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THE ROLE OF ACEMELLA OLERACEA IN MEDICINE- A REVIEW

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ABSTRACT

Over three-quarters of the world population relies mainly on plants and plant extracts for health care. More than 30% of the entire plant species, at one time or other was used for medicinal purposes. The herbal products today symbolise safety in contrast to the synthetics that are regarded as unsafe to human and environment. Medical plants play an important role in the management of diseases in developing countries where resources are meager. Among them *Acmella oleracea* are important for their therapeutical potentials. This article reviewed the biomedical applications of *Acmella oleracea* Toothache, Diuretic and renal stones, Scurvey, scabies, psoriasis, Hepatoprotective, malaria, rheumatisms, gastrointestinal diseases, other biomedical uses.

KEY WORDS: Acemella oleracea, rheumatism, headache, immunomodulatory, antioxidant.

1. INTRODUCTION

Acemella oleracea is an annual herb grows to a height of 15 - 30 cm. It belongs to the family Asteraceae. It is commonly known as Toothache plant. The whole plants can be used in the treatment of dysentery and rheumatism [1]. The decoction of the plant can be taken internally as a diuretic and able to resolve stones in the bladder, while a decoction of the roots can be used as a purgative [2] and the decoction of leaves and flowers are used toothache, stomatitis and stammering. It is also used as a defensive medicine for scurvy and stimulates digestion. Besides these medicinal uses, the flower heads have been used as a spice for appetizers by the Japanese. In this review a monograph will be produced that justifies the use of this plant in a wide range of applications.

2. *Scientific Classification*

Kingdom	:	Plantae
Phylum	:	Tracheophyta
Class	:	Magnoliopsida
Order	:	Asterales
Family	:	Asteraceae
Subfamily	:	Mimosoideae
Genus	:	*Acmella*
Species	:	*A. oleracea*

3. *Botanical Description*

Acemella oleracea is an Annual herb with erect stems, sometimes decumbent. The stems are prostrate or erect, often reddish, hairless. Leaves opposite, simple; broadly ovate to triangular, 5–11 cm long, 4–8 cm wide, base truncate to shortly attenuate, apex acute to shortly acuminate, margin dentate. Inflorescence a discoid head up to 2.5 cm × 1.5 cm; involucral bracts 15–18, 3-seriate, up to 8 mm × 1 mm, apex acute; receptacular bracts straw-coloured, often tinged purple-red, up to 6 mm × 1 mm. Disk flowers 400–620, corolla 5-merous, yellow, up to 3.5 mm long. Fruit an achene 2–2.5 mm × 1 mm; pappus consisting of 2 bristles Table.1.

4. Phytochemicals Of Spilanthes Spp

Phytochemicals are the chemical compounds that occur naturally in plants and have protective or disease-preventive properties. Different phytochemicals like alkaloids, glycosides, flavanoids, tannins, anthraquinones, saponins and cardiac glycosides have been reported in *Acmella calva* [3]. Alkamides are the most abundant phytochemicals present in genus *Spilanthes*. Alkamides have been identified in several species of *Spilanthes* including *S.acmella, S. americana, S. oppositifolia, S. ocymifolia, S. ciliata, S. calva* and *S. mauritiana.* Alkamides are bitter in taste and could stimulate salivation. Several secondary volatile metabolites like sesquiterpenes, alkamides and oxygenated compounds have been isolated and identified in *S. Americana* [4]. The most abundant alkamide found was spilanthol. Spilanthol has a strong pungent taste. It may produce local astringency and anaesthetic effects [5]. The molecular formula of spilanthol was determined as (2*E*, 6Z, 8E)-N-isobutylamide-, 6, 8-decatrienamide [6].

5. Biomedical Applications

5.1. Toothache Treatment

Acmella oleracea (*Spilanthes oleracea*) commonly known as the toothache plant. It derives the name of 'toothache' plant from the compound 'spilanthol', which is used to reduce the pain associated with toothaches and also it can induce saliva secretions [7]. Jansen, 1985 [8] reported that *Spilanthes oleracea* is used as anaesthetic for toothache and as an antipyretic. Chewing on the fresh or dried flower or using the extract will help deaden tooth pain. A plant used for centuries by the Inca people of Peru to relieve toothache. It acts as a natural anaesthetic. A tincture of the fresh or dried *S. oleracea* is used against toothache and gum problems in India [9]. So it is considered by Indians as a powerful stimulant and sialogogue (a herb that promotes an increased flow of saliva). Extracts from the plant is used as a pain-relieving oral gel with no known side-effects [10] described, *Spilanthes acmella* having a hot burning taste which causes salivation.

5.2. Diuretic and Renal Stones

Diuretics are drug which increase the formation of urine and thus remove excess extra cellular water from oedematous tissue. Drugs that induce diuresis are known as diuretics. *A. olerecea* has strong diuretic activity and the ability to dissolve urinary calculi [11]. *A. oleracea* have a strong diuretic action in rats was determined [12] by using cold water. The result showed that the highest dose of flowers tested possesses strong diuretic activity when given orally in single dose. The urine was slightly acidified and strongly suggests that the cold water extract is acting as a loop diuretic. Loop diuretics are the most powerful of all diuretics and these inhibit the Na+/K+/Cl- co-transporter system in the thick ascending loop of the nephron, thereby increasing natriuresis(excretion of sodium in the urine) and kaleuresis(excreting potassium in the urine [13, 14].

5.3. Scurvey, Scabies, Psoriasis

Scurvy is a condition caused by a lack of vitamin C (ascorbic acid) in the diet. Signs of scurvy include tiredness, muscle weakness, joint and muscle aches, a rash on the legs, and bleeding gums [15]. Extract of *A.olerecea* flower heads and roots are used as a preventive medicine for scurvy and stimulate digestion [16]. Scabies is an easily spread skin disease caused by a very small species of mite. Psoriasis is an autoimmune disease that affects the skin. Ayurvedic system of medicine *A.olerecea* flower heads and roots are used in treatment

of scabies, psoriasis, scurvy [17] and also leaves are used externally in treatment of skin diseases.

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5.4. Hepatoprotective

Liver plays an astonishing array of vital functions in the body. No specific allopathic medicines used as hepatoprotective. Herbal drugs are more widely used for hepatoprotectives. Hepatoprotective activity of S.acmella extracts against CCl_4-induced liver toxicity in rats was determined [18]. Suja et al. 2003 [19] Conducted the study on antihepatotoxic activity of *Spilanthes ciliate*. Pretreatment of the rats with oral administration of the plant ethanolic extracts-*Ixora coccinea*, *Rhinacanthus nasuta*, *Spilanthes ciliate. Spilanthes ciliate* prior to Aflatoxin B1 was found to provide significant protection against toxin induced liver damage.

5.5. Treatment for Malaria

Spilanthes spp. is used as traditional herbal medicines in Africa and India to treat malaria. A decoction of *S. oleracea* has been used as a traditional antimalarial in Africa [20]. Pandey *et al*. 2007 [21] conducted the study on antimalarial activity of three species of *Spilanthes* against malaria and filarial vector. They determined *Spilanthes calva* and *Spilanthus paniculata* have anti-malarial activity. *Acmella olerecea* contain spilanthol, which is effective against *Plasmodium falciparum* [22, 23] and malarial paraxysms. An ether extract of fresh flower tops is effective against anopheles mosquito larvae [3].

5.6. Treatment For Rheumatisms

Rheumatism or rheumatic disorder is a medical problem affecting the joints and connective tissue. The leaves of *Spilanthes acmella* have been used traditionally as tonic for the treatment of rheumatism, gout, sailagogine [24]. The whole plant can be used in the treatment of dysentery and rheumatism [25, 26].

5.7. Gastrointestinal Diseases

In Indo-China the plant is used to treat dysentery. Filipinos make use of the roots to treat constipation. The flower head is chewed by the Indonesians to promote salivation [27].

5.8. Beauty Care Cosmetics

Spilanthol, the active compound isolated from *Acmella oleracea*, is a fast-working myorelaxant. *Acmella oleracea* extract stimulates the contractile force of the fibroblasts

(cell/collagen fibre interaction increased), which will help to firm and tighten the dermis [28]. The plant extract is used widely in cosmetics as a myorelaxant. It is used to stimulate, reorganize and reinforce the collagen network in anti-age applications (antiwrinkle cream formulations) [29]. *Acmella oleracea* Extract (with water and alcohol) - Immediately limits micro-contractions that create then aggravate facial wrinkles. This reduction of wrinkles leads to significantly smoother skin.

5.9. Other Biomedical Uses

It protects the individual from colds and flu [30]. An extract of the leaves and flowers is traditionally used for the stomatitis, flu, cough, rabies diseases and tuberculosis, throat complaints, headache [31] and fever [32]. An Indian tribe used *S. acmella* to treat fungal skin conditions, such as athlete's foot, ringworm and nail infections. *Spilanthes acmella* flower heads were used as a remedy in India on children for stammering. In Indo-china plant is used to treat dysentery while the Filipinons make use of the roots to treat constipation.

6. Pharmacological Activity

Spilanthes spp are used for the treatment of various disorders including life-threatening diseases. Researchers have done different *in vivo* and in vitro pharmacological screenings to authenticate the traditional uses. These studies have revealed the potential of the plant to be developed as a curative agent from natural resources.

6.1. Anti-Inflammatory Effect

Chen et al. [33] conducted the study on Anti-inflammatory Effect of Spilanthol from *Spilanthes acmella* on Murine Macrophage by Down-Regulating LPS-Induced Inflammatory Mediators Results of this study suggest that spilanthol, isolated from *S. acmella*, attenuates the lipopolysaccharide-induced inflammatory responses in murine macrophages partly due to the inactivation of NF-κB, which negatively regulates the production of proinflammatory mediators. Aqueous extract of ariel part of *S. acmella,* in experimental animal models showed dose-dependent inhibition of paw edema and increased pain threshold indicating significant anti-inflammatory and analgesic properties [34]. Spilanthol shows signficant antiinflammatory activity on lipopolysaccharide-activated murine macrophage model RAW 264.7, partly from inactivation of NF-KAPPA B which negatively regulates production of pro-inflammatory mediators [35].

6.2. Analgesic

Different doses of aqueous extract of fresh flowers of *Spilanthes acmella* were orally administered to male rats and their analgesic potential was determined at different post treatment periods by using hot plate and tail flick tests. The analgesic activity is mediated supra-spinally accompanied with sedation [36].

6.3. Vasorelaxant Activity

The chloroform and ethylacetate extract of *S. acmella* on phenylephrine exerts maximal vasorelaxation in a dose-dependent manner, although less than acetylcholine-induced nitric oxide (NO) vasorelaxtion. Chloroform extract showed the highest vasorelaxation and antioxidant activity [37].

6.4. Immunomodulatory Activity

Immunomodulatory agents of plant and animal origin increase the immune responsiveness of the body against pathogens by activating primarily the non specific immune system. The leaves are used as immunomodulatory, adaptogenic, toothpaste, lithotriptic, antiscorbitic, ailagogine and digestive [24]. The leaves of *Spilanthes acmella* have been used traditionally as tonic for the immunostimulant activity [24].The herb exhibits general immunomodulator properties when used internally, boosting production of leucocytes and antiviral interferon as well as phagocyosis. The ethanol extract of leaves showed significant activation of macrophages and enhanced their function as compared to control, suggesting the herb as a potential natural drug for immunostimulant effect.

6.5. Antioxidant Activity

The antioxidant activity of methanol extracts of stem and leaves of *S. acmella* were measured using DPPH and superoxide radical scavenging assays [38]. The result showed the methanol extract of stem of *S. acmella* to have the highest superoxide radical scavenging activity while leaves showed maximum DPPH scavenging activity. In superoxide radical scavenging assay, highest radical scavenging activity was observed in stem and callus, while minimum superoxide radical scavenging activity was found in roots. In DPPH radical scavenging activity was found maximum in leaf and minimum in in root. Callus showed significant DPPH radical scavenging activity [38].

7. Biocidal Activity

7.1. Insecticidal Activity and Pesticidal Activity

Potential beneficial uses as an insecticide or antiseptic of the extracts of genus Spilanthes plants have been investigated. Several studies have reported that *S. acmella Murr.* or *S.mauritiana* extracts have significant insecticidal activity on mosquito larvae of various species [7]. Kadir et al. [39] Identified spilanthol as the active ingredient and showed that spilanthol was more acutely toxic to cockroaches by topical application than common pesticides such as carbaryl, lindane and bioresmethrin. The cockroaches showed tremors immediately after application and electrophysiological tests indicated a hyper-excitation of the cereal nerve followed by complete inhibition of nervous activity.

7.2. Antifungal Activity

Contrary to folk medicine use for thrush, extracts of *S. mauritiana* did not show activity against Candida albicans, antifungal activity was observed [40]. Different concentrations of *S. acmella* flower head extract (dried flower heads extracted with petroleum ether) were evaluated for antifungal activity (0.1 to 2.0 mg). The diameter of inhibition zones ranged from 0.1 to 2.3 cm with the increase in concentration of test solution. In all the organisms, the maximum zone of inhibition was observed at 2000 mg concentration [41].

7.3. Antibacterial Activity

Extracts of *S. mauritiana* were also screened against 105 bacterial strains including H. pylori, but found to have little antibacterial activity [40]. The different fractions were isolated from crude ethyl acetate extract of *S. acmella* and were studied against 27 strains of microorganisms. The results showed that fraction E3 completely inhibited the growth of *Corynebacterium diphtheriae* with MIC value of 128 µg/mL.

8. Toxicological Studies

8.1. Acute Toxicity

De et al. [42] reported the LD50 in mice to be 23 .5 mg/kg following intraperitoneal injection of an extract of *S Americana*. Clinical observations prior to death included irritability, trembling and convulsions. Intraperitoneal (IP) administration to rats of the extract of *S.americana* flowers resulted in rapid death accompanied by convulsions [43] the LD5o was estimated at 128 mg/kg by IP injection and 336 mg/kg by subcutaneous dosing. Extracts using hexane of freshly harvested flowers of *S. acmella* were bioassayed against *Aedes aegypti* (yellow fever mosquito) larvae and *Helicoverpa zea* (the corn earworm moth)

neonates. Spilanthol proved effective at killing mosquitoes, with an LD_{100} (at 24 hours) at a concentration of 12.5 µg/mL and showed 50% mortality at 6.25 µg/mL.The mixture of isomers of spilanthol showed a 66% weight reduction of *H. zea* neonate larvae at 250 µg/mL concentration after 6 days [7].

8.2. Neurotoxicity

Herdy et al. [44] reported that spilanthol interfered with the fast component of the action potential and caused depolarization in heart atrial nerve cells. Moreira et al. [45] produced rapid clonic-tonic seizures similar to epileptic seizures in rats at levels of 100 mg/kg *S.acmella var. oleracea* extracts by IP dosing. Following dosing, the animals had tremors and began to convulse in about two minutes. EEG recordings also show spiking activity by this time. A threshold for acute toxicity was observed since treated animals that did not die recovered to normal behavior and EEG recordings within an hour [42] evaluated the extract of *S. americana* flowers in several pharmacological tests on motor activity, central and peripheral nervous system function. The extract was reported to have a cholinergic action on the central nervous system as well as the common CNS stimulatory effect of anesthetics.

8.3. Genotoxicity

Extracts of *S. calvus* and eugenol were added to tobacco extracts in the Ames/Salmonella test [46]. Both materials significantly reduced the mutagenic activity of the tobacco extract. They also significantly inhibited the nitrosation of methylurea by nitrite to form the mutagenic nitrosourea.

9. CONCLUSION

This review has focused on the biomedical applications, Pharmacological activity, Biocidal Activity and Toxicological Studies. Biomedical applications, which includes treatment of Toothache, Diuretic and renal stones, Scurvey, scabies, psoriasis, Hepatoprotective, malaria, rheumatisms, gastrointestinal diseases, other biomedical uses. Pharmacological activity includes antioxidant activity, immunomodulatory activity, vasorelaxant activity, analgesic, anti-inflammatory Effect. Biocidal Activity includes Insecticidal activity and Pesticidal activity Antibacterial activity, Antifungal activity. Toxicological Studies includes Acute Toxicity, Neurotoxicity Genotoxicity of the plant *Acemella oleracea.*

Acemella oleracea is a plant with much potential and is useful in many diseases. Though *Acemella oleracea* has various medicinal applications, but it is the need of hour to explore its

medicinal values at molecular level with help of various biotechnological tools and techniques. Further studies should be conducted to elucidate the molecular mechanism of interaction of various plant based drugs with human in different diseases.

Conflict of interest statement: We declare that we have no conflict of interest.

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