. Using two different modes of ion scanning allowed us to fast qualitative and quantitative determination of cefazolin.

PHARMACOLOGICAL AND EXPERIMENTAL STUDY OF THE SEDATIVE DRUG "FLEGMEN"

N. Olimov[1], Z. Sidametova[2], B. Abdullaev[2]

1) Tashkent Pharmaceutical Institute, 100147, e-mail: pharmi@pharmi.uz
2) Tashkent Medical Academy, Farobi 2, Almazar District, Tashkent, Uzbekistan 100109

Introduction. Distress, due to pain, fear/anxiety, dyspnea, or delirium is common among critically ill patients. Distress may manifest clinically as agitation that is often associated with ventilator asynchrony and vital sign abnormalities. Regardless, distress needs to be treated to comfort the patient, ameliorate agitation that may interfere with supportive care, and attenuate increases in sympathetic tone, which may have untoward physiological effects.

Purpose. Common sedative-analgesic medications used to treat distress in critically ill adults. Identifying the cause of distress and using this information to select the optimal sedative-analgesic agent is discussed separately. The aim of the study was to evaluate effectiveness of the new sedative drug complex “Flegmen” in preclinical study.

Materials and Methods. The elemental composition of sedative assemblage "Flegmen" was analyzed by the method of mass spectrometry induction coupled plasma on the instrument ICP-MS 7500a AT the company "Agilent Technologies". Sedative assemblage "Flegmen" contains 39 elements. In the greatest number of macrocells in the sedative assemblage, "Flegmen" contains chlorine, phosphorous, bromine, sodium, chromium, titanium, zinc and strontium. Also set the content of calcium (9.6 μg), which relieves the consequences of stress. Amino acid composition was studied via analyzer. Identification of amino acids and their quantitative content in nanomolar was calculated according to the integrator, which is supplied with amino acid analyzer. Clinical studies were performed in the Republican Specialized Scientific-Practical Center (RSSPC) of Therapy and Medical Rehabilitation, the Department of Neurology, Departments of GP-therapy, Clinical Allergology, Propedeutics of Internal Diseases, Hematology, and Professional Diseases at the Tashkent Medical Academy.

Experiments and Results. The research included 30 patients who received the studied medicine, and 20 patients who received compared medicine while being on outpatient and inpatient treatment. Research included only 50 patients who were divided into two groups: the main and control. The main group included 17 women (56.6%) and 13 (43.3%) men, average age was 50.9 ± 3.03 years. 13 (65%) men and 7 (35%) women were included in control group, average age was 44.5 ± 2.09 years. A value of $p = 0.01$ is used here as estimation of the severity of action of the drug or different drug effects. "Flegmen" in the ratio of 1:10 was administered to the patients of the main group (30 people) 1/3 - 1/2 cup 2-3 times a day for 15 - 20 minutes before meals for 2–3 weeks on the background of basic therapy. Patients in the comparison group (20 people) took the drug Sedonik with similar effects.

Conclusion. It was confirmed that "Flegmen" is the most effective in the treatment of patients with various diseases followed by asteno-neurotic syndrome and neuroses that allows recommending for use in practical health care. According to the evaluation, "Flegmen" was found extremely tolerability in all 50 (100%) patients. Side effects were not revealed in the research.

FATTY-ACID COMPOSITION OF OIL EXTRACT "MEKRITEN"

N. K. Olimov[1], A. A. Mukhitdinov[1], L. G. Mezhlumyan[2]

1) Tashkent Pharmaceutical Institute, Tashkent, e-mail: pharm@bcc.com.uz
2) S.Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of Uzbekistan

Garlic (*Allium sativum*) has unique healing properties and is successfully used in folk medicine for the treatment of various diseases, including intestinal atony, hypertensive disease, atherosclerosis, diabetes mellitus, etc.

We have developed a special technology for obtaining an oil extract of garlic (the conventional name is "Mekriten"), which has a pronounced anti-inflammatory effect, from the raw material of the "South Violet" variety harvested in the Tashkent region.

Chemical analysis of "garlic oil" was carried out, and data on the composition and content of fatty acids were obtained.

The separation of the fat phase was carried out with a mixture of chloroform: aqueous methanol. In this case, the fat part was dissolved in chloroform, and the other components - in the water-methanol phase. The yield of the fat phase was 99.7%.

The composition and content of fatty acids in the fat phase and in the control sample was established by gas-liquid chromatography using a "Chrom-5" device.

Preparation of "Garlic Oil" (GO) samples and "Control" was carried out after their preliminary alkaline hydrolysis. Then, fatty acids were isolated from the hydrolysis products, which were converted into methyl esters with freshly prepared diazomethane. After that, the samples were analyzed by GLC.

TABLE 1. **Fatty Acid Composition,% GLC by Weight**

Acids	Sample	
	Control	GO
Capricious (10:00	–	0.2
Lauric (12:0)	–	0.2
Myristic (14:0)	0.1	0.8
Tetradecene (14:1)	–	Tr.
Palmitic (16:0)	6.1	7.7
Stearic (18:0)	0.9	0.2
Oleic (18:1)	19.8	27.3
Linoleic (18:2)	72.8	63.6
Arachidonic (20:0)	0.3	
$\Sigma_{sat.}$	7.4	9.1
$\Sigma_{unsat.}$	92.6	90.9

The total content of unsaturated acids (18:1 + 18:2) in the control and sample was 92.6 and 90.9%, accordingly. This index dropped by 2% in GO due to the increase of saturated acids 16:0.

Thus, a chemical analysis of "garlic oil" was carried out, and data on the content of fatty acids and protein were obtained. The results of fatty-acid and amino-acid compositions are presented.

INFLUENCE OF QUERCETIN ON MITOCHONDRIAL ATP-DEPENDENT POTASSIUM CHANNEL IN THE HEART

E. J. Komilov, N. A. Ergashev, U. G. Gayibov

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan, 100125, Tashkent, Mirzo Ulugbek str., 83, e-mail: info@biochem.uz

Flavonoids are one of the natural polyphenol compound groups. Nowadays, flavonoids are widely using in the prevention and treatment of a variety of pathological conditions in organism. It was shown, that quercetin inhibits mitochondrial breathing and oxidation phosphorylation processes, and these processes related with the second package of oxidation phosphorylation.

It is well known, the permeability of K^+-ions through the mitochondrial and cell membranes depends on the functioning of potassium channels. In this regard, influence of quercetin to potassium permeability trough ATP-dependant channel on mitochondrial membranes of rat heart was studied. The results were announced, that flavonoid quercetin in different concentrations activates the ATP-dependant potassium channel of heart mitochondria. It was obtained that quercetin in 10, 30 and 50 μM concentrations activates potassium permeability trough membranes of heart mitochondrion on 39%, 148% and 203%, respectively.

It was shown, that quercetin is the activator of ATP-dependant potassium channel of heart mitochondria, thus this flavonoid can be used as cardio protector in medicine.

SOURCES OF PLATYPHYLLINE AND ITS DERIVATIVES

Z. Ch. Abraeva, V. I. Vinogradova, R. A. Botirov

S. Yu.Yunusov Institute of the Chemistry of Plant Substances Academy of Sciences of Uzbekistan, 100170, M. Ulugbek st., 77, Tashkent, e-mail: z.abraeva@mail.ru

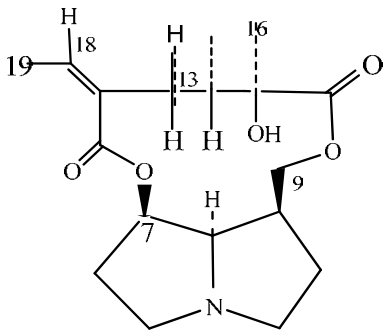
Senecio platyphylloides (*Asteraceae* family) is a perennial herbaceous plant. Dried grass of S. *platyphylloides* is used as a raw material for the production of platyphylline hydrotartrate.

We investigated the aerial part of *S. platyphylloides* from Georgia and China. The air-dry plant was extracted with 80% alcohol. After processing the yield of the total alkaloids and platyphylline hydrotartrate were the following:

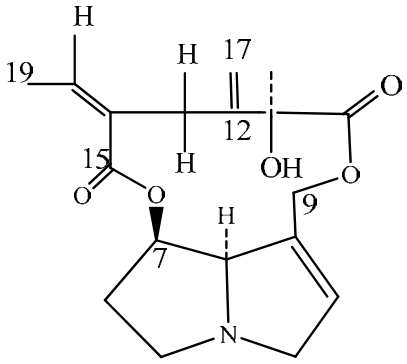
Growth place	Plant weight, kg	Chloroform amount of alkaloids, g	Amount of platyphylline hydrotartrate from air-dry mass of raw material, %
Georgia	13.5	105 (0.77%)	0.1-0.2
China	12.0	70 (0.58%)	0.05 *

*With an admixture of sarracine.

On the basis of the alkaloid seneciphylline concomitant with the alkaloid platyphylline the reactions with *N*-bromosuccinimide, bromine and thionyl chloride were carried out.



platyphylline



seneciphylline

STUDY ON THE SYNTHESIS OF EPOXY SOYBEAN OIL ACRYLATE

Xamxikamar Mamat, Danfeng Qin, Sanshuang Gao, Nuerbiya Yalikun, Guangzhi Hu

The Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi, 830011, e-mail: xamxikmr@ms.xjb.ac.cn

In this work, the epoxy soybean oil was prepared by oxidation of soybean oil with formate peroxide in petroleum. In order to obtain the optimum synthesis conditions of epoxy soybean oil, the experimental parameters were optimized. A best experimental can be obtained under the following conditions: The soybean oil (10 g) with half volume of petroleum were added to the formate peroxide (25 g) at about 30 °C; and then be soaked at 58 °C for 5 h. After the distillation treatment, the epoxy value, acid value and yield of the epoxy soybean oil are 6, <0.5 and 95%, respectively. Under the optimized experimental conditions, epoxidized soybean oil and acrylic acid were esterified to prepare epoxidized soybean oil acrylic acid and the characteristics of as-prepared product are acid value < 1, iodine value 38, and viscosity 16000 (25°C). Additionally, the influences of reactant proportion on the viscosity, viscosity index, flash point and, pour point were also investigated. The preparation process of spoxy soybean oil acrylate is simple, clean without high pressure and high temperature equipment, and facile to large-scale production.

DISTRIBUTION OF DYSTROPHIN GENE DELETIONS IN UZBEKISTAN POPULATION

U. T. Omonova[1], Yo. N. Madjidova[1], Z. Z. Ibragimov[2], K. T. Boboev[2]

1) Chair of "Neurology, Pediatric Neurology and Medical Genetics"
Tashkent Pediatric Medical Institute
2) Research Institute of Hematology and Blood Transfusion of the Ministry of Health of the Republic of Uzbekistan

Introduction. Duchenne (OMIM 310200) and its less severe allelic form Becker (OMIM 00376) muscular dystrophy (DMD/BMD) are common X-linked recessive hereditary neuromuscular diseases. DMD affects about 1 in 3500 to 4000 boys globally. These disorders result from heterogeneous mutations in the dystrophin gene. The DMD gene maps to the short arm of the X chromosome at band Xp 21. The DMD gene is the largest human gene with a length of approximately 2.3 Mb, and it contains 79 exons. It encodes for a14 kb mRNA, which is translated into a 427 kDa protein dystrophin. The dystrophin protein isinvolved in the linkage between the extracellular matrix and the cytoskeleton. DMD and BMD result from partial gene deletions (in approximately 60%), duplications (approximately 5%), point mutations and deletions/insertion offew nucleotides. Mutational analysis is complicated by the large size of the gene, although an accurate multiplex polymerase chain reaction (PCR) method using 19-exon and promoter region primers can detect to 98% of dystrophin deletions. The frequency and distribution of deletions of the dystrophin gene in patients with DMD and BMD show that there are different variants of exons between different populations.

The purpose. To describe the deletion characteristics of the dystrophin gene in Uzbek population of patients with Duchenne muscular dystrophy (DMD) or Becker muscular dystrophy (BMD).

Materials and Methods. Ninety one patients with dystrophinopathies (eighty four patients with Duchenne muscular dystrophy (DMD) and seven with Becker muscular dystrophy (BMD) were ascertained from both Uzbekistan. Diagnosis was based on clinical characteristics, elevated serum creatine kinase (CK) and electromyographic features. Genomic DNA extraction was carried out from the peripheral blood sample using DIAtom ™ genomic DNA extraction and purification Kit (Molecular Genetics Center, Moscow) following the manufacturer's instructions. The quantitative and qualitative analysis of genomic DNA was carried out by Spectrophotometer (NanoDrop 2000, USA) and agarose gel electrophoresis. DMD gene deletions were detected using multiplex PCR reactions. Samples were run in PCR machine (Corbett Palm Cycler, Australia). PCR products were resolved on 9% PAGE gels and the gels were analyzed for exonic deletions by the presence or absence of a corresponding band.The gel was stained with ethidium bromide (10 mg/ml) and visualized under UV transilluminator «UVT-1» (Biocom, Russia).

Result. Molecular analysis of DMD gene mutations was carried out by the multiplex PCR to identify the pattern of exon deletions in the dystrophin gene from DNA samples from 91 Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) patients. In this study, deletions were detected in 58/91 (63.7%) patients, and around 71.2 % localized in the mid-distal hotspot of the gene (on exons 47–53), 19 cases (32.8 %) with single-exon deletions, and 39 cases (67.2%) with multi-exonic deletions. The most frequent deleted exons were exon 50–51 (15.7 %) and exon 52 (13.7%). No deletion were detected in exons 32, 42, 60 Pm.

SIGNIFICANCE OF DETECTION OF G2014A GENE POLYMORPHISM ESR-α IN THE DEVELOPMENT OF OSTEOPOROSIS IN THE POPULATION OF UZBEKISTAN

Z. Z. Ibragimov, A. A. Yaryev, K. T. Boboev

Scientific-Research Institute of Hematology and Blood Transfusion,
Bunyodkor st., 42-a, Tashkent, Republic of Uzbekistan,
e-mail: info.niigem@minzdrav.uz

Osteoporosis (OP) - has a complex pathogenesis is multifactorial disease characterized by low bone mass and bone microstructural rearrangement, leading to increased bone fragility and risk of fracture. The causes of osteoporosis and osteoporotic fractures can be a genetic background, environmental factors and their interaction.Now, there are many genes associated with the development of Osteoporosis (OP), each of which, alone, having little effect in combination with other genes contributes to the overall phenotype of the patient. Among many candidate genes involved in the regulation of bone metabolism, an important role belongs to the estrogen receptor gene (ESR).

The aim of this study was to determine the association of polymorphism rs2228480 ESR1 gene with the risk of osteoporosis.

In total, this study involved 235 people were living in Uzbekistan, of which 98 patients with OP and the control group consisted of 137 conditionally healthy individuals with no history of fractures. Testing polymorphic locus 2014G> A (rs2228480), ESR1 gene PCR was performed on a real-time hermocycler Rotor Gene 6000. Statistical analysis of the results carried out using the statistical software package «Doctor Stat 2013".

The statistical analysis of allele frequencies and genotype polymorphism 2014G> A ESR gene between the main and population groups showed statistically significant differences. The frequency distribution of wild homozygous G/G genotype at OP was markedly lower than in the control (49.0% vs. 67,9%, P <0.005; OR = 0.45), that It can be considered as a protective factor against the risk of OP in carriers of this genotype. Frequency distribution of the genotype heterozygous G/A ESR1 gene in patients with OP up 42.9% (42/98) and 29.9% in the control group (41/137), respectively ($\chi2$=5.96; p=0.016; OR=1.98; 95%CI: 1.14-3.45). The frequency distribution of rs2228480 genotype A/A ESR1 gene in patients with OP was 8.1% (8/98) in the control group and 2.2% (3/137) respectively. The criterion $\chi2$ between the frequencies of genotypes in groups of patients with osteoporosis and control is at 6.56; df = 1; and p = 0.019; OR = 5.17; 95%CI: 1.31-20.37). According to the calculated odds ratio the presence of unfavorable genotype A/A significantly increases the risk of OP in 5.2 times. At the same time, examining the genotypes of G/A +A/A, we obtained the following values of the indicators in the group with control and OP: 51.0 (50/98) and 32.1 (44/137), which indicates that genotype data statistically significantly increased risk of OD 2.2 times ($\chi2$=8.51; p=0.0045; OR=2.2; 95%CI: 1.29-3.76). As a result of statistical analysis of polymorphism rs 2228480 alleles of ESR gene showed that the frequency of occurrence of “G” allele is Osteoporosis in 70.4%, whereas in the control group, 82.8% ($\chi2$=10.19; p=0.001; OR=0.49; 95%CI: 0.32-0.76). The study also revealed that detection of the unfavorable allele “A” Group to OP and control was 29.6% and 17.2%, respectively ($\chi2$=10.19; p=0.0016; OR=2.03; 95%CI: 1.31-3.15). It was revealed that in the basic group the association of polymorphism rs 2228480 ESR1 gene plays an important role in the osteoporosis (OP). In the presence of the allele A and hetero/homozygous genotypes (G/A and A/A), the frequency of detection of this polymorphism increases significantly, and the protective allele and genotype G and G/G reduces the risk of OP in the population of Uzbekistan.

ANALYSIS OF ASSOCIATION OF DRD4 GENES C521T POLYMORPHISM WITH THE SYNDROME OF DEFICIT OF ATTENTION WITH HYPERACTIVITY IN CHILDREN

S. N. Saidkhodzhaeva[1], Kh. Ya. Karimov[2], Yo. N. Madzhidova[1], K. T. Boboev[2], Mokhammad Dın A.[2]

1) Tashkent Pediatric Medical Institute
2) Research institute of hematology and blood transfusion

Presently the researchers of leading scientific centers of the developed countries of the world spare considerable attention the exposure of genes-candidates, participating in forming of syndrome of deficit of attention with hyperactivity (SDAH) in children. However, the number of work is small and the search for an associative link still gives contradictory results.

Purpose of work. Analysis of association of DRD4 genes C521T polymorphism with forming of SDAH in children of Uzbek nationality.

Materials and methods. The study included 94 children with SDAH (66-boys and 24-girls). As a control were used DNA samples of 97 conditional-healthy children of Uzbek nationality, of the same age and without the signs of SDAH (48 boy and 49 girls). Detection of polymorphism conducted with the use of test-system LTD. Liteh (Russia) on thermo cycler GeneAmp PCR-system 2700 (Applied Biosystems, USA). As an instrument of calculations used the package of applied «OpenEpi 2009, Version 2.3».

Results and discussion. In the studıed groups of patients and control group observed frequency distribution of genotypes did not deviate from EHW ($\chi 2 < 3.8$; $P > 0.05$). The comparative analysis of frequencies of genotypes and alleles of C521t Drd4 gene polymorphism between the groups of patients and control group did not expose statistically reliable distinctions ($\chi 2 < 3.8$; $P > 0.05$). Frequencies of genotypes of C/C, C/T and T/T were: 13.8%, 44.7% and 41.5% – in the general group of patients and 11.3%, 46.4% and 42.3% – in the control group accordingly. Frequencies of alleles of 521c and 521t were: 36, 7% and 63.8% – in general group and 34.5% and 65.5% – in control group. In the sub-group of girls, marked meaningful decrease of frequency of occurrence of 521T mutant allele as compared to the sub-group of boys (31.1% against 48.2%; $\chi 2=5.0$; $P=0.02$; OR=0.5; 95%;CI 0.25-0.92) and tendency to the increase on comparison with population selection (48.2% against 34.5%; $\chi 2=3.6$; $P=0.06$; OR=1.8; 95%;CI 0.96- 3.2).

Thus, it is established that this DNA locus independently not associated with the formation of SDAH. At the same time, detected expressed tendency to gender differences in the distribution of frequencies of alleles and genotypes.

STUDY OF BIOLOGICALLY ACTIVE SUBSTANCES OF *Ferula moschata* by GC- and HPLC-MS METHODS

A. B. Soliev[1], M. R. Tursunova[2], A. A. Mamadrakhimov[1], I. R. Mavlyanov[1], A. A. Khojimetov[1], M. Sh. Karimov[1]

1) Republican Scientific and Practical Center of Sports Medicine at the National Olympic Committee of Uzbekistan 100027, Almazar str., 6, Tashkent, Uzbekistan
2) "Dentafill Plyus" private company, 100209, Chortok-Magrib str., Tashkent, Uzbekistan, e-mail: malika.tursunova.1983@ mail.ru

Phytotherapy or herbal treatment for millennia remained an affordable and reliable means of fighting against human illnesses. Information about the properties of plants to use as medical drugs passed down from generation to generation. For therapeutic purposes, various parts of plants are used in the form of dry grass, root infusions, bark, flowers, leaves and juices, since the content of medicinal substances in different organs of the plant is not the same, and yet the presence and composition of these substances depend on the time of collection.

In this work, the main goal was to study the chemical composition of the root part of the *Ferula moschata* using modern gas chromatography and high-performance liquid chromatography coupled with mass spectrometry to assess their suitability for use in folk and sports medicine.

The *Ferula moschata* plant is an endemic species in the mountainous regions of Central Asia. In Uzbekistan, there are more than 50 species. In folk medicine, mainly the roots of the plant are used, containing 2-4% of essential oil, which gives a bitter-spicy taste. In medical practice, Ferula is used to treat convulsions, tuberculosis, plague, syphilis, whooping cough, toothache, nervous system diseases and other ailments, as well as a tonic, expectorant and anthelmintic.

In this work, the root part of the plant, collected from the mountainous regions of the Kashkadarya region, was examined. To study the chemical composition, the roots of the plant were divided into small pieces and ground on a mortar and pestle. Substances of fatty-lipid nature were extracted with hexane, while tannins were extracted in a 70% solution of ethyl alcohol. The extracts were filtered on a paper filter and centrifuged at 10000 rpm for 10 minutes and then either analyzed by a gas chromatography or by HPLC coupled with a triple quadruple mass spectrometer of Thermo Fisher Scientific, USA. Identification of the obtained chromatograms was carried out using the "NIST" library of reference mass spectra of natural compounds.

Analyzes revealed the presence in the root part of the plant a number of known biologically active substances belonging to such classes as sugars, glycans, isoflavones, terpenoids, saponins, etc. Among them, there are biologically active substances that are of pharmacological interest.

Currently, the study of the complete chemical composition of the root part of the plant is continuing, and the pharmacological properties of biologically active substances are being studied.

EFFECT OF SAFFLOWER EXTRACT AND QUERCETIN ON BLOOD GLUCOSE IN EXPERIMENTAL DIABETES

M. M. Mustafakulov, S. U. Irgasheva, T. M. Ishankhodjaev, M. K. Salokhutdinova, E. A. Ibragimova, B. R. Zainutdinov

Institute of Bioorganic Chemistry, Uzbekistan Academy of Sciences,
83 Mirzo Ulugbek Street 700125 Tashkent, Republic of Uzbekistan,
e-mail: mmustafakulov@bk.ru

Antioxidant properties of plant flavonoids are discussed in many works, interest to these classes of polyphenols is still high. In literature glucose-lowering properties of polyphenols are explained by their antioxidant ones facilitating partial restoration of pancreatic beta-cells resulting in increase of blood insulin. However, question if the flavonoids produce any effects on glucose utilization in the insulin-resistant tissue of animals with experimental diabetes is still unanswered.

The work was initiated to study effect of safflower and quercetin, a flavonoid, on some parameters of antioxidant system, on blood glucose and activity of glucose utilization enzymes in rat liver tissues in experimental diabetes model.

Outbred rats weighing 200-300g on standard diet were used as a model. Diabetes was induced with a single intra-abdominal injection of diabetogenic dose of alloxan (100 mg/kg of animal's weight). Blood glucose level approaching 120 mmol/l (in 10-12 days) safflower extract in the dose of 120 mg/kg, quercetin in the dose of 15 mg/kg and gliclazide, a commercially available hypoglycemic (control), in the dose of 0.4 mg/kg were administered *per os* every day for 10 days.

Our findings demonstrated that injected to rats with alloxan diabetes extract of safflower and quercetin caused reduction in blood glucose from 12 mmol/l to 6.0 mmol/l, while gliclazide reduced blood glucose to 7.0 mmol/l only. Safflower extract, quercetin, and gliclazide were found to cause significant reduction in thiobarbituric acid (TBA) products both in blood and liver tissue; activity of antioxidant system enzymes is differently directed one, excluding catalase, activity of which appeared to increase. The highest increase in the activity (by 30%) was registered after injection of quercetin; all values were lower than those in the intact animals. No significant differences were found in activity of superoxide dismutase and glutathione reductase after injection of safflower extract to animals with experimental diabetes. Quercetin was found to increase superoxide dismutase activity by 20%, but produces no significant changed in the activity of glutathione reductase.

Study on glucokinase activity in liver of rats with alloxan diabetes demonstrated that safflower extract, quercetin, and gliclazide caused increase in the activity of liver enzymes in rats with experimental diabetes with decline in blood glucose by 30, 25 and 18%, respectively. Safflower extract was shown to produce the most significant effect as compared with others.

Thus, hypoglycemic effect of safflower extract and quercetin seemed to be the result not only of partial restoration of pancreatic beta-cells, but of liver issues' glucokinase activity restoration.

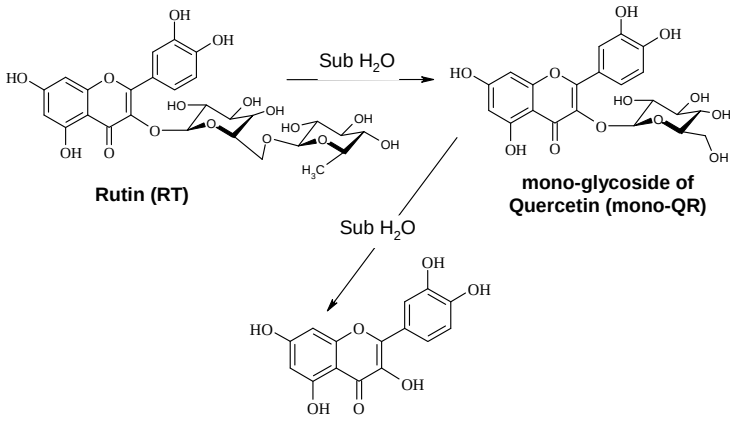
AN ACID-FREE TECHNIQUE FOR THE PREPARATION OF NATURAL ANTIOXIDANT QUERCETIN FROM RUTIN BY SUBCRITICAL WATER

E. V. Vetrova, E. V. Maksimenko, A. V. Lekar, S. N. Borisenko, S. S. Khizrieva, A. F. Bugaeva, N. I. Borisenko

Southern Federal University, Stachky Av. 194/2, Rostov-on-Don, 344090, Russia, e-mail: boni@ipoc.rsu.ru

Quercetin (QR) is a natural strong antioxidant of the plant origins. It is used for treating conditions of heart and blood vessels including “hardening of arteries” (atherosclerosis), high cholesterol, heart disease, circulation problems, preventing cancer, for treating chronic infections of the prostate, etc. The aim of this work was to development and study of an acid-free technique for the preparation of QR from rutin (RT) that requires no use of acids and toxic organic solvents.

For the first time, the subcritical water [1] that serves as a reactant and a solvent were used to obtain QR in good yields starting from RT. High-performance liquid chromatography combined with mass spectrometry was used to determine the quantitative and qualitative compositions of the obtained products.



That way requires no use of acids and/or toxic organic solvents. It has been shown that variation of only one parameter of the process (temperature of subcritical water) allows alteration to the composition of the hydrolysis products. The new method developed for the production of QR in subcritical water is environmentally friendly and faster than conventional hydrolysis methods that use acidic or enzymatic hydrolysis. The proposed technique has a potential for the future development of inexpensive and environmentally friendly technologies for the production of new pharmaceutical plant-based substances.

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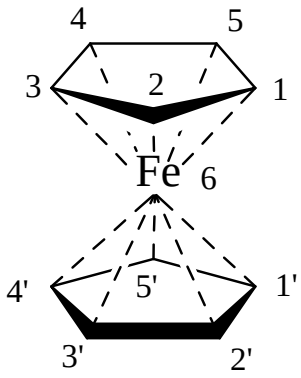
BIOLOGICALLY ACTIVE FERROCENE BIOSTIMULATORS

M. Kh. Mamarakhmonov[1], I. R. Askarov[1], L. I. Belen′kii[2], B. Tashkhodjayev[3]

1) Andijan State University, 170100, Andijan, University st. 129, Uzbekistan
2) ZIOC RAS, 119991 Moscow, Leninsky Prospekt 47, Russian Federation
3) S. Yu.Yunusov Institute of the Chemistry of Plant Substances Academy of Sciences of Uzbekistan, 100170, M. Ulugbek st., 77, Tashkent,

Studies of ferrocene derivatives (dicyclopentadienyl iron, Fc) have started long time ago [1]. In Russia, the first scientific research on ferrocene compounds [2] was carried out by a group of scientists under the supervision of Acad. A. N. Nesmeyanov. Scientists of INEOS RAS continue intensive scientific research to create highly effective ferrocene derivatives. In Uzbekistan, scientists under the guidance of prof. A. G. Makhsumov have synthesized many biologically active ferrocene derivatives.



Nowadays, theoretical and experimental studies on these classes of compounds are increasing, due to the presence among them of many compounds with high biological activity. For example, the patented ferro-stimulants “MAXIT”, “ADUMAKH” synthesized by the scientists of the ASU headed by prof. I.R.Askarov, are the regulators of plant growth. Preparations of the new generation "Ferand", "FerandMI", "Ferask" have been created on the basis of ferrocene, and recommended for the treatment of inflammatory processes. New unique biocles "Cyakrin AP-1" and "Cyacrin AndMos" approved by the Ministry of Public Health of Uzbekistan for use in surgical practice of parenchymal organs [3].

The discipline 02.00.09 .- "Chemistry of goods" the correct codes for all biostimulators as a finished product provides according to the chemical composition established by the physical-chemical methods of investigation, as well as by the results of quantum-chemical studies. The theoretical studies carried out by us, in particular, the ferrocene arylation process [4], have shown the convenience of using modern methods of quantum chemistry [5] to study the reactivity and mechanisms of these reactions.

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