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# *Acmella oleracea* Plant; Identification, Applications and Use as an Emerging Food Source – Review

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## ABSTRACT

*Acmella oleracea* (L.) R.K.Jansen belongs to the family Asteraceae is generally called “toothache plant”. Though *Acmella* genus has complex patterns, the cylindrical discoid capitula which owe agolden yellow color with red tip make it unique. It is an annual herb, occurring around the world and, is cultivated for horticultural, pharmacological (anti-inflammatory, antimicrobial, anesthetic, antioxidant, antiseptic, antiobesity and anticancer), insecticidal, personal care and culinary purposes. Spilanthol is the major alkamide available in *Acmella* plant, responsible for its unique sensorial effects. There have been remarkable promote in *A.oleracea* herb in multidisciplinary studies, and anumber of commercial products have been invented over the years. Its application in the food industry has been scarcely explored and make opportunities for further research. This review provides an updated overview of the growing conditions of the plant, identification methods, edibility as food, functional properties, phytochemicals, and other applications which opens future applications in food production.

## KEYWORDS

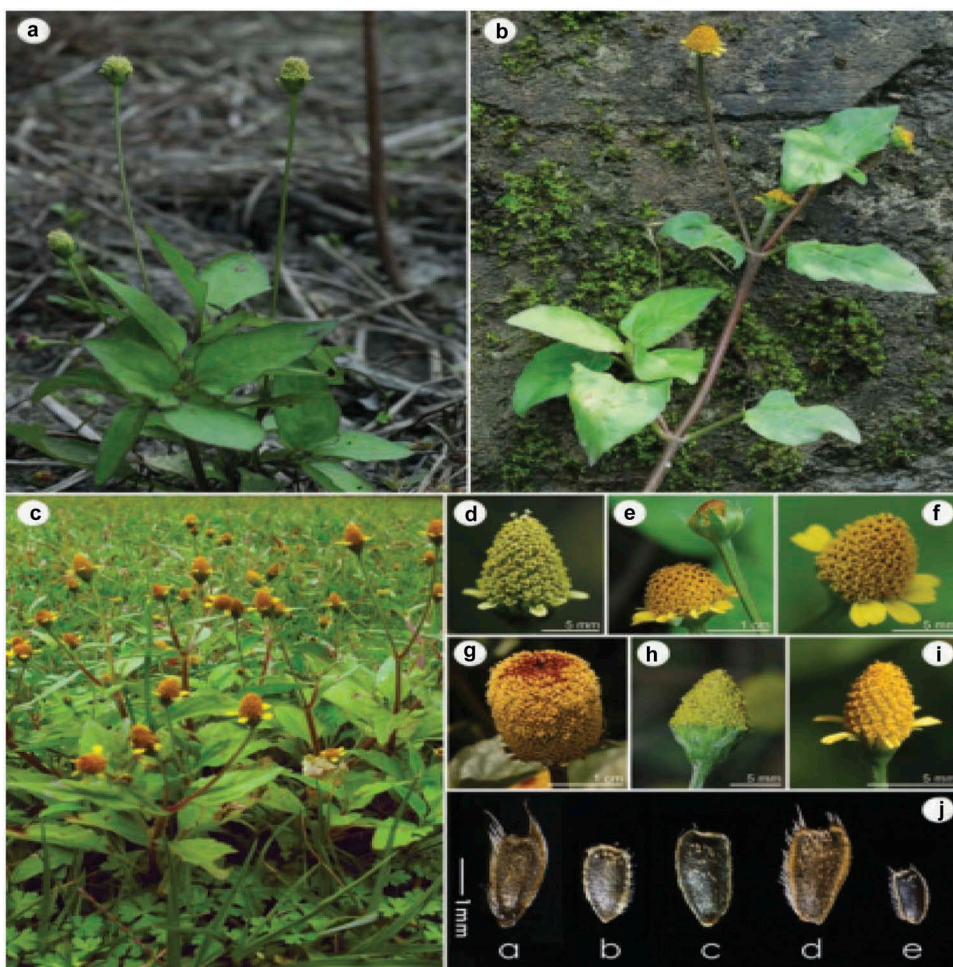
*Acmella oleracea*; food applications; functional property; spilanthol; antimicrobial

## Introduction

The genus *Acmella* which belongs to the family Asteracea comprises 30 species and nine additional infraspecific taxa.<sup>[1,2]</sup> One of the most distinguished members of the genus is *Acmella oleracea* (L.) R.K.Jansen due to its large cylindrical discoid capitula which owe aunique golden yellow color with the red tip (Figs. 1g and 2). *Acmella oleracea* (R.K. Jansen) is an annual herb that is occurring around the world including Sri Lanta, India, Nepal, China, Taiwan, Mexico, Bolivia, Brazil and regions such as Africa, America, and Asia.<sup>[3–5]</sup> It has been widely cultivated for horticultural, medicinal, insecticidal, and culinary purposes. Raw *Acmella* (jambu) have substantial amounts of nutrients.<sup>[6]</sup> Recent studies revealed that raw *Acmella* leaves are comprised with approximately 24.01% of protein, 1.54% of lipid, 63.38% carbohydrate, 62.61% fiber,10.92% of ash (dry basis), high amount of some mineral such as Ca,Mg and Cu, and amino acids such as asparagine, glutamic acid, valine and isoleucine.<sup>[7]</sup> Spilanthol is the major alkamide available in the *Acmella* plant, responsible for its unique sensorial effects.<sup>[8–10]</sup> In vitro studies have shown its anti-inflammatory<sup>[11]</sup>, antimicrobial<sup>[12]</sup>, anesthetic<sup>[13]</sup>, antipyretic, antioxidant<sup>[14,15]</sup>, insecticidal<sup>[5]</sup>, antiseptic, immune stimulation<sup>[16]</sup>, antiobesity, and

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**Figure 1.** Different species of *Acmella* plants (a) Habit of *Acmella brachyglossa*; (b) Habit of *Acmella ciliate*; (c) Habit of *Acmella uliginosa*; (d–j) radiate (d,f,i) and discoid (g,h) capitula; (d) *Acmella brachyglossa*; (e, f) *Acmella ciliate*; (g) ***Acmella oleracea***; (h) *Acmella paniculata*; (i) *Acmella uliginosa*; (j) achenes, the scalar bar = 1mm: (a) *Acmella brachyglossa*; (b) *Acmella ciliate*; (c) ***Acmella oleracea***; (d) *Acmella paniculata*; (e) *Acmella uliginosa*.<sup>[1]</sup>

anticancer effects. There have been remarkable promote in *Acmella oleracea* herb by multidisciplinary studies, and an intensified number of commercial products have appeared in the market as personal care products, health care products, and for culinary use over years.

*Acmella* is generally called as “toothache plant”<sup>[5,18–21]</sup> because of its ability to stimulate saliva production (sialagogue), numbing and tingling properties.<sup>[22]</sup> The other common names for *Acmella oleracea* L. include jambu, agrião do Pará, akmaella, spot flower, brede mafane and paracress.<sup>[5,7,23–27]</sup> This plant is popular among Brazilian (jambu) dishes due to their sensorial anesthetic and spicy properties.<sup>[25]</sup>

There is some doubt in the literature over the name of the genus and species of *Acmella* plant.<sup>[12,28–31]</sup> The monographs<sup>[1,5,24,32]</sup> on *Acmella* mentioned of false synonyms for *A.*



**Figure 2.** (a) Image of an *Acmella oleracea* (L) RKJansen plant.<sup>[17]</sup> (b) Flower pod of *Acmella oleracea* plant.

*oleracea* that appear on various websites.<sup>[32]</sup> Some of them state that the “accepted scientific name” is *Spilanthes acmella* (L.) Murr., but the photos on them clearly show *A. oleracea* vice versa.<sup>[5,15,33,34]</sup> In other articles, the plants named as *Spilanthes acmella* (L.) Murr. have yellowish (golden) flower pods and those plants are about 32–60cm in height.<sup>[35]</sup> Morphological, chromosomal and molecular evidence assist authentication of the genus into two genera: *Spilanthes* and *Acmella*, which can be clearly identified by at least eight morphological characters and by distinctive basic chromosome numbers.<sup>[36–38]</sup>

The genus *Acmella* has very complex patterns of morphological and chromosomal variation that have caused difficulties in demarcating taxa, especially at the specific and infraspecific levels.<sup>[5]</sup> The monograph also stated that the “currently accepted name” for *Spilanthes acmella* (L.) Murr. is *Blainvillea acmella* (L.) Philipson.<sup>[5]</sup> There is another article discussed a Mexican plant that they called *Acmella oppositifolia*, while the local name was Chilcuage.<sup>[39]</sup> There are also five different species of *Acmella* in Taiwan (Fig. 1) that contain spilanthal.<sup>[1]</sup> Finally, there is an article that lists *S. acmella* and *S. oleracea* as two separate plants.<sup>[40]</sup>

Chung et al.<sup>[1]</sup> revealed that the identification of this plant through the appearance and color of the inflorescence. *Acmella oleracea* flower pod is generally 3.5–0.5mm in diameter, occasionally two per capitulum, apex acute; palea stramineous, often with a purple-tinged when young but other species are having apod without a red tip.<sup>[1]</sup>

The genus is attributed to a number of medicinal, antimicrobial, larvicidal,<sup>[41]</sup> and insecticidal properties due to the presence of bioactive compounds, one of them is isobutyl amides,<sup>[9]</sup> which is used in folk medicine for the treatment of several disorders including stomatitis and colds. However, there is a serious constraint of recurrent availability of the material in mass scale which in turn is needed for the extraction of secondary metabolites.<sup>[42]</sup> Moreover, there is a lack of complete nutritional composition analysis for each part of the plant. Over the past few decades, many products have been developed by extracting the active ingredient (spilanthal) in the fields of pharmacological products, cosmetics, and food.<sup>[25,43]</sup> Its application in the food industry has been scarcely explored

and make opportunities for further research. This review provides an updated overview of the growing conditions of the plant, identification methods, edibility as food, potential functional properties, phytochemicals and other applications in which an avenue will be open for the future application of *Acmella* plant in food production.

### Growing conditions and macroscopy

The plant is mostly cultivated in fresh cultivation areas and grows best in clay soil which is rich in organic matters. *Acmella* is grown in low open spaces and may ascend up to an altitude of about 1200m.<sup>[12,26]</sup> *A. oleracea* is an annual herb up to 90-cm tall usually sown in April and can attain matures within 6–8 months.<sup>[1]</sup> Hind and Biggs<sup>[17]</sup> have stated that *A. oleracea* is grown wild in Brazil and it prefers humid and very damp soil even can be grown in lake margins. It is easily get wilted, accordingly should be planted in rich soil with high moisture.<sup>[44]</sup> Even though it is an annual herb, it can be grown in a protected glass during winter. It does not root frequently at the nodes, so it is unlikely to spread far, hence dense planting is recommended. It can be grown in the ground or as a potted herb. In Sri Lanka, this plant is called as Akmaella,<sup>[26]</sup> and it has been identified in the areas of Uwa, Western and Central provinces. It can be found in damp soil in villages, pasture lands, paddy fields, along ditches, marshy meadows, old clearings, on open hillsides and the rocky shores of rivers, and roadsides. It thrives best in soil rich in compost.

Stems generally decumbent to ascending and green to red in color, glabrous texture. Petioles are about 2–6.5cm long, narrowly winged, glabrous or very sparsely pilose. Leaf blades are broadly ovate to deltate. Capitula (compact head of structures) are discoid 10.5–23.5mm high, 11–17mm in diameter<sup>[5]</sup> (Fig. 1g). *Acmella oleracea* is characterized by its large and cylindrical discoid capitula, a feature that is unique for the genus. For centuries, this highly ornamental plant has been admired for its medicinal value and widely cultivated around the world. In Taiwan, *Acmella oleracea* is commonly cultivated for its horticultural and medicinal properties, especially for relieving toothache. Chung et al.<sup>[1]</sup> revealed that the identification of this plant through the appearance and color of the inflorescence. *Acmella oleracea* flower pods are generally 11–27mm in diameter and often with a purple-red tinged while other species are having a pod without a red tip (Figs. 1 and 2).

### Edible nature as a food

*Acmella* is known as jambu, agrião bravo, or agrião do Pará in Brazil. The plant is used in local dishes (Brazil), among which are tacacá (soup) and duck in tucupi sauce (a broth made by the fermentation of the liquid extracted from wild manioc) as well as in Japanese dishes. Additionally, extracts of the *Acmella* plant are used as a food-flavoring agent in the cuisines all over the world.<sup>[45]</sup> Recent studies have proved that raw *Acmella* has nutritional value compared to boiled form. *Acmella* comprised with substantial amount of protein (24.01%), ash (10.92%), total fiber (62.61%) some mineral such as Ca (2551.56mg/100 g), Mg (734mg/100 g) and Cu (2.09mg/100 g), and amino acids such as asparagine (32.01mg/g), glutamic acid (28.26mg/g), valine (14.55mg/g) and isoleucine (14.19mg/g).<sup>[7,23]</sup> Nevertheless, *Acmella* is not well known in the rest of the world<sup>[7,23]</sup>; it is used as an appetite stimulant in Brazil and Japan.<sup>[46,47]</sup>

Some people sense the spilanthal-induced tingling of the tongue unpleasant; nevertheless, cooked parts of plant lose its strong flavor and can be used as a green leafy vegetable.<sup>[48,49]</sup> This vegetable is mainly cultivated and consumed in the Northern region of Brazil as a seasoning in foods.<sup>[50]</sup> The leaves and stem are frequently consumed either cooked or used as a seasoning to enhance the flavor of other food items.<sup>[14,51]</sup> In America, these raw leaves are consumed as a pungent flavoring for salads.<sup>[26,51]</sup> The aerial part of the plant is hot in taste and produces numbness or tingling sensation in the mouth upon mastication. This sensation is present in the plant leaves and yellow flower.<sup>[8,25,52]</sup> *Acmella oleracea* (L.) R.K. Jansen is commonly used as a condiment in local dishes because of its pungent flavor in northern Brazil.<sup>[52]</sup> Moreover, tea made from its buds and leaves is consumed as a beverage by some communities which is having analgesic properties. Thus, *A. oleracea* is consumed as food or tea, and there are reported studies on its polysaccharide isolation, structural characterization, and antiulcer activity of hot aqueous extraction of *A. oleracea* leaves.<sup>[23]</sup>

## Functional properties

Different extracts of *A. oleracea* have been reported to hold numerous important functions.<sup>[11]</sup> Table 1 gives a summary of functional activities of *Acmella oleracea* plant extract, including antibacterial effect, antifungal effects,<sup>[69]</sup> larvicidal effects,<sup>[53,57,70]</sup> analgesic<sup>[71]</sup>, antiwrinkling agent, antioxidant,<sup>[72]</sup> female aphrodisiac,<sup>[68]</sup> antiobesity properties, etc.

Hexane extract of the flower bud was earlier accounted to act as a larvicide against three important mosquito species such as *Anopheles stephensi*, *A. culicifacies*, and *Culex quinquefasciatus*.<sup>[41]</sup> The decoctions obtained from the leaves and flowers of this plant are used as remedies for toothache, stomatitis, constipation, peptic ulcers, liver abscess, stammering and anesthetic effect in folk medicine over a hundred years.<sup>[8,21,25,40,62]</sup>

Recent studies have revealed that the hydroethanolic extract from leaves of *A. oleracea* have very low ecotoxicity and can be used against *Culex quinquefasciatus* and *Aedes aegypti* because of lower environmental impact.<sup>[54]</sup> Besides this, the plant was also reported to show antimicrobial activity against bacteria such as *Klebsiella pneumoniae*, *Bacillus subtilis*, and *Escherichia coli* as well as an antifungal activity against *Aspergillus niger*.<sup>[12,58,73]</sup> Also, Borate and Disale have successfully found the possible inhibition effect of leaf and inflorescence extracts tested against seven different bacteria named *Bacillus megaterium*, *B. subtilis*, *B. cereus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Micrococcus luteus*, and *Pseudomonas aeruginosa*.<sup>[74]</sup> In 2012, ethanol extracts of *A. oleracea* were found to be effective against the foodborne pathogens like *E. coli*, *Pseudomonas* spp., *Bacillus* spp., *Klebsiella* spp., *Staphylococcus* spp. and even *Salmonella* spp.<sup>[59]</sup> This antimicrobial potential of this plant could be used in the food industry for hygiene management as well as food safety management.

Mouse treated with methanol extract also presented an anti-inflammatory function which can suppress neutrophilic inflammation in the lungs of the treated animal.<sup>[60]</sup> In addition, it is used to control skin hyperpigmentation or control the enzymatic browning and also used in making natural products in topical wound care.<sup>[43,46]</sup> Furthermore, *Acmella* is used to combat insects and parasites in folk medicine. Benelli et al.<sup>[4]</sup> have proven the insecticidal effect of *Acmella* essential oil, especially the potential of terpenes as

Table 1. Functional activities of *Acmella* extracts.

Activity	Tested model/application	Extraction method/usage		Reference
		Part of the plant	Extracted solvent/method	
Larvicidal effect/Insecticidal effect	<i>Anopheles stephensi</i> , <i>A.culicifacies</i> , <i>Culex quinquefasciatus</i>	Seedling leaf explants of <i>Acmella oleracea</i>	Hexane, hydro ethanol	[4,41,42,53-55]
	<i>Aedes aegypti</i>	<i>Acmella oleracea</i>	Hexane	[10,56]
	<i>Tuta absoluta</i> (Tomato pest)	<i>Acmella oleracea</i> whole plant	Methanol	[27]
	<i>Rhipicephalus microplus</i> , <i>Dermacentor nitens</i>	Leaves, stems and flower	Ethanol	[57]
	<i>Amblyomma cajennense</i>	Arial partsof <i>Acmella oleracea</i> (L.) R.K. Jansen	Petroleum ether Ethanol Double distilled water	[3,58]
Antibacterial	<i>Klebsiella pneumoniae</i> , <i>Bacillus subtilis</i> and <i>Escherichia coli</i>	Flower pod of <i>Acmella oleracea</i>	Ethanol	[59]
Antifungal	<i>Klebsiella spp.</i> , <i>P.aurogenosa</i> , <i>Salmonella</i> , <i>Bacillus spp.</i> , <i>Escherichia coli</i>	Splianthes acmella Flowers	Petroleum ether Ethanol Double distilled water	[58]
	<i>Aspergillus Niger</i>	Whole plant	Methanol	[60]
Anti-inflammatory effect	HEK 293 and RAW 264.7 cells neutrophilic inflammation in the lungs of the treated animal (mouse)	<i>S.acmella</i> Murray- whole plant	Methanol	[8,52]
Analgasic	Mice	Flower of <i>Acmella oleracea</i>	Ethanol	[52]
Antinociceptive(chemical and thermal) effect	Adult male mice were treated by intraperitoneal route	Flowers of <i>Acmella oleracea</i> (L.) R.K. Jansen	Ethanol	[8,25,40]
Local anesthetic effect	Folk medicine	Leaves, specially flower pod	-	[61]
Gastro protective and gastric healing effect	Rat	Leaves of <i>Acmella oleracea</i> (L.) R.K. Jansen	Water extract	[62]
Antiflatulent effect (against constipation and peptic ulcer)	Folk medicine	Whole plant	Boil with water	[62]
	Against cirrhosis and liver abscess	Flower of <i>Acmella</i>	Crushing to keep in mouth	[62]
Anti- toothache/induce saliva secretion	Folk medicine	Flower of <i>Acmella</i>	Crushing to keep in mouth	[21,25,28,62,63]
Antioxidant	Hydroxyl radical scavenging and Hydrogen peroxide radical scavenging assays	Arial parts of <i>Acmella oleracea</i>	Methanol extracts	[14]
Blood brain barrier permeability/ Prevent skin hyper pigmentation/ control the enzymatic browning	Permeation through Caco-2 cell monolayer	Flower of <i>Acmella</i>	Ethanol	[64]
	Tyrosinase inhibition activity- UV-vis method.	Whole plant of <i>Acmella oleracea</i>	Methanol extracts- dichloromethane and hexane fractions	[43]
Enhance salty taste/ Anti- wrinkling Property	Mouse taste bud cells	<i>Acmella oleracea</i>	Splianthol	[22]
	Inhibit contractile activity in subcutaneous face muscles.	Whole plant of <i>Acmella oleracea</i>	Using polar solvent	[65]
Anti-obesity	Mouse 3T3-L1 pre-adipocytes	Leaves/flower	-	[66]
Cytotoxic effect	Hela and V79 carcinoma cells	Arial parts of <i>Acmella oleracea</i>	Methanol	[14]
	<i>Rhipicephalus sanguineus</i> , <i>Rhipicephalus microplus</i>	Arial parts of <i>Acmella oleracea</i>	Ethanol	[43,67]
Anaesthetic effect	Juvenile tambaqui - <i>Colossoma macropomum</i>	Flower pods of <i>Splianthes acmella var oleracea</i> (L.)	Supercritical fluid extraction-ethanol	[68]
Reproductive toxicity (female aphrodisiac)	Zebra fish ( <i>Danio rerio</i> )	Fresh flowers of <i>Acmella oleracea</i>	Hydroethanolic extract	[11]

biopesticides. Complete studies have not been done yet to reveal the exact mechanisms of action responsible for analgesic and anti-inflammatory activities of this plant. However, flavonoids are known as target prostaglandins that are involved in the late phase of acute inflammation and pain perception.<sup>[75]</sup> In 2018, Xu and others have revealed that spilanthol in the *Acmella* plant enhances sodium chloride responses in taste bud cells.<sup>[22]</sup> Therefore, it could be utilized as a salt taste enhancer. Moreover, recent studies have revealed the reproductive and developmental toxicity of the hydroethanolic extract of *Acmella oleracea*. De Souza et al.<sup>[11]</sup> have studied reproductive and developmental toxicity of the hydroethanolic extract taken from fresh flowers against zebrafish and resulted in few gonad tissue alterations, without interfering in reproduction and significantly increased egg deposition. They have stated that some reactions of spilanthol metabolism are linked to its toxicity, such as hydroxylation, C-oxidation, N-glucuronidation, N-acetylation, epoxidation, and glutathionation. Barbas et al.<sup>[68]</sup> have observed anesthetic and antioxidant properties of *Acmella* pod extracts obtained through supercritical fluid extraction towards *Colossoma macropomum*. The effects of the plant extract may differ depending on the type of cells treated, the type of extraction, temperature used in extraction, and solvents used in the extraction process.<sup>[75,76,86]</sup> Therefore, more in-depth studies of the biological activities of this plant are needed to be carried. Since this is an edible plant which shows beneficial activities in multidisciplinary applications, *Acmella* could be considered as a functional food ingredient in nutraceutical development.

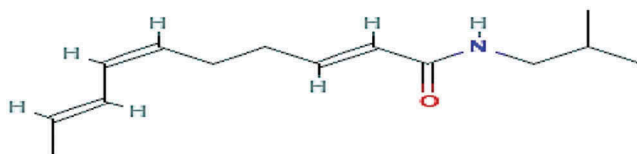
## Phytochemicals

Extensive phytochemical investigations of *Acmella oleracea* plant had previously been reported. It constitutes a diverse group of compounds. It was found to contain many important bioactive compounds such as spilanthol, amyriester, stigmasterol, miricilic alcohol glycosides, sitosterol, saponins, and triterpenes which are responsible for therapeutic uses.<sup>[14,77–80]</sup> As a result of phytochemical studies, alkyl amides such as 3-acetylauritolic acid,  $\beta$ -sitostenone, scopoletin, vanillic acid, trans-ferulic acid, and trans-isoferulic acid have been found<sup>[9,53]</sup> (Table 2).

**Table 2.** Phytochemical compounds in *Acmella oleracea* plant.

Category	Name of the compound	Part of the plant	References
Alkamide	Spilanthol, undeca-2E,7Z,9E-trienoic acid isobutylamide, 2E)-N-(2-methylbutyl)-2-undecene-8,10-diyamide, deca-6,9-dihydroxy-(2E,7E)-dienoic acid isobutylamide, deca-8,9-dihydroxy-(2E,6Z)-dienoic acid isobutylamide, nona-2,3-dihydroxy-6,8-dienoic acid 2-phenylethylamide	Leaf, flower pod, whole plant	[3,24,42,43,47,53,63,79,81,82]
Phytosterols	$\beta$ -sitostenone, stigmasterol, $\alpha$ - and $\beta$ -amyriins	-	[83]
Essential oils	Limonene and $\beta$ -caryophyllene	Flower pod	[84]
Terpenes	$\beta$ caryophyllene, $\beta$ pinene, myrcene, caryophyllene oxide, limonene	Flower pod	[4,84]
Esters	(7Z,9E)-2-oxo-undeca-7,9-dienyl 3-methylbut-2-enoate (acmellonate)	Whole Plant	[85]
Aromatic compound <sup>[83]</sup>	Vanillic acid	Vanillic acid	Whole Plant





**Figure 3.** (2E,6Z,8E)-N-Isobutyl-2,6,8-decatrienamide (spilanthol).

**Table 3.** Phytochemical screening results (qualitative) for different parts of the *Acmella oleracea* plant.

Part of the plant	Solvent	Extraction method	Alkaloids	Flavonoids	Saponin	Steroid Glycosides	Tannins	Terpenoids	References
Leaf	Methanol	Soxhlet	+	+	+	+	+	NM	[78]
Stem			+	+	+	+	+	NM	
Flower			+	+	+	+	+	NM	
Flower	Water	Maceration	+	-	+	NM	+	+	[102]

+, presence; - absence; NM, not mentioned.

Among the chemical components, spilanthol (C<sub>14</sub>H<sub>23</sub>NO, 221.339 g/mol) is considered to be the major active compound that can impart various important biological activities.<sup>[24,28,86–89]</sup> Spilanthol is an important secondary metabolite that is claimed to be responsible for antioxidant, antimicrobial, neuroprotective, insecticidal, anticancer and anti-inflammatory bio-activities. Spilanthol was first isolated and characterized by Gerber<sup>[91]</sup> from *A.oleracea*.<sup>[14,15,17,24,80,90–93]</sup> The plants in which spilanthol present are often called as toothache plant because of its analgesic property.<sup>[3,40,63,86,94–96]</sup> There were a number of studies that have been carried out on account of a broad range of biological activities exerted by spilanthol.<sup>[24]</sup> Its IUPAC name is (2E,6Z,8E)-N-Isobutyl-2,6,8-decatrienamide (Fig.3) which is an unsaturated alkamide with a relative polar amide and a less polar fatty acyl. This amphiphilic nature (hydrophilic and hydrophobic) creates the advantage of extracting spilanthol from *Acmella* plants using either ethanol, water, methanol, hexane, petroleum ether or supercritical carbon dioxide, etc.<sup>[9,28,63,72,97,98–101]</sup> The review article which was written by Barbosa et al.<sup>[24]</sup> has mentioned the biological functions of spilanthol (analgesic, antinociceptive, antioxidant, anti-inflammatory, antiwrinkle, antimicrobial, diuretic toothache relief, etc.). Although human toxicity of spilanthol has not been extensively tested, it is (*Acmella oleracea*) consumed for a long time as an edible plant. The spilanthol content in different parts of the plant has not been determined.

Research studies of qualitative studies on *Acmella oleracea* have proved the presence of alkaloids, flavonoids, saponins, steroid glycosides, and tannins (Table 3) in all parts of the plant (leaves, stems, and flower heads).

## Applications

Traditionally, *A.oleracea* is used for the treatment of flatulence, constipation, peptic ulcer, liver abscess, intestinal infection, stammering, toothache, stomatitis, etc.<sup>[48,62,72]</sup> Both flower and leaves of *Acmella* have a pungent taste accompanied by tingling and numbness; accordingly, they have been used as a spice for appetizers and as folk medicine for throat difficulties.<sup>[28,103]</sup> The flower head extract was used as a flavoring material for dentifrices and gum. Rather than dysentery, it has been used for the treatment of snakebite and

articular rheumatism. Besides these medicinal uses, the aqueous extract of the plant is used as astupefying agent for fishes in small rivers and streams.<sup>[14]</sup> Extracts of *A. oleracea* had been found to exert certain activities such as antimicrobial, antioxidant, diuretic, larvicidal, analgesic and mosquitocidal activities.<sup>[3]</sup> Tinctured products made from Paracress in Ireland are used for anti-fungal treatments in adults.<sup>[33]</sup> It is widely used in cooking and also popularly used to treat toothaches, tuberculosis, and anemia and as appetite stimulant in Brazil.<sup>[46,104]</sup>

Acmella plant has got important chemical properties, a fact that arouses the interest of the pharmaceutical industry, due to the occurrence of spilanthol, one of the major chemical constituents of the flowers and leaves of this species.<sup>[9,27]</sup> Spilanthol in Acmella can be absorbed through the skin, endothelia gut, oral mucosa and blood-brain barrier.<sup>[24,105]</sup> According to diverse traditional usage and pharmacological potential, *A. oleracea* is considered to be a good alternative to various commercial drugs<sup>[25]</sup> including in producing toothpaste too.<sup>[35]</sup> There are many literatures that disclosed the biological importance of spilanthol which is one of the major active ingredients in Acmella plant. A recent analysis on patent review referring the keyword “spilanthol” has provided 1444 records, over 20 years (1999–2016) including pharmacological, cosmetic<sup>[65,106–108]</sup>, extraction and sensorial applications.<sup>[25]</sup> *S. acmella* has long been used in traditional Asian medicine to treat various ailments, including pulmonary dysfunction.<sup>[80]</sup> Most recently, one of the studies has been done on evaluating the reproductive and developmental toxicity of the hydro-ethanolic extract of *Acmella oleracea*.<sup>[11]</sup> In the latter mentioned study, parent zebrafish which were subjected to treatments resulted in few gonad tissue alterations, without interfering in reproduction and significantly increased egg deposition.

## Future trends

The results from literature anthology of plant Acmella related to the bioactive alkalamide spilanthol over a period of 20 years made it possible to see the state of the art of spilanthol employed to food, cosmetic and pharmaceutical industries. Considering the vast amount of patents involving the food industry, this study contributes to this area, as it presents different technological ways to apply spilanthol, which helps to visualize opportunities and to boost innovation for new products. Recent research opens the new directions to study this plant in depth by analyzing nutrition composition on different parts of the plant, extracting proteins which could be used to produce active food packaging (nanomaterials), nutraceutical developments, using antimicrobial properties in food processing and sanitizing, evaluating the sensory properties, studies on toxicity of the extracts, introducing preserving techniques, etc. Acmella is a perishable commodity which is having higher water content.<sup>[50]</sup> Therefore, new methods in preserving raw materials will have to be researched in future. Also, antimicrobial properties of this plant could be applied for new package material productions with antiseptic properties using novel technologies as well as for the food hygienic management. Currently, synthetic chemicals are used in manufacturing sanitizers used for the food industry. Hence, there is a higher market demand to develop plant-based sanitizer for food handlers.<sup>[102]</sup> Since the plant is rich in phytochemicals causing anesthetic properties, studies should be further continued in toxicology, safety, and allergy aspects. More studies have to be on hydroethanolic extract to analyze reproductive and developmental toxicity of the *Acmella oleracea* plant extracts which has

important implications for studies of nonintentional pharmaceutical treatments. And a larger number of functional properties could be used to production of nutraceuticals that are demanded by consumers. Currently, this herb is used as aculinary ingredient in limited areas over the world. Hence, popularizing of this plant as aspic can bring immense benefits because of its higher functional properties, nutritional aspects as well as sensorial properties.

## Conclusion

Throughout this review, it has been shown that *Acmella* plant (*Acmella oleracea* (L.) R.K. Jansen) is a rich plant in important functional properties such as antibacterial effect, antifungal effects, gastroprotective, larvicidal effects, analgesic, antioxidant, flavor-enhancing, and antiobesity properties and edible nature.

Therefore, *Acmella* is a promising source of natural antiseptic properties to replace synthetic ones in food products; moreover, the inclusion of *Acmella* in food formulations may also provide valuable improvement against different illnesses. However, more studies about its toxicity and the potential application in food products will have to be determined along with the effects on different sensory and nutritional properties.

## Conflict of interests

The authors declare that they have no conflict of interests.

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## References

- [1] Chung, K.F.; Kono, Y.; Wang, C.M. Notes on *Acmella* (Asteraceae: Heliantheae) in Taiwan. *Bot. Stud.* **2008**, *49*, 10.
- [2] Mabberley, D.J.; Corner, E.J.H. A Portable Dictionary of Plants, Their Classification and Uses: Utilizing Kubitzki's the Families and Genera of Tascular Plants. In *Mabberley's Plant-Book*; Mabberley, D. J., Ed.; University Press: Cambridge, **2017**. ISBN:9781107115026. <https://www.cambridge.org/gb/academic>.
- [3] Dubey, S.; Maity, S.; Singh, M.; Saraf, S.A.; Saha, S. Phytochemistry, Pharmacology and Toxicology of *Spilanthes acmella* : A Review. *Adv. Pharmacol. Sci.* **2013**, 1–9. DOI: [10.1155/2013/423750](https://doi.org/10.1155/2013/423750).
- [4] Benelli, G.; Pavela, R.; Drenaggi, E.; Maggi, F. Insecticidal Efficacy of the Essential Oil of Jambú (*Acmella oleracea* (L.) R.K. Jansen) Cultivated in Central Italy against Filariasis Mosquito Vectors, Houseflies and Moth Pests. *J. Ethnopharmacol.* **2019**, *229*, 272–279. DOI: [10.1016/j.jep.2018.08.030](https://doi.org/10.1016/j.jep.2018.08.030).
- [5] Jansen, R.K. The Systematics of *Acmella* (Asteraceae-heliantheae). *Syst. Bot. Monogr.* **1985**, *8*, 1. DOI: [10.2307/25027614](https://doi.org/10.2307/25027614).
- [6] Seal, T.; Chaudhuri, K.; Pillai, B. Traditionally Used by the Local People of Meghalaya State in India. *Asian J. Plant Sci.* **2013**, *12*(4), 171–175. DOI: [10.3923/ajps.2013.171.175](https://doi.org/10.3923/ajps.2013.171.175).
- [7] Neves, D.A.; Schmiele, M.; Pallone, J.A.L.; Orlando, E.A.; Risso, E.M.; Cunha, E.C.E.; Godoy, H. T. Chemical and Nutritional Characterization of Raw and Hydrothermal Processed Jambu

- (*Acmella oleracea* (L.) R.K. Jansen). *Food Res. Int.* **2019**, *116*, 1144–1152. DOI: [10.1016/j.foodres.2018.09.060](https://doi.org/10.1016/j.foodres.2018.09.060).
- [8] Greger,H. Alkamides: ACritical Reconsideration of aMultifunctional Class of Unsaturated Fatty Acid Amides. *Phytochem. Rev.* **2016**, *15*(5), 729–770. DOI: [10.1007/s11101-015-9418-0](https://doi.org/10.1007/s11101-015-9418-0).
- [9] Ramsewak,R. Bioactive N-Isobutylamides from the Flower Buds of *Spilanthes acmella*. *Phytochemistry* **1999**, *51*(6), 729–732. DOI: [10.1016/S0031-9422\(99\)00101-6](https://doi.org/10.1016/S0031-9422(99)00101-6).
- [10] Moreno,S.C.; Carvalho,G.A.; Picanço,M.C.; Morais,E.G.; Pereira,R.M. Bioactivity of Compounds from *Acmella oleracea* against Tuta Absoluta (Meyrick) (Lepidoptera: Gelechiidae) and Selectivity to Two Non-Target Species. *Pest Manag. Sci.* **2012**, *68*(3), 386–393. DOI: [10.1002/ps.2274](https://doi.org/10.1002/ps.2274).
- [11] de Souza,G.C.; Matias Pereira,A.C.; Viana,M.D.; Ferreira,A.M.; da Silva,I.D.R.; de Oliveira, M.M.R.; Barbosa,W.L.R.; Silva,L.B.; Ferreira,I.M.; Dos Santos,C.B.R. *Acmella oleracea* (L.) R. K.Jansen Reproductive Toxicity in Zebrafish: An in Vivo and in Silico Assessment. *Evid. Based Complement. Alternat. Med.* **2019**, *2019*, 1–19. DOI: [10.1155/2019/1237301](https://doi.org/10.1155/2019/1237301).
- [12] Rani,A.S.; Murty,U.S. Evaluation of Antimicrobial Activity of *Spilanthes acmella* Flower Head Extract. *J.Nat. Remedies* **2005**, *5*(2), 170–171.
- [13] Chakraborty,A.; Devi,B.K.; Sanjebam,R.; Khumbong,S.; Thokchom,I. Preliminary Studies on Local Anesthetic and Antipyretic Activities of *Spilanthes acmella* Murr. In Experimental Animal Models. *Indian J.Pharmacol.* **2010**, *42*(5), 277. DOI: [10.4103/0253-7613.70106](https://doi.org/10.4103/0253-7613.70106).
- [14] Lalthanpuui,P.B.; Lalruatfela,B.; Vanlaldinpuia,K.; Lalremsanga,H.T.; Lalchhandama,K. Antioxidant and Cytotoxic Properties of *Acmella oleracea*. *Med. Plants - Int. J. Phytomedicines Relat. Ind.* **2018**, *10*(4), 353. DOI: [10.5958/0975-6892.2018.00051.5](https://doi.org/10.5958/0975-6892.2018.00051.5).
- [15] Franca,J.V.; Queiroz,M.S.R.; Do Amaral,B.P.; Simas,N.K.; da Silva,N.C.B.; Leal,I.C.R. Distinct Growth and Extractive Methods of *Acmella oleracea* (L.) R.K. Jansen Rising Different Concentrations of Spilanthol: An Important Bioactive Compound in Human Dietary. *Food Res. Int.* **2016**, *89*, 781–789. DOI: [10.1016/j.foodres.2016.09.018](https://doi.org/10.1016/j.foodres.2016.09.018).
- [16] Rojas,J.J.; Ochoa,V.J.; Ocampo,S.A.; Muñoz,J.F. Screening for Antimicrobial Activity of Ten Medicinal Plants Used in Colombian Folkloric Medicine: APossible Alternative in the Treatment of Non-Nosocomial Infections. *BMC Complement. Altern. Med.* **2006**, *6*(1), 2. DOI: [10.1186/1472-6882-6-2](https://doi.org/10.1186/1472-6882-6-2).
- [17] Hind,N.; Biggs,N. Plate 460. *Acmella oleracea* Compositae. *Curtis's Bot. Mag.* **2003**, *20*(1), 31–39. DOI: [10.1111/1467-8748.00368](https://doi.org/10.1111/1467-8748.00368).
- [18] Ramírez-Chávez,E.; Molina-Torres,J.; Ríos-Chávez,P. Natural Distribution and Alkamides Production in *Acmella radicans*. *Emirates J.Food Agric.* **2011**, *23*(3), 275–282.
- [19] Ratnasooriya,W.D.; Pieris,K.P.P.; Samaratunga,U.; Jayakody,J.R.A.C. Diuretic Activity of *Spilanthes acmella* Flowers in Rats. *J.Ethnopharmacol.* **2004**, *91*(2–3), 317–320. DOI: [10.1016/j.jep.2004.01.006](https://doi.org/10.1016/j.jep.2004.01.006).
- [20] Jayaweera,D.M.A. *Medicinal Plants. Part 111*; National Science Council of Sri Lanka: Colombo, Sri Lanka, **1981**.
- [21] Joseph,B.; George,J. The Role of *Acmella Oleracea* in Medicine- A Review. *World J.Pharm. Res.* **2013**, *2*, 2781–2788.
- [22] Xu,J.; Lewandowski,B.C.; Miyazawa,T.; Shoji,Y.; Yee,K.; Bryant,B.P. Spilanthol Enhances Sensitivity to Sodium in Mouse Taste Bud Cells. *Chem. Senses* **2019**, *44*(2), 91–103. DOI: [10.1093/chemse/bjy069](https://doi.org/10.1093/chemse/bjy069).
- [23] Nascimento,A.M.; de Souza,L.M.; Baggio,C.H.; de Werner,M.F.P.; Maria-Ferreira,D.; da Silva,L.M.; Sasaki,G.L.; Gorin,P.A.J.; Iacomini,M.; Cipriani,T.R. Gastroprotective Effect and Structure of aRhannogalacturonan from *Acmella oleracea*. *Phytochemistry* **2013**, *85*, 137–142. DOI: [10.1016/j.phytochem.2012.08.024](https://doi.org/10.1016/j.phytochem.2012.08.024).
- [24] Barbosa,A.F.; de Carvalho,M.G.; Smith,R.E.; Sabaa-Srur,A.U.O. Spilanthol: Occurrence, Extraction, Chemistry and Biological Activities. *Rev. Bras. Farmacogn.* **2016**, *26*(1), 128–133. DOI: [10.1016/j.bjp.2015.07.024](https://doi.org/10.1016/j.bjp.2015.07.024).
- [25] Silveira,N.; Sandjo,L.P.; Biavatti,M.W. Spilanthol-Containing Products: APatent Review (1996–2016). *Trends Food Sci. Technol.* **2018**, *74*, 107–111. DOI: [10.1016/j.tifs.2018.02.012](https://doi.org/10.1016/j.tifs.2018.02.012).

- [26] Lim,T.K. *Edible Medicinal and Non-Medicinal Plants, Fruits*; Springer: Dordrecht, 2014; Vol. 3. pp 469–472. DOI: [10.1007/978-94-007-2534-8](https://doi.org/10.1007/978-94-007-2534-8).
- [27] Cruz,P.B.; Barbosa,A.F.; Zeringóta,V.; Melo,D.; Novato,T.; Fidelis,Q.C.; Fabri,R.L.; de Carvalho,M.G.; Oliveira Sabaa-Srur,A.U.; Daemon,E.; etal. Acaricidal Activity of Methanol Extract of *Acmella oleracea* L.(Asteraceae) and Spilanthol on Rhipicephalus Microplus (Acari: Ixodidae) and Dermacentor Nitens (Acari: Ixodidae). *Vet. Parasitol.* **2016**, 228, 137–143. DOI: [10.1016/j.vetpar.2016.08.026](https://doi.org/10.1016/j.vetpar.2016.08.026).
- [28] Nakatani,N.; Nagashima,M. Pungent Alkamides from *Spilanthus acmella* L.Var. *Oleracea clarke*. *Biosci. Biotechnol. Biochem.* **1992**, 56(5), 759–762. DOI: [10.1271/bbb.56.759](https://doi.org/10.1271/bbb.56.759).
- [29] Favoreto,R.; Gilbert,B. *Acmella oleracea* (L.) R.K.Jansen (Asteraceae)-Jambu. *Rev. Fitos* **2013**, 5(1), 83–91.
- [30] Lin,W.C. *Wild Flowers of Taiwan-the 1300 Species Found in Lower Elevation*; Recreat. Press: Taiwan, 2005; Vol. 3, pp. 382.
- [31] Spilanthes- *Spilanthus acmella*. *Annie's Remedy Essential Oils of Herbs*. 2018. <https://www.anniesremedy.com/spilanthus-acmella.php>
- [32] Nicolas,V.C. *Acmella oleracea*-the-Toothache-Plant; Mecklenburgh Square Garden; 2017. <http://mecklenburghsquaregarden.org.uk/acmella-oleracea-the-toothache-plant/>
- [33] Evergreen Health foods. A.Vogel Spilanthus Paracress, Evergreen.ie, Ireland. 2019. <https://www.evergreen.ie/a-vogel-spilanthus-paracress?nosto=magento-recent>
- [34] Navarro-González,I.; González-Barrio,R.; García-Valverde,V.; Bautista-Ortín,A.; Periago,M. Nutritional Composition and Antioxidant Capacity in Edible Flowers: Characterisation of Phenolic Compounds by HPLC-DAD-ESI/MSn. *Int. J.Mol. Sci.* **2014**, 16(1), 805–822. DOI: [10.3390/ijms16010805](https://doi.org/10.3390/ijms16010805).
- [35] Savadi,R.; Yadav,R.; Yadav,N. Study on Immunomodulatory Activity of Ethanolic Extract of *Spilanthus acmella* Murr. *Leaves* **2010**, 1(2), 204–207.
- [36] Jansen,R.K. Systematics of Spilanthus (Compositae: Heliantheae). *Syst. Bot.* **1981**, 6(3), 231. DOI: [10.2307/2418284](https://doi.org/10.2307/2418284).
- [37] Reshmi,G.R.; Rajalakshmi,R. Three New Combinations in *Acmella* (Asteraceae: Heliantheae). *Trop. Plant Res. Int. J.* **2016**, 3, 67–69
- [38] Rahman,M.M.; Khan,S.A.; Hossain,G.M.; Jakaria,M.; Rahim,M.A. *Acmella radicans* (Jacq.) R.K. Jansen (Asteraceae) - ANew Angiosperm Record for Bangladesh. *Jahangirnagar Univ. J. Biol. Sci.* **2016**, 5(1), 87–93. DOI: [10.3329/jujbs.v5i1.29747](https://doi.org/10.3329/jujbs.v5i1.29747).
- [39] Molinatorres,J.; Salgado-Garciglia,R.; Ramirez-Chavez,E.; Del Rio,R.E. Purely Olefinic Alkamnides in Heliopsis Longipes and *Acmella* (Spilanthus) Opositifolia. *Biochem. Syst. Ecol.* **1996**, 24(1), 43–47. DOI: [10.1016/0305-1978\(95\)00099-2](https://doi.org/10.1016/0305-1978(95)00099-2).
- [40] Tiwari,K.L.; Jadhav,S.K.; Joshi,V. An Updated Review on Medicinal Herb Genus Spilanthus. *Zhong Xi Yi Jie He Xue Bao= J.Chin. Integr. Med.* **2011**, 9(11), 1170–1178. DOI: [10.3736/jcim20111103](https://doi.org/10.3736/jcim20111103).
- [41] Pandey,V.; Agrawal,V. Efficient Micropropagation Protocol of *Spilanthus acmella* L. Possessing Strong Antimalarial Activity. *Vitro Cell. Dev. Biol. - Plant* **2009**, 45(4), 491–499. DOI: [10.1007/s11627-008-9184-4](https://doi.org/10.1007/s11627-008-9184-4).
- [42] Pandey,V.; Chopra,M.; Agrawal,V. In Vitro Isolation and Characterization of Biolarvicidal Compounds from Micropropagated Plants of *Spilanthus acmella*. *Parasitol. Res.* **2011**, 108(2), 297–304. DOI: [10.1007/s00436-010-2056-y](https://doi.org/10.1007/s00436-010-2056-y).
- [43] Barbosa,A.F.; Silva,K.C.B.; de Oliveira,M.C.C.; de Carvalho,M.G.; Sabaa Srur,A.U.O. Effects of *Acmella oleracea* Methanolic Extract and Fractions on the Tyrosinase Enzyme. *Rev. Bras. Farmacogn.* **2016**, 26(3), 321–325. DOI: [10.1016/j.bjp.2016.01.004](https://doi.org/10.1016/j.bjp.2016.01.004).
- [44] Reshmi,G.R.; Rajalakshmi,R. Drought and UV Stress Response in *Spilanthus acmella* Murr., (Tooth-Ache Plant). *J.Stress Physiol. Biochem.* **2012**, 8(4), 110–129.
- [45] EFSA. Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific Opinion on Flavouring Group Evaluation 303 (FGE.303): Spilanthol from Chemical Group 30. *EFSA J.* **2011**, 9(3), 1995. doi:[10.2903/j.efsa.2011.1995](https://doi.org/10.2903/j.efsa.2011.1995).
- [46] Yamane,L.T.; de Paula,E.; Jorge,M.P.; de Freitas-blanco,V.S.; Junior,Í.M.; Figueira,G.M.; Anholetto,L.A.; de Oliveira,P.R.; Rodrigues,R.A.F. *Acmella oleracea* and Achyrocline

- Satureioides as Sources of Natural Products in Topical Wound Care. *Evid. Based Complement. Alternat. Med.* **2016**, 2016, 1–9. DOI: [10.1155/2016/3606820](https://doi.org/10.1155/2016/3606820).
- [47] Leng,T.C.; Ping,N.S.; Lim,B.P.; Keng,C.L. Detection of Bioactive Compounds from *Spilanthes acmella* (L.) Plants and Its Various in Vitro Culture Products. *J.Med. Plants Res.* **2011**, 5(3), 371–378.
- [48] Paulraj,J.; Govindarajan,R.; Palpu,P. The Genus *Spilanthes* Ethnopharmacology, Phytochemistry, and Pharmacological Properties: A Review. *Adv. Pharmacol. Sci.* **2013**, 1–22. DOI: [10.1155/2013/510298](https://doi.org/10.1155/2013/510298).
- [49] Lalthanpuii,P.B.; Lalawmpuii,R.; Lalchandama,K. Study on the Phytochemical Constituents and Some Biological Activities of the Toothache Plant *Acmella Oleracea*, Cultivated in Mizoram, India. *Res. J.Pharmacogn. Phytochem.* **2017**, 9(3), 152. DOI: [10.5958/0975-4385.2017.00028.0](https://doi.org/10.5958/0975-4385.2017.00028.0).
- [50] Gomes,F.P.; Osvaldo,R.; Sousa,E.P.; de Oliveira,D.E.C.; de Araújo Neto,F.R. Drying Kinetics of Crushed Mass of ‘Jambu’: Effective Diffusivity and Activation Energy. *Rev. Bras. Eng. Agríc. EAmbient.* **2018**, 22(7), 499–505. DOI: [10.1590/1807-1929/agriambi.v22n7p499-505](https://doi.org/10.1590/1807-1929/agriambi.v22n7p499-505).
- [51] Bailey,L.H. *Manual of Cultivated Plants; Most Commonly Grown in the Continental United States and Canada*, Revised ed.; The Macmillan C: NewYork, 1949.
- [52] Nomura,E.C.O.; Rodrigues,M.R.A.; da Silva,C.F.; Hamm,L.A.; Nascimento,A.M.; de Souza,L. M.; Cipriani,T.R.; Baggio,C.H.; de Werner,M.F.P. Antinociceptive Effects of Ethanolic Extract from the Flowers of *Acmella oleracea* (L.) R.K. Jansen in Mice. *J.Ethnopharmacol.* **2013**, 150(2), 583–589. DOI: [10.1016/j.jep.2013.09.007](https://doi.org/10.1016/j.jep.2013.09.007).
- [53] Simas,N.K.; da Dellamora,E.C.L.; Schripsema,J.; Lage,C.L.S.; de Filho,A.M.O.; Wessjohann, L.; Porzel,A.; Kuster,R.M. Acetylenic 2-Phenylethylamides and New Isobutylamides from *Acmella oleracea* (L.) R.K.Jansen, aBrazilian Spice with Larvicidal Activity on *Aedes Aegypti*. *Phytochem. Lett.* **2013**, 6(1), 67–72. DOI: [10.1016/j.phytol.2012.10.016](https://doi.org/10.1016/j.phytol.2012.10.016).
- [54] de Araújo,I.F.; de Araújo,P.H.F.; Ferreira,R.M.A.; Sena,I.D.S.; Lima,A.L.; Carvalho,J.C.T.; Ferreira,I.M.; Souto,R.N.P. Larvicidal Effect of Hydroethanolic Extract from the Leaves of *Acmella oleracea* L.R.K.Jansen in *Aedes aegypti* and *Culex quinquefasciatus*. *South Afr. J.Bot.* **2018**, 117, 134–140. DOI: [10.1016/j.sajb.2018.05.008](https://doi.org/10.1016/j.sajb.2018.05.008).
- [55] Saraf,D.K.; Dixit,V.K. *Spilanthes acmella* Murr.: Study on Its Extract Spilanthol as Larvicidal Compound. *Asian J.Exp. Sci.* **2002**, 16, 11.
- [56] Chhetri,L.B. Tomato Leafminer (*Tuta absoluta*) an Emerging Agricultural Pest: Control and Management Strategies: A Review. *World Sci. News* **2018**, 14, 9–17.
- [57] Anholeto,L.A.; de Oliveira,P.R.; Rodrigues,R.A.F.; Dos Spindola,C.S.; Labruna,M.B.; Pizano, M.A.; de Castro,K.N.C.; Camargo-Mathias,M.I. Potential Action of Extract of *Acmella oleracea* (L.) R.K. Jansen to Control *Amblyomma cajennense* (Fabricius, 1787) (Acari: Ixodidae) Ticks. *Ticks Tick-Borne Dis.* **2017**, 8(1), 65–72. DOI: [10.1016/j.ttbdis.2016.09.018](https://doi.org/10.1016/j.ttbdis.2016.09.018).
- [58] Bedi,P.S.; Jamwal,S.; Ellali,N.Z.M. Antimicrobial Activity of *Spilanthes acmella* and its Chemical Composition. *Saudi Journal of Medical and Pharmaceutical Sciences.* **2017**, 3, 8.
- [59] Sharmin,M.; Das,K.K.; Acharjee,M. Estimation of Microbiological Propagation and Antimicrobial Traits of the Frequently Accessible Flowers. *Stamford J.Microbiol.* **2015**, 4 (1), 19–23. DOI: [10.3329/sjm.v4i1.22756](https://doi.org/10.3329/sjm.v4i1.22756).
- [60] Kim,K.H.; Kim,E.J.; Kwun,M.J.; Lee,J.Y.; Bach,T.T.; Eum,S.M.; Choi,J.Y.; Cho,S.; Kim,S.J.; Jeong,S.I. Suppression of Lung Inflammation by the Methanol Extract of *Spilanthes acmella* Murray is Related to Differential Regulation of NF-KB and Nrf2. *J.Ethnopharmacol.* **2018**, 217, 89–97. DOI: [10.1016/j.jep.2018.02.011](https://doi.org/10.1016/j.jep.2018.02.011).
- [61] Maria-Ferreira,D.; da Silva,L.M.; Mendes,D.A.G.B.; Cabrini,D.; de,A.; Nascimento,A.M.; Iacomini,M.; Cipriani,T.R.; Santos,A.R.S.; de Paula Werner,M.F.; etal. Rhamnogalacturonan from *Acmella oleracea* (L.) R.K. Jansen: Gastroprotective and Ulcer Healing Properties in Rats. *PLoS One* **2014**, 9(1), e84762. DOI: [10.1371/journal.pone.0084762](https://doi.org/10.1371/journal.pone.0084762).
- [62] Neamsuvan,O.; Ruangrit,T. ASurvey of Herbal Weeds that are Used to Treat Gastrointestinal Disorders from Southern Thailand: Krabi and Songkhla Provinces. *J. Ethnopharmacol.* **2017**, 196, 84–93. DOI: [10.1016/j.jep.2016.11.033](https://doi.org/10.1016/j.jep.2016.11.033).

- [63] Sharma,A.; Kumar,V.; Rattan,R.S.; Kumar,N.; Singh,B. Insecticidal Toxicity of Spilanthol from *Spilanthes acmella* Murr. Against *Plutella xylostella* L. *Am. J.Plant Sci.* **2012**, 03(11), 1568–1572. DOI: [10.4236/ajps.2012.311189](https://doi.org/10.4236/ajps.2012.311189).
- [64] Veryser,L.; Taevernier,L.; Joshi,T.; Tatke,P.; Wynendaele,E.; Bracke,N.; Stalmans,S.; Peremans,K.; Burvenich,C.; Risseeuw,M. Mucosal and Blood-Brain Barrier Transport Kinetics of the Plant N-Alkylamide Spilanthol Using in Vitro and in Vivo Models. *BMC Complement. Altern. Med.* **2016**, 16(1), 177. DOI: [10.1186/s12906-016-1159-0](https://doi.org/10.1186/s12906-016-1159-0).
- [65] Demarne,F.; Passaro,G.; Gattefosse,S.A. Use of an *Acmella Oleracea* Extract for the Botulinum Toxin-like Effect Thereof in an Anti-Wrinkle Cosmetic Composition. U.S. Patent7,531,193. Issued May 12, **2009**.
- [66] Huang,W.C.; Peng,H.L.; Hu,S.; Wu,S.J. Spilanthol from Traditionally Used *Spilanthes acmella* Enhances AMPK and Ameliorates Obesity in Mice Fed High-Fat Diet. *Nutrients* **2019**, 11(5), 991. DOI: [10.3390/nu11050991](https://doi.org/10.3390/nu11050991).
- [67] De Oliveira,P.R.; Anholetto,L.A.; Rodrigues,R.A.F.; Arnosti,A.; Bechara,G.H.; de Carvalho Castro,K.N.; Camargo-Mathias,M.I. Cytotoxic Effects of Extract of *Acmella oleracea* in the Ovaries and Midgut of *Rhipicephalus Sanguineus* Latreille, 1806 (Acari: Ixodidae) Female Ticks. *J.Microsc. Ultrastruct.* **2019**, 7(1), 28. DOI: [10.4103/JMAU.JMAU\\_16\\_18](https://doi.org/10.4103/JMAU.JMAU_16_18).
- [68] Barbas,L.A.; Maltez,L.C.; Stringhetta,G.R.; de OliveiraGarcia,L.; Monserrat,J.M.; da Silva,D. T.; Heinzmann,B.M.; Sampaio,L.A. Properties of Two Plant Extractives as Anaesthetics and Antioxidants for Juvenile Tambaqui *Colossoma Macropomum*. *Aquaculture* **2017**, 20(469), 79–87. DOI: [10.1016/j.aquaculture.2016.12.012](https://doi.org/10.1016/j.aquaculture.2016.12.012).
- [69] Molina-Torres,J.; Salazar-Cabrera,C.J.; Armenta-Salinas,C.; Ramírez-Chávez,E. Fungistatic and Bacteriostatic Activities of Alkamides from *Heliopsis longipes* Roots: Affinin and Reduced Amides. *J.Agric. Food Chem.* **2004**, 52(15), 4700–4704. DOI: [10.1021/jf034374y](https://doi.org/10.1021/jf034374y).
- [70] Gasquet,M.; Delmas,F.; Timon-David,P.; Keita,A.; Guindo,M.; Koita,N.; Doumbo,O. Evaluation in Vitro and in Vivo of aTraditional Antimalarial. *Malarial 5. Fitoterapia-Milano* **1993**, 64, 423.
- [71] Cilia-López,V.G.; Juárez-Flores,B.I.; Aguirre-Rivera,J.R.; Reyes-Agüero,J.A. Analgesic Activity of *Heliopsis longipes* and Its Effect on the Nervous System. *Pharm. Biol.* **2010**, 48(2), 195–200. DOI: [10.3109/13880200903078495](https://doi.org/10.3109/13880200903078495).
- [72] Abeysinghe,D.C.; Wijerathne,S.M.N.K.; Dharmadasa,R.M. Secondary Metabolites Contents and Antioxidant Capacities of *Acmella oleraceae* Grown under Different Growing Systems. *World J.Agric. Res.* **2014**, 2(4), 163–167. DOI: [10.12691/wjar-2-4-5](https://doi.org/10.12691/wjar-2-4-5).
- [73] Fabry,W.; Okemo,P.O.; Ansorg,R. Antibacterial Activity of East African Medicinal Plants. *J. Ethnopharmacol.* **1998**, 60(1), 79–84. DOI: [10.1016/S0378-8741\(97\)00128-1](https://doi.org/10.1016/S0378-8741(97)00128-1).
- [74] Borate,P.P.; Disale,S.D. Studies on Antibacterial Activity of *Acmella oleracea* (L.) Murr. *Int. J.Pharm. Sci. Health Care.* **2013**, 5(3), 7.
- [75] Narayana,K.R.; Reddy,M.S.; Chaluvadi,M.R.; Krishna,D.R. Bioflavonoids Classification, Pharmacological, Biochemical Effects and Therapeutic Potential. *Indian J.Pharmacol.* **2001**, 33(1), 2–16.
- [76] Dhanani,T.; Shah,S.; Gajbhiye,N.A.; Kumar,S. Effect of Extraction Methods on Yield, Phytochemical Constituents and Antioxidant Activity of *Withania Somnifera*. *Arabian J. Chem.* **2017**, 10, S1193–S1199. DOI: [10.1016/j.arabjc.2013.02.015](https://doi.org/10.1016/j.arabjc.2013.02.015).
- [77] Lemos,T.L.G.; Pessoa,O.D.L.; Matos,F.J.A.; Alencar,J.W.; Craveiro,A.A. The Essential Oil of *Spilanthes acmella* Murr. *J.Essent. Oil Res.* **1991**, 3(5), 369–370. DOI: [10.1080/10412905.1991.9697962](https://doi.org/10.1080/10412905.1991.9697962).
- [78] Abeysiri,G.R.P.I.; Dharmadasa,R.M.; Abeysinghe,D.C.; Samarasinghe,K. Screening of Phytochemical, Physico-Chemical and Bioactivity of Different Parts of *Acmella oleraceae* Murr. (Asteraceae), aNatural Remedy for Toothache. *Ind. Crops Prod.* **2013**, 50, 852–856. DOI: [10.1016/j.indcrop.2013.08.043](https://doi.org/10.1016/j.indcrop.2013.08.043).
- [79] Cheng,Y.B.; Liu,R.; Ho,M.C.; Wu,T.Y.; Chen,C.Y.; Lo,I.W.; Hou,M.F.; Yuan,S.S.; Wu,Y.C.; Chang,F.R. Alkylamides of *Acmella oleracea*. *Molecules* **2015**, 20(4), 6970–6977. DOI: [10.3390/molecules20046970](https://doi.org/10.3390/molecules20046970).

- [80] Greger,H.; Hofer,O.; Werner,A. New Amides from *Spilanthes oleracea*. *Monatshefte Für Chemie/Chemical Monthly* **1985**, 116(2), 273–277. DOI: [10.1007/BF00798463](https://doi.org/10.1007/BF00798463).
- [81] De Alcantara,B.N.; Kobayashi,Y.T.; Barroso,K.F.; da Silva,I.D.R.; de Almeida,M.B.; Barbosa, W.L.R. Pharmacognostic Analyses and Evaluation of the in Vitro Antimicrobial Activity of *Acmella oleracea* (L.) RK Jansen (Jambu) Floral Extract and Fractions. *J.Med. Plants Res.* **2015**, 9(4), 91–96. DOI: [10.5897/JMPR2014.5680](https://doi.org/10.5897/JMPR2014.5680).
- [82] Spelman,K.; Depoix,D.; McCray,M.; Mouray,E.; Grellier,P. The Traditional Medicine *Spilanthes Acmella*, and the Alkylamides Spilanthol and Undeca-2E-Ene-8,10-Diynoic Acid Isobutylamide, Demonstrate in Vitro and in Vivo Antimalarial Activity: Anti-Malarial Activity of *Spilanthes acmella*. *Phytother. Res.* **2011**, 25(7), 1098–1101. DOI: [10.1002/ptr.3395](https://doi.org/10.1002/ptr.3395).
- [83] Prachayasittikul,S.; Suphamong,S.; Worachartcheewan,A.; Lawung,R.; Ruchirawat,S.; Prachayasittikul,V. Bioactive Metabolites from *Spilanthes acmella* Murr. *Molecules* **2009**, 14(2), 850–867. DOI: [10.3390/molecules14020850](https://doi.org/10.3390/molecules14020850).
- [84] Baruah,R.N.; Leclercq,P.A. Characterization of the Essential Oil from Flower Heads of *Spilanthes acmella*. *J.Essent. Oil Res.* **1993**, 5(6), 693–695. DOI: [10.1080/10412905.1993.9698310](https://doi.org/10.1080/10412905.1993.9698310).
- [85] Ley,J.P.; Blings,M.; Krammer,G.; Reinders,G.; Schmidt,C.O.; Bertram,H.J. Isolation and Synthesis of Acmelonate, aNew Unsaturated Long Chain 2-Ketol Ester from *Spilanthes acmella*. *Nat. Prod. Res.* **2006**, 20(9), 798–804. DOI: [10.1080/14786410500246733](https://doi.org/10.1080/14786410500246733).
- [86] Rios,M.Y.; Olivo,H.F. *Natural and Synthetic Alkamides. Studies in Natural Products Chemistry*; Elsevier, **2014**; Vol. 43, pp 79–121. DOI: [10.1016/B978-0-444-63430-6.00003-5](https://doi.org/10.1016/B978-0-444-63430-6.00003-5).
- [87] Prachayasittikul,V.; Prachayasittikul,S.; Ruchirawat,S.; Prachayasittikul,V. High Therapeutic Potential of *Spilanthes acmella*: A Review. *EXCLI J.* **2013**, 12, 291–312.
- [88] Castro-Ruiz,J.; Rojas-Molina,A.; Luna-Vázquez,F.; Rivero-Cruz,F.; García-Gasca,T.; Ibarra-Alvarado,C. *affinin* (Spilanthol), Isolated from *Heliopsis longipes*, Induces Vasodilation via Activation of Gasotransmitters and Prostacyclin Signaling Pathways. *Int. J.Mol. Sci.* **2017**, 18 (1), 218. DOI: [10.3390/ijms18010218](https://doi.org/10.3390/ijms18010218).
- [89] Borges,L.D.S.; Vieira,M.A.; Marques,M.O.; Vianello,F.; Lima,G.P. Influence of Organic and Mineral Soil Fertilization on Essential Oil of *Spilanthes oleracea* Cv. Jambuarana. *Am. J.Plant Physiol.* **2012**, 7(3), 135–142. DOI: [10.3923/ajpp.2012.135.142](https://doi.org/10.3923/ajpp.2012.135.142).
- [90] Purushothaman,Y.; Gunaseelan,S.; Vijayakumar,S.D. *Spilanthes acmella* and Its Medicinal Uses– AReview. *Asian J.Pharm. Clin. Res.* **2018**, 11(6), 45. DOI: [10.22159/ajpcr.2018.v11i6.24697](https://doi.org/10.22159/ajpcr.2018.v11i6.24697).
- [91] Gerber,E. Ueber die Chemischen Bestandteile der Parakresse (*Spilanthes oleracea*, Jacquin). *Arch. Pharm. (Weinheim)* **1903**, 241(4), 270–289. DOI: [10.1002/artdp.19032410404](https://doi.org/10.1002/artdp.19032410404).
- [92] Wang,Z.; Lu,X.; Lei,A.; Zhang,Z. Efficient Preparation of Functionalized (E,Z) Dienes Using Acetylene as the Building Block. *J.Org. Chem.* **1998**, 63(12), 3806–3807. DOI: [10.1021/jo980440x](https://doi.org/10.1021/jo980440x).
- [93] Yasuda,I.; Takeya,K.; Itokawa,H. The Geometric Structure of Spilanthol. *Chem. Pharm. Bull. (Tokyo)* **1980**, 28(7), 2251–2253. DOI: [10.1248/cpb.28.2251](https://doi.org/10.1248/cpb.28.2251).
- [94] Dandin,V.S.; Naik,P.M.; Murthy,H.N.; Park,S.Y.; Lee,E.J.; Paek,K.Y. Rapid Regeneration and Analysis of Genetic Fidelity and Scopoletin Contents of Micropropagated Plants of *Spilanthes oleracea* L. *J.Hortic. Sci. Biotechnol.* **2014**, 89(1), 79–85. DOI: [10.1080/14620316.2014.11513052](https://doi.org/10.1080/14620316.2014.11513052).
- [95] Martin,R.; Becker,H. Spilanthol-Related Amides from *Acmella Ciliata*. *Phytochemistry* **1984**, 23(8), 1781–1783. DOI: [10.1016/S0031-9422\(00\)83490-1](https://doi.org/10.1016/S0031-9422(00)83490-1).
- [96] Hajdu,Z. *An Ethnopharmacological Survey Conducted in the Bolivian Amazon, and Identification of N-Alkylamides and Lignans from Lepidium Meyenii and Heliopsis Helianthoides Var. Scabra with Effects on the Central Nervous System*; Szegedi Tudományegyetem: Szeged, Hungary, **2014**. DOI:[10.14232/phd.2483](https://doi.org/10.14232/phd.2483).
- [97] Dias,A.M.A.; Santos,P.; Seabra,I.J.; Júnior,R.N.C.; Braga,M.E.M.; de Sousa,H.C. Spilanthol from *Spilanthes acmella* Flowers, Leaves and Stems Obtained by Selective Supercritical



- Carbon Dioxide Extraction. *J.Supercrit. Fluids* **2012**, *61*, 62–70. DOI: [10.1016/j.supflu.2011.09.020](https://doi.org/10.1016/j.supflu.2011.09.020).
- [98] Rai,M.K.; Varma,A.; Pandey,A.K. Antifungal Potential of *Spilanthes calva* after Inoculation of Piriformospora Indica. Das Antimyzetische Potential Von *Spilanthes calva* Nach Inokulation Von Piriformospora Indica. *Mycoses* **2004**, *47*(11–12), 479–481. DOI: [10.1111/j.1439-0507.2004.01045.x](https://doi.org/10.1111/j.1439-0507.2004.01045.x).
- [99] Singh,M.; Chaturvedi,R. Screening and Quantification of an Antiseptic Alkylamide, Spilanthol from in Vitro Cell and Tissue Cultures of *Spilanthes acmella* Murr. *Ind. Crop Prod.* **2012**, *36*(1), 321–328. DOI: [10.1016/j.indcrop.2011.10.029](https://doi.org/10.1016/j.indcrop.2011.10.029).
- [100] Singh,M.; Chaturvedi,R. Evaluation of Nutrient Uptake and Physical Parameters on Cell Biomass Growth and Production of Spilanthol in Suspension Cultures of *Spilanthes acmella* Murr. *Bioprocess Biosyst. Eng.* **2012**, *35*(6), 943–951. DOI: [10.1007/s00449-012-0679-3](https://doi.org/10.1007/s00449-012-0679-3).
- [101] Bae,S.S.; Ehrmann,B.M.; Ettefagh,K.A.; Cech,N.B. AValidated Liquid Chromatography-Electrospray Ionization-Mass Spectrometry Method for Quantification of Spilanthol in *Spilanthes acmella* (L.) Murr. *Phytochem. Anal.* **2010**, *21*(5), 438–443. DOI: [10.1002/pca.1215](https://doi.org/10.1002/pca.1215).
- [102] Uthpala,T.G.G.; Navaratne,S.B. Developing Herbal Based Liquid Sanitizer to Maintain Personal and Environmental Hygiene as aDisaster Resilience. *Capacity Building for Research and Innovation in Disaster Resilience, Ascent Conference*; National Science Foundation: Sri Lanka **2019**; pp. 86–96. DOI:[10.1177/1753193419870403](https://doi.org/10.1177/1753193419870403).
- [103] Barbosa,A.F.; Sabaa-Srur,D.F.; Maia,J.G.S.; Sabaa-Srur,A.U.O. Microbiological and Sensory Evaluation of Jambu (*Acmella oleracea* L.) Dried by Cold Air Circulation. *Food Sci. Technol.* **2016**, *36*(1), 24–29. DOI: [10.1590/1678-457X.6827](https://doi.org/10.1590/1678-457X.6827).
- [104] Lorenzi,H.; Matos,F.J.D.A. *Plantas Medicinais No Brasil: Nativas EExóticas.* **2002**.
- [105] Veryser,L.; Wynendaele,E.; Taevernier,L.; Verbeke,F.; Joshib,T.; Tatke,P.; Spiegeleer,B.D. N-Alkylamides: From Plant to Brain. *Funct. Foods Health Dis.* **2014**, *4*(6), 264. DOI: [10.31989/ffhd.v4i6.6](https://doi.org/10.31989/ffhd.v4i6.6).
- [106] Belfer,W.A. Cosmetic Composition to Accelerate Repair of Functional Wrinkles. U.S. Patent 8,025,907, September 27, **2011**.
- [107] Shanthi,P.; Amudha,P. Evaluation of the Phytochemical Constituents of *Acmella calva* (DC) RK Jansen. *IntJPharma Bio. Sci.* **2010**, *1*(4), B308–B314.
- [108] Cosmetic pioneers in Brazil. *Natura Brazil-Anti-Aging Detox Night Cream 30+ - Chronos*; Cosmetic pioneers in Brazil; **2019**. <https://www.naturabrasil.fr/en-us/skincare/anti-aging-detox-night-cream-30-chronos-40ml-50205997>