REVIEW PAPER

JMS Journal of Medical Science

The medicinal properties of clove with special focus on antimicrobial effect: a systematic review

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Keywords: clove, *syzygium aromaticum*, eugenol, antibacterial, antifungal, antioxidant

Received 2024-10-22
Accepted 2024-12-26
Published 2024-12-31

How to Cite: Verma A, Toshi N, Mungi V, Mehta A. The medicinal properties of clove with special focus on antimicrobial effect: a systematic review. Journal of Medical Science. 2024 December;93(4);e1156. doi:10.20883/medical.e1156

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doi: https://doi.org/10.20883/medical.e1156

ABSTRACT

Clove, the dried flower bud of the *Syzygium aromaticum* tree, has been used for thousands of years in traditional medicine for its medicinal properties. One of the most well-known properties of clove is its antimicrobial activity attributed to a compound called eugenol. It has been found to be effective against a wide range of microorganisms, including bacteria, viruses, fungi, and parasites. In addition to its antimicrobial activity, clove has also been found to have anti-inflammatory, antioxidant, and pain-relieving properties. These properties make it an ideal natural remedy for a wide range of conditions, including toothaches, sore throat, and skin infections. With this background a systematic review was conducted wherein we explored the articles relevant to the research questions through databases like PubMed, Scopus, Web of Science, etc. Out of 150 articles explored, 30 were selected through online and snowballing literature searches. Out of these, 19 were original research articles, 8 systematic reviews, and three books/online resources. The selected articles were further assessed on quality reporting. In the current scenario of increasing prevalence of bacterial infections and emergence of multidrug resistant strains it is essential to explore alternative options like herbal antimicrobials to combat this problem.

Introduction

Clove, the dried flower bud of the *Syzygium aromaticum* tree, has been used for thousands of years in traditional medicine for its medicinal properties. One of the most well-known properties of clove is its antimicrobial activity.

Clove contains a compound called eugenol, which is responsible for its antimicrobial activity. Eugenol has been found to be effective against

a wide range of microorganisms, including bacteria, viruses, fungi, and parasites. In particular, it has been found to be effective against some of the most common bacterial and fungal pathogens, such as *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* [1,2].

In addition to its antimicrobial activity, clove has also been found to have anti-inflammatory, antioxidant, and pain-relieving properties. These properties make it an ideal natural remedy for a wide range of conditions, including toothaches, sore throat, and skin infections [3,4].

Clove oil is the most commonly used form of clove in traditional medicine, and it is used as a natural remedy for toothaches, sore throat, and skin infections. The oil is also used as a natural remedy for headaches and as an insect repellent [5].

With this background a systematic review was conducted wherein we explored the articles relevant to the research questions through databases like PubMed, Scopus, Web of Science, etc. Out of 150 articles explored, 30 were selected through online and snowballing literature searches. Out of these, 19 were original research articles, 8 systematic reviews, and 3 books/online resources. The selected articles were further assessed on quality reporting.

Table 1. Taxonomy and Scientific Clssification of Clove.

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Myrtales
Family	Myrtaceae
Genus	Syzygium
Species	aromaticum

Clove oil can also be used as a natural preservative for food, as it has been found to be effective in preventing the growth of bacteria and fungi. The oil can be added to food products in small amounts to help preserve their freshness.

Clove oil is also commonly used in aromatherapy, as its strong, spicy aroma is believed to have a soothing and relaxing effect on the mind and body [6].

Syzygium aromaticum, commonly known as clove, is a small, evergreen tree native to tropical regions. It is also referred to as *Eugenia aromaticum* or *Eugenia caryophyllata*. The plant produces highly aromatic, unopened flower buds that are harvested and dried for use as a spice. The spice is widely recognized by the same name as the tree and is often used in its plural form as "cloves" [7].

Cloves are highly valued for their culinary, medicinal, and commercial uses. As a culinary spice, cloves are widely used for their strong aroma and pungent taste, which adds a unique flavor to various dishes from different cuisines around the world. The essential oil extracted from the buds is highly valued for its flavoring and perfuming properties, as well as its medicinal properties, such as antiseptic, analgesic, and anesthetic effects [5].

The origins of clove can be traced back to the Spice Islands (Maluku Islands), where it played a central role in the early spice trade. Cloves were highly prized and were considered a valuable commodity that was sought after by traders from all over the world. Even today, clove remains an important spice and is used in various applications, including cooking, perfumery, and medicine. Its unique flavor and medicinal properties make it a popular ingredient in a variety of traditional and modern preparations [5].

The Myrtle family Myrtaceae, to which the clove tree belongs, is a group of dicotyledon plants categorized under the order Myrtales. This family is comprised of 130–150 genera and has over 3000 species, including popular plants like guava, myrtle, allspice, eucalyptus, and feijoa. The species in this family are typically woody, with essential oils, and have flower parts in multiples of four or five. Although the flowers usually have a base number of five petals, some genera have very minute or even absent petals. The stamens are usually numerous, brightly coloured, and easily noticeable. The leaves of the Myrtaceae family are simple, alternate or opposite, evergreen, and have an entire margin. A notable feature of this family is that the phloem can be found on both sides of the xylem, not just outside, as is common in most other plants [8].

The clove tree, *Syzygium aromaticum*, is a conical evergreen that grows to a height ranging from ten to 20 meters, having large oval leaves and crimson flowers in numerous groups of terminal clusters. The flower buds are at first pale in colour and gradually become green, after which they develop into a reddish brown or bright

red when they are ready for collecting. Cloves are harvested when 1.5 to two centimetres (cm) long and consist of a long calyx, terminating in four spreading sepals and four unopened petals that form a small ball in the centre. The flower buds are strongly aromatic and impart a flavour that can be described as hot and pungent [9].

The term "clove" derives from the French word clou, meaning nail, as the buds resemble small, irregular nails in shape. According to the Food and Agriculture Organization (FAO), Indonesia produced almost 80 percent of the world's clove output in 2005, followed at a distance by Madagascar and Tanzania. Cloves are also cultivated in Pakistan, India, Sri Lanka, Mauritius, and the West Indies. Cloves are one of the world's most essential, popular, and useful plants, It is commonly used as a culinary spice, adding a strong aroma and pungent flavor to a variety of dishes. The essential oil extracted from cloves is also highly prized for its various uses in flavourings, perfumes, and medicinal properties, including antiseptic, analgesic, and anaesthetic properties [10].

Chemical compounds isolated from clove

A diverse array of phenolic compounds is found in clove, one of the major vegetal sources of these compounds. Clove contains various phenolic compounds such as flavonoids, hydroxybenzoic acids, hydroxycinnamic acids, and hydroxyphenyl propens, with eugenol being the predominant bioactive compound present in fresh plant material. Gallic acid is also present in high concentrations, with 783.50 mg/100 g fresh weight, along with other gallic acid derivatives such as hydrolyzable tannins, which are present in concentrations of 2,375.8 mg/100 g. Additionally, the clove plant contains other phenolic acids like caffeic, ferulic, ellagic, and salicylic acids, as well as flavonoids like kaempferol and quercetin and their glycosylated derivatives, albeit in lower concentrations [11].

The clove flower buds can contain up to 18% essential oil, with eugenol accounting for approximately 89% of the oil content, while eugenol acetate and β-caryophyllene make up 5% to 15%. α-humulene is another important compound present in the essential oil of clove, with concentrations of up to 2.1%. β-pinene, benzaldehyde, farnesol, limonene, 2-heptanone, and ethyl hexanoate are some other compounds of volatile nature that are present in clove oil [4].

Biologically active compounds

Eugenol is the primary compound responsible for the unique and strong aroma of cloves. It is present in the essential oil obtained from cloves and constitutes a significant portion ranging from 72 to 90 percent of the oil's composition. Eugenol is widely known for its potent antiseptic and anaesthetic properties and is commonly used in mouthwashes and germicides [3].

Apart from eugenol, there are several other active compounds found in cloves that contribute to their various medicinal properties. Acetyl eugenol, beta-caryophyllene, and vanillin are among the other essential oils present in cloves, while crategolic acid, tannins, and gallotannic acid are non-volatile compounds with pharmacological activity [12].

Methyl salicylate, one of the major constituents of wintergreen oil, is also present in cloves and acts as a painkiller.Flavonoids such as eugenin, kaempferol, rhamnetin, and eugenitin also add up to its medicinal benefits. Oleanolic acid, stigmasterol, and campesterol are some triterpenoids that have been identified in clove extracts [13].

The combination of these active compounds is responsible for the numerous therapeutic properties of cloves, including their analgesic, antiseptic, anti-inflammatory, antioxidant, and anticancer effects. The use of cloves as a traditional medicine dates back centuries and continues to be an important part of many natural medicine practices around the world [14].

Medicinal properties of clove

Antibacterial and antifungal properties

The antimicrobial properties of clove have been extensively studied against various bacteria and fungi. Sofia et al. conducted a study to assess the antimicrobial effects of several Indian spice plants, including cinnamon, garlic, ginger, mint, mustard, and clove, against food-borne patho-

gens such as *Escherichia coli (E. coli), Staphylococcus aureus*, and *Bacillus cereus*. The results showed that only clove's aqueous extract, at a concentration of 3%, demonstrated complete bactericidal activity against all the tested pathogens. At a lower concentration of 1%, clove extract displayed significant inhibitory activity [15].

Another study by Dorman and Deans evaluated the antibacterial activity of black pepper, clove, geranium, nutmeg, oregano, and thyme against 25 strains of Gram-positive and Gram-negative bacteria. The oils with the broadest spectrum of activity were oregano, thyme, and clove, respectively [16].

Clove, oregano, bay, and thyme essential oils' antibacterial activity against *E. coli* O157:H7 was tested, with different levels of inhibition observed. Additionally, formulations containing eugenol and carvacrol encapsulated in a non-ionic surfactant were tested against *E. coli* O157:H7 and *Listeria monocytogenes*. The results demonstrated that eugenol could be used to inhibit the growth of these microorganisms on food-contact surfaces [17].

Rana et al. investigated the antifungal activity of clove oil against different strains and reported that it was most effective against Mucor sp., followed by *Microsporum gypseum, Fusarium moniliforme NCIM 1100, Trichophyton rubrum, Aspergillus sp.,* and *Fusarium oxysporum* MTCC 284. The antifungal activity of eugenol was demonstrated by the lysis of spores and micelles in the chromatographic analysis [18].

The efficacy of pure clove oil or clove oil mixed with rosemary oil was assessed against various bacteria, including *Staphylococcus epidermidis, Staphylococcus aureus, Bacillus subtilis, E. coli, Proteus vulgaris,* and *Pseudomonas aeruginosa*. The results indicated minimum inhibitory concentrations ranging from 0.062% to 0.500% (v/v), highlighting the potential use of clove oil as an anti-infectious agent or food preservative [19].

Eugenol and carvacrol's anticandidal activity was evaluated in a vaginal candidiasis model, and the results indicated that these compounds could be promising antifungal agents for the treatment and prophylaxis of vaginal candidiasis [20].

Furthermore, a study demonstrated that eugenol and cinnamaldehyde inhibited the growth of 31 strains of *Helicobacter pylori* at 2 µg/mL after 9 and 12 hours of incubation, respectively, without developing resistance. The activity and stability of these compounds were also examined at low pH values since *Helicobacter pylori* resides in the stomach [21].

Solid lipid nanoparticles containing eugenol were developed using stearic acid, caprylic triglyceride, and Poloxamer 188 at various concentrations by a modified hot homogenisation ultrasonication method. The particles were characterised by their particle size, polydispersity index, morphology, zeta potential, crystalline state, and encapsulation efficiency [22].

Anti-oxidant effects

Based on the database created by the United States Department of Agriculture, Perez-Jimenez et al. classified the 100 richest dietary sources of polyphenols and concluded that spice plants have the highest polyphenol content, followed by fruits, seeds, and vegetables [23].

Among all spices, cloves contain the highest amounts of polyphenol and antioxidant compounds. Shan et al. identified and quantified the main phenolic compounds in 26 spices by high-performance liquid chromatography and in vitro antioxidant activity analysis. Results showed that clove had the highest antioxidant activity and polyphenol content [24].

The antioxidant activity of aqueous extracts of clove was tested by different in vitro methods, and clove and other plants proved to have enormous potential as food preservatives. The powerful antioxidant activity of ethanol and aqueous extracts of clove and lavender may be attributed to their strong hydrogen-donating ability, metal-chelating ability, and scavenging of free radicals, hydrogen peroxide, and superoxide [25].

A study exposed male rats to hepato-toxic and nephrotoxic stress showed higher antioxidant effect of eugenol when compared to *S. aromaticum* oil and *Nigella sativa* oil [4].

Oxidative stress can also impact brain cells leading to cognitive decline and memory deficits. A study on mice's brain demonstrated the positive effects of clove oil in reducing oxidative stress. Implications of clove oil in reverting memory and learning deficits in some cases need to be studied more [26].

Anti-viral properties

Researchers conducted a study to test the antiviral activity of eugeniin, a compound derived from

S. aromaticum and *Geum japonicum*, against various herpes virus strains. The results showed that eugeniin was effective at a concentration of 5 µg/mL, and it was found that one of the primary targets of eugeniin was the inhibition of viral DNA synthesis through the inhibition of viral DNA polymerase. This finding suggests that eugeniin has the potential to be developed as an antiviral drug [4].

In another study, researchers examined the antiviral activity of aqueous extracts from several plants, including *S. aromaticum, Geum japonicum, Rhus javanica*, and *Terminalia chebula*, against *Herpes simplex* virus type 1 (HSV-1) when combined with acyclovir. The results showed that the combination of these extracts with acyclovir exhibited strong synergistic activity against HSV-1, with the strongest activity observed in the brain compared to the skin. Furthermore, it was demonstrated that these combinations were non-toxic to mice. These findings suggest that a combination of these plant extracts and acyclovir may be an effective treatment option for HSV-1 infections [27].

Analgesic action

Since the 13th century, clove has been employed as an analgesic for relieving toothaches, joint pain, and spasms. The main compound responsible for this activity is eugenol. It has been observed that the mechanism of action involves the activation of calcium and chloride channels in ganglion cells. This activation, in turn, leads to a reduction in pain. The analgesic effect of clove can also be attributed to the voltage-dependent effects of eugenol in sodium and calcium channels and in receptors expressed in the trigeminal ganglion. The activation of these channels and receptors contributes to the analgesic effect of clove. Another study has shown that the analgesic effect of clove is due to the action of eugenol as a capsaicin agonist. Eugenol has also been reported to have significant peripheral antinociceptive activity [28].

Studies have also shown the benefits of cloves in reducing metastasis of some cancers when given along with the chosen therapy. It is not proven to cure cancers individually but can be beneficial during recovery [29].

Toxicity and pharmacokinetics

According to scientific research, the consumption of clove essential oil in concentrations lower than 1,500 mg/kg is considered safe. Moreover, the World Health Organization (WHO) has established that the acceptable daily intake of clove for humans is 2.5 mg/kg of body weight. However, the toxicity of clove oil was tested in two species of aquarium fish, namely *Danio rerio* and *Poecilia reticulata*. The results showed that the medium lethal concentrations (LD50) at 96 hours were (18.2 ± 5.52) mg/mL and (21.7 ± 0.8) mg/mL, respectively [4].

When eugenol, the main component of clove essential oil, is administered orally, it is quickly absorbed and reaches the plasma and blood in a short period. The mean half-lives for plasma and blood are approximately 14.0 hours and 18.3 hours, respectively. It has been hypothesized that a cumulative effect may occur, which could be associated with the relief of neuropathic pain after repeated daily administrations [30].

Conclusion

Clove is a powerful natural remedy that has been used for centuries for its medicinal properties. Its antimicrobial activity is one of the most well-known properties of clove and it is effective against a wide range of microorganisms. Clove has also been found to have anti-inflammatory, antioxidant, and pain-relieving properties, making it a versatile natural remedy. Clove oil is the most commonly used form of clove in traditional medicine, it is widely used in dental care, aromatherapy, and food preservation. The potential of plant-based antimicrobials like cloves, neem, and turmeric may help devise an effective strategy to reduce antibiotic misuse and break the resistance among microbes.

Acknowledgements

Conflict of interest statement
The authors declare no conflict of interest.

Funding sources
There are no sources of funding to declare.

Authorship
All authors contributed significantly in the process and approved to the final version of manuscript.

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