

Review article

Phytochemistry and Bioactive Potential of *Acronychia pedunculata*: A Comprehensive Review

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Abstract

Acronychia pedunculata (Rutaceae) is a tropical plant widely distributed in Southeast Asia and has been traditionally used for medicinal and nutritional purposes. Phytochemical investigations reveal a diverse array of bioactive compounds, including acetophenone monomers and dimers, prenylated flavonoids, meroterpenoids, arylketones, alkaloids, sterols, lignans, and tocopherols, which are distributed across leaves, stems, roots, bark, flowers, and fruits. These compounds exhibit multiple biological activities, such as anti-inflammatory, antioxidant, antimicrobial, cytotoxic, neuroprotective, and enzyme inhibitory effects. Notably, compounds such as evolitrine, acrovestone, acronynoid B, and acetophenone dimers demonstrate potent cytotoxicity against various cancer cell lines and neuroprotective activity via modulation of apoptosis-related pathways (e.g., caspases, Bcl-2, and Akt/FoxO3a). Essential oils from the plant, particularly those derived from the bark, exhibit applications in food preservation, fermentation inhibition, and mosquito repellency. Due to the scattered nature of these studies and the diversity of bioactive compounds, this review aims to comprehensively summarize the phytochemistry, biological activities, and potential applications of *A. pedunculata*. Despite promising activities, studies on nutritional composition, pharmacokinetics, toxicity, and standardization remain limited, highlighting the need for further research.

Keywords: *Acronychia pedunculata*; flavonoids; anti-inflammatory; cytotoxicity; neuroprotection; essential oil

1. Introduction

Acronychia pedunculata (L.) Miq., is an aromatic shrub or small tree in the family *Rutaceae*. The species is widely distributed throughout the tropical and subtropical regions of South and Southeast Asia, including India, Sri Lanka, Malaysia, Indonesia, Thailand, and Vietnam (Kim-Anh et al., 2024). Traditionally, many parts of *A. pedunculata*—such as the leaves, fruit, bark, and roots—have been used in folk medicine to treat colic, fever, rheumatism, infections, skin disorders, and indigestion. Historically, several species of the genus

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Acronychia have been used medicinally by indigenous communities in Asia and Australia to treat diarrhea, bacterial infections, fever, and stomach ailments (Epifano et al., 2013).

Phytochemical studies on *A. pedunculata* revealed the presence of various groups of secondary metabolites, including coumarins, alkaloids, flavonoids, phenolics, lignans, and terpenoids (Hapuarachchi et al., 2020). Notably, the essential oil of aerial parts is rich in monoterpenes and sesquiterpenes, such as β -caryophyllene, germacrene D, limonene, β -pinene, and α -humulene, which contribute to its characteristic aroma and biological properties. These chemical components are associated with a wide range of biological activities (Lesueur et al., 2008).

Studies have shown that extracts and essential oils from aerial and underground parts of *A. pedunculata* exhibit significant antioxidant, anti-inflammatory, antibacterial, cytotoxic, insecticidal, and enzyme-regulating activities (Ratnayake et al., 2019). These findings support its applications and highlight its potential value in the development of natural therapies, food preservatives, and cosmetic ingredients. Furthermore, interest in *A. pedunculata* has increased due to the increasing demand for essential oils and plant-derived phytochemicals with multifunctional biological activities (Câmara et al., 2024).

Despite numerous individual studies, a comprehensive synthesis of the phytochemical composition, bioactivities, and practical applications of *A. pedunculata* remains limited. Therefore, this review aims to provide an updated overview of its phytochemical composition, essential oil properties, pharmacological properties, and potential applications in the food, pharmaceutical, and cosmetic industries. By integrating the current findings, this paper highlights the research gaps and opportunities for future research on this underexploited but biologically promising plant.

2. Bioactive Ingredients of *Acronychia pedunculata*

2.1 Phytochemical screening

Recent studies have shown that *A. pedunculata* contains a wide range of secondary metabolites. In Sri Lanka, Hapuarachchi et al. (2020) qualitatively analyzed leaves and stem bark, noting the presence of carbohydrates, glycosides, tannins, saponins, alkaloids, flavonoids, phenols, and terpenoids, suggesting that this species possesses a diverse secondary metabolite system. Similarly, studies conducted in Vietnam of stems, leaves, and fruits of *A. pedunculata* also confirmed the presence of various groups of compounds such as flavonoids, coumarins, saponins, reducing sugars, lipids, sterols, and essential oils (Van et al., 2025). The similarities between reports on various plant parts suggest that secondary metabolite accumulation is extensive throughout the plant.

When compared with other species in the same genus, *A. acidula*—a species of the same genus—is reported to contain glycosides, saponins, triterpenes, flavonoids, but no alkaloids or tannins (Wright et al., 2020). This suggests that *A. pedunculata* has a richer compound spectrum, especially the presence of alkaloids and tannins, which were not observed in *A. acidula*. This difference may reflect the unique biochemical characteristics of each species in the genus *Acronychia* and implies a different potential for biological activity.

On a broader scale, an overview of secondary metabolism in the genus *Acronychia* shows that species in this genus often accumulate a variety of characteristic compounds such as acetophenones, quinoline alkaloids, acridone alkaloids, flavonoids, cinnamic acid derivatives, lignans, coumarins, steroids, and triterpenes (Epifano et al., 2013). These data are consistent with the findings in *A. pedunculata* and highlight the richness of alkaloids,

coumarins, and phenolic compounds – groups of compounds known to possess a wide range of potent biological activities.

Overall, the results from the available studies suggest that *A. pedunculata* is a phytochemically rich species, possessing a wide range of compounds with potential pharmacological value. This contributes to explaining the diverse biological activities reported for this plant in traditional medicine and modern research.

2.2 Isolated compounds and structural characterization

Studies on the leaves and branches of *A. pedunculata* have shown that these parts are rich sources of acetophenone compounds (Table 1). Kozaki et al. (2014) isolated three new acetophenone monomers (1–3), along with an isoprenylated acetophenone 1-[2',4'-dihydroxy-3',5'-di-(3"-methyl-2"-butenyl)-6'-methoxy]phenylethanone and a benzofuran acetophenone acronyculatin E. In addition, sterol (β -sitosterol, stigmasterol) and lignan (sesamin) compounds were also detected, contributing to the chemical diversity in the leaves and branches. These acetophenones were structurally elucidated by spectroscopic methods, and some derivatives showed biological activities, e.g., inhibition of DNA polymerase and cancer cell growth.

In addition to acetophenones, the leaves and branches also contain new meroterpenoids, named acronynoids A–G (Yang et al., 2024), with some compounds possessing unique carbon skeletons never before seen, such as acronynoid A with a pentacyclic ring system 6/6/6/9/4. These compounds were evaluated for their angiogenesis inhibitory activity, of which acronynoid B showed the strongest efficacy in *in vitro* and *in vivo* tests.

Recent studies have also noted the presence of the alkaloid evolitrine (Ratnayake et al., 2019), a new prenylated acetophenone acronyrone A–C (Lv et al., 2022), and the acetophenone–alkaloid hybrid acroquinolone A & B (Panyasawat et al., 2022). In addition, other compounds such as tocopherol and alkaloids, including kokusaginine (0.1%) and evolitrine (0.05%) were also detected in the leaves and branches (de Silva et al., 1979). This suggests that this fraction is a potential source of diverse bioactive compounds for pharmacological research and biological applications.

Flowers of *A. pedunculata* were identified as a rich source of polyphenolic compounds and acetophenones. Lekphrom et al. (2025) isolated a new polyisoprenylated benzofuran acetophenone named acronyculatin S, along with several known acetophenones, such as demethylacrovestone, acrovestone, and acroflavone A. In addition to acetophenones, the flower also contains prenylated flavonoids (3,5,4'-trihydroxy-3',8-dimethoxy-7-(3-methylbut-2-enyloxy)flavone), furanocoumarins (xanthotoxin, isopimpinellin), and furoquinoline alkaloids (N-methylflindersine). The presence of these compounds not only expands the chemical range of the flower but also highlights its diverse biological potential, including antioxidant, anti-inflammatory and cell physiology-regulating effects.

From the root bark, studies have shown that this part is rich in characteristic arylketones and acetophenones. Kumar et al. (1989) isolated a new arylketone, 1-[2',4'-dihydroxy-3',5'-di-(3"-methylbut-2"-enyl)-6'-methoxy]phenylethanone, in addition to known acetophenones such as acronylin and acrovestone, coumarin (bergapten), and triterpenoid (β -amyrin). These compounds provide evidence of potential biological activity, particularly anti-inflammatory and anti-cancer effects. In addition, the isolation of these bioactive compounds from root bark also shows that compound-specific isolation methods can yield unique derivatives with potent biological activity.

Table 1. Synthesis of compounds isolated from *A. pedunculata*

Parts	Compound Group	Isolated Compounds	References
Stem and leaves	Acetophenone monomers	1–3	Kozaki et al. (2014)
	Acetophenone isoprenylated	1-[2',4'-dihydroxy-3',5'-di-(3"-methyl-2"-butenyl)-6'-methoxy]phenylethanone (4)	
	Benzofuran acetophenone	Acronyculatin E (5)	
	Sterol	β -sitosterol, stigmasterol	
	Lignan	Sesamin	
	Meroterpenoids	Acronynoids A–G	Yang et al. (2025)
	Alkaloid	Evolitrine	Ratnayake et al. (2019)
	Acetophenones prenyl	Acronyrone A–C	Lv et al. (2022)
	Acetophenones	Acetophenones 4–5	
	Hybrid compounds acetophenone–alkaloid	Acroquinolone A & B	Panyasawat et al. (2022)
	Tocopherol	Tocopeduncunal	de Silva et al. (1979)
	Alkaloid	Kokusaginine (0.1%), evolitrine (0.05%)	
Flowers	Acetophenone polyisoprenylated benzofuran	Acronyculatin S	Lekphrom et al. (2025)
	Acetophenones	Demethylacrovestone, acrovestone, acroflavone A	
	Prenyl flavonoid	3,5,4'-trihydroxy-3',8-dimethoxy-7-(3-methylbut-2-enyloxy)flavone	
	Furanocoumarins	Xanthotoxin, isopimpinellin	
	Alkaloid furoquinoline	N-methylflindersine	

Table 1. Synthesis of compounds isolated from *A. pedunculata* (continued)

Parts	Compound Group	Isolated Compounds	References
Root bark	Arylketone	1-[2',4'-dihydroxy-3',5'-di-(3"-methylbut-2"-enyl)-6'-methoxy]phenylethanone	Kumar et al. (1989)
	Acetophenone	Acronylin, acrovestone	
	Coumarin	Bergapten	
	Triterpenoid	β-amyrin	
Trunk bark	Arylketone	1-[2',4'-dihydroxy-3',5'-di-(3"-methylbut-2"-enyl)-6'-methoxy]phenylethanone	Han et al. (2004)
	Arylketone	1-[2,4-Dihydroxy-6-methoxy-3,5-bis(3-methylbut-2-en-1-yl)]ethanone	Pathmasiri et al. (2005)
	Arylketone	Acrovestenol	Kouloura et al. (2012)
	Acetophenone dimers	Acropyrone, acropyranol A, acropyranol B	
	Dimers	Acrovestone, acrovestenol, acrofolione A, acrofolione B	
	Monomer	Acronyline	
	Furoquinoline alkaloids	4 alkaloids	
	Acetophenone	Acrophenone A, B , and C	Ito et al. (2016)
	Dimers	Acrovestone, acropyrone, and acrovestenol	
Roots	Quinoline alkaloids	2,3-methylenedioxy-4,7-dimethoxyquinoline; evolitrine; γ-fagarine; skimmianine; kokusaginine; maculosidine; sesamolin; yangambin	Cui et al. (1999)
Fruits	Prenyl flavonoid	Acroflavone	Wisetsai et al. (2022)

Similarly, the stem bark is a rich source of arylketones, acetophenone dimers and monomers, and furoquinoline alkaloids. Han et al. (2004) reported 1-[2',4'-dihydroxy-3',5'-di-(3"-methylbut-2"-enyl)-6'-methoxy]phenylethanone with COX-2 inhibitory activity, while Pathmasiri et al. (2005) obtained acrovestenol and related compounds, which may contribute to the observed biological activities. Kouloura et al. (2012) isolated acetophenone dimers (acropyrone, acopyranol A/B) along with known dimers (acrovestone, acrovestenol, acrofolione A/B), monomer acronyline, and four furoquinoline alkaloids, demonstrating that the stem bark is a source of structurally and biologically diverse acetophenone compounds. Furthermore, novel acetophenones (acrophenone A–C) and dimers (acrovestone, acropyrone, and acrovestenol) were reported to exhibit significant inhibitory activity on leukemia cells (Ito et al., 2016), highlighting their potential applications in medicinal research.

The roots also contain a rich set of quinoline alkaloids, including 2,3-methylenedioxy-4,7-dimethoxyquinoline, evolitrine, γ -fagarine, skimmianine, kokusaginine, maculosidine, sesamolin, and yangambin (Cui et al., 1999). These alkaloids play important roles in diverse biological effects, especially antibacterial, anti-inflammatory, and enzyme-regulating activities, and open up potential research directions for new alkaloid derivatives.

Finally, the fruit of the plant was identified as a novel source of prenylated flavones, notably acroflavone (Wisetsai et al., 2022). Although the number of studies on the fruit is limited, the occurrence of prenylated flavones suggests that the fruit may also play an important role in the exploitation of bioactive compounds, with potential applications in pharmaceuticals, functional foods, and biocosmetics.

Overall, flowers, root bark, stem bark, roots and fruits of *A. pedunculata* contain diverse phytochemical compounds including acetophenones, flavonoids, coumarins, alkaloids, meroterpenoids, tocopherols, triterpenoids, and lignans. The different chemical distributions among parts not only reflect the biological adaptations of the plant, but also suggest opportunities for the exploitation of bioactive compounds for pharmaceutical, food, and cosmetic research.

3. Chemical Composition of *A. pedunculata*

3.1 Ash

Current nutritional research on the medicinal plant *A. pedunculata* is highly limited, with most available data focusing only on the leaves and stem bark sourced from Sri Lanka (Hapuarachchi et al., 2020). These initial studies primarily provide general indices, specifically ash content and moisture/loss on drying.

The total ash content of the leaves (40.38%, dry basis) is considered exceptionally high when compared to many other medicinal herbs, which typically range from 5-20% (Radha et al., 2021). While high total ash may indicate a richness in essential minerals, the relatively high percentage of acid-insoluble ash (12.64% in leaves) is a significant concern. This fraction is indicative of inorganic contaminants like silica or soil particles clinging to the leaf surface. For practical applications in herbal medicine or functional foods, this necessitates rigorous consideration of sample cleaning and standardization methods before use.

In contrast, the stem bark shows a lower total ash content (20.42%), lower water-soluble ash, and lower moisture, reflecting its different physiological role—one focused on structure and protection rather than active metabolism and water exchange (Pojić et al., 2015).

3.2 Essential oil

The essential oil of *A. pedunculata* has been analyzed in various parts of the plant, including the leaves, fruits, roots, stems, and aerial parts. The results revealed pronounced variation in both the composition and relative abundance of constituents (Table 2). In the fruits, the essential oil yield was determined to be 0.167% (Van et al., 2025), a relatively low extraction level compared with many other Rutaceae species, yet still containing compounds with notable biological potential.

Table 2. Some main components (%) in the essential oil of *A. pedunculata* parts

Component	Aerial Parts (Lesueur et al., 2008)	Root (Kim-Anh et al., 2024)	Fruit (Diep et al., 2023)	Leaves (Van et al., 2021; Van et al., 2025)	Stem (Diep et al., 2023)
α-Pinene	57.4	63.9	21.4	1.57-21.2	-
Camphene	0.3	0.9	-	-	-
β-Pinene	0.9	1.2	0.4	-	-
Myrcene	1.4	0.8	0.6	-	-
p-Cymene	0.1	0.4	-	-	-
Limonene	1.1	3.9	3.5	-	-
Cineole-1,8	0.1	-	-	-	-
(Z)-β-Ocimene	2.3	0.4	5.4	-	-
(E)-β-Ocimene	1.1	0.1	16.5	10.91	-
Linalool	2.1	-	12.5	-	6.5
α-Copaene	0.9	5.4	-	-	0.7
(E)-β-Caryophyllene	13.6	2.4	13.0	30.40-57.63	-
α-Humulene	1.6	0.6	7.0	0.31	-
δ-Cadinene	0.3	2.5	1.1	1.14	-
Caryophyllene oxide	3.0	-	7.2	-	35.3
Germacrene D	-	2.3	0.2	11.80	-
β-Eudesmene	-	2.0	-	-	-
α-Selinene	-	2.9	1.5	0.83	0.5

Note: “-” not detected

From Table 2, across most plant parts, α -pinene is the predominant component, accounting for 57.4% in the aerial parts (Lesueur et al., 2008), 63.9% in the roots (Kim-Anh et al., 2024), and ranging from 1.57-21.2% in the leaves (Van et al., 2021; Van et al., 2025). These differences reflect the organ-specific distribution and influence of environmental growth conditions, which ultimately affect the characteristic aroma and biological properties of the essential oil. α -Pinene, a well-known monoterpene, possesses anti-inflammatory, antimicrobial, and antioxidant activities, suggesting that the leaves and roots of *A. pedunculata* could serve as promising sources for medicinal applications.

Other monoterpenes, such as camphene, β -pinene, myrcene, p-cymene, and limonene occur at lower proportions (typically <5%) but contribute to the overall fragrance profile and, to some extent, the biological activity. For instance, (Z)- β -ocimene and (E)- β -ocimene exhibit substantial variability, with (E)- β -ocimene of 16.5% in the fruits and 10.91% in the leaves, contributing to antimicrobial and antioxidant properties (Diep et al., 2023; Van et al., 2025).

Sesquiterpenes and their derivatives—including (E)- β -caryophyllene, α -humulene, α -copaene, δ -cadinene, caryophyllene oxide, and germacrene D—generally occur at lower levels but play important roles in anti-inflammatory and antimicrobial activity. Notably, (E)- β -caryophyllene accounts for 30.4-57.63% in the leaves, indicating that the leaves are particularly rich in bioactive sesquiterpenes. Although α -humulene represents a smaller fraction (~0.31-1.6%), it is recognized for its anti-inflammatory properties, complementing the activity of (E)- β -caryophyllene (Van et al., 2021; Van et al., 2025).

When compared with a related species, *Acronychia acuminata*, the differences in essential oil composition are evident. In *A. acuminata*, α -pinene constitutes 33.7%, β -caryophyllene 3%, and other compounds such as aromadendrene and spathulenol contribute ~5-6% (Brophy et al., 2004). In contrast, *A. pedunculata* displays markedly higher levels of α -pinene (57.4%) and (E)- β -caryophyllene (13.6%), along with greater diversity in minor monoterpenes and sesquiterpenes. These distinctions indicate that each *Acronychia* species possesses a unique essential oil profile and distinct biological potential (Lesueur et al., 2008).

Despite their low abundance, minor monoterpenes and sesquiterpenes remain important due to potential synergistic interactions with major constituents. For example, linalool (12.5% in fruits) and α -copaene (5.4% in roots), though present at modest levels, contribute to aroma and exhibit antimicrobial and antifungal properties (Diep et al., 2023; Kim-Anh et al., 2024). Oxidized sesquiterpene derivatives, such as caryophyllene oxide, although limited in the leaves, also participate in anti-inflammatory mechanisms and enzyme inhibition.

A notable observation is that several compounds—including camphene, β -pinene, myrcene, p-cymene, and α -selinene—occur at very low levels or are undetected in certain plant parts, indicating uneven distribution influenced by organ type and environmental conditions (Table 2). This highlights the importance of harvesting practices, plant part selection, and extraction conditions in determining the quality and biological activity of the essential oil.

In summary, the essential oil profile of *A. pedunculata* is characterized by the dominance of α -pinene and (E)- β -caryophyllene, complemented by a diverse array of minor constituents. However, current studies remain limited, particularly in the evaluation of the biological activities of minor compounds. Therefore, further research is required to investigate compound interactions, seasonal and geographical variation, and comprehensive assessments of antimicrobial, antioxidant, and anti-inflammatory activities across different plant parts.

4. Biological Activities

4.1 Antioxidant activity of *A. pedunculata*

Studies on the leaves of *A. pedunculata* have demonstrated significant antioxidant potential both *in vitro* and *in vivo*. Ethanol extracts of the leaves (EELA) show strong activity in scavenging radicals (DPPH assay, 2,2-diphenyl-1-picrylhydrazyl) with a half maximal effective concentration (EC₅₀) value of 33.4 µg/mL (Ratnayake et al., 2019), indicating potent activity comparable to or exceeding that of many other species within the same genus. Beyond *in vitro* assays, EELA also shows *in vivo* efficacy by markedly reducing serum lipid peroxidation in rats, underscoring its potential to protect cell membranes from oxidative stress (Lekphrom et al., 2025).

In addition, the leaf extract displays dose-dependent inhibition of nitric oxide (NO) radicals, with an EC₅₀ value of 209.7 µg/mL (Ratnayake et al., 2019). This suggests that EELA may play a role in mitigating inflammation and modulating NO-associated oxidative stress, a key mediator in many chronic inflammatory disorders.

Several isolated compounds from this species also contribute to its biological activity. For instance, acrotrione B exhibits moderate antibacterial activity against Gram-positive bacteria, such as *Staphylococcus aureus*, *Bacillus cereus*, and *B. subtilis*, with Minimum Inhibitory Concentration (MIC) values ranging from 16-64 µg/mL. These findings indicate that the prenylated acetophenones or polyphenolic derivatives in this species possess not only antioxidant capacity but also antimicrobial effects (Wisetsai et al., 2023).

Moreover, studies on antihistamine activity further highlight the species' anti-allergic potential. Both EELA and the alkaloid evolitrine inhibit histamine-induced wheal formation on the skin, with inhibition rates of 29% and 35%, respectively, demonstrating their ability to modulate allergic responses and inflammation via histamine-mediated pathways (Ratnayake et al., 2019).

In summary, current evidence reveals that the leaves of *A. pedunculata* are a rich source of antioxidant and anti-inflammatory compounds, acting through diverse mechanisms such as radical scavenging, NO inhibition, and antihistamine effects. However, existing research has focused predominantly on the leaves, while other plant parts, such as the roots, fruits, and stems, remain largely understudied regarding antioxidant activity or other biological properties. This highlights the need for broader investigations across different plant organs, integrating quantitative phytochemical analysis and biological assays to provide a more comprehensive assessment of this species' potential applications in medicinal and functional food industries.

4.2 Antibacterial activities of *A. pedunculata*

Acronychia pedunculata has been shown to possess notable antibacterial potential across multiple plant parts, including the leaves, stem bark, roots, flowers, and fruits, with activity varying depending on the organ and the type of extract (Table 3). An *in vitro* study on fresh extracts from the plant (Ankenda) demonstrated that a combination of stem bark and leaves produced the largest inhibition zone against *Staphylococcus aureus* (mean diameter 11.67 mm), compared with extracts of stem bark (11.00 mm) or leaves alone (9.00 mm). The minimum inhibitory concentration (MIC) of the combined extract was 10⁻² mg/mL, suggesting a synergistic interaction between plant parts that enhances antibacterial efficacy (Muthukuda & Jayakody, 2021). These findings support the traditional medicinal use of this species in Sri Lanka for treating skin infections and wounds.

Table 3. Antibacterial activities of *A. pedunculata*

Part	Compounds/Extracts	Bacterial Strain	Methods/ Results	References
Leaves, bark	Combined extracts	<i>S. aureus</i>	Inhibition zone diameter: 11.67 mm; MIC = 10 ⁻² mg/mL	Muthukuda & Jayakody (2021)
Stem bark	Extract	<i>B. cereus</i> : 7.3-7.4 mm	Inhibition zone diameter	Karunathilaka et al. (2016)
Leaves	Extract	<i>S. aureus</i> : 10.3-12 mm; <i>B. cereus</i> : 10-13 mm	Inhibition zone diameter	Karunathilaka et al. (2016)
Seed	Extract	<i>S. aureus</i> : 7.2-12.8 mm <i>B. cereus</i> : 7.6-8.6 mm	Inhibition zone diameter	Karunathilaka et al. (2016)
Roots	Extract	<i>B. cereus</i> : 8.1-8.4 mm	Inhibition zone diameter	Karunathilaka et al. (2016)
Fruit	Acrovestone	<i>B. subtilis</i>	MIC = 1 mg/mL (compare to chloramphenicol MIC = 4 mg/mL)	Wisetsai et al. (2023)
Flower	Extract	<i>S. aureus</i> , <i>B. cereus</i> : 9.0-13.8 mm	Inhibition zone diameter	Karunathilaka et al. (2016)
	Acronyculatin S, Demethylacrovestone	Methicillin-resistant <i>S. aureus</i> , <i>B. subtilis</i>	MIC = 2-8 µg/mL	Lekphrom et al. (2025)

Other studies from Sri Lanka have likewise reported antibacterial activity in extracts from the leaves, bark, roots, flowers, and seeds, with inhibition zones ranging from 7.2–13.8 mm against *S. aureus* and *B. cereus*, indicating a widespread distribution of antibacterial constituents throughout the plant (Karunathilaka et al., 2016).

The fruits of *A. pedunculata* also contain potent antibacterial constituents. Acrovestone exhibited antibacterial activity comparable to or stronger than

chloramphenicol against *B. subtilis*, with an MIC of 1 mg/mL—lower than that of reference antibiotics, such as chloramphenicol (MIC = 4 mg/mL), kanamycin (MIC = 8 mg/mL), and vancomycin (MIC = 2 mg/mL) (Wisetsai et al., 2023).

Compounds isolated from the flowers such as acronyculatin S and demethylacrovestone demonstrated remarkable activity against methicillin-resistant *S. aureus* (MRSA) and *B. subtilis*, with MIC values of only 2-8 µg/mL (Lekphrom et al., 2025). These results highlight that flowers are also a rich source of polyisoprenylated acetophenones with strong antibacterial properties.

Overall, the available data indicate that *A. pedunculata* possesses a broad antibacterial capacity due to the presence of acetophenones, alkaloids, and polyphenols distributed across multiple plant parts. Antibacterial activity is evident not only in crude extracts but also in isolated compounds, particularly prenylated acetophenones and benzofuran derivatives. However, most current studies have focused predominantly on Gram-positive bacteria, while data on gram-negative pathogens and detailed mechanisms of action remain limited. Future research should therefore be expanded to include these aspects to better elucidate the full therapeutic potential of this species.

4.3 Anti-inflammatory activity of *A. pedunculata*

The anti-inflammatory activity of *A. pedunculata* has been documented in multiple plant parts, with the leaves serving as a particularly rich source of bioactive anti-inflammatory compounds (Table 4). Specifically, the 70% ethanol leaf extract (EELA) exhibits strong inhibition of acute carrageenan-induced paw edema in rats, with a dose of 200 mg/kg producing up to 78% edema suppression after 5 h, indicating that the leaves contain constituents capable of effectively modulating acute inflammatory responses. Moreover, evolitrine, a compound isolated from the leaves, demonstrates both anti-inflammatory and significant analgesic effects; at a dose of 50 mg/kg, it produces anti-inflammatory activity comparable to indomethacin (5 mg/kg) and analgesic effects superior to aspirin (100 mg/kg) (Ratnayake et al., 2019). These findings highlight the importance of the leaves as a source of multi-mechanistic bioactives that inhibit inflammatory mediators and reduce free radical production.

The stem bark also plays a prominent role in the anti-inflammatory potential of this species. Two representative compounds—1-[2,4-dihydroxy-6-methoxy-3,5-bis(3-methylbut-2-en-1-yl) phenyl]ethanone and acrovestenol—have been shown to act through COX-2 inhibition, thereby reducing prostaglandin synthesis, with inhibitory effects of 68% at 500 µM and an IC₅₀ of 142 µM, respectively (Pathmasiri et al., 2005). Thus, stem bark not only provides anti-inflammatory compounds but also targets key biochemical pathways involved in inflammation, supporting its relevance in traditional medicine and its potential in pharmaceutical development.

In addition, the stems contain dimeric acetophenones such as acrofolione A, which possess both anti-inflammatory and cytotoxic activities against cancer cell lines, including NALM-6, K562, and HPB-ALL. This compound induces apoptosis by increasing caspase-3/7 activity, decreasing survivin levels, altering mitochondrial membrane potential, and suppressing cell proliferation (Matsui et al., 2019). These findings suggest that certain stem-derived compounds exhibit anti-inflammatory effects linked to apoptosis regulation and direct modulation of immune or inflammation-related cells, offering dual therapeutic potential in anti-inflammatory and anticancer applications.

Table 4. Anti-inflammatory activity of *A. pedunculata*

Parts	Compounds/ Extracts	Active Type	Mechanism/ Result	References
Leaves	70% ethanol extract (EELA)	Anti-inflammatory	Inhibition of acute carrageenan-induced paw edema in mice, dose of 200 mg/kg inhibited 78% of edema after 5 hours	Ratnayake et al. (2019)
Leaves	Evolitrine	Anti-inflammatory	Dose 50 mg/kg: anti-inflammatory effect equivalent to Indomethacin 5 mg/kg; stronger pain relief than Aspirin 100 mg/kg	
Stem bark	1-[2,4-Dihydroxy-6-methoxy-3,5-bis(3-methylbut-2-en-1-yl)phenyl]ethanone	Anti-inflammatory	Inhibition of COX-2-catalyzed PG biosynthesis by 68% at 500 μ M	Pathmasiri et al. (2005)
Stem bark	Acrovestenol	Anti-inflammatory	COX-2 inhibition with IC_{50} = 142 μ M	
Stem	Acrofolione A	Anti-inflammatory/ cytotoxic	Inhibition of NALM-6, K562, HPB-ALL cells; increased caspase 3/7 activity, decreased survivin, induced apoptosis	Matsui et al. (2019)

Finally, the essential oil from *A. pedunculata* fruits also demonstrates notable anti-inflammatory properties. The fruit essential oil inhibits nitric oxide (NO) production with an IC_{50} of 14.62 mg/mL, comparable to dexamethasone, indicating that the fruits represent an effective natural source of anti-inflammatory agents (Diep et al., 2023). Combined with evidence from the leaves, stem bark, and stems, these findings underscore the concept that multiple parts of *A. pedunculata* collectively contribute to diverse bioactive anti-inflammatory compounds, highlighting the species' potential for development into safe, effective, and multifunctional medicinal products.

4.4 Anticancer/neuroprotective activity of *A. pedunculata*

The anticancer activity of *A. pedunculata* has been investigated across various parts of the plant—including the leaves, bark, stem, and fruits—and has been demonstrated through both *in vivo* and *in vitro* studies. These studies indicate that the species contains numerous compounds capable of modulating inflammatory responses, while some compounds also exhibit antioxidant properties, thereby enhancing cellular protection (Table 5).

In the roots, the anticancer activity of *A. pedunculata* has been documented, with alkaloids such as evolitrine and skimmianine showing potent inhibitory effects on the BC1 breast cancer cell line, with effective dose 50% (ED₅₀) values of 5.8 and 5.6 µg/mL, respectively. These alkaloids also act on the drug-resistant KB-V1⁺ cell line, with ED₅₀ values ranging from 2.9 to 4.4 µg/mL, highlighting their potential in treating multidrug-resistant cancers. In contrast, other root-derived alkaloids such as kokusaginine and maculosidine exhibit only weak activity against KB-V1⁺ cells (ED₅₀ ~4.4-4.5 µg/mL), illustrating the variability in bioactivity among compounds from the same plant part and suggesting specificity in their mechanisms of action toward different cancer cell lines (Cui et al., 1999).

In the stem, acetophenone dimers such as acrofolione A and B also contribute significantly to anticancer activity. Acrofolione A demonstrates stronger inhibition on NALM-6, K562, and HPB-ALL cell lines compared with acrofolione B and induces apoptosis through increased caspase 3/7 activity and decreased expression of the anti-apoptotic protein survivin (Matsui et al., 2019). These mechanisms show that compounds from the stem not only suppress cancer cell proliferation but also promote programmed cell death, offering promising prospects for anticancer drug development based on acetophenone dimers.

Studies on the bark further reveal dual biological potential. Compounds such as 3,5-dimethoxybenzaldehyde and evolitrine exhibit both anti-inflammatory effects and antibacterial activity (MRSA, *B. cereus*, IC₅₀ = 8 µg/mL). This underscores that certain compounds can integrate multiple biological mechanisms, indirectly supporting anticancer effects through the regulation of inflammation and oxidative stress (Nathabumroong et al., 2023).

Extracts of the leaves of *A. pedunculata* contain compounds such as evolitrine that display anticancer activity alongside anti-inflammatory effects (Ratnayake et al., 2019). These extracts inhibit edema while also exhibiting antioxidant capacity, thereby helping to protect cells from oxidative stress associated with cancer progression. Additionally, some leaf-derived compounds have been shown to activate retinoid X receptor- α (RXR α) transcription in a dose-dependent manner, suggesting potential roles as gene-regulating ligands for anticancer therapy (Lv et al., 2022).

Notably, the compound acrovestone (AVT), found in the stem, leaves, and roots, has been studied for its neuroprotective effects. AVT reduces glutamate-induced toxicity in SH-SY5Y cells by modulating apoptotic pathways, including decreasing activation of ERK1/2, Bim, BAX, caspase-3, -7, and -9, while increasing levels of anti-apoptotic proteins Bcl-2/Bcl-xL (Worasrihirun et al., 2025). Simultaneously, AVT regulates the Akt/FoxO3a pathway, reducing acute oxidative stress and demonstrating strong potential as a neuroprotective therapeutic candidate.

Table 5. Anticancer/neuroprotective activity of *A. pedunculata*

Parts	Compound	Active Type	Mechanism/ Result	References
Fruit	Fruit essential oil	Anti-inflammatory	Inhibition of NO production, IC ₅₀ = 14.62 mg/mL, equivalent to dexamethasone	Diep et al. (2023)
Root	Evolitrine, skimmianine	Anti-cancer	Inhibition of BC1 breast cell line (ED ₅₀ 5.8-5.6 µg/mL), KB-V1 ⁺ cell line (ED ₅₀ 2.9 – 4.4 µg/mL)	Cui et al. (1999)
Root	Kokusaginine, maculosidine	Anti-cancer	Weak activity on KB-V1 ⁺ strain (ED ₅₀ ~4.4-4.5 µg/mL)	Cui et al. (1999)
Stem	Acrofolione A	Anti-cancer	Inhibition of NALM-6, K562, HPB-ALL; increased apoptosis, activated caspase 3/7, decreased survivin	Matsui et al. (2019)
Stem	Acrofolione B	Anti-cancer	Inhibits NALM-6 cells; less effective than A	
Stem bark	3,5-Dimethoxybenzaldehyde, evolitrine	Anti-inflammatory / Anti-cancer	Inhibition of MRSA or <i>B. cereus</i> ; IC ₅₀ = 8 µg/mL (bacterial cells)	Nathabumrong et al. (2023)
Leaves	Evolitrine	Anti-cancer / anti-inflammatory	Leaf extract inhibits edema and has antioxidant effects to support anti-cancer treatment.	Ratnayake et al. (2019)

Table 5. Anticancer/neuroprotective activity of *A. pedunculata* (continued)

Parts	Compound	Active Type	Mechanism/ Result	References
Stem / Leaves / Root	Acrovestone (AVT)	Neuroprotection	Inhibition of glutamate toxicity on SH-SY5Y cells; reduction of apoptosis by regulation of ERK1/2, Bim, BAX, caspase-3, caspase-7, caspase-9; increase of Bcl-2/Bcl-xL; modulation of Akt/FoxO3a	Worasrihirun et al. (2025)
Leaves	-	RXR α activation	Dose-dependent transcriptional activation of the retinoid X- α receptor	Lv et al. (2022)
Fruit	Essential oil	Anti-cancer	IC ₅₀ on SK-LU-1, MCF-7, HepG2 = 5.47–9.22 μ g/mL; simultaneously inhibits NO, anti-inflammatory	Diep et al. (2023)

Finally, the essential oil from the fruits also contributes to anticancer activity, with IC₅₀ values ranging from 5.47 to 9.22 μ g/mL against the SK-LU-1, MCF-7, and HepG2 cell lines. It also inhibits nitric oxide (NO) production and exhibits anti-inflammatory effects (Diep et al., 2023). These findings indicate that multiple parts of *A. pedunculata* harbor multifunctional compounds with both anticancer and anti-inflammatory properties, supporting their potential for development into multi-target therapeutic agents.

5. Application Assessment and Prospects

5.1 Applications of *A. pedunculata*

Recent studies have demonstrated that the essential oil extracted from the bark of *A. pedunculata* exhibits outstanding effectiveness in inhibiting the fermentation of Kithul sap (*Caryota urens*). When applied at a concentration of 3 mL of bark essential oil, parameters such as pH and Brix value remained stable, the turbidity of the solution was reduced, and the ethanol content decreased markedly to 2.09% compared to the control. Moreover, the essential oil showed pronounced antibacterial activity, significantly reducing microbial

colony counts, indicating its potential as a natural fermentation inhibitor to improve both the quality and yield of Kithul treacle and syrup production (Tharuka et al., 2025).

In addition, extracts from the leaves, bark, stems, and fruits of *A. pedunculata* have long been used in local traditional medicine as remedies for wounds, scabies, and intestinal infections due to their antifungal and antibacterial properties. The fruits and leaves are also widely utilized in food preparation, highlighting the multifunctional role of this species in daily community life (Chandrika & Ratnayake, 2022).

Beyond its medicinal and culinary applications, the essential oil and monoterpenic alcohols from *A. pedunculata* leaves have demonstrated biological activities in repelling mosquitoes, killing larvae, and eliminating adult mosquitoes, suggesting promising applications in the prevention of mosquito-borne diseases (Kumar et al., 2022).

5.2 Safety assessment: Toxicity and cytotoxicity of *A. pedunculata*

Studies on the toxicity of *A. pedunculata* leaves indicate that leaf extracts are virtually non-toxic, even at very high doses. In an acute limit dose toxicity test, the leaf extract caused no mortality in mice and did not induce any behavioral changes, clinical abnormalities, fluctuations in body weight, or alterations in key biochemical parameters reflecting liver and kidney function, even at a dose of 5,000 mg/kg body weight (Ratnayake et al., 2019). These results suggest that leaf extracts of this species have a high safety profile, providing a strong scientific basis for their use in traditional medicine and plant-based applications.

In addition, preliminary phytochemical studies of leaves and other plant parts have evaluated antiproliferative activity. Specifically, certain compounds isolated from the leaves were tested against gastrointestinal cancer cell lines, including HCT-116, RKO, and SW480, with compound 5 exhibiting significant inhibition of cell proliferation, with IC₅₀ values ranging from 0.24 to 5.3 μ M (Yang et al., 2024). These findings not only reinforce the safety profile of leaf extracts but also highlight their potential for the development of natural anticancer agents.

In summary, the available data indicate that *A. pedunculata* is a safe plant source containing bioactive compounds with promising pharmacological potential. A number of compounds have been shown to be suitable for medicinal and food applications, and provide a foundation for further studies on toxicity, pharmacology, and anticancer activity.

5.3 Potential and challenges for development of *A. pedunculata*

Current studies indicate that *A. pedunculata* is a botanically rich source of diverse bioactive compounds, offering significant potential for applications in medicine, food, and the pharmaceutical industry. Across its leaves, bark, stem, roots, fruits, and flowers, numerous classes of compounds have been isolated, including acetophenone monomers and dimers, meroterpenoids, prenylated flavonoids, alkaloids, arylketones, tocopherols, as well as sterols and lignans (Kozaki et al., 2014). These compounds exhibit a wide range of biological activities—not only antibacterial, anti-inflammatory, and antioxidant properties, but also neuroprotective, anticancer, analgesic, and modulatory effects on oxidative stress-related biological pathways (Matsui et al., 2019; Worasrihirun et al., 2025). For instance, compounds such as evolitrine, acrovestone, acronynoid B, and AVT have demonstrated the ability to inhibit cancer cell lines, reduce glutamate-induced apoptosis, and activate neuroprotective mechanisms while regulating key signaling pathways including Akt/FoxO3a and the caspase cascade (Matsui et al., 2019; Worasrihirun et al., 2025).

Essential oils and extracts from various plant parts also present strong practical application potential. The bark essential oil has been shown to inhibit the fermentation of *Caryota urens* sap, maintaining higher pH and Brix values while markedly reducing ethanol content, along with demonstrating strong antibacterial activity. This highlights its promising application in the food sector, particularly in natural sugar and syrup processing (Tharuka et al., 2025). Furthermore, extracts from the leaves, bark, stem, and fruits are widely used in traditional medicine for treating ulcers, scabies, and intestinal infections, while mosquito-repellent and larvicidal activities have also been documented (Kumar et al., 2022; Ratnayake et al., 2019).

However, despite these promising attributes, the species still faces several research challenges. Nutritional and phytochemical studies remain limited, especially regarding fruits and roots, making cross-study comparisons difficult (Hapuarachchi et al., 2020). Moreover, many strongly bioactive compounds isolated from the plant have not yet been thoroughly evaluated for pharmacokinetics, long-term toxicity, or clinically safe dosage ranges (Ratnayake et al., 2019; Yang et al., 2024). Additionally, variations in essential oil composition and active compound levels across different geographical sources, seasons, and plant parts present challenges for extraction standardization and product development (Van et al., 2025; Lesueur et al., 2008; Kim-Anh et al., 2024).

In summary, *A. pedunculata* is a highly promising plant species endowed with diverse bioactive properties and broad application potential—from traditional medicine and functional foods to modern pharmaceutical developments. Nevertheless, the successful development of products from this species requires more in-depth scientific investigation and comprehensive evaluation of toxicity, safe dosage, and compound stability. Moreover, better standardized extraction protocols to ensure effective and sustainable utilization are needed.

6. Conclusions

Acronychia pedunculata represents a rich source of bioactive compounds with significant potential for pharmaceutical, nutraceutical, and industrial applications. The plant exhibits diverse biological activities, including anti-inflammatory, antioxidant, antimicrobial, cytotoxic, and neuroprotective effects, mediated by multiple molecular mechanisms such as apoptosis induction, caspase activation, COX-2 inhibition, and modulation of oxidative stress pathways. Essential oils and extracts also demonstrate practical applications in food preservation, fermentation control, and vector management. However, despite its promising bioactivity, current research on the nutritional profile, toxicity, pharmacokinetics, and standardization of extracts is limited. To translate these findings into safe and effective products, further studies are required to optimize extraction methods, validate biological effects *in vivo*, and ensure consistent chemical composition across plant sources. Ultimately, *A. pedunculata* holds considerable promise; however, realizing its full potential will depend on a comprehensive scientific evaluation and standardization.

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8. Authors' Contributions

Conceptualization: LPTQ; Data curation: PMH and PTQ; Formal analysis: LBBP and PTQ; Investigation: LTN; Methodology: LPTQ and LTN; Supervision: LPTQ and LBBP; Validation: PMH and LPTQ; Writing - original draft: LPTQ and LTN; Writing - review and editing: LPTQ.

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9. Conflicts of Interest

The authors declare that there are no conflicts of interest related to this article.

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