Review Article



Spilanthes acmella: Ethnobotanical And Pharmacological Activities

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ABSTRACT

Spilanthes acmella is found in tropical and subtropical region of India. It has diversified medicinal properties such as analgesic, antiseptic, antioxidant and diuretic activity. It belongs to family Asteraceae, and subfamily Mimosoideae. The various parts such as stem leaves and flowers that are responsible for different pharmacological actions. The whole plant except root shows some medicinal use. The ethanolic extract of flower part of *Spilanthes acmella* shows the local anesthetic effect. It is also used in Beauty care cosmetics and the whole plant is responsible for it. It has many secondary metabolites. In this review article we have given brief information about pharmacological activities, extraction methods, spiritual uses, phytochemistry, multiple traditional uses and history of plant. This review will give an insight to all the scientific information about *Spilanthes acmella* to the scientific community.

Keywords: Spilanthes acmella, phytochemistry, cultivation, spiritual property, traditional uses, pharmacological activities.

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INTRODUCTION

pilanthes acemella Murr. or "Akarkara" of family Asteraceae, marked by star shaped flowers, is used in folk medicines since ancient times to treat severe tooth pain, infections of throat and gums, paralysis of tongue and psoriasis¹. It is also used as immuno modulator. It has various properties such as antiseptic, analgesic, antioxidant, anti-malarial, immune-modulator and diuretic properties¹. India is one of the twelve-mega heterogenietal countries in the world and has almost 17,000 flowering plants. Among the 25 hotspots in the world, the Eastern Himalayas and the Western Ghats are the two hotspots of India. Herbal drugs play an important role in health care programs especially in developing countries². Spilanthes acmella commonly known as 'akarkara' is an annual hairy herb, up to 32-60 cm. tall with numerous stems of marigold yellow flowers².

Cultivation

Spilanthes acmella can be grown as an annual in most climates. It is frost-sensitive but perennial in warm climates. Commissary Spilanthes estates have been established to address the need for sustainable supplies of standardized, high quality raw materials. *Spilanthes acmella* grows well in full sun to partial shade reaching a height of 12 to 15 inches with a spread of 24 to 30 inches. It prefers rich, moist, well-drained soil with a pH of 6.1 to

6.5. It is easily established started from seeds directly sown in the garden or indoors pots. Seed should be sown in flats. *Spilanthes acmella* can also propagate through stem cuttings. It needs regular watering and thrives well in high humidity in well-drained soils. The optimal temperature for germinating the seeds is 20-24°C (67-75°F).



Figure 1: *Spilanthes acmella* in medicinal garden of SRMS CET Pharmacy Bareilly.



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It is important to sow the seeds by burrowing them to about only 1/4 inch deep as they require light to stimulate germination. Germination takes approximately 1-2 weeks. For the best germination results, it is recommended to grow indoors in sterilized potting soil. A black earth and peat moss mixture works well. Always keep soil moist but never soggy. Once the seedlings have at least 2 sets of leaves they can be transplanted when the danger of frost has passed⁹. For utilizing the leaves and flowers of Spilanthes acmella, the whole plant can be harvested by cutting the plant to about 6". It will grow back and can be harvested again during the season. For harvesting the roots of the plant, the entire plant is plucked out and the roots are cut and separated from the plant. The harvested plant parts can be shade dried and stored in a dry place to avoid moisture and contamination⁹.

Spiritual beliefs

Antiseptic and analgesic properties, its extract is used in oral health care for the treatment of sore throat, oral ulcer, gingivitis, and general toothache³. Acmella oleracea is also used for clinical diseases such as anemia, hemorrhage, cancer, dysentery, gastro- intestinal ulcer, rheumatism, scurvy, stammering, and xerostomia and snake bite^{13.} It is also used in many other diseases such as blood disorder. It likewise has insecticidal potency against the pest Tuta absoluta, and vectors of infectious diseases including Aedes aegyptii²³. It is commonly known as toothache plant, eyeball plant, paracres and spot plant. There are throughout60 species of genre Spilanthes which have been reported from different areas and regions of the world. From all of these 5 species occur in India namely Spilanthes acmella Murr, S.acmella L.var.oleraceae Clarke, S.calva L., S.calva, S.paniculata and S.mauritiana L. from all these species Spilanthes acmella is an acutely threatened species⁴.

Taxonomic Classification

Subkingdom Tracheobionta	Tracheobionta	
Phylum Tracheophyta		
Division Magnoliophyta		
Superdivision Spermatophyte		
Class Magnoliopsida		
Sub Class Asteridae		
Order Asterales		
Family Asteraceae	Asteraceae	
Subfamily Mimosoideae	Mimosoideae	
Genus Spilanthes		
Species Acmella	Acmella	

Language Synonym

Names of Spilanthes acemella in different countries

India: Akarkara

Indonesia : Jotang, jocong and Dung getang

Chinese : San lu cao, Xiao tong chui, Tian wen cao, Bian di hong.

Japanese : Supirentesu panikurata

Malaysai : Subhang nenek

Thailand :Raan

History

Spilanthes having two species was first described by Jacquin (1760), Spilanthes insipida and S. urens. Richard (1707) described Spilanthes in having ray florets and lack of pappus which differ acmella as a genus of five species. Cassini (1722) suggested that Acmella might be treated better as a section within Spilanthes. De Candolle (1736) trailed Cassini's suggestion and sighted two sections, namely sect. Salivaria DC. Still some of the Indian treatises have followed the broader concept of the genus Spilanthes⁴. The leaves are eaten as a vegetable in India. Fresh as well as broiled leaves are used in dishes. The raw leaves are used as flavoring for salads soups and meats⁵. The Asteraceae constitutes one of the largest vascular plant family, with 30,000 species and over 1100 genera⁶. Leaf blades and flowers of the herb are also used to treat leucorrhoea in females among people of tribes in Bangladesh⁷. The entire slip paste of *Spilanthes acmella* is also used as "poisonous sting" in Chittagong hill tracts of Bangladesh where the plant is also known as Jhummosak²⁷. Spilanthes acmella var oleracea, also known as Acmella oleracea, Spilanthes acmella and most commonly as jambú, is a native plant original from the tropics of Asia and South America³⁸. Spilanthes acmella refers to the induce saliva important medicinal plant distributed in the tropical and subtropical, locality around the world with flourished source of therapeutic and medicinal constituents. The main constituents, namely, "spilanthol" and "acmellonate" are sometimes used to reduce the pain associated with toothaches and can secretion⁷.

Traditional use

This plant is very prominent among the archaic tribal community; special cuisine is prepared from this plant in theological festival. The destitute people offered this plant simultaneously with the "Ajeng Dues" in Dobur Uie. In particular, this plant is eminent as a folklore countermeasure for toothache and for throat and gum contagion⁴⁵. The flowers are crippled and utilized at the locus of toothache, eccentrically in "Irula tribe of Hasanur hills in abrade district of Tamil Nadu" where it is established by the local name "Mandal Poo Chedi" .afar from Tamil Nadu, root paste of the bush is used in throat problems in Betul and Chindwara district of Madhya Pradesh⁷. The plant is also published to be used as panacea (Sumatra), as stimulant, for toothache (Sudan), for stomatitis (Java), and for wound healing (India) In



Cameroon, the plant is utilised as a snakebite remedy and in the medication of articular rheumatism ⁷.

Table 1: Traditional uses and applications of different partsof Spilanthes acmella plant

Health Care	Treatment	Plant part Used
Medical	Rheumatism, fever Diuretics Flu, cough, rabies diseases, Tuberculosis, antimalarials, Antibacterial	Leaves, flowers
	Antifungal, skin diseases Immunomodulatory, Antiscorbutic, Local anesthetics Digestive, Obesity control (lipase inhibitor)	Leaves
	Snakebite	Whole plant
Dental	Toothpaste	Leaves
	Toothache	Leaves, Flower
	Periodontal disease	Flower heads, Roots
Beauty care cosmetics	Fast acting muscle relaxant Anti wrinkle	Whole plant

Medicinal Uses

Spilanthes acmella is a paramount medicinal plant, widely known as toothache plant which reduces the pain confederated with toothaches and induce salivation. For centuries *Spilanthes acmella* has been widely grown for horticultural, harmacological, medicinal, insecticidal, and culinary purposes and application for this purpose is still widespread in different parts of the world. Whole plant of *Spilanthes acmella* is enriched with secondary metabolites, which relinquish a plethora of medicinal uses to the plant. Various parts of this herb possess diverse pharmacological activities, which include antimicrobial, antipyretic, local anaesthetic, bio-insecticide, anticonvulsant, antioxidant, aphrodisiac, analgesic, diuretic, toothache relieve and anti-inflammatory effects³⁹.

The compact regulation of inflammatory feedback is important because exuberance of inflammatory responses cause severe inflammatory diseases, aforesaid (IBD) inflammatory bowel disease, rheumatoid arthritis and atherosclerosis. However, soundly regulated inflammation can extricate the human body from infectious diseases. Consequently, the discovery of candidates holding anti inflammatory properties is a valuable strategy for the treatment of severe inflammatory states¹⁰.

Pharmacological Activities

Local Anaesthetics

Local anaesthetics (LAs) are drugs which act upon topical application or local injection cause reversible loss of sensory sensation, especially of pain, in a restricted area of the body. They arrest the generation and conductance of nerve impulse at all parts of the neurone where they come in contact with skin without causing any structural damage. Thus, not only sensory but also motor impulses are interrupted when a local anaesthetics is applied or given to a mixed nerve, resulting in muscular paralysis and loss of autonomic control as well¹².

• The local anaesthetic (LAs) activity of Plant material environment.

- Its origin.
- Moisture content.
- Degree of processing.
- Particle size.

It is being carried out using two different animal models such as intracutaneous application, in guinea pigs using NUPERCAINE as standard (suitable for determining degree of anaesthesia) and plexus anaesthesia in frog using cocaine as standard (used for determining onset of anaesthesia). The mean onset of local anaesthetic action was very potent which could be attributed to the presence of alkyl amides ⁴⁹. The whole plant of S.acemella is used in the local anaesthetic effect.

Antipyretic Activity

Antipyretic reduce body temperature in fever, but do not cause hypothermia in normothermic individuals. Fever in the interim of infection is produced through the procreation of pyrogens in addition to ILs, TNFa, induce PGE2 production interferons which in hypothalamus raise its temperature set point⁴⁰. NSAIDs block the action of pyrogens but not that of PGE2 injected into the hypothalamus. The isoform present at this site appears to be COX-2 (possibly COX-3 also). However, fever can occur through non-PG mediated mechanisms as well¹². Spilanthes acmella was evaluated by yeast induced methods, a general method used for the induction of pyrexia. Inhibiting properties of lipo-oxygenase and cyclooxygenase were due to the presence of flavonoids had been suggested by reports. plentiful studies were carried over varying doses of yeast which culminated in varied quantities of flavonoids extracted¹¹.

Anti Inflammatory Activity

The most important mechanism of anti inflammatory action of NSAIDs is considered to be inhibition of PG synthesis at the site of injury. The anti inflammatory vigor of different compounds hardly corresponds with their potency to inhibit COX. Nimesulide is an effective anti inflammatory but comparatively weak COX inhibitor. PGs are eclusively one of the arbitraters of inflammation; inhibition of COX does not afflict the production of other mediators like LTs, PAF, cytokines, etc. Inflammation is the outcome of concerted participation of a large number of vasoactive, chemotactic and proliferative factors at different stages, and there are many targets for anti inflammatory action¹. Various studies had reported the anti-inflammatory properties of *Spilanthes acmella* on carrageenan, an initiator of hind paw derangement and a



standard phlogistic agent to study anti-inflammatory activity. Analytical reports show significant dosedependent reticence of paw oedema. The conclusions obtained indicated the extracts to be less efficient as to the standard drug mentioned by the researchers earlier. Researchers have also announced the existence of analgesic properties when combined with acetic acid and have prooved to induce abdominal constriction as revealed by a popular methodology, namely tail flick method²⁴. The results obtained with these plant extracts proved to be more efficient and effective as to tail flick method thus could be explored as peripherally acting analgesic. The presence of flavonoids was found to be the powerful inhibitors of prostaglandins which were effective at the later stages of acute inflammation¹¹.

Analgesic Activity

Analgesics, also called painkillers, are medications that relieve differing types of pain from headaches to injuries to arthritis. Anti-inflammatory analgesics dwindle inflammation, and opioid analgesics alter the way the encephelon perceives pain. Some analgesics are often bought over the counter, others require a prescription³³. They also demonstrated the analgesic activity of *Spilanthes acmella* using acetic acid induced abdominal constriction and tail flick method. The aqueous excerpt produced better results as compared to tail flick method which meant that the plant can be explored as peripherally acting analgesic and diuretic potency.

Diuretic Activity

These are constituents which cause a net debt of Na+ and water in urine output. Diuretics are among the foremost widely prescription drugs. Utilization of diuretics for the administration of hypertension has outstripped their use in edema. Availability of diuretics has also had a major impact on the understanding of renal physiology⁵².

The diuretic potential of *Spilanthes acmella* whole plant as well as fresh flowers, extracted using cold water extract method showed strong diuretic activity when given orally in a single dose⁵⁶. The diuresis lured by the *Spilanthes acmella* flowers was endowed to be strong with intensity mimicing to that of furosemide and accompanied by remarkable increases in both urinary Na+ and K+ levels. The onset of the diuretic effect of the aqueous extract was immensely rapid, and it also had a fairly long duration of action⁵⁷.

Anti Oxidant Activity

Antioxidant activity can be defined as a limitation or inhibition of nutrient oxidation (especially lipid and protein) by restraining oxidative chain reaction. Antioxidant capability of leaves of *Spilanthes acmella* was also examined recently by the researchers and that they found that the potent antioxidant activity within the crude ethanol extract of the leaf blades of the plant was attributed to the presence of flavanoids , tannins and phenolic compounds⁴⁴.

Anti-malarial Activity

Malaria may be a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes. It is preventable and curable. In 2019, there have been an estimated 229 million cases of malaria worldwide⁴⁹. A larvicide is a type of insecticide used to control mosquitoes indoors and outdoors around your home. They work by killing mosquito larvae before they will grow into adults. When used consistent with product label instructions, larvicides don't harm people, pets, or the environment³⁷. Spilanthol is simpler even at low doses against eggs and pupae. In pupae, it seems to figure on systema nervosum as evident by abnormal movement like jerks, spinning and uncoordinated muscular activity. This implied that the drug disturbed the nerve conduction somewhere⁵⁵. The mortality of pupae briefly span of your time upon exposure to the drug also indicated that spilanthol greatly disturbs the continued processes of histolysis and histogenesis. Many researchers also reported spilanthol as a potent larvicidal agent⁹.

Aphrodisiac Activity

To achieve better concupiscence has led to the event and use of various substances referred to as aphrodisiacs. An aphrodisiac enhances drive or pleasure by crossing the blood brain barrier and mimicking or stimulating some area of arousal within the central systema nervosum ⁴⁴. Aphrodisiac effect of the plant extract has been studied in male rats. They stated that mount latency, intromission latency, ejaculation frequency and post ejaculatory interval were increased in a dose-dependent manner after oral administration of extract. Although exact quantification of these improvements was not given, estimation derived from graphs suggested that after 9 days of 150 mg/kg dose, the improvements were reduced in mount latency, intromission latency, and post ejaculatory latency⁵². These benefits were more significant 9 days after supplementation relative to 14 days, suggesting a build-up effect. The plant proved to be superior to Viagra altogether aspects studied except proerectile properties⁶².

Anti-nociceptive Activity

Antinociceptive activity. Antinociception also referred to as nocioception/nociperception is that the body's response to potentially toxic stimuli, like harmful chemicals (e.g., capsaicin, formalin), mechanical injury (e.g., cutting, crushing), or adverse temperatures (heat and cold) by the sensory nervous system³⁶. Antinociceptive potency of the crude ethanolic extract of S. acemella adopting ethanoic acid induced writhing model in mice is available elsewhere in literature. The animals of test groups received test substance at the dose of 250 and 500 mg/kg weight. Positive control group was administered Diclofenac sodium (standard drug) at the dose of 25 mg/kg body weight, and vehicle control group was treated with 1% Tween 70 in water at the dose of 10 mL/kg body weight. Test samples, standard drug, and control vehicle



were administered orally 30 min before intraperitoneal administration of 0.7% acetic acid. After an interim of 15 min, the mice were contemplated to be writhing (constriction of abdomen, turning of trunk, and extension of hind legs) for five min. Crude ethanol extract of S. acemella leaves was found to possess significant antinociceptive activity⁵⁷.

Immunomodulatory action

A substance that stimulates or suppresses the system and should help the body fight cancer, infection, or other diseases. Specific immunomodulating agents, like monoclonal antibodies, cytokines, and vaccines, affect specific parts of the system. Also called immune system modulator⁴⁷. Hexane and chloroform extracts of Spilanthes acmella were found to suppress nitric oxide production in stimulated macrophages at 70 mcg/ mL by 72% and 75%, respectively. Isolated spilanthol demonstrated dosedependent prevention of macrophage activation with 60% and 20% production of nitric oxide at 90 and 360 5ØßM concentrations, respectively ⁴⁹. These inhibitory properties were accompanied by less nitric oxide synthetase and cyclooxygenase-2 mRNA and protein content, less cytokine production from macrsophages, and less nF-kB activation in the nucleus⁹.

Bioinsecticidal Activity

Biopesticides include naturally occurring substances that control pests (biochemical pesticides), microorganisms that control pests (microbial pesticides), and pesticidal substances produced by plants containing added genetic material (plant-incorporated protectants) or PIPs⁵⁵.

Bio-insecticides are small insects or microorganisms that are naturally present within the environment to regulate other insects from destroying the crop fields. For example, ladybugs and praying mantis combat scale insects for aphids which feed on plant sap⁵³.

Anticonvulsant Activity

A convulsant may be a drug which induces convulsions or epileptic seizures, the other of an anticonvulsant. These drugs generally act as stimulants at low doses, but aren't used for this purpose thanks to the danger of convulsions and consequent excitotoxicity⁵⁷. Several insecticidal compounds have been reported in *Spilanthes acmella*. Extract of *Spilanthes acmella* plant in rats was reported to induce full convulsions amid typical electrographic seizures in the electroencephalogram³⁹.

Insecticidal Toxicity of Spilanthol

Extract of Spilanthol from the flower heads of *Spilanthes acmella* was found to move against P. xylostella⁵⁶. The extracts from Spilanthes were most toxic against different mosquito species (i.e., Anopheles, Culex, and Aedes). The insecticidal peculiarity was attributed to spilanthol as well as alkamides. Besides, non-volatile sesquiterpenoids, saponins were also reported⁵⁴. Ethanol extract of flower heads of Spilanthes has shown a potent ovicidal,

insecticidal and pupacidal activity at dose of 7.5 ppm concentration against Anopheles, Culex, and Aedes mosquito⁴⁴. The hexane excerpt of preserved flower buds of Spilanthes acmella (3 N-isobutylamides: spilanthol, undeca- 2E, 7Z, 9E-trienoic acid isobutylamide and undeca2E-en-7,10-diynoic acid isobutylamide) was found active against Aedes aegypti larvae. The ethanolic extracts of Spilanthes acmella (whole plants) were segregated against early 4th instar larvae of Culex guinguefasciatus^{60.} The constituent Spilanthol was delineated to be toxic contrary for adults of P. americana. It is one of the most potent compound in comparison with conventional insecticides like carbaryl, lindane, and bioresmethrin ⁶⁵. The Spilanthes acmella floweret head extract also found to be effectual in controlling the Spodoptera litura, an polyphagous, hazardous agriculture pest²⁹.

Antimicrobial Activity

The different fractions were isolated from crude ethyl acetate extract of *Spilanthes acmella* and were studied against 9 strains of microorganisms⁶¹. The results showed that fraction E3 completely inhibited the growth of Corynebacterium diphtheriae with MIC value of 19 μ g/mL. The antibacterial activity is also reported from the flower head extract of *Spilanthes acmella* ⁵⁹.

Antibacterial: Anything that destroys bacteria or suppresses their growth or their ability to breed. Heat, chemicals cognate chlorine, and antibiotic drugs are all having antibacterial properties. Many antibacterial products for cleaning and hand washing are sold today ³⁵. The antibacterial activity is of two types, bactericidal and bateriostatic which means that the bactericidal agents kill the bacteria and bacteriostatic agents inhibits the growth of bacteria these are the mode of action of these two type of agents⁵⁷. The plant part which is used for antibacterial activity is stems of spilanthes acemella, and it is shown by in vitro callus and also it's potential against gram negative bacteria harbouring bla gens³⁴.

Antimicrobial drugs are the best contribution of the 20th century to therapeutics. Their advent changed the outlook of the physician about the facility drugs can wear diseases. They are one among the few curative drugs. Their importance is magnified within the developing countries, where infective diseases predominate. As a class, they are one of the foremost frequently used also as misused drugs¹². Drugs in this class differ from all others in that they are designed to inhibit/kill the infecting organism and to possess no/minimal effect on the recipient. ^[52]The leave of Spilanthes acemella shows the antimicrobial activity³⁷. The methanol and standard of ethyl acetate extract against bacterial strain Klebsiella pneumoniae as it showed more inhibition zone than the standard drug Doxycycline¹⁹.

Antifungal Activity: These are actives used for superficial as well as deep (systemic) fungal infections. A disquietening trend after 1950s is that the rising prevalence of more sinister sort of fungal infections which are, to an outsized extent, iatrogenic. These are associated with the utilization



of broad-spectrum antibiotics, corticosteroids, anticancer/immunosuppressant drugs, artificial dentures, implants and indwelling catheters, and emergence of AIDS. As a result of breakdown of host defence mechanisms, saprophytic fungi easily invade living tissue¹². Aspergillus parasiticus, Aspergillus niger, Fusarium oxysporum and Fusarium moniliformi were the four different fungal species against which Spilanthes acmella had been active, which was demonstrated using inflorescence extracts of various concentrations²¹. Every concentration of the test solution was found to inhibit at varying degrees of sensitivity against the fungal species¹¹.

Laxative Activity

These are drugs that promote evacuation of bowels. A distinction is sometimes made according to the intensity of action. (a) Laxative or aperients milder action, elimination of soft but formed stools. (b) Purgative or cathartic: stronger action leading to more fluid evacuation.

Many drugs in low doses act as laxative and in larger doses as purgative¹². The whole plant is used as a laxative *Spilanthes acmella* appear to contain substance(s) that possess significant laxative activity. Bisacodyl is widely used stimulant laxative in the management of constipation, which effectively antagonized constipation induced by atropine ⁴.

CONCLUSION

Spilanthes acmella has long been used as a spice for appetizers and as a folk medicine for toothache, as an antiseptic, and for other therapeutic activities. Several components of this herb, such as spilanthol, (2E)-N-(2methylbutyl)-2-undecene-8,10-diynamide, (2E,7Z)-Nisobutyl-2,7-tridecadiene-10,12-diynamide, (7Z)-Nisobutyl-7-tridecene-10,12-diynamide, and undeca-2E,7Z,9E-trienoic acid isobutylamide, have been isolated and characterized ^{23, 41}. However, the bioactive compounds involved in anti-inflammation are not yet revealed. This study has isolated the anti-inflammatory bioactive spilanthol, demonstrating compound, significant suppression effects on inflammatory responses⁴². This is is often the primary report back to identify the antiinflammatory component, spilanthol, of Spilanthes acmella. Spilanthol dose-dependently inhibits the production of nitrous oxide, due to inhibition of inducible nitrous oxide synthase (iNOS) protein expression and the respective alterations of inducible nitrous oxide synthase (iNOS) gene transcription. Overexpression of inducible nitrous oxide synthase (iNOS) is generally accompanied by inflammatory disorders, in which inflammatory cytokines like IL-1 and TNF-R are liable for various acute and chronic responses to inflammatory diseases⁵⁰.

Proinflammatory cytokines are important mediators of inflammatory responses. IL-1, IL-6, and TNF-R serve as endogenous pyrogens that cause fever by initiating metabolic changes in the hypothalamic thermoregulatory center during inflammation. These cytokines oversee the inflammatory acknowledgement and stimulate the fabrication of acute phase reactants. This study indicates that spilanthol markedly reduces the production of inflammatory cytokines (IL-1, IL- 6, TNF-R) in LPS-treated murine RAW 264.7 macrophages, which could possibly ameliorate the pain and sore. togetherly spilanthol do constrain the expression of COX-2, downsizing the advancement of inflammatory responses. These annihilation effects are partly because of the inactivation of NF- κ B. Results reveal that spilanthol dose-dependently impede the phosphorylation of I κ B in cytoplasm of the cells.

REFERENCES

- 1. Baruah RN., Leclercq PA Characterization of the essential oil from flower heads of *Spilanthes acmella*. Journal of Essential Oils Research, 1993;5: 693:695
- 2. Chase, CR. and Pratt, R., Fluorescence of Powdered Vegetable Drugs with Particular Reference to Development of a System of Identification., Journal of American Pharmaceutical Associaiton, 1949 (Sci. ed.); 38: 324-331.
- 3. Kumar KS. ,Phytochemical and Pharmacognostic investigations of *Spilanthes acmella* Murr. World Journal of Pharmacy and Pharmacetical Sciences, 2016;4(11):978-988.
- Leng Tan Chee, Ning Shu Ping, Boey Peng Lim and Chan Lai Keng, Detection of bioactive compounds from *Spilanthes acmella* (L.) plants and its various in vitro culture products. Journal of Medicinal Plants Research 2011;5(3):371-378.
- Pavunraj M, Baskar K., Phytopesticidal effects of *Spilanthes* acmella (L.). Murr. Leaves on three economically important lepidopteron insect pests. Journal of Coastal Life Medicine 2014; 2(7):549-554.
- 6. Nagashima M, Nobuji N. Two sesquiterpenes from *Spilanthes acmella* L. Chem Expr 1991;6(12): 993-996.
- Nakatani N and Nagashima M, Pungent alkamides from Spilanthes acmella L. var. oleraceae Clarke. Biosci., Biotech. Biochem 1992;56:759-762.
- 8. Oliver-Bever BEP, Medicinal plants in tropical West Africa. Cambridge University Press, 1986 Cambridge, UK.
- 9. Shimada T, Gomi T. (1995). Spilanthol-rich essential oils for manufacturing toothpastes or other oral compositions. Chem. Abstr. 122, 322237).
- 10. Yadav R. et al Phytochemical Screening of *Spilanthes acmella* plant parts. International Journal of Pharmaceutical Erudition 2012;1(4):43-48.
- Schwartz WB. Effect of sulphanilamide on salt and water excretion in congestive heart failure. N Engl J Med. 1949; 240:173.
- 12. Kirtikar KR, Basu BD. Indian Medicinal Plants, 2nd Edn. Dehradun: International Book Distributors, 1988.
- Yoganarasimhan SN. Medicinal Plants of India, Vol. II, Bangalore: India Karnataka, Interline Publishing Pvt. Limited, 1996.
- 14. The Wealth of India, A dictionary of India Raw Materials and Industrial Products. C.S.I.R. New Delhi: publication and Information Directorate New Delhi, 1988.



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- 15. Nadkari AK. Indian Material Media, Bombay: Popular Prakashan Pvt. Ltd., 1976. 6. Rastogi BN. Compendium of Indian Medicinal Plants, Vol. II, CDRI Lucknow:
- 16. Nakatani N and Nagashima M. Pungent alkamides from *Spilanthes acmella*, L. var. oleracea Clarke. Biosci biotech biochem. 1992; 56(5): 759-762.
- Shimada T and Gomi T. Spilantholrich essential oils for manufacturing toothpastes or other oral compositions. JP Pat 07090294; [Chem Abstr 1995; 122, 322237].
- Nagashima M and Nakatant N. LCMS analysis and structure determination of pungent alkamides from *Spilanthes acmella*, Murr. Flowers. Lebenson Wiss Technol. 1992; 25(5): 417-421.
- 19. Lemos TLG et al. The essential oils of *Spilanthes acmella* , Murr. J of Essential Oil Res. 1991; 3(5): 369-370.
- 20. Nagashima M and Nobuji N. Two sesquiterpenes from *Spilanthes acmella*, L. Chem Expr. 1991; 6(12): 993-996.
- 21. Penteado et al. Carotenoids and provitamin-A activity of vegetable leaves consumed in Northern Brazil. Rev Farm. Bioquim University, Sao Paulo 1986; 22(2): 97-102.
- 22. Amal MK and Sudhendu M. Analysis of free amino acid content in pollen of nine Asteraceace species of known allergenic activity. Ann Agric Environ Med. 1998; 5(1): 17-20.
- 23. Ratnasooriya W D et al. Diuretic activity of *Spilanthes acmella* flowers in rats. J Ethnopharmacol. 2004; 2-3(91): 317-320.
- 24. Chakraborty A et al. Preliminary studies on antiinflammatory and analgesic activities of *Spilanthes acmella* in experimental animal models. Indian J Pharmacol. 2004; 36(3): 148-150.
- 25. Wongsawatkul O et al. Vasorelaxant and Antioxidant Activities of *Spilanthes acmella* Murr. Int J Mol Sci. 2008; 9(12): 2724–2744.
- 26. WHO Quality control method for medicinal plant materials. Delhi: IJRPC 2011, 1(1) Rajesh et al. 61 A.I.T.B.S. Publishers & Distributors, 2002.
- 27. Harbone JB. Phytochemical Methods A Guide to Modern Techniques of plant analysis, 2nd edn. New York: Chapman and Hall London, 1984.
- 28. Ghosh MN. Fundamentals of Experimental Pharmacology, 2nd Edn. Kolkata: Scientific Book Agency, 1984.
- 29. Rao VS and Fonteles MC. Effects of nifedipine on renal responses to several diuretic agents in rats. J Pharm Pharmacol. 1991; 43:741-3.
- Vogel GH and Vogel WH. Drug Discovery and Evaluation: Pharmacological Assays. Germany: Springer-Verlag Berlin Heidelberg, 1997.
- Lipschitz WL and Hadidian KA. Bioassay of Diuretics. Journal of Pharmacology Experiments and Therapeutics 1943; 79: 97-110.
- 32. Guyton AC. Blood pressure control special role of the kidneys and body fluids. Science. 1991; 252: 1813-6.

- Maghrani M, Zeggwagh N, Haloui M and Eddouks M. Acute diuretic effect of aqueous extract of Retama raetam in normal rats. J Ethnopharmacol. 2005; 99: 31–35.
- 34. Haloui M, Louedec L, Michel JB and Lyoussi B. Experimental diuretic effects of Rosmarinus officinalis and Centaurium erythraea. J Ethnopharmacol. 2000; 71:465-72.
- 35. Rao NK, Reddy RK. Threatened plants of Tirupati and its environs. Howarh. An Assessment of Threatened Plants of India. 1983;167-8.
- 36. Pandey V, Agrawal V. Efficient micropropagation protocol of *Spilanthes acmella* L. possessing strong antimalarial activity. In Vitro Cell Dev Biol-Plant 2009;45:491-99.
- Prasad MM, Seenaya G. Effects of spices on growth of red halophilic cocci isolated from salt cured fish and solar salt. Food Res Int. 2000;33:793-98.
- Sabitha AR, Suryanarayana UM. Antifungal potential of flower head extract of *Spilanthes acmella* Linn. African J Biomed Res 2006;9:67-9.
- Sharma S, Shahzad A, Shahid M, Jahan N. An efficient in vitro production of shoots from shoot tips and antifungal activity of *Spilanthes acmella* (L.) Murr. Int J Plant Dev Biol. 2012;6:40-5.
- 40. Amer A, Mehlhorn H. Larvicidal effects of various essential oils against Aedes, Anopheles, and Culex larvae (Diptera, Culicidae). Parasitol Res. 2006;99:466-72.
- 41. Chakraborty A, Devi RKB, Rita S, Sharatchandra K, Singh TI. Preliminary studies on anti-inflammatory and analgesic activities of *Spilanthes acmella* in experimental animal models. Indian J Pharma. 2004;36:148-50.
- 42. Wu LC, Fan NC, Lin MH, Chu IR, Huang SJ, Hu CY, Han SY. Anti-inflammatory effect of Spilanthol from *Spilanthes acmella* on murine macrophage by down-regulating LPSinduced anti-inflammatory mediators. J Agric Food Chem. 2008;56:2341-9.
- 43. Savadi RV, Yadav R, Yadav N. Study on immunomodulatory activity of ethanolic extract of *Spilanthes acmella* Murr. leaves. Indian J Nat Prod Res. 2010;1:204-7.
- 44. Ekanem AP, Wang M, Simon JE, Moreno DA. Antiobesity properties of two African plants (*Afromomum meleguetta* and *Spilanthes acmella*) by pancreatic lipase inhibition. Phytotherapy Res. 2007;21:1253-5.
- 45. Tanwer BS, Choudhary R, Vijayvergia R. In vitro and in vivo comparative study of primary metabolites and antioxidant activity in *Spilanthes acmella* Murr. Int J Biotech Biochem. 2010;6:819-25.
- Sharma G, Gupta V, Sharma S, Shrivastava B, Bairva R. Toothache plant *Spilanthes acmella* Murr.: a review. J Natural Conscious. 2010;1:135-42.
- Prachayasittikul S, Suphapong S, Worachartcheewan A, Lawung R, Ruchirawat S, Prachayasittikul V. Bioactive metabolites from *Spilanthes acmella* Murr. Molecule 2009;14:850-67.
- Singh M, Chaturvedi R. Improved clonal propagation of Spilanthes acmella Murr. For production of scopoletin. Plant Cell Tiss Organ Cult. 2010;103:243-53.



- 49. Chandra S, Sharma HP, Chandra R, Jha S. Medicinal herbs-Spilanthes species: a review. Pharmbit. 2007;15:17-22.
- 50. Saritha KV, Prakash E, Ramamurthy N, Naidu CV. Micropropagation of *Spilanthes acmella* Murr. Biol Plant. 2002;45:581-4.
- 51. Haw AB, Keng CL. Micropropagation of *Spilanthes acmella*, a bio-insecticide plant through proliferation of multiple shoots. J App Hortic. 2003;5:65-8.
- 52. Saritha KV, Naidu CV. Direct shoot regeneration from leaf explant of *Spilanthes acmella*. Biol Plant. 2008;52:334-8.
- 53. Deka P, Kalita MC. In vitro clonal propagation and organogenesis in *Spilanthes acmella* (L.) Murray: a herbal pesticidal plant of north-east India. J Plant Biochem Biotech. 2005;14:69-71.
- 54. Singh SK, Rai MK, Asthana P, Sahoo L. An improved micropropagation of *Spilanthes acmella* L. through transverse thin cell layer culture. Acta Physiol Plant. 2009;31:693-98.
- 55. Singh M, Chaturvedi R. Screening and quantification of an antiseptic alkylamide, spilanthol from in vitro cell and tissue cultures of *Spilanthes acmella* Murr. Industrail Crop Prod. 2012;36:321-28.
- 56. Sandal I, Bhattacharya A, Ahuja PS. An efficient liquid culture system for tea shoot proliferation. Plant Cell Tiss Organ Cult. 2001;65:75–80.
- 57. Mackinney G. Absorption of light by chlorophyll solution. J Biol Chem. 1941;140:315-22.

- MacLachlan S, Zalik S. Plastid structure, chlorophyll concentration and free amino acid composition of chlorophyll mutant of barley. Can J Bot. 1963;41:1053-62.
- 59. Sahai A, Shahzad A. High frequency in vitro regeneration system for conservation of *Coleus forskohlii*: a threatened medicinal herb. Acta Physiol Plant. 2013;35:473-81.
- 60. Banerjee S, Tripathi J, Verma PC, Dwivedi PD, Khanuja SPS, Bagchi GD. Thidiazuron-induced high-frequency shoot proliferation in *Cineraria maritima* Linn. Curr Sci. 2004;87:1287-90.
- 61. He SS, Liu CZ. Plant regeneration of an endangered medicinal plant *Hydrastis canadensis* L. Sci Hort. 2007;113:82-86.
- Huetteman CA, Preece JE. Thidiazuron: a potent cytokinin for woody plant tissue culture. Plant Cell Tiss Organ Cult. 1993;33:105-19.
- 63. Radhika K, Sujatha M, Nageshwer Rao T. Thidiazuron stimulates adventitious shoot regeneration in different safflower explants. Biol Plant. 2006;50:174-9.
- Malek MA, Bari Miah MA, Al-Amin M, Khanam D, Khatun M. In vitro regeneration in pointed gourd. Bangladesh J Agri Res. 2007;32:461-71.
- 65. Dhar U, Joshi M. Efficient plant regeneration protocol through callus for *Saussurea obvallata* (DC.) Edgew. (Asteraceae): effect of explant type, age and plant growth regulators. Plant Cell Rep. 2005;24:195-200.
- Mohapatra H, Barik DP, Rath SP. In vitro regeneration of medicinal plant *Centella asiatica*. Biol Plant. 2008;52:339-42.

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