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Phytochemical Constituents and Pharmacological Effects of Baeckea Frutescens: A Review

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Abstract: *Baeckea frutescens* is a medicinal species widely used in traditional practices and known for its rich phytochemical diversity, yet its pharmacological profile remains fragmented across multiple studies. This systematic review aims to integrate current evidence on the phytochemical constituents and pharmacological activities of *B. frutescens*, focusing on anti-inflammatory, antimicrobial, antioxidant, anticancer, wound-healing, and insecticidal effects. A literature evaluation was conducted using previously compiled research comprising 16 studies from China, Indonesia, Malaysia, and Southeast Asia, covering chemical isolation, essential oil analysis, in vitro assays, in vivo experiments, and computational approaches. The results indicate that *B. frutescens* contains meroterpenoids, phloroglucinol derivatives, flavonoids, phenolics, and terpenes that collectively contribute to significant modulation of NF-κB, MAPK, TLR4–MyD88, and COX-related pathways. Essential oils and polar extracts exhibit broad antimicrobial and antioxidant activities, while cytotoxic and wound-healing assays demonstrate promising therapeutic potential. Insecticidal studies further highlight ecological relevance through antifeedant and repellent properties. Overall, the review confirms *B. frutescens* as a pharmacologically versatile species with strong prospects for drug discovery and functional applications. However, further mechanistic and in vivo investigations are needed to strengthen its translational value.

Keywords: *Baeckea frutescens*; Mechanisms; Pharmacological activities; Phytochemical constituents

Introduction

Beackea frutescens is a member of the Myrtaceae family, has long been recognized as a traditional medicinal plant in Southeast Asia and Southern China. Ethnopharmacologically, this plant has been used to treat fever, cough, inflammation, and skin wounds (Alqahtani et al., 2013). One of its scientific attractions lies in its diverse essential oils and secondary metabolites, making it a potential natural source of active compounds for pharmaceutical and therapeutic cosmetic applications (Kamarazaman et al., 2024). Studies on B. frutescens have shown that its essential oil contains major constituents such as α-pinene, 1,8-cineole, and linalool, which are known to possess significant biological activities, including antioxidant and antibacterial effects (Huong et al., 2023; Xu et al., 2021). This complex phytochemical profile indicates that the plant holds substantial potential for further development in natural product-based pharmaceuticals, although many aspects of its bioactivities have not yet been fully elucidated.

Over the past two decades, scientific exploration of B. frutescens has progressed considerably. Researchers have successfully isolated various bioactive compounds such as flavonoids, meroterpenoids, phloroglucinol derivatives, and C-methylated chromones, which exhibit a wide range of pharmacological activities (Hou et al., 2020; Zhou et al., 2018). The anti-inflammatory, antibacterial, and antioxidant activities of its extracts have been demonstrated through both in vitro and in vivo studies, reinforcing its ethnopharmacological

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claims as a medicinal plant with real therapeutic benefits (Wahyuni et al., 2022). Furthermore, modern scientific approaches such as network pharmacology and molecular docking have been employed to identify the molecular mechanisms of its active compounds, including their roles in inhibiting the NF-κB and PI3K–Akt signaling pathways associated with inflammatory processes (Guo et al., 2025; Yu et al., 2017). This multidisciplinary approach underscores that B. frutescens has a strong scientific foundation as a candidate natural bioactive material for the development of modern herbal medicines.

Over the past two decades, scientific exploration of B. frutescens has progressed rapidly. Researchers have successfully isolated various bioactive compounds such as flavonoids, meroterpenoids, phloroglucinol derivatives, and C-methylated chromones, all of which exhibit broad pharmacological activities (Guo et al., 2025; Hou et al., 2020; Zhou et al., 2018). The anti-inflammatory, antibacterial, and antioxidant activities of the plant's extracts have been demonstrated through both in vitro and in vivo assays, reinforcing its ethnopharmacological claims as a medicinal plant with real therapeutic benefits (Wahyuni et al., 2022). Furthermore, modern scientific approaches such as network pharmacology and molecular docking have been applied to identify the molecular mechanisms of its active constituents, including their roles in inhibiting the NF-κB and PI3K–Akt signaling pathways associated with inflammation (Guo et al., 2025; Yu et al., 2017). This multidisciplinary framework highlights the strong scientific foundation of *B. frutescens* as a natural bioactive candidate for modern herbal drug development.

Despite the growing number of publications investigating the therapeutic benefits of *B. frutescens*, the available knowledge remains partial and not yet integrated comprehensively. Most studies emphasize phytochemical characterization without extensively linking it to the underlying mechanisms of pharmacological activity (Aizo et al., 2024). As a result, the causal relationship between compound structure and biological function remains insufficiently understood. A comprehensive mapping of the plant's chemical components and biological effects would greatly support the direction of future applied research (Luo et al., 2020). For instance, Kamarazaman et al. (2024) reported that *B. frutescens* extract can accelerate wound healing by increasing the expression of TGF-β, IL-1β, VEGF, and MMP-2, which play important roles in tissue regeneration. These findings reveal the plant's strong potential in the development of regenerative therapies and natural-based medical cosmetics.

Beyond pharmacological aspects, research on *B. frutescens* is also driven by the strategic value of Asia's local biodiversity, which remains underutilized. Jemi et al. (2023) demonstrated that differences in extraction solvents lead to variations in oleoresin compound profiles, which directly impact the biological activities of the extracts. This supports the urgency of systematic research to integrate the existing data in order to produce a comprehensive knowledge map of the plant's chemical constituents and bioactivities. With the advancement of research methodologies integrating phytochemistry, molecular biology, and bioinformatics, systematic review efforts on *B. frutescens* are becoming increasingly important to identify knowledge gaps and future research directions (Guo et al., 2025). Such comprehensive evaluations will strengthen the scientific basis for developing evidence-based phytopharmaceutical and natural cosmetic products.

This study aims to systematically review the entire scientific literature related to *B. frutescens*, with a focus on its chemical constituents and pharmacological effects. The primary objective is to identify the major secondary metabolites that have been isolated, categorize the pharmacological activities demonstrated through various research methods, and analyze the relationship between chemical structures and their corresponding biological mechanisms (Yu et al., 2017; Zhou et al., 2018). Additionally, this study seeks to evaluate the plant's potential in the development of phytopharmaceuticals and natural health products. For example, Hou et al., (2020) identified new meroterpenoid compounds with strong antioxidant activity, while Xu et al., (2021) demonstrated the potential of *B. frutescens* essential oil as a natural antibacterial agent. These findings underscore that a systematic investigation will provide a strong scientific foundation for further development of the plant in various pharmaceutical applications.

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Method

This research is a systematic review using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) method which is carried out systematically by following the correct stages or research protocol (Parums, 2021; Sarkis-Onofre et al., 2021). A systematic review is a method that utilizes reviews, studies, structured evaluations, classifications, and categorizations of previously generated evidence (Krnic Martinic et al., 2019; Pollock & Berge, 2018). The steps involved in conducting a systematic review are thoroughly planned and well-structured, making this method very different from one that merely presents a literature study.

Literature Search Process

First, a computerized literature search was conducted using the Publish or Perish application. The combined keywords used were: "B. frutescens chemistry compound" and "pharmacology." Articles were filtered based on title, abstract, and keywords or across all text fields, followed by full-text reviews to identify studies included in this literature review (de la Torre-López et al., 2023; Dennstädt et al., 2024; Natukunda & Muchene, 2023). The initial search yielded a total of 112 articles. Next, we set a publication year range from 2016 to 2025 to ensure the inclusion of recent literature, resulting in 65 articles that reported on the topic Phytochemical Constituents and Pharmacological Effects of B. frutescens.

Eligibility Criteria

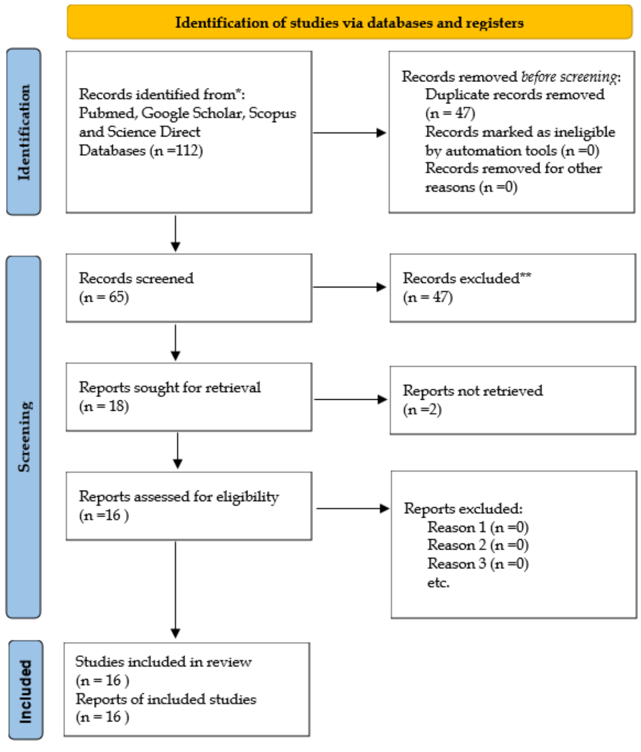
Inclusion and exclusion criteria were established to ensure that the 4 results obtained represented a relevant set of studies for this systematic review. The studies included in this systematic review were selected based on the following inclusion criteria: 1) Population: *B. frutescens*; 2) Quantitative or qualitative studies from open-access journals; 3) Reporting data related to research findings; 4) All studies written in English and published between 2016 and 2025.

Data Collection and Synthesis

After considering the inclusion and exclusion criteria, 16 articles were included in this systematic review. We carefully examined these articles. The extracted variables included publication year, number of participants/respondents, research design, data analysis, and key findings. Furthermore, we reported issues related to the Phytochemical Constituents and Pharmacological Effects of B. frutescens in order to draw a conclusion

Result and Discussion

The literature search was conducted using the Publish or Perish application on four search engines, namely PubMed, Google Scholar, Scopus, and Web of Science. From the literature search using the predetermined keywords, a total of 112 publications were obtained. The literature was then screened using the inclusion criteria and based on the relevance to the topic, resulting in 16 articles that met the criteria. A more detailed description can be seen in Figure 1. The stages of the literature search are described in the Figure 1.



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Figure 1. Systematic review strategy based on PRISMA

Distribution country is an essential step in examining the development of research. This analysis not only illustrates how scientific attention toward this species is geographically distributed, but also reflects research capacity, scientific focus, and the academic collaborations established across different countries. In the Author Affiliation Country Distribution, contributions originate from China, Indonesia, Malaysia, and collaborative efforts across Southeast Asian countries. The Author Affiliation country Distribution are described in the Figure 2.

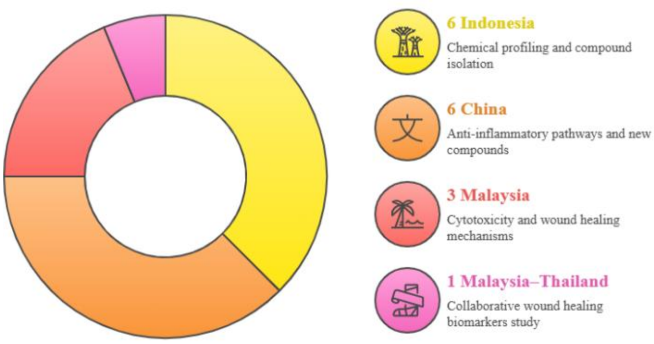


Figure 2. Author Affiliation country Distribution

In the review table of *Phytochemical Constituents and Pharmacological Effects of B. frutescens* above, the plant *B. frutescens* contains several chemical constituents along with their pharmacological effects.

Table 1. Riview of Phytochemical Constituents and Pharmacological Effects of B. frutescens

Author and Years	Result	Chemical Constituents Identified	Methods Used	Pharmacological Effects
Jemi et al. (2023)	GC-MS revealed diverse monoterpenes and sesquiterpenes.	1,8-Cineole, α-Humulene, Caryophyllene oxide, Linalool, α-Terpineol, Quinic acid	Fractionation, GC-MS	Antifungal, anti-inflammatory, antimicrobial, cytotoxic
Herawati et al. (2022)	Qualitative identification of metabolites.	Tannins, saponins, alkaloids, steroids, triterpenoids, quinones	Harborne phytochemical tests	Potential antioxidant, antimicrobial
Yu et al. (2017)	Suppresses inflammatory signaling.	Essential oil components including p-cymene	RAW264.7 assays, NO, Western blot	Anti-inflammatory
Ito et al. (2016)	Five new phloroglucinols; antiproliferative.	Baeckenones G–K, ursolic acid, humulene dioxide	Extraction, MPLC, NMR	Antiproliferative
Hou et al. (2020)	Novel meroterpenoids with anti-inflammatory activity.	Frutescones S, T, U	HR-ESI-MS, NMR, NO assay	Anti-inflammatory
Luo et al. (2020)	Discovery of 24 PTA compounds.	PTA compounds	Isolation, synthesis, NMR, HPLC-MS	Antifeedant
Zhou et al. (2018)	Flavonoids inhibit COX-1/COX-2.	Myricetin derivatives; methylchromone	HPLC, NMR, COX assays	Anti-inflammatory, antioxidant
Li et al. (2024)	Essential oils effective against D. citri.	Eucalyptol, α-pinene, β-caryophyllene, linalool	GC-MS, repellent assays	Insecticidal
Lin et al. (2021)	Blocks TLR4–MyD88–NF-κB & MAPK.	Frutescone O	RAW264.7 assays	Strong anti-inflammatory
Wahyuni et al. (2022)	32 compounds identified; strong antibacterial activity.	β-Ocimene, eucalyptol, β-myrcene, α-humulene, α-terpineol	Steam distillation, GC-MS	Antibacterial
Shahruzaman et al. (2019)	Selective cytotoxicity on MCF-7.	Tannins, triterpenoids, flavonoids, phenolics	Soxhlet, MTT	Anticancer
Nisa et al. (2017)	Rich in phenolics/flavonoids; strong antioxidant.	Phenolics, flavonoids	Folin, DPPH	Antioxidant, antibacterial
Guo et al. (2025)	PI3K-Akt inhibition confirmed.	Chromone derivatives, baeckein E	Docking, in vivo	Anti-inflammatory, anti-RA
Kamarazaman et al. (2024)	Promotes fibroblast/keratinocyte proliferation.	Myricetin & quercetin derivatives	In vitro + in vivo	Wound healing
Aizo et al. (2024)	Essential oil validated for soap formulation.	1-Ethyl-3-methylbenzene	ATR-FTIR, GC-MS	Antibacterial potential
Xu et al. (2021)	Essential oil rich in monoterpenes; strong antibacterial/antioxidant.	1,8-Cineole, α-pinene, linalool, eugenol	GC-MS, antibacterial & antioxidant assays	Antibacterial, antioxidant

Anti-Inflammatory Effects

NF-κB / MyD88 Pathway–Related Studies

Anti-inflammatory research on *B. frutescens* is dominated by mechanistic studies from China, particularly those focusing on macrophage-mediated inflammatory pathways. One important study demonstrated that extracts and fractions of *B. frutescens* significantly inhibited MyD88-dependent NF-κB activation, reduced NO production, and suppressed iNOS, TNF-α, and IL-6 expression in MALP-2-stimulated RAW264.7 cells (Yu et al., 2017). These findings validate the ethnomedicinal use of the plant for inflammation-related disorders.

However, although the researchers identified multiple lipophilic components, they did not isolate individual active compounds, limiting correlation between chemistry and mechanism. Later, a highly targeted study identified Frutescone O as a meroterpenoid that directly modulates TLR4–MyD88–NF-κB and MAPK pathways in LPS-stimulated macrophages, thereby confirming the anti-inflammatory potential of a single, structurally defined molecule from the plant (Lin et al., 2021). Even though this study relied solely on in vitro systems, its clear mechanistic results significantly advance the understanding of compound-specific inflammatory modulation. Additional research on new meroterpenoids, including Frutescone S–U, reported strong NO inhibition at low micromolar concentrations, further supporting the anti-inflammatory relevance of this metabolite class (Hou et al., 2020). Together, these studies establish that *B. frutescens* contains several compound groups capable of regulating key inflammatory pathways with therapeutic potential.

Cyclooxygenase-Related Anti-Inflammatory Activity

Flavonoid-based anti-inflammatory research on *B. frutescens* has identified unique structural variants that exhibit selective inhibition of cyclooxygenase enzymes (Al-Khayri et al., 2022). Zhou et al. (2018) isolated several flavonoids and methylchromone derivatives—such as myricetin and quercetin glycosides—which demonstrated meaningful inhibition of COX-1 and COX-2. These findings indicate that phenolic and flavonoid compounds in *B. frutescens* are capable of modulating arachidonic-acid-derived inflammatory pathways. While these assays were performed only at the enzymatic level, they clearly support the potential of these compounds as anti-inflammatory agents. Structural features such as galloylation and methylation appeared to influence the magnitude of COX inhibition. Despite the lack of mechanistic validation using cell or animal models, this research provides a foundation for future anti-inflammatory drug development from the flavonoid subclass of *B. frutescens*. When viewed together with studies involving NF-κB and TLR4 inhibition, these findings support a multimodal anti-inflammatory profile within the species.

Antimicrobial Effects

Essential Oil Antibacterial Activity

Antimicrobial activity is another widely documented property of *B. frutescens*, particularly through its essential oil components (Mahfudh et al., 2025). A study from Kalimantan showed that steam-distilled leaf oil containing β-ocimene, eucalyptol, β-myrcene, α-humulene, and α-terpineol produced notable inhibitory zones against *Escherichia coli*, confirming strong antibacterial potential (Wahyuni et al., 2022). Although the study assessed only one bacterial species, the results align with several traditional claims of antimicrobial activity. Likewise, Xu et al., (2021) characterized essential oils rich in 1,8-cineole, α-pinene, and linalool and found significant antibacterial effects against *Staphylococcus aureus*, expanding the antimicrobial profile to include Gram-positive bacteria. These findings suggest that monoterpenes and sesquiterpenes collectively contribute to antimicrobial action through possible membrane disruption or oxidative damage. Furthermore, phenolic-rich polar extracts demonstrated strong antimicrobial effects against *E. coli* and *Salmonella typhi*, reinforcing the presence of multiple antimicrobial compound groups within the species (Nisa et al., 2017). Although mechanistic details remain limited, convergence of evidence across essential oil and polar extract studies confirms the broad antibacterial potential of *B. frutescens*.

Antioxidant Effects

Antioxidant effects of *B. frutescens* have primarily been documented in studies evaluating phenolic and flavonoid content. Nisa et al. (2017) reported high phenolic and flavonoid concentrations in ethanol extracts, accompanied by strong DPPH-based radical scavenging activity with IC_{50} values below 50 µg/mL. These results imply that the antioxidant capacity is largely due to phenolic hydroxyl groups capable of neutralizing reactive oxygen species. Although no cellular oxidative stress models were used, the study's quantitative analysis supports the relevance of phenolics as major antioxidant contributors. In addition, flavonoids identified by Zhou et al. (2018) exhibited antioxidant properties in parallel with anti-inflammatory effects, suggesting dual functionality. Essential oils rich in linalool, eugenol, and 1,8-cineole also showed meaningful antioxidant activity (Xu et al., 2021), demonstrating that volatile components contribute to non-polar antioxidant effects. Collectively, these studies reveal that both polar and non-polar constituents of *B. frutescens* contribute to antioxidant capacity, reinforcing the species' potential for oxidative-stress-related disorders.

Anticancer Effects

Anticancer research on *B. frutescens* has identified both polar and non-polar compounds with cytotoxic and antiproliferative effects. Shahruzaman et al. (2019) demonstrated that ethanol extracts from branches selectively inhibited the proliferation of MCF-7 breast cancer cells and interfered with glucose uptake, suggesting a metabolic disruption mechanism. Although specific active compounds were not isolated, the results indicate potential therapeutic value. Furthermore, Nisa et al. (2016) isolated five new phloroglucinol derivatives—Baeckenones G–K—which exhibited antiproliferative activity against A549 lung cancer and PSN-1 pancreatic cancer cell lines. The IC_{50} values ranging from 11.8 to 19.2 µM suggest significant potency. As the study did not evaluate apoptosis or cell-cycle modulation, the mechanistic basis remains unclear.

Still, the findings confirm that *B. frutescens* contains multiple compound classes with cytotoxic potential. Given that both crude extracts and purified compounds demonstrate anticancer effects, the species appears to be a promising source of future anticancer agents.

Wound-Healing Effects

The wound-healing potential of *B. frutescens* has been demonstrated through in vitro and in vivo studies using ethanolic leaf extracts. Kamarazaman et al. (2024) found that the extract enhanced fibroblast and keratinocyte proliferation and upregulated growth factors such as TGF-β, IL-1β, VEGF, and MMP-2, indicating accelerated tissue regeneration. These biomarkers are essential in re-epithelialization, angiogenesis, and extracellular matrix remodeling. The presence of flavonoid derivatives such as myricetin and quercetin glycosides is believed to contribute to this activity. Even though the study did not pinpoint specific signaling pathways, the combination of molecular and cellular evidence strongly supports the wound-healing utility of *B. frutescens*. This research extends the plant's pharmacological relevance beyond antimicrobial and anti-inflammatory domains into tissue repair and dermatological applications.

Antifeedant and Insecticidal Effects

A unique pharmacological dimension of *B. frutescens* relates to its ecological defense properties, particularly concerning insecticidal and antifeedant effects. Luo et al. (2020) identified 24 novel phloroglucinol–terpene adducts (PTAs) that exhibited strong antifeedant activity against *Plutella xylostella*. The structural complexity of these compounds, involving phloroglucinol cores fused with terpene moieties, indicates a sophisticated evolutionary defensive mechanism. In addition, Li et al., (2024) demonstrated that essential oils of *B. frutescens* showed repellent and toxic effects against *Diaphorina citri*, with key constituents such as eucalyptol, α-pinene, and β-caryophyllene contributing significantly. Although these insect-related studies are not directly linked to human pharmacology, they reveal important ecological and biochemical functions of the plant. Moreover, the presence of compounds with both insecticidal and anti-inflammatory potential highlights structural versatility within the species.

Other Relevant Pharmacological and Applied Findings

Beyond medicinal and ecological applications, *B. frutescens* has been investigated for its potential in herbal product formulation. Aizo et al. (2024) reported that ATR-FTIR and GC-MS validation confirmed the stability of essential oil components during saponification processes used in soap manufacturing. The persistence of compounds such as 1-ethyl-3-methylbenzene and other VOCs suggests that antibacterial and anti-inflammatory properties may remain active in finished products. Although the research is formulation-oriented and lacks pharmacological assays, it demonstrates practical applications for health-related consumer goods. This study highlights the plant's utility in applied natural product science, complementing the pharmacological evidence provided by other investigations

Conclusions

The collective evidence from previous studies demonstrates that *B. frutescens* contains diverse phytochemicals—including meroterpenoids, phloroglucinol derivatives, flavonoids, phenolics, and essential oil constituents—that contribute to a broad spectrum of pharmacological activities. The plant exhibits notable anti-inflammatory effects through modulation of NF-κB, MAPK, MyD88–TLR4, and COX-related pathways, while antimicrobial and antioxidant activities are supported by both volatile and non-volatile compounds. Cytotoxic analyses reveal significant antiproliferative potential in cancer models, and wound-healing studies show enhanced cell proliferation and upregulation of key growth factors involved in tissue repair. Additional insecticidal and formulation-based findings further highlight the species' ecological and applied value. Overall, these studies position *B. frutescens* as a promising source of bioactive compounds with therapeutic and functional potential, although more targeted mechanistic and in vivo investigations are required to fully elucidate its medicinal applications.

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Author Contributions

AWS as the main author created the concept or idea for the article, N and NS designed the method used, conducted research, analyzed the data until finished.

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Conflicts of Interest

The authors declare no conflict of interest.

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