# A review on

# Pharmacological activities and bioactive compounds of *Eucalyptus globulus*

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

Submitted To

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# APPROVAL

This project paper, A Review on Pharmacological activities and bioactive compounds of *Eucalyptus globulus*, submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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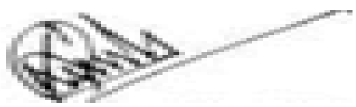
# DECLARATION

I hereby declare that this project report, "A Review on Pharmacological activities and bioactive compounds of *Eucalyptus globulus*", is done by me under the supervision of Dr. Md. Sarowar Hossain, Associate Professor, Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University. I am declaring that this Project is my original work. I also declare that neither this project nor any part thereof has been submitted elsewhere for the award of Bachelor or any degree.

Supervised By



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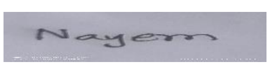


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***My Parents***

***The persons who always encourage me in every sphere of my life.***

## Abstract

According to its vast range of intriguing bioactivities, which are mostly related to the multiplicity of phytochemical elements in the plant parts, *Eucalyptus globulus*. is one of the most commonly used medicinal plants worldwide. There is an immediate need to investigate new antimicrobial components from botanical sources, of which medicinal plants are the most promising. The rising crisis of pathogen resistance for conventional antibiotics is regarded a global concern for the waning efficacy of antibiotics. Furthermore, the global scientific community has been driven to find plant-derived antioxidants and antimicrobials due to the developing limitations on synthetic antioxidants. Due to rising public health knowledge and dependence on natural substances as alternative options, this poses a significant global concern. Additionally, synthetic pharmacological side effects can be prevented. Additionally, plant extracts and their oil could be utilized as eco-friendly plant-based treatments for the management of weeds, insects, and plant pathogens, reducing the need for synthetic chemicals. Thus, the purpose of this review is to draw attention to the richness of the *E. globulus* plant, which contains valuable bioactive components, antioxidants, antimicrobials, phytoremediation, and herbicidal activities. This review will also lay the foundation for the creation of new agrochemicals, pharmaceuticals, and food preservatives. They might also offer potential economic uses to make up for the drawbacks of synthetic antioxidants.

**keywords**: antimicrobial activity; antioxidant activity; *E. globulus*; essential oil; herbicidal activity; 1,8-cineole; phytoremediation

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# Chapter one
# Introduction

## 1. Introduction

*E. globulus* is a member of the Myrtaceae family; the genus *Eucalyptus* has more than 700 species of evergreen deciduous trees with straighter trunks that are native to Australia [1]. The Tasmanian blue gum or "the blue gum" are two names for it. Nowadays, due to its simple adaptation to environmental factors, ease of culture, quick rate of increase, and rise in the woody biomass, E. globulus is widely grown around the world [2–5]. Infected regions can also be used to plant it [6]. There is no doubt that Eucalyptus can respond to biotic and abiotic challenges by preferentially producing defensive chemicals, primarily mono- and sesquiterpenes, as well as certain hydrocarbons and quinones [7]. *E. globulus* has drawn interest from scientists and environmentalists worldwide as a result. utilized frequently in the pulping process as a rapidly expanding supply and for the crucial it produces oil from its flowers. It is frequently utilized in the business world for numerous uses. Various species of eucalyptus essential oil is one of the top 18 most traded essentials. oils all around the world. Consequently, there is growing emphasis as a result. weighed in favor of their benefits as raw materials that can be employed in food, medicine, both in academic and commercial studies [8-9] are cosmetics. They include *E. globulus Labill*. is the primary source of eucalyptus leaf oil that is consumed worldwide [10]. The blades are exactly lanceolate, alternating, with yellowish petioles, and measure 10 to 30 cm long by 2.5 to 5 cm wide. They are excellent sources of natural oil and are green on both surfaces [11]. Usually, the oil Hydrodistillation was used to recover the majority of the chemical components. can be acquired using this technique [13]. The fundamental oil output varies between 1–3% [14]. The Eucalyptus leaf essential oil has a chemical makeup that is a complicated combination of materials, typically made up of 20 to 54 parts, each with a different function levels [15]. Especially oxygenated monoterpenes made up the oil. together along with monoterpene hydrocarbons (18.33–12.45%) (80.6–87.32%). The leaf essential oil that was extracted is generally light yellow in color and has a pleasing, camphor-like scent [16]. This oil has the following physical characteristics: an optical rotation of +1.5956, a pH (22 °C) of 4.9, a dielectric constant ranging from 1.4657 0.0070 to 1.4693 0.00057 [17], and a specific gravity of 0.913 to 0.919 g/cm3. Acid value, saponification value, hydroxyl value, and iodine value are the chemical parameters of the recovered leaf essential oil that are 0.5945, 19.576, 31.61, and 41.52, correspondingly [18]. All of the aforementioned physicochemical characteristics are thought to be important for determining oil quality, particularly for marketing. Monoterpene oxide 1,8-cineole (also referred as eucalyptol) is the main component of eucalyptus plants' essential oil. Cosmetics, fragrances, and flavors frequently use eucalyptol. This can be attributed to its flavor and nice spicy scent. Additionally, it is utilized as cough suppressants and mouthwash [19]. The presence of 1,8-cineole is the primary factor determining the important oil's commercial worth [20]. As a result, the Nigerian-grown E. globulus lacks 1,8-cineole and contains -phellandrene, which has a significant cytotoxic effect, making the oil acceptable for mosquitocidal applications but unsuitable for medicinal uses [21]. Numerous academics have been interested in eucalyptus leaf oil because it covers a broad range of biological potentials, including effectiveness against both bacteria that are both Gram-positive and Gram-negative [22] as well as having a significant antibacterial activity towards gum disorders [23]. As a result, it can be used in dental treatment.  products because it possesses anti-inflammatory and antifungal properties as well as possibilities for treating diabetes [25]. It also has insecticidal, acaricidal, and repellent properties. insecticide that degrades naturally [40]; effective against biological nematodes, phytopathogens [8,23], Additionally, it has anthelmintic activity [26] and is a natural preservative Additionally, the use of this leaf extracts in "folk medicine, in the treatment respiratory issues, such as a cold, a cough, a runny nose, a sore throat, asthma, and nasal sinusitis, bronchitis, and congested According to a research from Germany, aromadendrene, which has antibacterial properties, is the primary constituent in the essential oil of hydro-distilled fruits. However, Bey-Ould Si Said et al. [27] found that globulol, which makes up the majority of the fruit oils recovered from plants in Algeria's north-east, predominates (23.6%). Fruit essential oils are rich in Fruit oil is a promising option for use in the fight against germs because of its antibacterial action [28]. food and pharmaceutical industries. Extracts from leaves and roots have antioxidant, anti-inflammatory, and anticancer properties, which are associated with a higher concentration of plant phytoconstituents.

Leaf extracts also have the ability to be fungicidal, have allelopathic potential, be antihyperglycemic, have the potential to be anticancer, be antibacterial, and be neuroprotective [29]. Leaf extracts are also currently used as dietary supplements and in cosmetic applications [30]. Antioxidant and antibacterial properties are present in the E. globulus stump, which is referred to as "the basal section of the tree" and includes the near-ground stem portion and the woody roots that remain after "stem felling" [31]. The proposed study's objective is to give recent data on the phytochemical, properties of the E that are antibacterial, antioxidant, and globulus plant components, in addition to the reasons affecting the plant's ability to produce essential oils as well as their eco-friendly uses. This could facilitate the gathering of useful data for the plant's prospective usage as a priceless resource. supplier of various substances, for a variety of uses.

Figure 1: *Eucalyptus globulus* [32]

**1.1 Habitat of *Eucalyptus globulus***

While *Eucalyptus globulus* may grow on a variety of soil types, it is more prevalent and abundant on soils made from quartz and granodiorite rocks. It grows best in thick, well-drained soil or somewhat fertile loams. On ill-drained, very calcareous, or highly alkaline soils, blue gum does not naturally form. Nowhere does E. globulus occur spontaneously with less than 50 cm of annual precipitation, and the majority of its appearances are in regions with an average annual rainfall of 60 to 110 cm. Its elevational range is roughly

1100 m, which is close to sea level. [33] This species can be found in several frost environments. Sites near the coast rarely get frost, whereas higher altitude locations may see more than 70 frosts annually. E. globulus only occurs naturally within coordinates 31 and 43 degrees S in Tasmania, Victoria, and New South Wales. The Ottway Ranges, islands in the Bass Straits, southeastern Tasmania, and Wilson's Promontory in Victoria are the places where this plant is most prevalent. [31] While within a specific region blue gum is strongly linked to a constrained range of habitats, E. globulus has been most frequently associated with other Eucalyptus species throughout its natural range. With stands of different Eucalyptus species occupying areas peculiar to each species, a mosaic pattern frequently develops. [34] One of the eucalyptus species that is frequently cultivated is eucalyptus globulus. Its appeal has been attributed to its quick expansion and versatility in a variety of site situations. Only temperate places with harsh winters, tropical regions at low altitudes with consistently high temperatures, and areas with protracted hot and dry seasons have it unsuccessful. Because of severe defeat from collapse, cracking, and warping, the quickly growing wood has shown to be inappropriate for sawn timber. It has served as acceptable firewood, fence posts, mining timber, paper pulp, rayon pulp, shelter belts, and a species for ornamental landscaping. [35] Captain Robert Waterman brought E. globulus to California in 1853. He described it as an ornamental plant with rapid growth. Blue gum was being grown for professional reasons by 1870. "The section inside the impact of the moderate coast environment is most conducive for its optimal development," Sellers wrote in 1910. Although Southern California's northern coast counties and coastal valleys have particularly frugal rates of growth, the Santa Clara, Sacramento, and other valleys around San Francisco Bay tend to have the fastest rates of timber output. [36] The blue gum groves on the arid slopes and crests of the Coast Range hills attribute their survival primarily to the frequent fogs, as they typically fail in dry locations. The lowlands leading into San Francisco Bay, meanwhile, are the most suitable area in California for growing E. globulus due to fog wetness. Where the water table is very high, blue gum will flourish and can even withstand some time in excess moisture. [37]

**Taxonomy**

Kingdom: Plantae

Phylum: Magnoliophyta

Class: Magnoliopsida

Order: Myrtales

Family: Myrtaceae

Genus: Eucalyptus

Species: *E. globulus*

Subspecies: *E. globulus*

## 1.2 Literature review

### 1.2.1 Therapeutic Effect, Chemical Composition, Ethnobotanical Profile of *Eucalyptus globulus:*

Everywhere in the world, the essential oil (EO) of E. globulus has a very unique makeup. 1,8-cineole (Compound 64), macrocarpal C (Compound 22), terpenes (Compound 23–92), oleanolic acid (Compound 21), and tannins make up the majority of an important oil's constituents (Compound 93-99). We looked through in vitro and in vivo articles and examined information about E. globulus's chemical makeup, therapeutic potential, and mode of action. Numerous therapeutic effects, which include antibacterial, antifungal, antidiabetic, anticancer, anthelmintic, antiviral, antioxidant, anti-inflammatory, protection against UV-B, wound healing impact, and immune system stimulation, were depicted by essential oils and extracts of the leaves, stump, wood, root, and fruits of E. globulus. Additionally, the industry uses eucalyptus leaf extract as a food ingredient.

### 1.2.1 **Phytochemical and pharmacological profile of *Eucalyptus globulus:***

The Myrtaceae family of myrtle plants includes a diverse genus of blooming trees and bushes called Eucalyptus. The utilization of medicinal plants for the treatment and cure of various ailments has been practiced for centuries, and they play a significant role in global health. Generally referred to as "blue gum," eucalyptus contains compounds like flavonoids, alkaloids, tannins, and propanoids that are found in the plant's leaf, root, and stems. The pharmaceutical and phytochemical research reviewed here supports the medicinal efficacy of Eucalyptus globulus, which possesses a range of benefits including anti-inflammatory, anti-cancer, antibacterial, and antiseptic qualities.

# Chapter two
# Purpose of the study

## 2.1 Purpose of the study

- The purpose of this study was to determine knowledge of *Eucalyptus globulus*, its sources of information, and justifications for not going through screening if they had not already had the efficacy tested for.
- To know the different pharmacological option for the management of many diseases.
- To find out the different natural component which have therapeutic efficacy for the treatment of various pharmacological manifestation.
- To know the source & mechanism of those natural products.

# Chapter three
# Methodology

### 3.1 Methodology

Utilizing the PUBMED (including Medline) and Google Scholar databases, me gathered the pertinent experimental literature detailing the pharmacological effects of natural products on *Eucalyptus globulus*. When looking for related research, utilized the keywords "natural product of *Eucalyptus globulus*, therapeutic efficacy of *Eucalyptus globulus*." After the initial investigation was finished, we eliminated duplicates and non-English literature. The NCBI PubChem website was used to cite the chemical compositions of compounds made from natural sources. A piece of the information was collected by directly reading previous research articles, while the other part came from scouring the internet for pertinent data. All of the information gathered from prior study publications was numerically coded and imported.

# Chapter four
# Results & Discussion

### 4.1.1 Bioactive Components

Table 1 lists the many plant portions that multiple studies found to contain significant levels of diverse bioactive substances. The medicinal effects of the plant are caused by these phytochemicals. Except for a few data 1,8-cineole is the predominant component in the essential oils of leaves in the majority of investigations, with varying percentages (Table

1). The extract of leaves also contained tannins, saponins, terpenoids, glycosides, alkaloids, phenolic compounds, steroids, cardiac glycosides, terpenes, reducing sugars, carbohydrates, resins, acidic substances, and flavonoids, according to a phytochemical examination. [41]

| **Compound Name** | Plant name | Pharmacological activities | Mechanism | Reference |
|---|---|---|---|---|
| 1,8-cineole | Root tubers and leaves of Ipomoea batatas | Induction of apoptosis | ↑CFP/YFP | [34] |
| rutin, tannic acid | Syzygium aromaticum | Induction of apoptosis | Bcl-2, XIAP | [54] |
| pinene | Rhamnus | Inhibition of apoptosis | HOCl/OCl-, p-Akt | [55] |
| alloaromadendrene | Leaves of Pterogyne nitens Tul. | Inhibition of apoptosis | caspase-3, -8, -9 | [35] |

Table 1: : Plants parts of *Eucalyptus globulus*

Table 1. [42] had reported previously on the essential oil from the harvested leaves' anthelmintic efficacy. It has been suggested that this is because the oil contains beneficial phytoconstituents such borneol, linalool, cineol, geranyl acetate, anethol, and saffrol. The essential oil from leaf tissue also contained more flavonoids than phenols, according to phytochemical and fingerprint assessments, while the Fourier Transform Infrared Spectrophotometer demonstrated the presence of polyphenolic compounds like rutin, tannic acid, vanillic acid, and ascorbic acid, which are extensively used in the food industry. Additionally, the 1,8 cineole (29%), -pinene (16.9%), and -pinene (16%) major constituents of the essential oil were identified by the gas chromatography study. Table 1

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cassic acid, it is well recognized that these described compounds have intriguing uses in medicine and pharmaceuticals. [47]

### 4.1.2 Factors Influencing the Essential Oil Composition of Plants

As shown in Table 1, several research primarily focused on the variability of the essential oil composition obtained from plant leaves, which are thought to be the primary commercial source of 1,8-cineole. The diversity in essential oil constituents connected geographical regions to phonological stages, environmental factors, fluctuations, chemo type occurrence, and extraction techniques. [48] 1,8-cineole is one of the principal components of eucalyptus leaf oil (Eucalyptol). It has the empirical formula C10 H18O and is a cyclic ether. Recent research has shown how powerful eucalyptol is and how effective its antibacterial capabilities are Depending on the particular species, it varies in percentage and antibacterial action. The principal constituent of the leaf essential oil from plants grown in Algeria is identified by GC as -terpinene (94.48%), and 1,8-cineole (1,8-cineole) is the major component of some prior discoveries that also characterize the various important ingredients from plants growing in other places (3.20%) [58]. Furthermore, Benabdesslem et al. [49] stated that the primary component in Algerian-grown E. globulus plants (southwest Algeria) is p-cymene (20.24%). The authors came to the conclusion that Eucalyptus leaves from the same province, as well as their essential oils, can be used for the influenza virus, as inhaled steroids and as a replacement for foreign goods. Both of the aforementioned research ran counter to what Harkat-Madouri et al. found. The essential oil output and content were significantly influenced by the phenological stage. On Eucalyptus plants grown in Tunisia, Salem et al. [50] discovered that plants cultivated at the late fructification stage produced the highest oil yield (0.32% w/w), compared to plants cultivated at the vegetative and full flowering stages (0.11 and 0.14% w/w, respectively). This result was associated with the growth of essential oil's secretory structures, which are frequently linked to plant ontogeny. [51] Environmental factors also had a significant impact on how plants grew and produced essential oils. Furthermore, the growth phase also changed the components of the essential oils, so during the vegetative and full flowering stages. Usman et al. [52] discovered that D-limonene and m-cymene chemotypes were the most prevalent chemicals (23.5 and 24.8%, respectively) identified in the leaf oil obtained during the dry and wet seasons, respectively, of the E. globulus plant growing in north-central Nigeria. In contrast to the oil obtained (0.2% w/w) by distillation process [53], hydrodistillation produced a higher quantity of oil yield from E. globulus leaves, including such 1.1 and 1.21% of essential oil (w/w), based on the fresh weight of the mature leaves [54]. While classical hydrodistillation was preferable to steam distillation, the aromatic oil produced by steam distillation was suitable for food manufacturing as a flavoring ingredient from plants.

| **Compound** | **Efficacy** | **Mechanism** | **Reference** |
|---|---|---|---|
| terpinene | Induction of apoptosis | caspase-3, -8, -9 | [45] |
| eudesmol | Inhibition of proliferation | Bcl-2, XIAP | [46] |
| Juncusol | Inhibition of proliferation | tubulin polymerization | [47] |
| betulonic | cell cycle arrest Inhibition of proliferation | ROS | [48] |
| Mitomycin C | cell cycle arrest Inhibition of proliferation | caspase-3, -7 ↓Bcl2-L1 | [49] |

| | | | |
|---|---|---|---|
| Naringenin oxime | cell cycle arrest Inhibition of proliferation | caspase-3 | [50] |
| Notoginsenoside | Inhibition of proliferation | Bax, p-PTEN | [51] |
| Osthole | Inhibition of proliferation | Bax,c-caspase-3, -9 proteins | [52] |
| Piperine | mitochondrial dysfunction | PCNA, VEGF | [53] |
| Tf-CT-ME | apoptosis Inhibition of proliferation | ↑c-caspase-3 ↓Bcl-2/Bax | [54] |
| Thymoquinone | Inhibition of migration and invasion | Bax,E-cadherin | [55] |

Table 2: Bioactive Compounds

### 4.1.3 Antioxidant Activity of E. globulus.

As the harmful impacts of synthetic antioxidants were more widely known, a number of researchers worldwide were inspired to find alternative antioxidants of plant origin. In this context, it has previously been reported that the antioxidant properties of several Eucalyptus plant components (leaves, fruits, roots, and stump wood) as well as their essential oils can be used as chemical preservatives and to reduce oxidative stress-related disorder with higher IC50 values (136.87 L/mL) as comparable to the common antioxidant ascorbic acid, the leaf essential oil of E. globulus cultivated in Nigeria revealed a low antioxidant capacity. [55] This might be explained by the removal of some elements from the leaf oil, namely 1,8-cineole, as well as the potential antagonistic effects of other elements in eucalyptus oil. Contrarily, Luis et al. reported that the essential oil of Eucalyptus globulus has a notable antioxidant activity by scavenging DPPH radicals with an IC50 value of (2.90 0.35 v/v), compared to Eucalyptus radiata's IC50 value (4.56 0.70 v/v). [56] This may be due to the synergistic interaction of the other oil constituents as well as the fact that 1,8-cineole is present as the primary constituent solely in E. globulus essential oil. This was viewed as a positive outcome that encouraged the E. globulus essential oil as a viable all-natural replacement to offset the drawbacks effects of artificial antioxidants, particularly in regard to food preservation. [57] According to Salem et al. the increased antioxidant activity was found at the full blossoming and fructification stage, hence there was a favorable correlation here between essential oils and oil content and its capacity as an antioxidant. Additionally, the aerial sections' essential oil demonstrated both a moderate lowering power efficacy and a powerful DPPH scavenging capacity. [58] as comparison to ascorbic acid and butylated hydroxyanisole, correspondingly. Furthermore, the 1,8-cineole, -terpineol, and methyleugenol's effects on metal chelation were thought to be the reasons why the ferrous ions of the essential oils obtained at the vegetative and full blooming stages had a stronger chelating ability than oil obtained at the fructification stage. Intriguingly, Usman et al. investigated the impact of seasonal variation on the antioxidant activity of Eucalyptus essential oil and showed that the leaf essential oil harvested during the rainy season was richer in oxygenated mono- and sesquiterpenoids. [59] This was evidenced in its higher DPPH radical scavenging capacity as well as considerable protection of human subject’s authority as tried to compare to the leaf essential oil collected during the dry season. Currently, Sharma et al. The leaf methanol extract had the highest IC50 value, which was 23 g/mL, followed by the leaf ethyl acetate extract and the leaf hexane extract, which had IC50 values of 29 and 65 g/mL, correspondingly. The scientists linked the extract's high phenolic concentration to the extract's greatest action for BHT

(IC50 = 17 g/mL) and vitamin E (IC50 = 26 g/mL) [60]. Similar conclusions were reached by Nile and Keum, who found that the leaves of the methanol extract had a significant antioxidant efficacy as measured by their ability to scavenge DPPH radicals and reduce their iron content as well as their ability to scavenge OH radicals. The polar isolates of the E. globulus stumps had a considerable antioxidant ability with a lower IC50 value than the non-polar extract when tested utilizing the DPPH and -carotene bleaching test methods (n-hexane). [61] This was due to the fact that the polar isolates were able to efficiently remove the phenolic components, which helped to explain the stumps' economic significance as the oldest section of the tree. Additionally, stump isolates' capacity to prevent lipid peroxidation suggested that they might be used as natural preservatives, especially for foods with a high fat content. Its (2020) discovered that the limited results of the ethanol root extract of E. globulus demonstrated a strong antioxidant activity thru the DPPH radical scavenging possibility, encouraging an inhibition that directly linked with the connection between the antioxidant activity and root content of phenolics and flavonoids, which recommended that the roots were a promising source of natural antioxidants for lowering reactive oxygen species in biological systems. Furthermore, crude extracts from the bark and fruit possessed antioxidant properties that might be used to counteract the negative effects of synthetic antioxidants by substituting them for pure molecules like plant-derived antioxidants. [62]

| **Compound Name** | Pharmacological activities | Mechanism | Reference |
|---|---|---|---|
| methyleugenol's | **Antioxidant Activity** | ↑CFP/YFP | [23] |

| | | | |
|---|---|---|---|
| butylated hydroxyanisole | **Antioxidant Activity** | Bcl-2, XIAP | [24] |
| Eucalyptus radiata's | **Antioxidant Activity** | HOCl/OCl-,  p-Akt | [25] |
| alloaromadendrene | **Antioxidant Activity** | caspase-3, -8, -9 | [26] |

Table 3: Antioxidant Activity of *E. globulus*

### 4.1.4 Antibacterial Activity

the growing concern over traditional antimicrobial agents' efficacy, a serious global threat was created by the expanding multidrug resistance pathogens as well as.  There is a need to look into natural alternatives that have strong antibacterial properties.  eradicating infectious diseases that were becoming a greater danger to human health. [63] so that The antimicrobial effects of various plant components and their essential oils have been Gram-positive and Gram-negative bacterial strains have been extensively studied, as Table 2's summary demonstrates that E. A promising antibacterial agent with numerous medicinal uses is globulus. Additionally, the effectiveness of eucalyptus essential oil versus bacterial species as plant component extracts are ascribed to the following: [64]

| Plant Parts | Solvent Used | Method Used | Target Species |
|---|---|---|---|
| Leaves | Essential oil | Agar diffusion technique | *Staphylococcus aureus* CECT 4459<br>*Escherichia coli* O157:H7 CECT 4267 |
| Aerial parts | Essential oil | Disc diffusion assay | *Salmonella enteritidis* (CECT 4155)<br>*Escherichia coli* (CECT 4267)<br>*Pseudomonas aeruginosa* (CECT 110)<br>*Staphylococcus aureus* (CECT 239)<br>*Enterococcus faecium* (CECT 239)<br>*Listeria monocytogenes* (CECT 935)<br>*Listeria monocytogenes* EGD-e |
| Leaves | Essential oil | Agar disc diffusion method | *Staphylococcus aureus* ATCC 25923<br>*Escherichia coli* ATCC 25922<br>*Pseudomonas aeruginosa* ATCC 27853<br>*Phylococcus aureus*<br>*Escherichia coli*<br>*Pseudomonas aeruginosa*<br>*klebsiella pneumoniae*<br>*Proteus mirabilis*<br>*Streptococcus* pyogenes<br>*Morganella morganii*<br>*Providencia stuartii*<br>*Enterobacter cloacae*<br>*Acinetobacter baumannii*<br>*Citrobacter freundii*<br>*Salmonella infantis* |
| Leaves | Essential oil | Agar disc diffusion and dilution broth methods | *Escherichia coli*<br>*Staphylococcus aureus* |
| Leaves | Essential oil | Agar dilution method | *Helicobacter pylori* ATCC 700392 |
| Leaves | Methanol extract | Cup-plate method | *Staphylococcus aureus*<br>*Bacillus subtilis* |
| Leaves | Ethyl acetate | Agar well diffusion method | *Lactobacillus acidophilus* (MTCC-*447)<br>*Lactobacillus casei* (MTCC-1423)<br>*Staphylococcus aureus* (MTCC-890)<br>*Streptococcus mutans* (MTCC-96) |
| Fruits | Aqueous methanol (80%) | Disc diffusion method | *Staphylococcus aureus* ATCC 6538<br>*Bacillus subtilis* ATCC 6633<br>*Klebsiella pneumoniae* E 47 |
| Leaves | Oil encapsulated silica nanoparticle | Agar well diffusion method | *Escherichia coli* (ATCC 25922) |

Table 4: Antibacterial activities reported in different parts of *E. globulus* [65]

Fruit essential oils that had been isolated had strong antimicrobial effects on evaluated for multi-drug resistance. Additionally, the fusion of 1,8-cineole and Fruit oil-derived aromadendrene increased resistance via an addition and anti-Staphylococcus aureus, anti-Streptococcus pyogenes, and other methicillin-resistant bacteria comparable to utilizing a combined chemical, and Bacillus subtilis. The antibiotic The greatest amount of oxygenated monoterpenes (87.32%) was found to be effective in The synergism was caused by eucalyptus leaf oil and other minor ingredients as well. The methanolic leaf extract's antibacterial properties against S. bacteria and B. subtilis, possibly be explained by the tannins and saponins present. Similar to this, leaf extracts had anticariogenic efficacy because they contained the sesquiterpene alpha-farnesene, which paved the way for the development of potent medications for the treatment of dental caries [66]. The E. globulus essential oil or leaf extracts combined with medications had the strongest antibacterial efficacy against P. aeruginosa. Furthermore, Goldbeck et al. noted a synergism impact when Streptococcus mutans was treated with a mixture of E. globulus and E. urograndis essential oils. Additionally, a correlation between the strongest antibacterial activity and the higher concentration of 1,8-cineole (71%) in E. globulus comparison to E. urograndis (36%), supporting the possible use of E. globulus essential oil. According to Lus et al, it was discovered that essential oils had an additive effect on Acinetobacter baumannii strains when used in combination with ciprofloxacin, chloramphenicol, and tetracycline. The mixture of essential oil with cefoperazone and piperacillin, on the other hand, had no synergistic effects against by the aforementioned strains. [56] The high concentration of 1,8-cineole and -pinene in the essential oil isolated from the leaves was linked to the potent antibacterial effectiveness. However, according to Quatrin et al, nano-emulsions were inefficient against the Gram-negative bacterium, which is typically prevalent in immunocompromised patients, and only contained a tiny portion of eucalyptus essential oil (5%) in them. [69] In contrast to the water and ethanol leaf extracts, the methanol extract of leaves demonstrated a good antibacterial activity versus S. mutans, S. aureus, and E. coli. This was due to the separation of significantly varied components by methanol in comparison to other extracts. An analogous pattern was seen in the Eucalyptus aqueous ethanol leaf extract, which also demonstrated antibacterial activity against by the investigated species. [67] The occurrence of multiple bioactive compounds was cited by the authors as a possible explanation for the additive or synergistic action. When used against S. aureurs, the aqueous extract of E. globulus leaves exhibited the same mechanism of action as ampicillin. In contrast to the water and ethanol leaf extracts, the methanol extract of leaves demonstrated a good antibacterial activity versus S. mutans, S. aureus, and E. coli. This was due to the separation of significantly varied components by methanol in comparison to other extracts. An analogous pattern was seen in the Eucalyptus aqueous ethanol leaf extract, which also demonstrated antibacterial activity against investigated species. [34] The occurrence of multiple bioactive compounds was cited by the authors as a possible explanation for the additive or synergistic action. When used against S. aureurs, the aqueous extract of E. globulus leaves exhibited the very same mechanism of action as ampicillin. Broadly speaking, gram-negative microorganisms were much more resilient to eucalyptus extracts and essential oil than gram-positive bacteria. Additionally, the leaf extracts had no effect on Gram-negative bacteria, which can be attributed to their outer lipopolysaccharide membrane, whereas it had an antibacterial effect exclusively on Gram-positive bacteria because of its high phenol content. There has been few research on the effectiveness of E. globulus leaves and stumps as antifungal agents (Table 3), despite the fact that eliminating fungal diseases that are resistant to antibiotics is a serious challenge worldwide, for instance in the case of Candida spp. and other fungal genera. Trying to find a new therapeutic approach is also thought to be of utmost relevance because of the rise in cases of Candida spp. infection and the threat of drug resistance. The abundance of plant parts with a variety of phytochemical elements has been linked to the induced antifungal efficacy (Table 1), which is a practical means of preventing fungal infections. [35]

### 4.1.5 Antifungal Activity

There has been few research on the effectiveness of *E. globulus* leaves and stumps as antifungal agents (Table 3), despite the fact that eliminating fungal diseases that are resistant to antibiotics is a serious challenge worldwide, for instance in the case of Candida spp. and other fungal genera. Trying to find a new therapeutic approach is also thought to be of utmost relevance because of the rise in cases of Candida spp. infection and the threat of drug resistance. The abundance of plant parts with a variety of phytochemical elements has been linked to the induced antifungal efficacy (Table 1), which is a practical means of preventing fungal infections. The substantial anti-candidal activity of E. globulus essential oil suggests that mouthwash therapies may be possible. Comparable to how Eucalyptus crude extract outperformed the antifungal nystatin (used to treat fungal infections of the skin, mouth, vagina, and intestinal tract) by a factor of two, *Eucalyptus* crude extract was twice as effective against C. albicans. This is likely due to the high concentration of 1,8-cineole (85.8%) in the leaf essential oil. The primary microbe that causes fungal infections worldwide, C. albicans, was the target of antifungal and antibiofilm activity in nanoemulsions utilizing legally procured *E. globulus* essential oil. [70]

| Plant Parts | Solvent Used | Method Used | Target Species |
|---|---|---|---|
| Leaves | Essential oil | Micro dilution method | *Candida albicans* ATCC 90028<br>*Candida albicans* 15B |
| leaves | Essential oil | Agar-well diffusion method | *Candida* spp. |
| Leaves | Essential oil | Broth microdilution assay | *Candida albicans* ATCC 10231 |
| Leaves | Methanol extract | Cup-plate method | *Trichophytor rubrum* |
| Leaves | Essential oil | Cylinder plate method | *Aspergillus niger*<br>*Candida albicans* |
| Stump | n-hexane, ethanol, methanol, and 75% aqueous ethanol | Disc diffusion assay | *Candida albicans* ATCC 90028<br>*Candida tropicalis* ATCC 750 |
| Leaves | Essential oil incorporated into chitosan films | Agar diffusion assay | *Candida albicans*<br>*Candida parapsilosis* |
| Leaves | Essential oil | Agar diffusion method | *Trichophyton* spp.<br>*Aspergillus* spp. |
| Leaves | Nanoemulsions containing oil | Broth microdilution technique | *C. albicans* (ATCC 14053)<br>*C. tropicalis* (ATCC 66029)<br>*C. glabrata* (ATCC 66032) |
| Aerial parts | Essential oil | Disk diffusion assay | *Candida albicans* ATCC 10231 |
| Leaves | Essential oil | Double-dilution micro-plate assay | *C. albicans1*<br>*C. albicans2* |
| Leaves | Zinc oxide nanoparticles from essential oil | Agar well diffusion method | *Candida albicans* |

Table 5: Antifungal activities reported in different parts of *E. globulus* [45]

The Tunisian Eucalyptus aerial parts' essential oil was shown to have a strong fungus-fighting ability against C. larger than the antifungal (Amphotericin) albicans B), in particular the crucial essential oil harvested during the fruiting period, as opposed to the essential oil achieved during the entire flowering and vegetative periods. This was most likely due to the Plant immune mechanisms during fruit development or changes in oil composition Considering that the oil includes significant levels of -pinned and p-cymene at the height of its essential oil output throughout the maturation process. Additionally, when Eucalyptus essential oil and amphotericin B were applied together, the MIC value for Eucalyptus essential oil alone against C. albicans significantly decreased, falling from 1000 to 31.25 g/mL [70]. In a similar manner, Bogavac et al. [71] demonstrated the essential oil's robust antifungal activity as a promising substitute for vaginal C. albicans strains that were multi drug resistance to traditional antifungals.

### 4.1.6 Future Perspectives

The above-mentioned motivate findings corroborate the use of various *E. globulus* plant part extracts and their essential oils as antioxidant and antimicrobial officials that encourage additional clinical trials, which should be implemented to confirm the above-mentioned findings for additional medical uses. [72] Additional studies should be conducted to investigate the synergistic or antagonistic relationships from among complex mixes of essential oils in order to gain a thorough grasp of all the bioactive chemical pathways involved in all the investigated bioactive components. [79] Additionally, additional research needs to be done on the mechanism of action following the combination of traditional antibiotics and oils, which might also affect many targets simultaneously. To address the low penetration of natural antimicrobial drugs into the microbe biofilm matrix, which can be accomplished using nanocarriers, more research is necessary. Therefore, more research will be required in the case of employing biosynthesized nanoparticles to establish the influence of their cytotoxicity, with a focus on improving the methods for phenolic component extraction and chemical characterization for potential extraction quality enhancement. [8]

# Chapter five
# Conclusion

## 5.1 Conclusion

The examination of *Eucalyptus globulus* trees harvested for pulpwood at ages 1 1–4 years on plantations revealed that this species has a high cellulose and comparatively low lignin content. The chemical makeup of the trees varied among them and among the four distinct geographic areas. For cellulose content, this heterogeneity was noticeably greater. For the examples examined, an age restriction of 12 years was the upper limit for a low wood extractive content because wood extractives rose with age. *Eucalyptus globulus* bark contains more extractives and more cases than the tops, which share a chemical makeup with bolewood. Leaves, particularly those with small diameters, are composed primarily of extractives and have relatively little cellulose.

# Chapter six
# Reference

## Reference

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