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Clove (*Syzygium aromaticum*): Processing, bioactives, and applications

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Abstract

Clove (*Syzygium aromaticum* (L.). Merr & L.M. Perry) is a widely used spice valued for its rich aroma and potent biological properties. This article highlights the traditional and modern processing techniques of clove in a detailed manner, including harvesting, destalking, drying, and storage, with a focus on quality retention. It explores both volatile (e.g., eugenol) and non-volatile (e.g., tannins, sterols) compounds responsible for its therapeutic efficacy. The paper also presents an overview of clove's pharmacological applications, such as antimicrobial, antidiabetic, anticancer, antioxidant, and anti-inflammatory activities. Technological advancements in extraction and nanoencapsulation have enhanced its application in functional foods, pharmaceuticals, and green packaging. This review emphasizes the significance of optimized processing and bioactive preservation for maximizing the medicinal and commercial potential of clove.

Keywords: Bioactive compounds, clove, eugenol, functional foods, food processing

Introduction

India is known as the "home of spices." Widely accepted as spices and flavorings in human nutrition and disease treatment, spices have played a significant role in the history of civilization, exploration, and commerce. Spices are essential to the culinary technique of flavouring food. For thousands of years, spices such as cloves, oregano, mint, thyme, and cinnamon have been used as food preservatives and in herbal medicines due to their antioxidant and antimicrobial properties. The antibacterial, antifungal, antiviral, and anticancer properties of spice plants are now widely recognized. Cloves stand out from other spices due to their powerful antioxidant and antibacterial properties. Traditional medicinal practices such as Unani, Siddha, Ayurveda, and Chinese medicine have thrived on these plants. According to world spice trade statistics, cloves are the second most important spice in the world after black pepper (Ahmad *et al*. 2022).

The word "clove" derives from the French and English words "clov" and "clout", both meaning "nail", due to the resemblance of the clove tree bud to a broad-headed nail. There is evidence for use of clove by the Chinese in the third century BC. Cloves were introduced to Europe in 1265. Before the Portuguese located the island of Moluccas in the 16th century, its origin and origins were unknown (Idowu *et al*. 2021) The French successfully introduced the clove tree to Mauritius and Réunion in 1770, from where it spread to Zanzibar. Before the arrival of the British, cloves were an established crop in Sri Lanka as early as 1796. The East India Company introduced cloves to India in the 18th century. Currently, Indonesia is the world's largest producer of cloves, accounting for more than 80% of output, followed by Madagascar, Tanzania (Zanzibar and Pemba), and Comoros (Danthu *et al*. 2020). It is called "Lavanga" in Sanskrit and has been used in India since ancient times (Kembauw *et al*. 2021). With continuous advances in processing, handling and pharmacological applications of cloves, their role in modern medicine and functional foods is expanding. Clove extracts have been studied for their potential in diabetes management, cancer prevention, and antimicrobial resistance, making them a promising ingredient in pharmaceutical and nutraceutical formulations. Furthermore, advancements in extraction technologies and nanoencapsulation are enhancing the bioavailability and efficacy of clove-derived compounds, paving the way for their broader applications in the food and pharmaceutical industries.

Profile of clove

Production

The clove trees are small evergreen trees that can reach a height of 12-20 m. It thrives in coastal areas, where temperatures range from 15 to 30 °C, rainfall is average, and there is a distinct dry season; the optimum level of rainfall is 1750 to 2500 mm per year. It is a plant found at low elevations (Hassan *et al*. 2023). It requires a warm humid tropical climate and can be cultivated from sea level up to elevations of about 900 m above mean sea level. Though it grows best at lower elevations (below 300 m), it can also adapt to higher altitudes under suitable climatic conditions (Kerala Agricultural University 2019). The young leaves of the clove tree are bright pink and mature to a greenish-yellow color. Flower heads form a series of between three to ten flowers petals in each cluster. The major clove-growing regions are Indonesia, Tanzania, Madagascar, Malaysia, Brazil, Sri Lanka, Haiti, and India. They are mainly cultivated by small farmers in Indonesia, Madagascar, the Comoros, Tanzania (Zanzibar and Pemba), and Sri Lanka. Indonesia remains the largest producer fulfilling over 80% of its own demand while Zanzibar and Pemba have periodically supplied the Indonesian *kretek* industry during supply constraints (Danthu *et al*. 2020). Clove was grown on 40,610 ha in Indonesia in 2001 (Thomas *et al*. 2023). In India, clove is cultivated in Tamil Nadu, Kerala, Karnataka, and the Andaman and Nicobar Islands. The cultivation is being done effectively on the western slopes of the Western Ghats in the Kanyakumari district. Tirunelveli, Nilgiris, Cumbum, Kumali, and Burliar are among the other viable clove gardens in Tamil Nadu. India's domestic market of cloves is approximately 4000 tonnes per year. Clove farming is primarily limited to southern India, and clove gardens were reportedly established with a few seedlings obtained from Mauritius (Cortés-Rojas *et al*. 2014).

Processing of clove

Harvesting

Clove harvesting begins when the trees are mature-typically between 8-10 years of age, or 6-8 years in regions like Maluka. The unopened flower buds, found at the tips of branches, are hand-picked carefully without damaging the branches. Harvesting often requires scaffolding. High-quality cloves are identified by a brownish-black colour post-curing, full crowns, a slightly rough texture, and minimal wrinkling. The buds at harvest generally contain around 12% moisture and up to 2% foreign matter (Farooqi *et al*. 2005).

Destalking

Post-harvest, the separation of clove buds from their stalks is carried out manually. This involves gently holding a cluster in one hand and using the palm of the other to twist and apply pressure until the buds fall off. It is essential that this process is conducted under hygienic conditions to prevent contamination. Both the work surface and the hands of the processor must be thoroughly clean. After separation, the buds and stems are dried separately. Notably, the stems are not wasted; they are utilized in the extraction of distilled clove oil (Pruthi *et al*. 1998).

Drying

Timely drying is crucial, as delays may lead to fermentation and degradation of the spice quality. Clove buds are usually sun-dried by spreading them evenly on clean mats, ensuring they are regularly raked and turned for uniform exposure and color development. During drying, buds transition from a pale red to a rich brown hue, indicating proper dehydration. The drying process typically spans 4 to 5 days under ideal sunny conditions.

Overly rapid drying may cause cloves to become brittle, shriveled, and lose their desired plump texture. The ideal moisture content after drying should range between 8% and 10%. A properly dried clove can be identified by its crisp snap when broken. During the monsoon or periods of low sunlight, mechanical dryers-such as tray dryers-are recommended. Hot air drying at temperatures between 60°C and 70°C provides consistent results, with the drying time ranging from 5 to 9 hours depending on the size of the batch and equipment used. The typical drying ratio is 1:4 moreover, Poorly dried cloves, which appear pale and underdeveloped, are commonly referred to as "khuker" (Pruthi *et al*. 1998; Hassan *et al*. 2023).

Winnowing

Winnowing is performed to eliminate residual dust and debris from the dried cloves. Traditionally, this process is carried out using large woven baskets that allow fine particles to be separated from the buds through gentle tossing. In addition to manual techniques, mechanical winnowers and small-scale air classifiers are available in the market, which improve efficiency and consistency by removing finer impurities such as sand, husk particles, and other extraneous matter.

Packaging and storage

Packaging of cloves is done using polythene or laminated pouches of various sizes catering to the demands of different market segments. Moisture-proof, airtight packaging is essential to preserve flavor, prevent spoilage, and extend shelf life. The use of heat-sealing machines ensures a secure seal. Labels should be clear, providing comprehensive information including the product name, brand (if applicable), manufacturer details, weight, manufacturing and expiry dates, and a list of any added ingredients. In some export markets, following the rules may mean giving extra traceability information like barcodes, producer codes, and batch numbers (Ratri *et al*. 2020). The cloves must be completely dry before storage to avoid mold growth and spoilage. Storage should be in airtight containers and placed in cool, dry environments away from direct sunlight. The storage facility must be clean, well-ventilated, and free from pests and strong odors. Cloves are highly absorbent and can take on the scent of nearby items, which can compromise their aroma and flavor. Periodic checks should be performed to detect any signs of moisture or fungal contamination. If moisture absorption occurs, cloves should be re-dried to a moisture level of around 10% before being returned to storage. It is also advisable to install insect screens and maintain high sanitation standards to protect against infestations (Farooqi *et al*. 2005).

Bioactive compounds

Clove is a rich source of both volatile and non-volatile bioactive compounds, which are primarily responsible for its distinct aroma, flavor, and wide range of therapeutic applications. Volatile components refer to compounds that easily vaporize at relatively low temperatures. These are typically found in the essential oil fraction of plants and contribute significantly to their aroma and therapeutic properties. In cloves, these volatile oils are derived from various parts of the plant, including the leaves, stalks, flower buds (gems), and fruits. The extraction and analysis of these bioactive constituents are carried out using solid-liquid extraction techniques followed by Gas Chromatography-Mass Spectrometry (GC-MS) for compound identification (Krishnan *et al*. 2017; Krishnan *et al*. 2018; Joseph *et al*. 2024; Lavanya *et al*. 2024; Joseph *et al*. 2025). The yield and composition of essential oils in clove vary considerably with geographical location, seasonal variations and varietal differences. Additionally, the age of the plant at harvest, pretreatment and post-distillation handling, and the type of distillation technique adopted significantly affect the efficiency and quality of oil recovery (Gupta *et al.* 2021). Among the various volatile constituents, eugenol is the most predominant compound present in clove oils. Eugenol is well-documented for its antimicrobial, antioxidant, and analgesic properties, making it a valuable component in pharmaceutical formulations, food preservation, and cosmetic applications (Bakkali *et al*. 2008; Choudhary *et al*. 2025).

In contrast, non-volatile components refer to compounds that do not readily evaporate and generally remain as stable solids or liquids under standard conditions. These bioactive substances contribute to the long-term medicinal and functional effects of clove, even in the absence of aroma. Clove is known to contain several non-volatile phytochemicals, including tannins, sterols, triterpenes, and flavonoids, each exhibiting significant antioxidant, anti-inflammatory, and antimicrobial activities (Anita Dua *et al*. 2014; Raja Rajeshwari *et al*. 2025). These compounds, though not aromatic, play an equally vital role in the pharmacological potential of clove. Together, the volatile and non-volatile constituents of clove represent a powerful combination of sensory and therapeutic attributes, reinforcing its significance in food, health, and wellness industries.

The clove essential oil is mainly derived from flower buds, but are also present in the leaves, stalks, and fruits. Clove fruits are especially abundant in phenylpropanoids and terpenoids. Eugenol (4-allyl-2-methoxyphenol) is the most predominant and pharmacologically significant compound, comprising approximately 70-90% of clove essential oil depending on plant part, age, and extraction method (Prashar *et al*. 2006; Chaieb *et al*. 2007). Eugenol exhibits antimicrobial, antioxidant, anti-inflammatory, and analgesic properties. Its phenolic structure, characterized by a hydroxyl group bonded to an aromatic ring with a methoxy substitution, facilitates its ability to scavenge free radicals and disrupt microbial membranes. Other volatile constituents include eugenyl acetate (4-allyl-2-methoxyphenyl acetate), β-caryophyllene (a bicyclic sesquiterpene), α-humulene, methyl eugenol, and benzyl alcohol, which are present in variable concentrations and contribute to clove's therapeutic range.

Eugenyl acetate, often found in concentrations ranging from 10-17%, enhances clove's aromatic profile and augments eugenol's anti-inflammatory properties via cyclooxygenase (COX) pathway modulation (Gertsch *et al*. 2008). β-Caryophyllene, accounting for 5-12% of the essential oil, is notable for its CB2 receptor agonist activity, making it an unique non-psychoactive phytocannabinoid with immunomodulatory and analgesic benefits. GC-MS has served as a primary analytical method for characterizing these compounds. Studies by (R. Juma *et al*. 2024; Abdelmuhsin *et al*. 2025; Mustafa *et al*. 2025) underscore the compositional variation in clove essential oil as influenced by agro-climatic factors, post-harvest processing, and the choice of distillation technique. Seasonal shifts and varietal differences, such as between Zanzibar and Ambon cultivars, result in significant changes in the relative concentrations of major oil components. This, in turn, alter both flavor intensity and pharmacological efficacy. Further, Kumar *et al*. (2021 and Prakash *et al*. (2025) highlighted that oil and eugenol content are heavily impacted by harvesting time and plant maturity, with younger buds generally producing oils richer in eugenol.

In contrast to the highly aromatic and volatile essential oil fraction, clove also contains a diverse array of non-volatile bioactive compounds that contribute significantly to its medicinal value, particularly in contexts that do not rely on aroma or vaporized constituents. These include tannins, flavonoids, triterpenoids, sterols, and organic acids, many of which are present in the residual plant material after oil extraction or in ethanolic and aqueous extracts. Notable among these are gallic acid, ellagic acid, kaempferol, quercetin, rhamnetin, and stigmasterol-all of which exhibit pronounced antioxidant, anti-inflammatory, and antimicrobial effects. Unlike the volatile phenylpropanoids, these compounds are generally stable at ambient conditions and persist longer in the body, lending themselves to applications in nutraceuticals and therapeutic supplements (Tian *et al*. 2014). For instance, kaempferol and quercetin are known to neutralize reactive oxygen species (ROS) and inhibit lipid peroxidation, thereby mitigating oxidative damage in cells and tissues. Similarly, gallic and ellagic acids are hydrolyzable tannins that not only enhance antioxidant potential but also exert antimicrobial effects by chelating metal ions and altering membrane integrity in microbial cells (Rajeshwari *et al*. 2024).

Clove's triterpenoids such as oleanolic acid and ursolic acid, although less abundant than eugenol, have shown anti-inflammatory and hepatoprotective properties in animal studies. The presence of β-sitosterol and stigmasterol, plant sterols structurally similar to cholesterol, contributes to lipid-lowering effects and supports cardiovascular health. These non-volatile compounds are generally extracted using solid–liquid techniques, often involving ethanol or methanol as solvents, and are identified via High-Performance Liquid Chromatography (HPLC) or LC-MS/MS. Study by (Krishnan *et al*. 2017; Krishnan *et al*., 2018) emphasized that traditional decoction and maceration methods used in Ayurvedic preparations retain substantial amounts of these compounds, explaining clove's efficacy in chronic inflammatory and metabolic disorders despite the absence of its characteristic aroma. Moreover, (Rajeshwari *et al*. 2024) observed that clove polyphenols downregulate pro-inflammatory cytokines and inhibit COX and LOX pathways in cell-based assays, confirming their role in immune regulation. Therefore, while the volatile constituents contribute immediate and sensory-linked pharmacological effects such as analgesia and antiseptic activity, the non-volatile phytochemicals are more suited for sustained therapeutic applications. Together, these volatile and non-volatile fractions create a synergistic matrix that underpins clove's comprehensive bioactivity across systems including gastrointestinal, immune, cardiovascular, and dermatological health.

Therapeutic and biological applications

Antidiabetic activity

Cloves have garnered considerable scientific interest for its antidiabetic potential. A growing body of evidence underscores clove's multifaceted mechanisms in combating type 2 diabetes mellitus (T2DM), highlighting its ability to regulate glycemic parameters, modulate metabolic enzymes, and attenuate oxidative stress and inflammation. Several studies have identified clove's bioactive constituents-particularly eugenol, dehydrodieugenol, and dehydrodieugenol B as potent modulators of diabetes-related pathways. Ahmad *et al*. (2020), Shukla *et al*. (2020) and Ruyati *et al*. (2024) demonstrated that clove extract effectively down regulated key gluconeogenic genes such as glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK), mimicking insulin's role in hepatic glucose metabolism. This gene modulation is critical in reducing hepatic glucose output and improving overall glycemic control. *In vitro* and *in vivo* studies corroborate clove's ability to inhibit carbohydrate-hydrolyzing enzymes such as α-glucosidase and α-amylase in a dose-dependent manner. This enzymatic inhibition slows the breakdown of polysaccharides into glucose, thereby blunting postprandial hyperglycemia-a key therapeutic goal in T2DM management (Ijarotimi *et al*. 2018).

In a significant rodent model study, Pei *et al*. (2019) reported that the oral administration of clove extract led to a substantial reduction in fasting blood glucose, total cholesterol, LDL, and triglycerides, while elevating HDL levels. These lipid-modulating effects were accompanied by enhanced insulin sensitivity and improved adiponectin levels, indicating systemic metabolic improvements. Importantly, clove's antihyperglycemic effect extends to its influence on insulin signaling pathways. (Yang *et al*. 2020) showed that clove extract activates the AMP-activated protein kinase (AMPK) pathway, which enhances GLUT4 translocation in skeletal muscles-facilitating increased glucose uptake independent of insulin. This is especially beneficial in insulin-resistant states. Interestingly, (Atsumi *et al*. 2001) provided early insight into clove's molecular interactions, showing that dehydrodieugenol and dehydrodieugenol B demonstrate high binding affinity to Peroxisome Proliferator-Activated Receptors (PPARs). These nuclear receptors play pivotal roles in lipid metabolism, glucose homeostasis, and inflammation regulation, suggesting additional therapeutic avenues for clove in metabolic syndrome. Its antidiabetic efficacy is attributed to its diverse pharmacological actions: modulation of glucose metabolism genes, inhibition of digestive enzymes, improvement of insulin signaling through AMPK activation, and suppression of inflammatory cytokines. These synergistic effects position clove as a compelling phytotherapeutic agent for diabetes management. Nevertheless, while preclinical data are promising, rigorous human clinical trials are essential to validate these findings and establish standardized dosing protocols.

Anticancer activity

Commonly, the cytotoxic and apoptosis methods are followed for the anticancer studies (Vignesh *et al*. 2012; Lakshmipraba *et al*. 2013; Vignesh *et al*. 2013; Vignesh *et al*. 2016; Lakshmipraba *et al*. 2017). Clove essential oil has exhibited strong cytotoxic and antimutagenic activity against a range of cancer cell lines, such as colon (HCT 116- Human colon cancer cell line), breast (MCF-7 Michigan Cancer Foundation 7, MDA-MB-231 M D Anderson - Metastatic Breast - 231), liver (HepG2- human hepatoblastoma cell line), cervical (HeLa- Henrietta Lacks), prostate (DU-145- human prostate cancer cell line), and esophageal (TE-13 Tracheoesophageal) cancers, with little effect on normal human peripheral blood lymphocytes (Baskaran *et al*. 2012; Gunaseelan *et al*. 2022). Further, the methanol extract of clove has been reported to suppress the SOS response, a DNA repair process for damage, by inhibiting mutagen-induced activity in *Salmonella typhimurium* strains. Studies also demonstrate the prevention of carcinogenesis by clove, as evidenced in a mouse model of skin carcinogenesis initiated by 9,10-dimethylbenz(a)anthracene, where its antimutagenic activity ranged from 34.11% to 79.74% against *S. typhimurium* TA100 and TA98 mutant strains (Baskaran *et al*. 2010; Manoharan *et al*. 2011; Baskaran *et al*. 2018). Eugenol, along with a few other extracts like sesquiterpenes, b-caryophyllene, b- caryophyllene epoxide, a-humulene, and humulene epoxide demonstrated strong anti- cancerous properties by activating the detoxifying enzyme glutathione-S-transferasein mouse liver small intestine (Manoharan *et al.* 2010; Shanmugam *et al*. 2010).

Anti-inflammatory and immunomodulatory

Clove exhibits significant anti-inflammatory and immunomodulatory properties, primarily attributed to its major bioactive compound, eugenol (Leela & Sapna, 2008). These properties have been substantiated through various *in* *vitro* and *in vivo* studies, highlighting clove's potential in managing inflammatory conditions and modulating immune responses. Eugenol exerts its anti-inflammatory effects by targeting key inflammatory mediators and pathways. Notably, it inhibits the cyclooxygenase-2 (COX-2) enzyme, leading to a reduction in prostaglandin E2 (PGE2) synthesis, a pivotal molecule in the inflammation cascade. Additionally, eugenol suppresses the nuclear factor-kappa B (NF-κB) signaling pathway, which regulates the expression of various pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) (Kim *et al*. 2003). In murine macrophage models, clove and eugenol have demonstrated the ability to modulate cytokine production. Specifically, clove extract inhibited the production of IL-1β, IL-6, and IL-10, while eugenol selectively suppressed IL-6 and IL-10 levels. These findings suggest that clove components can modulate immune responses by influencing cytokine profiles.

Further supporting its anti-inflammatory potential, clove essential oil (CEO) has been shown to reduce the expression of inflammatory biomarkers in human dermal fibroblasts. CEO significantly decreased levels of vascular cell adhesion molecule-1 (VCAM-1), interferon gamma-induced protein 10 (IP-10), and collagen III, indicating its role in mitigating inflammation and promoting tissue repair (Han *et al*. 2017). Moreover, eugenol's immunomodulatory effects extend to the modulation of macrophage activity. Studies have reported that eugenol can suppress Nitric oxide (NO) production and influence macrophage polarization, thereby contributing to immune regulation. These actions underscore eugenol's potential in managing immune-related disorders. These properties position clove as a promising natural agent for the management of inflammatory and immune-related conditions. However, further clinical studies are warranted to fully elucidate its therapeutic potential and establish standardized dosing regimens (Rajeshwari *et al*. 2024).

Aphrodisiac

Clove has garnered considerable attention for its potential aphrodisiac properties. Traditionally used in Ayurveda and Unani systems for enhancing sexual vigour and treating reproductive ailments, modern research has begun to substantiate these ethnomedical uses. The aphrodisiac effects of clove are primarily attributed to its bioactive constituents-most notably eugenol and β-caryophyllene-which exert hormonal and neurovascular modulatory effects conducive to sexual stimulation and fertility enhancement. Experimental pharmacological studies have demonstrated that clove extract can positively influence sexual performance in male rodents. Dasofunjo et *al*. (2013) reported that oral administration of aqueous clove extract significantly improved mounting and intromission frequency, as well as ejaculation latency in male rats. These behavioural changes were accompanied by increased levels of serum testosterone and heightened activity of steroidogenic enzymes such as 17β-hydroxysteroid dehydrogenases, which are essential for androgen biosynthesis and testicular function (Ghai *et al*. 2016). Similarly, Anand *et al.* (2009) and Haidl *et al.* (2011) found that clove extract enhanced spermatogenic parameters, including sperm count, motility, and morphology in mice, suggesting potential benefits for male fertility (Benkirane *et al*. 2022).

One of the critical factors contributing to these effects is the antioxidant activity of eugenol, which helps protect testicular tissue from oxidative stress, a known disruptor of hormonal balance and spermatogenesis. By scavenging ROS and reducing lipid peroxidation, eugenol preserves the structural and functional integrity of reproductive organs, thus supporting healthy sexual function. In addition to its antioxidant effects, β-caryophyllene, a bicyclic sesquiterpene found in clove oil, has been shown to interact with cannabinoid receptors (particularly CB2), which are implicated in anti-inflammatory and neuroendocrine regulation pathways that may further support libido and fertility (Gertsch *et al*. 2008). Interestingly, Tajuddin *et al*. (2004) evaluated the impact of a 50% ethanolic extract of clove and reported a consistent enhancement of sexual activity in normal male mice without adverse effects such as gastric ulceration or hepatotoxicity. This positions clove as a safe natural candidate for long-term sexual health supplementation (Rodrigues *et al*. 2004). Their findings further reinforced the role of clove as a vasodilatory and androgen-enhancing agent, crucial for erectile function and libido.

However, studies also caution that the aphrodisiac effects of clove are dose-dependent. Raji *et al*. (2006) and Adio *et al*. (2024) observed that while low to moderate doses of clove extract stimulate sexual behaviour and hormone levels, excessive intake may lead to testicular toxicity and suppression of reproductive hormone synthesis (Kuiate *et al*. 2006). Thus, careful consideration of dose and formulation is vital when using clove therapeutically for reproductive enhancement. Beyond pharmacological models, clove is now being integrated into functional foods and nutraceutical products aimed at improving sexual wellness. Its incorporation into dietary supplements may offer a natural means to manage libido, erectile dysfunction, and hormone-related disorders, especially when combined with other adaptogenic or antioxidant herbs. As scientific validation continues to align with traditional knowledge, clove's place as a botanical aphrodisiac becomes increasingly justified.

Antimicrobial activity

Clove exhibits potent antimicrobial properties against a wide array of microorganisms, including Gram-positive and Gram-negative bacteria, fungi, and antibiotic-resistant strains. Eugenol's antimicrobial efficacy is primarily attributed to its ability to disrupt microbial cell membranes, leading to increased permeability and leakage of vital intracellular components. This disruption compromises the integrity of the cell membrane, resulting in cell death. Additionally, eugenol interferes with enzyme activity and inhibits the synthesis of essential proteins and nucleic acids within microbial cells. *In vitro* studies have demonstrated clove oil's effectiveness against various pathogens. For instance, Nuñez *et al*. (2012) reported that clove essential oil exhibited significant microbicidal activity against *Escherichia coli, Staphylococcus aureus,* and *Pseudomonas aeruginosa*, with a 5-log reduction in bacterial counts observed at specific concentrations. Similarly, Alanazi *et al*. (2022) found that clove oil inhibited the growth of multiple bacterial strains, including *Klebsiella pneumoniae, Enterobacter cloacae*, and *Salmonella paratyphi*, with minimum inhibitory concentrations (MICs) ranging from 0.016 to 2.4 mg/mL. These findings underscore clove oil's broad-spectrum antibacterial activity.

In addition to these findings, several other studies have evaluated clove-based products using methods such as disc diffusion, well-diffusion, and MIC assessments (Vignesh *et al*. 2012; Pandiyarajan *et al*. 2013; Harinee *et al*. 2019; Periasamy *et al*. 2023; Yashwant *et al*. 2023). These studies confirmed the superior antimicrobial properties of clove-derived formulations against common pathogens. Clove essential oil has been shown to be effective against bacterial genera such as *Streptococcus, Staphylococcus, Pneumococcus,* and *Enterococcus* (Pruthi *et al*. 1998; Abdul *et al.* 2024). Even clove extract at a concentration of 1% has demonstrated significant antibacterial activity. Chromatographic analyses identify eugenol as the major antimicrobial component, primarily acting by causing spore and micelle lysis. Fu *et al*. (2007) supported this mechanism, suggesting that eugenol inhibits microbial membrane function and macromolecular synthesis. Furthermore, Devi *et al*. (2010) reported that eugenol and cinnamaldehyde, at a concentration of 2 g/mL, inhibited the growth of *Helicobacter pylori* within 9-12 hours.

Beyond its antibacterial properties, clove oil also exhibits antifungal activity. It has been shown to be effective against *Candida albicans*, a common fungal pathogen responsible for oral and vaginal infections. The antifungal mechanism involves the disruption of fungal cell walls and inhibition of ergosterol synthesis, which is essential for maintaining fungal cell membrane integrity. Notably, clove oil has demonstrated efficacy against biofilm-forming bacteria. A study by Kunicka-Styczyńska *et al*. (2020) revealed that clove essential oil significantly reduced biofilm formation by *Alicyclobacillus acidoterrestris* on technical surfaces, highlighting its potential application in food industry sanitation. It has also been investigated for its potential in treating infections caused by multidrug-resistant organisms. Alanazi *et al*. (2022) explored the antibacterial activity of clove bud oil against methicillin-resistant *Staphylococcus aureus* (MRSA) in a rat wound infection model. The study found that clove oil exhibited significant antibacterial effects, reducing microbial load and promoting wound healing. These findings suggest that clove oil could serve as an adjunct or alternative to conventional antibiotics in managing resistant infections. Eugenol, demonstrates substantial antimicrobial activity against a diverse range of pathogens, including bacteria, fungi, and antibiotic-resistant strains. Its mechanisms involve disrupting microbial membranes, inhibiting essential enzymes, and preventing biofilm formation. These properties position clove oil as a promising natural antimicrobial agent for applications in medicine, dentistry, food preservation, and sanitation.

Pharmacological activities: antinociceptive, larvicidal, and antiplatelet effects

Historically, clove had been in use since the thirteenth century as a natural remedy for pain. Clove demonstrates notable antinociceptive activity-a term that refers to the ability of a substance to block the detection of painful or injurious stimuli by sensory neurons. Eugenol exerts this effect by modulating pain perception pathways, including the inhibition of voltage-gated sodium and calcium channels, which play a crucial role in transmitting nociceptive signals. Its antispasmodic and analgesic properties have made it a traditional therapeutic agent for managing toothaches, muscular spasms, and joint pain (Tajuddin *et al*. 2004).

In addition to pain relief, clove oil has shown potent larvicidal activity, particularly in controlling the larvae of mosquito species responsible for vector-borne diseases like dengue fever. Its efficacy has been documented against *Aedes aegypti, Anopheles albimanus, and Culex quinquefasciatus,* making it a promising botanical insecticide in tropical regions such as Brazil and Southeast Asia (Gulcin *et al*, 2004; Idowu *et al*. 2021). The larvicidal effect is primarily attributed to eugenol's ability to disrupt respiratory and neurological functions in insect larvae. Furthermore, clove also exhibits antiplatelet activity, contributing to cardiovascular health. Studies have shown that a combination of eugenol and acetyl eugenol effectively inhibits platelet aggregation induced by arachidonic acid, adrenaline, and collagen, thus reducing the risk of thrombus formation (Fu *et al*. 2007).This suggests that clove extracts may have therapeutic potential in the management of cardiovascular disorders such as thrombosis and atherosclerosis.

Antiviral activity

The antiviral properties of clove are attributed to its essential oil, which is rich in phenylpropanoids, monoterpenals, and monoterpenols-classes of compounds with demonstrated antiviral efficacy *in vitro* (Bakkali *et al*. 2008). Among the key active constituents, eugenol and eugeniin have emerged as particularly effective agents against a range of viruses. Eugenol exhibits multiple mechanisms of antiviral action. One prominent strategy involves disruption of the viral envelope and capsid, which impairs viral entry into host cells. This physical disruption leads to inactivation of the virus even before it can initiate infection. Eugenol also interferes with viral attachment and penetration, critical early stages in the infection cycle. Furthermore, it modulates inflammatory responses by downregulating host cytokines such as TNF-α and IL-6, which may help reduce the severity of infection-related inflammation (Benencia *et al*. 2000). Laboratory studies provide compelling evidence of clove's effectiveness against both DNA and RNA viruses. For instance, Astani *et al*. (2011) reported that clove oil inhibited replication of herpes simplex virus type 1 (HSV-1) by over 90% at non-toxic concentrations. Supporting this, Ogata *et al*. (2000) identified eugeniin, a flavonoid derived from clove, as a selective inhibitor of HSV-1 DNA polymerase, thereby directly halting viral genome replication. This specificity positions eugeniin as a strong candidate for therapeutic development against herpes infections. Its action extends to hepatitis C virus (HCV) as well. Pandey *et al*. (2024) demonstrated that clove extract achieved 90% inhibition of HCV replication at 100 μg/mL, indicating a potent antiviral effect at relatively low concentrations. Bachir *et al*. (2012), also documented substantial reductions in viral titers in HCV-infected cell cultures following treatment with clove-derived compounds.

In the case of influenza A virus also, clove shows promise. Eugenol has been shown to interrupt a crucial viral replication mechanism by preventing the dissociation of the Beclin1–Bcl2 complex, thereby obstructing autophagy processes that the virus exploits for proliferation (El-Saber *et al*. 2020). Notably, clove's antiviral benefits are not confined to clinical settings. In the context of food safety, Otunola *et al*. (2022)seeds, bark, roots, rhizomes, buds, etc found that a clove-ginger infusion significantly decreased feline calicivirus titers, a model used to mimic human norovirus. This reduction was observed both when the virus was pretreated with the extract and during active infection, highlighting clove's potential as a natural food-grade antiviral additive and its exhibits strong antiviral potential through both direct virucidal action and inhibition of viral replication pathways. Its constituents-particularly eugenol and eugeniin-have shown efficacy against a range of viruses including HSV-1, HCV, influenza A, and norovirus surrogates. These findings support the development of clove-based therapeutics and preservatives, warranting further investigation through clinical trials and formulation research.

Antioxidant properties

Eugenol, the principal bioactive component of clove oil, plays a central role in clove's antioxidant capacity. Eugenol exhibits its antioxidant action by chelating metal ions and scavenging free radicals, thereby preventing oxidative damage to cellular structures. In addition to its antioxidative function, eugenol also acts as a photocytotoxin and participates in photochemical reactions that further contribute to its biological activity (Basava Prasad *et al*. 2022; Basava *et al*. 2023). Experimental studies have demonstrated that clove oil, even at a low concentration of 0.005%, possesses antioxidant efficacy comparable to 0.01% of synthetic antioxidant butylated hydroxytoluene (BHT) (Basava *et al*. 2023; Kiriti *et al*. 2023). Its ability to effectively chelate ferric ions (Fe^{3+}) inhibits the formation of hydroxyl radicals, which are among the most damaging reactive oxygen species (Chaieb *et al*. 2007). Owing to these characteristics, clove oil is considered an excellent natural antioxidant with promising applications in both the medical field and food preservation systems (Yashwant *et al*. 2023; Charu *et al*. 2024).

Mosquito-repellent and insecticidal activities

Clove oil demonstrates significant mosquito-repellent and insecticidal properties, making it a promising natural alternative to synthetic chemical agents. Its essential oil has shown effective repellency against several mosquito species, including *Culex quinquefasciatus*, which is a known vector of diseases such as malaria, dengue, and filariasis. In addition to its repellent action, clove oil exhibits potent insecticidal activity against a variety of parasitic and storage pests. It has been proven lethal to *Anopheles dirus, Pediculus capitis* (head lice), *Culex pipiens* larvae, *Sitophilus zeamais*, and *Tribolium castaneum* (Idowu *et al*. 2021). When used in combination with isoeugenol, the oil significantly suppresses the reproductive development of *Sitophilus zeamais*. Furthermore, eugenol, an acaricidal compound present in clove oil, has been shown to effectively control house dust mites such as *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*. Clove oil has also demonstrated efficacy as a fumigant against Japanese termite infestations, reinforcing its role in integrated pest management (Gulcin *et al*. 2004).

Applications and future perspectives

Clove has enormous promise in the culinary and pharmaceutical sectors (Leela & Sapna 2008).Clove extracts are natural preservatives with potent antibacterial and antioxidant qualities in the food industry. Table 1 and Figure 1 illustrate the various applications and transformations of clove and its derivatives in these sectors. Additionally, with improvements in nanoencapsulation enhancing the release of antimicrobial agents, edible films infused with clove essential oil offer an environmentally beneficial substitute for plastic packaging (Radünz *et al*. 2019). Clove's strong flavor may complement animal alternatives and cuisine advances as the market for plant-based foods grows. Through transdermal patches or controlled-release capsules, its analgesic and anti-inflammatory qualities-which are already used in dental care-could be extended to the treatment of arthritis and chronic pain.

Clove and its principal active compound, eugenol, have long been valued in dentistry for their analgesic, anti-inflammatory, antiseptic, and antimicrobial properties. Clove oil is traditionally applied to relieve toothache by numbing peripheral nerves and inhibiting bacterial growth. Epidemiological studies demonstrate that clove oil, eugenol, and eugenyl acetate significantly inhibit tooth decalcification caused by acidic challenges, acting comparably to fluoride in remineralization potential, thus showing promise as adjuncts in preventive dental treatments (Kim *et al*. 2012; Nakai *et al*. 2012). In clinical formulations, zinc oxide-

Table 1. Application of clove and its benefits in food

Category	Application	Key benefits	References
Baked foods	Used as a natural preservative in baked goods	Extends shelf life, prevents mold growth, maintains flavor, texture, and sensory properties	(Sung *et al*. 2012; Shukla *et al*. 2020)
Milk products	Antibacterial agent in cheese production	Inhibits bacterial growth for up to a month without affecting taste	(Fadilah *et al*. 2017)
Processed food	Added as a flavoring agent with antibacterial and antioxidant properties	Enhances food safety but may affect sensory quality at high concentrations	(Thapa *et al*. 2019)
Meat, poultry, and seafoods	Applied to meat and seafood for preservation	Prevents bacterial growth, delays lipid oxidation, maintains color, texture, and flavor	(Cansian *et al*. 2017; Perumal *et al*. 2021)
Vegetables	Used as a natural disinfectant for fresh-cut vegetables	Extends shelf life, replaces synthetic fungicides, and maintains nutritional quality	(Musthafa *et al*. 2016; Phothisuwan *et al*. 2020)
Packaging materials	Incorporated into biodegradable films for food packaging	Inhibits microbial growth, enhances antioxidant properties, and extends food shelf life	(Kaur *et al*. 2019; Barajas-Álvarez *et al*. 2021)

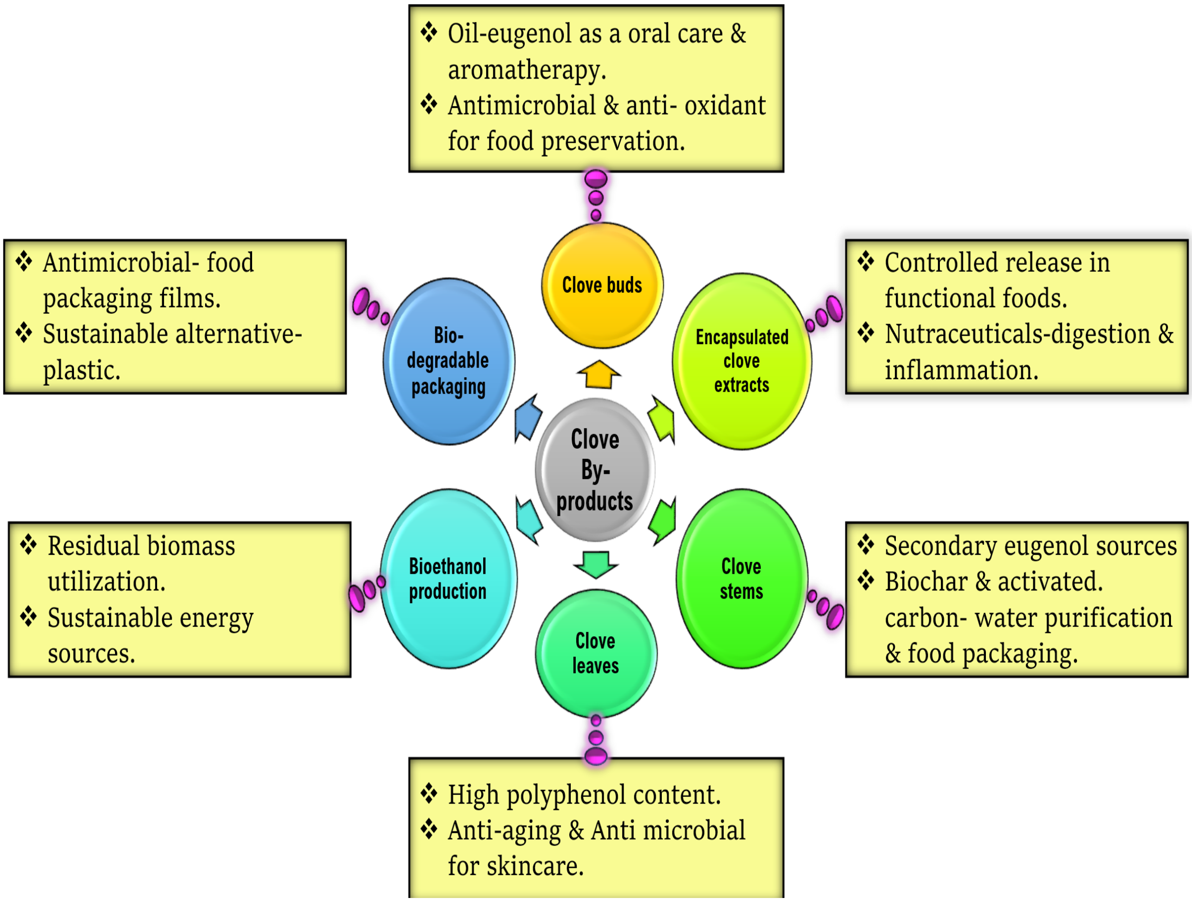

Fig. 1. Value addition in clove and its by-products

eugenol (ZOE) cement combining zinc oxide with clove-derived eugenol is widely used as a temporary filling, lining, or dressing for dry sockets; it soothes inflamed pulp tissue and provides antibacterial action, although it may interfere with resin polymerization when used concurrently. Furthermore, innovative delivery systems such as mucoadhesive eugenol tablets and herbal dental gels incorporating clove oil offer sustained therapeutic release for managing periodontal inflammation and acute dental pain (Gupta *et al*. 2004; Manikandan *et al*. 2016).

Clove may also be able to stop the growth of cancer cells, according to research, which makes it a viable option for supplementary oncology treatments (Suresh *et al*. 2007). Additionally, lipid-based carriers may improve the therapeutic efficacy of clove bioactive in medication formulations, and nanoencapsulation methods may improve the bioavailability and controlled management of these bioactive. The requirement for standardization and regulatory permissions, which need for precise extraction procedures and clinical validations, are obstacles to the broad use of clove-based products. Enhancing product development, processing, and harvesting practices for clove in the food and pharmaceutical sectors-while optimizing the extraction of bioactive compounds-can significantly improve quality and efficiency. Furthermore, integrating contemporary technologies such as artificial intelligence (AI) and machine learning can accelerate research and innovation in this field.

Conclusion

Clove (*Syzygium aromaticum*), a historically treasured spice, continues to gain scientific and commercial traction due to its potent bioactive constituents-chief among them eugenol and a host of polyphenolic compounds that exhibit robust antimicrobial, antioxidant, anti-inflammatory, and anticancer properties. This review underscores the critical role of optimized post-harvest processing-from harvesting and pretreatment to drying, packaging, and storage in safeguarding the integrity and efficacy of these bioactives. Innovations in extraction technologies, nanoencapsulation, and lipid-based delivery systems are enhancing clove's applications across pharmaceuticals, functional foods, and biodegradable packaging. With the rising consumer shift towards natural and sustainable ingredients, clove essential oil is being explored as a green alternative to synthetic preservatives. However, the path to broader adoption demands rigorous clinical validation, standardization of extraction protocols, and regulatory alignment. Leveraging precision processing and AI-driven research can accelerate the development of clove-derived therapeutics and bioactive-rich food solutions. Thus, clove not only reaffirms its place in culinary tradition but also emerges as a versatile agent for future health, nutrition, and environmental innovation.

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