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Phytochemical and Ethnopharmacological Review of *Acmella oleracea* (Toothache Plant) in Asia with Descriptive Analysis of Its Antimicrobial Potential

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Abstract

This review consolidates recent literature on *Acmella oleracea* (syn. *Spilanthes acmella*), especially those that have been carried out in Asia. Major scientific databases, such as PubMed, ScienceDirect, SpringerLink, Scopus, and Google Scholar, were used to conduct a systematic literature review. Results indicate that *Acmella oleracea* contains a variety of phytochemicals, including N-alkylamides such as spilanthol, flavonoids, terpenoids, and phenolic compounds, which contribute to its analgesic, anti-inflammatory, antioxidant, and antibacterial effects. The widespread traditional use of traditional ethnopharmacology is confirmed by reports of the use of ethnopharmacology in countries like India, Thailand, and the Philippines in the treatment of pain, wound healing, and infection treatment. The antimicrobial potential against *Staphylococcus aureus* and *Escherichia coli* is further confirmed by pharmacological studies. The toxicological evidence shows that there is a wide safety margin at standard doses, but slight hepatic and renal alterations have been noted in animal models at high doses. Although promising pharmacologically, studies are restricted to a large extent to in vitro models. More research is needed to emphasize standardized techniques of extraction, in vivo or human clinical trials to define the efficacy and safety level. *Acmella oleracea* proves to be a good potential source of natural therapeutic agents in modern medicine that have their roots in culture.

Keywords: *Acmella oleracea; Spilanthes acmella;* Phytochemistry; Ethnopharmacology; Antimicrobial activity; Traditional medicine

1. Introduction

Acmella oleracea (L.) R.K. Jansen, or *Spilanthes acmella*, or the "toothache plant", or jambu, is a yellow-orange capitula perennial plant of the family Asteraceae that is characterized by a pungent and tingling sensation when the florets are chewed. The species is commonly grown and dispersed around the tropical and subtropical areas, including Asia. In addition to its culinary uses, the plant has bioactive compounds, including N-alkylcamphorides (spilanthol) and flavonoids, terpenoids, and phenolic compounds, which have sparked considerable interest in its ethnopharmacological use. The phytochemicals have a large spectrum of pharmacological actions, which include analgesic, anti-inflammatory, antioxidant, and antibacterial.

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Recent research has increased the scientific facts of *Acmella oleracea*. Aktar et al. [1] reported a variety of phytochemical constituents, flavonoids, tannins, phenolic compounds, and alkamides, which lend it a wide biological profile. The plant is still of interest in Asia, where traditional medicine is still part of healthcare and may develop natural antibacterial and therapeutic compounds [2].

The purpose of this review is to synthesize existing scientific data on the phytochemical makeup and ethnopharmacological applicability of *Acmella oleracea* in Asia, as well as to descriptively examine its antimicrobial importance.

2. Methods

A systematic literature review was performed to find studies published from 2015 to 2025 that focus on *Acmella oleracea* (also known as *Spilanthes acmella*) research in Asia. We used the following keywords to search for relevant articles in several scientific online databases, such as PubMed, ScienceDirect, SpringerLink, Mendeley, Scopus, and Google Scholar: "*Acmella oleracea*," "toothache plant," "phytochemical composition," "ethnopharmacology," "antimicrobial activity," and "Asia." To make the search results more specific, Boolean operators like "AND" and "OR" were used.

The review included only peer-reviewed journal articles published in English. Publications were selected based on specific inclusion criteria, which encompassed (a) studies on phytochemical constituents, (b) reports of traditional medicinal uses in Asian countries, and (c) tests of antimicrobial or pharmacological activity. The review incorporated various types of studies, including review articles, in vivo and in vitro studies, and ethnobotanical surveys. Articles that were duplicates or not available in full text were excluded.

Key aspects such as study objectives, methodology, plant parts utilized, solvent systems employed, and reported bioactivities were summarized from the selected articles. The most recent and methodologically rigorous research was prioritized for synthesis [1,3].

2.1. Botanical and Taxonomic Profile

Acmella oleracea, a member of the *Asteraceae* family, is indigenous to South America yet is extensively cultivated in India, Thailand, and the Philippines. Conducting precise phytochemical and pharmacological studies on *Acmella oleracea* necessitates a comprehensive understanding of its taxonomic classification. Historically, nomenclature confusion, particularly regarding its association with the genus *Spilanthes*, has posed challenges for research standardization. The accepted scientific name, as proposed by Spinozzi et al. [4], addresses these discrepancies and provides clarity that is essential for advancing research efforts.

2.1.1. Taxonomic Classification

- Kingdom: *Plantae*
- Division: *Tracheophyta*
- Class: *Magnoliopsida* (Angiosperms)
- Order: *Asterales*
- Family *Asteraceae* (Compositae)
- Genus: *Acmella*
- Species: *Acmella oleraceae*

2.1.2. Synonym and Nomenclature

The currently accepted binomial name for the Toothache Plant is *Acmella oleracea* [4]. In historical scientific literature, it is often referred to by its synonyms, *Spilanthes oleracea* and *Spilanthes acmella*.

Nomenclature confusion has arisen due to the numerous morphological similarities between the genera *Acmella* and *Spilanthes*. However, chromosomal analyses and detailed phytochemical studies have confirmed that these are separate genera [4]. Locally, this plant is commonly known as Jambu or Paracress. The name Toothache Plant reflects its traditional use as an analgesic.

2.1.3. Morphology

Acmella oleracea is a perennial herb that flourishes in warmer climates, such as the Philippines, where it is frequently cultivated as an annual. It typically reaches a height between 20 and 60 cm.

- Stems: long, branching, and slightly brown.
- Leaves: Dark green in color, heart-shaped or cordate, and oppositely arranged on the stem.
- Inflorescence: The most distinguishing feature of the plant is its conical, discoid flower head. At the apex, it has yellow with a distinctive reddish-brown spot. This inflorescence has the richest source of primary bioactive compounds.
- Root System: It develops fibrous roots.

2.2. Distribution and Habitat

A. oleracea represents a cultivated species indigenous to tropical regions.

- Geographic Range: The toothache plant is extensively cultivated across various tropical and subtropical regions [6], including significant areas of South America such as Brazil and Peru, in addition to regions in Africa and Southeast Asia, notably the Philippines, India, and Indonesia.
- Habitat: This species exhibits a preference for full sunlight and thrives in well-drained, humus-rich soils. It is predominantly found in humid environments, frequently located in pastures, adjacent to ditches, and along riverbanks [4]. The extensive traditional utilization of this plant throughout Asia underscores its remarkable adaptability to a diverse array of climatic conditions.

2.3. Ethnopharmacological and Traditional Uses in Asia

People in Asia have used *Acmella oleracea*, also known as the toothache plant, for a long time to treat pain and other common problems. The alkylamide spilanthol in it is what gives it its well-known numbing or tingling effect. This has made it a popular natural remedy for toothache and oral inflammation in both formal traditional medicine and rural folk medicine [7, 8].

Studies of plants and their uses in India, Thailand, Indonesia, and the Philippines show that *Acmella oleracea* is often used to treat dental pain, oral infections, wounds, and fevers in the form of chewed flower heads, leaf infusions, or topical pastes [3, 7]. These widespread uses in different Asian cultures show that people have passed down a common traditional knowledge of the plant's pain-relieving and antiseptic properties over the years.

Recent studies support these traditional claims, calling *Acmella oleracea* one of Asia's best ethnomedicinal plants because it can reduce pain, inflammation, and infections [1, 2, 4, 9].

Table 1 Ethnopharmacological and Traditional Uses of *Acmella oleracea* in Asia

Country/Region	Local Name	Common Preparation or Form Used	Traditional Use(s)	Supporting Ethnopharmacological Notes
Philippines	"Toothache herb," "Biri "	Crushed leaves or decoction of aerial parts	Applied to toothache, to cleanse wounds, and to treat insect bites; occasionally made into a fever remedy	In the country, it is widely used as a numbing agent and a weak antiseptic.
India (Assam, Meghalaya, Tamil Nadu)	Toothache plant, "Akkakara," "Maanjit"	Fresh flower heads chewed or leaves crushed and applied directly	Application as a sedative in mild cases; to treat oral pain, sore throat and mouth ulcers	Tribal medicine: thought to enhance salivation, and reduce toothache
Thailand	"Phak-Khi-Khao," "Raan"	Flower heads chewed raw or	Used to treat toothache, colds, and mouth infections	Highly regarded in Thai natural medicine as an analgesic and antiseptic agent

		boiled with other herbs		
Indonesia (Java, Sumatra)	"Jotang"	Leaf paste or decoction applied to skin; also cooked as food	Used as a tonic and digestive aid, applied to wounds, and used on skin infections	It is culinary and medicinal; it has been traditionally regarded as a warming herb that enhances circulation
China (Southern provinces)	"Gui yuan ju"	Flower heads infused in alcohol or oil	Applied on swelling, toothache and small wounds.	Traditional medicine attributes its cooling and pain-relieving effects to its essential oils
Nepal	"Maaratii"	Fresh flower heads chewed	Cures toothache, inflamed gums and mouth	Widespread in the herbal markets of highlands; commonly prepared with clove to take care of the mouth
Malaysia	"Subang nenek"	Infused oil or crushed leaf poultice	Topically applied to the skin by infusion or crushing	Known as a domestic herbal remedy that has antiseptic effect.

Overall, people in Asia have traditionally used *Acmella oleracea* in the ways shown in Table 1. It lists the plant's local names, how to prepare it, and some of the most common medicinal uses that people have reported from different countries. People all over the world use the plant in different ways, but most people use it to ease toothache, heal cuts and scrapes, lower fever, and keep small infections at bay. People in Asia use *Acmella oleracea* a lot to treat minor infections and ease pain, as shown in Table 1. People in India, the Philippines, and Thailand often chew on the flower heads or put crushed leaves on their wounds to help with cuts, mouth sores, and toothaches. Scientists have now found that spilanthol is a natural substance that can kill germs. It is what makes the drug work. These results back up what people have always thought about the plant's healing powers and show that old remedies can still lead to new scientific research.

2.4. Phytochemistry of *Acmella oleracea*

2.4.1. Qualitative Phytochemical Profile

Acmella oleracea is a notable species from the *Asteraceae* family. It produces a wide range and specialized array of secondary metabolites [6]. Phytochemical screening confirms the presence of several major classes of compounds. These compounds support the plant's medicinal properties and pharmacological activities [4].

Primary Compound Classes

N-Alkylamides: This is the most important chemical group. N-Alkylamides, especially Spilanthol, determine the plant's biological activity. Other key alkylamides include the new alkylamide (2E,5Z)-N-isobutylundeca-2,5-diene-8,10-diynamide and known analogs such as (2E)-N-isobutyl-2-undecene-8,10-diynamide and (2E,6Z,8E)-N-(2-methylbutyl)-2,6,8-decatrienamide. These compounds feature an unsaturated aliphatic chain attached to an isobutyl amine group. This structure causes the characteristic pungency and local anesthetic effects [6].

Phenolic Compounds: Phenolics are widespread throughout the plant matrix. This group includes phenolic acids such as trans-ferulic acid, trans-isoferulic acid, and vanillic acid. Several flavonoids are also present. Phenolics act as metal chelators and radical scavengers, which is essential for the plant's strong antioxidant activity [9].

Coumarins: Coumarins are aromatic lactones. Scopoletin is the primary coumarin identified. Scopoletin is a known phytoalexin, which has a key role in the plant's defense mechanisms. Generally, coumarins contribute to anti-inflammatory and hepatoprotective bioactivities.

Triterpenoids and Sterols: These lipophilic compounds closely resemble mammalian hormones in structure. Main compounds include the pentacyclic triterpenoid 3-acetylaleuritolic acid and the sterols β-sitostenone and stigmasterol. Additionally, α- and β-Amyrin derivatives and Lupeol have been identified. These metabolites exhibit cytotoxic and anti-inflammatory effects. They are primarily extracted with nonpolar solvents.

Other Components: *Acmella oleracea* also contains essential oils such as myrcene and d-limonene. Qualitative tests show the presence of saponins and tannins. This complex chemical profile supports the plant's various traditional uses. The major phytochemical classes and bioactive constituents are summarized in Table 2.

Table 2 Major Phytochemical Classes and Bioactive Compounds Identified in *Acmella oleracea*

Compound Class	Notable Compounds	Key Activity/Property	Source
N-Alkylamides	Spilanthol, (2E,5Z)-N-isobutylundeca-2,5-diene-8,10-diynamide, (2E)-N-isobutyl-2-undecene-8,10-diynamide	Local anesthetic, Analgesic, Pungent taste	10.3390/molecules20046970
Phenolic Compounds	trans-Ferulic acid, trans-isoferulic acid, vanillic acid, Flavonoids	Antioxidant, Free radical scavenging	10.3390/molecules20046970
Coumarins	Scopoletin	Anti-inflammatory, Phytoalexin	10.3390/pharmaceuticals16050697
Triterpenoids/Sterols	3-acetylaleuritolic acid, beta-sitostenone, stigmasterol, alpha-/beta-Amyrin, Lupeol	Cytotoxic, Anti-inflammatory	10.3390/molecules20046970
Essential Oils	d-Limonene, myrcene	Volatile aroma, Mild biological effects	10.3390/pharmaceuticals16050697

2.4.2. Quantitative Composition and Notable Compounds

Quantitative phytochemical analysis of *Acmella oleracea* primarily involves determining the concentrations of its characteristic N-alkylamides, especially spilanthol, and assessing antioxidant capacity via total phenolic and flavonoid content. High-performance liquid chromatography (HPLC) and ultra-fast liquid chromatography (UFLC), in combination with mass spectrometry, are employed to generate detailed profiles of compound concentrations.

N-Alkylamides: Spilanthol and Its Derivatives

Spilanthol ((2E,6Z,8E)-N-isobutyl-2,6,8-decatrienamide) is the most abundant and biologically active N-alkylamide in *Acmella oleracea*. Its concentration varies depending on the plant part, cultivation conditions, and extraction method. Spilanthol consistently functions as the primary chemical marker for quality assessment.

Table 3 Quantitative Analysis of Spilanthol in Different Extracts of *Acmella oleracea*

Class	Compound	Reported Concentration	Plant Part/ Extract	Analytical Technique	Source
Alkylamides	Spilanthol	1.72 mg/g Dried Matter	Aerial Parts (*in vitro* seedlings)	HPLC-DAD/MS	10.3390/molecules20046970
		5.69 mg/g Dried Matter	Aerial Parts (Hydroalcoholic extract)	HPLC-DAD/MS	10.3390/molecules20046970
		245.93 µ/mL	Flower Heads (Ethanol Extract)	HPLC-DAD	10.3390/molecules29030612
		97/7% Relative Content	Hydroethanolic Extract of Flowers	UHPLC-ESI-QTOF-MS/MS	10.3390/pharmaceuticals16050697

		84.52 ± 0.81 mg/g	Flower	HPLC-PDA	10.3390/molecules20046970
	Concentrated Spilanthol	63.4 mg/g Dried Extract	Aerial Parts (Hexane Fraction)	HPLC-DAD/MS	10.3390/molecules20046970

Naturally, the spilanthol concentration is highest in the flowers and inflorescences. This alkamide is primarily responsible for the pronounced pungent and numbing sensation. Recent analytical methods have identified up to seven additional alkamides in the methanolic extract. Quantitative variations are presented in Table 3.

Total Phenolic and Flavonoid Content

The concentrations of polyphenols and flavonoids are directly associated with the antioxidant and anti-inflammatory activities of *Acmella oleracea* extracts. Quantifying these compounds allows assessment of overall bioactive quality.

Table 4 Total Phenolic and Flavonoid Content of *Acmella oleracea* Extracts

Parameter	**Value**	**Plant Part/ Extract**	**Analytical Technique**	**DOI**
Total Phenolic Content (TFC)	11.19 mg/g Dried Matter Gallic Acid Equivalent	Roots (*in vitro* seedlings)	Folin-Ciocalteu	10.3390/ijms25168886
	11.45 ± 0.17 mg Gallic Acid Equivalent/g	Hydroponically Grown Plants	Folin-Ciocalteu	10.3390/ijms25168886
	12.33 ± 0.92 mg QE/g		Aluminum Nitrate method	10.3390/ijms25168886
	8.37 mg Gallic Acid Equivalent/g	NADES Extract	Folin-Ciocalteu	10.3390/molecules29030612
	14.50 mg QE/mL		Aluminum Chloride method	10.3390/molecules29030612

Antioxidant Activity

Quantifying antioxidant activity provides functional data on the extracts' ability to neutralize free radicals. This confirms the biological efficacy suggested by the TPC/TFC values. The total phenolic and flavonoid contents are shown in Table 4.

Table 5 Antioxidant Activity of *Acmella oleracea* Extracts Based on DPPH Assay

Assay	**Activity Measure**	**Plant Part/Extract**	**Source**
DPPH Radical Inhibition	IC_{50} = 44.50 ± 4.46 µg/mL	Methanolic Leaf Extract (AOM)	10.3390/ijms25168886
	63.56 ± 13.01 (RAA% of Quercetin)	Methanolic Leaf Extract (AOM)	10.3390/ijms25168886

Other Compounds

The use of Ultra-Fast Liquid Chromatography Quadrupole Time-of-Flight Mass Spectrometry (UFLC-QTOF-MS) has enabled the tentative identification and semi-quantification of individual phenolic compounds which offers more detailed analysis than total content measurements [9]. The identified components include:

- Phenolic acids: Vanillic acid and derivatives.

- Flavonoids: Quercetin and its glycosides.
- Other alkamides: Not more than seven additional N-alkylamide analogues have been identified alongside spilanthol, each contributing to the overall biological effects [9].

The collective quantitative data establishes essential benchmarks necessary for the development of standardized and effective *Acmella oleracea* extracts. The antioxidant activity results based on DPPH assay are summarized in Table 5.

3. Discussion

3.1. Pharmacological Activities

From 2015 to 2025, research has increasingly shown the versatility of *Acmella oleracea*, mainly because of its bioactive N-alkylamides (spilanthol), flavonoids, triterpenoids, and phenolic compounds. These biologically active components have demonstrated antimicrobial, antioxidant, anti-inflammatory, analgesic, and immunomodulatory effects [1, 4, 10].

3.1.1. Antimicrobial Activity

Acmella oleracea's antibacterial activity is one of the most studied pharmacological components. Ethanol and methanol extracts from the flowers and leaves of *Acmella oleracea* showed significant inhibitory effects against both Gram-positive bacteria and Gram-negative bacteria. This includes *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* [1]. Likewise, Spinozzi et al. [4] concluded that spilanthol-rich extracts compromise microbial cell membranes, hence diminishing bacterial viability. Turcov et al. [9] have reported similar strong antibacterial and antifungal activities in methanolic and aqueous extracts. This supports the use of the plant in traditional medicine for oral and wound infections.

3.1.2. Other Pharmacological Activities

In addition to antimicrobial activity, *Acmella oleracea* has also been shown to have anti-inflammatory and immunomodulatory effects. In this context, Maxim et al. [8] showed dose-dependent inhibition of nitric oxide and reactive oxygen species in vitro, indicating possible clinical applications in diseases mediated by inflammation. In some cases, high levels of flavonoids and phenolic compounds correlate with detectable DPPH and ABTS radical-scavenging capacities [2, 9]. All these bioactivities provide justification for the use of *Acmella oleracea* in the traditional medicine of multiple Asian communities for the treatment of infections, toothache, and inflammation.

3.2. Toxicological Profile and Safety Considerations

With most available studies focusing on acute and subchronic toxicity in animal models, toxicological data on *Acmella oleracea* remain limited. However, existing evidence suggests that the plant has a relatively wide safety margin when used within traditional therapeutic doses. Furthermore, studies have reported that ethanolic and aqueous extracts of *Acmella oleracea* did not produce significant adverse effects on vital organs, hematological parameters, or body weight at moderate doses in rodents [1, 4]. Although, high doses or prolonged exposure to ethanolic extracts have shown mild hepatic and renal alterations in animal studies, suggesting cautious dosing and further toxicological evaluation.

The major bioactive compound, spilanthol, has also shown low in-vitro cytotoxicity. On the other hand, higher concentrations may cause transient irritation or mucosal numbness, consistent with its traditional use for toothache relief [2]. Excessive intake, however, has not been extensively evaluated, and standardized toxicity data across extract types and preparation methods are lacking.

Moreover, no significant allergenic or teratogenic effects have been reported, but human clinical data are limited, and most findings come from short-term experimental models. Just like many medicinal plants, variations in solvent extraction, dosage, and plant origin can affect safety outcomes. Further toxicological profiling, dose-response studies, and long-term safety evaluations, particularly in human populations, are needed to establish clear safety thresholds and clinical relevance.

Research Gap and Future Research

Acmella oleracea has been examined for its phytochemical composition and pharmacological effects; however, most evidence comes from in-vitro studies. Aktar et al. [1] and Spinozzi et al. [4] examined the plant and identified a significant presence of flavonoids, phenolics, and alkamides. Nonetheless, many findings remain unverified by *in-vivo*

or clinical studies. Moreover, ethnopharmacological reports from Asia often rely on descriptive narratives that show little standardization in preparation methods, dosages, and bioassay protocols, making it difficult to compare studies.

Future researches should focus on *in-vivo* and clinical investigation to show that *Acmella oleracea* has antibacterial and therapeutic capabilities. According to Sharma and Arumugam [7], using standardized methods to extract and test key bioactive compounds makes the data more reliable and enables a comprehensive safety assessment. You might also want to know that Asian types work differently in different areas and have different phytochemical profiles. If these problems are fixed, the reasons for using *Acmella oleracea* carefully and its chances for drug development will be better.

4. Conclusion

This study investigates the phytochemical properties, traditional medicinal uses, and antimicrobial potential of *Acmella oleracea*, commonly known as the Toothache Plant, in Asia. By synthesizing scientific findings with traditional knowledge, the research highlights the plant's significance as both a cultural remedy and a scientifically validated source of therapeutic compounds.

Research from various peer-reviewed studies confirms that *Acmella oleracea* contains a variety of significant bioactive compounds, including spilanthol, flavonoids, alkylamides, and phenolic acids. These compounds underpin its analgesic, anti-inflammatory, antioxidant, and antimicrobial properties, thereby providing a scientific rationale for the plant's longstanding use in traditional Asian medicine for alleviating toothaches, treating wounds, and managing minor infections. The consistent ethnopharmacological applications across diverse cultures underscore its reliability, accessibility, and therapeutic value.

Moreover, the study notes that while traditional uses have been supported by in-vitro analyses, further research is necessary to establish standardized formulations, dosage safety, and clinical efficacy. Conducting in vivo and human trials would yield stronger evidence for its integration into contemporary pharmaceutical and therapeutic practices.

Acmella oleracea presents a promising medicinal plant that bridges the gap between folk healing traditions and scientific innovation. Its enduring application and growing scientific interest reflect its potential as a source of natural antimicrobial and therapeutic agents. With continued research and proper standardization, this plant could significantly contribute to the development of safe, affordable, and culturally rooted treatments in modern medicine.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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