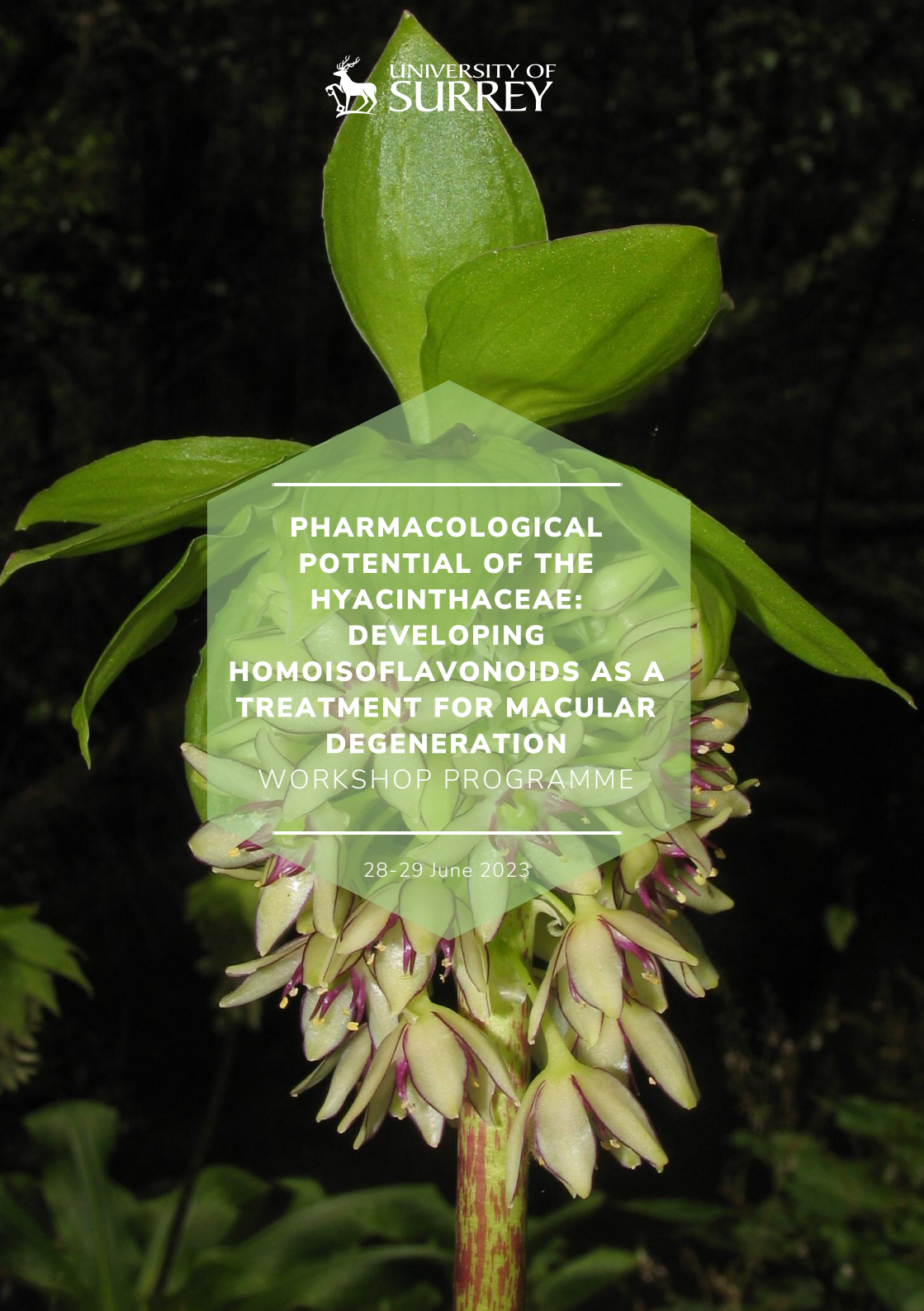

UNIVERSITY OF SURREY

PHARMACOLOGICAL POTENTIAL OF THE HYACINTHACEAE: DEVELOPING HOMOISOFLAVONOIDS AS A TREATMENT FOR MACULAR DEGENERATION

WORKSHOP PROGRAMME

28-29 June 2023

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WELCOME MESSAGE FROM THE CONFERENCE CHAIR

Dulcie Mulholland

Welcome to our second conference on the Hyacinthaceae. The first meeting in 2012 led to many new collaborations, and I hope this one will also.

We have a very wide-ranging program, with ethnobotanists, taxonomic botanists, pharmacologists and natural products and synthetic chemists contributing.

Much more has been discovered since the last meeting about the pharmacological activity of compounds from the Hyacinthaceae and the taxonomic relationships between these plants. The anti-angiogenic activity of the homoisoflavonoids means they have great potential in the development of an eye drop therapy for the treatment of macular degeneration. The anti-cancer, anti-inflammatory activity and the potential for the treatment of cardiovascular conditions have been demonstrated. These are all very important in treating ailments of our ageing population.

We are very pleased to have with us Mrs Geraldine Hoad and Mr Peter Bloomfield from the Macular Society. We have delegates from many countries: Malaysia, USA, Austria, Thailand, South Africa, Spain, South Korea and post graduate students from various parts of the world attending. We are also pleased to have delegates from Kew and Wisley Gardens. Welcome to you all.

I hope you will enjoy the variety of lectures, the visit to Albury vineyard and the trip to Wisley Gardens.

Conference Chair:
Professor Dulcie Mulholland, University of Surrey

Administrative support:
Ms Linda Bennett, University of Surrey and Ms Louise Jones, Institute of Advanced Studies

PROGRAMME

DAY 1 – WEDNESDAY 28 JUNE

Innovation for Health Building, Room 02 EFH 01

(BST)	
08.45 – 09.15	Registration, Coffee, Tea and Pastries
09.15 – 09.25	Welcome by Workshop Chair
09.25 – 09.35	Address by Geraldine Hoad and Dr Peter Bloomfield, Macular Society
	Chairperson: Prof Dulcie Mulholland
09.35 – 10.15	**Lecture 1: Prof Neil Crouch: Reflections on scientific endeavour associated with the Hyacinthaceae of southern Africa**
10.15 – 10.55	**Lecture 2: Prof Tim Corson: Homoisoflavonoids for Macular Degeneration: The Evidence So Far**
10.55 – 11.10	Tea, Coffee and Biscuits
	Chairperson: Dr Moses Langat
11.10 – 11.50	**Prof Mario Martinez-Azorin: How many genera must be accepted in Hyacinthaceae? Do we know its real diversity?**
11.50 – 12.10	**Dr Sianne Schwikkard: Homoisoflavonoids and Chalcones for the Treatment of Pterygium**
12.10 – 12.30	**Dr Walter Knirsch: A case presentation of a patient with a wet Age Related Macular Disease (wet AMD)**
12.30 – 13.30	Cold Conference Lunch with Poster viewing
	Chairperson: Prof Neil Crouch
13.30 – 14.10	**Dr Nor Hadiani Ismail: Search for Dengue Antiviral Compounds from an Indigenous Malaysian Plant, *Goniothalamus lanceolatus***
14.10 – 14.35	**Dr Eduard Mas-Claret: Bufadienolides and anti-angiogenic homoisoflavonoids from *Rhodocodon cryptopodus*, *Rhodocodon rotundus* and *Rhodocodon cyathiformis***
14.35 – 14.55	**Elisha Griffin: Synthetic Homoisoflavonoids for the Treatment of Choroidal Neovascularization**
14.55 – 15.15	**Hannah Jefford: Homoisoflavonoids from the Asparagaceae family for use against ocular angiogenesis**
15.15 – 15.30	Tea, Coffee, Cake
	Chairperson: Professor Martin Pfosser
15.30 – 15.50	**Dr Linda Langat: Antiproliferative Bufadienolides from the Bulbs of *Drimia altissima***
15.50 – 16.05	**Dr María Ángeles Alonso Vargas: What is *Urginea aurantiaca*? New data on this enigmatic Moroccan species**
16.05 – 16.45	**Dr John David. The missing piece: a detailed phylogeny of the Hyacinthinae**
16.45 – 17.30	Poster Session: 1. Dr Watcharee Waratchareeyakul: Antioxidant Activities of Extracts of *Ochna integerrima* 2. Dr Nurulfazlina Edayah Rasol: Unveiling the Medicinal Secrets: Exploring Malaysia's *Goniothalamus lanceolatus* Miq. for Anticancer Discoveries 3. Kamatshi Sishtla: In vitro Assessment Reveals Antiangiogenic Potential of Homoisoflavonoids 4. Hannah Hall: New insights into the taxonomy of Hyacinthinae Parl. 5. Yanisa Olaranont: Cytotoxic ent-abietane diterpenoids, banyangmbolides A-E, from the leaves of *Suregada occidentalis* 6. Hanady Kadhim: Modification of Protein Synthesis Inhibitor Antibiotics to Improve Efficacy/Safety
17.45	Bus to Vineyard from Senate House, University of Surrey
18.30 - 21.30	Albury Vineyard event

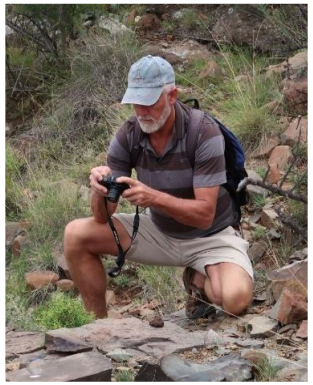
DAY 2 – THURSDAY 29 JUNE

Innovation for Health Building, Room 02 EFH 01

(BST)	
08.45 – 09.15	Registration, Coffee, Tea and pastries
	Chairperson Prof Timothy Corson
09.15 – 09.55	**Prof Martin Pfosser: Biogeography and Phylogeny of Subfamily Hyacinthoideae with Special Emphasis on the Mediterranean and Eurasian Taxa**
09.55 – 10.35	**Prof Seo Seung-Yong: Total synthesis of homoisoflavonoids and preclinical development for wet age-related macular degeneration (AMD)**
10.35 – 11.00	**Dr Michael Pinter: Fragrant beauties – insights into the genus *Tenicroa* Raf**
11.00 – 11.15	Tea, Coffee and Biscuits
11.15 – 11.45	**Group Discussion: The way ahead**
12.00	Transport to Wisley Gardens
	Lunch at Wisley Gardens
17.00	Return by Bus from Wisley Gardens

ABSTRACTS AND PARTICIPANTS

Neil Crouch



Neil Crouch graduated at the University of Natal in Pietermaritzburg (Ph.D Natal) before joining the National Botanical Institute (what is now SANBI) as an ethnobotanist in 1994. He headed the institute's Ethnobotany Unit for over 20 years before concentrating on the promotion and development of South Africa's bioprospecting and biotrade economy. Although his current activities focus primarily on sustainable use issues and resource management, he has historically undertaken research on traditional plant use by the Zulu nation, particularly on medicinal plants. This interest in traditional medical practices led to his involvement as SANBI Principal Investigator in a number of state sponsored bioprospecting consortia, in teams that sought to develop medicinal plants as new drugs to treat malaria, exposure to the exciting fields of ethnobotany and biosystematics, with with ferns, hyacinthacs and succulents of particular research interest. He is an Honorary Professor in the School of Chemistry & Physics at the University of KwaZulu-Natal in Durban..

Reflections on scientific endeavor associated with the Hyacinthaceae of southern Africa

Author: *Neil R. Crouch*
Institute: *School of Chemistry & Physics, University of KwaZulu-Natal, South Africa*

Within the Flora of southern Africa (FSA) region three subfamilies of the Hyacinthaceae are distributed widely in both winter- and summer-flowering regions. However, it is within the latter distribution range that bulbs of this large family are extensively used in traditional medicine, ranking amongst the most popular species in informal trade. Prior to interest being shown in the pharmacologically valuable properties of some medicinal members of the Hyacinthcaeae, both horticulture and stock poisoning had already attracted attention to the family. Early chemical interest was stimulated by a desire to learn the nature of the toxic principles of both homicidal agents and plants linked to the death of livestock.

Given their prominent role in both healing and homicide the family has in recent decades attracted the interest of ethnobotanists, pharmacologists,

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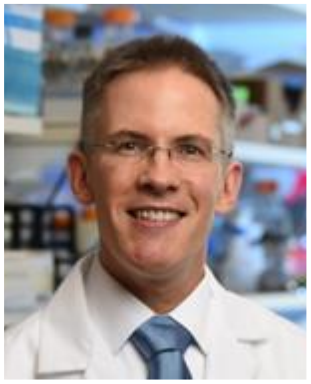
phytochemists and toxicologists. As a group showing major radiative diversification in southern Africa, the Hyacinthaceae represents a large and academically interesting group of underexplored and under-researched plants, which inevitably have attracted significant attention from taxonomists and bioprospectors alike. This presentation reflects on three decades of personal scientific engagement with the Hyacinthaceae, as an ethnobotanist supporting natural products, pharmacology and taxonomic studies, and looks back on a period of intense scientific interest and oftentimes controversy associated with Hyacinthaceae systematics. Consideration is made of substantial recent improvements in our understanding of phylogenetic relationships and genus circumscriptions that improve the interpretation of traditional medicinal practices, and which should inform rational and efficient drug discovery within the family.

Timothy W. Corson



Tim Corson is Professor and Chair of the Department of Pharmacology and Toxicology at Indiana University School of Medicine in Indianapolis, IN, USA. He also has appointments in the Departments of Ophthalmology and Biochemistry and Molecular Biology. He holds Hon BSc, MSc, and PhD degrees from the University of Toronto and completed a postdoctoral fellowship in chemical biology at Yale University before establishing his lab in Indiana. His group focuses on identifying new small molecules and molecular targets to block ocular neovascularization. Multiple protein targets and compounds identified by the group have been patented, and optioned or licensed to industry. Dr. Corson has published more than 80 research papers and holds current funding from the National Institutes of Health, the Retina Research Foundation, and the Reeves Foundation.

Homoisoflavonoids for Macular Degeneration: The Evidence So Far

Author: *Timothy W. Corson*
Institute: *Department of Pharmacology and Toxicology, Eugene and Marilyn Glick Eye Institute, Department of Ophthalmology, Indiana University School of Medicine*

Age-related macular degeneration (AMD) is one of the leading causes of blindness globally. Two forms are recognized. The more common is “dry” AMD, which is a chronic degenerative disease of the retinal cells driven by aging, oxidative stress, and inflammation. The “wet” or neovascular form of AMD (nAMD) is less common but more frequently leads to more profound vision loss and is characterized by aberrant angiogenesis within or below the region of the retina responsible for central, high-resolution vision, called the macula. To date only one drug for dry AMD has been approved (the complement inhibitor pegcetacoplan). While there are several drugs for nAMD, these are all currently biologics targeting vascular endothelial growth factor (VEGF) signaling that must be injected intravitreally (directly into the eyeball). There is thus a pressing need for new therapeutic approaches, notably small molecules acting by novel mechanisms that could be more easily delivered. Since the identification of a homoisoflavanone called cremastranone from Cremastra appendiculata as antiangiogenic, considerable work over the last two decades has characterized both natural-source and synthetic homoisoflavonoids as having potential for nAMD therapy based on antiangiogenic activity. These compounds target unexpected cellular proteins and have led to new biological understanding of neovascularization. However, homoisoflavonoids’ potential for dry AMD therapy remains unexplored. In this presentation, I will review the pathophysiology of both forms of AMD, the preclinical evidence that homoisoflavonoids are antiangiogenic, and the possibilities for future studies looking towards clinical testing.

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Mario Martínez-Azorín

Graduated in Biology at the University of Alicante (Spain). PhD on Taxonomy and Systematics of *Ornithogalum* s.l. Professor of Botany at Dept. Environmental Sciences and Natural Resources, University of Alicante, Spain. Main interests in taxonomy, systematics and biogeography of Hyacinthaceae.

How many genera must be accepted in Hyacinthaceae? Do we know its real diversity?

Authors: *Mario Martínez-Azorín*[*1], Manuel B. Crespo[1], María Ángeles Alonso-Vargas[1], Michael Pinter[2]*
Institute: [1]*Depto. de Ciencias Ambientales y Recursos Naturales (dCARN), Universidad de Alicante, P.O. Box 99, Alicante E-03080, Spain*
[2]*Division of Plant Sciences, Institute of Biology, NAWI Graz, Karl-Franzens University Graz, Holteigasse 6, Graz 8010, Austria*

The taxonomy and systematics of Hyacinthaceae, especially considering genera circumscription, have been controversial in recent decades, with contrasting taxonomic treatments proposed based on preliminary and partial studies that have focused on morphology and/or solely plastid DNA sequence data.

Some authors have recognized only two genera in subfamily Urgineoideae, with a very broadly conceived *Drimia*, while others have accepted several genera that, although better defined morphologically, were doubtfully monophyletic. Our latest phylogenetic analyses involving four plastid DNA regions (trnL intron, trnL-F spacer, matK, and the trnCGCA-ycf6 intergenic region), a nuclear region (Agt1), and a selection of 40 morphological characters covers 293 samples and ca. 160 species of Urgineoideae (ca. 80% of its global diversity). Our data yielded phylogenetic trees with 31 well-defined clades or lineages, most corresponding to previously described genera, although some have required description or revised circumscription.

A similar case occurs in subfamily Ornithogaloideae where the accepted genera range from a single genus extremely variable in morphology to several genera better characterized in morphologically. Our phylogenetic work based on extensive sampling and combination of plastid and nuclear regions also evidence the existence of 19 lineages that can be accepted at genus rank and are linked to a defined biogeography.

As with other monocot families, a considerable degree of homoplasy was observed in morphological characters in the Hyacinthaceae, especially in those groups with unspecialized flowers; nonetheless, consistent syndromes of traditional and novel characters are shown to support clade recognition at genus rank.

Our taxonomic work in the last decades has facilitated the description of 9 genera and 59 species of Hyacinthaceae, and evidence the urgent need of further taxonomic work in the group with the promise of exciting future findings and new chemical compounds to be found.

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Sianne Schwikkard

I completed my PhD in Natural Products Chemistry at the University of Kwazulu-Natal, South Africa in 1998. The complexity and beauty of natural compounds fascinated me and has led to a life-long pursuit of both novel compounds from plant sources as well as the synthesis of these compounds. Plants can produce a range and diversity of chemical entities unparalleled by synthetic efforts and displaying an unsurprising range of biological activities. My research career was developed through a post-doctoral fellowship at Virginia Tech under Professor David Kingston, followed by a post-doctoral position at the Rand Academic University under Professor Fanie Van Heerden. I spent a short 18 months working in the petrochemical industry for Sasol Technology before relocating to the UK and working for Professor Keith Jones at Kingston University.
I spent 11 years as a part-time lecturer at Kingston University and research associate at Surrey University before I joined Kingston University full time in

Continued ►

September 2015. My current research focuses on diseases of the eye characterised by neovascularisation and the development of novel antimicrobial compounds, with a focus on drug-resistant bacteria.

Homoisoflavonoids and Chalcones for the Treatment of Pterygium

Authors: *Sanaz Sandig Baheran, Ola Deri, Ali A. Al-Kinani, Raid G. Alany, Sianne L. Schwikkard**
Institute: *School of Life Sciences, Pharmacy and Chemistry, Kingston University, Kingston-upon-Thames, KT1 2EE, United Kingdom*

Pterygium is a disease of the conjunctiva of the eye. It is a fleshy growth that usually starts in the corner of the eye and once it begins to cover the cornea, can have an effect on a patient's vision, in addition to causing discomfort. Pterygium has tumour like qualities due to its invasive nature and high degree of recurrence after removal. The exact cause is not clear, but it appears to be linked to exposure to UV radiation and environmental factors such as dust and wind. There is some suggestion of a hereditary link and people with pinguecula have a higher incidence of pterygium.

Pterygium is usually treated surgically with adjunctive therapies to help prevent recurrence. These treatments include the use of antibiotics such as mitomycin C, anti-inflammatory drugs such as Loteprednol etabonate, anti-metabolites such as 5-fluorouracil and antiangiogenic agents. The nature of the disease suggests that the inhibition of VEGF may have benefits in treating the condition, particularly in preventing recurrence after surgical removal. The use of anti-VEGF biologicals such as Bevacizumab have seen some success.

The potential of small natural products such as chalcones and homoisoflavonoids as antiangiogenic, antioxidant and anti-inflammatory agents is gaining prominence. A range of these molecules have been synthesised and shown to inhibit angiogenesis and reduce inflammation at nontoxic concentrations. Some initial formulation studies have demonstrated that solubility can be improved without any loss of activity.

Walter Knirsch

1981 Dr.med. at the Karl Franzens University, Graz, Austria
Since 1990 in office as Ophthalmologist in Kapfenberg
2012 Mag. rer. nat. at the Karl Franzens University, Graz
Since 2000 numerous excursions to Madagascar in collaboration with the Botanical Garden Vienna and the Botanical Garden Tsimbazaza in Antananarivo, Madagascar

A case presentation of a patient with a wet Age Related Macular Disease (wet AMD)

Author: *Walter Knirsch*
Institute: *Pharmaceutical Sciences / Medical University, Karl Franzens University, Graz Universitätspl. 3, 8010 Graz*

The aim of the presentation: The burden and complications of the therapy;

The Golden Standard: therapy with anti VEGF
Corticosteroid therapy
Non-steroidal anti-inflammatory drugs

Conclusion: we need novel therapies

Nor Hadiani Ismail

Professor Dr Nor Hadiani Ismail obtained her Ph.D. in natural product chemistry from Universiti Putra Malaysia in 1999. Her PhD thesis entitled Chemistry and Biological Activity of the Roots of Morinda elliptica won the Tan Sri Ong Kee Hui medal for the Best Postgraduate Thesis 1999 by Institut Kimia Malaysia. She is a professor in Chemistry at the Faculty of Applied Sciences and currently serving as the director of Atta-ur-Rahman Institute for Natural Products Discovery, Universiti Teknologi MARA. The institute focuses on discovery of bioactive compounds from Malaysian plants and microbial sources towards several target diseases such as diabetes, cancer, malaria and dengue. With almost 200 research publications, she was recognized as Top Research Scientist Malaysia in 2017. A fellow of the Malaysian Chemical Institute and Malaysian Academy of Science, Prof Nor Hadiani is the current president of Malaysian Natural Product Society.

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Search for Dengue Antiviral Compounds from an Indigenous Malaysian Plant, *Goniothalamus lanceolatus*

Authors: *Nor Nadirah Abdullah[1,2], Adlin Afzan[2], Murizal Zainol[2], Syahrul Imran Abu Bakar[1], Mohd Ridzuan Mohd Abd Razak[2] and Nor Hadiani Ismail[1]*
Institute: *[1]Atta-ur-Rahman Institute for Natural Product Discovery, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor, Malaysia; Faculty of Applied Science UiTM, 40450 Shah Alam, Selangor, Malaysia; [2]Herbal Medicine Research Centre, Institute for Medical Research, National Institutes of Health, Ministry of Health, No. 1 Jalan Setia Murni U13/52, Seksyen U13, Setia Alam, 40170 Shah Alam, Selangor Darul Ehsan, Malaysia*

In our continuing search for bioactive compounds, we scrutinized the chemical constituents present in the leaves of *G. lanceolatus* Miq., an endemic plant from the rainforest of Sarawak, Malaysia. As these leaves are traditionally used by the indigenous population as a mosquito repellent and to treat fever, we were inspired to examine the plant for potential anti-dengue activity. Preliminary screening showed that at a concentration of 50 µg/ml, the dichloromethane extract of these leaves was able to inhibit 90.9% of Dengue Virus Type-2 (DENV-2). Dose-dependent plaque assays gave an IC50 of 4.16 µg/ml with a selectivity index (SI) of 5.82. Chemical profiling of the active fraction using high-resolution mass spectrometry (UHPLC-ESI-Orbitrap), via data-dependent MS/MS experiments dereplicated nine styryllactones from reference standards, and eighteen styryllactones were further annotated by a molecular database search. Seven styryllactones were isolated from this active fraction. Bis-styryllactone goniolanceolatin A was further evaluated using quantitative reverse transcription qRT-PCR to determine the viral RNA level. The qRT-PCR data showed that the IC50 value for the compound was 5.07 µg/mL, and its corresponding SI value of 5.30. Docking studies of goniolanceolatin A showed that it can form binding interactions with crucial amino acids of the Envelope (E) of DENV proteins.

Eduard Mas-Claret

I completed my PhD in Organic Chemistry at the University of Surrey (United Kingdom) in 2018, supervised by Dr Daniel Whelligan, followed by a post-doctoral position at the Natural Products group of the University of Surrey under Prof. Dulcie Mulholland. Currently a Research Fellow at the Royal Botanic Gardens, Kew, my research focusses on the development of new formulations for the plant-based insecticide Pyrethrum (*Tanacetum cinerariifolium*). My research interests include organic synthesis, natural products and computational methods to aid structure elucidation of chiral molecules.

Bufadienolides and anti-angiogenic homoisoflavonoids from *Rhodocodon cryptopodus*, *Rhodocodon rotundus* and *Rhodocodon cyathiformis*

Authors: Hannah Whitmore[1], Kamakshi Sishtla[2], Walter Knirsch[3], Jacky L. Andriantiana[4], Sianne Schwikkard[4,5], Eduard Mas-Claret[1,6], Sarah M. Nassief[1], Sani M. Isyaka[1,6], Timothy W. Corson[2], Dulcie A. Mulholland[1,7]
Institute: [1]Natural Products Research Group, Department of Chemistry, University of Surrey, Guildford GU2 7XH, United Kingdom; [2]Eugene and Marilyn Glick Eye Institute, Department of Ophthalmology, Indiana University School of Medicine, 1160 W. Michigan St., Indianapolis, IN 46202, USA; [3]Institute of Plant Sciences, NAWI Graz, Karl-Franzens University Graz, Holteigasse 6, A-8010 Graz, Austria; [4]Parc Botanique et Zoologique de Tsimbazaza, Rue Fernand Kassanga, Antananarivo 101, Madagascar; [5]School of Life Sciences, Pharmacy and Chemistry, Kingston University, Kingston-upon-Thames KT1 2EE, United Kingdom; [6]Biological Chemistry, Royal Botanic Gardens, Kew, Kew Green, Richmond, TW9 3AE, United Kingdom; [7]School of Chemistry and Physics, University of KwaZulu-Natal, Durban, South Africa

Abnormal retinal vascularization is the leading cause of conditions associated with vision loss in developed countries, such as age-related macular degeneration (AMD) or diabetic retinopathy. The current approach for their treatment is based on inhibitors of the vascular endothelial growth factor (VEGF). However, up to 30% of patients are non-responsive to these drugs, which are also linked to ocular and systemic side effects. For that reason, there is an urgent need for small antiangiogenic molecule leads to supplement the existing biologics. Homoisoflavonoids have previously shown potent

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antiangiogenic activity *in vitro* and *in vivo* in animal models of ocular neovascularisation, together with promising synergistic effects with existing VEGF inhibitors. In this work, the phytochemistry of three species of *Rhodocodon* (Scilloideaea subfamily of the Asparagaceae family), endemic to Madagascar, *R. cryptodus*, *R. rotundus* and *R. cyathiformis*, was investigated. Two homoisoflavonoids 3S-5,7-dihydroxy-(3'-hydroxy-4'-methoxybenzyl)-4- chromanone **1** and 3S-5,7-dihydroxy-(4'-hydroxy-3'-methoxybenzyl)-4-chromanone **2** were isolated, together with three cinnamic acid derivatives, four bufadienolides and a coumarin. The antiangiogenic activity of the two homoisoflavonoids was tested against human retinal microvascular endothelial cells (HRECs), giving excellent GI50 results of 0.13 μM and 0.49 μM respectively. Moreover, compound **2** showed a 100-fold specificity for HRECs over other tested cell lines. Its high antiangiogenic activity and promising specificity make compound **2** a suitable candidate in the development of new treatments against ocular neovascularization.

Elisha Griffin

Graduated from the University of Surrey in 2021. Currently undertaking a PhD in the natural products group under Professor Dulcie Mulholland at the University of Surrey. Researching potential of synthetic, derivatized homoisoflavonoids to treat macular degeneration and associated ocular diseases. Main interests in synthetic organic chemistry.

Synthetic Homoisoflavonoids for the Treatment of Choroidal Neovascularization

Authors: Elisha Griffin[1], Dulcie Mulholland[1], Sianne Schwikkard[2], Timothy Corson[3]
Institute: [1]Natural Products Research Group, Department of Chemistry, University of Surrey, Guildford GU2 7XH, United Kingdom; [2]School of Life Sciences, Pharmacy and Chemistry, Kingston University, Kingston-upon-Thames, KT1 2EE; [3]Department of Pharmacology and Toxicology, Eugene and Marilyn Glick Eye Institute, Department of Ophthalmology, Indiana University School of Medicine

The process of choroidal neovascularization is associated with debilitating ocular diseases such as age-related macular degeneration, retinopathy of prematurity and proliferative diabetic retinopathy, the former of which is the most prevalent cause of blindness in the ageing population. The existing treatments for these diseases consist of monoclonal antibodies and decoy receptors that bind to vascular endothelial growth factor to prevent excessive angiogenesis of the ocular vasculature. These high molecular weight biologics must be introduced to the patient via intravitreal injection, a painful process which is associated with a range of undesirable side effects and resistance issues. Homoisoflavonoids are a class of naturally occurring compounds that have been isolated from plant families such as *Asparagaceae*, species of which have been long used by traditional healers in Eastern and Southern Africa. Both synthetic and isolated homoisoflavonoid compounds have been shown previously to possess antiproliferative and antiangiogenic activities against human retinal endothelial cells (HRECs). This presents an exciting opportunity for the development of an alternative small molecule biologic to treat diseases associated with choroidal neovascularisation, which may provide a less invasive route of administration. Though homoisoflavonoid compounds may be found in nature, synthetic derivatives with a range of non-naturally derived heteroatoms and functional groups may provide exciting biological activity. We describe our syntheses of derivatised (*E*)-3-benzylidene-4-. chromanones and 3- benzylchromanes (Fig.1). Initial screening showed promising results, with two synthetic homoisoflavonoids exhibiting growth inhibitory concentrations of 4.9 μM and 12 μM against the proliferation of HRECs.

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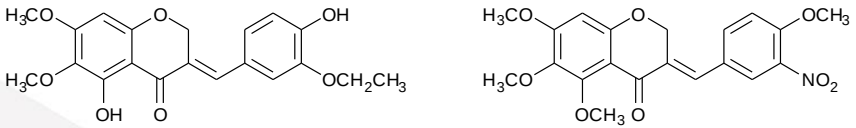

Fig. 1 Examples of synthetic (*E*)-3-benzylidene-4-chromanone homoisoflavonoids

Hannah Jefford

Graduated from the University of Surrey with an MChem in Chemistry, in 2021. Currently working towards a PhD in Natural Products Chemistry under the supervision of Professor Dulcie Mulholland at the University of Surrey. Researching phytochemistry of various species from the Asparagaceae family in search of homoisoflavonoids to treat macular degeneration. Main interests include natural products chemistry and organic synthesis

Homoisoflavonoids from the Asparagaceae family for use against ocular angiogenesis

Authors: Hannah Jefford[1], Dulcie Mulholland[1], Moses Langat[2], Timothy Corson[3]
Institute: [1]Natural Products Research Group, Department of Chemistry, Faculty of Engineering and Physical Science, University of Surrey, Guildford, GU2 7XH, UK, [2]Jodrell Laboratory, Department of Natural Capital and Plant Health, Royal Botanic Gardens, Kew, Richmond, TW9 3DS, UK, [3]Eugene and Marilyn Glick Eye Institute, Department of Ophthalmology, Indiana University School of Medicine, Indianapolis, IN 46202, USA

Natural products chemistry involves the extraction of potentially active compounds from plants. A class of these active compounds is called homoisoflavonoids and they are frequently extracted from the Asparagaceae family. They are regarded as hopeful pharmacological candidates due to their anti-inflammatory, anti-bacterial and antioxidant effects. Due to their anti-bacterial and anti-inflammatory activity, these plants are often used in traditional medicine. In addition, homoisoflavonoids have been shown to exhibit antiangiogenic activity, reducing the excessive formation of blood vessels. Several homoisoflavonoids have been investigated as prospective treatments for various major causes of blindness: proliferative diabetic retinopathy, retinopathy of prematurity and wet age-related macular degeneration. These are all characterised by abnormal blood vessel growth at the back of the eye. As homoisoflavonoids are small molecules, they have potential for delivery as eye drops.

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Homoisoflavonoids extracted from various plants in the Asparagaceae family, and synthesised homoisoflavonoids, have been screened for antiangiogenic activity. More recently, homoisoflavonoids extracted from *Eucomis bicolour*, *Eucomis autumnalis* and *Scilla peruviana* were screened and it has been determined that there are important structure-activity relationships. Notably, the presence and position of methoxy groups, the presence of the 3,9-double bond and the configuration at the chiral centre (C-3) are all important in the activity of the compound. Figure 1 shows a compound with antiangiogenic activity extracted from *Eucomis autumnalis*, with a GI50 value of 0.67 μM. From this screening, targeted synthesis and further extractions from plants in the *Scilla* genus has taken place, in order to increase our library of compounds for screening. In addition, the dichloromethane extract of *Scilla bifolia* is being investigated for homoisoflavonoids and the ease of separation, with the potential that this species can be farmed.

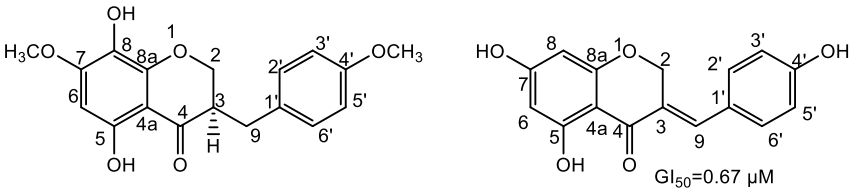

Fig. 1 Homoisoflavonoid from *Scilla peruviana* (left) and homoisoflavonoid with anti-angiogenic activity from *Eucomis autumnalis* (right)

Linda Langat

Obtained her PhD in Chemistry, and Masters in Toxicology at the University of Surrey (United Kingdom). Her PhD on the novel anticancer compounds from the Scilloideae subfamily was supervised by Prof. Dulcie Mulholland. Linda is a Research Fellow at the University of Surrey working on developing analytical methods for quantification of anti-oomycete diterpenoids from Larch.

Antiproliferative Bufadienolides from the Bulbs of *Drimia altissima*

Authors: Linda Langat[1], Moses Langat[2], Wolfgang Wetschnig[3], Walter Knirsch[3] and Dulcie A. Mulholland[1]
Institute: [1]Natural Products Research Group, Department of Chemistry, University of Surrey, Guildford, GU2 7XH, UK; [2]Science Department, Royal Botanic Gardens Kew, Kew Green, Richmond, TW9 3AE, UK; [3]Institute of Biology, NAWI Graz, University of Graz, 8010 Graz, Austria

In this study we report the chemistry and antiproliferative effects of bufadienolides from the bulbs of South African *Drimia altissima*. *D. altissima* (L.f.) Ker Gawl (syn, *Urginavia altissima* (L.f.) Speta, (Hyacinthaceae) is widespread in sub-Saharan Africa, and investigations into the phytochemistry of the bulbs collected from South Africa (as *U. altissima*), Ethiopia (as *D. altissima*), and Kenya (as *U. altissima*) have been reported previously. Herein, we report undescribed, bufadienolides, drimianins A – G (**1**-**7**) (Fig. 1). *D. altissima* is considered toxic and has been reported to cause serious loss of livestock in south and east Africa and northern Zimbabwe. The antiproliferative properties of bufadienolides from skin secretions of Chinese toads against three cancer cell lines, KB, HL-60, and MH-60,8 and the antiproliferative activity of bufatrienolides from *Urginea depressa* prompted the investigation of the possible antiproliferative activities of the isolated drimianins A – G. Drimianins A-G were evaluated by National Cancer Institute (NCI) against a panel of human tumour cell lines, using the NCI-validated protocol. Drimianin E (**5**) showed promising antiproliferative activity against several cancer cell lines including the CNS SF-539 (GI50 = 3nM), non-small lung A549/ATCC (GI50 = 4nM), prostate DU-145 (GI50 = 6nM), leukemia CCRF-CEM (GI50 = 7nM), colon HCT-116 (GI50 = 5nM) and renal cancer lines (GI50 ≤ 12nM).

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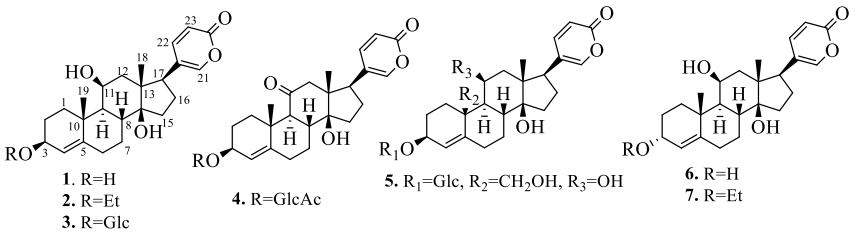

Fig. 1 *Drimianins A – G (1 -7) isolated from the bulbs of Drimia altissima*

María Ángeles Alonso Vargas

Graduated in Biology at the University of Alicante (Spain). PhD in Botany. Lecturer in Botany at Dept. Environmental Sciences and Natural Resources, University of Alicante, Spain.
Main interests are taxonomy, systematics and biogeography of Hyacinthaceae, Amaranthaceae, Frankeniaceae, Tamaricaceae and Caryophyllaceae.

What is *Urginea aurantiaca*? New data on this enigmatic Moroccan species

Authors María Ángeles Alonso-Vargas, Mario Martínez-Azorín* & Manuel B. Crespo
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Urginea aurantiaca H.Lindb. was described from plants collected in bud in the High Atlas of Morocco. This collection flowered in cultivation and was related to *Urginea fugax*, but differed by the longer peduncle, larger and cinnamon coloured bulbs, smaller orange flowers (tepals 8-9mm long), and flowering time around June, instead of August-October. No mention of the diurnal or nocturnal flowering time of the species was included in the protologue. The type collection H1237873 shows two bulbs with inflorescences lacking leaves. Flowers appear to be subcampanulate, with tepals suberect, very small, only ca. 5 mm long. The illustration in the protologue shows the same two plants with small flowers, fitting the previous description.

Maire (1933, 1958) combined Lindberg's species respectively as variety and subspecies of *Urginea noctiflora*, based on the apparently shared nodding nocturnal flowers with reflexed tepals with typical U. *noctiflora*, but differing in widely expanded filaments at the base and the straight leaves. Stearn (1978) suggested the convenience of assuming the two taxa accepted by Maire as a good species. Several herbarium collections from Morocco fit Maire's concept of U. *aurantiaca*, based on the nocturnal, nodding orange flowers with basally expanded filaments and strongly reflexed tepals.

Battaglia (1958) studied caryology of *Urginea aurantiaca* material collected by R. Nègre in 1952 near Chichaoua, West of Marrakech in Morocco. The plants were cultivated at Fordham University in New York and the described morphology and photograph of the flowering plant on August 1958 fit Lindberg's concept and the type collection, showing suberect smaller flowers on short pedicels.

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Moreover, the detailed caryological study of Battaglia (1958) concluded that the studied samples from Chichaoua were 2n=20+1–2B and closely related to the caryotype of *Urginea fugax*.

Our recent field work in Morocco facilitated the study of fresh material of what Maire (1958) had considered *Urginea noctiflora* subsp. *aurantiaca*. Our inedit phylogenetic study of two Moroccan populations from Chichaoua and Douar Shémch reveals their close relation to *Urginea fugax* and *Spirophyllos noctiflorus* clade, where the three species share biogeography. However, further studies are needed to ascertain whether our studied samples represent Lindberg's *Urginea aurantiaca*, based on their remarkable flower divergence with regard to the type collection. We have noticed that buds never open until they reach about 9–10 mm long, and the type collection includes suberect open flowers with very short tepals (c. 5 mm long) disposed on very short pedicels. Further, Lindberg did not mention in the protologue the typical nocturnal flowering of his species, a distinct character unmistakable in cultivation.

John David

Dr John David is Head of Horticultural Taxonomy at RHS Garden Wisley. His main research interest is into the taxonomy of *Narcissus* and *Nerine* (Amaryllidaceae), but more recently has extended into the "little blue bulbs" (Hyacinthinae). He is Chairman of the International Commission for the Nomenclature of Cultivated Plants and the RHS's Nomenclature and Taxonomy Advisory Group. He is also involved with invasive non-native plants in horticulture, covering both the identification and legislative aspects.

The missing piece: a detailed phylogeny of the Hyacinthinae

Authors: David, J.C.[1], Hall, H.[2], Könyves, K.[1], Culham, A.[2]
Institute: [1]Science & Collections, Royal Horticultural Society, RHS Garden Wisley, UK; [2]School of Biological Sciences, University of Reading, Whiteknights, Reading, UK

Following the ground-breaking paper by Speta (1998) and the molecular analysis by Pfosser & Speta (1999), there has

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been relatively little attention given to the Eurasian clade of the Hyacintheae, in contrast with the Southern African taxa and the other tribes of the Scilloideae. The papers by Ali et al. (2012) and Buerki et al. (2012) have confirmed the basic structure of the phylogeny of the subtribe, and added a few further taxa, but neither paper concentrates on the subtribe alone. There has been some inconsistency in and resistance to taking up the genera recognised by Speta for this subtribe, which expands the widely accepted 8 or 9 genera to 20 genera. The limited sampling in previously published trees, combined with the lack of readily visible morphological characters to support the genera recognised by Speta has possibly contributed to the limited acceptance of them. This presentation will provide and discuss data from our current research into the phylogeny of the subtribe based on whole plastome sequences for 159 samples. It recovers the three main clades of the subtribe (Scilla, Fessia and Hyacinthoides clades by Pfosser & Speta) and shows broad congruence with the more narrowly circumscribed genera but also highlights some areas where further investigation is needed.

Martin Pfosser

Graduated at the University of Agriculture, Vienna (Austria). Fellowship of the Japan Society for the Promotion of Science at Tohoko University. Assistant Professor at the Institute of Microbiology and Genetics and the Institute of Botany and Evolutionary Biology of Vienna University. Since 2003 Head of Botany Department, Biocenter Linz of the Museum of Upper Austria. Main interests in molecular phylogeny and biogeography of Hyacinthaceae.

Biogeography and Phylogeny of Subfamily Hyacinthoideae with Special Emphasis on the Mediterranean and Eurasian Taxa.

Authors: Martin Pfosser, Hanna Schneeweiß & Syed Shujait Ali

Subfamily Hyacinthoideae of family Hyacinthaceae shows a bimodal distribution pattern with a primary center of diversification in Africa south of the Sahara and a secondary center of diversification north of the Sahara with a present distribution of the north-

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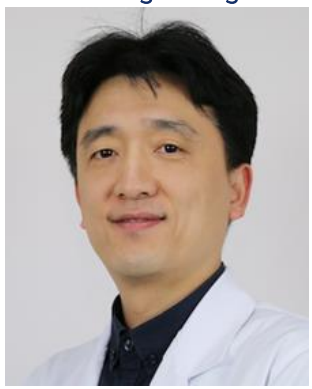
hemispheric members covering a large area from the Atlantic islands in the west and reaching Japan as its easternmost point.

Based on molecular data subfamily Hyacinthoideae can be further divided into three monophyletic tribes: The monotypic tribe Pseudoprospereae, the tribe Massonieae with members found from Africa south of the Sahara and Madagascar to Arabia and India, and tribe Hyacintheae containing the remaining Eurasian and Mediterranean taxa.

Phylogenetically based historical biogeographic reconstructions have shown that a single colonization event from sub-Saharan Africa to the Mediterranean region, followed by rapid diversification and radiation resulted in the monophyletic tribe Hyacintheae. Dated trees suggest that dispersal to Eurasia took place at about 15 Ma at the time when the formation of the Gomphotherium land bridge (19 Ma) allowed the free exchange of floras and faunas between Africa and Eurasia. High support values at the basal branching points of Massonieae and Hyacintheae also suggest a vicariance event. Dating of this event at about 18 Ma is consistent with the accelerated African aridification in the early Miocene due to the uplift of the continent and the formation of the East African Rift Valley.

In tribe Hyacintheae, *Barnardia sinensis* (*Scilla scilloides*-relationship) from Japan, China and Korea occupies the earliest branching position. Based on morphology and karyology this group has been reported to include also Barnardia numidica, a species known from the western Mediterranean (North Africa, Balearic Islands). Detailed molecular and karyological investigations have now shown that the western Mediterranean Barnardia is not related to the East Asian group but shows affinities to *Scilla* s.l. species from Greece and Albania.

Seo Seung-Yong



Seo Seung-Yong earned his Ph.D. in 2004 and M.S. in 2000 from Seoul National University, where he conducted his studies under the guidance of Professor Young-Ger Suh. Seo Seung-Yong's Bachelor of Science degree in Pharmacy was also obtained from Seoul National University in 1998. Since 2012, he has served as a Professor at the College of Pharmacy, Gachon University. Prior to joining Gachon University, from 2008 to 2012, he held an Assistant Professor position at the College of Pharmacy, Woosuk University. From 2006 to 2008, he worked as a postdoctoral researcher at Yale University under the supervision of Professor Craig M. Crews. Additionally, from 2004 to 2006, he pursued postdoctoral research at Seoul National University.

Total synthesis of homoisoflavonoids and preclinical development for wet age-related macular degeneration (AMD)

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Institute: College of Pharmacy, Gachon University, 191 Hambakoero, Yeonsu-gu, Incheon 21936, Republic of Korea

An antiangiogenic homoisoflavanone, cremastranone, has been synthesised for the first time and shows potential as a lead molecule for the treatment of angiogenesis-induced ocular diseases. We report the asymmetric synthesis and structural elucidation of cremastranone by dynamic kinetic asymmetric transfer hydrogenation. Synthetic cremastranone and its optimised analogue SH-11037 showed inhibitory effects on the proliferation, migration and tube formation ability of human retinal microvascular endothelial cells, key steps in pathological angiogenesis, and blocked retinal neovascularisation in animal models. Despite their potent efficacy, the mechanism of these compounds was not fully understood. To identify targets of homoisoflavonoid-binding proteins, different types of photoaffinity probes were synthesised in which benzophenone and biotin were attached to homoisoflavonoids using PEG linkers. The chemical probes identified ferrochelatase (FECH), a haem synthesis enzyme, and soluble epoxide hydrolase (sEH), an epoxy fatty acid metabolism enzyme, as targets for an anti-angiogenic homoisoflavonoid that inhibited FECH and sEH activity in vitro and in vivo. These findings suggest a potential target for neovascular eye diseases. In addition, we identified potent small molecule FECH inhibitors through high-throughput screening, with anti-angiogenic activity in vitro and promising results in a mouse model of choroidal neovascularisation. This work provides insight into the development of therapeutic agents targeting ocular neovascularisation and diseases involving FECH activity.

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Michael Pinter

*1985, Graz, Austria. 2020 PhD (Dr. rer. nat.) in Botany at the Karl – Franzens-University Graz (KFU), topic: "A revised generic concept of the subfamily Urgineoideae (Hyacinthaceae)", 2012 MSc. (Mag. rer. nat.) in Botany at KFU; 2008 BSc. (Bakk. rer. nat.) in Plant function, bioindication and environmental monitoring at KFU. 2005 – 2020 Study of biology (main focus in systematic botany) at the KFU. Currently head of education at the Natural History Museum / Universalmuseum Joanneum Graz and lecturer at the Institute of Biology, Division Plant Sciences, KFU Graz. 2012 – 2013 Herbarium Assistent and lecurer at the Institute of Plant Sciences, KFU Graz. 2008 – 2009 Herbarium Assistent at the Natural History Museum in Graz. Member of the editorial board of Phyton - Annales Rei Botanicae and member of several associations related to the fields of the main scientific interests. Various research trips to Africa (Gambia, Lesotho, Madagascar, Namibia, Senegal, South Africa, Tansania), the Arabian Peninsula (Oman) and the Mediterranean Basin (Croatia, Montenegro, Slovenia).

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Fragrant beauties – insights into the genus *Tenicroa Raf.*

Author: Michael Pinter
Institute: Department of Syst. Botany and Geobotany, Karl-Franzens-Universität Graz, Holteigasse 6, 8010 Graz/Austria

Unlike other genera of Hyacinthaceae, species of the genus *Tenicroa*, have been placed by time in eight different genera. In the very beginning, the early known species were treated as Anthericum (Jacquin 1794, 1797; Willdenow 1799). Up to now, they had been assigned to genera like *Albuca* (Ker Gawler 1805, 1818, 1821), *Drimia* (Jessop1977, Goldblatt & Manning 2000, Manning & Goldblatt 2003, 2018), *Ornithogalum* (Kunth 1843), *Phalangium* (Poiret 1804), *Pilasia* (Rafinesque 1837), *Sypharissa* (Salisbury 1866, Obermeyer 1980), and *Urginea* (Steinheil 1834, Duthie 1928, Adamson 1942, Lewis 1952). These nomenclatural changes have produced an intricate situation reflected in the extensive synonymy, which is due to the lack of comprehensive research on the individual species of the genus over a long period of time.

Tenicroa is characterized by having (mostly) synanthous leaves and sheathing cataphylls with raised darker (purple or brown) transversal ridges enclosing their bases. The flowers are sweetly scented, diurnal, stellate at full anthesis with the white tepals subpatent, free and having a distinct narrow, reddish-brown or greenish band. The stamens are suberect to spreading, slightly curved, with subbasifixed anthers, and the ovary ovate-oblong to oblong-globose, with an elongate, deflexed and curved or sigmoid style, and papillate stigma. The genus is distributed in South Africa and southwestern Namibia, having its highest diversity in the Cape winter rainfall region.

In our latest taxonomic revision of the genus, the morphology of the different species was examined on the basis of living material, fixations and herbarium specimens. In this context, we described four new species, and presented two new combinations, which means that the genus now consists of 12 accepted species.

Having a closer look at *Tenicroa* and its story of discovery, which seems in some parts fairytale-like, the presentation gives a historic overview, as well as insights into the different species.

Nadjat Azizi

Nadjat Azizi was born in Algeria, She is currently an Associate Professor and Team Leader (Biotechnology) at the University of Algiers 1 - Benyoucef Benkhedda. She received the B.Sc, M.Sc in Plant Sciences and Biotechnology. And Ph.D. in Genetics, Molecular Physiology of Plants at the University of Sciences and Technology Houari Boumediene (USTHB, Algiers, Algeria). Her area of interest revolves around several axes including karyosystematics, evolutionary genetics, and the biogeography of geophytes. With several classic cytogenetic works (Establishment and analysis of karyotypes; Idiograms; Analysis of meiosis) on several genera (Muscari, Squilla, Battandiera, Ornithogalum) as well as the Identification and Taxonomy of Asparagales (Morphology and anatomy). She also carried out molecular cytogenetics work (Fluorescence In Situ Hybridization (FISH) and flow cytometry) and phylogenetic analyses on the genus Bellevalia.

Biosystematic studies among species of Hyacinthaceae from Algeria

Authors: Nadjat Azizi[1]*, Rachid Amirouche[2] and Nabila Amirouche[2]
Institute: [1]University of Algiers 1 Benyoucef Benkhedda, 02 rue Didouche Mourad, 16002 Algiers, Algeria; [2]University of Sciences and Technology Houari Boumediene, 16111 El-Alia, Algiers, Algeria

The Mediterranean region is one of the most important hotspot of biological diversity. Species occuring particularly in North Africa, are well adapted to climate change and possesses a high pharmacological potential. Here, we will present some results from taxonomic investigations, nomenclatural updates and chorology of species belonging to the Hyacinthaceae family present in the flora of Algeria. Sampling was carried out on natural populations from various ecogeographical conditions. This study involved 14 taxa: *Bellevalia variabilis* Freyn, *Squilla maritima* (L.) Steinh., *S. undulata* (Desf.) Mart.-Azorín et al., *Spirophyllos noctiflorus* (Batt. & Trab.) Mart.-Azorín et al., Stellarioides sessiliflora (Desf.) Speta, *Prospero autumnale* (L.) Speta, *Bellevalia mauritanica* Pomel, *Dipcadi serotinum* (L.) Medik., *Muscari neglectum* Guss. ex Ten., *M. comosum* (L.) Mill., *M maritimum* Desf., *Barnardia numidica* (Poir.) Speta, *Battandiera amoena* (Batt.) Maire, and *Urginea fugax* (Moris) Steinh.

Karyological analysis reveals diversified chromosomal numbers and basic

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numbers. The diploid taxa are S. sessiliflora (2n = 10, x = 5), *M. comosum*, *M. maritimum*, B. numidica and *B. amoena* (2n = 18, x = 9), *S. undulata*, U. fugax and *S. noctiflorus* (2n = 20, x = 10). The others taxa were polyploids : *B. variabilis* is tetraploid (2n = 16, x = 4*), D. serotinum* octaploid (2n = 32, x = 4) and *P. autumnale* hexaploid (2n = 42, x = 7). *B. mauritanica* shows two ploidy levels, tetraploid and octaploid (2n = 16 and 32 with x = 4). *M. neglectum* constitutes a polyploid series with 2n = 45, 2n = 54 and 2n = 72 (x = 9).

In perspective, it would be interesting to link polyploidy, which plays a major role in the ecological adaptation of species, to the ability of polyploids to produce molecules of pharmacological interest.

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POSTER SESSION

Watcharee Waratchareeyakul

Graduated PhD at the University of Surrey, UK. Assistant Professor at Rambhai Barni Rajabhat University, Thailand. My research interests are natural products, organic synthesis and virtual screening.

Antioxidant activities of extracts of *Ochna integerrima*

Authors: Watcharee Waratchareeyakul, Kanjana Pinakase and Retima Keawlek
Institute: Department of Chemistry, Rambhai Barni Rajabhat University, Chanthaburi, Thailand

This research aims at comparing the antioxidant activities of extracts from the bark, wood and petals of *Ochna integerrima* using the DPPH radical scavenging technique.

The bark of *O. integerrima* showed the highest antioxidant activity. The antioxidant activities of hexane, dichloromethane and methanol extracted from the bark of *O. integerrima* obtained IC_{50} = 278.22, 388.91 and 411.61 $\mu g.ml^{-1}$, respectively.

According to the wood, the wood extracts exhibited a weak antioxidant activity which was lower than that of the bark but higher than that of the petals. The antioxidant activities of hexane, dichloromethane and methanol extracted from the wood of *O. integerrima* offered IC_{50} = 376.49, 419.96 and 540.56 $\mu g.ml^{-1}$, respectively.

Moreover, the antioxidant activities of hexane, dichloromethane and methanol extracted from the petals extracts showed IC_{50} = 903.33, 529.98 and 450.44 $\mu g.ml^{-1}$, respectively.

In addition, the antioxidant activities of extracts from the bark, wood and petals of *O. integerrima* are significantly lower than that of butylated hydroxytoluene (IC_{50} = 66.99 $\mu g.ml^{-1}$) and ascorbic acid (IC_{50} = 9.19 $\mu g.ml^{-1}$).

Nurulfazlina Edayah Rasol

Dr. Nurulfazlina Edayah Rasol earned her Ph.D. in Natural Product Chemistry (Analytical) from Universiti Teknologi MARA, Malaysia in 2020. Her Ph.D. thesis focused on the study of Alkaloids, Styryl Lactones, and Acetogenin from The Roots of Goniothalamus Lanceolatus Miq. and Their Antiproliferative Activity, resulting in the publication of four papers, including one in the prestigious Journal of Natural Products. During her postgraduate studies, she gained extensive experience in phytochemistry, particularly in the analysis of various Malaysian plant species using advanced chromatography techniques such as Preparative and Recycling HPLC. Currently, Dr. Edayah holds the position of senior lecturer in the Department of Chemistry and Environment at the Faculty of Applied Sciences and research fellow at the Atta-ur-Rahman Institute for Natural Products Discovery (AuRIns), Universiti Teknologi MARA. Within the institute, she serves as a consultant and resource person for the high-end instrument, Orbitrap FusionTM TribridTM Mass Spectrometry.

Unveiling the Medicinal Secrets: Exploring Malaysia's *Goniothalamus lanceolatus Miq.* for Anticancer Discoveries

Authors: Nurulfazlina Edayah Rasol[1,2], Nur Vicky Bihud[1,2], Fasihuddin B. Ahmad[3], Chun-Wai Mai[4], Nor Hadiani Ismail[1,2]
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Malaysia's rich biodiversity encompasses a wide array of plant species renowned for their valuable medicinal properties. These plants not only contribute to the country's natural heritage but also hold significant national value. In this study, we focused on investigating the phytochemical components of *Goniothalamus lanceolatus* Miq., an indigenous plant species exclusively found in Sarawak, Malaysia. Locally known as Gertimang or Selukai, this plant has a rich history of traditional use by native communities for its medicinal benefits in treating cancer, skin infections, and fever. To uncover the potential therapeutic compounds, present in *G. lanceolatus* Miq., we employed advanced mass spectrometry (MS) identification and isolation techniques on the plant's barks and roots. Through our meticulous approach, we discovered a total of 30 chemical compounds, including 11 previously unidentified styryl lactones and alkaloids. Cytotoxicity assessments revealed the promising activity of specific compounds such as 6*S*-goniothalamin, (6*S*,7*S*,8*R*)-8-chlorogoniodiol, (-)-ent-goniothalamin oxide, (–)-goniolanceolactam, goniolanceolatin B, and goniolanceolatin D against human lung and colorectal cancer cell lines, demonstrating their potential as novel anticancer agents. This research offers valuable scientific insights and lays the groundwork for future exploration in discovering potential anticancer agents, especially Malaysian plant species. Integrating traditional medicinal practices with modern scientific validation also will reinforce the importance of preserving and utilizing natural resources in healthcare systems.

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Kamatshi Sishtla

Kamakshi Sishtla graduated with a Bachelor of Science degree from the University of Illinois Urbana-Champaign. She joined Dr. Brian Kay's lab at Argonne National Laboratory where she used phage display technology and small molecule screening to identify inhibitors of proteins involved in bacterial pathogenesis. She moved to Dr. Timothy Corson's lab at the Indiana University School of Medicine in 2011. While she has worked on several different projects in the Corson Lab, a large focus is on characterizing small molecules for antiangiogenic potential in vitro with the aim of developing new treatments for neovascular eye diseases. When she's not in the lab, her hobbies include experimenting in the kitchen and her garden.

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In vitro Assessment Reveals Antiangiogenic Potential of Homoisoflavonoids

Authors: Kamakshi Sishtla[1], Sianne Schwikkard[2], Hannah Whitmore[3], Dulcie A. Mulholland[3], Timothy W. Corson[1]
Institute: [1]Department of Pharmacology and Toxicology, Eugene and Marilyn Glick Eye Institute, Department of Ophthalmology, Indiana University School of Medicine; [2]School of Life Sciences, Pharmacy and Chemistry, Kingston University, Kingston-upon-Thames, KT1 2EE; [3]Natural Products Research Group, Department of Chemistry, University of Surrey, Guildford GU2 7XH, United Kingdom

Pathological ocular neovascularization is implicated in several blinding eye diseases such as retinopathy of prematurity, diabetic retinopathy, and neovascular age related macular degeneration. Homoisoflavonoid rich plants have long been used in traditional medicine and numerous purified compounds from a range of species have proven antiangiogenic in vitro and in vivo. To test a compound's antiangiogenic potential, we recapitulate three stages of angiogenesis: proliferation, migration, and tubule formation using ocular endothelial cells. Discussion of two homoisoflavonoids provides examples of how these assays are applied. Regioisomers RC.B-1 ((S)-5,7-dihydroxy-3-(3-hydroxy-4-methoxybenzyl)chroman-4-one) and RR.B-4 ((S)-5,7-dihydroxy-3-(4-hydroxy-3-methoxybenzyl)chroman-4-one) were isolated from Rhodocodon campanulatus and R. rotundus respectively. We first tested the antiproliferative effect of both compounds on primary Human Retinal microvascular Endothelial Cells (HRECs) using alamarBlue, a resazurin reagent which reacts to the reducing environment of viable cells. Seven concentrations of each compound plus the vehicle DMSO were tested in this assay to determine the concentration at which 50% of maximal growth is inhibited (GI50). To test the specificity of their antiproliferative effect, we also tested compounds on non-endothelial, ocular cell lines such as human retinal pigment epithelial cells (ARPE19), and two ocular cancer cell lines (92-1 and Y-79). We then tested compounds' ability to affect the endothelial cell property of migration with a scratch-wound assay and determined percentage inhibition of migrated cells compared to the DMSO vehicle. Finally, we tested compounds in vitro with a Matrigel tube formation assay which tests both migration and morphogenesis capacities of HRECs. We determined percentage of total tubule length formed by cells exposed to compound vs. DMSO. While both compounds showed potent antiproliferative effect on HRECs with sub-micromolar GI50, RR.B-4 was more selective with mid to high micromolar GI50 against the other ocular cell lines tested. As both compounds had very similar effects on tube formation and migration of HRECs, RR.B-4 is the better candidate for further testing as an antiangiogenic compound in an ocular context. These in vitro angiogenesis assays yield much information about the specificity and antiangiogenic potential of compounds, at a relatively low cost of both time and reagents. They serve as an essential gatekeeping step before moving lead compounds into much more expensive and labor intensive in vivo testing in mouse models of disease.

Hannah Hall

Third year PhD student at the University of Reading and the Royal Horticultural Society. Investigating the taxonomy and evolution of the Mediterranean subtribe Hyacinthinae (Asparagaceae, Scilloideae). Interested in botany, horticulture and molecular phylogenetics.

New insights into the taxonomy of Hyacinthaceae Parl.

Authors: Hannah Hall, Alistair Cultham, Kalman Konyves, John David
Institute: University of Reading, Royal Horticultural Society

Hyacinthus orientalis L. is perhaps one of the most familiar members of Hyacinthinae in cultivation and has a long history of use in ornamental horticulture. Together with *H. transcaspicus* and *H. litwinovii* it currently forms a genus. Analysis using next generation DNA sequencing across the broader *Hyacinthinae* reveals Hyacinthus to be split and interleaved with *Othocallis*, elements falling in *Fessia* and sister to the monotypic *Pfosseria* and *Zagrosia*. Phylogenetic patterns match elements of the biogeography of the group suggesting that redefinition of generic boundaries is needed.

Yanisa Olaranont

Yanisa Olaranont is a PhD student in the Department of Plant Science at Mahidol University, Thailand. Her research spans various intriguing areas, including plant anatomy, plant physiology, plant molecular biology, phytochemistry, and plant-fungal interactions, which form the focal point of her PhD thesis. She is currently enhancing her skills in plant chemistry techniques and actively participating in research projects on secondary metabolites within the plant genera Vepris and Suregada at the Jodrell Laboratory, Royal Botanic Gardens, Kew.

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Cytotoxic ent-abietane Diterpenoids, Banyangmbolides A-E, from Leaves of *Suregada occidentalis*

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The leaf extract of herbarium specimen material of *Suregada occidentalis* collected in Banyang Mbo Wildlife Sanctuary, Southwest Region, Cameroon, has yielded five undescribed ent-abietane diterpenoids, banyangmbolides A-E, (1-5), and four known diterpenoids, gelomulides A (6), B (7), D (8) and O (9). The structures of the isolated compounds were elucidated based on NMR, IR, ECD and HRESIMS. Compounds 5, 7 and 8, showed 48-55% inhibition at 200 µM against FM-55-M1 human melanoma cells. The isolated compounds did not show signs of stimulating growth of serum starved human dermal fibroblast cells at concentrations up to 20 µM. Authors declare no conflict of interest.

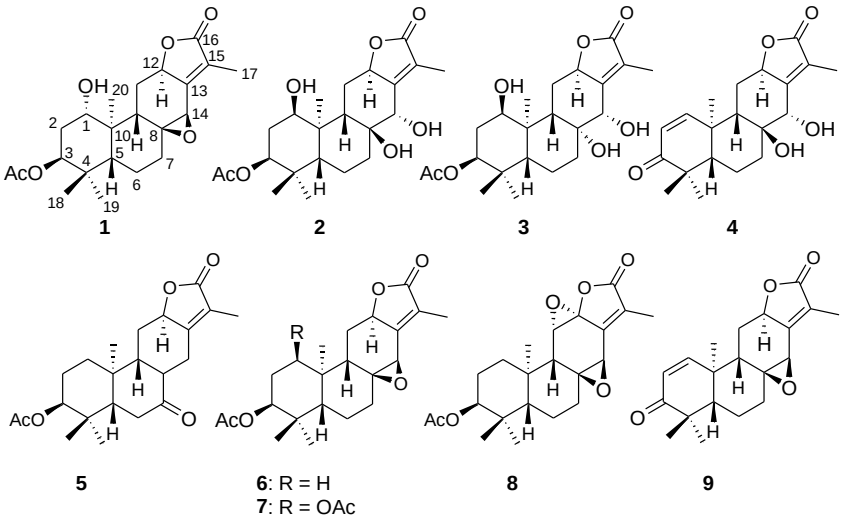
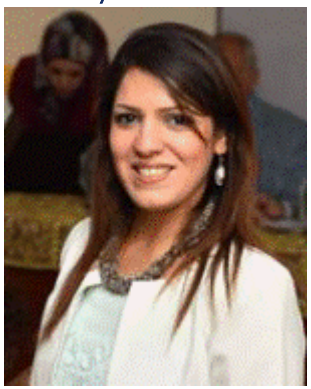


Fig 1 Compounds isolated from S. occidentalis

Hanady Kadhim



I am Hanady Kadhim a 4th year PhD student in Organic Chemistry. My research focuses on modifying an old antibiotic (Chloramphenicol) in order to improve its efficacy and reduce its toxicity. The research includes full synthesis and investigating the bioactivities of the novel compounds against different gram-positive and gram-negative bacteria. I have a B.Sc. and M.Sc. in chemistry and Biochemistry from Al-Nahrain University/ Baghdad-Iraq and 6 years in teaching and research in higher education in Kurdistan University/ Iraq. In 2020 I got the award of An Associate Fellowship in Higher Academy (AFHEA) Education form Kingston University and the Advance HE.

Modification of Protein Synthesis Inhibitor Antibiotics to Improve Efficacy/Safety

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Chloramphenicol is an old antibiotic that is seldom prescribed because of concerns over its toxicity, especially towards human mitochondria. Nevertheless, in some cases (e.g., multi-drug resistant brain abscess) chloramphenicol is the only effective drug.1 In this project, chloramphenicol is to be improved by the synthesis of new analogues, based on recent literature precedent for cytotoxicity and microbiological testing. Isosteric replacement of CH by N has profound effects on physicochemical properties2 and intra- and intermolecular interactions that can translate to improve pharmacological profiles.3 Correspondingly, the first chloramphenicol analogues in this project incorporate a nitrogen in the aromatic ring. Further analogues rely on isosteric replacement of the nitro group by 3,4-difluoride and the synthesis of azo-chloramphenicol tripeptide derivatives.

The synthetic reaction pathway entailed seven steps with a Stille coupling as the key stage. Bromination with NBS followed by Gabriel synthesis and aldol reaction completed the essential carbon skeleton.

Molecular docking was performed using AutoDock Vina with Chimera and PyMOL in order to predict the best tripeptide combination with high binding affinity for the 50S subunit of the 70S ribosome4.

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