

## **Eugenol as Potential Medicine- Review**

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**Type of manuscript:** Review

**Running title :** Potential medicine- Eugenol

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## ABSTRACT

Eugenol is a naturally occurring phenolic molecule that is used in dentistry. Eugenol is also used as a topical anaesthetic agent in dentistry. Moreover it has many pharmacological effects like anaesthetic and analgesic action in dentistry, and also antibacterial, anti-oxidant effects. Eugenol and thymol were found to possess general anesthetic properties. Since it is a phytochemical constituent, it exhibits highly potent anti-cancer activities that have been attributed to their effect on multiple signalling and apoptotic pathways. It illustrates potent antibacterial potential against the numerous strains of gram positive and gram negative bacteria. Eugenol damages the cell membrane and a cell wall which then induces cell lysis in gram positive and gram negative bacteria. It is also used as an irritant, sensitiser, flavouring agent, root canal medicaments in dentistry. Clove oil or eugenol can be used as local anesthetic and also used as an anesthetic agent in several fish species. In this review study, an elaborate role of eugenol as a potential medicine is required. The review of the scientific literature was done in the preparation of manuscript. The systems and databases were searched for relevant articles from Pubmed and Google scholar. Databases of individual journals were searched for keywords in this review. The aim of this study is to analyse the role of eugenol as potential medicine. The published article was selected from the year 1980 to 2020. In this review, 47 articles were reviewed. Hence future research should be aimed at identifying different activities of eugenol.

**Keywords:** Eugenol, Antibacterial agent, Clove oil, Dentistry, Antioxidants, Anaesthetics.

## INTRODUCTION :

Eugenol is an aromatic molecule found in several plants and used in dentistry for analgesic and antiseptic purposes. It inhibits pro-inflammatory medication including nitric oxide synthase, cyclooxygenase and lipoxygenase. It also regulates ion channels involved in pain signalling. Eugenol exerts anaesthesia when inhibition of sodium current is considered as one of the mechanisms [1]. It is a photogenic bioactive component that is frequently found in diversified herbal plants possessing well defined functional properties. Prominent sources of eugenol are clove, cinnamon, tulsi and pepper that is common everywhere. Various extraction methods have been practised globally in nutraceuticals from the plants. Eugenol has been approved to encompass numerous beneficial aspects against oxidative stress, inflammation, cancer, disorders, hyperglycaemia[2]. Eugenol plays an important role in dental and oral hygiene to patients. It is used as a flavour, irritant, sensitiser and produces local anesthetic. Ability of the zinc oxide eugenol-based endodontics sealers is used to influence the periapical tissue healing, and is considered in the view of use in all anti-inflammatory and toxic properties. Dental materials containing eugenol used mostly in dental clinics and hospitals. Whenever zinc oxide eugenol is applied to the dental cavity, a small amount of eugenol diffuses through the dentin to the pulp. Even low concentration leads to anti-inflammatory local anaesthetic on pulp [3]. Use of zinc oxide eugenol temporary filling may facilitate pulpal healing and on the other hand, eugenol concentrations when high, leads to cytotoxic effects, direct application of eugenol to the pulp

tissue may result in the extensive tissue damage. Ability of the zinc oxide eugenol-based sealers has anti-inflammatory and toxic properties [4]. Moreover Eugenol is known to have a detrimental effect on both composite resin and dentin bonding agents, It is identified that there is no significant leakage observed when it is treated with eugenol containing and eugenol free dental temporary cements [5]. Eugenol, usually in combination with zinc oxide, is used in dentistry as wound dressings, impression materials and temporary filling materials. Dental material containing eugenol can have some harmful effects and zinc oxide eugenol have been shown to give cytotoxic effects on the cell culture. Treatment of rat mucosa with pure eugenol or clove oil will cause denaturation of proteins, swelling and necrosis. It is sometimes considered to be irritating agents to the tissues [6]. Eugenol and Eugenol containing cements can alter the surface of the cured composite resins. This may be due to the combined effects of eugenol, the suitable properties of temporary cement and rubbing action required to remove the cement. Reaction between bisGMA and eugenol results in softening followed by mechanical abrasion that is also found on the tissue surface [7]. Eugenol is considered as an effective promising anaesthetic in fish culture because of its low cost, efficacy and safety margin for fish and lack of toxicity to humans. Clove oil may be appropriate for use in the commercial aquaculture situations [8]. Eugenol has a potential role in alleviating and preventing chronic disease such as cancer, inflammatory reactions and other conditions. It possesses multiple antioxidant properties [9]. Eugenol has attracted attention mainly due to its anti-inflammatory properties. It is volatile and insoluble and acts as skin irritant. The cytotoxic, antioxidant and anti-inflammatory effects of eugenol were assessed in human neutrophils, and keratinocytes [10]. It is a natural capsaicin congener widely used in dentistry. It inhibits voltage activated sodium and calcium channels in TRPV 1 independent manner. Eugenol also inhibits voltage gated potassium channels to be an irritable action of eugenol [11]. It has the ability to allay tooth pain. Indication of voltage gated sodium channel and activation of TRPV 1 results that eugenol also serve as local anaesthetic for other pathological pain conditions [12]

Previously our team had conducted numerous clinical trials [13–19] and lab animal studies [20–24] and in-vitro students [25–27] over the past 5 years. Our team has rich experience in research and we have collaborated with numerous authors over various topics in the past decade [28][29–51]. Now we are focussing on epidemiological surveys. This idea for this survey stemmed from the current interest in our community.

### **EUGENOL AS TOPICAL ANESTHESIA:**

Eugenol is a topical analgesic agent widely used in dental clinics. To elucidate the molecular mechanisms underlying its energetic action, it is investigated the effect of eugenol on high-voltage activated calcium currents in primary afferent dental neurons[52]. It is expected that clove oil might replace widely used topical anaesthetic benzocaine there by reducing the dosage of the drugs the patient receives, lowering cost on dentists and allowing more patients to benefit from cheap and largely available topical anaesthetic. Although local anaesthetic injection used to alleviate pain and reduce anxiety. Topical anaesthetic is used to reduce the pain [53]. This

natural anaesthetic agent can also be used in aquaculture medium. Improper clove oil may decrease the fish viability, distort physiological data or result in death of fishes. Method of preparations and precautions for administration changes fish behaviour and its potential for compromising fish health and effectiveness of water quality parameters [54]. Essential oil extracted from the dried flower buds of clove oil used as anaesthetic to relieve pain and promote healing and also used in fragrances and flavouring industries [55]. Benzocaine, eugenol and menthol are effective anaesthetic for the use with freshwater organisms. Benzocaine did not promote any toxic effect on fish. Compared to other topical anaesthetics and natural phenolic compounds, eugenol has been considered as a better anaesthetic agent topically used in dentistry and also in some animals etc... Although it does not cause any side-effect being used as a topical anaesthetic[56] . Improper clove oil will cause such effects. It can also exhibit some other effects like cytotoxic effects, antibacterial effects, anti-oxidant, anti-inflammatory effects [57]. It is an aromatic molecule found in several plants. It inhibits pro-inflammatory mediators and inhibits sodium currents in the concentration dependent manner[58]. It is also used as a corneal anaesthetic when applied topically, being included with lidocaine. Sub anaesthetic doses of eugenol produced a good local anesthetic when used with sub anaesthetic dose of lidocaine[59].

#### **PHARMACOLOGICAL ACTIONS OF EUGENOL:**

Eugenol, as a pharmacological agent has been widely used in dentistry. Eugenol exhibits a pharmacological action on almost all systems. It possesses significant antioxidant, anti-inflammatory and cardiovascular properties. Metabolism is identified and has been used as a penetration enhancer[60]. Eugenol and essential oils have been found to reduce raised blood sugar level, triglycerides and cholesterol levels and activities of LDH, GPT, and Alkaline phosphatase. Several studies have been reported that therapeutic potential activities of ocimum sanctum, tulsi and several plants can exhibit antidiabetic, cardiovascular, hypolipidemic and hepatoprotective activities [61]. And essential oils can exhibit some antibacterial activity [62]. Corneal penetration of eugenol is important for successful fungal keratitis treatment. It has potent antifungal activity against candida, aspergillus and dermatofibrosis. It is used in the treatment of keratomycosis .It is a simple photochemical constituent exhibiting highly potent anti-cancer activities which have been attributed to their effects on multiple signalling and apoptotic pathways [63]. And anti-cancer effects of eugenol are investigated against colon cancer cells. The results show that a molecular mechanism of eugenol induces apoptosis in human colon cancer cells [64]. Clove oil polyphenol eugenol illustrates potent antibacterial activity against gram positive and gram negative bacteria. It damages the cell membrane and cell wall, inducing cell lysis[65].

#### **EUGENOL IN DENTISTRY:**

Eugenol also acts as a topical anaesthetic in dentistry. Although it is widely used in dentistry, its molecular mechanism for anaesthetic property is little. Previous research has identified that eugenol in dentistry can inhibit the sodium currents in dental afferent neurons of a rat. It

contributes to its analgesic effect[66]. Eugenol odour can evoke memories and unpleasant dental experiences and may contribute to dental anxiety and fear. It is seen that odour brings negative conditioning towards the dental office [67]. Zinc oxide eugenol has been used widely in dentistry for indirect pulp capping, and acts as a temporary root canal sealer. It is identified that free radicals are known to have a greater effect on cancer cells than the normal cells. Oxidative eugenol is likely to have a greater cytotoxic effect on tissue cells than bis-eugenol [68]. Eugenol has been approved to encompass aspects against oxidative stress, inflammation and cancer. Our institution is passionate about high quality evidence based research and has excelled in various fields ([46,47,69–77]. Application in dentistry, pulpal irritation such as pulp inflammation and aspiration of the pulpal cells are more common. Temporary zinc oxide eugenol restoration should not be inserted in deep carries without linear or bases covering the exposed dentinal tubules [78].

### **OTHER FEATURES:**

Eugenol can be used as a local irritating agent that can lead to cytotoxic effects. It is used as a root canal irrigant, root canal medicament and also as a temporary cement. Eugenol has certain pathobiological effects. They can have the ability to inhibit polymerisation of resins [79]. Eugenol inhibits inflammatory and regulates redox status. It is effective in administration for the management of acute pancreatitis. The compound is very promising for versatile applications, and the design of new drugs based on the pharmacological effects of eugenol could be beneficial[80].

### **CONCLUSION :**

This review has access to the properties of Eugenol, especially topical anaesthetic properties of using clove oil. Other pharmacological effects on the use is noted. Hence future researchers should be aimed at different activities of clove oil, method of identification and properties over Benzocaine like drugs as anaesthetics. Elaborated articles on topical anaesthetic is required mostly.

### **ACKNOWLEDGEMENT:**

We thank saveetha dental college for the support to conduct the study or review.

### **AUTHOR CONTRIBUTIONS:**

The authors have carried out the study by collecting data from search engines and drafted the manuscript by necessary information. They have aided in conception of the topic, have participated in the review and have supervised in preparation of manuscript. The authors have participated in the study design and have coordinated in developing the manuscript. All authors have discussed the study details among themselves and contribute to the final manuscript.

### **CONFLICT OF INTEREST:**

No potential conflict of interest relevant to this article was reported.

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