

## Pharmacological Action of Clove (*Syzygium aromaticum*)

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### Abstract

*Syzygium aromaticum* or Clove has been used traditionally as a spice for thousands of years, and provides a rich and spicy addition to our favourite recipes. Cloves are also essential in the manufacturing of herbal medicine such as Indian Ayurvedic medicine and Chinese medicine. Phenolic compounds such as eugenol show antioxidant capacity and free radical scavenging activity. Constituents of the oil also include methyl amyl ketone, methyl salicylate,  $\alpha$  and  $\beta$ -humulene, benzaldehyde,  $\beta$ -ylangene and chavicol.

**Keywords:** eugenol; antimicrobial; anti-inflammatory; anti-cancerous

### Introduction

Plants are one of the most important and traditional sources of medicines [1]. The important advantages claimed for therapeutic uses of medicinal plants in various ailments are their safety besides being economical, effective and their easy availability [2]. *Syzygium aromaticum* or Clove has been used traditionally as a spice for thousands of years, and provides a rich and spicy addition to our favourite recipes [3]. Hussain et al. [4] described in his article that cloves are famous for its spices and widely used in cooking throughout the world especially in the Europe and Asia. Cloves are also essential in the manufacturing of herbal medicine such as Indian Ayurvedic medicine and Chinese medicine [5]. Khan et al. [6] updated that clove is rich in minerals such as calcium, iron, phosphorus, sodium, potassium, and vitamin A and vitamin C. They also described in his article that the health benefits of clove oil can be attributed to its antimicrobial, antifungal, antiseptic, antiviral, aphrodisiac and stimulating properties. Ahmad et al. [7] reported that clove oil is a major component of eugenol which is used to reduce pain in the nerves during tooth extraction usually when there is complication known as "dry socket". Markowitz et al. [8] reported that eugenol also forms cement when it is mixed with Zinc Oxide and applied to the tooth as temporary filling of cavities and its oils are also used in the production of antibiotics for its antimicrobial properties. Martinez et al. [9] updated that their potential uses as alternative remedies for the treatment of many infectious diseases and also noted that essential oils and extracts of various species of edible and medicinal plants, herbs, and spices constitute very potent natural biologically active agents. The objective of our present research was to explore the pharmacological activity and investigate the mechanism of action of clove oil and its main component.

### Botanical Description:

Kingdom –Plantae  
Phylum –Angiosperms  
Order- Myrtales  
Family –Myrtaceae  
Genus –*Syzygium*  
Species –*aromaticum*

### Phytochemistry

Clove contains 14-20% of volatile oil that includes eugenol, acetyleugenol, sesquiterpenes ( $\alpha$ - and  $\beta$ -caryophyllenes) and small quantities of esters, ketones and alcohol [10]. Singh et al., [11] reported that clove also contains tannins, sitosterol and stigmasterol. Mittal et al., [12] reported that other essential oil ingredients of clove oil are vanillin, crategolic acid, tannins, galloannic acid, methyl salicylate, flavonoids eugenin, kaempferol, rhamnetin, eugenitin and triterpenoids like oleanolic acid. Lim et al. [13] described in his paper that the constituents of the oil also include methyl amyl ketone, methyl salicylate,  $\alpha$  and  $\beta$ -humulene, benzaldehyde,  $\beta$ -ylangene and chavicol.

### Pharmacological Activities

Phenolic compounds such as eugenol show antioxidant capacity and free radical scavenging activity. [14]. Gulsin [15] reported that the antioxidant activity of eugenol and one of its isomers isoeugenol has been studied by using iron-mediated lipid peroxidation and auto-oxidation of Fe<sup>2+</sup>. Solmaz

et al. [16] reported that eugenol had the inhibitory effect on lipid peroxidation. Antioxidant activity of eugenol is potent to form complexes with reduced metals [17]. Nejad et al. [18] reported that isoeugenol causes a decrease in the formation of iron-oxygen chelate complex, which is the initiating factor of lipid peroxidation.

Hemaiswarya, and Doble, [19] investigated that the combination of eugenol with two antibiotics, vancomycin and a  $\beta$ -lactam, showed an increased membrane damage in bacteria which means a synergistic effect. It has been also demonstrated that penetration of vancomycin and  $\beta$ -lactam, in combination with eugenol, has increased and resulted in more antimicrobial effect [20]. Atsumi et al. [21] reported that eugenol at the concentrations of 16 to 128  $\mu\text{g/mL}$ , decreased the hemolytic activity and the release of tumor necrosis factor alfa (TNF- $\alpha$ ) in a dose dependent manner. Adefegha et al. [22] also found that depending on the concentration of eugenol, production of staphylococcal enterotoxin has been reduced significantly. As a result, it is suggested that eugenol could be used as a food additive because of the inhibitory effect on growth of bacteria and suppressive effect on the production of exotoxins of *S. aureus*. Investigations of anti-inflammatory effects of eugenol, have suggested that this compound is able to suppress the expressions of cyclooxygenase II enzyme [23]. Eugenol dimers can inhibit the expression of cytokines in macrophages, which are stimulated by polysaccharides [24]. Krasimir et al. [25] reported that eugenol also has an inhibitory effect on cell proliferation via suppression of NF-Kappa B (NF-kB) and the activation of NF-kB induces reduction in the incidence of gastric tumors. Manikandan et al. [26] noted that eugenol can also modulate the expression of NF-kB target genes which are responsible for the regulation of cell proliferation and cell survival. Feng and Lipton, [27] reported that eugenol has been found to exert antipyretic activity in rabbits when given intravenously and intragastrically and may reduce fever through a similar central action to allopathic antipyretic drugs such as acetaminophen. It has also been found to have a preventive effect on dopamine depression and lipid peroxidation, which can protect depression induced by 6-hydroxyl dopamine [28]. Fabio et al. [29] investigated that eugenol has prevented depression by decreasing the lipid peroxidation and stimulating reduced glutathione (GSH) and also noted some inhibitory effects of such spices on the activity of Na<sup>+</sup>/K<sup>+</sup> ATPase in kidney and intestine. It is also possible that spices have toxic effects on mitochondrial function which leads to decrease in ATP level which influence the mechanism of cell growth, viability and aging. Akbar et al. [30] updated that the toxic effects of anesthetic doses of eugenol on African clawed frogs demonstrated damage in kidney and some morphological alteration and cell apoptosis in renal cells. The cytotoxic effects of eugenol, induction of reactive oxygen species (ROS) production and reduced levels of GSH have been studied in human submandibular cell line and suggested that formation of benzyl radicals is the main cause of low GSH of eugenol is found to be related to ROS-independent mechanisms [31]. Akbar et al. [30] also described in his research paper that eugenol is also found potential to decrease the activity of dehydrogenase enzymes in human osteoblastic cells in a dose dependent manner. They also evaluated the cytotoxic effects of eugenol on human pulp cells and also the expression of molecular markers in osteogenic differentiation. Observations suggested that eugenol used for endodontic treatment, may have cytotoxic effects on the normal function of stem cells [30]. Marchase et al. [32] studied that the cytotoxicity of eugenol was in three different malignant and nonmalignant human derived cells. The malignant Hep G2 hepatoma cells, malignant Caco-2 colon cells and nonmalignant human VH10 fibroblasts were chosen to determine the cytotoxicity of eugenol. They noted in his experiment that eugenol was found to be toxic in human VH10 fibroblasts and Caco-2 colon cells but not in Hep G2 hepatoma cells. Furthermore, eugenol has been found to induce apoptosis by destruction the mitochondrial membrane potential and production of reactive oxygen species. Eugenol showed different degrees of cytotoxicity in HL60 cancer cells and inhibited the cell growth by 50% at a concentration of 23.7  $\mu\text{M}$ . It was found that eugenol is able to inhibit the proliferation of melanoma cells. Such effect resulted in a considerable delay in tumor growth and about 40% decrease in the size of tumor.

chemopreventive effect of eugenol on DNA damage induced by 7,12 dimethylbenzanthracene (DMBA) has been evaluated in MCF-7 cells [32]. Kumar et al. [33] discussed that eugenol is able to suppress the DMBA activation and acts as a potential chemo preventive compound. The also noted that after oral administration of eugenol for two weeks in rodents, the frequency of micro nucleated erythrocytes was decreased significantly. The results provided that eugenol has the capacity of mutagenicity in male mouse and causes mutation, particularly in the anaphase of polychromatic erythrocytes of male mouse [33]. Sarrami et al. [34] also observed several adverse effects after use of dental products which contain eugenol. Localized irritation of the skin; ulcers, allergic dermatitis, tissue necrosis and rarely even anaphylactic-like shock have been reported in different studies [34]. The allergic capacity of eugenol containing fragrance was evaluated in approximately 24,000 individuals. Findings reported that 25.5% of health care workers, 16.5% of non-health care workers, 39.39% of metal workers and 16.3% of people in other occupations showed allergic reactions to eugenol. Yongjian et al. [35] analyzed the antitermitic and antifungal activities of flower buds essential oil from *Syzygium aromaticum* and its dominant constituents. The essential oil components were analysed by gas chromatography and the major compound of essential oil was eugenol. The results demonstrated that at the dosage of clove essential oil had 100% mortality to *Reticulitermes chinensis* after testing for 5 d. Furthermore, they found eugenol killed all termites after testing for 3 d, with an LC50 value of 12.1 mg/g. They also concluded that eugenol was principal antifungal and natural wood preservatives. Srivastava [36] noted that the action of plant derived molluscicides decrease the level of serotonin and inhibit prostaglandins synthesis by inhibiting 5-lipoxygenase and leukotriene which affect the CDCs and reduce the release of ovulation hormone, resulting a decrease in the fecundity of treated snail.

## Conclusion

This review discusses pharmacological activities of all the phytoconstituents isolated from *S. aromaticum* till date. The main constituents of clove essential oil are phenylpropanoides such as carvacrol, thymol, eugenol and cinnamaldehyde. The major pharmacological activities of clove are antimicrobial, anti-inflammatory, anesthetic, analgesic, antioxidant and anticancer. Some other activities are aphrodisiac, mosquito repellent, insecticidal and antipyretic. All the major activities of clove are explained and appreciable results have been reported regarding the various activities discussed in the review. Furthermore, considering its versatile medicinal uses, there is an ample scope for future research.

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