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## SPILANTHES ACMELLA: A UNIQUE MEDICINAL HERB

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### ABSTRACT

An essential medicinal plant, *Spilanthescmella* is found in tropical and subtropical regions, primarily in South America and India. It is commonly referred to as the "toothache plant," as it may both stimulate salivation and lessen the discomfort associated with toothaches. This plant has a variety of extracts and active metabolites that have beneficial pharmacological properties in different regions of the plant. According to a literature review, it possesses a variety of pharmacological actions, such as antimicrobial, antinociception, diuretic, vasorelaxant, anti-human immunodeficiency virus, antifungal, antipyretic, local anesthetic, bioinsecticide, anticonvulsant, antioxidant, aphrodisiac, analgesic, and pancreatic lipase inhibitor properties. The phytochemistry, pharmacology, toxicity, and traditional applications of this plant are all covered in detail in this paper. The toothache plant, *Spilanthescmella*, has long been utilized in ayurvedic medicine for dental conditions. Numerous research on its phytochemicals have been published, based on its historical use in food and medicine. An overview and general description of the plant species, bioactive metabolites, and significant pharmacological activities, such as preparation, purification, and large-scale in vitro synthesis, are given in this review. The links between the bioactive chemicals' structures and activities have been examined. It is possible to show that *S. acmella* has a wide range of bioactive qualities and is widely used in medicine, healthcare, cosmetics, and dietary supplements by taking into account data from the literature. Being a nutritious food, it has a great therapeutic value and lots of room to grow.

**Keywords:** Anti-Inflammatory, Analgesic, Antipyretic, Local Anesthetic, Bioinsecticide, Anticonvulsant, Antioxidant.

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### I. INTRODUCTION

People are finding that the growing demand for herbal medications and their acceptability in the global market due to their strong pharmacological potential and high therapeutic value are true blessings. To introduce ayurvedic medications as first-line treatments, however, research, standardization, and validation of their potency, safety, and effectiveness are required. Popular asteraceae and kingdom Plantae plant *Spilanthescmella* has long been used therapeutically to cure a variety of illnesses.<sup>[1]</sup> *S. acmella* Murr., also referred to as Phak-KradHauwaen in Thai, has been used in traditional remedies to cure a variety of conditions, including fever, flu, cough, rabies illnesses, TB, malaria, bacterial infections, skin conditions, scurvy, and stomach ulcerative disorders [2-10]. It has also been shown that *S. acmella* Murr. has the ability to regulate immunological response [9], promote digestion, and manage obesity [11,12]. Due to the plant species' strong local anesthetic effects, tooth pain has also been effectively relieved by using it [13].

When it comes to pharmacology, *S. acmella* Murr. has demonstrated a broad variety of bioactivities. These include antipyretic [15], diuretic [18,19], antifungal [17], anti-inflammatory [16], vasorelaxant [18,19], antioxidant [20,21], antiplasmodial [6], and antibacterial [22]. Furthermore, from *S. acmella* Murr. preparations, a range of physiologically active compounds were recovered, such as 3-acetylaleuritolic acid, vanillic acid, bsitostenone, scopoletin, ferulic acid, and isoferulic acid [23]. Studies conducted on mice have revealed that spilanthol has sexual qualities in addition to the advantages already mentioned [24]. A penile erection, mounting frequency, intromission frequency, and ejaculation frequency improvement that lasted for at least two weeks after the animal was weaned off of the medication also showed that men's sexual performance was improved by the treatment.[25]

## II. TAXONOMICAL CLASSIFICATION

<b>Kingdom</b>	Plantae
<b>Subkingdom</b>	Tracheobionta
<b>Phylum</b>	Tracheophyta
<b>Division</b>	Magnoliophyta
<b>Super division</b>	Spermatophyte
<b>Class</b>	Magnoliopsida
<b>Sub Class</b>	Asteridae
<b>Order</b>	Asterales
<b>Family</b>	Asteraceae
<b>Subfamily</b>	Mimosoideae
<b>Genus</b>	Spilanthes
<b>Species</b>	Acmella <sup>[26,27]</sup>

**Synonyms:** Jambu, Toothache plant, Electric daisy, Buzz buttons, Schezuan buttons, Jotang, jocong and Dung getang, Akarkara, Jotang, jocong and Xiao tong chui, Tian wencao, Bian di hong. [26,28]

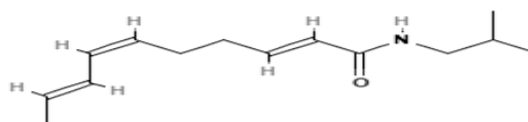
**Botanical description:**



**Figure No.01.** Flowers of plant S.acmella



**Fig.No.2:** leaves of plant S.acmella



**Fig.No.3:** Structure of S. Acmella

Approximately 60 species of the genus *Spilanthes* (Compositae or Asteraceae) are found worldwide in tropical and subtropical areas, including Africa, America, Borneo, India, Sri Lanka, and Asia [29]; [30]. Brazilian in origin, *S. acmella* is grown all year round as a decorative or therapeutic plant. At 40–60 cm in height, it is an annual or short-lived plant. Low germination rate or poor vegetative propagation are two of its growing conditions [30, 31]. It is cultivated in moist areas. When handled, the leaves and blooms of this plant cause tingling and numbness and have a strong flavor [30]. The plant species has been widely used as a traditional medicine, for example, for fever, rheumatism, and toothaches [31], as a fresh vegetable [30], and as a spice for Japanese appetizers [32].

### Phytochemicals :

A variety of bioactive chemicals may be present in medicinal plants used in traditional medicine, and these compounds may have important physiological effects on human health. Isobutyl amide derivatives [33], amino

acids,  $\alpha$ - and  $\beta$ -amyrin esters, myricyl alcohol, including sitosterol glucosides [34], and triterpenoid [35] have all been found to be present in *S. acmella* phytochemically. Alkamides have been identified as secondary metabolites in eight plant families, including Asteracea [36]. The most important alkamide in the genus *Spilanthes* is spilanthol. Alkamides are thought to be the most abundant phytochemicals in the species.

The primary volatile substance in *S. Acmella* that is in charge of a number of biological processes is called spilanthol, or N-isobutylamide. (2E, 6Z, 8E)-N-isobutylamide-2,6,8-decatrienamide is the clarified structure of spilanthol [37]. Spilanthol has been found in the mother plant, flower heads, and in vitro plantlets of *S. acmella*, according to a gas chromatography-mass spectrometry (GC-MS) investigation [38]. The main metabolites of *S. acmella* that exhibit potent antioxidant action are phenolics (vanillic acid, trans-ferulic acid, and trans-isoferulic acid) and stigmasteryl glucoside [39]. The bioactive components of *S. Acmella* have exceptional pharmacological activity, according to the literature. Numerous bioactivities, such as local anesthetic and antipyretic [40], diuretic [41], antifungal [42], antiplasmodial [43], antimicrobial [44], and insecticidal activities [45], are demonstrated by *S. acmella*'s pharmacological properties.

#### **Traditional uses:**

Because of its numbing qualities, an extract from the leaves and blossoms is traditionally used to treat toothaches, stomatitis, fever, cough, rabies illnesses, TB, and throat complaints[46]. Fever and rheumatism have also been treated with it [47, 48]. It can dissolve urinary calculi and has potent diuretic action[49]. Additionally, it demonstrates antibacterial, antiseptic, and antimalarial qualities[46]. The leaves have several applications such as digestive, lithotriptic, antiscorbutic, immunomodulatory, adaptogenic, and ailagogene [50]. The plant's most potent antiseptic alkaloid, pilanithol, is powerful against blood parasites even at very low concentrations and poisonous to most invertebrates, but innocuous to warm-blooded animals[51]. Chewing the flower heads of *S. acmella* can act as a haemostatic, analgesic, and pain reliever in addition to relieving toothache[52].

The Ayurvedic medical system uses flower heads and roots to treat a variety of conditions, including scabies, psoriasis, scurvy, gum infections, periodontosis, paralysis of the tongue, children's stammering, and mouthwashes [53–55]. Excellent antimicrobial activity against red halophilic cocci from salt-cured fish was another trait that *S. acmella* possessed[46]. Its extract is a potent ingredient in cosmetics for beauty care that works quickly to relax muscles and hasten the healing of functional wrinkles[56]. In anti-aging applications, such as anti-wrinkle cream compositions, the plant extract was also utilized to stimulate, reorganize, and reinforce the collagen network[56,57]. When applied as an insecticide, spilanthol has strong larvicidal, pupicidal, and ovicidal properties [58]. A fungal skin ailment that includes athlete's foot, ringworm, and nail infections was treated with *S. acmella* by an Indian tribe [58].

### **III. PHARMACOLOGICAL ACTION**

#### **1. Toothache**

*Spilanthesacmella* is commonly referred to be an anti-toothache herb. People chewed on the strong flower heads of the plants to relieve themselves of dental ache, throat issues, or tongue paralysis. Spilanthol is the component that's accountable for this.[60]

#### **2. Local Anesthesia**

The lack of feeling in a specific region of the body resulting from blockage of the conduction process or decrease of excitement in nerve terminals is known as local anesthesia.(61)

Research conducted by Chakraborty and colleagues demonstrated the effectiveness of xylocaine as a local anesthetic.[62]

#### **3. Dentifrice**

Mouth rinses and dental pastes have been made with spilanthol. In addition to improving hunger by increasing salivation, the goal is to deliver a long-lasting fresh minty flavor. People with toothaches can brush more easily because the spilanthol in it also has a minor anesthetic effect.[63]

#### **4. Anti BacterialActivity**

According to research by Noor Jahan et al., the ethanolic extract of *Spilanthesacmella* exhibited antimicrobial activity against a variety of bacteria, including *Salmonella typhi*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Enterococcus faecalis*, and resistant bacteria with the

Blagene.In [64] Gram positive and gram negative activity against 27 different bacterial strains is also demonstrated by S. Acmeella's Agar Dilution Assay.Reference [65]

#### 5. Anti-fungal Activity

The antifungal activity of S. Acmeella is just marginal. Nonetheless, it has been demonstrated that they are active against the fungus *Microsporiumgypseum* and *Cryptococcus neoformans*, which are frequent opportunistic infections in AIDS patients.[66]

#### 6. Periodontitis

Gum irritation is the cause of periodontitis. Chewing on the roots and flower heads has been used to treat periodontitis and has been demonstrated to reduce gum inflammation.[67]

#### 7. Diuretic and Renal Stones

As a result, diuretics help excrete more water from oedematous tissue by increasing the production of urine. "Diuretics" are medications that cause diuresis to occur. Strong diuretic action and urinary calculi dissolution are two of *A. oleracea's* medicinal qualities [68]. Cold water was used to establish [69] that *A. oleracea* had a potent diuretic effect in rats. The findings indicated that when taken orally in a single dose, the maximum dosage of flowers examined exhibited potent diuretic action. Strong evidence that the cold water extract is functioning as a loop diuretic is provided by the urine's modest acidity.Inhibiting the  $\text{Na}^+/\text{K}^+/\text{Cl}^-$  co-transporter system in the thick ascending loop of the nephron increases natriuresis (the expulsion of salt from the urine) and kaleuresis (the expulsion of potassium from the urine). Loop diuretics are the strongest kind of diuretics [70,71]

#### 8. Immunostimulant Activity

In addition to being reported to have immunostimulant effect, *S. acmeella* leaves have been traditionally employed as a sialogogue, tonic, and in the treatment of gout, rheumatism, and gout [72]. Several experimental models were used to conduct the inquiry. By boosting the amount of macrophages with the largest number of cells on the fifteenth day, the EtOH leaf extract demonstrated notable immunomodulatory action [72]. Alkamides, pungent amides, tannins, sugars, carotenoids, essential oils, sesquiterpenes, and amino acids were among the chemicals found in *S. acmeella* leaves [73], [74], [75],[77], and [77]. It has been documented that spilanthol stimulates the immune system and reduces the inflammatory response in mouse Raw 264.7 macrophages [78]. Moreover, certain alkamides are ingested to strengthen the immune system, which helps treat respiratory infections and colds. and influenza [79].

#### 9. Antimutagenic Activity

A chloroform extract of *S. calva* flower buds inhibited mutagenicity in a dose-dependent manner. Utilizing the Ames salmonella/microsome experiment, *S. calva* extract demonstrated a greater degree of mutagenesis inhibition (86.4%) [80]. These extracts include high concentrations of alkamides and flavonoids, which may be the cause of their action.

#### 10. Anticancer Activity

*Spirulina's* anticancer activity was evaluated in an immortal neuroblastoma with spontaneous malignant genesis, demonstrating tumoricidal effects at concentrations ranging from 10  $\mu\text{g}/\text{mL}$  to 5  $\text{mg}/\text{mL}$ . The results are regarded as poor since they did not show any pattern of tumoricidal effects with anticancer screen category 5 [81].

#### 11. Antipyretic Activity

For a long time, antipyretics have been made from a variety of medicinal plants, such as *S. acmeella* (flower and aerial aqueous) extracts (Chakraborty et al., 2010[82]). According to Elumalai et al. (2012)[83], fever, or pyrexia, is typically brought on by the secondary effects of infection, tissue damage, inflammation, transplant rejection, cancer, and other illnesses. The aforementioned effects trigger the production of pro-inflammatory mediators, specifically cytokines such as interleukin  $1\beta$ ,  $\alpha$ ,  $\beta$ , and  $\text{TNF-}\alpha$ . As a result, the body produces more prostaglandin E2 (PGE2), which raises body temperature [83]. The results of the research demonstrated that the aerial aqueous extract of *S. acmeella* had antipyretic efficacy against pyrexia produced by Brewer's yeast. Plant species possess antipyretic effect due to flavonoids [84,85], which were shown to be the main inhibitors of either lipoxygenase (LOX) or cyclooxygenase (COX) [86]. It is well recognized that flavonoids target prostaglandins during the latter stages of acute pain and inflammation. [87]

### 12. Anti-inflammatory and Analgesic:

Aqueous extract of arial 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[17]. Spilanthol shows significant anti-inflammatory activity on lipopolysaccharide-activated murine macrophage model RAW 264.7, partly from Anti-inflammatory and Analgesic: Aqueous extract of arial 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[17]. Spilanthol shows significant anti-inflammatory activity on lipopolysaccharide-activated murine macrophage model RAW 264.7, partly from Anti-inflammatory and Analgesic: Aqueous extract of arial 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[17]. Spilanthol shows significant anti-inflammatory activity on lipopolysaccharide-activated murine macrophage model RAW 264.7, partly from Anti-inflammatory and Analgesic: Aqueous extract of arial 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[17]. Spilanthol shows significant anti-inflammatory activity on lipopolysaccharide-activated murine macrophage model RAW 264.7, partly from Anti-inflammatory and Analgesic: Aqueous extract of arial 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[17]. Spilanthol shows significant anti-inflammatory activity on lipopolysaccharide-activated murine macrophage model RAW 264.7, partly from Anti-inflammatory and Analgesic: Aqueous extract of arial 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[17].

### 13. Anti-inflammatory and Analgesic

The aqueous extract of *S. acmella*'s arial portion shown strong anti-inflammatory and analgesic activities in experimental animal models by inhibiting paw edema in a dose-dependent manner and increasing pain threshold[88]. NF-KAPPA B's inactivation, which negatively affects the synthesis of pro-inflammatory mediators, is one of the ways that spilanthol exhibits significant anti-inflammatory effect in lipopolysaccharide-activated murine macrophage model RAW 264.7[89]. Using the tail flick and hot plate tests, the analgesic efficacy of various dosages of aqueous extract of fresh flowers was determined in male rats at various post-treatment intervals. The sedative effect is complemented by supraspinal analgesic activity[91].

### 14. Vasorelaxant and antioxidant activity

The plant extracts elicited vasorelaxation action by partial endothelium generated nitric oxide and prostaglandin-I<sub>2</sub> in a dose-dependent manner. It is noteworthy that the ethyl acetate extract of *S. Acmella* demonstrated rapid vasorelaxation action at nanogram levels, given that it is the most powerful antioxidant in the diphenyl picryl hydrazine assay (DPPH assay). Conversely, chloroform extracts exhibited the largest content of antioxidants and the strongest vasorelaxation action [92,93]. Researchers found that the presence of tannins, flavonoids, and phenolic substances [94–96] contributed to the antioxidant potentiality of *S. acmella* leaf extracts.

### 15. Bioinsecticide and convulsant activity

For the genus *Spilanthes*, there were about 42 recognized species. Numerous insecticidal chemicals have been shown to be present in *Spilanthes alba*, *Spilanthes mauritiana*, *Spilanthes mauritiana oleracea*, *Spilanthes mauritiana ocymifolia*, and *S. acmella* [97-99]. When the typical electrographic convulsions in the electroencephalogram were accompanied, the hexanic extract of *S. acmella* was shown to cause epilepsy in rats [93].

### 16. Antimalarial activity

Malaria is treated with *S. acmella*, a traditional remedy used in Africa and India [100]. Pharmacological analysis revealed that two strains of *Plasmodium falciparum* (the chloroquine-resistant K1 strain originated from Thailand and the PFB strain originated from Brazil) were susceptible to the antimalarial effects of spilanthol (1) and acetylenic alkamide (undeca-2E-ene-8,10-diyonic acid isobutylamide, or UDA) (3), which were separated from the root EtOH extract of *S. acmella*. With an IC<sub>50</sub> ranging from 5.8 to 41.4 µg/mL, both compounds were shown to have antimalarial action, with spilanthol being the most effective. Semi-purified *S. acmella* compounds were shown to have much better antiplasmodial action as evidenced by the decreased IC<sub>50</sub> value. These compounds were extracted using centrifugal partition chromatography (CPC) and electrospray ionization-ion trap-time of flight-mass spectrometry (ESI-IT-TOF-MS)[101].N-alkylamides' synergistic effects in the investigated substances may be the cause of this. The in vitro root hexane extract of regenerated *S. Acmella* also shown 100% larvicidal activity, resulting in the lowest values of LC<sub>50</sub> and LC<sub>90</sub> against filarial vectors and malaria [102]. A larger active principle content was suggested to be present in the regenerated plant species

compared to field-grown ones. Furthermore, the research revealed *S. acmella*'s potential for both malaria therapy and prevention. [103]

#### IV. CONCLUSION

In the traditional medical system of India, *Spilanthescmella* is a well-known herb with a variety of pharmacological actions and little side effects. We provided a detailed summary of ethnobotany, phytochemistry, pharmacology, and toxicity in this paper. This plant's phytoconstituents and extracts have been demonstrated to elicit a variety of pharmacological responses, including diuretic, antimalarial, anticonvulsant, analgesic, and anti-inflammatory actions. This herb is most commonly used in South America and India to treat toothaches. *Spilanthescmella* is also traditionally used as a stomachic, stimulant, antidiarrheal, and infrequently as a treatment for TB. Numerous researches have shown that the whole plant possesses aphrodisiac, anti-inflammatory, antioxidant, antinociception, immunomodulator, and insecticidal properties in addition to local anesthesia. However, it has been demonstrated that the floral component contains diuretic, vasorelaxant, antifungal, and pancreatic lipase inhibitory qualities. We are able to evaluate *Spilanthescmella* because of its many traditional uses and pharmacological reactions. The scientific community will receive a succinct summary of all the scientific material from this evaluation.

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