MEDICINAL PROPERTIES OF *EUCALYPTUS GLOBULUS* AND ITS UTILIZATION IN THE SYNTHESIS OF CAO NANOPARTICLES

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ABSTRACT: The plant *E. globulus (E. globulus)*, is a cosmopolitan tree commonly found in plain areas, and has a great deal of potential for medical applications. It has a diverse nature of chemical components with strong medicinally important constituents. This review explores the pharmacological properties of *E. globulus* highlighting its many applications for both human and animal medicines. *E. globulus* contains a variety of phytochemical constituents in leaves, stems, and roots, such as flavonoids, alkaloids, tannins, and propanoids. Numerous studies have shown that *E*.ucalyptus *globulus* possesses a wide range of qualities, including astringent, antibacterial, anticancer, and anti-inflammatory effects. Literature regarding the phytochemicals compounds of the plant are studied in the current review article. The bioactive compounds in Eucalyptus are found to be explored for their potential to combat antibiotic-resistant bacteria, making them a valuable resource in the ongoing battle against superbugs. In conclusion, Eucalyptus species offer a vast array of pharmacologically active compounds with diverse therapeutic applications. Continued research and clinical trials are essential to fully unlock and validate the medicinal potential of these remarkable plants.

Keywords: *E. globulus* , phytochemicals, astringent, propanoids, antioxidant, antibacterial.

(Received 15.04.2024 Accepted 01.06.2024)

INTRODUCTION

An Australian native evergreen tree known as *E. globulus* Labial (Lan An) is commonly cultivated for pulp and firewood in Mediterranean and subtropical regions. The leaves of E. globules have long been used to treat bronchitis and asthma. Herbal tea is also made with them. Recent studies have also identified characteristics that are antibacterial, antifungal, anthelmintic, and anti-diabetic (González-Burgos, 2018).

In the wild, *E. globulus* trees can grow to heights of 60 to 80m. Usually smooth, the plant's brown or yellowish-brown bark peels off in long strips to reveal a white or grayish surface that resists rot and can readily detach from the stem. The age of the tree also affects the color of its leaves (Pereira, 2014; Tyagi, 2011; Araujo, 2010). The flower buds are arranged singly in the leaf axils on a sessile or up to 5 mm long condensed peduncle. The flowers are at their largest between May and January, and they are white with numerous white, cream, yellow, or red stamens (Ali, 2020).

The Mirtaceae family of eucalyptus globules contains many crucial therapeutic plants. Their components and essential oils offer insecticidal qualities against pest insects. Large amounts of minerals, vitamins, and amino acids can be found in *E. globulus* (Nesamani, 1999).

The Myrtaceae family includes the tall, evergreen eucalyptus tree or shrub. Despite having originated in Tasmania and Australia, it has quickly spread to other nations. Therefore, unless the species from which it is obtained is specified, the term "Eucalyptus oil" is scientifically useless. Numerous eucalyptus tree species produce essential oils, with some species having more pungent foliage than others and oils from each species having unique properties. The use of eucalyptus leaf extracts in food additives and cosmetic formulations has been authorized. The eucalyptus species is distinguished for its quick growth. In their native habitat, several of these species grow to enormous proportions and rank among the tallest trees on Earth. Nearly all of the species go by the name "gum trees." There is a long history of valuable medical uses for *E. globulus* . A lot of research has gone into extracting different natural products to test for antimicrobial activity, but the antimicrobial activity of these items when combined has not received as much attention. Numerous members of the Myrtaceae family's genus

Eucalyptus are among these medicinal plants and are used throughout the world to cure a wide range of illnesses, including microbial infections (Ahmad, 2021).

The Myrtaceae family of myrtle plants includes a diverse genus of blooming trees and bushes called Eucalyptus. Various qualities of *E. globulus* , including anti-inflammatory, anti-cancer, antibacterial, and antiseptic (Sawalha, 2021). Various qualities of *E. globulus* , including anti-inflammatory, anti-cancer, antibacterial, and antiseptic (Sawalha, 2021).

Figure 1.1: Eucalyptus globules

Figure 1.2: Eucalyptus globules (Mirtaceae)

In the following section, a summary of the most common varieties of nanoparticles (NPs) is provided. Nanotechnology is extensively applied across numerous scientific fields. Focusing on NP-related products and their applications, NPs hold significant potential in various areas, including drug delivery, cancer treatments, bacterial targeting as alternatives to antibiotic treatments, and the prevention of bacterial infections through antibacterial vaccines. Specifically, because of their unique characteristics, inorganic nanometal oxide NPs like calcium oxide (CaO), magnesium oxide (MgO), copper oxide (CuO), zinc oxide (ZnO), and titanium

dioxide (TiO2) stand out. These nanoparticles are recognized for their safety, stability, and multifunctionality, making them highly valuable in diverse biomedical and technological applications. Their unique characteristics enable them to perform effectively in targeted therapeutic interventions and the development of new antimicrobial strategies, thereby offering promising advancements in both medical treatments and preventive healthcare.

Photochemical Chemical composition: The root, stem, and leaf of *E. globulus* are rich in flavonoids, alkaloids, tannins, and propanoids, among other phytochemicals. These substances have a wide range of possible uses. Calcium oxide nanoparticles, known for their high surface area and magnetic properties, can be synthesized using green methods involving *E. globulus* . These nanoparticles, which can be either spherical or faceted, serve as effective adsorbents for removing dyes from various solutions. Their size can be accurately measured using powder x-ray diffraction techniques.

Extensive research has been carried out to isolate phytoconstituents from different parts of E. globulus. Many volatile chemicals, including 1,8-cineole (eucalyptol), aromadendrene, globulol, ß-pinene, pipertone, and ß-terpinen-4-ol, as well as allo-aromadendrene, are present in the plant's leaves and shoots. Dextrin and sucrose are extracted from honey and flowers using an acidic solution. At 79.85%, eucalyptol makes up a sizable portion of the essential oil (EO). Additionally, this essential oil has a high concentration of oxygenated monoterpenes, albeit the exact amount varies depending on the type of Eucalyptus. Geographical location influences these components' variations, which in turn impacts the biological activity of essential oils. Aromatherapy, phytotherapy, perfumery, cosmetics, and food manufacturing are just a few of the businesses that heavily utilize essential oils (EO), particularly in China, India, South Africa, Portugal, Brazil, and Tasmania..

The composition of lipophilic extractives in the acetone extract from the chloroform-soluble portion of *E. globulus* wood has been studied in detail. Solid-phase extraction using aminopropyl-phase cartridges was used to separate the lipid extract into four fractions with increasing polarity. The complete lipid extract and its fractions were analyzed using gas chromatography and gas chromatography-mass spectrometry using capillary columns heated to a high temperature. Sterols, sterol esters, fatty acids, steroids, ketones, hydrocarbons, and triglycerides are among the main compounds found. There were also trace amounts of waxes, tocopherols, mono- and triglycerides, and fatty alcohols. A-terpineol (2.54%), terpinen-4-ol (0.34%), 1,8-eucalyptol (72.71%), and linalool (0.24%) were among the sesquiterpenes containing oxygen that made up the majority of the essential oils.(Brito, Silva, Leão, & Almeida, 2008).

The primary component of eucalyptus oil is eucalyptol, sometimes referred to as 1,8-cineole. Different studies have reported varying amounts of essential oil and its constituents in *E. globulus* . At least 2% (v/w) of the leaves' essential oil is 1,8-cineole, which makes up at least 70% (w/w) of the leaves. 54–61% 1,8-cineole, 19.5–24.3% ß-pinene, 6.7–9.1% limonene, 2.1–5.4% ß-terpinyl acetate, and 3.6–7.7% sesquiterpenes have all been shown to be present in freshly collected leaves. Different preparation techniques, including steam distillation, might cause some compounds to hydrolyze. According to a different source, fresh *E. globulus* leaves have a volatile oil content of 1.87% and a 1,8-cineole content of 35.7%. Phytosterols are present in chloroform and methanol extracts of the leaves, but not in aqueous or petroleum ether extracts. Many extraction methods were used to identify the main core groupings. (Brito, Silva, Leão, & Almeida, 2008).

To synthesize calcium oxide nanoparticles, green methods using *E. globulus* can be highly effective. These nanoparticles have unique properties, including high surface area and magnetic behavior, making them suitable for applications such as adsorbents for dye removal from solutions. Powder X-ray diffraction is a valuable tool for determining the precise size of these nanoparticles. Research indicates that the isolation of phytoconstituents from E. globulus involves separating the plant's organs, which contain diverse compounds like volatile substances in the leaves and shoots. The extraction of essential oils reveals a high percentage of eucalyptol, contributing to the oil's composition and its biological activities, influenced by geographic and species variations. The use of essential oils spans numerous industries, underscoring their importance and versatility.

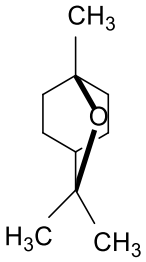
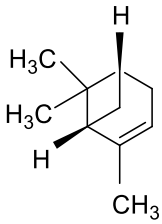
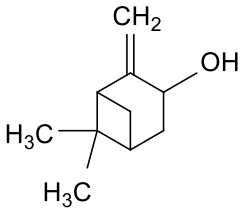
By understanding the intricate composition and potential applications of phytochemicals and nanoparticles derived from *E. globulus* , researchers can explore new avenues for utilizing these natural resources in various scientific and industrial fields.

Classification

The following is *E. globulus* ' taxonomy: Plantae is the kingdom of plants; Tracheobionta is the subkingdom of vascular plants; Magnoliophyta is the division of flowering plants; Super_division: Spermatophyta is the division of seed plants; Genus: Eucalyptus L'Hér. - Gum; Class: Magnoliopsida - Dicotyledons; Subclass: Rosidae; Order: Myrtales; Family: Myrtaceae - Myrtle family;

This classification highlights plant's place within the broader categories of the plant kingdom, from the general characteristics of plants down to the specific genus Eucalyptus, known for its characteristic gum trees.

Chemical structure of Eucalyptus globules

Name	1,8-cineol	α-pinene	L-pinocarveol
			
Synonyms	Eucalyptol 1,8-epoxy-p-menthane cajeputol	α-pinene oxide (1R,5R)-2-pinene	10- pinen-3-ol
Formula	$C_{10}H_{18}O$	$C_{10}H_{16}$	$C_{10}H_{16}O$
Average Mass (g/mol)	154.24	136.23	152.23
Role	Food additives known as flavoring agents are used to enhance a food's flavor or aroma.	Plants release metabolites	Plants release metabolites

Pharmacological properties: There have been numerous pharmacological actions associated with *E. globulus* leaf extract, including anti-inflammatory, antioxidant, antibacterial, and antihistaminic (Irshad *et al*., 2014).

Antihistaminic Properties: Ethanol and hexane extracts of *E. globulus* fruit and leaves have demonstrated the ability to inhibit histamine release from RBL-2H3 cells in an IgE-dependent manner. This indicates a potential role for these extracts in managing allergic reactions by preventing mast cell degranulation and subsequent histamine release, which can alleviate symptoms associated with allergies (Tailor *et al*., 2020).

Anti-Inflammatory Effect: Eucalyptus oil (EO)'s aromatic components are well known for its analgesic, anti-inflammatory, and antipyretic qualities. One of EO's main ingredients, eucalyptol, has been demonstrated to be a strong inhibitor of cytokine production. Studies conducted by Juergens and colleagues have shown that eucalyptol may successfully inhibit the production of TNF-α, IL-1, leukotriene B4, and thromboxane B2 in human blood monocytes. This implies that eucalyptol could be helpful in the long run for controlling bronchial asthma patients' airway irritation. Furthermore, eucalyptol's anti-inflammatory properties were validated in a double-blind, placebo-controlled trial including patients with severe asthma, emphasizing the plant's promise as a mucolytic treatment for upper and lower respiratory conditions. (Iravani, 2011).

Antibacterial Activity: Leaf extracts from *E. globulus* have shown strong antibacterial properties. There was an effective reduction of oral pathogenic bacteria with a minimum inhibitory concentration (MIC) of 0.20 ml in a 50% ethanol extract of the leaves. The extract has shown significant antibacterial activity against Porphyromonas gingivalis and Streptococcus mutans. It is 50% soluble in ethanol. Additionally, utilizing 200 clinical samples from patients with respiratory tract infections, the antibacterial qualities of E. globulus leaf extract were examined against a range of microorganisms, including Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae, and Haemophilus influenzae. (Siddiqui *et al*., 2021).

Fifty-six isolates of Staphylococcus aureus, twenty-five isolates of Streptococcus pyogenes, twelve isolates of Streptococcus pneumoniae, and seven isolates of Haemophilus influenzae were used in the study to assess the antibacterial activity of *E. globulus* leaf extract. According to the findings, these species' MIC50, MIC90, and minimum bactericidal concentration (MBC) values were 64 mg/L, 32 mg/L, and 16 mg/L; 128 mg/L, 64 mg/L, and 32 mg/L; and 512 mg/L, 128 mg/L, and 64 mg/L, in that order. These results demonstrate the strong antibacterial properties of E. globulus leaf extract, indicating the need for additional research to determine whether it can be used therapeutically to treat respiratory tract infections. (Salari *et al*., 2006).

Sinus Relief: Eucalyptus has also been shown to provide relief from sinus infections. Persistent congestion and headaches often indicate a sinus infection rather than a common cold. Eucalyptus is known to facilitate easier breathing for individuals with asthma, and its effectiveness extends to alleviating symptoms of sinus infections. The aromatic compounds in eucalyptus oil help reduce inflammation and clear mucus from the

airways, providing relief from sinus congestion and associated headaches (Hassanein *et al*., 2021).

Cytotoxic: Numerous extracts and separated elements from species of Eucalyptus have demonstrated the ability to be harmful to cells. The cytotoxicity of compounds produced from eucalyptus has been assessed in two noteworthy investigations by calculating the concentration needed to block 50% of cell growth (IC50). The initial investigation concentrated on a formylated triterpene called Clodoaldo that was taken from Eucalyptus cladocalyx leaves. The HL-60 myeloid leukemia cell line was significantly deadly to this chemical. The second research looked at Eucalyptus benthamii's cytotoxic effects in vitro. The activity of eucalyptus oil (EO) and many terpene components, such as α-pinene, terpinen-4-ol, and γ-terpinene, was evaluated against a range of pathogenic cell lines, such as HeLa (cervical cancer cells), J774A.1 (murine macrophage tumor), and Jurkat (T leukemia cells). When compared to other herbal treatments, the results showed that EO was more toxic to the Jurkat and HeLa cell lines than any one terpene. This suggests that E. benthamii may be a potential alternative source of cytotoxic chemicals. This research highlights how EO's cytotoxic effects on particular cell types may be used to treat particular disorders. The toxicity of EO is a serious worry, though. Numerous incidences of negative consequences following EO intake have been reported in scientific literature, particularly in youngsters. Among the symptoms include burning in the mouth and throat, nausea, and vomiting. For example, within 30 minutes of inadvertently consuming EO, a 3-year-old kid had central nervous system depression. 41 cases of EO poisoning in children under 14 during seven years are highlighted in reports by Day *et al*. and Webb and Pitt, highlighting the significance of precautionary measures and careful handling of EO to prevent unintentional poisoning. (Irshad *et al*., 2014).

Anti-diabetic activity: The herb *E. globulus* is frequently used to treat diabetes. E. globulus substantially alleviated weight loss and lowered hyperglycemia when added to the drinking water (2.5 g/l) and diet (62.5 g/kg) of mice. Additionally, an aqueous extract of E. globulus (0.5 g/l) markedly improved glucose metabolism in many ways: in mice's abdomen muscles, it increased 2-deoxy-glucose transport by 50%, facilitated 90% of glucose absorption into glycogen, and raised glucose oxidation by 60%. These encouraging findings suggest that *E. globulus* may be a useful dietary supplement for controlling hyperglycemia during treating diabetes. Additionally, it holds potential as a source for developing new, effective oral medications for diabetes management. Beyond its applications in diabetes, the bioactive compounds in *E. globulus* are being explored for their broader pharmacological properties, which include anti-inflammatory, antibacterial, and antioxidant activities. This positions *E. globulus* not only as a critical component in dietary therapies but also as a prospective foundation for innovative drug development, enhancing the therapeutic arsenal available for various chronic conditions (Iravani, 2011).

Calcium Oxide (CaO) Nanoparticle synthesis: Calcium oxide nanoparticles, or CaO NPs, are prospective drug delivery agents since they are used in synaptic delivery, photothermal and photodynamic treatment. CaO NPs have several uses outside of the biomedical industry, including in electronics, environmental cleanup, sensors, and catalysis. (V. Kumar *et al*., 2019). Calcium oxide (CaO) is a critical substance widely used in numerous domains, including catalysis, cosmetics, and ceramics, for controlling microorganisms. It also serves as an inorganic antimicrobial agent. Based on its chemical composition, CaO is categorized under the alkaline earth metals in the periodic table (Marquis, Ramasamy, Banwarilal, Munusamy, & Biology, 2016).

Given the rich diversity of tropical plants in Indonesia, employing tropical biomass or its extracts for CaO biosynthesis presents a valuable scientific challenge due to the efficiency and environmental friendliness of this method. The capability of metabolite chemicals found in plant materials to act as biological reducers for metal production is well-documented (Akhtar, Panwar, Yun, & Engineering, 2013). Flavonoid compounds, a prominent class of secondary metabolites in plant tissues, have proven effective as reducing agents for metal ions. Depending on the plant type, many flavonoids naturally exhibit colors in various shades, such as red, pink, and purple.

Calcium oxide's extensive use spans across catalysis, cosmetics, ceramics, and as an inorganic antibacterial agent to inhibit microbial growth. As an alkaline earth metal, CaO's chemical makeup positions it within the periodic table's alkaline earth group. The vast diversity of tropical plants in Indonesia suggests that using tropical biomass or its extracts for CaO biosynthesis is a scientific challenge worth pursuing due to the method's efficiency and eco-friendliness. Chemicals in plant materials, such as biomass, are well-recognized as biological agents in metal production (Mustafa, Tahir, Sultan, & Akhtar, 2013). Flavonoid compounds, a crucial class of secondary metabolites in plant tissues, are particularly effective as reducing agents for metal ions. Various flavonoids naturally produce pigments in hues like red, pink, and yellow, depending on the plant's characteristics.

In the past decade, there has been a significant focus on nanotechnology, particularly on exploring the electrical, optical, and magnetic properties of nanomaterials. Numerous nanoparticle-based therapeutics have demonstrated increased effectiveness and reduced

toxicity in drug delivery, overcoming biological barriers and providing selective drug delivery options. These unique properties can be harnessed for extensive nano-biomedical applications (Choi & Han, 2018). To manufacture nanoparticles, several plants have been used, including Oat (*Avena sativa*), aloe vera (*Aloe barbadensis* Miller), Tulsi (*Osimum sanctum*), alfalfa (*Medicago sativa*), Neem (*Azadirachta indica*), Lemon (*Citrus limon*), Coriander (*Coriandrum sativum*), lemon grass (*Cymbopogon)* and Mustard (*Brassica juncea*) (J. Singh *et al*., 2018)

Conclusion: A thorough analysis of the literature reveals that eucalyptus species are an important source of a wide range of compounds with pharmacological and therapeutic value, such as terpenoids and essential oils, which are widely utilized in aromatherapy. Many eucalyptus species have been the subject of in-depth study because of their diverse pharmacological properties. Analgesic (pain-relieving), hepatoprotective (liver-protecting), antifungal, anti-inflammatory, antibacterial, antidiabetic, antioxidative, antiviral, antitumor, and anticancer characteristics are some of these actions. The essential oils derived from Eucalyptus species are particularly noted for their therapeutic potential. These oils contain compounds such as cineole, which contribute to their efficacy in treating respiratory conditions and enhancing mental clarity. The terpenoids present in Eucalyptus also exhibit significant biological activities, adding to the plant's medicinal value. In addition to their internal medicinal uses, Eucalyptus oils are commonly used in topical applications for their antiseptic and soothing properties. They can be found in many different items, such as lotions, ointments, inhalants, and massage oils. While aromatherapy is appreciated for its pleasant experience, affordability, and minimal side effects (except for rare allergic reactions), the scientific evidence supporting its effectiveness, particularly for patients undergoing medical treatments, remains limited. Despite the widespread anecdotal reports and traditional use, more rigorous clinical studies are needed to substantiate the therapeutic claims of aromatherapy using Eucalyptus essential oils. Moreover, the potential of Eucalyptus species extends beyond human medicine. Studies have shown their effectiveness in veterinary medicine, offering natural alternatives for treating infections and inflammatory conditions in animals.

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