



REVIEW ARTICLE

Bioactive molecular properties and technological applications of clove essential oil

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Abstract

Clove essential oil, extracted from *Syzygium aromaticum* flower buds, has garnered attention owing to its diverse bioactive properties and applications across industries. This review explores the chemical composition, biological activities and technological applications of this plant. The major bioactive compounds of the oil, including eugenol, eugenyl acetate, β -caryophyllene and α -humulene, contribute to its potent antioxidant, antimicrobial, anti-inflammatory and analgesic properties. These bioactivities have been extensively studied using *in vitro* and *in vivo* models, showcasing the oil's potential as a natural alternative to synthetic compounds. Clove essential oil is used in the food, pharmaceutical, cosmetic and agricultural industries as a natural preservative, flavor enhancer, antimicrobial agent and biopesticide. Its incorporation into drug delivery systems, such as nanoemulsions and nanoparticles, has shown promise for enhancing stability, bioavailability and efficacy. However, challenges in large-scale production, standardization of extraction methods, stability issues and environmental concerns need to be addressed. This review also discusses the toxicological profile and regulatory aspects of this oil, emphasizing safety and quality control. Future research directions include exploring the synergistic effects of other natural compounds, developing personalized medicine applications and optimizing sustainable production practices. The global market for clove essential oil is influenced by trends in the spice industry and the demand for organic products. Its cost-effectiveness compared to synthetic alternatives and potential for developing value-added products present significant economic opportunities.

Keywords

antimicrobial; biopesticide; clove essential oil; eugenol; food industry; pharmaceutical applications

Introduction

Clove essential oil, extracted from the dried flower buds of the clove tree (*Syzygium aromaticum* L.), is renowned for its high eugenol content, which constitutes a substantial portion of its chemical composition (1–3). Historically, this essential oil has been used in traditional medicine across diverse cultures because of its therapeutic properties. In herbal medicine, it has been applied topically to mitigate pain and promote healing and is also employed in the fragrance and flavoring industries (4).

The utilization of clove oil can be traced back to antiquity, where it was esteemed for its aromatic qualities and employed in both perfumery and food preservation (2).

Furthermore, its antibacterial, antifungal and antioxidant properties have been extensively documented, highlighting its traditional use in treating oral infections and other microbe-related health issues (5,6).

In contemporary contexts, clove essential oil is of considerable significance across various industries. Within the health and pharmaceutical sectors, its antimicrobial, anti-inflammatory, analgesic, anesthetic, antinociceptive and anticancer properties render it valuable for the development of therapeutic products (1,7,8). Additionally, the antioxidant properties of these oils contribute to food preservation and safety, facilitating their application in the food industry (9).

Moreover, in the cosmetics and fragrance sectors, clove oil is utilized for its aromatic qualities and role in flavoring formulations (2). Its application as an insecticidal agent underscores its versatility, offering eco-friendly alternatives to synthetic chemicals for pest management (10). Furthermore, the potential of clove oil in veterinary contexts, particularly in combating ectoparasites in cattle, underscores its significance in agricultural practice (11).

The comprehensive chemical composition, historical applications and extensive industrial significance of clove essential oil continue to affirm its enduring value across various

fields. While its traditional uses have established a foundational basis, contemporary research and applications are progressively expanding its utilization in innovative and sustainable ways.

This review explores the diverse applications and significance of clove essential oil across various sectors, including health, pharmaceuticals, food, cosmetics, agriculture and pest control. This review examines the historical uses, chemical composition and therapeutic properties of clove oil, emphasizing its enduring value and potential for innovative applications in contemporary contexts.

Chemical composition of clove essential oil

Clove essential oil, extracted from *Syzygium aromaticum*, comprises several bioactive compounds with diverse applications (Table 1). Eugenol is the predominant compound, accounting for at least 50 % of the oil. Eugenol is well-known for its antimicrobial, antioxidant and anti-inflammatory properties, rendering it a crucial component of various medicinal and cosmetic products (2).

Clove essential oil contains several notable compounds (Fig. 1), including eugenyl acetate, β -caryophyllene and α -humulene. These constituents enhance the therapeutic potential of the oil, with β -caryophyllene recognized for its anti-inflammatory properties and α -humulene for its potential anticancer effects (12).

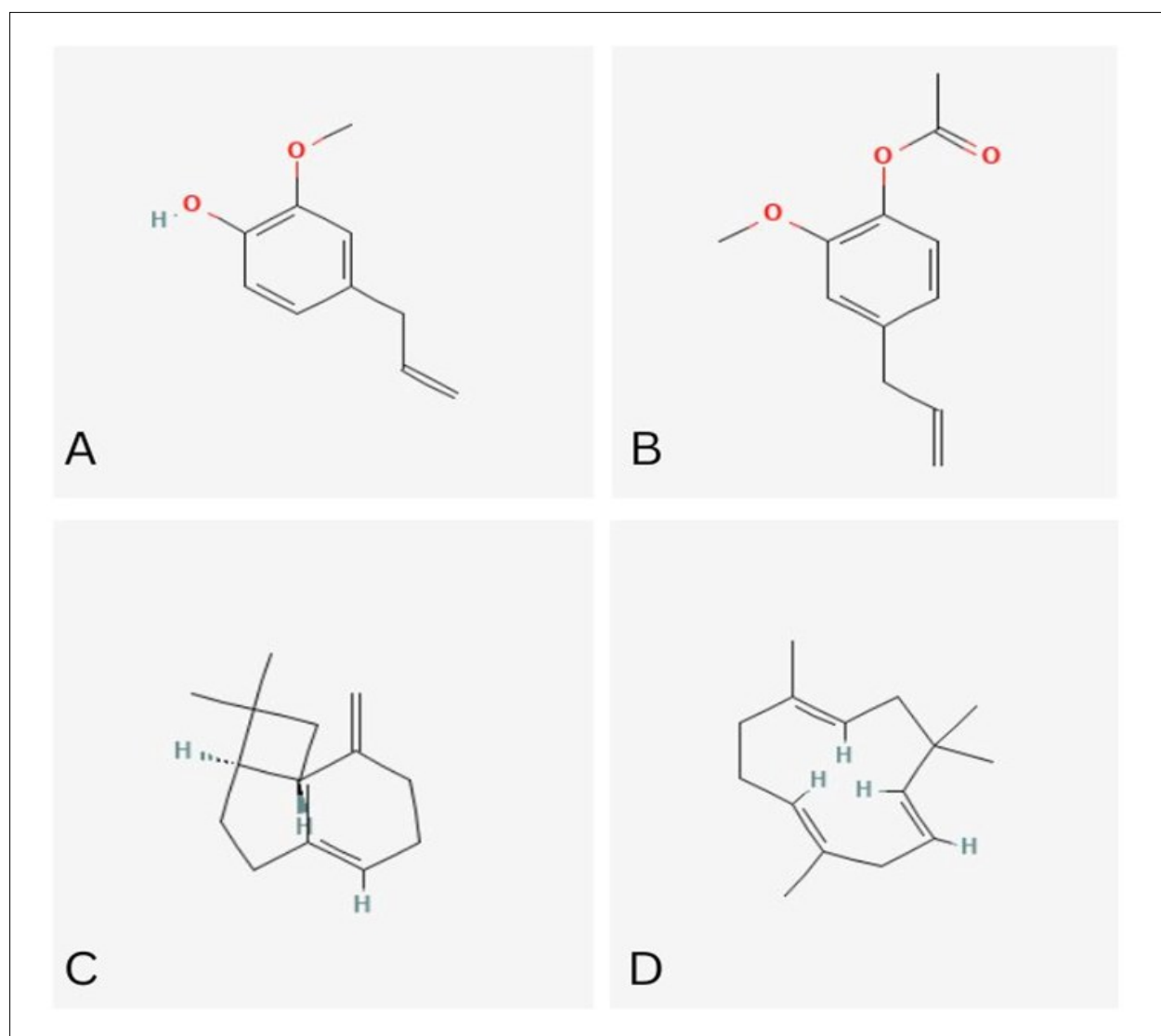


Fig. 1. Chemical structures of major bioactive compounds present in clove (*Syzygium aromaticum*) essential oil. (A) Eugenol; (B) Eugenyl acetate; (C) β -caryophyllene; (D) α -humulene

Clove essential oil is recognized for its phenolic content, which confers significant antioxidant activity. This characteristic is beneficial in food preservation and pharmaceutical applications, as it aids in protecting against oxidative stress and prolonging the shelf life of products (1,13). In summary, the bioactive components of clove essential oil highlight its historical applications in traditional medicine and offer potential for contemporary uses in health, food and pharmaceuticals because of their potent biological activities.

Table 1. Major bioactive compounds that are present in clove essential oil

Compound name	Bioactivity
Eugenol	The primary constituent of clove oil, recognized for its analgesic, anesthetic and antimicrobial properties, comprises at least 50 % of the oil (2,12).
Eugenyl acetate	A phenolic compound that contributes to the fragrance and antimicrobial activity of the oil (12,14).
β-caryophyllene	A sesquiterpene known for its anti-inflammatory and potential anticancer activities. It enhances the oil's insecticidal and antifungal effects (2,14).
α-humulene	Another sesquiterpene contributing to the anti-inflammatory and anticancer potential of the oil is α -copaene (2,14).

The antimicrobial, antioxidant and anti-inflammatory properties of these compounds are essential for the varied applications of clove essential oil in the cosmetics, food and pharmaceutical industries.

Factors affecting the chemical composition

The chemical composition of clove essential oil varies owing to several factors, including the extraction methods, geographical origin and environmental conditions. The predominant constituent of clove essential oil is eugenol, which typically accounts for 80 % or more of the oil's composition, as documented in studies of clove oil from various regions (2,3).

Extraction methods

Various extraction techniques are pivotal in determining the concentrations of primary volatile compounds in clove oil. Methods such as hydro-distillation, steam distillation and ultrasound-assisted extraction yield different levels of key components, including eugenol and eugenyl acetate. Each technique has distinct advantages and limitations that influence the final composition of the extracted oil. For instance, steam distillation has been shown to produce a high percentage of eugenol in certain studies (1,2). Selection of an extraction method can substantially impact the quality and chemical profile of clove oil. Variables such as temperature, pressure and extraction duration can affect the yield and composition of volatile compounds. Furthermore, novel extraction techniques, such as supercritical fluid extraction and Microwave-Assisted Extraction (MAE), are being investigated to enhance the efficiency and selectivity of isolating desired compounds. Understanding the influence of different extraction methods on the concentration of volatile compounds is crucial for optimizing the production of high-quality clove oil for diverse applications in the food, pharmaceutical and cosmetic industries.

Geographical and environmental factors

The composition can also vary based on the location of clove

cultivation. The clove essential oil obtained from Turkey had a composition comparable to that of cloves from their native regions, indicating that clove plants tend to maintain their chemical profiles despite different growing conditions (3).

Plant parts used and cultivation conditions

The specific parts of the plant used (e.g., buds, stems and leaves) can result in differences in oil composition. The environmental conditions during cultivation, such as temperature and humidity, also play a role in the nutritional uptake by the plant, thereby affecting the chemical composition of the essential oil.

Chemical interactions and bioactivities

The prevalent presence of eugenol in clove essential oil contributes to various bioactive properties, including antimicrobial and antioxidant activities. This compound, along with others such as **β -caryophyllene**, contributes to the efficacy and application of oils in various industries (7,15).

Methods of extraction and analysis

Clove essential oil is extracted using various methods, each of which influences the oil's composition and biological activities. The two primary extraction techniques are hydro-distillation and supercritical CO₂ extraction. Hydro-distillation typically utilizes a Clevenger apparatus to isolate essential oils rich in eugenol and other compounds, such as carvacrol and thymol (1,16). This traditional method establishes a baseline composition for analyzing the chemical and biological properties of oils.

The supercritical CO₂ extraction method is a contemporary technique that achieves a higher concentration of essential oils while preserving a greater proportion of the oil's volatile compounds, thereby enhancing its antimicrobial and antioxidant properties (17). This method has demonstrated superior extraction yields and enhanced antimicrobial activities compared to hydro-distillation (18). Furthermore, supercritical extraction is more effective in maintaining the sensitivity and efficacy of active compounds against various pathogens, providing a distinct advantage in biological applications, such as antibacterial and antioxidant activities (17).

Gas Chromatography-Mass Spectrometry (GC-MS) is commonly used to identify and quantify the constituents of clove essential oil. This analytical technique has consistently demonstrated that eugenol is the predominant compound, which significantly contributes to the antioxidant and antimicrobial properties of the oil (14,16). Furthermore, Raman spectroscopy has been applied to detect adulteration in clove oil, enabling the identification of pure oil and potential additives such as benzyl alcohol or vegetable oils through spectral analysis (19).

The selected extraction method significantly impacts not only the yield but also the concentration of essential compounds, thereby influencing the oil's applicability in the fields of health and wellness, food, cosmetics and pharmaceuticals. Ongoing advancements in extraction and analytical technologies continue to enhance the usability and efficacy of clove essential oil, while preserving its natural properties (20).

Bioactive molecular properties of clove essential oil

Antioxidant properties

Clove Essential Oil (CEO), extracted from the buds of *Syzygium aromaticum*, demonstrates significant antioxidant properties,

primarily due to its predominant component eugenol (21). The antioxidant potential of this essential oil has been thoroughly investigated in both *in vitro* and *in vivo* studies.

Mechanisms of antioxidant action

CEO functions as an antioxidant by scavenging free radicals, such as DPPH and by inhibiting oxidative processes, including lipid peroxidation. The phenolic compounds present in clove oil, particularly eugenol, are integral to its radical-scavenging capability (22). Furthermore, eugenol and other phenolic compounds contribute to the reduction of oxidative stress by upregulating *in vivo* antioxidants such as superoxide dismutase (SOD), glutathione (GSH) and catalase (CAT) (23).

In vitro and *in vivo* studies

In vitro analyses have demonstrated that clove oil exhibits potent radical scavenging activities, achieving an IC₅₀ of 0.2 µg/mL compared to synthetic antioxidants such as tert-butylated hydroxytoluene, which have an IC₅₀ of 11.5 µg/mL (22). Another study highlighted its significant antioxidant potential, with a DPPH IC₅₀ value of 4.82×10^{-2} µg/mL and a reducing power EC₅₀ value of 3.47×10^{-2} µg/mL (21). *In vivo*, a polyphenol-rich extract from clove buds demonstrated substantial antioxidant and anti-inflammatory activities by enhancing antioxidant enzyme activities while inhibiting oxidative stress and inflammation in animal models (23).

Comparison with other natural antioxidants

CEO has been favorably compared with other natural antioxidants, such as cinnamon and thyme oils. Research has indicated that the antioxidant properties of eugenol, the principal constituent of clove oil, are positively associated with the inhibition of lipid oxidation and reduction of oxidative stress in biological systems (24). It has been proposed that clove oil exhibits superior antioxidant activity compared to the other oils examined, which is attributable to its high eugenol content (24). Moreover, a synergistic combination of clove and cinnamon oils has demonstrated enhanced antioxidant efficacy compared to their individual use, potentially offering more effective protective mechanisms against oxidative damage when employed as natural preservatives in food and pharmaceutical applications (25).

Antimicrobial properties

CEO exhibits substantial antimicrobial properties, including antibacterial, antifungal and antiviral activities, making it a promising candidate for developing novel antimicrobial agents.

Antibacterial activity

CEO exhibits significant antibacterial activity against a range of food spoilage bacteria, pathogens and antibiotic-resistant microorganisms, including Methicillin-Resistant *Staphylococcus aureus* (MRSA). The oil is effective against bacteria such as *Bacillus subtilis*, *Pseudomonas fluorescens*, *Staphylococcus aureus* and *Vibrio parahaemolyticus* (26). These robust antibacterial properties are primarily attributed to the main active compounds present in the oil, such as eugenol, which penetrates bacterial cells and disrupts their cellular functions.

Antifungal activity

In addition to its antibacterial properties, CEO exhibits potent antifungal effects. It is effective against pathogenic fungi, such as *Aspergillus flavus* and demonstrates antifungal activity against various fungal strains, underscoring its utility in inhibiting the

growth of fungi, such as *Candida* spp. and *Aspergillus niger* (27,28). The essential oil exerts antifungal effects by altering the permeability of fungal cell membranes, thereby interfering with cellular enzyme systems.

Antiviral potential

The antiviral properties of CEO, along with those of other essential oils, have been extensively investigated, demonstrating its capacity to inhibit viral replication across various host cell lines. The oil and its constituents exhibit significant antiviral effects by disrupting multiple stages of viral infection and replication, including viral entry, adsorption and replication within the host cells (29). These mechanisms typically involve binding to viral envelope proteins, thereby preventing the virus from attaching to the host cells.

CEO demonstrates a broad range of antimicrobial properties, which are essential for addressing resistant strains of bacteria, fungi and viruses. These properties offer a promising foundation for further development into therapeutic and preventive applications in both the medical and food industries.

Anti-inflammatory properties

CEO exhibits significant anti-inflammatory properties, primarily due to its principal component, eugenol. The molecular mechanisms responsible for its anti-inflammatory effects involve the suppression of cytokine production and modulation of signaling pathways. *In vitro* studies have indicated that clove oil and eugenol at specific noncytotoxic concentrations can inhibit the production of pro-inflammatory cytokines, such as IL-1β, IL-6 and IL-10, by murine macrophages. This inhibitory effect occurs either prior to or following lipopolysaccharide (LPS) stimulation, suggesting both preventive and therapeutic potential for modulating immune responses (30).

The anti-inflammatory properties of CEO have been investigated using both *in vitro* and *in vivo* models. *In vivo* experiments, such as the paw edema test, it revealed that CEO nanogels exhibited significant anti-inflammatory and antinociceptive effects. These results suggest potential applications in treating conditions characterized by inflammation and pain (31). Furthermore, studies have demonstrated that clove oil can effectively inhibit biofilm formation in resistant strains of *Helicobacter pylori*, thereby enhancing its role in managing inflammation-related disorders (32).

The potential applications of clove essential oil in treating inflammatory disorders are promising. Notably, its integration into controlled release nanoparticulate systems, such as nano-emulsions and nanofibers, has been developed to enhance anti-inflammatory properties. These formulations have demonstrated significant efficacy in addressing induced skin inflammation in animal models, suggesting their potential as alternatives to nonsteroidal anti-inflammatory drugs, which are often associated with adverse effects (33).

The anti-inflammatory properties of CEO, substantiated by both molecular and applied research, underscore its potential as a natural therapeutic agent for treating inflammatory conditions. The integration of *in vitro* evidence, such as cytokine inhibition, with *in vivo* studies demonstrating effective resolution of inflammation supports its therapeutic promise in various inflammatory disorders (30,31).

Analgesic properties

CEO, extracted from the dried flower buds of *Eugenia caryophyllata*, exhibits notable analgesic properties through various mechanisms in diverse experimental models. The oil is primarily composed of phenylpropanoids, such as eugenol, which are associated with a broad spectrum of biological activities, including analgesic effects (14).

Mechanisms of pain relief

CEO exerts analgesic effects, predominantly through the activity of eugenol, its principal component. In experimental models, the systemic administration of CEO has demonstrated antinociceptive effects on acute pain, such as corneal and formalin-induced pain, primarily through its interactions with opioid and cholinergic receptors. The analgesic action of the oil was comparable to that of morphine, underscoring its potential as a natural alternative for pain management (34,35).

Studies on acute and chronic pain models

Topical and systemic applications of CEO have been investigated across various pain models. In acute experimental contexts, such as the formalin test, nano-emulsion formulations of clove oil exhibit significant anti-nociceptive properties, effectively mitigating both inflammation and pain perception. These findings indicate that clove oil nano-emulsions may be effective in managing both acute and chronic pain (31). Additionally, clove oil has been shown to substantially diminish pain perception in mice, yielding a pronounced analgesic effect in acetic acid-induced writhing and hot plate assays (35).

Comparison with conventional analgesics

In pain management, CEO exhibited efficacy comparable to that of conventional analgesics in certain experimental contexts. In the hot plate test, clove oil significantly increased pain reaction latency, like the effects of morphine. Furthermore, in anti-inflammatory models, clove oil demonstrated effects similar to those of aspirin and indomethacin, effectively reducing edema and inflammatory responses (35). This positions clove oil as a viable alternative or complementary intervention to synthetic analgesics in pain therapy.

The dual action of CEO on nociception and inflammation, particularly due to its eugenol content, highlights its potential as a natural analgesic in both acute and chronic pain.

Other bioactive properties

CEO, primarily composed of eugenol, exhibits several significant bioactive properties, including anticancer, antiparasitic and insecticidal effects.

Anticancer potential

Eugenol, the principal constituent of CEO, has been associated with a range of pharmacological properties, notably its significant anticancer effects. Research has demonstrated that eugenol can exert effects on various cancer cell lines by inhibiting cell proliferation and modulating several signaling pathways that are essential for cancer progression. Its simple chemical structure, characterized by active sites in the hydroxyl, allylic and aromatic groups, makes eugenol a promising compound for the development of novel anticancer agents (36).

Antiparasitic activities

CEO exhibits significant antiparasitic properties and has been employed in the treatment of various parasitic infections, including those caused by *Leishmania* species. The antiparasitic efficacy of essential oils is crucial for developing novel therapeutic agents, especially considering the increasing resistance to conventional antiparasitic medications (37).

Insecticidal properties

The use of essential oils, such as those extracted from cloves, as insecticides presents an environmentally sustainable alternative to synthetic pesticides. These oils demonstrate considerable insecticidal efficacy against a range of pests owing to their neurotoxic properties, including the modification of octopamine receptors and inhibition of acetylcholine esterase activity in insects. The natural compounds present in these oils can disrupt the physiological functions of pests, thereby mitigating pest-related damage (38).

The bioactive properties of CEO highlight its potential in therapeutic and pest management applications, presenting a natural alternative that reduces reliance on synthetic chemicals.

Technological applications of CEO

Food industry applications

CEO has garnered significant attention in the food industry owing to its diverse applications, including its function as a natural preservative, flavor enhancer and ingredient in the formulation of functional foods.

Use as a natural preservative

CEO exhibits notable antimicrobial and antifungal properties, rendering it a viable natural substitute for synthetic preservatives in the food industry. Its primary component, eugenol, effectively inhibits various foodborne pathogens by diminishing their migration, adhesion and biofilm formation (39,40). This antimicrobial efficacy is advantageous for prolonging the shelf life of food products, thereby ensuring safety and quality without the negative health implications associated with the use of synthetic additives (2).

Flavor enhancement in food products

CEO is extensively employed for its aromatic properties, which are attributed to its high concentration of volatile compounds, such as eugenol and β -caryophyllene. These compounds are responsible for the rich and distinct flavor of olive oil, which is widely used to enhance the flavor of food products and beverages (1,14). The robust taste and aroma of essential oils make them desirable for augmenting the sensory properties of food, providing a natural and appealing flavor profile that complements various culinary creations.

Development of functional foods

The bioactive compounds present in CEO play a significant role in formulating functional foods that offer health benefits beyond basic nutrition. Eugenol, along with other phytochemicals found in clove oil, demonstrates antioxidant, anti-inflammatory and anticancer properties, rendering them valuable for the development of foods that promote health and well-being (1,12). Furthermore, the encapsulation of CEO has been investigated to enhance its stability and augment its functional properties in food applications, thereby ensuring its effectiveness in delivering health benefits (41).

These diverse applications highlight the potential of CEO to address consumer demands for natural, safe and health-promoting food products in the modern market.

Pharmaceutical applications

CEO, extracted from *Syzygium aromaticum*, has attracted considerable interest in the pharmaceutical industry because of its bioactive constituents, notably eugenol. These compounds exhibit antioxidative, antimicrobial and antifungal properties, rendering them valuable for drug formulation (1,22).

In drug delivery, CEO has been successfully integrated into micro- and nano-emulsions to enhance its therapeutic potential. These delivery systems improve the solubility of hydrophobic components, thereby increasing the bioavailability and biological activity of the essential oils. Research has shown that CEO-based nano-emulsions exhibit superior antimicrobial and antioxidant activities compared to free CEO, attributed to the increased surface area and stability of nanodroplets (42,43). Furthermore, essential oil microemulsions have demonstrated enhanced penetration capabilities, primarily because of their terpenic constituents, which protect volatile essential oil components from degradation (44).

Moreover, CEO has potential for the development of both topical and oral pharmaceutical formulations. When encapsulated within suitable carriers, such as hydroxypropyl beta-cyclodextrin, CEO can exhibit controlled and sustained release properties, potentially enhancing its therapeutic efficacy over an extended period (45). This encapsulation technique also improves the stability and bioactivity of the oil, confirming its applicability in pharmaceutical contexts (45).

Recent investigations have examined the potential of CEO as a novel therapeutic agent. For example, research assessing its anticancer properties has demonstrated that nano-emulsions of CEO exhibit greater cytotoxic activity against certain cancer cell lines than free clove EO (41,46). Additionally, the potent antimicrobial properties of the oil render it an effective natural alternative for treating infections caused by both Gram-positive and Gram-negative bacteria, as well as yeast (5).

CEO has considerable potential for the development of novel therapeutic agents for various pharmaceutical applications. This potential is facilitated by diverse drug delivery systems, formulation strategies and the oil's intrinsic bioactive properties.

Cosmetic and personal care applications with CEO

CEO has extensive applications in the cosmetic and personal care industries because of its rich composition of bioactive compounds, including eugenol, β -caryophyllene and α -humulene. These compounds confer a wide array of beneficial properties, rendering CEO a valuable ingredient in skin care, oral care and aromatherapy products.

Use in skincare products

CEO is widely recognized for its antimicrobial and antioxidant properties, which are particularly advantageous in skin care formulations. Its capacity to inhibit microbial activity renders it an effective component for addressing skin conditions that are susceptible to bacterial infections, such as acne. Furthermore, the antioxidant properties of clove oil protect the skin from oxidative stress, thereby enhancing skin health and potentially mitigating premature aging (1,2). Nevertheless, caution is warranted in its

application because of its potential cytotoxicity at elevated concentrations, which can pose risks to skin cells, including fibroblasts and endothelial cells (4). Therefore, its incorporation into skincare products must be meticulously formulated and balanced to optimize its benefits while minimizing the adverse effects.

Applications in oral care formulations

CEO is extensively used in oral care because of its antiseptic properties. It is effective against both Gram-positive and Gram-negative bacteria, making it a preferred option for natural remedies for oral infections (5). Additionally, its analgesic properties enhance its use in products intended for pain relief during dental procedures. Furthermore, clove oil is frequently incorporated into products such as toothpaste and mouthwash, where it aids in microbial control and imparts a refreshing aroma that augments oral hygiene.

Development of aromatherapy products

Aromatherapy represents another domain in which CEO is extensively utilized, primarily because of its soothing and calming properties. The distinctive warm aroma of clove oil is frequently incorporated into scent blends to facilitate relaxation and alleviate stress. Within the context of aromatherapy, CEO is esteemed for its potential analgesic and anti-inflammatory properties, which may assist in the management of chronic pain and inflammation when used in diffusers or for topical applications (19). In summary, the applications of CEO in cosmetics, oral care and aromatherapy underscore its versatility, reflecting a combination of biological activities that are beneficial to human health. Nevertheless, appropriate formulation and dosage are essential to optimize efficacy while minimizing potential adverse effects.

Agricultural applications

This substance exhibits considerable potential for diverse agricultural applications owing to its rich composition of bioactive compounds, including eugenol, eugenyl acetate and β -caryophyllene. Its extensive utility is ascribed to its antimicrobial, antifungal, antioxidant, insecticidal and plant growth-promoting activities.

Biopesticide formulations

CEO is valued for its insecticidal properties, making it a valuable component in biopesticide formulations. Empirical studies have demonstrated its efficacy against a range of agricultural pests, notably *Callosobruchus maculatus*, a prevalent pest that affects stored beans. Exposure to CEO results in reduced oviposition and impaired population growth in these pests, positioning CEO as a promising natural alternative to synthetic pesticides (47). Furthermore, CEO has been shown to exhibit insecticidal activities comparable to those of synthetic insecticides, such as deltamethrin, thereby offering an environmentally friendly solution for pest management (47).

Postharvest preservation

Clove oil exhibits substantial antifungal properties against pathogens that cause spoilage of stored crops, thereby playing a crucial role in post-harvest preservation. Its integration into edible coatings and active packaging materials, such as those utilized for bananas, enhances shelf life and mitigates post-harvest losses by inhibiting the growth of pathogenic fungi. When incorporated into starch-based films, CEO forms a protective barrier against fungal infections, thus prolonging the freshness and edibility of fruits and

vegetables. The combination of consumer acceptability and efficacy renders CEO a promising candidate for post-harvest management strategies (48).

Soil fumigation and plant growth promotion

The application of CEO in soil fumigation plays a significant role in managing soil-borne pathogens because of its potent antimicrobial properties. Although specific studies directly associating CEO with soil fumigation are limited, its broad-spectrum antimicrobial efficacy against various bacterial and fungal pathogens indicates potential applications in enhancing soil health and promoting plant growth by reducing pathogen loads (5). Additionally, the antioxidant properties of CEO may improve soil quality, thereby fostering healthier plant growth (5).

CEO has numerous advantages in agricultural applications, functioning as a natural biopesticide, prolonging the shelf life of harvested crops and potentially enhancing soil and plant health through its antimicrobial and antioxidant properties. The incorporation of AI into agricultural systems can reduce dependence on synthetic chemicals and promote sustainable and environmentally friendly farming practices. The increasing interest in natural compounds, driven by consumer demand for healthier and eco-friendly pest management solutions, further highlights the significance of clove oil in modern agriculture (2,14).

Industrial applications

CEO has diverse industrial applications owing to its antimicrobial, antioxidant and functional properties. Its utility extends across various sectors, including packaging, cleaning products and biofuel production.

Packaging applications

CEO is extensively acknowledged for its application in food packaging materials because of its significant antimicrobial and antioxidant properties. The integration of clove oil into packaging films has been demonstrated to effectively reduce microbial proliferation, extends the shelf life of food products and enhances food safety and quality. For example, when incorporated into chitosan emulsions and films, CEO functions as a natural preservative, inhibiting spoilage pathogens such as *Fusarium graminearum* and *Escherichia coli* without the need for synthetic additives (49). Nanoclay-soy protein films augmented with clove oil exhibit notable enhancements in tensile strength and active release properties, rendering them suitable for active food packaging applications (13). Moreover, clove oil has been shown to improve the mechanical properties and antimicrobial efficacy of cellulose-based films used in packaging, highlighting its potential as a bioactive agent for sustainable packaging solutions (50).

Cleaning and disinfection products

Owing to its potent antimicrobial properties, CEO is used in cleaning and disinfection products, demonstrating efficacy against both Gram-positive and Gram-negative bacteria (42). Various studies have shown that nano-emulsions exhibit enhanced antimicrobial effectiveness, achieving more rapid microbial inhibition than free essential oil forms, thereby making them ideal for incorporation into surface cleaners and sanitizers (41). Beyond its bactericidal activity, clove oil contributes significant aromatic qualities, enhancing consumer products by combining efficacy with pleasant sensory experiences.

Potential in biofuel production

Although the utilization of CEO in biofuel production is not as extensively documented as its applications in packaging and antimicrobial contexts, its high eugenol content and versatile chemical structure suggest potential utility in this domain. The chemical constituents of clove oil may serve as substrates or chemical precursors in advanced biofuel production. Although specific studies on the direct application of clove oil in biofuel production are lacking, the interest in its antibacterial and antioxidant properties indicates its potential for future exploration in this field, reflecting broader trends in the utilization of bio-based materials (51).

In conclusion, the diverse properties of CEO highlight its increasing significance across various industrial sectors, focusing on enhancing sustainability, safety and functionality.

Safety and regulatory aspects

Toxicological studies

Numerous studies have examined the safety and regulatory considerations of CEO, particularly its toxicological profile, encompassing acute and chronic toxicities, genotoxicity and allergenicity.

Acute and chronic toxicity

Numerous studies have investigated the toxic effects of CEO. Acute toxicity evaluations have demonstrated substantial toxicity against specific organisms. For example, assessments involving *Artemia salina* have determined a lethal concentration (LC50) of 0.5993 µg/mL, indicating significant toxicity at elevated doses (52). Conversely, in mammalian models, a study observed no signs of toxicity or mortality at an oral dose of 1000 mg/kg in rats over 90-day period, suggesting a relatively safe profile at certain dosages (53).

Genotoxicity and mutagenicity

Studies have evaluated the genotoxic potential of the constituents of CEO. For instance, a formulation incorporating essential oils exhibited no mutagenic effects across various mutagenicity assays, including bacterial reverse mutation tests (Ames test) and mammalian erythrocyte micronucleus assays. These findings suggest that CEO and analogous formulations may not pose genotoxic risks when used appropriately (53).

Allergenicity and sensitization potential

The allergenic potential of CEO is well documented, as eugenol, its primary constituent, is a recognized allergen capable of eliciting reactions in susceptible individuals. While acute studies in mammals have demonstrated no adverse effects under controlled conditions, the possibility of allergenic responses in humans necessitates caution, particularly for products intended for dermal application (54).

The findings indicate that while CEO presents certain toxicological risks, its safety profile is generally deemed acceptable under specific conditions and at specific dosages. However, further research, particularly involving human subjects, is essential to thoroughly understand its allergenic potential and ensure its safe application.

Regulatory status and guidelines

The regulatory status and guidelines for CEO, particularly focusing on FDA regulations, European Union (EU) regulations, EFSA opinions and international standards for quality control, involve several aspects.

FDA regulations on CEO use

In the United States, the regulation of essential oils falls under the jurisdiction of the Food and Drug Administration (FDA) in accordance with the Federal Food, Drug and Cosmetic Act, CEO is predominantly utilized for its flavoring properties and possesses antiseptic properties. It is frequently classified as "Generally Recognized as Safe" (GRAS) for specific applications in the food industry. However, certain uses, particularly those involving therapeutic claims, necessitate adherence to FDA regulations, which may entail additional research and approval processes to verify safety and efficacy (4).

EU regulations and EFSA opinions

Within the EU, CEO is regulated as a flavoring agent and food additive. The European Food Safety Authority (EFSA) is responsible for evaluating the safety of flavorings, including CEO, which has notably high eugenol content. The regulations established by the EU ensure that these substances adhere to safety standards when they are incorporated into food products. Furthermore, clove oil is used in cosmetic products, where it must comply with the Cosmetic Products Regulation (Regulation (EC) No. 1223/2009) to guarantee consumer safety (1,2).

International standards for quality control

International standards, such as those established by the International Organization for Standardization (ISO), offer comprehensive guidelines for the quality assurance of essential oils, including that of clove oil. These standards encompass the chemical composition, purity and testing methodologies to ensure that products are not adulterated and comply with specific safety and quality benchmarks. The implementation of quality control measures is imperative because of the prevalence of adulteration within the essential oil market, which can compromise both efficacy and safety (19).

The global market for CEO necessitates compliance with established regulations and standards to ensure the production of high-quality and safe products for consumer use and industrial applications. Although the regulatory framework may differ across regions, adherence to the standards set by the FDA, EU and international bodies is crucial for the safe incorporation of CEO s into various products.

Future perspectives and challenges

Emerging applications and research directions

The investigation of CEO in emerging applications and research trajectories underscores several promising prospects, particularly in the context of nanotechnology-based delivery systems, synergistic interactions with other natural compounds and potential applications in personalized medicine.

Nanotechnology-based delivery systems

CEO has been extensively investigated for incorporation into nanotechnology-based delivery systems to enhance its stability, bioavailability and efficacy. The application of nanotechnology enables CEO to address challenges related to volatility and low water solubility. For example, CEO has been optimized into nano-emulsions, which can augment its antimicrobial and antioxidant properties. These nano-emulsions have demonstrated improved stability and enhanced the bioactivity of clove oil when encapsulated in nanoparticles, such as in the formulation of stable nano-emulsions for therapeutic and food preservation

applications (41,55,56).

Synergistic effects with other natural compounds

CEO is recognized for its bioactive constituents, such as eugenol, which exhibit notable synergistic effects when combined with other natural compounds. These combinations can augment the antimicrobial and therapeutic properties of CEO, providing a comprehensive strategy for the treatment of infections and diseases. For example, the integration of CEO into soy protein-montmorillonite films has demonstrated a synergistic effect that enhances the tensile strength and antimicrobial properties of the films, indicating their potential applications in food packaging and preservation (13).

Potential in personalized medicine

The integration of CEO into personalized medicine is supported by its extensive range of bioactivities, including antimicrobial, antioxidant, anti-inflammatory and anticancer properties (2,12). Personalized medicine seeks to customize treatments to meet individual patient needs by utilizing the unique properties of CEO to effectively address specific health conditions. This approach necessitates an understanding of the role of bioactive components of CE in human health, potentially employing their encapsulated forms for targeted therapy, thereby enhancing therapeutic outcomes and reducing side effects. In summary, the future prospects of CEO in emerging applications are promising owing to advancements in nanoencapsulation, synergistic applications with other natural compounds and its potential in personalized treatment strategies. These directions not only capitalize on the inherent properties of CEO but also address the limitations of its traditional use in contemporary clinical and industrial applications.

Challenges in large-scale production and application

The large-scale production and utilization of CEO face several challenges, particularly in terms of standardization, stability and environmental sustainability.

Standardization of extraction and quality control methods

The methods employed for extracting CEO play a crucial role in determining its chemical composition and biological efficacy. Commonly used techniques include hydro-distillation, steam distillation, ultrasound-assisted extraction and MAE. Each of these methods differentially influences the concentration of principal compounds, such as eugenol, β -caryophyllene and α -humulene, thereby affecting the standardization and quality control of the oil (1,2). Recent advancements in nano-emulsion technologies present opportunities to improve the solubility and stability of clove oil; however, the development of a standardized methodology remains a significant challenge (41).

Stability and bioavailability issues

The hydrophobic characteristics of CEO impede its integration into aqueous-based formulations because of solubility challenges (42). Although nano-emulsions can enhance bioavailability and stability, they are intrinsically unstable and prone to alterations in average droplet size during storage, which compromises their efficacy (41). Micro-fluidization techniques have been devised to augment the antimicrobial activity and stability of oils; nevertheless, maintaining stability over prolonged periods and under diverse environmental conditions remains a substantial concern (15).

Environmental and sustainability concerns

The sustainability of CEO production presents a significant challenge. Extraction processes typically require substantial energy input and may not conform to the principles of green chemistry. Enzymatic methods for synthesizing derivatives, such as eugenyl acetate, offer potential for mitigating environmental impact; however, these methods require further optimization and evaluation for scalability (52). Additionally, clove cultivation in tropical and subtropical regions must balance local ecological impacts with production demands, particularly given its increasing application in various industries (2).

These challenges underscore the necessity for continued research aimed at optimizing extraction techniques, enhancing the stability and bioavailability of CEO formulations and developing sustainable practices that address both environmental and industrial aspects of CEO production.

Economic aspects and market trends

CEO is of considerable economic significance and has potential applications across various industries. It demonstrates promising market trends, cost-effectiveness compared to synthetic alternatives and presents opportunities for the development of value-added products.

Global market analysis of CEO

CEO is predominantly produced in regions such as Indonesia, Madagascar, Comoros, Tanzania and Sri Lanka, where clove trees are cultivated. This essential oil, noted for its high eugenol content, has diverse applications in the cosmetics, dentistry, agro-food and traditional medicine sectors (57). The global clove oil market is shaped by trends within the spice industry and the consumption patterns of traditional products, such as Indonesia's kretek cigarettes. Additionally, the international demand for organic products and sustainable farming practices has the potential to enhance market growth, given that the oil is classified as an organic material derived from green chemistry (57).

Cost-effectiveness compared to synthetic alternatives

CEO is a promising alternative to synthetic preservatives and chemicals in various applications owing to its significant antimicrobial, antioxidant and insecticidal properties. It competes with synthetic chemicals based on several factors: it is biodegradable, generally non-toxic at appropriate doses and demonstrates multimodal action against pathogens and pests (7,58). These attributes render CEO an appealing candidate for substituting synthetic additives, particularly in the food and pharmaceutical industries, where health concerns regarding synthetic substances are increasing (40).

Potential for developing value-added products

The potential for developing value-added products from CEO is substantial, particularly considering its role in innovative applications such as nanoemulsions. These formulations enhance the bioavailability and stability of clove oil, thereby augmenting its efficacy as an antimicrobial and antioxidant (41,42). Nanoemulsified configurations of clove oil hold promise for advancements in food safety by serving as natural preservatives and could significantly impact the pharmaceutical industry by enhancing the therapeutic applications of eugenol. Furthermore, the use of oil in the green synthesis of nanoparticles for antibacterial activity represents another innovative avenue for

product development (56). The integration of clove oil into these value-added products not only opens new markets but also contributes to sustaining the livelihoods of producers in clove-producing regions (57). However, strategic measures must be implemented to ensure product quality and authenticity, as issues of adulteration remain a barrier to market integrity (19). Overall, CEO presents robust economic opportunities with its diverse applications, cost-effectiveness over synthetic alternatives and potential for innovation in value-added products.

Discussion

This review highlights the diverse bioactivities of CEO, primarily attributed to its main component, eugenol. CEO exhibits significant antioxidants, antimicrobial, anti-inflammatory and analgesic properties, as evidenced by both *in vitro* and *in vivo* studies. These activities underscore its potential as a natural alternative to synthetic preservatives, therapeutic agents and pesticides. Compared to other natural essential oils, CEO demonstrates superior radical-scavenging and antimicrobial effects, thereby reinforcing its utility in food safety, pharmaceutical formulations, cosmetics and sustainable agriculture. Nonetheless, challenges persist regarding the variability in chemical composition due to extraction methods, geographical origin and environmental factors. Issues related to stability, bioavailability and potential cytotoxicity at high concentrations also limit its widespread application. Emerging technologies, such as nano-emulsions, encapsulation and controlled-release systems, offer promising solutions for enhancing stability and efficacy. Future research should prioritize the standardization of extraction processes, assurance of safety and the integration of CEO into advanced delivery systems. Overall, CEO represents a multifunctional bioactive compound with substantial industrial and therapeutic potential, meriting further investigation for sustainable application.

Conclusion

In conclusion, CEO demonstrates considerable versatility and potential in various industries and applications. Its potent bioactive properties, including antimicrobial, antioxidant, anti-inflammatory and analgesic effects, make it a valuable natural ingredient in food preservation, pharmaceutical formulations, cosmetics and agricultural applications. The primary component of this oil, eugenol, is largely responsible for these beneficial activities. While clove oil shows promise as an alternative to synthetic chemicals in numerous areas, challenges persist regarding the standardization of extraction methods, stability in formulations and assurance of sustainable production practices. Ongoing research is necessary to optimize the delivery systems, explore the synergistic effects with other natural compounds and develop novel applications in personalized medicine. From an economic perspective, the global market for CEO continues to expand, driven by the increasing consumer demand for natural products. However, careful consideration of safety and regulatory aspects is crucial as applications expand. Overall, CEO is a multifaceted natural resource with significant potential for innovation and development across diverse sectors, warranting continued scientific investigation and commercial exploration.

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Authors' contributions

BK contributed to the conceptualization of the study, conducted the literature search and prepared the original draft of the manuscript and editing. AKP was responsible for performing critical review and contributed to figure generation. SP assisted in review and editing process. SKC contributed through critical review of the work. MB provided supervision. All authors read and approved the final manuscript.

Compliance with ethical standards

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