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Compound Content and Bioactivity of Eucalyptus sp Species

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Abstract

The genus Eucalyptus is widely recognized as an important natural resource, both economically and therapeutically, with a wide variety of species spread throughout the world. With the increasing resistance to antimicrobials and the need for safe and effective natural alternatives, essential oils (EOs) and extracts from Eucalyptus have garnered significant attention due to their potential bioactivity. This comprehensive review aims to analyze the chemical composition and bioactivity of various Eucalyptus species. The methodology involved systematic data extraction regarding yield, chemical profiles (identified via GC-MS, HPLC, etc.), and evaluation of various biological activities such as antimicrobial, antioxidant, anti-inflammatory, antidiabetic, cytotoxic, insecticidal, and herbicidal activities. The results showed that Eucalyptus EOs and extracts have highly variable chemical compositions, dominated by terpenoids such as 1,8-cineole and α-pinene, influenced by genetic and environmental factors. The observed bioactivity was very strong, particularly against bacteria (especially Gram-positive), fungi, and biofilms. In addition, Eucalyptus extract exhibits significant antioxidant capacity, anti-inflammatory and analgesic effects, as well as antidiabetic, cytotoxic, and insecticidal properties. Overall, Eucalyptus is a promising source of bioactive compounds, supporting potential applications in the pharmaceutical, cosmetic, food, and agricultural industries. Further research, including in vivo studies and clinical trials, is needed to fully validate the efficacy and safety of Eucalyptus-based products.

Abstrak

Genus *Eucalyptus* dikenal sebagai sumber daya alam yang penting secara ekonomi dan terapeutik karena memiliki banyak spesies yang tersebar di berbagai wilayah dunia. Meningkatnya resistansi antimikroba dan kebutuhan terhadap alternatif alami yang aman mendorong perhatian terhadap minyak atsiri dan ekstrak *Eucalyptus* sebagai sumber senyawa bioaktif. Tinjauan ini bertujuan menganalisis komposisi kimia dan aktivitas biologis berbagai spesies *Eucalyptus* melalui pengumpulan data mengenai rendemen, profil senyawa yang diidentifikasi menggunakan GC-MS, HPLC, dan metode lainnya, serta pengujian aktivitas antimikroba, antioksidan, antiinflamasi, antidiabetes, sitotoksik, insektisida, dan herbisida. Hasil kajian menunjukkan bahwa komposisi kimianya sangat bervariasi dan umumnya didominasi oleh terpenoid, terutama 1,8-sineol dan α-pinena, yang dipengaruhi oleh faktor genetik dan lingkungan. Minyak atsiri dan ekstraknya menunjukkan aktivitas kuat terhadap bakteri, khususnya bakteri Gram-positif, jamur, dan biofilm. Selain itu, ditemukan pula aktivitas antioksidan, analgesik, antidiabetes, sitotoksik, dan insektisida. Secara keseluruhan, *Eucalyptus* berpotensi dikembangkan untuk industri farmasi, kosmetik, pangan, dan pertanian, meskipun studi *in vivo* dan uji klinis masih diperlukan untuk memastikan efektivitas dan keamanannya.

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Introduction

From ancient times to the modern era, medicinal plants have occupied a central position in human health practices, serving as a primary source for the prevention and treatment of various infectious diseases and other health disorders (Dogara *et al.*, 2024; Ahmed & Shrivastava, 2019). This historical role has become increasingly prominent in recent decades, marked by a significant surge in interest in the use of natural medicines derived from plants. This increased attention is driven by various factors, including global concerns about the worsening antibiotic resistance crisis and awareness of the potential side effects of synthetic compounds (Ghaffar *et al.*, 2015; Elaissi *et al.*, 2012; Putri *et al.*, 2024). Natural products extracted from plants are widely recognized for their advantageous characteristics, such as better safety profiles, lower toxicity, and relatively economical costs compared to synthetic alternatives. These attributes make natural products a highly promising and sought-after choice in various industrial sectors, including pharmaceuticals, cosmetics, and food (Dogara *et al.*, 2024; Sukhikh *et al.*, 2022; El Shiekh *et al.*, 2025).

Among the world's diverse flora, the genus Eucalyptus (family Myrtaceae) stands out as one of the most important and globally widespread genera of flowering trees and shrubs, with over 900 species and subspecies (Barbosa *et al.*, 2016; El Shiekh et al., 2025; Alvarez *et al.*, 2021). Although native to Australia, the extraordinary adaptability of Eucalyptus to diverse environmental conditions, combined with its rapid growth rate, has facilitated its extensive cultivation in various regions worldwide, particularly in subtropical and Mediterranean climates (El Shiekh *et al.*, 2025; Shala & Gururani, 2021). Eucalyptus' dominance in the forestry industry is not limited to the production of wood, fiber, cellulose, and pulp for the paper industry but is also renowned for its leaves rich in essential oils (EOs) (El Shiekh *et al.*, 2025; Vieira *et al.*, 2021). Eucalyptus essential oil ranks among the 18 most traded essential oils globally, affirming its status as an essential source of natural chemicals with highly diverse and functionally beneficial bioactive qualities (Shala & Gururani, 2021). Interestingly, the utilization of residues from the pulp and paper industry, such as Eucalyptus leaves and branches, offers valuable opportunities for EO production, transforming waste into value-added products (Salvatori *et al.*, 2023; Vieira *et al.*, 2021).

Eucalyptus essential oils are a complex blend of various volatile compounds that give this plant its distinctive aroma. Its chemical composition is dominated by terpenoids, particularly monoterpenoids, with smaller amounts of sesquiterpenoids. Additionally, EOs contain oxygen-containing compounds such as alcohols, aldehydes, ethers, esters, ketones, and phenols (El Shiekh *et al.*, 2025; Belaid *et al.*, 2023). This diversity of compounds underpins the broad spectrum of bioactivity documented through various phytopharmacological studies. Eucalyptus EOs have been shown to possess antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, and wound-healing properties (El Shiekh *et al.*, 2025). Specifically, 1,8-cineole (eucalyptol) is often identified as the primary component in many Eucalyptus species, responsible for most of its therapeutic properties, particularly in addressing respiratory issues (Shala & Gururani, 2021; Hadj-Moussa *et al.*, 2024; Čmiková *et al.*, 2023). However, some Eucalyptus chemotypes may have other compounds as dominant components, such as linalool in certain E. globulus or citronellal in E. citriodora, which also exhibit significant bioactivity (Hadj-Moussa *et al.*, 2024; Barbosa *et al.*, 2016).

The ongoing search for new antimicrobial agents is crucial in the era of antibiotic resistance, which has led to increased treatment costs and prolonged treatment duration (Dogara *et al.*, 2024). Eucalyptus EOs offer diverse mechanisms of action, which may reduce the likelihood of resistance development in pathogens compared to single antibiotics. Numerous studies have confirmed the effectiveness of Eucalyptus essential oils against Gram-positive bacteria, which are often more sensitive than Gram-negative bacteria, as well as their activity against fungi and even viruses (Elaissi *et al.*, 2012; Ghaffar *et al.*, 2015; Čmiková *et al.*, 2023). Additionally, oxidative stress, a trigger for various chronic diseases including diabetes, can be addressed by the strong antioxidant properties of Eucalyptus EOs, which are rich in phenolic compounds and flavonoids (Dogara *et al.*, 2024; Park *et al.*, 2023; Singab *et al.*, 2011; Idris *et al.*, 2020). Its ability to act as an anti-inflammatory, pain reliever, and even as a nematicide and herbicide further expands its potential applications (Salvatori *et al.*, 2023; Rodrigues & Faria, 2021; Kouki *et al.*, 2022).

Although many studies have highlighted the potential of Eucalyptus, there are still gaps in our comprehensive understanding of the chemical variability of EOs between species, the factors that influence this composition, and how these variations correlate with a broader spectrum of bioactivity. Therefore, this review aims to synthesize and analyze existing literature on the compound content and bioactivity of various Eucalyptus species in depth. Specifically, this study will elaborate on data regarding the chemical composition of EOs and extracts, their effectiveness as antimicrobial agents (antibacterial, antifungal, antiviral), antioxidants, and anti-inflammatory agents, as well as highlight their potential applications in the pharmaceutical, cosmetic, food, and agricultural industries as sustainable natural alternatives.

Method

Extraction Method

The methods used to obtain essential oils (EO) or extracts (e.g., hydrodistillation, steam distillation, solvent extraction with various polarities, ultrasonic extraction), as well as the yields obtained (Barbosa *et al*., 2016; Park *et al*., 2023; Hadj-Moussa *et al*., 2024; Atmani-Merabet *et al*., 2018; Alvarez *et al*., 2021; Sukhikh *et al*., 2022).

Chemical Composition Analysis

The techniques used for the identification and quantification of compounds (e.g., GC-MS, GC-FID, HPLC, NMR, UV-Vis, FTIR), as well as the main compounds identified and their percentages (Ghaffar *et al*., 2015; Elaissi *et al*., 2012; Čmiková *et al*., 2023; Khedhri *et al*., 2023). Differences in chemotypes were also noted (Hadj-Moussa *et al*., 2024; Elaissi *et al*., 2012).

Bioactivity Evaluation

- **Antimicrobial Activity**

The methods used (e.g., disk diffusion, broth microdilution), target microorganisms (Gram-positive bacteria, Gram-negative bacteria, fungi, viruses), and efficacy parameters (inhibition zone, MIC, MBC, MFC) (Elaissi *et al*., 2012; Ghaffar *et al*., 2015; Čmiková *et al*., 2023; Park *et al*., 2016).

- **Antioxidant Activity**

The methods used (e.g., DPPH, ABTS, FRAP, ORAC) and the parameters measured (IC_{50}, TEAC, RSA) (Park *et al*., 2023; Dogara *et al*., 2024; Singab *et al*., 2011).

- **Anti-inflammatory and Antinociceptive Activities**

Test models (e.g., acetic acid-induced writhing test, formalin-induced paw licking test), as well as the parameters evaluated (Salvatori *et al*., 2023).

Data Analysis

The extracted data will be analyzed qualitatively and comparatively to identify consistency, variation, and correlation between findings. This analysis will include Synthesis of Major Compounds, Comparison of Bioactivity, Correlation of Composition and Activity, and Identification of Trends and Gaps. Synthesis of Major Compounds Identify the most frequently found and dominant chemical compounds in various Eucalyptus species and plant parts, and highlight the factors that influence composition variation (e.g., geographic location, extraction method, chemotype). Comparison of Bioactivity Evaluate the relative effectiveness of Eucalyptus in various bioactivities, comparing results between different species, types of extracts, and testing methods. Special attention will be given to activities that show significant potential as natural alternatives. Correlation of Composition and Activity Analyzing the extent to which chemical composition, particularly the presence of certain compounds or specific chemotypes, correlates with the type and strength of observed bioactivity. Identification of Trends and Gaps Identify general trends in Eucalyptus research, as well as knowledge gaps that require further investigation, such as more detailed mechanisms of action or in vivo studies and clinical trials.

Results

Extraction Yield

The yield of essential oil (EO) from Eucalyptus leaves shows significant variability, ranging from 0.06% to 9% based on dry weight, depending on the species, plant organ, environmental conditions, and extraction method used (El Shiekh *et al*., 2025; Shala & Gururani, 2021; Barbosa *et al*., 2016). Some studies report an average EO yield of approximately 1.84% (w/w) after hydrodistillation (Ghaffar *et al*., 2015). Varieties such as E. cinerea and E. sideroxylon are reported to yield high yields of around 3% (Sebei et al., 2015), while E. bicostata can reach 2.85% (Kouki *et al*., 2022) and E. lesouefii up to 5.2% (Ameur *et al*., 2021). Extraction methods also influence yield; solvent extraction with high polarity solvents such as methanol and ethanol generally produces higher extract yields compared to non-polar solvents, with E. viminalis reaching 42.5% with methanol (Alvarez *et al*., 2021). Ultrasonic treatment (US) can increase the dry matter yield of the extract, with the highest results observed at an extraction time of 20–25 minutes (Sukhikh *et al*., 2022).

Chemical Composition

Chemical analysis of EOs and Eucalyptus extracts using techniques such as GC-MS, GC-FID, and HPLC identified hundreds of compounds, with terpenoids dominating. Monoterpenes and sesquiterpenes are the main components, along with oxygenated compounds such as alcohols, aldehydes, ethers, esters, ketones, and phenols (El Shiekh *et al.*, 2025).

Some of the main chemical components that are dominant and frequently reported include 1,8-Cineole (Eucalyptol), α-Pinene, Citronellal, Linalool, p-Cymene, Spathulenol, Flavonoids and Phenolics.

Variations in chemical composition are strongly influenced by genetic factors, environmental conditions (climate, soil, altitude), phenological stage, and extraction methods (Barbosa *et al.*, 2016; Elaissi *et al.*, 2012; Atmani-Merabet *et al.*, 2018; Alvarez *et al.*, 2021). The phenomenon of chemotypes, where the same species exhibit different chemical profiles, is frequently observed (Hadj-Moussa *et al.*, 2024; Elaissi *et al.*, 2012).

General Bioactivity

Antimicrobial Activity

EOs and Eucalyptus extracts exhibit strong antibacterial activity against various pathogenic microorganisms (El Shiekh *et al.*, 2025; Ghaffar *et al.*, 2015; Elaissi *et al.*, 2012; Čmiková *et al.*, 2023). Gram-positive bacteria (e.g., Staphylococcus aureus, Bacillus subtilis, Listeria monocytogenes, Bacillus cereus) are generally more sensitive to Eucalyptus EOs than Gram-negative bacteria (e.g., Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae) (Elaissi *et al.*, 2012; Ghaffar *et al.*, 2015; Sebei *et al.*, 2015). Beberapa spesies, seperti *E. odorata*, *E. citriodora*, *E. maideni*, *E. astrengens*, dan *E. bicostata*, menunjukkan aktivitas antibakteri yang sangat tinggi (Elaissi *et al.*, 2012; Ghaffar *et al.*, 2015; Sebei *et al.*, 2015). Significant antifungal activity has also been reported, particularly against Candida albicans and various microscopic fungi (Čmiková *et al.*, 2023; Shala & Gururani, 2021). EOs from E. globulus have even been reported to be twice as effective as nystatin against C. albicans (Shala & Gururani, 2021). Antimicrobial effects are often associated with synergies between major and minor components, rather than a single dominant compound (Hadj-Moussa *et al.*, 2024; Elaissi *et al.*, 2012). Essential oils formulated in nanoemulsion form exhibit strong antimicrobial and antibiofilm activity against oral pathogens, with low toxicity to human cells (Batista *et al.*, 2024). Eucalyptus globulus and Eucalyptus pellita essential oils also exhibit antibacterial activity against fish pathogenic bacteria (Edwardsiella tarda, Vibrio harveyi, Staphylococcus iniae) (Park *et al.*, 2016; Astiani *et al.*, 2014; Nur Alam *et al.*, 2024).

Antioxidant Activity

EOs and Eucalyptus extracts exhibit strong antioxidant properties, capable of neutralizing free radicals and reducing oxidative stress (Dogara *et al.*, 2024; Park *et al.*, 2023; Singab *et al.*, 2011). This activity correlates positively with high phenolic and flavonoid content (Alvarez *et al.*, 2021; Idris *et al.*, 2020; Singab *et al.*, 2011). Methanol extracts from E. citriodora and 50% ethanol extracts from E. globulus showed very high antioxidant activity (Idris *et al.*, 2020; Park *et al.*, 2023).

Anti-inflammatory and Analgesic Activities

Eucalyptus EO is effective in reducing inflammation and pain (El Shiekh *et al.*, 2025; Salvatori *et al.*, 2023). 1,8-cineole and α-pinene are the main components often associated with this effect, working through the inhibition of inflammatory mediators (Salvatori *et al.*, 2023). Animal studies have demonstrated significant antinociceptive and anti-inflammatory effects, possibly involving opioid pathways (Salvatori *et al.*, 2023).

Discussion

Variability in Yield and Chemical Composition

The EO yield from Eucalyptus leaves shows substantial fluctuations, ranging from 0.06% to 9% (El Shiekh *et al.*, 2025; Shala & Gururani, 2021; Barbosa *et al.*, 2016). This variability reflects the complexity of interactions between internal factors (genetic, species, plant age, plant organ) and external factors (climate conditions, soil type, elevation, harvest season, collection time) (Barbosa et al., 2016; Elaissi et al., 2012; Atmani-Merabet *et al.*, 2018; Alvarez *et al.*, 2021). For example, species such as E. cinerea and E. sideroxylon in Tunisia can produce high EO yields (around 3%), while ultrasonic extraction methods have also been shown to significantly increase the dry matter content of the extract, achieving optimal results at a duration of 20–25 minutes (Sukhikh *et al.*, 2022).

The chemical profile of Eucalyptus essential oils is dominated by terpenoids, particularly monoterpenes and sesquiterpenes, along with various oxygenated compounds (El Shiekh *et al.*, 2025; Belaid *et al.*, 2023). 1,8-cineole (eucalyptol) is the most prominent component in many species, with concentrations that can exceed 70% (Shala & Gururani, 2021; Elaissi *et al.*, 2012; Čmiková *et al.*, 2023). However, the phenomenon of chemotypes is very common, where the same species exhibit different dominant compound profiles. For example, some E. globulus may be dominated by linalool instead of 1,8-cineole (Hadj-Moussa *et al.*, 2024), while E. citriodora is known for its dominance of citronellal (Barbosa *et al.*, 2016). Factors such as geographical location (e.g., Tunisia vs. Pakistan) and extraction methods (hydrodistillation vs. solvent extraction) also contribute to this variation, influencing the types and quantities of compounds extracted (Ghaffar *et al.*, 2015; Alvarez *et al.*, 2021). Polar extracts from Eucalyptus leaves tend to be richer in phenolic compounds and flavonoids, such as quercetin, luteolin, and chlorogenic acid, which play important roles in biological activity (Park *et al.*, 2023; Singab *et al.*, 2011; Alvarez *et al.*, 2021).

Correlation between Chemical Composition and Bioactivity

Antimicrobial Activity

Eucalyptus essential oils consistently demonstrate strong efficacy against various microbial pathogens. Gram-positive bacteria (e.g., Staphylococcus aureus, Bacillus subtilis, Listeria monocytogenes, Bacillus cereus) generally exhibit higher sensitivity than Gram-negative bacteria (e.g., Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae) (Elaissi *et al.*, 2012; Ghaffar *et al.*, 2015; Sebei *et al.*, 2015). This difference can be attributed to the more complex structure of Gram-negative bacterial cell walls, which limits the penetration of hydrophobic compounds in EOs (Elaissi *et al.*, 2012). Compounds such as 1,8-cineole, linalool, and α-pinene are often the primary contributors to antimicrobial activity (Čmiková *et al.*, 2023; Hadj-Moussa *et al.*, 2024). However, some studies emphasize that the synergy between major and minor components produces optimal antimicrobial effects, surpassing the activity of individual compounds (Hadj-Moussa *et al.*, 2024; Elaissi *et al.*, 2012; Miguel *et al.*, 2018).

In addition, Eucalyptus EOs also exhibit significant antifungal activity, particularly against Candida albicans and other microscopic fungi (Čmiková *et al.*, 2023; Shala & Gururani, 2021). The potential of EOs to inhibit bacterial biofilm formation has also been demonstrated, offering an alternative solution to antibiotic resistance caused by biofilms (Khedhri *et al.*, 2023; Čmiková *et al.*, 2023; Batista *et al.*, 2024). The use of Eucalyptus EO-based nanoemulsions enhances antimicrobial and antibiofilm activity while reducing cytotoxicity on human cells, promising applications in oral health products (Batista *et al.*, 2024).

Antioxidant Activity

Aktivitas antioksidan yang kuat dalam EOs dan ekstrak *Eucalyptus* sebagian besar dikaitkan dengan kandungan senyawa fenolik dan flavonoid yang tinggi (Park *et al.*, 2023; Singab *et al.*, 2011; Alvarez *et al.*, 2021; Idris *et al.*, 2020). Senyawa-senyawa ini bekerja dengan menetralkan radikal bebas, mereduksi ion logam, dan menghambat peroksidasi lipid, sehingga berkontribusi pada perlindungan terhadap stres oksidatif (Dogara *et al.*, 2024). Variasi dalam pelarut ekstraksi sangat memengaruhi perolehan senyawa antioksidan, dengan pelarut polar seperti metanol dan etanol umumnya menghasilkan ekstrak dengan kapasitas antioksidan yang lebih tinggi (Park *et al.*, 2023; Alvarez *et al.*, 2021).

Anti-inflammatory and Analgesic Activities

Senyawa seperti 1,8-cineole dan α-pinene, yang melimpah di banyak spesies *Eucalyptus*, merupakan kontributor utama efek anti-inflamasi dan analgesik (Salvatori *et al.*, 2023; El Shiekh *et al.*, 2025). Mekanisme yang diusulkan melibatkan penghambatan jalur inflamasi dan mediator nyeri, seperti enzim siklooksigenase dan sitokin pro-inflamasi (Salvatori *et al.*, 2023; El Shiekh *et al.*, 2025). Studi *in vivo* pada hewan telah menunjukkan bahwa EOs *Eucalyptus* dapat secara signifikan mengurangi respons nyeri dan peradangan, bahkan menunjukkan interaksi dengan jalur opioid (Salvatori *et al.*, 2023).

Application Potential and Research Gaps

Overall, the synthesized results confirm that Eucalyptus species are a very promising natural resource with a wide variety of chemical compounds and a broad spectrum of bioactivity. The potential applications are diverse, including development New antimicrobial agents, Natural antioxidants, Anti-inflammatory and analgesic agents, Biopesticides, Cosmetics and personal care products.

However, there is a research gap that needs to be filled. Many of the studies reviewed focused on in vitro evaluations, so more in vivo studies and controlled clinical trials are needed to validate efficacy and safety in living organisms and humans (Dogara et al., 2024; El Shiekh et al., 2025; Sukhikh et al., 2022). A deep understanding of the molecular mechanisms underlying the observed bioactivity is also limited. Additionally, investigations into the synergistic or antagonistic effects of compound combinations in EOs and extracts, as well as the development of optimized formulations for stability and delivery (e.g., nanoemulsions), will be crucial for translating these research findings into effective and safe commercial products. Optimization of extraction methods, including environmentally friendly and sustainable approaches, is also an important area for further research (Sukhikh et al., 2022).

Conclusion

This comprehensive review aims to synthesize and analyze the chemical compound content and bioactivity spectrum of various Eucalyptus species, highlighting the great potential of this genus as a multifunctional natural resource.

Studies indicate that Eucalyptus essential oils (EO) and extracts exhibit highly diverse chemical compositions, dominated by terpenoids, particularly 1,8-cineole, α-pinene, and citronellal. This diversity is greatly influenced by genetic, environmental, and extraction method factors, leading to chemotype differences between species and locations (Barbosa *et al.*, 2016; El Shiekh *et al.*, 2025; Hadj-Moussa *et al.*, 2024; Park *et al.*, 2023).

Overall, Eucalyptus is an extraordinary natural resource for the development of new therapeutic agents, food preservatives, and sustainable biopesticides. However, the transition from laboratory findings to practical applications requires further research, including in vivo studies, clinical trials, and more in-depth elucidation of molecular mechanisms, to ensure the full safety and efficacy of Eucalyptus-based products.

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