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Toothache plant: A comprehensive review focusing on its applications in dental health



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ARTICLEINFO	A B S T R A C T
Article Type: Review	The contemporary era showcases a growing emphasis on alternative medicine, specifically the utilization of ethnomedicine, which has gained significant attraction in recent times. This
Article History: Received: 3 April 2024 Accepted: 30 May 2024 epublished: 25 December 2024	review explores the curative properties and ethnomedicinal utilization of the "Toothache plant" belonging to the Asteraceae family, the most common weed in crop fields. "Toothache plant" has added noteworthy attention in dentistry due to its unique properties. The toothache plant is well-known for providing numbing and analgesic effects by simply chewing the flowers due to the presence of active compounds such as Spilanthol. The analgesic property makes the plant a potential candidate for natural pain relievers, particularly in dentistry.
<i>Keywords:</i> Oral diseases, Phytometabolites, Spilanthes paniculata, Herbal medicine, Toothache plant	Besides its dental application, this plant is used as an antidote for snake bites. This review summarises the ethnomedicinal values and clinical applications of the toothache plant, with a particular focus on oral health care, and the findings presented herein are anticipated to help in future research.

Implication for health policy/practice/research/medical education:

The toothache plant has local anesthetic properties and exhibits efficacy in treating several oral ailments, including oral ulcers, oral cancer, and periodontitis. Its analgesic property makes the plant a potential candidate for natural pain relievers, particularly in dentistry.

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Introduction

The most prevalent oral diseases include dental caries, gingivitis, and periodontitis. Several medicinal methods including ointments, mouth rinses, and pain relievers, have been effective in maintaining oral health; however, they come with challenges. Alcohol-based mouth rinses may lead to substantial inflammation and irritation, potentially causing the shedding of the protective epithelial layer. This shedding can result in the emergence of canker sores and the teeth may become discolored as a result (1). Oral ointments and gels used to treat various oral diseases often have an unpleasant taste and odor, which is unacceptable by patients. In this context, the genus Spilanthes is regarded as a traditional medicine for treating several disorders, particularly oral ailments. Six species in India represent the genus (2). One such

species is Spilanthes paniculata, commonly known as the toothache plant, which has attracted the attention of researchers as it holds the potent secret of anesthetic and analgesic properties. The toothache plant has numerous therapeutic potentials, and the herb is extensively used as a folk medicine in many regions of the world. This is commonly employed in the treatment of rheumatism, tuberculosis, and rabies, as well as gastrointestinal problems, fever, flu, cough, and headache. The plant is also well appreciated for its diuretic effect, endorsing increased urine production and aiding in the detoxification of toxins from the body (3). Moreover, this plant is a rich source of minerals and vitamins, especially vitamin C, which makes it beneficial in curing scurvy caused by the deficiency of vitamin C (3). The roots and flower heads are well known for the healing of scabies and psoriasis. The leaves

also aid in controlling obesity and help alleviate various skin disorders (4). Additionally, the toothache plant is considered a powerful herb for stimulating digestion. The leaves and flowers are known to treat leucorrhoea, a condition characterized by abnormal vaginal discharge (5,6). This plant is also widely used in the treatment of several oral ailments. Chewing the flower heads of toothache plants can give an instant anesthetic effect. Earlier studies of the toothache plant have emphasized its traditional therapeutic applications, particularly its anesthetic and analgesic effects. Studies often focus on its ethnobotanical significance, phytochemical analysis, and pharmacological properties. Some studies have also investigated its potential applications in non-oral health issues. While previous studies have discussed the therapeutic potential of toothache plants, there is still a need for a complete evaluation that consolidates existing knowledge and delves deeper into its clinical applications (3). This review article aims to fill this gap by offering an in-depth comprehensive overview of the toothache plant's taxonomic position, global distribution, active phytocompounds, and clinical applications.

The findings of this study are anticipated to provide information regarding the therapeutic benefits of the toothache plant in treating oral disorders. Furthermore, it may inspire further study into the development of novel oral health products or treatments employing the unique properties of this plant.

Methods

A comprehensive and fundamental literature review was conducted to collect the various phytoconstituents, and therapeutic uses with special reference to oral health and clinical trials of the toothache plant. Several online databases were evaluated such as EBSCO, Scopus, PubMed, NCBI, and Google Scholar between 2008 and 2023 years with the keywords "Spilanthes", "Toothache plants", "*Spilanthes acmella*" and "*Spilanthes paniculata*". The key data-gathering resources for this review article were the papers published by several reputable publishers such as Springer, Taylor & Francis, Elsevier, and Hindawi. In this study, we gathered many biological activities of the toothache plant, which will provide researchers with a thorough understanding of the clinical and pharmacological activities.

Taxonomic position and common uses

The genus *Spilanthes* encompasses approximately 300 species, six of which are found in India: *Spilanthes paniculata* DC., *Spilanthes oleracea, Spilanthes radicals* Jacq., *Spilanthes uliginosa* Sw., *Spilanthes ciliata* Kunth and *Spilanthes calva* DC (2). *S. paniculata* belongs to the Asteraceae family with the following taxonomic position: Kingdom: Plantae Phylum: Tracheophyta

Class: Magnoliopsida Order: Asterales Family: Asteraceae Genus: Spilanthes Species: *paniculata, oleracea, radicals, uliginosa, ciliata, calva*

The English names of this plant include toothache plant, para cress, electric daisy, and ting flowers. Besides this, in India, there are various vernacular names for the plant such as Akarkar in Hindi, Biribiri in Odia, Palluvedanachedi in Malayalam, Maratiteega in Marathi, Mandal poo chedi in Tamil Nadu (7). In other countries, it is called Jhummosak in Bangladesh and Bhuin Timur in Nepali (8). Spilanthes species due to their easy availability, are extensively used for culinary purposes. The flowers and leaves when consumed give a numbing and tingling sensation. The leaves can be incorporated into salads to enhance the flavors. Fresh and dried leaves can also be added to stews and soups by combining the leaves with garlic and chilies. Additionally, the oil or extract of the toothache plant can be used as a flavoring agent in chewing gums and chewing tobacco. Beyond its culinary practices, the plant is used in cosmetics as an anti-wrinkle agent due to its antioxidant properties. Interestingly, in many parts of India, the plant is used as a traditional remedy for snake bites (9).

Botanical description

Toothache plant, a member of the Asteraceae family with its distinctive inflorescence, is considered the most prominent plant family. Another striking feature of the Asteraceae family is stamens with united anthers. The botanical description of the different species of toothache plants is summarized in Table 1.

Ecological condition and global distribution

The genus Spilanthes thrives in direct sunlight at temperatures ranging from 65 to 85 degrees Fahrenheit. The herb grows best in loamy, well-drained soil with a pH of 6.1 to 6.5. Although they flourish in bright sunshine, they are sensitive to cold temperatures and cannot tolerate freezing temperatures, therefore, they cannot endure a frosty climate. All the species of toothache plants relatively require low maintenance and grow rapidly. Spilanthes species are found throughout the world's tropical and subtropical zones (10). Brazil, South America, Bangladesh, China, Colombia, Borneo, Ecuador, Africa, Malaya, India, Indonesia, Nepal, Papua New Guinea, Peru, Solomon Islands, Sri Lanka, Taiwan, Thailand, and Vietnam are its native regions. In India, it is widely distributed to Andhra Pradesh, Assam, Chhattisgarh, Goa, Gujarat, Himachal Pradesh, Kerala, Karnataka, Meghalaya, Maharashtra, Madhya Pradesh, Odisha, Rajasthan, and Tamil Nadu (11).

The toothache plant is a prevalent species in many regions of Odisha. It is commonly seen in fields of

Table 1. The botanical description of different species of toothache plants

Species	Foliage	Inflorescence	Stem	Root	Figure
Spilanthes paniculata	Ovate to lanceolate in shape with a pointed tip. They have smooth and shiny surfaces that are arranged alternately along the stem	Cone-shaped yellow flower heads. They are disc-like, solitary, and borne in panicles carried on stalks ranging from 2.5-16 cm in length. Achenes are ovoid	Branched, thick, amaranths, ascending, and can grow up to 30 cm long. Each stem bears flowers.	Cylindrical, featuring a brown color on their external surface and have hairy rootlets	
Spilanthes calva*	Stalked, ovate to ovate, lanceolate, pointed tip, base narrow	Panicled spot flower, heads are disc-like without any ray floret 2.5-16 cm long stalk	Vranched, erect, or ascending, and can grow up to 30 cm long	Cylindrical, brown color on their external surface, and have hairy rootlets	
Spilanthes oleracea*	Egg-shaped triangular with a toothed leaf margin	Yellow and red flower heads sometimes have a red color center.	Prostrate or erect, often reddish, hairless.	Cylindrical, brown color on their external surface and have hairy rootlets	
Spilanthes filicaulis [*]	Ovate, base attenuate, margins dentate, narrowly winged	Yellow or slightly orange with many disc florets,	Sappy, reddish or purplish, glabrous	Cylindrical, brown color on their external surface, and have hairy rootlets	
Spilanthes uliginosa*	Simple and opposite leaves and oval shape	Conical yellow heads, borne by a very long peduncles, achenes with ciliated margin	Cylindrical, branched, fleshy, slightly striated.	Pivoting, densely branched	
Spilanthes ciliata*	Ovate, base rounded, serrate margins	Yellow flower heads, axillary, subglobose	Terete stems	Cylindrical, rooting at lower nodes	

The "*" mark images were taken from Google.

sugarcane, paddy, and black and green gram as a weed. It is often available in all the districts of Odisha; however, it is abundant in the districts of Angul (12), Bolangir (12), Bhadrak (13), Cuttack (14), Dhenkanal (15), Kendrapara (16), Khordha (17), Malkangiri (18), Mayurbhanj (12), and Sundargarh (12). The distribution of toothache plants in Odisha within India is presented in Figure 1.

Phytochemicals present in "Toothache plant"

In different species of the genus Spilanthes, several phytometabolites with distinct features are present that aid in treating several ailments. The Gas chromatography with mass spectra (GCMS) analysis of *S. filicaulis* leaves has revealed 10 phytocompounds with 13-octadecenal and Ar-turmerone being the predominant ones (19).

Leng et al studied and concluded that spilanthol was the major phytocompound found in the mother plant, flower heads, and in vitro plantlets of *Spilanthes acmella*. Spilanthol exhibits a distinct anesthetic effect accompanied by increased saliva flow (20). In addition, studies reported that *S. calva* dry extracts contained phenolics (459.89 mg gallic acid equivalent per gram) flavonoid (123.59 mg quercetin per gram), and tannins (22.83 mg gallic acid equivalent per gram) (21). Phenolics are well known for their antioxidant properties; flavonoids have been reported to have anti-tumor, anti-viral, and anti-inflammatory activities. Tannins have been reported to possess antimicrobial and anti-carcinogenic properties (22).

Begum et al studied the GCMS analysis of the essential oil from the inflorescence of *S. calva* DC and identified seven phytocompounds caryophyllene oxide (24.14%), caryophyllene (22.19%), limonene (21.79%) and myrcene

(9.02%), as significantly dominating compounds (23). Masoko studied Spilanthes mauritiana extracts and revealed the presence of tannins (23.9±1.18 mg gallic acid equivalent per gram)), phenols (52.47± 2.29 mg gallic acid equivalent per gram), and flavonoids (25.1 \pm 0.79 mg quercetin per gram) (24). Sharma et al studied the GCMS of S. ciliata extract and revealed the presence of 15 different compounds in the oil. 11-Tridecene-2R-1,3,3-trimethyl-4T-(3-methyl-2-buten-1-yl)-1-ol, 1T-cyclohexanol, pentadecanoic acid, 1-hexacosanol, nonadecane, and hexatriacontane were found to be the major constituents (25). Uraku studied the leaf extract of S. uliginoia; the major phytocompounds identified were hexadecanoic acid, hepta-9, 10, 11-trienoic acid, octadecenoic acid, 5-hydroxylmethyl heptadecane, docosane aldehyde, and 1-ethoxyoctadecane (26). Furthermore, Zhu et al reported that the essential oil of S. paniculata contained sesquiterpene hydrocarbons (41.16%), monoterpene hydrocarbon (15.86%),monoterpenoids (14.62%), sesquiterpenoids (8.46%) and others (18.11%). Sesquiterpenes have antimicrobial activity. Monoterpenes have antiviral, antioxidant, and anti-inflammatory properties. This analysis provides valuable insights into the phytochemical profile of toothache plants and provides further understanding of its therapeutic properties (27).

A study conducted on the free amino acids of the pollen of *S. acmella* revealed approximately 4% amino acids. Among these amino acids, tyrosine is present in high concentrations (1.800 mol/mg dry weight). In addition, amino-n butyric acid, aspartic acid, glycine, histidine, proline, and a few unknown amino acids that did not match the standard amino acids were also detected (Figure

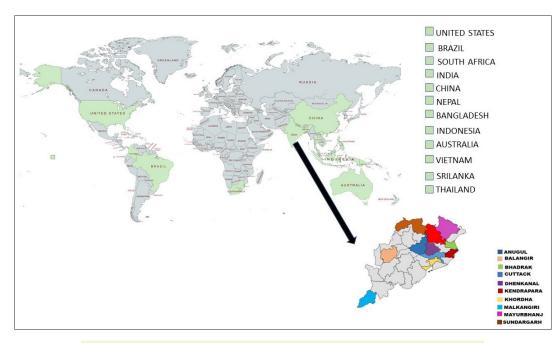


Figure 1. The global distribution as well as the distribution of toothache plants in Odisha, India.

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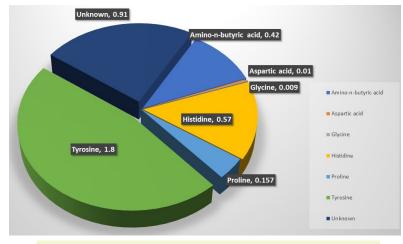


Figure 2. Pie chart showing the free amino acids present in Spilanthes acmella.

2). Glycine is recognized for its anti-aging and immuneboosting ability, whereas proline plays a crucial role in protein synthesis and is essential in the wound healing process (28) (Table 2).

Role of spilanthol

Spilanthol ($C_{14}H_{23}$ NO), the principal phytocompound present in almost all species of toothache plants, with a molecular weight of 221.339 g/mol exerts several pharmacological activities such as analgesic, antiinflammatory, anticancer, antioxidant, and antimicrobial activities (31). Several studies were carried out for the evaluation of the analgesic effect of spilanthol. Studies revealed that spilanthol within 30 seconds after administration at 1×10^{-4} M concentration induced the release of gamma-aminobutyric acid (GABA) (32). The effectiveness in inducing analgesia was quantified by determining its median effective dose (ED50), which was found to be 6.98 mg/kg (31). The mechanism underlying the analgesic effect of spilanthol is due to the increased level of release of GABA within the temporal cerebral cortex (33). GABA is an amino acid that serves as an inhibitory neurotransmitter, thereby lessening the capacity of a nerve cell to receive, generate, or transmit chemical signals to the neighboring nerve cells (34).

It has also been reported that spilanthol inhibits inducible nitric oxide synthase (iNOS) expression; nitric oxide (NO) production protects from NO-dependent cell death and suppresses inflammatory transcription factors (TFs) such as NF- κ B, ATF4, FOXO1, IRF1, ETS, and AP1 (35).

Nanoparticles present in "Toothache plant"

The nanoparticles derived from plants are well recognized for their non-toxic and eco-friendly nature. These nanoparticles have a wide range of applications, including antifungal, antioxidant, antibacterial, and anticancer properties. According to several studies, it has been reported that various species of *Spilanthes* species can produce diverse types of nanoparticles. Durga et al studied the green synthesis of silver nanoparticles using selected *Spilanthes* Jacq. species from South India. Among

Table 2.	The p	hytochemicals	present in diffe	rent species of	Toothache plants
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Name of phytochemicals	Species	Functions	References
Spilanthol	Spilanthes acmella	Analgesic, anti-inflammatory, neuroprotective	(29)
β-Pinene	S. paniculata Acmella uliginosa	Antibacterial, antidepressant, cytotoxic, and antimicrobial	(27,29)
Limonene	S. Acmella S. paniculata	Antitumor, antiviral, anti-inflammatory, and antibacterial agents	(27,29)
2-Tridecanone	S. paniculata	Flavour and fragrance agents	(27)
Caryophyllene oxide	A. uliginosa	Antifungal	(30)
Germacrene D	A. uliginosa S. paniculata	Antibacterial and antifungal activities	(27,30)
Vanillic acid	S. acmella	Antiinflammatory, antioxidant	(29)
α-Amyrin	S. acmella	Antiinflammatory, antinociceptive	(29)
β-bisabolene	A. uliginosa S. paniculata	Antitumor, antioxidant	(27,30)

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the species examined, *S. uliginosa* exhibited a significant and prominent peak, whereas a narrow peak was detected followed by *Spilanthes ghoshinis*, and *S. radicans* (36). Researchers successfully synthesized rod-shaped silver nanoparticles using the aqueous leaf extract of *S. calva* (37). Silver nanoparticles have been used in medicine due to their antimicrobial activity and biofilm formation inhibition (38). Paul et al synthesized zinc nanowires from the leaf extracts of *S. acmella* (39). Zinc nanoparticles are currently used in healthcare for wound healing, preparation of anti-cancer medicines, antimicrobial agents, and implant coating (40). These findings hold promise for unlocking therapeutic applications in future research.

Toxicology of Toothache plant

Several toxicity studies were conducted on the "Toothache plant" and it was observed that the plant was safe for use without any toxic effects. The toxicity of *S. acmella* plant extract was evaluated on zebrafish embryos, and it was found that there was no toxic impact observed at the highest concentration tested (20% v/v), whereas the lowest observable sublethal effect concentration was 10%. The crude extract of *S. acmella*, when used in animal feed, was found to be safe for use at concentrations ranging from 0.01% v/v and 1% v/v with no adverse effects on animals (9).

The extracts of *S. acmella*, which contained phytoconstituents including spilanthol and alkamide exhibit a detrimental effect on a wide range of insect species, including mosquitos. Sesquiterpenoids and saponins found in the plant have also been associated with insecticidal effects (9,41). Ethanol and hexane extracts of plant components, when used at low concentrations, exhibited significant efficiency in controlling mosquito larvae, including ovicidal and pupacidal activities (42).

Pharmacological properties of Toothache plants

The toothache plant has multiple pharmacological activities, including anticancer, antipyretic, anesthetic, antioxidant, and many more due to the presence of phenolics, flavonoids, and other phytoconstituents which are summarized below.

The toothache plant has been shown to have anticancer and antiproliferative properties on different cancer cell lines. The ethyl acetate and ethanolic extracts of flowers of *S. paniculata* showed antiproliferative effects on hepatic carcinoma cells, which have been attributed to the presence of rich amounts of phenols and flavonoids (43). The essential oil obtained from the whole plant of *Acmella oleracea* showed cytotoxicity towards breast adenocarcinoma (IC50 87.80 µg/mL) and melanoma (IC50 130.9 µg/mL) cell lines (44). *S. acmella* showed an inhibitory effect against liver cancer and colon cancer, which was attributed to the presence of alkaloids, proteins, and flavonoids (45).

Antioxidant activity

The *Spilanthes* species are known for their antioxidant properties due to the presence of tannins, flavonoids, and phenolic substances. The methanolic root extracts of *S. acmella* using the DPPH free radical scavenging method showed effective antioxidant activity (46). The ethanol, methanol, and chloroform extracts of *S. paniculata* showed significant antioxidant activities, which were attributed to flavonoids (47). *S. mauritiana* showed minimal antioxidant activity in hexane, methanol, acetone, and dichloromethane extracts against the DPPH assay (24).

Local anesthetic activity

The toothache plant is well appreciated for its local anesthetic property owing to the presence of alkamide. The local anesthetic activity of *S. acmella* was evaluated using different animal models: intracutaneous wheal in guinea pigs and plexus anesthesia in frogs; the results showed that *S. acmella* could be used as a potent source of anesthetic agent (48).

Antibacterial activity

The crude extracts of *S. oleracea* showed potent antimicrobial activity against oral bacteria: Streptococcus mutans and Lactobacillus species (49). The methanolic extract of *S. calva* (DC) leaves was evaluated for antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*; Staphylococcus aureus showed maximum antimicrobial activity whereas no sensitivity was found for *E. coli* (50). The antibacterial activities of the whole plant extracts of *S. mauritiana* were evaluated using hexane, methanol, acetone, and dichloromethane extracts against *E. coli*, *Pseudomonas aeruginosa, Enterococcus faecalis*, *S. aureus*, which the hexane extract had an average minimum inhibitory concentration value of 2.50 mg/mL, followed by methanol extract (1.72 mg/mL), acetone and dichloromethane extracts (1.96 mg/mL) (24).

Antipyretic activity

The antipyretic efficacy of *S. acmella* was tested using the yeast-induced technique where the temperature of the pyretic rats was reduced from the first to the third hour (48). The ethanolic extract, n-hexane, and ethyl acetate soluble fractions of *S. paniculata* leaves were also evaluated, which showed a significant reduction in the temperature of the mice (51).

Diuretic activity

The diuretic effect of the ethanolic extracts of leaves of *S. acmella* Murr. Was evaluated; the extract showed an increase in total urine volume and electrolytes excretion (sodium Na⁺, potassium K⁺, and chloride Cl⁻) (52). The diuretic activity of aqueous extract of *S. paniculata* flowers

was also tested in rats; the study revealed that the three different doses tested (100 mg/kg, 300 mg/kg, 500 mg/kg) significantly increased urine volume, conductivity, Na+ and K+ contents as compared to the control group (54) (Table 3).

Based on their pharmacological activities, toothache plants can be employed in dental care in a variety of ways. Both the extracts and essential oils obtained from the plant can be administered topically to oral ulcers and infected gums to offer an anesthetic effect and combat microbial infections. Furthermore, toothache plant extracts can be incorporated into oral gels, and mouthwashes to treat specific mouth problems such as oral infections, gingivitis, and periodontitis.

Applications of "Toothache Plant" in dentistry

The use of toothache plants has a wide range of potential applications in dentistry. Crushed flowers and leaves were placed in the region of pain for immediate alleviation from odontalgia (toothache). When chewed, the leaves and flowers of toothache plants induce a numbing effect, thereby relieving the toothache and inflammation. The numbing effect is primarily attributable to spilanthol, which is considered to be the most predominant alkamide found in the toothache plant (3). Spilanthol, which is accountable for the bitter taste, stimulates the salivary glands and induces salivation. Chewing the leaves creates a burning sensation and increases salivation. Chewing the roots and flower heads of the toothache plant aids in alleviating periodontal pain and treating gum inflammation (Figure 3). The tincture of flower heads and roots is placed in the affected areas to get relief from gingivitis and bleeding gums. The leaves of the toothache plant have long been used for treating stomatitis (54). This herb is widely renowned for improving speaking fluency by curbing stammering (4).

Clinical trials

There are a few clinical trials reported in the literature for the genus *Spilanthes*; however, there ARE no clinical trial conducted on the species *S. paniculata*. The effects of *S. calva* DC root extracts were compared with herbal and synthetic dentifrices on oral microflora using an in vitro human tooth model. The findings indicated that the root

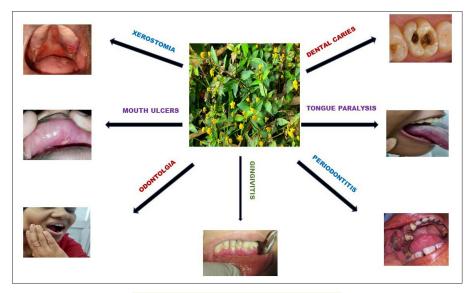


Figure 3. Dental applications of toothache plant.

Activity	Species	Findings	References
Anticancer	Spilanthes paniculata; Acmella oleracea, S. acmella	Antiproliferative effects on hepatic carcinoma, adenocarcinoma and melanoma, liver cancer, and colon cancer cell lines.	(43-45)
Antioxidant	S. acmella, S. paniculata, S. mauritiana	Significance antioxidant properties.	(24,46,47)
Anesthesia	S. acmella	Potent source of anesthesia.	(48)
Antibacterial	S. oleracea, S. calva (DC), S. mauritiana	Strong antimicrobial activity against antibacterial activity.	(24,49,50)
Antipyretic	S. acmella, S. paniculata	Significant reduction in the temperature of pyretic rats.	(48,51)
Diuretic	S. acmella, Murr., S. paniculata	Substantial increase in urine volume, conductivity, and Na+ and K+ content in rats.	(52,53)

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extracts possessed inhibitory activities against different oral microflora; these root extracts could be used in singly or in combination with other herbal and synthetic dentifrices, especially for diabetic patients (55). The effect of an ointment with A. oleracea and 20% benzocaine was determined as a topical anesthetic for the buccal mucosa and concluded that A. oleracea ointment use was effective and safe in reducing pain from needle insertion in the methodology used in their study (56). de Cássia Costa da Silva et al conducted an in vivo animal study to assess the novel mucoadhesive containing S. acmella extract as an oral mucosal topical anaesthetic agent. They formulated the film using chitosan and tested it with three different doses of S. acmella extract. To evaluate the efficacy of the mucoadhesive films, the researchers employed the tail flick test in mice and concluded that the chitosan-based oral mucoadhesive film of S. acmella ethanolic extract could be considered as a promising alternative to topical anesthetic formulations owing to its high permeation and low toxicity level (57). Mohite et al conducted a study to investigate the local anesthetic efficacy of the gel prepared from the fresh flower buds of S. acmella Murr and the roots of Anacyclus pyrethrum DC. They compared it with 2% lignocaine gel as a positive control. They evaluated the actions of these agents as intraoral topical anesthetic agents in children for reducing pain due to needle sticks before inferior alveolar nerve block administration. They concluded that the herbal local anesthetic gel containing S. acmella and roots of A. pyrethrum was equally effective as the standard 2% lignocaine gel in reducing pain caused by needle stick before inferior alveolar nerve block administration. The herbal gel was found to be a good alternative to the lignocaine gel (58) (Table 4).

Conclusion and future prospective

The therapeutic potential of all toothache plants broadens beyond oral health, making them beneficial for treating various health ailments. Owing to its antimicrobial, anesthetic, and anticancer capabilities, plant extracts hold promise in developing innovative dental treatments for managing oral diseases. However, it is worth noting that the knowledge surrounding the use of toothache

Table 4. Clinical trials of Toothache plants

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plants in the field of dentistry is still limited. The objective of this review was to consolidate and update available information, aiming to contribute to future advancements in oral healthcare research. By enhancing our understanding of toothache plants and their potential applications, we can pave the way for improved oral health treatments and tactics in the future.

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Authors' Contribution

Conceptualization: Sanat Kumar Bhuyan. Formal analysis: Nihar Ranjan Panda. Investigation: Arun Kumar Pradhan. Methodology: Sanat Kumar Bhuyan. Supervision: Sanat Kumar Bhuyan. Writing-original draft: Soumya Subhashree Satapathy. Writing-review & editing: Ruchi Bhuyan.

Conflict of interests

The authors state that they have no conflicts of interest, financial or otherwise.

Ethical considerations

The duplication and plagiarism were considered and checked using Turnitin software.

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References

- Kowitz GM, Lucatorto FM, Cherrick HM. Effects of mouthwashes on the oral soft tissues. J Oral Med. 1976;31(2):47-50.
- 2. Paulraj J, Govindarajan R, Palpu P. The genus *Spilanthes* ethnopharmacology, phytochemistry, and pharmacological properties: a review. Adv Pharmacol Sci. 2013;2013:510298. doi: 10.1155/2013/510298.

Species	Aim of the study	Conclusion	References	
Spilanthes calva	The effect of <i>S. calva</i> DC root extracts on oral microflora using in vitro human tooth model	<i>S. calva</i> DC root extracts show repressive activities against oral microflora.	(55)	
Acmella oleracea	The efficacy of <i>A. oleracea</i> as a topical anaesthetic for the buccal mucosa	A. oleracea gel use was safe and effective in reducing needle insertion pain.	(56)	
Spilanthes acmella	Developing a chitosan-based mucoadhesive films using <i>A. oleracea</i> extract for oral mucosa topical anesthesia	The <i>S. acmella</i> mucoadhesive film was shown to be harmless and effective topical anaesthesia.	(57)	
Spilanthes acmella	Comparing <i>S. acmella</i> Murr gel and 2% lignocaine gel as an intraoral topical anesthesia in children	S. acmella Murr gel was found to be a good substitute for lignocaine gel.	(58)	

- Srinath J, Laksmi T. Therapeutic potential of *Spilanthes* acmella-a dental note. Int J Pharm Sci Rev Res. 2014;25(1):151-3.
- Rani AS, Sana H, Sulakshana G, Puri ES, Keerti M. Spilanthes acmella-an important medicinal plant. Int J Minor Fruits Med Aromat Plants. 2019;5(2):15-26.
- Baruah S, Brahma D, Upadhya P. Phytochemical study of some selected medicinal plants and its ethnobotanical importance to the indigenous communities of Assam. Med Plants Int J Phytomed Relat Ind. 2018;10(2):145-50. doi: 10.5958/0975-6892.2018.00023.0.
- 6. Santesson CG. Several drugs of the Cameroon district and their native uses. Arch Bot. 1926;20(3):1-34.
- Revathi P, Parimelazhagan T. Traditional knowledge on medicinal plants used by the Irula tribe of Hasanur hills, Erode district, Tamil Nadu, India. Ethnobotanical Leaflets. 2010;2010(2):4.
- Biswas A, Bari MA, Roy M, Bhadra SK. Inherited folk pharmaceutical knowledge of tribal people in the Chittagong Hill Tracts, Bangladesh. Indian J Tradit Knowl. 2010;9(1):77-89.
- Dubey S, Maity S, Singh M, Saraf SA, Saha S. Phytochemistry, pharmacology and toxicology of *Spilanthes acmella*: a review. Adv Pharmacol Sci. 2013;2013:423750. doi: 10.1155/2013/423750.
- Reshmi GR, Rajalakshmi R. Three new combinations in *Acmella* (Asteraceae: Heliantheae). Trop Plant Res. 2016;3(1):67-9.
- Cook CD. Aquatic and Wetland Plants of India: A Reference Book and Identification Manual for the Vascular Plants Found in Permanent or Seasonal Fresh Water in the Subcontinent of India South of the Himalayas. Oxford University Press; 1996.
- 12. Singh H. Ethnomedicinal uses of some wild flowers in Sundargarh, Mayurbhanj, Angul and Bolangir districts of Odisha. Ethnobotany. 2013;25:115-9.
- Panda T, Mishra N, Rahimuddin S, Pradhan BK, Mohanty RB. Distribution pattern and multifarious use of weeds in rice agro-ecosystems of Bhadrak district, Odisha, India. Trop Plant Res. 2019;6(3):345-64. doi: 10.22271/tpr.2019. v6.i3.045.
- Panda M, Samal RN, Bhatta KS, Lenka S, Patra HK, Nanda S. Diversity and distribution of vascular macrophytes in Ansupa Lake, Odisha, India. Int J Bonorowo Wetl. 2018;8(1):1-12. doi: 10.13057/bonorowo/w080101.
- Pradhan I, Chauhan M, Dimri R, Kumar S. Common medicinal plants of Dhenkanal (Odisha), India. Medico-Biowealth of India vol IV. APRF Publishers; 2021. p. 147-65.
- 16. Sankar JG, Satapathy KB. Weed diversity of Rabi crops and their ethnomedicinal uses in Kendrapara district of Odisha, India. Int Res J Biol Sci. 2015;4(3):33-8.
- 17. Noor N, Satapathy KB. Phytodiversity of Dhauli Giri Hill and its adjoining area, Odisha, India: a floristic approach. Plant Arch. 2020;20(1):2093-102.
- Prusti AB, Behera KK. Ethnobotanical exploration of Malkangiri district of Orissa, India. Ethnobotanical Leaflets. 2007;2007(1):14.
- 19. Ojo OA, Ogunlakin AD, Gyebi GA, Ayokunle DI, Odugbemi AI, Babatunde DE, et al. Profiling the antidiabetic potential of GC-MS compounds identified from the methanolic extract of *Spilanthes filicaulis*: experimental and

computational insight. J Biomol Struct Dyn. 2023:1-22. doi: 10.1080/07391102.2023.2291828.

- Leng TC, Ping NS, Lim BP, Keng CL. Detection of bioactive compounds from *Spilanthes acmella* (L.) plants and its various in vitro culture products. J Med Plants Res. 2011;5(3):371-8.
- 21. Ramproshad S, Das R, Mondal B, Saha L. Phytochemical evaluation and antioxidant activities of *Spilanthes calva* DC. PharmacologyOnLine. 2019;1:289-300.
- Bankova VS, Popov SS, Marekov NL. A Study on flavonoids of propolis. J Nat Prod. 1983;46(4):471-4. doi: 10.1021/ np50028a007.
- 23. Begum J, Bhuiyan MN, Chowdhury JU. Essential oil from inflorescence of *Spilanthes calva* DC. Bangladesh J Bot. 2008;37(2):217-8.
- 24. Masoko P. Phytochemical analysis, antioxidant and antibacterial properties of *Spilanthes mauritiana* used traditionally in Limpopo province, South Africa. J Evid Based Complementary Altern Med. 2017;22(4):936-43. doi: 10.1177/2515690x17746774.
- Sharma R, Zimik M, Arumugam N. Isolation and GCMS characterization of certain non-polar compounds from *Spilanthes ciliata*. Int J Pharm Biol Sci. 2018;8(4):889-903.
- 26. Uraku AJ. GC/MS determination of bioactive constituents of methanol fraction of *Spilanthes uliginosa* (Sw) leaves. Res J Med Plant 2016;10(1):42-54.
- 27. Zhu SM, Zhu L, Tian YJ, Yin YC. Composition and antimicrobial activity of the essential oil of *Spilanthes paniculata* growing wild on the Gaoligong Mountains, China. Asian J Chem. 2012;24(2):607-10.
- Mondal AK, Parui S, Mandal S. Analysis of the free amino acid content in pollen of nine Asteraceae species of known allergenic activity. Ann Agric Environ Med. 1998;5(1):17-20.
- Baruah RN, Leclercq PA. Characterization of the essential oil from flower heads of *Spilanthes acmella*. J Essent Oil Res. 1993;5(6):693-5. doi: 10.1080/10412905.1993.9698310.
- Maimulyanti A, Prihadi AR. Chemical composition of essential oil and hexane extract and antioxidant activity of various extracts of *Acmella uliginosa* (Sw.) Cass flowers from Indonesia. Agric Nat Resour. 2016;50(4):264-9. doi: 10.1016/j.anres.2015.11.002.
- Barbosa AF, de Carvalho MG, Smith RE, Sabaa-Srur AU. Spilanthol: occurrence, extraction, chemistry and biological activities. Rev Bras Farmacogn. 2016;26(1):128-33. doi: 10.1016/j.bjp.2015.07.024.
- Cilia-López VG, Juárez-Flores BI, Aguirre-Rivera JR, Reyes-Agüero JA. Analgesic activity of *Heliopsis longipes* and its effect on the nervous system. Pharm Biol. 2010;48(2):195-200. doi: 10.3109/13880200903078495.
- Ogura M, Cordell GA, Quinn ML, Leon C, Benoit PS, Soejarto DD, et al. Ethnopharmacologic studies. I. Rapid solution to a problem--oral use of *Heliopsis longipes--by* means of a multidisciplinary approach. J Ethnopharmacol. 1982;5(2):215-9. doi: 10.1016/0378-8741(82)90045-9.
- 34. Ochoa-de la Paz LD, Gulias-Cañizo R, Ruíz-Leyja ED, Sánchez-Castillo H, Parodí J. The role of GABA neurotransmitter in the human central nervous system, physiology, and pathophysiology. Rev Mex Neurocienc. 2021;22(2):67-76. doi: 10.24875/rmn.20000050.
- 35. Bakondi E, Singh SB, Hajnády Z, Nagy-Pénzes M, Regdon

Z, Kovács K, et al. Spilanthol inhibits inflammatory transcription factors and iNOS expression in macrophages and exerts anti-inflammatory effects in dermatitis and pancreatitis. Int J Mol Sci. 2019;20(17):4308. doi: 10.3390/ ijms20174308.

- Durga KV, Cherian P, Sheela D. Green Synthesis of Silver Nanoparticles and Antimicrobial Activity from *Spilanthes* Jacq. Species from South India. 2020. Available from: https://ssrn.com/abstract=3598035.
- Rethinam R, Jeyachandran R. Green synthesis of silver nanoparticles using aqueous leaf extract of *Spilanthes calva* DC. World J Pharm Res. 2016;5(11):822-8. doi: 10.20959/ wjpr201611-7211.
- Bapat RA, Chaubal TV, Joshi CP, Bapat PR, Choudhury H, Pandey M, et al. An overview of application of silver nanoparticles for biomaterials in dentistry. Mater Sci Eng C Mater Biol Appl. 2018;91:881-98. doi: 10.1016/j. msec.2018.05.069.
- Paul N, Khole E, Jagtap S, Tribhuvan H, Kakde G, Kuwar P. Green synthesis of zinc nanowires using *Spilanthes acmella* leaf extract. Pharm Biosci J. 2016;4(3):45-7. doi: 10.20510/ ukjpb/4/i3/107861.
- 40. Jha S, Rani R, Singh S. Biogenic zinc oxide nanoparticles and their biomedical applications: a review. J Inorg Organomet Polym Mater. 2023:1-16. doi: 10.1007/s10904-023-02550-x.
- Krishnaswamy NR, Prasanna S, Seshandri TR, Vedantham TN. α-and β-amyrin esters and sitosterol glucoside from *Spilanthes acmella*. Phytochemistry. 1975;14(7):1666-7. doi: 10.1016/0031-9422(75)85386-6.
- Saraf DK, Dixit VK. Spilanthes acmella Murr.: study on its extract spilanthol as larvicidal compound. Asian J Exp Sci. 2002;16(1-2):9-19.
- Mishra A, Roy S, Maity SI, Yadav RK, Keshari AK, Saha S. Antiproliferative effect of flower extracts of *Spilanthes paniculata* on hepatic carcinoma cells. Int J Pharm Sci. 2015;7(1):130-4.
- 44. Jerônimo LB, Santos PV, Pinto LC, da Costa JS, de Aguiar Andrade EH, Setzer WN, et al. *Acmella oleracea* (L.) R.K. Jansen essential oils: chemical composition, antioxidant, and cytotoxic activities. Biochem Syst Ecol. 2024;112:104775. doi: 10.1016/j.bse.2023.104775.
- 45. Singh S, Verma SK, Singh SK. In vitro investigation of anticancer potential of *Spilanthes acmella*. J Pharm Sci Res. 2020;12(1):124-8.
- 46. Sana H, Sabitha Rani A, Sulakshana G. Determination of antioxidant potential in *Spilanthes acmella* using DPPH assay. Int J Curr Microbiol Appl Sci. 2014;3(7):219-23.
- Haque SH, Lopa SD, Das BK. Evaluation of antioxidant potential of *Spilanthes paniculata*. Int J Pharm Pharm Sci. 2015;7(8):390-2.

- Chakraborty A, Devi BR, Sanjebam R, Khumbong S, Thokchom IS. Preliminary studies on local anesthetic and antipyretic activities of *Spilanthes acmella* Murr. in experimental animal models. Indian J Pharmacol. 2010;42(5):277-9. doi: 10.4103/0253-7613.70106.
- 49. Onoriode O, Oshomoh EO. Antibacterial activity of methanol and chloroform extracts of *Spilanthes oleracea* plant on isolated pathogenic oral bacteria. J Appl Sci Environ Manage. 2018;22(2):237-45. doi: 10.4314/jasem. v22i2.15.
- Ali MS, Islam MS, Rahman MM, Islam MR, Islam ME, Islam MR. Antibacterial and cytotoxic activity of methanol extract of *Spilanthes calva* (DC) leaves. Int J Pharm Sci Res. 2011;2(7):1707-11.
- Hossain MM, Ahamed SK, Dewan SM, Hassan MM, Istiaq A, Islam MS, et al. In vivo antipyretic, antiemetic, in vitro membrane stabilization, antimicrobial, and cytotoxic activities of different extracts from *Spilanthes paniculata* leaves. Biol Res. 2014;47(1):45. doi: 10.1186/0717-6287-47-45.
- 52. Yadav R, Kharya MD, Yadav N, Savadi R. Diuretic activity of *Spilanthes acmella* Murr. leaves extract in rats. Int J Res Pharm Chem. 2011;1(1):57-61.
- Ali SA. Diuretic activity of aqueous extract of *Spilanthes paniculata* flower in rats. Int J Green Pharm. 2015;9(3):162-6.
- 54. Joseph B, George J, Jeevitha MV. The role of *Acemella oleracea* in medicine-a review. World J Pharm Res. 2013;2(6):2781-8.
- 55. Vyas YK, Chandrashekhra KT, Bhatnagar M, Sharma K. Effect of *Spilanthes calva* DC. root extract, herbal and synthetic dentifrices on oral microflora using in vitro human tooth model. J Herb Med Toxicol. 2009;3(1):141-8.
- Fosquiera E, Andrade L, Rotta I, Chaves S, Uchida D, Gazim Z. Effectiveness of Acmella oleracea for topical anesthesia on buccal mucosa. Int Association Dent Res. 2012:28(3)20-3.
- 57. de Cássia Costa da Silva R, Campos DR, de Oliveira P, Laguna AG, de Souza Magalhães V, Cid YP, et al. Efficacy of chitosan gel mucoadhesive containing doxycycline associated or not to meloxicam as adjuvant to treatment of gingivitis in dogs with periodontal disease. Rev Bras Med Vet. 2016;38(Suppl 2):40-4.
- 58. Mohite VA, Baliga S, Thosar N, Rathi N, Khobragade P, Srivastava R. Comparative evaluation of a novel herbal anesthetic gel and 2% lignocaine gel as an intraoral topical anesthetic agent in children: Bilateral split-mouth, singleblind, crossover in vivo study. J Indian Soc Pedod Prev Dent. 2020;38(2):177-83. doi: 10.4103/jisppd_Jisppd_226_20.

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