REVIEW ON EUCALYPTUS: PHYTOCHEMICAL PROFILE, EXTRACTION TECHNIQUES, AND PHARMACOLOGICAL APPLICATIONS IN FOOD AND MEDICINE

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ABSTRACT

One of the eucalyptus species, Eucalyptus globulus, is a plant used extensively in medicine because it produces essential oil (1). *The most advantageous portion of eucalyptus is usually thought to be the leaves. Bioactive substances such gallic acid, cypellocarpin A, eucaglobulin, cuniloside, and (1S, 2S, 4R)-trans-2-hydroxy-1,8-cineole;-D-glucopyranoside are found in the essential oils that are derived from these plants. These bioactive substances have anti-inflammatory, antibacterial, and antioxidant qualities.*

The yield and bioactive component content of essential oils are both greatly impacted by the extraction technique selected. Many extraction techniques are used, such as steam distillation, water distillation, water-steam distillation, microwave assisted extraction (MAE), ultrasound assisted extraction (UAE), and maceration. The purpose of this review is to examine these extraction techniques as well as the major variables influencing the extraction procedure used to produce E (2,3,5).

Keywords:-eucalyptus, phytochemicals, medicinal properties, extraction techniques, food applications

Introduction

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As a member of the Myrtaceae family, eucalyptus is widely grown for its therapeutic qualities all over the world (4-9). Eucalyptus globulus is the most notable species of eucalyptus among the many others. Essential oil from Eucalyptus globulus, which is mostly extracted from its leaves, is used in flavoring, cosmetics, healthcare, and pharmaceutical industries. The essential oil, which is abundant in bioactive components, has antibacterial, anti-inflammatory, and antioxidant effects (10-14). Eucalyptus essential oil improves flavor and aroma in food products and acts as a natural preservative. Secondary metabolites found in eucalyptus leaves include aldehyde, ketone, monoterpene, sesquiterpene, and 1,8-cineole (eucalyptol).The standard essential oil's cineole level shouldn't be higher than 70%. The species, geographic location, time of year, leaf age, harvest period, and extraction technique are some of the variables that affect the essential oil's chemical composition. The selection of the extraction technique has a major influence on the essential oil's chemical composition and production. High-quality essential oil production is ensured while maintaining bioactive chemicals by the use of efficient extraction techniques as distillation with water or steam, microwave assisted extraction (MAE), ultrasound-Assisted Extraction (UAE), and maceration (15-20). The purpose of this paper is to clarify the different extraction techniques used to extract the essential oil from Eucalyptus globulus.

Taxonomy

The Eucalyptus species are categorized as flowering plants and are part of the kingdom Plantae. Eucalyptus globulus, E. citriodora, E. staigeriana, E. radiata, E. camaldulensis, E. laxophleba, E. cinerea, E. saligna, E. tereticornis, and E. leocoxylon are some of the prominent species that they belong to (21-22).

Kingdom	**Plantae**
Sub-kingdom	Tracheobionta
Super-division	Sprematophyta
Division	Flowering plants
Class	Dicotlydeons
Sub-class	Rosidae
Order	Myrtales
Family	Myrtaceae
Genus	Eucalyptus
Species	*Eucalyptus globulus*, *E. citriodora*, *E. staigeriana*, *E. radiata*, *E. camaldulensis*, *E. laxophleba*. *E. cinerea, E. saligna, E. tereticornis*and *E. leocoxylon*

Morphology

Officially classified as an evergreen tall tree, eucalyptus can grow to a height of 40–70 meters and has a straight, robust trunk that is 0.6–2 meters in diameter. Its alternating, glossy, waxy green petiolate leaves frequently droop downward. The eucalyptus tree's blossoms are covered in many fluffy stamens that might be white, cream, yellow, pink, or red in color. An operculum, a cap made

of fused sepals, petals, or both, encloses these stamens. The operculum sheds when stamens expand, which is one of the genus Eucalyptus's distinguishing traits (23-25).

The age of the plant and the degree of furrowing determine the thickness, hardness, and color of the eucalyptus tree's bark. Older eucalyptus trees yearly lose a bark layer that adds to the diameter increase in the stem.

Chemical Composition

Eucalyptus globulus leaves include chemical compounds such as α-pinene, camphene, β-pinene, y-terpinene, cis-β-ocimene, fenchol 1, 7, 7-trimethylbicyclo hept-5-en-2ol, pinocarveol, 5, 5-dimethylene-3-hylenebicyclo heptan-2-one, 2, 6-dimethyl-1, 5, 7-octatrien-3-ol, isobornylformate, terpien-4-ol, α-terpineol, trans-carveol, 2-methylene-5-(1-methylethenyl), cyclohexanol, 3, 7-dimethyl-2, 6-octadien-1-ol, exo-2-hydroxycineole, geranyl acetate, isoledene, isopulegol acetate, α-terpineol acetate, α-gurjunene, (-)-cis-carvyl acetate, β-panasinsene, β-gurjunene, alloaromadendrene, aromadendrene, 2-phenylethyl isovalerate, eudesma-4(14), 11-diene, α-guaiene, (+)-ledene, cubenol, ledol, spathulenol, (-)-globulol, α-cadinol, Y-eudesmol, undetermined, α-eudesmol, β-eudesmol 3 (24-28).

Results and Discussion on Usefulness of Eucalyptus

Antioxidant

"Eucalyptus globulus stands out among the spectrum of tree species for having the highest antioxidant activity in its essential oil. The strongest antioxidants are found in fruits, next in immature flowers (30-32). Out of all the main constituents, γ-terpinene exhibits the strongest antioxidant capacity. Furthermore, the essential oil that is derived from the leaves of Eucalyptus globulus demonstrates notable antioxidant qualities. The two main derivative chemicals found in Eucalyptus globulus are globulusin A and eucaglobulin (33-38). They both show concentration-dependent DPPH free radical scavenging and have inhibitory action greater than ascorbic acid."

Anticancer

The abundance of bioactive chemicals in eucalyptus oil, including α-pinene, γ-terpinene, and terpinen-4-ol, is responsible for its anticancer activities. Studies show that terpinen-4-ol exhibits antitumor action by either causing caspase-dependent apoptosis in human melanoma cells or by specifically causing necrosis and cell-cycle arrest in melanoma cells. Terpinen-4-ol has been shown to suppress the growth of colorectal, pancreatic, gastric, and prostate malignancies in a dose-dependent way (0.005–0.1%) in studies conducted on human cell lines produced under tumor circumstances (40).

Additionally, studies on the cytotoxic potential of terpenes such as γ-terpinene, terpinen-4-ol, and α-pinene as well as essential oil derived from young and mature Eucalyptus benthamii leaves have yielded encouraging results. The essential oil extracted from young leaves shown more potent cytotoxic effects on Jurkat (T leukemia cells), J774A.1 (murine macrophage tumor), and HeLa (cervical cancer) cells when compared to α-pinene and γ-terpinene.

Young leaves may be cytotoxic because to changes in mitochondrial enzymatic activity, which can cause damage to the mitochondria and increase membrane permeability, which can ultimately

lead to cell death. Extracted from the leaves of Eucalyptus cladocalyx, cladocalol has also shown cytotoxic effects on the HL-60 myeloid leukemia cell line. Furthermore, cytotoxic effects of α-phellandrene isolated from various species of eucalyptus have been observed.

Antidiabetic

Anti-diabetic qualities are demonstrated by Eucalyptus globulus. It has been discovered that eucalyptus consumption at particular dosages or concentrations (62.5 g/kg in food and 2.5 g/litre in drinking water) lowers hyperglycemia (41). An aqueous eucalyptus extract was found to enhance 90% of the incorporation of glucose into glycogen, 60% of the glucose oxidation rate, and 50% of the glucose transport in an albino mouse experiment. Numerous further serological investigations have also suggested that regular consumption of eucalyptus at predetermined doses may help lessen the harm that streptozotocin causes to the pancreatic β-cells, which may make it a useful dietary supplement for diabetes.

Anti-inflammatory

Eucalyptus oil contains a variety of chemicals that have analgesic, antipyretic, and anti-inflammatory effects. One of the main ingredients in Eucalyptus globulus leaves, eucalyptol, functions as a potent cytokine inhibitor and helps treat bronchial asthma, respiratory tract infections, and other conditions that are susceptible to steroids. The ability of eucalyptol to inhibit the synthesis and production of interleukin-1beta (IL-1β), thromboxane B2, leukotriene B4, and tumor necrosis factor-alpha (TNF-α) in human blood monocytes suggests that it has the potential to be a powerful cytokine inhibitor for the long-term management of airway inflammation in bronchial asthma and other steroid-sensitive disorders.

Moreover, eucalyptol's anti-inflammatory properties have been evaluated in individuals with severe asthma, suggesting that it may find use both as an anti-inflammatory agent and as a novel medication to treat upper and lower respiratory conditions (42).

Antibacterial

Antimicrobial activity of Eucalyptus globulus has been observed against gram-positive (Staphylococcus aureus, Enterococcus faecium, and Listeria monocytogenes) and gram-negative (Salmonella enteritidis, Escherichia coli) microorganisms. Its antibacterial effect is caused by two compounds: para-isopropylphenol and α-terpineol. Eight phloroglucinol-sesquiterpene coupled components and three new compounds, called macrocarpals (H, I, and J), are extracted from eucalyptus leaves. These compounds have antibacterial effects against some oral pathogenic microbes.

Furthermore, Eucalyptus globulus leaf dried methanolic extract has shown antibacterial activity against S. aureus, E. coli, Pseudomonas aeruginosa, and Candida albicans. Six bacteria are also susceptible to the antibacterial properties of eucalyptus tereticornis essential oil: S. aureus, Bacillus cereus, E. coli, Micrococcus luteus, Proteus mirabilis, and Alcaligenes faecalis. The most sensitive to Eucalyptus globulus essential oil among the studied bacterial strains were found to be Haemophilus influenzae, Haemophilusparainfluenzae, and Stenotrophomonas maltophilia, followed by Streptococcus pneumoniae and Streptococcus agalactiae. The maximum activity for H. influenzae, H. parainfluenzae, and S. maltophilia was found at a concentration of

1.25 µl/ml. The range of 0.56 to 4.50 mg/ml is the minimum inhibitory concentration (MIC) for eucalyptus oil (42).

Antiviral and anti-fungal

Research evaluating antiviral efficacy revealed a moderate level of effectiveness against the mumps virus. The Eucalyptus globulus essential oil has demonstrated antiviral characteristics against both Herpes simplex virus (HSV) 1 and 2. Epstein-Barr virus activity was strongly inhibited by euglobal -G1, -G2, and -G3. The tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA) was able to significantly block the activation of Epstein-Barr virus (EBV) when Euglobal-G1 and G5, which were extracted from E. grandis leaves, were exposed to it. At 50%, 75%, and 100% concentrations, treating human facial demodicosis with recently made camphor oil (E. globulus) with or without glycerol dilutions produced a full cure. The antifungal effects of E. globulus leaf extracts and oil were demonstrated by a progressive inhibition of Malassezia furfur's growth on Sabouraud's dextrose agar medium.The essential oil that was extracted from E. globulus Labill showed antifungal activity against A. parasiticus and A. flavus. In the headspace volatile assay, 100% inhibitory concentration was reported at 1000 µL, and in the contact assay, it was at 1000 µL. At 200 µL of essential oil concentration, there was a partial suppression of aflatoxin B1 synthesis in the volatile assays. The range of 1.13 to 9 mg/ml is the minimum fungicidal concentration of eucalyptus oil (4).

Antiseptic

For centuries, people have used this plant as an antiseptic to treat respiratory tract infections, such as colds, the flu, sore throats, and chest infections caused by bronchitis or even pneumonia. Eucalyptus oil is recognized as one of the strongest antiseptics in its class, exhibiting strong disinfection qualities.

Antimalarial

It is well known that eucalyptus globulus is a frequently utilized antimalarial herb in Brazil. Plasmodium falciparum development was successfully inhibited by ethanol-water extracts when given intragastrically to mice at a dosage of 75 mg/ml, demonstrating antimalarial action.

Antihelminthic

Anti-helminthic qualities are exhibited by phytochemicals including safrole, borneol, cineol, linalool, geranyl acetate, and antheol. In tropical areas, hookworm infestations are treated with eucalyptus-chloroform solution. The essential oil of Eucalyptus globulus showed notable anti-helminthic efficacy at concentrations of 0.05, 0.1, and 0.15 ml/ml in an investigation on adult Indian earthworms (Pheretimaposthuma) (36).

Wound healing activity

Evan's blue-treated rabbits received an intradermal injection of 0.1 ml of essential oil produced from leaves, which increased the body's ability to repair wounds more quickly. During the observation time, this effect was seen to last for six hours.

Insecticidal property

The toxicity of eucalyptol against Pediculushumanus capitis, or human head lice, is demonstrated. It's also commonly used as an anti-feedant, especially for insects that bite. When used by humans

as insect repellents, eucalyptus-based products can shield users from biting insects for up to eight hours. However, the length of protection depends on the oil's dosage.

Food and medicinal uses

Since ancient times, eucalyptus has been used in both cooking and medicine. In many parts of India and South Africa, the leaves were frequently cooked to make tea, and the belief was that this would help with colds, sore throats, fever, flu, and even diabetes mellitus. Fresh eucalyptus leaves were also chewed to strengthen the gums in various parts of South Africa. The food sector has taken an interest in eucalyptus essential oils because of their potential as safe-for-consumption decontaminating agents(39).

Eucalyptus essential oil is used as a flavoring agent in a variety of products, usually at low quantities (0.002%), including baked goods, drinks, candies, and meat products. It's also utilized for food preservation, including beverages. Its usage in foods at concentrations of 5 mg/kg or less, as well as in candies and confectionary at concentrations of 15 mg/kg or less, has been approved by regulatory organizations such as the European Council. Not only can volatile oils and their ingredients improve flavor, but they also prolong shelf life by preventing microbiological growth in candies and soft drinks.

Chewing gum and candies containing eucalyptus oil can help strengthen gums, freshen breath, and lower oral bacteria counts. Research has demonstrated that incorporating eucalyptus essential oil into minced beef prolongs the shelf life of the meat and demonstrates antibacterial action against common infections such as S. aureus and E. coli. Furthermore, it has been noted that eucalyptus essential oil extends the shelf life of cheese, yogurt, pork, and fruit juices (40).

The application of eucalyptus essential oil in hurdle technology for food preservation has been popular in recent years. Tested against a variety of strains of yeast, varying doses of eucalyptus oil shown inhibitory effects on yeast growth. Furthermore, food-borne pathogens like Salmonella typhi, Shigella dysenteriae, Listeria monocytogenes, and Streptococcus pyogenes are all susceptible to the antibacterial properties of eucalyptus essential oil.

Essential oils, such as eucalyptus oil, are used as antimicrobial agents in food packaging systems because of their hydrophobic properties. These oils are hydrophobic due in part to the presence of monoterpenes, which repel water vapor inside the packaging and act as a barrier to preserve the food goods that are being stored.

Extraction Method

There are two types of essential oil extraction techniques: traditional techniques and cutting-edge techniques. The traditional process consists of solvent extraction, steam distillation, and hydrodistillation. The contemporary technique consists of three steps: hydrodistillation with microwave assistance, ultrasound assisted extraction, and supercritical fluid extraction (42).

Hydro-distillation

This procedure is an example of a conventional method for essential oil extraction. This method involves heating a solution of plant material and water, or occasionally additional solvents, to extract the essential oil. The essential oil vaporises due to the heat and is subsequently condensed back into a liquid state in a condenser. In a different chamber, the resultant liquid is then divided

into its constituent parts, usually water and essential oil.
This approach is comparatively simple to use and can be applied on a local or large scale. Because of the quick extraction procedure, it has the benefit of conserving the extract's chemical composition while reducing losses. It is energy-efficient as well.
For example, 15 grams of sample were distilled for 5 hours after being submerged in 300 milliliters of water to extract eucalyptus essential oil. While the oil extracted by Soxhlet extraction and Supercritical Fluid Extraction (SFE) had both volatile and heavier molecular weight components, the oil obtained through hydro-distillation contained only volatile chemicals. After hydro-distillation extraction, the output of eucalyptus oil rose from 3.1% after one hour to 3.8% after five hours (42).

Steam distillation

This is a common procedure used to extract compounds that are sensitive to temperature, like hydrocarbons, oils, and resins. Usually insoluble in water, these substances have the potential to dissolve at their boiling temperatures. This process works by separating a compound or combination of compounds at a temperature that is lower than the material being extracted (about 100°C at atmospheric pressure, or close to the boiling point of water). This enables volatile substances with boiling points ranging from 150 to 300°C to evaporate at water temperature.
The substance to be distilled is covered with water vapor instead of being submerged in water. Following their condensation in a condenser, the chemicals carried by the water vapor are divided into components that comprise water and essential oils. After the essential oil cools and condenses into a liquid, it is collected in a separator flask, which is a container that is placed underneath the condenser. The essential oil usually floats on top of the water when the water and essential oil in this flask separate.
This technique is frequently used to extract Eucalyptus globulus essential oils. The technique generally employs either fresh or dry leaves, producing essential oil that ranges from 1.0% to 2.4% of the fresh weight when using either type of leaf (30).

Solvent extraction

Solubility is a prerequisite for the liquid-to-liquid separation process known as solvent extraction. This method is widely used in many different industries, such as the manufacture of biodiesel, vegetable oil processing, and perfumes. It is especially useful for getting huge amounts of oils at a reasonable price and for removing essential oils from fragile or heat-sensitive plants.
The leaves of Eucalyptus globulus are cleaned and then allowed to air dry for four days, or until the average humidity level reaches approximately 9%. After that, they are sieved and ground to produce particles that are smaller than 0.5 mm, and then they are placed inside plastic bags that are sealed. Using aqueous ethanol as the solvent, the extraction is done in an orbital shaker with temperature control. A 100 ml Erlenmeyer flask containing two grams of leaf powder and a solid-to-liquid ratio of 1:20 g/mL is shaken at 120 rpm. The resultant extract is then vacuum-filtered via filter paper, and the resulting filtrate is analyzed. The obtained extraction yields varied between 24.4% and 33.1% (47).

Supercritical fluid extraction

Supercritical Fluid Extraction (SFE) is a separation technique in which a supercritical fluid is used as the solvent to extract a component from a matrix. Compounds are frequently extracted using this technique from liquid or solid matrices. The supercritical fluid that is typically employed is carbon dioxide (CO2), though it can also be adjusted by adding other solvents, such as methanol or ethanol. Higher yields, greater diffusion coefficients, less viscosity, and enhanced extract quality in terms of functional and biological activities are some benefits of using SFE as opposed to traditional approaches. But one disadvantage of SFE is that it can be expensive because of the equipment needed, and it can be difficult to manage or use.

The leaves of Eucalyptus globulus are extracted by air-drying them for two days and then oven-drying them for five hours at 103°C. The dried samples are next sieved using a sieve shaker and pulverized with a knife grinder. Glass wool is inserted at both ends of the SC CO2 extraction vessel to stop substrate access, and five grams of eucalyptus leaves are weighed and added to the tank. After the proper pressure and temperature have been reached, SFE is started, and the gas CO2 flow rate is always set at 2 L/min.

In order to reduce the amount of volatile compounds lost as a result of CO2 sublimation, the extracted material is collected in an amber bottle and placed in an ice bath for dynamic extraction. Any deposits in the pipes are cleaned with ethanol and mixed with the extracted material that has been collected in the bottle. Next, rotary evaporation is applied to the mixture, and the extract is weighed. As temperature and pressure rise, the resulting oil yield rises as well, reaching 2.99% to 3.39% at 50°C and 2.51% to 4.66% at 70°C. In comparison to hydrodistillation, solvent extraction, and ultrasonic-assisted extraction methods, the extraction of E. globulus employing this approach at a pressure of 350 bar, temperature of 80°C, and CO2 flow rate of 12 g/min provided the highest percentage (3.6%) (28).

Microwave-assisted hydro-distillation

The term "microwave-assisted hydro-distillation" describes the hydro-distillation procedure carried out with a microwave oven's help. It has been demonstrated that this novel technique dramatically cuts down on the amount of solvent needed as well as the extraction time. In addition, compared to conventional methods, it uses less energy and produces less CO2 into the atmosphere, minimizing its negative effects on the environment. Furthermore, it has been discovered that Microwave-Assisted Hydro-distillation improves the extracted essential oil's quality.

The ratio of raw materials to water in this process of extracting essential oil from Eucalyptus globulus leaves is kept at 1:3 mL/g. Usually, the extraction procedure requires 60 minutes and 450W of microwave power. With these specifications, an essential oil yield of 2.65 mg/L (ground material) is achieved, with eucalyptol making up about 38.771% of the oil as its main component (40).

Ultrasound-assisted extraction

One method that is well-known for its effectiveness in extracting valuable compounds is ultrasound-assisted extraction. For the purpose of extracting essential oils, this process is most beneficial when used on flowers, leaves, or seeds. When compared to other procedures, ultrasound-assisted extraction delivers higher yields in a shorter amount of time, despite its relatively

expensive cost.
Studies have indicated that the yields of Eucalyptus globulus leaves extracted with ultrasonic assistance are 2.2% higher than the yields obtained with hydro-distillation and extraction procedure A. Organic acids, esters, and aliphatic saturated hydrocarbons are among the significant chemicals that can be extracted with this technique (19).

Limitations

There are certain drawbacks to eucalyptus in addition to its many positive attributes. Consuming eucalyptus oil is normally only safe at low quantities, usually between 0.05 and 0.2 milliliters per day. Increased dosages may cause side effects include nausea, headaches, diarrhea, and stomach pain. Consuming more than 3.5 milliliters of eucalyptus essential oil daily has the potential to be lethal.
Irritation may result when directly applying undiluted eucalyptus essential oil to the skin. As a result, it is best to use diluted eucalyptus oil, ideally at concentrations lower than 3.5 ml. Considering these possible dangers, it's crucial to keep eucalyptus oil out of children's reach to avoid overuse or inadvertent consumption.

Conclusions

Eucalyptus trees of various varieties are grown in many parts of the world. This tree is rich in phytochemicals in every part of it, and the essential oils that are produced from its leaves and fruits have unique fragrances and a host of health benefits, such as antioxidant, antifungal, anticancer, antidiabetic, and antibacterial qualities. Interestingly, eucalyptus essential oil has a higher antioxidant activity than ascorbic acid.
Eucalyptus oil is used in the food business to make antimicrobial packaging, candies, and chewing gum. It is also used in aromatherapy as a stress reliever and cold and cough treatment. But when it comes to food applications, it's important to keep the essential oil quantities modest because large concentrations might have negative consequences like nausea and diarrhoea. Despite the paucity of study on eucalyptus's culinary uses, there is a rising need to investigate this plant's potential for improving flavor and lengthening the shelf life of several food categories.

Conflict of interest

The authors report no conflicts of interest.

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