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A review on therapeutic potential of *Acmella oleracea* (L.): A medicinal Herb

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Abstract

Acmella oleracea (L.), commonly known as the toothache plant or “Jambu,” is an ethnomedicinally important herb extensively used in traditional healthcare systems across Asia, Africa, and South America. The species is characterized by a rich phytochemical profile, with N-alkylamides, particularly spilanthol, being the principal bioactive constituents responsible for its distinctive sensory effects and therapeutic activities. The present manuscript provides a critical overview of the botanical characteristics; geographical distribution, traditional uses, phytochemical composition, and experimentally validated pharmacological properties of *A. oleracea*, which contain various secondary metabolites, including triterpenoids, steroidal glycosides, phenolic compounds, fatty acids, coumarins, and volatile compounds, contribute to a wide range of biological activities such as antimicrobial, antioxidant, anti-inflammatory, antinociceptive, diuretic, immunomodulatory, and pancreatic lipase inhibitory effects. Preclinical studies demonstrate notable efficacy against oral pathogens, oxidative stress, inflammatory pain models, and immune modulation pathways, supporting its traditional applications. Collectively, the available evidence highlights *A. oleracea* as a promising source of bioactive molecules for the development of plant-based therapeutics and functional products.

Keywords: *Acmella oleracea*, spilanthol, N-alkylamides, Ethnopharmacology, antimicrobial activity, antioxidant potential, medicinal plants

1. Introduction

The *Acmella* genus, classified under the Asteraceae family, contain about 30 different species. Among various species, *Acmella oleracea* is considered one of the most important (Cheng *et al.*, 2015) [4]. The flowers of this plant are golden-yellow in colour with red tips, arranged in a characteristic round and tubular shape called discoid capitulum (Uthpala, & Navaratne 2020) [19]. *Acmella* has significant medicinal value due to its wide range of bioactive compounds. It is commonly called as the “Toothache Plant” because of its use in relieving tooth pain. The entire plant has various health benefits. In northern regions of Brazil, this plant is called as “Jambu”. Because of its medicinal value, this is also used for the traditional cooking. The flowers are often added to vegetable dishes, adding flavour and having a mild numbing effect (Rondanelli *et al.*, 2020) [13]. Traditionally, all parts of the plant including flowers, leaves, and stems are known for their use in folk medicine to relieve a wide range of ailments.

In Brazilian homes, especially in the Amazon region, *Acmella oleracea* is commonly employed in traditional medicine for treating throat infections, mouth ulcers, and even mild fevers. When the flowers and leaves of plants are chewed, they produce a unique tingling, numbing or mouth-watering sensation on the lips and tongue. This sensory effect is arises due to spilanthol content which is a bioactive compound found in high concentration in the plant. Spilanthol is belongs to N-Alkylamide group that acts as a natural local anesthetic and analgesic (Alperth *et al.*, 2024) [3]. It interacts with nerve endings and temporarily blocks pain signals, making it especially useful in treating toothaches, gum inflammation, and oral discomfort.

2. Scientific classification

The scientific classification of *A. oleracea* is given in the table below (Table 1).

Table 1: Scientific classification of *Acmella oleracea* (Aktar *et al.*, 2024) ^[1]

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Asterales
Family	Asteraceae
Genus	<i>Acmella</i>
Species	<i>A. oleracea</i> (L.)

Apart from its pain-relieving activity, spilanthol contain antimicrobial, antifungal and anti-inflammatory properties. These features make *Acmella oleracea* a valuable for the development of herbal-based dental care products, such as gels, mouthwashes, and toothpaste aimed at reducing oral infections and inflammation (Sawant & Kareppa, 2022) ^[16]. Both the leaves and flowers of this species serve as important sources of bioactive compounds and are widely used in traditional remedies and culinary practices.

3. Leaves

Acmella oleracea leaves are soft, and dark green in colour, and range in shape from oval to lanceolate, with noticeable venation and finely serrated edges. They are arranged alternately along the stem and grow on slender petioles. When the leaves are crushed, a special aroma is released due to the essential oils they contain. The leaves are reservoir of some beneficial constituents, including alkylamides (notably spilanthol), flavonoids, and various phenolic compounds. These chemicals contribute to the pharmacological activities such as antibacterial, anti-inflammatory, antioxidant and pain-relieving properties (Dubey *et al.*, 2013) ^[6]. Traditionally, the leaves are used to prepare a decoction to treat fever, oral infections, sore throat and joint pain associated with arthritis. Their ability to stimulate saliva flow also makes them effective in managing oral dryness and speech difficulties (Savant *et al.*, 2022) ^[16]. The fresh leaves of *Acmella oleracea* are also consumed as food in

some regions and this is used for salads or lightly cooked food as a leafy green in South American and Asian cuisines.

4. Flowers

Flowers of *Acmella oleracea*, a member of the Asteraceae family, are unique in their structure and form. They are arranged in a dense, cylindrical, disc-shaped head known as the capitulum. Unlike many flowering plants in this family, *Acmella oleracea* does not have petal-like ray florets and has only tubular disc florets. These flowers usually display a bright yellow colour with a red or maroon center, which gives them a distinctive look. Flowers are borne on long stalks and are located in the axils of the leaves. They are soft and fleshy, which contributes to their edible and medicinal uses. One of the most significant chemical constituents of the flowers is spilanthol. Spilanthol is a alkylamide which have anti-wrinkled activity and used in many skin care products. *Acmella oleracea* flowers are frequently used to treat the mouth ulcer because of its antimicrobial, antioxidant and anti-inflammatory activity (Sanap *et al.*, 2023) ^[15].

5. Habitat

Acmella oleracea is primarily native to Peru and Brazil, but they also grow in China, Taiwan, India. It can also be planted in moist continental climates such as the Moscow region as an annual plant (Matyushin *et al.*, 2017) ^[10]. *Acmella oleracea* mainly thrives in warm, sunny and humid climate. It prefers sandy soil, which is rich in organic matter. It grows best in areas with moderate to high rainfall and is sensitive to frost. It is mainly found in low-lying areas, open fields, road sides, damp grassland and domestic gardens (Kamatou *et al.*, 2008) ^[8].

6. Ethnobotanical Uses of *Acmella oleracea*

A. oleracea is widely cultivated and used in indigenous communities of Asia, Africa, and South America due to its medicinal value. (Table 2) (Yadav *et al.*, 2023 & Mipun *et al.*, 2022) ^[21, 111]

Table 2: Traditional Medicinal Uses:

Use	Part Used	Region/Community
Anti-inflammatory for sore throat	Leaves	Peru, Africa
Relief from toothache and mouth pain	Fresh Flower heads	Amazonian tribes, India, Brazil
Treatment of scurvy and vitamin deficiency	Leaves (rich in vitamin C)	India
Fever and cold symptoms	Leaf decoction	Nigerian traditional medicine
Treatment of parasitic worms (anthelmintic)	Roots and stems	Brazil and Amazonian tribes
Wound healing and skin infections	Leaf poultice	African tribes
Digestive aid	Whole plant	Southeast Asia
Aphrodisiac and tonic	Flowers heads and roots	Ayurveda, Unani, Brazilian Folk use

7. Secondary Metabolites:

Acmella oleracea is rich in secondary metabolites, namely triterpenoids, steroidal, steroidal glycosides, phenolic

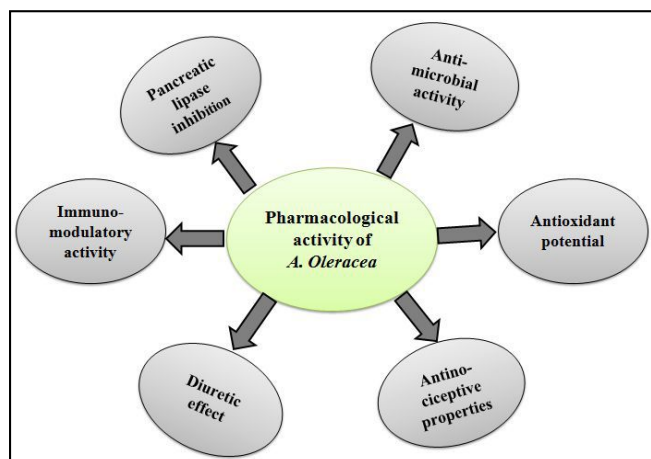
compounds, coumarins, volatile compounds and N-alkylamides, etc. (Table 3).

Table 3: Secondary metabolites reported in *Acmella oleracea* and their biological activities

Compound class	Representative compounds	Reported biological activities	Reference
Triterpenoids	3-Acetylaleuritic acid, β -sitosterone, stigmasterol	Anti-inflammatory, antiviral, and anticancer activities	Dubey <i>et al.</i> , 2013 [6]
Steroidal glycosides	Stigmasteryl-3-O- β -D-glucopyranoside, β -sitosteryl-3-O- β -D-glucopyranoside	Antitumor, antidiabetic, and antibacterial activities	
Fatty acids	<i>n</i> -Hexadecanoic acid, <i>n</i> -tetradecanoic acid	Anti-inflammatory, antibacterial, and antioxidant activities	
Phenolic compounds	Vanillic acid, trans-ferulic acid, trans-isoferulic acid	Antioxidant, anti-inflammatory, anti-aging, and anticancer activities	Weintraub <i>et al.</i> , 2020 [20]
Coumarins	Scopoletin	Antioxidant, anti-inflammatory, antimicrobial activities; potential roles in neuroprotection, cancer prevention, and anticoagulation	Joseph <i>et al.</i> , 2013 [7]
Volatile compounds	β -Pinene, myrcene, (E)-caryophyllene, caryophyllene oxide, germacrene D, β -phellandrene, spilanthal, acmellonate	Anti-inflammatory, analgesic, and neuroprotective activities	Kamatou <i>et al.</i> , 2008 [8]
N-alkylamides	Isobutylamides, methylbutylamides, phenylbutylamides	Anti-inflammatory, antimicrobial, and analgesic effects	Kavallieratos <i>et al.</i> , 2023 [9]

8. Pharmacological activity of *A. oleracea*

A. oleracea has a diversity of pharmacological activity, including antimicrobial activity, antioxidant potential, antinociceptive properties, diuretic effect, immunomodulatory activity and pancreatic lipase inhibition (Figure 1), details of these activities are as follows:

**Fig 1:** Pharmacological diversity of *A. oleracea*.

8.1 Antimicrobial Activity

Antimicrobials are chemicals commonly used to prevent or treat infections by killing or inhibiting the growth of harmful microorganisms, such as bacteria, viruses, fungi, and parasites. They work by targeting vital biological processes such as enzyme function, genetic mutations or cell wall formation (Russell *et al.*, 1991) [14]. In a study conducted on *Acmella oleracea*, methanolic leaf extracts were evaluated for antibacterial activity through the disc diffusion technique. It was tested against both Gram positive as well as gram negative bacteria. The inhibition zone ranged from 10 mm to 26 mm, showing that the plant extract has mild to moderate antibacterial activity. The strongest effect was observed against *Vibrio mimicus*, with a maximum inhibition zone of 23 mm (Alam and Akash 2023) [2]. These findings suggest that *A. oleracea* has the potential to be used as a natural antimicrobial agent. Further studies showed that both hydroethanolic and aqueous extracts of *Acmella oleracea* were effective against *Streptococcus mutans*, bacteria associated with dental plaque. These extracts had a minimum inhibitory

concentration (MIC) and minimum bactericidal concentration (MBC) of 125 μ g/ml. The leaves and flowers of the plant were found to contain high amounts of spilanthal-a major active compound (Aktar *et al.*, 2024) [1].

In a biofilm reduction test, using 500 μ g/ml of the extract reduced *S. mutans* activity by more than 50%, a result similar to that obtained with chlorhexidine mouthwash (0.12%). This suggests that this extract rich in spilanthal may be useful in dental products for the prevention of dental caries. Different extraction solvents ethanol, water and petroleum ether were used to test the antibacterial properties of dried *Acmella oleracea* flower buds. Ethanolic extracts obtained from cold water dried flowers showed greater antibacterial effects than sun dried flowers. These extracts produced inhibition zones of 12-18.8 mm against several harmful microbes including *E. coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. The research also tested extracts of *A. oleracea* on skin and intestinal bacteria found in animals. Whole and fragmented plant parts were active against a variety of bacteria and fungi when used at various concentrations (up to 1000 mg/mL). Spilanthal was identified in the extract using chromatography methods. A study showed that chloroform extract of *A. oleracea* reduced the growth of *Salmonella typhi* at an MIC of 31.25 mg/mL. Plates treated with 100 mg/ml extract showed bacterial inhibition after 18 h. Through the well diffusion method, the antibacterial activity of the plant was evaluated against several pathogens such as *Streptococcus salivarius*, *Pseudomonas aeruginosa*, *S. viridian*, *S. mutans*, *Neisseria catarrhalis* and *Bacillus megaterium*. The chloroform extract was particularly potent against *S. viridians*, whereas the aqueous extract worked well against *N. catarrhalis* and *S. mutans*. The methanol extract was effective against *B. megaterium* and *P. aeruginosa*. However, the water extract had no significant antimicrobial effect on the microorganisms tested (Thompson *et al.*, 2012 and Uthpala *et al.*, 2021) [17, 18].

8.2 Antioxidant Potential:

When free radicals accumulate in excess in the body, they cannot be neutralized, resulting in oxidative stress, which is an imbalance between harmful oxidative processes and protective antioxidant defenses. Free radicals are unstable molecules, formed primarily in mitochondria, which can damage proteins and other cellular structures, potentially

leading to a number of health problems. Antioxidants help by neutralizing these radicals, thereby reducing the damage they cause to the body (Mo *et al.*, 2021) ^[12].

It has been found that adding *Acmella oleracea* extract to bearberry, using a technique called supercritical extraction, significantly increases its antioxidant capacity. Scientists use different testing methods like ABTS, DPPH and ORAC to measure this activity (da Silva *et al.*, 2023) ^[5]. Spilanthol, one of the major bioactive compounds, was identified through advanced techniques such as GC-FID (gas chromatography-flame ionization detection), TLC (thin layer chromatography), and FTIR-ATR (Fourier transform infrared-attenuated total reflectance). In another study, extract of jambu flower (*Acmella oleracea*) was found to have powerful antioxidant properties, suggesting it could be used as a natural preservative in beer. The researchers treated the plant powder with a mixture of hydrochloric acid and methanol to separate the phenolic compounds and then assessed the antioxidant capacity through DPPH and ABTS tests. The radical scavenging capacity of each sample was measured using Trolox ($\mu\text{mol/g}$ dry weight) and compared with a standard reference. Among the different plant parts, leaves, stems and flowers of *A. oleracea* showed significantly higher levels of antioxidants (Weintraub *et al.*, 2020) ^[20]. In particular, the methanolic extract obtained from the stem of *A. oleracea* showed strong antioxidant activity when tested with hydrogen peroxide and hydroxyl radical scavenging methods. This extract also showed the effect of neutralizing free radicals in a concentration dependent manner. Moreover, MTT assay indicated that the extract could decrease the survival of cancer cells, such as HeLa and V79 cell lines. Of all the plant parts tested, stem extracts had the strongest activity against superoxide radicals, while leaves were most effective in neutralizing DPPH radicals (Aktar *et al.*, 2024) ^[1].

8.3 Antinociceptive Properties

Given the variation in pain perception between individuals, understanding the underlying mechanisms of antinociception is essential for effective pain management. Tools such as the Temporal Summation of Pain (TASP) help identify individuals with increased or decreased sensitivity to pain, which is important for developing personalized treatment strategies. The growing body of research targeting neuropathic and inflammatory pain has emphasized the importance of tailored approaches for varying patient populations experiencing chronic or internal pain syndromes (Aktar *et al.*, 2024) ^[1].

The antinociceptive potential of the methanolic extract of *Acmella oleracea* has been validated through both *in vivo* and *in silico* methods. These effects are primarily due to inhibition of the neurogenic and inflammatory responses seen in formalin-induced nociception mode. Molecular docking analysis further demonstrated that the plant alkylamides functionally bind to CB1/CB2 and TRPV1 receptors, which play key roles in nociceptive modulation. Importantly, the crude methanol extract did not induce the adverse effects associated with cannabinoid-based treatments, such as seizures or hyper locomotion. These findings highlight the therapeutic promise of *A. oleracea* alkylamides as new antinociceptive agents. For the first time, this study establishes a link between these compounds and the modulation of the endocannabinoid and vanilloid signaling pathways. Further pharmacological investigations

into the hexanic fraction (HF) and isobutylalkylamide (IBA) demonstrated significant antinociceptive (0.1 μg) and pronociceptive (30 μg) effects via intraplantar administration in murine models. In the context of glutamate-induced nociception, low doses of HF and IBA significantly decreased pain responses in both the neurogenic and inflammatory phases. This analgesic effect was mediated via TRPV1 (transient receptor potential vanilloid 1) regulation and was independent of endogenous opioid system activation. Additionally, compound 48/80-induced nociception and mast cell degranulation in the hind paw were reduced following high-frequency stimulation (HF). According to Dallazzane *et al.*, (2018), both agents were shown to decrease nociceptive responses through mechanisms involving TRPA1 activation.

8.4 Diuretic Effect

Acmella oleracea, particularly its fresh flowers, has been investigated for its potential diuretic activity. In experimental studies, aqueous extracts prepared by cold maceration of fresh flowers were evaluated for their effects on urinary output. Administration of high doses of the extract resulted in a significant increase in urine volume following a single dose, indicating a pronounced diuretic response. The observed effect was comparable in magnitude to that of furosemide, a widely used loop diuretic.

In addition to increased urine output, a significant elevation in urinary sodium (Na^+) and potassium (K^+) excretion was recorded, suggesting enhanced electrolyte elimination. Furthermore, the urine produced following extract administration exhibited a slightly acidic pH, indicating that the extract may exert a mechanism of action similar to that of loop diuretics. Phytochemical analyses of *A. oleracea* flowers have revealed the presence of bioactive constituents such as N-isobutylamides, alkaloids, and amino acids, which may collectively contribute to the observed diuretic activity. The extract was also characterized by a rapid onset and prolonged duration of action, which may reduce the frequency of administration required for therapeutic efficacy. These findings support the traditional use of *A. oleracea* flowers as a natural diuretic and suggest their potential application as a safer alternative for managing conditions associated with fluid retention. However, further studies focusing on dose optimization, mechanism of action, and clinical safety are required to validate its therapeutic utility (Dubey *et al.*, 2013 and Aktar *et al.*, 2024) ^[6, 1].

8.5 Immunomodulatory Activity

Studies have shown that hexane and chloroform extracts of *Acmella oleracea* can reduce the production of nitric oxide in activated immune cells called macrophages. When used at a concentration of 80 micrograms per milliliter (mcg/mL), the hexane extracts reduced nitric oxide levels by 72%, while the chloroform extract caused a greater reduction of up to 85%. Animal and plant immunomodulatory drugs increase the body's responsiveness against infections by primarily activating the non-specific immune system. The leaves functions as immunomodulatory, adaptogenic, toothpaste, lithotriptic, antiscorbutic, ailagogene, and digestive. *Acmella oleracea* leaves are reported to be used traditionally as a tonic for the immune system stimulation. Internally consumed, the herb is known to exhibit general immunomodulatory activity, promoting white blood cell production (leucocytes) and antiviral interferon production

and phagocytic function. Leaf ethanolic extract exhibited macrophage immunostimulation and increased function compared to control, demonstrating the herb's potential as a herbal immunomodulatory compound (Dubey *et al.*, 2013 and Joseph *et al.*, 2013) ^[6, 7].

8.6 Pancreatic Lipase inhibition

The ethanolic flower extract of *Acmella oleracea* demonstrated a 40% inhibition of pancreatic lipase activity *in vitro* at a concentration of 2 mg/mL. In comparison, *Aframomum melegueta* exhibited a higher inhibition rate of approximately 90%, indicating greater lipase inhibitory activity. Furthermore, an extract concentration of 0.75 mg/mL from *A. melegueta* produced stronger pancreatic lipase inhibition than *A. oleracea* (Dubey *et al.*, 2013) ^[6].

9. Conclusions

The accumulated ethnobotanical knowledge and experimental evidence clearly indicate that *Acmella oleracea* is a pharmacologically significant medicinal plant with multifunctional therapeutic potential. Its bioactivity is largely attributed to spilanthol and related N-alkylamides, along with a diverse array of secondary metabolites that collectively confer antimicrobial, antioxidant, analgesic, anti-inflammatory, diuretic, immunomodulatory, and metabolic regulatory effects. The demonstrated efficacy of leaf and flower extracts, particularly in oral health management and pain modulation, supports the plant's long-standing traditional use and its relevance in modern phytotherapy. Despite encouraging preclinical findings, the translation of *A. oleracea* into evidence-based medicinal applications remains limited by the lack of standardized extracts, comprehensive toxicological assessments, and well-controlled human clinical studies. Future research should therefore focus on bioavailability, mechanism-based pharmacology, formulation development, and clinical validation to facilitate the safe and effective integration of *A. oleracea*-derived products into contemporary healthcare systems.

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