

ANTINOCICEPTIVE, ANTI- INFLAMMATORY, AND ANTIMICROBIAL ACTIVITIES OF ACMELLA OLERACEA: FROM BIOACTIVE CONSTITUENTS TO EMERGING PRECLINICAL AND CLINICAL EVIDENCE

**ATIVIDADES ANTINOCICEPTIVA, ANTI-INFLAMATÓRIA E
ANTIMICROBIANA DE ACMELLA OLERACEA: DOS CONSTITUINTES
BIOATIVOS ÀS EVIDÊNCIAS PRÉ-CLÍNICAS E CLÍNICAS EMERGENTES**

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ABSTRACT

Acmedella oleracea (L.) R.K. Jansen, popularly known as jambu, is an Amazonian species traditionally used for culinary and medicinal purposes and characterized by the presence of bioactive metabolites, particularly N-alkylamides such as spilanthol. This review critically synthesizes the evidence concerning the antinociceptive, anti-inflammatory, and antimicrobial activities of *A. oleracea*, considering the bioactive constituents associated with these effects, the experimental models employed, and the progression of evidence from preclinical studies toward human investigations. A narrative review with a structured literature search was conducted using PubMed and SciELO, complemented by Google Scholar, with the literature updated through September 2026. Experimental evidence indicates that *A. oleracea* extracts and some of their constituents, particularly spilanthol, exert antinociceptive and anti-inflammatory effects in different experimental models and display activity against microorganisms of biomedical relevance. Recent studies have expanded this evidence to neuropathic and postoperative pain models, inflammatory processes, antifungal and antivirulence effects, and pain-related clinical applications. However, substantial heterogeneity in plant preparations, chemical composition, concentrations or doses, experimental models, and formulations limits direct comparisons among studies. Moreover, part of the human evidence derives from multicomponent formulations, preventing the observed effects from being attributed exclusively to *A. oleracea*. Overall, the available evidence supports the pharmacological relevance of the species, particularly at the preclinical level, while clinical evidence remains emerging and indication-specific. Further studies using chemically standardized preparations, mechanistic validation, rigorous safety assessment, dose–response characterization, and well-designed

clinical trials are required to establish the therapeutic relevance of *A. oleracea*.

Keywords: *Acmella oleracea*; spilanthol; antinociception; inflammation; antimicrobial activity.

RESUMO

Acmella oleracea (L.) R.K. Jansen, popularmente conhecida como jambu, é uma espécie amazônica utilizada tradicionalmente para diferentes finalidades alimentícias e medicinais e caracterizada pela presença de metabólitos bioativos, especialmente alquilamidas como o espilantol. Esta revisão sintetiza criticamente as evidências relacionadas às atividades antinociceptiva, anti-inflamatória e antimicrobiana de *A. oleracea*, considerando os constituintes bioativos associados a esses efeitos, os modelos experimentais empregados e a evolução das evidências pré-clínicas para investigações em humanos. Foi realizada uma revisão narrativa com busca estruturada da literatura nas bases PubMed e SciELO, complementada pelo Google Acadêmico, considerando estudos pertinentes ao escopo da revisão e uma atualização da literatura até 2026. As evidências experimentais indicam que extratos de *A. oleracea* e alguns de seus constituintes, particularmente o espilantol, apresentam efeitos antinociceptivos e anti-inflamatórios em diferentes modelos, além de atividade frente a microrganismos de interesse biomédico. Estudos recentes ampliaram a investigação para modelos de dor neuropática, processos inflamatórios, fatores de virulência fúngica e aplicações clínicas relacionadas à dor. Entretanto, a heterogeneidade dos extratos, das concentrações, dos modelos experimentais e das formulações utilizadas limita comparações diretas entre os estudos. Além disso, parte das evidências em humanos deriva de formulações multicomponentes, impossibilitando atribuir os efeitos observados exclusivamente a *A.*

oleracea. Em conjunto, os achados sustentam a relevância farmacológica da espécie e justificam investigações adicionais, particularmente estudos padronizados de composição, mecanismos de ação, segurança, dose-resposta e eficácia clínica.

Palavras-chave: *Acmella oleracea*; espilantol; antinocicepção; inflamação; atividade antimicrobiana.

1. INTRODUCTION

Acmella oleracea (L.) R.K. Jansen (Asteraceae), popularly known as jambu, is an edible and medicinal species strongly associated with the Amazon region, particularly northern Brazil, where its leaves and inflorescences are widely consumed and incorporated into traditional practices. Beyond its importance in regional cuisine, the species has attracted pharmacological interest because of its characteristic sensory effects and its traditional use in the management of toothache, oral discomfort, pain, and inflammatory conditions. These ethnobotanical applications, together with the increasing characterization of its chemical composition, have stimulated investigations into its potential biological and pharmacological properties (Rondanelli et al., 2020; Spinozzi et al., 2022; Lee, 2026).

The phytochemical profile of *A. oleracea* comprises several classes of secondary metabolites, including N-alkylamides, phenolic compounds, flavonoids, and volatile constituents. Among them, spilanthol (affinin) is the most extensively investigated and is commonly regarded as an important chemical marker of the species. Its abundance and biological properties have made it a major focus of studies addressing the pharmacological potential of jambu, although the biological effects of *A. oleracea* should not be

attributed to this compound alone. The composition of plant extracts may vary according to plant organ, cultivation conditions, extraction procedure, and other experimental factors, and additional constituents may contribute to the biological responses observed in complex preparations (Blanco et al., 2018; Spinozzi et al., 2022; Radulović et al., 2024; Lee, 2026).

Among the pharmacological properties investigated for *A. oleracea*, antinociceptive and anti-inflammatory activities are particularly relevant because of their relationship with the traditional use of the plant for pain relief. Experimental evidence has associated extracts and isolated constituents with modulation of nociceptive and inflammatory responses through different mechanisms and molecular targets. Studies involving spilanthol, for example, have demonstrated anti-inflammatory activity in cellular models, while other investigations have explored mechanisms involving inflammatory enzymes and signaling pathways (Blanco et al., 2018; Stein et al., 2021). More recent research has expanded this field toward neuropathic pain and human investigations, indicating a transition from predominantly mechanistic and preclinical evidence to an emerging, although still limited, clinical evidence base.

Antimicrobial activity represents another important component of the pharmacological profile of the species. Extracts and spilanthol-containing preparations have been investigated against microorganisms of biomedical relevance, including oral bacteria. Peretti et al. (2021), for instance, reported bactericidal and antibiofilm activity against *Streptococcus mutans*, with differences among *A. oleracea* subtypes and their spilanthol content. More recently, research on spilanthol isolated from *A. oleracea* demonstrated effects on the metabolism and a relevant virulence factor of

Cryptococcus neoformans, extending the antimicrobial discussion beyond antibacterial activity and highlighting the need to consider both bacterial and fungal models when evaluating the species.

Despite the increasing number of studies, interpretation of this body of evidence remains challenging. Investigations differ substantially in plant material, extraction procedures, chemical standardization, concentrations or doses, experimental models, biological endpoints, and formulations. Furthermore, evidence obtained with isolated spilanthol cannot automatically be extrapolated to crude extracts or to the plant as consumed traditionally. Conversely, biological responses observed with complex extracts cannot necessarily be attributed exclusively to spilanthol. These distinctions become particularly important when interpreting recent human studies, some of which have evaluated *A. oleracea* as part of multicomponent preparations rather than as a single intervention.

Recent reviews have broadened the understanding of the botany, ethnopharmacology, phytochemistry, and biological activities of *A. oleracea* (Lee, 2026), while systematic evidence synthesis has also begun to address specific pharmacological domains, including antibacterial properties within the genus *Acmella*. Nevertheless, the simultaneous relationship among antinociceptive, anti-inflammatory, and antimicrobial evidence, the bioactive constituents implicated in these effects, and the progression from experimental observations toward human investigation warrants a more focused analysis.

Accordingly, this review critically synthesizes the evidence concerning the antinociceptive, anti-inflammatory, and antimicrobial activities of *A. oleracea*, with particular attention to the

bioactive constituents associated with these effects, the experimental models used to investigate them, and the extent to which current knowledge has progressed from mechanistic and preclinical observations toward clinical investigation. By distinguishing among different levels of evidence and identifying methodological and translational limitations, the review seeks to provide a more critical framework for assessing the pharmacological potential of *A. oleracea* and for defining priorities for future research.

2. METHODOLOGY

This study was conducted as a narrative review with a structured literature search. Narrative reviews are particularly useful for integrating evidence from heterogeneous study designs, discussing the development of knowledge within a field, and identifying conceptual and methodological gaps, provided that the scope and procedures used to identify and interpret the literature are transparently described (Green; Johnson; Adams, 2006; Ferrari, 2015; Snyder, 2019). This approach was considered appropriate because the evidence on the pharmacological properties of *A. oleracea* encompasses phytochemical investigations, in vitro assays, animal models, mechanistic studies, and human investigations that differ substantially in design and outcomes.

The review was based on the literature survey originally conducted for the undergraduate research project and subsequently updated to incorporate recent evidence relevant to the scope of the present article. The original search was conducted in PubMed and SciELO, with Google Scholar used as a complementary search source. Search terms included combinations of “*Acmella oleracea*”, “jambu”, “spilanthol”, “alkylamides”, “antinociceptive activity”, “anti-

inflammatory activity”, “antimicrobial activity”, and related terms, using the Boolean operators AND and OR when applicable. The initial survey focused primarily on studies published between 2018 and 2024, while earlier publications were considered when necessary to provide relevant pharmacological, phytochemical, or historical context.

For the present review, the literature search was updated through 23 September 2026, maintaining the same thematic scope and prioritizing peer-reviewed studies directly addressing *A. oleracea*, its extracts, or its bioactive constituents in relation to antinociceptive, anti-inflammatory, antibacterial, or antifungal effects. Original studies involving in vitro and in vivo models and human investigations were prioritized as primary evidence. Review articles were used primarily to contextualize the field, identify additional relevant studies, and support broader aspects of ethnopharmacology and phytochemistry.

Studies were considered relevant when they provided experimental or clinical evidence directly related to the pharmacological domains addressed in this review or contributed to understanding the bioactive constituents associated with these effects. Publications focusing exclusively on ornamental, culinary, agricultural, insecticidal, or other biological applications outside the defined pharmacological scope were not considered part of the core evidence. Studies involving other species of *Acmella* without clearly distinguishable data for *A. oleracea* were also excluded from the primary synthesis.

The selected literature was qualitatively analyzed according to the biological activity investigated, type of extract, fraction or isolated

compound evaluated, experimental model, principal outcomes, and level of evidence. Particular attention was given to distinguishing findings obtained with whole or fractionated extracts from those obtained with isolated compounds, especially spilanthol, as well as results obtained with *A. oleracea* alone from those derived from multicomponent formulations. Evidence was organized into three major pharmacological domains—antinociceptive, anti-inflammatory, and antimicrobial activities—and interpreted according to its mechanistic, preclinical, or clinical nature. Because the study was designed as a narrative rather than a systematic review, no meta-analysis or formal risk-of-bias assessment was performed (Green; Johnson; Adams, 2006; Ferrari, 2015; Snyder, 2019).

3. RESULTS AND DISCUSSION

3.1. Phytochemical Basis And The Central Role Of Spilanthol

The pharmacological interest in *Acmella oleracea* is closely associated with its chemically diverse secondary metabolism, which includes N-alkylamides, phenolic compounds, flavonoids, terpenoids, and other lipophilic constituents. Among these compounds, spilanthol (N-isobutyl-2E,6Z,8E-decatrienamide) has received particular attention because it is one of the most characteristic N-alkylamides of the species and has been repeatedly investigated in relation to its sensory and pharmacological effects (Blanco et al., 2018; Spinozzi et al., 2022; Lee, 2026).

Importantly, however, the phytochemical composition of *A. oleracea* should not be regarded as uniform. The concentration of spilanthol and the relative abundance of other constituents may vary according to the plant organ, genotype or subtype, cultivation

conditions, developmental stage, and extraction procedure. Peretti et al. (2021), for example, demonstrated differences in spilanthol content among *A. oleracea* subtypes and related these chemical differences to variations in antibacterial and antibiofilm activity against *Streptococcus mutans*. More recent investigations have further reinforced the influence of extraction conditions on the recovery of spilanthol and other bioactive constituents, emphasizing chemical standardization as an important prerequisite for reproducible pharmacological comparisons.

Although spilanthol is the most frequently investigated constituent, attributing the pharmacological properties of *A. oleracea* exclusively to this compound would oversimplify the available evidence. Flavonoids, phenolic compounds, terpenoids, and other N-alkylamides have also been reported in the species, and their presence contributes to the chemical complexity of extracts (Spinozzi et al., 2022; Radulović et al., 2024; Lee, 2026). Nevertheless, the identification of a compound in an extract and the independent pharmacological activity previously described for that compound do not demonstrate that it is responsible for the biological effect of the *A. oleracea* preparation. Such attribution requires experimental evidence linking chemical composition to biological response.

This distinction is particularly relevant when comparing studies using crude extracts, fractions, spilanthol-rich preparations, and isolated spilanthol. Differences in pharmacological responses among these preparations may reflect variations in spilanthol concentration, the presence of additional constituents, extraction selectivity, bioavailability, or interactions within the phytochemical matrix. Claims of synergistic action should therefore be made

cautiously unless synergy has been experimentally demonstrated rather than inferred from the greater activity of a complex extract.

From this perspective, spilanthol is best considered a major pharmacologically relevant constituent and useful chemical marker of *A. oleracea* rather than the sole determinant of its biological activity. This framework is important for interpreting the antinociceptive, anti-inflammatory, and antimicrobial evidence discussed in the following sections, particularly because these activities have been investigated using chemically distinct preparations that are not necessarily pharmacologically equivalent.

3.2. Antinociceptive And Analgesic Evidence: From Experimental Mechanisms To Human Studies

The antinociceptive activity of *Acmella oleracea* is among the pharmacological properties most closely related to its traditional use, particularly its application for toothache and oral discomfort. This effect has been investigated using crude extracts, alkylamide-rich preparations, isolated natural alkylamides and, more recently, formulations evaluated in humans. Collectively, these studies support a biologically plausible antinociceptive action, although the magnitude and mechanisms of the response depend on the chemical composition of the preparation, dose, route of administration, and experimental pain model.

Early experimental evidence demonstrated that an ethanolic extract obtained from *A. oleracea* flowers produced antinociceptive effects in mice in different nociception models (Nomura et al., 2013). Although this study predates the main temporal range adopted in the present review, it provided an experimental basis for subsequent

investigations seeking to identify the compounds and mechanisms associated with the analgesic properties traditionally attributed to the species. Importantly, evidence obtained with a chemically complex flower extract does not establish which constituent is responsible for the observed response, but it provided a rationale for later studies focusing particularly on alkylamides.

A major contribution to the mechanistic understanding of these effects was provided by Dallazen et al. (2018), who investigated natural alkylamides obtained from *A. oleracea* and compared their effects with those of a synthetic isobutylalkyl amide. The study demonstrated that structurally related alkylamides may produce distinct local antinociceptive and pronociceptive responses and implicated transient receptor potential vanilloid 1 (TRPV1) in these effects. Molecular docking analyses provided additional support for potential interactions with this receptor; however, computational predictions should be interpreted as mechanistic support rather than direct evidence of receptor binding under physiological conditions. Particularly relevant is the observation that alkylamides may produce different, and under some experimental conditions opposing, nociceptive responses, indicating that their pharmacology cannot be interpreted as a simple and uniform analgesic effect (Dallazen et al., 2018).

Subsequent work extended these findings to inflammatory pain. Dallazen et al. (2020) investigated alkylamides obtained from *A. oleracea* flowers and a synthetic analogue in experimental models of inflammatory pain. Their results reinforced the antinociceptive potential of these compounds while also indicating that structural differences among alkylamides influence their pharmacological responses. These findings suggest that the activity of *A. oleracea*

cannot be predicted solely from total alkylamide or spilanthol content; the chemical identity of individual constituents and the biological context in which they are evaluated must also be considered.

The experimental evidence was subsequently expanded to more complex pain conditions. Dallazen et al. (2022) evaluated natural alkylamides from *A. oleracea* in mouse models of neuropathic and postoperative pain, extending previous observations beyond acute and inflammatory nociception. This progression is important because neuropathic and postoperative pain involve mechanisms that differ, at least partially, from those operating in conventional acute nociception models. The study therefore broadened the preclinical relevance of *A. oleracea*-derived alkylamides while reinforcing the importance of compound structure, concentration, and pain model in determining pharmacological response.

Mechanistic investigation has also continued through the evaluation of potential molecular targets. Yien et al. (2023) examined alkylamides isolated from *A. oleracea* and reported antinociceptive effects together with molecular docking analyses involving cannabinoid and TRPV1 receptors. These findings support the hypothesis that the antinociceptive properties of *A. oleracea* alkylamides may involve multiple molecular targets rather than a single pharmacological pathway. Nevertheless, docking results represent predictions of molecular interaction and should not be considered equivalent to functional receptor assays. Thus, while cannabinoid and TRPV1 pathways constitute plausible mechanistic candidates, their relative contribution to the effects of individual alkylamides requires further experimental clarification.

More recently, Ferrara et al. (2025) investigated hydroalcoholic extracts obtained from the aerial parts and roots of *A. oleracea* in a cellular model related to chemotherapy-induced neuropathic damage. The extracts were chemically characterized and contained phenolic compounds and alkylamides, including spilanthol. Their effects in SH-SY5Y cells provided evidence of neuroprotective potential and expanded the investigation of *A. oleracea* toward cellular mechanisms relevant to chemotherapy-induced neuropathy. These findings, however, should be distinguished from direct demonstration of antinociceptive activity in an animal or human pain model. Rather, they provide mechanistic and neuroprotective evidence that complements the in vivo findings obtained in neuropathic pain models by Dallazen et al. (2022).

The close relationship between nociception and inflammation also requires careful interpretation. Reduction of pain-related behavior may result partly from modulation of inflammatory processes rather than exclusively from direct interference with nociceptive signaling. Conversely, demonstration of anti-inflammatory activity does not necessarily establish an analgesic effect. Antinociceptive and anti-inflammatory activities should therefore be regarded as interconnected but distinct pharmacological outcomes. For this reason, evidence involving inflammatory enzymes, mediators, and signaling pathways is examined separately in the following section.

The transition from experimental models to human investigation has become increasingly evident in recent years. Silva et al. (2026) evaluated a bioadhesive film containing *A. oleracea* extract for reducing post-bleaching dental sensitivity in a randomized clinical trial involving 72 volunteers. The study compared the experimental *A. oleracea* preparation with placebo and a conventional

desensitizing treatment containing potassium nitrate and sodium fluoride. This investigation is particularly relevant because it moves beyond experimental nociception and evaluates a clinically measurable pain-related outcome in humans. Nevertheless, the findings relate to a specific dental-sensitivity condition and should not be generalized to analgesic efficacy in other painful disorders.

Other recent human investigations require additional caution because *A. oleracea* has frequently been evaluated as part of multicomponent formulations, including combinations with *Boswellia serrata* or conventional pharmacologically active substances. These studies are relevant to the development of *A. oleracea*-containing products but cannot establish the independent analgesic efficacy of the species. In such formulations, the observed response may result from *A. oleracea*, the other active components, or interactions among them. They should therefore be regarded as evidence of potential clinical applications of *A. oleracea*-containing formulations rather than direct confirmation of the independent antinociceptive activity of the plant.

Overall, the available literature reveals a progressive development of the evidence, from the antinociceptive activity of crude extracts to investigations of individual alkylamides, molecular targets, inflammatory, neuropathic, and postoperative pain models, neuroprotective mechanisms, and, more recently, human applications. The evidence remains strongest at the preclinical level, whereas clinical evidence is emerging but still limited and indication-specific. Future investigations should prioritize chemically standardized preparations, quantitative characterization of spilanthol and other alkylamides, dose–response relationships, mechanistic validation of proposed molecular targets, and

controlled clinical trials capable of determining the specific contribution of *A. oleracea* to analgesic outcomes.

3.3. Anti-Inflammatory Evidence And Proposed Mechanisms

The anti-inflammatory activity of *Acemella oleracea* is closely related to, but mechanistically distinct from, its antinociceptive effects. Whereas reduction of inflammatory signaling may contribute to pain relief, evidence of antinociception alone should not be interpreted as proof of anti-inflammatory activity. Studies directly evaluating inflammatory mediators, cellular responses, enzymatic targets, and inflammation-associated tissue alterations therefore provide a more appropriate basis for assessing this pharmacological property.

Among the bioactive constituents investigated, spilanthol has emerged as an important candidate for mediating anti-inflammatory effects. Blanco et al. (2018) isolated spilanthol from *A. oleracea* using extraction procedures developed within a green chemistry approach and evaluated its anti-inflammatory activity in vitro. Their findings provided direct evidence that isolated spilanthol can modulate inflammatory responses, strengthening the hypothesis that this N-alkylamide contributes substantially to the activity observed in *A. oleracea* preparations. This study is particularly relevant because the use of an isolated constituent reduces some of the interpretative uncertainty inherent to crude extracts, in which multiple compounds may contribute simultaneously to the biological response.

Evidence from animal models further supports the anti-inflammatory potential of spilanthol. Freitas-Blanco et al. (2019)

evaluated the compound in a murine model of intestinal mucositis induced by 5-fluorouracil and reported attenuation of intestinal damage associated with the inflammatory process. This model is considerably more complex than an isolated cellular assay because mucositis involves epithelial injury, inflammatory responses, and alterations in intestinal tissue. The findings therefore extend the evidence for spilanthol beyond *in vitro* activity. Nevertheless, protection against chemically induced mucositis represents a specific experimental condition and should not be generalized as evidence of efficacy across inflammatory diseases.

An important mechanistic contribution was subsequently provided by Stein et al. (2021), who investigated ethanolic extracts of *A. oleracea* and isolated spilanthol and identified chymase inhibition as a relevant component of their anti-inflammatory activity. Chymase is a serine protease released predominantly by mast cells and participates in the generation or activation of mediators involved in inflammatory and tissue-remodeling processes. The demonstration that both *A. oleracea* extracts and isolated spilanthol can interfere with this enzymatic target provides a more specific mechanistic basis for the anti-inflammatory effects attributed to the species (Stein et al., 2021).

The comparison between extract and isolated-compound studies is particularly informative. The activity of isolated spilanthol demonstrates that this molecule is pharmacologically active independently of the complete phytochemical matrix. However, activity observed with ethanolic or other complex extracts cannot automatically be attributed exclusively to spilanthol. *A. oleracea* contains additional N-alkylamides, phenolic compounds, flavonoids, and terpenoid constituents that may contribute to inflammatory

responses through different biochemical pathways. At present, the available evidence supports a prominent role for spilanthol but does not demonstrate that it is the sole determinant of the anti-inflammatory activity of the plant.

This distinction also has implications for claims of synergism. The chemical complexity of *A. oleracea* extracts makes interactions among constituents biologically plausible, but the presence of several compounds with individually reported anti-inflammatory properties does not, by itself, demonstrate synergistic activity. Demonstrating synergy requires appropriate comparative experiments with isolated constituents and defined combinations. Consequently, enhanced or broad activity of a crude extract should not be interpreted as evidence of synergism unless such interactions have been experimentally established.

More recent studies have broadened the biological context in which the anti-inflammatory potential of *A. oleracea* is being investigated. Research involving tissue repair and wound-healing models has reported biological responses consistent with modulation of inflammatory and regenerative processes. A recent investigation of *A. oleracea* leaf extract, for example, explored its bioactive potential in the context of wound healing (*Journal of Ethnopharmacology*, 2025, art. 118866). Such studies are relevant because successful tissue repair depends on a coordinated inflammatory response rather than indiscriminate suppression of inflammation. However, wound-healing activity is a multidimensional outcome involving cell proliferation, extracellular matrix remodeling, oxidative balance, and other processes; it therefore should not be used as isolated proof of an anti-inflammatory mechanism.

Another relevant issue is the relationship between chemical standardization and pharmacological interpretation. Variability in plant organ, cultivation conditions, extraction solvent, extraction technology, and spilanthol concentration can generate preparations with substantially different chemical profiles. Consequently, apparently divergent anti-inflammatory responses among studies may reflect not only differences in biological models but also differences in the preparations being tested. Reporting the concentration of spilanthol and, where possible, other major constituents is therefore important for reproducibility and for establishing meaningful dose–response relationships.

Taken together, current evidence supports anti-inflammatory activity at the preclinical level, with spilanthol representing the most consistently investigated constituent and chymase inhibition providing one experimentally supported mechanistic pathway. Nevertheless, the anti-inflammatory pharmacology of *A. oleracea* appears to be more complex than a single compound–single target relationship. The heterogeneity of extracts and experimental models, limited chemical standardization across studies, and scarcity of clinical investigations specifically designed to evaluate inflammatory outcomes currently prevent firm conclusions regarding therapeutic efficacy in humans. Future studies should combine chemically characterized preparations with defined inflammatory biomarkers, dose–response analyses, and mechanistically oriented experimental designs to determine how spilanthol and other constituents contribute individually or collectively to the anti-inflammatory effects of the species.

3.4. Antimicrobial Activity: Antibacterial And Antifungal Evidence

The antimicrobial potential of *A. oleracea* has been investigated against different microorganisms, with evidence involving crude extracts, chemically characterized preparations, and isolated constituents. However, the available studies vary considerably in extraction method, plant material, microorganism, concentration, and antimicrobial endpoint. Consequently, the term “antimicrobial activity” encompasses heterogeneous experimental evidence and should not be interpreted as indicating a uniform or broad-spectrum effect of the species.

Among the better-characterized antibacterial investigations, Peretti et al. (2021) evaluated aqueous and hydroethanolic extracts obtained from different *A. oleracea* subtypes against *Streptococcus mutans*, a bacterium strongly associated with dental caries and cariogenic biofilms. The authors determined spilanthol content and investigated both bactericidal and antibiofilm activities, allowing chemical differences among plant preparations to be considered together with their biological responses. This approach is particularly relevant because it moves beyond a simple demonstration of growth inhibition and addresses biofilm formation, a phenotype of substantial biomedical importance due to the increased tolerance of biofilm-associated microorganisms to environmental stress and antimicrobial interventions.

The findings of Peretti et al. (2021) also reinforce an issue discussed in the previous sections: different preparations of *A. oleracea* should not be regarded as chemically or pharmacologically equivalent. Differences in spilanthol content among subtypes were accompanied by differences in biological activity against *S. mutans*. Although such an association supports the pharmacological relevance of spilanthol, correlation between its concentration and

antimicrobial response does not by itself establish that spilanthol is solely responsible for the effect. Other constituents present in the extracts may contribute to bacterial growth inhibition or interference with biofilm development.

Evidence accumulated for *Acmella* species has subsequently been examined in a systematic literature review focused on antibacterial properties (Shuid et al., 2026). The review identified activity against microorganisms including *Streptococcus mutans* and *Staphylococcus aureus*, while also highlighting substantial methodological heterogeneity among studies. Although these findings support the broader antibacterial potential of the genus, evidence obtained from other *Acmella* species should not be automatically extrapolated to *A. oleracea*. Species-specific identification, plant material, extraction procedures, and antimicrobial assays remain essential when interpreting the pharmacological potential of jambu itself.

Another important consideration is the nature of the antimicrobial endpoint. Inhibition zones, minimum inhibitory concentrations (MIC), minimum bactericidal concentrations (MBC), and antibiofilm assays provide different types of information and should not be treated as interchangeable measures of antimicrobial potency. Agar diffusion results, for example, are influenced not only by antimicrobial activity but also by the ability of compounds to diffuse through the culture medium. For chemically complex and relatively lipophilic plant preparations, such methodological differences can substantially affect apparent activity. Therefore, studies providing quantitative MIC or MBC values and chemically characterized preparations offer stronger comparative information than screening based exclusively on inhibition-zone measurements.

Antifungal evidence has also been reported for spilanthol. A study published in 2021 investigated this alkylamide in experimental models of vulvovaginal candidiasis and identified it as a promising antifungal compound against *Candida* spp. These findings broadened the antimicrobial relevance of *A. oleracea*-derived spilanthol beyond bacterial models and preceded more recent investigations addressing its effects on fungal metabolism and virulence. Nevertheless, as with other preclinical findings, antifungal activity demonstrated under experimental conditions should not be directly extrapolated to therapeutic efficacy in humans (Fabri et al. 2021).

More recent evidence has extended the antimicrobial investigation of *A. oleracea* beyond bacteria. A 2025 study evaluated spilanthol obtained from *A. oleracea* against *Cryptococcus neoformans*, an opportunistic pathogenic yeast. Rather than restricting the analysis to fungal growth inhibition, the investigators examined metabolic alterations and effects on an important virulence-associated phenotype. The study demonstrated that exposure to spilanthol altered fungal metabolism and impaired a relevant virulence factor of *C. neoformans* (Silva, 2025). This represents an important expansion of the antimicrobial evidence because it suggests that the biological effects of spilanthol may involve interference with microbial physiology and pathogenicity in addition to direct effects on growth.

The distinction between antimicrobial and antivirulence activity is particularly important in interpreting these findings. Reduction of a virulence factor may decrease the pathogenic potential of a microorganism without necessarily producing fungicidal activity at the same concentration. Conversely, growth inhibition does not

reveal which pathogenic mechanisms are affected. The *C. neoformans* study therefore contributes mechanistic information that complements conventional susceptibility assays and broadens the pharmacological relevance of spilanthol beyond the antibacterial models more commonly investigated for *A. oleracea*.

Nevertheless, the antimicrobial evidence remains predominantly in vitro. Activity demonstrated against planktonic cells or biofilms under controlled laboratory conditions does not establish therapeutic efficacy in an infected organism. Bioavailability, metabolism, achievable tissue concentrations, toxicity to host cells, microbial environment, and pharmacokinetic properties may substantially alter activity in vivo. This limitation is especially relevant for spilanthol and other lipophilic constituents, whose physicochemical characteristics influence solubility, formulation, and delivery.

The available evidence also does not justify describing *A. oleracea* as a substitute for established antimicrobial therapy. Rather, current findings identify the species and spilanthol as sources of bioactive molecules deserving further antimicrobial investigation. From a translational perspective, the most promising directions include chemically standardized extracts, purified compounds, topical or oral formulations, antibiofilm applications, and studies targeting microbial virulence. These approaches require comparative experiments with reference antimicrobials, standardized susceptibility methods, evaluation against resistant clinical isolates, cytotoxicity assessment, and subsequent validation in appropriate in vivo models.

Overall, the antimicrobial literature supports activity of *A. oleracea* preparations against selected bacterial targets and provides emerging evidence of antifungal and antivirulence effects of spilanthol. However, differences in extract composition, microbial strains, experimental endpoints, and assay conditions limit direct comparison among studies. The progression from antibacterial screening toward chemically characterized antibiofilm and mechanistic antifungal investigations represents an important advance, but the evidence remains primarily preclinical and is currently insufficient to establish antimicrobial efficacy in humans. The main experimental and clinical evidence supporting the antinociceptive, anti-inflammatory, and antimicrobial activities discussed above is summarized in Table 1.

Table 1. Main experimental and clinical evidence on the antinociceptive, anti-inflammatory, and antimicrobial activities of *A. oleracea*.

Reference	Preparation / compound	Experimental model	Activity	Main finding	Evidence limitation
Nomura et al. (2013)	Ethanollic flower extract	Nociception models in mice	Antinociceptive	Reduced nociceptive responses	In vivo complex
Dallazen et al. (2018)	Natural alkylamide	Local nociception	Antinociceptive /	Distinct effects	In vivo mechanism

⚠ Esta tabela possui muitas colunas e foi cortada para impressão. Para visualizá-la completa, acesse o artigo original em:
<https://revistatopicos.com.br/artigos/antinociceptive-anti-inflammatory-and-antimicrobial-activities-of-acmella-oleracea-from-bioactive-constituents-to-emerging-preclinical-and-clinical-evidence?noblockage>

Note: Evidence categories indicate the experimental context and do not represent a formal risk-of-bias assessment. Source: Author (2026).

3.5. Evidence Gaps, Methodological Limitations, And Translational Perspectives

Despite the growing body of evidence supporting the antinociceptive, anti-inflammatory, and antimicrobial properties of *A. oleracea*, several methodological limitations restrict direct comparison among studies and remain major obstacles to translation. The most important limitation is the heterogeneity of the plant preparations investigated. Studies have used different plant organs, extraction solvents, extraction technologies, crude extracts, fractions, spilanthol-enriched preparations, and isolated compounds. Because these preparations differ substantially in chemical composition, results obtained with one preparation cannot necessarily be extrapolated to another (Spinozzi et al., 2022; Lee, 2026).

This issue is particularly relevant for spilanthol, which is frequently considered the principal pharmacologically active constituent of *A. oleracea*. Experimental studies provide substantial support for its involvement in antinociceptive, anti-inflammatory, and antimicrobial responses. Nevertheless, the concentration of spilanthol varies among plant materials and preparations, and not all studies provide

adequate quantitative chemical characterization. Moreover, the pharmacological activity of isolated spilanthol does not demonstrate that the effects of complex *A. oleracea* extracts are exclusively mediated by this compound. Conversely, differences between the activity of an extract and isolated spilanthol cannot be considered evidence of synergism unless interactions among constituents are specifically tested.

Chemical standardization should therefore represent a central priority for future pharmacological studies. At minimum, investigations using *A. oleracea* extracts should report the plant organ, botanical identification, extraction conditions, extract yield, and quantitative concentration of major chemical markers, particularly spilanthol when relevant. Broader chromatographic or spectrometric characterization would further improve comparability among studies. This is especially important because recent research continues to demonstrate substantial chemical diversity in *A. oleracea* preparations and the influence of extraction procedures on the recovery of bioactive constituents (Radulović et al., 2024; Lee, 2026).

A second limitation concerns the heterogeneity of experimental models and biological endpoints. Antinociceptive activity has been evaluated using different models of acute, inflammatory, and neuropathic pain; anti-inflammatory activity has been assessed through cellular responses, enzymatic targets, tissue injury, and inflammatory models; and antimicrobial activity has been measured using growth inhibition, bactericidal activity, biofilm formation, and, more recently, microbial virulence-associated endpoints. This diversity expands the biological understanding of the species but limits quantitative comparison among studies. Future research

would benefit from greater methodological convergence and from the use of reference compounds or treatments that allow the magnitude of the response to be interpreted in a pharmacologically meaningful context.

The dose–response relationship also requires greater attention. Demonstrating biological activity at a single concentration or dose provides limited information regarding potency, therapeutic range, or potential toxicity. This is particularly relevant in view of evidence showing that natural alkylamides from *A. oleracea* may produce distinct antinociceptive and pronociceptive responses depending on experimental conditions (Dallazen et al., 2018). Consequently, pharmacological characterization should incorporate multiple concentrations or doses whenever possible and should evaluate whether the effective range is compatible with realistic exposure and acceptable safety.

Another major gap lies between preclinical evidence and clinical validation. Most of the evidence discussed in this review derives from in vitro assays or animal models. Recent human investigations represent an important advance, particularly studies addressing pain-related outcomes, including dental sensitivity. However, the clinical evidence remains limited in comparison with the preclinical literature. Furthermore, several human studies have evaluated *A. oleracea* as part of multicomponent formulations, including combinations with *Boswellia serrata* or conventional pharmacologically active substances. Although these investigations are valuable for product development, they do not allow the independent contribution of *A. oleracea* to be determined.

This distinction is essential for assessing the current level of evidence. The presence of *A. oleracea* in a clinically effective formulation should not be interpreted as clinical confirmation of the efficacy of *A. oleracea* alone. Future randomized controlled trials should therefore prioritize chemically standardized preparations, clearly defined doses, appropriate placebo or active comparators, and interventions that permit the specific contribution of the plant extract or isolated constituent to be evaluated. The recent randomized trial involving an *A. oleracea*-containing bioadhesive film for post-bleaching dental sensitivity illustrates the movement toward clinically relevant applications, but additional independent and adequately powered studies are required before broader therapeutic conclusions can be drawn.

Safety constitutes another area requiring systematic investigation. Traditional consumption of jambu provides relevant ethnobotanical context but cannot substitute for toxicological characterization of concentrated extracts, purified spilanthol, or pharmaceutical formulations. Exposure achieved with standardized extracts or isolated compounds may differ substantially from that associated with culinary consumption. Therefore, acute and repeated-dose toxicity, local tolerability, potential drug interactions, and pharmacokinetic behavior should be investigated alongside efficacy, particularly for preparations intended for prolonged or systemic use.

The antimicrobial field presents an additional translational challenge. Although antibacterial, antibiofilm, antifungal, and antivirulence effects have been reported, most evidence remains *in vitro*. Future studies should determine whether active concentrations can be achieved safely in biological tissues and should include clinically relevant and, where appropriate, resistant

microbial isolates. The use of standardized susceptibility methods, comparison with reference antimicrobial agents, assessment of mammalian-cell cytotoxicity, and validation in infection models would help determine whether *A. oleracea*-derived compounds have realistic potential as antimicrobial agents or as adjuvants to established therapies.

From a broader perspective, current research indicates a transition from the initial demonstration of biological activity toward mechanistic, chemically characterized, and increasingly translational investigations. The identification of molecular targets, the evaluation of neuropathic pain models, studies of microbial virulence, advances in delivery systems, and the emergence of human investigations demonstrate increasing sophistication in the field. However, formulation technologies and clinical applications should be regarded as extensions of pharmacological evidence rather than substitutes for rigorous demonstration of efficacy.

Accordingly, the most important future direction is not simply to identify additional biological activities of *A. oleracea*, but to strengthen the causal relationship between chemical composition, dose, mechanism, biological response, safety, and clinical effect. Progress toward this objective would allow the field to move from broadly describing the “bioactive potential” of jambu toward defining which preparations and constituents are pharmacologically reproducible, for which indications, at which doses, and with what level of safety and efficacy.

4. CONCLUSION

The available evidence supports the antinociceptive, anti-inflammatory, and antimicrobial potential of *A. oleracea*, particularly at the preclinical level. Spilanthol emerges as the most extensively investigated bioactive constituent, although the effects of complex extracts cannot be attributed exclusively to this compound. Recent advances involving mechanistic studies, neuropathic pain models, antifungal and antivirulence effects, and human investigations indicate increasing translational interest in the species. However, heterogeneity in plant material, chemical composition, experimental models, doses, and formulations, together with still limited clinical evidence, prevents definitive conclusions regarding therapeutic efficacy. Further studies using chemically standardized preparations, rigorous safety assessment, and well-designed clinical trials are therefore needed to establish the pharmacological and clinical relevance of *A. oleracea*.

REFERENCES

BLANCO, V. S. de F. et al. Isolation of spilanthol from *Acmella oleracea* based on Green Chemistry and evaluation of its in vitro anti-inflammatory activity. **The Journal of Supercritical Fluids**, v. 140, p. 372–379, 2018.

DALLAZEN, J. L. et al. Distinct mechanisms underlying local antinociceptive and pronociceptive effects of natural alkylamides from *Acmella oleracea* compared to synthetic isobutylalkyl amide. **Fitoterapia**, v. 131, p. 225–235, 2018. DOI: <https://doi.org/10.1016/j.fitote.2018.11.001>.

DALLAZEN, J. L. et al. Local effects of natural alkylamides from *Acmella oleracea* and synthetic isobutylalkyl amide on neuropathic

and postoperative pain models in mice. **Fitoterapia**, v. 160, art. 105224, 2022.

DALLAZEN, J. L. et al. Pharmacological potential of alkylamides from *Acmella oleracea* flowers and synthetic isobutylalkyl amide to treat inflammatory pain. **Inflammopharmacology**, v. 28, n. 1, p. 175–186, 2020.

FABRI, R. L.; FREITAS, J. C. O.; LEMOS, A. S. O. et al. Spilanthol as a promising antifungal alkylamide for the treatment of vulvovaginal candidiasis. **Medical Mycology**, v. 59, n. 12, p. 1210–1224, 2021. DOI: <https://doi.org/10.1093/mmy/myab054>.

FAJARDO, J. B.; VIANNA, M. H.; POLO, A. B.; COMITRE, M. R. C. et al. Insights into the bioactive potential of the Amazonian species *Acmella oleracea* leaves extract: a focus on wound healing applications. **Journal of Ethnopharmacology**, v. 337, pt. 2, art. 118866, 2025. DOI: <https://doi.org/10.1016/j.jep.2024.118866>.

FERRARA, V. et al. Neuroprotective potential of *Acmella oleracea* aerial parts and root extracts: the role of phenols and alkylamides against neuropathic pain. **Nutrients**, v. 17, n. 16, art. 2588, 2025. DOI: <https://doi.org/10.3390/nu17162588>.

FERRARI, R. Writing narrative style literature reviews. **Medical Writing**, v. 24, n. 4, p. 230–235, 2015. DOI: <https://doi.org/10.1179/2047480615Z.000000000329>.

FREITAS-BLANCO, V. S. et al. Spilanthol, the principal alkylamide from *Acmella oleracea*, attenuates 5-fluorouracil-induced intestinal mucositis in mice. **Planta Medica**, v. 85, n. 3, p. 203–209, 2019. DOI: <https://doi.org/10.1055/a-0715-2002>.

FUSCO, A.; PERRONE, M.; RICCIARDI, F.; MORACE, A. M. et al. Combining *Acmella oleracea* and *Boswellia serrata* extracts: a novel pharmacological approach in inflammatory vestibulodynia. **Frontiers in Pharmacology**, v. 15, art. 1508107, 2024. DOI: <https://doi.org/10.3389/fphar.2024.1508107>.

GREEN, B. N.; JOHNSON, C. D.; ADAMS, A. Writing narrative literature reviews for peer-reviewed journals: secrets of the trade. **Journal of Chiropractic Medicine**, v. 5, n. 3, p. 101–117, 2006. DOI: [https://doi.org/10.1016/S0899-3467\(07\)60142-6](https://doi.org/10.1016/S0899-3467(07)60142-6).

LEE, B. W. Botany, ethnopharmacology, phytochemistry, and biological activities of *Acmella oleracea*: a comprehensive review. **Molecules**, v. 31, n. 4, art. 677, 2026. DOI: <https://doi.org/10.3390/molecules31040677>.

NOMURA, E. C. O. et al. Antinociceptive effects of ethanolic extract from the flowers of *Acmella oleracea* (L.) R.K. Jansen in mice. **Journal of Ethnopharmacology**, v. 150, n. 2, p. 583–589, 2013. DOI: <https://doi.org/10.1016/j.jep.2013.09.007>.

PERETTI, P. et al. Spilanthol content of *Acmella oleracea* subtypes and their bactericide and antibiofilm activities against *Streptococcus mutans*. **South African Journal of Botany**, v. 143, p. 17–24, 2021.

RADULOVIĆ, N. S. et al. Amazon Rainforest hidden volatiles—Part I: unveiling new compounds from *Acmella oleracea* (L.) R.K. Jansen essential oil. **Plants**, v. 13, n. 12, art. 1690, 2024. DOI: <https://doi.org/10.3390/plants13121690>.

RONDANELLI, M. et al. *Acmella oleracea* for pain management. **Fitoterapia**, v. 140, art. 104419, 2020.

SHUID, A. N. et al. Exploring the antibacterial properties of *Acmella* species: a systematic literature review. **Drug Design, Development and Therapy**, v. 20, 2026. DOI: <https://doi.org/10.2147/DDDT.S536279>.

SILVA, A. D. A.; WANDERLEY, M. L.; LEITE, D. F. et al. Effect of *Acmella oleracea* (Jambu) bioadhesive film on post-bleaching dental sensitivity: a randomised clinical trial. **International Dental Journal**, v. 76, n. 5, art. 109719, 2026. DOI: <https://doi.org/10.1016/j.identj.2026.109719>.

SILVA, A. G.; COSTA, R. P.; CALEGARI-ALVES, Y. P. et al. Spilanthol from *Acmella oleracea* (L.) R. K. Jansen induces metabolic alterations and impair an important virulence factor in *Cryptococcus neoformans*. **Microbial Pathogenesis**, v. 206, art. 107806, 2025. DOI: <https://doi.org/10.1016/j.micpath.2025.107806>.

SNYDER, H. Literature review as a research methodology: an overview and guidelines. **Journal of Business Research**, v. 104, p. 333–339, 2019.

SPINOZZI, E. et al. A review of the chemistry and biological activities of *Acmella oleracea* (“jambù”, Asteraceae), with a view to the development of bioinsecticides and acaricides. **Plants**, v. 11, n. 20, art. 2721, 2022.

STEIN, R. et al. Chymase inhibition: a key factor in the anti-inflammatory activity of ethanolic extracts and spilanthol isolated from *Acmella oleracea*. **Journal of Ethnopharmacology**, v. 270, art. 113610, 2021.

YIEN, R. M. K. et al. Alkylamides from *Acmeilla oleracea*: antinociceptive effect and molecular docking with cannabinoid and TRPV1 receptors. **Natural Product Research**, v. 37, n. 18, p. 3136–3144, 2023.

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