

Eugenol as a Bioactive Compound: Current Knowledge and Future Perspectives

Shaik Shabana ¹, Mandla Jaya Divya², Kamsali Sowmya³, Karivemula Lalitha⁴, Momin Umme Sulaim ⁵, Nemakallu Maheswari ⁶, **Chakali Ayyanna^{7*}**

¹ Assistant Professor, Department of Pharmacology, Creative Educational Society's College of Pharmacy, Chinnatekur, Kurnool, and Andhra Pradesh-518218, India.

^{2,3,4,5&6} Department of Pharmacology, Creative Educational Society's College of Pharmacy, Chinnatekur, Kurnool, and Andhra Pradesh-518218, India.

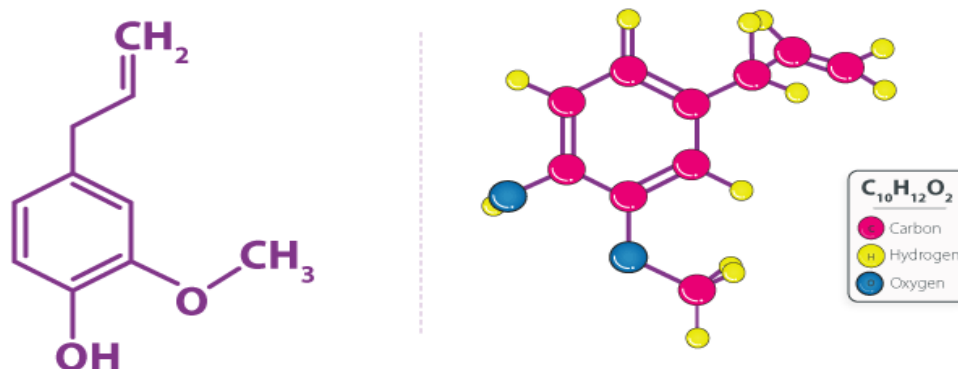
⁷Associate Professor, Department of Pharmacology, Creative Educational Society's College of Pharmacy, Chinnatekur, Kurnool, and Andhra Pradesh-518218, India

Abstract: The main bioactive component of clove oil, eugenol, is known for a variety of pharmacological and medicinal uses. It works well against a variety of illnesses and ailments because of its strong antibacterial, anti-inflammatory, analgesic, and antioxidant properties. By preventing biofilm formation on medical devices, exhibiting anticandidal activity, and having leishmanicidal activities on *Leishmania amazonensis*, eugenol exhibits antimicrobial potential. Its neuroprotective advantages include antidepressant and antipyretic properties, as well as possible uses in the treatment of Alzheimer's disease. Additional pharmacological actions include cytotoxicity to HeLa cells, chemo preventive properties, vasorelaxant activity, and the capacity to lessen lesions in the gastrointestinal mucosa. Its effectiveness in rheumatoid arthritis, antihyperglycemic action in metabolic disorders, and alleviation of gastrointestinal dysfunction in rats generated by restraint stress that resembles IBS is also supported by experimental evidence. These complex effects highlight the therapeutic promise of eugenol; nonetheless, pharmacokinetic limits, stability problems, and dose-dependent toxicity still pose difficulties for clinical use. This study summarises the available data on the bioactivity of eugenol and outlines potential future applications in a variety of medical fields for both prevention and treatment.

Key words: Eugenol, antioxidant, anti-inflammatory, analgesic, and antibacterial activities, neuroprotective, chemopreventive effects, cytotoxicity.

1. INTRODUCTION

Around 80 to 90 percent of clove (*Syzygium aromaticum*) oil's essential oil content is made up of eugenol (4-allyl-2-methoxyphenol), a naturally occurring phenolic molecule that is also significantly present in cinnamon, basil, nutmeg, and other aromatic plants ^[1]. It is a pale-yellow, fragrant, oily liquid that is frequently used in culinary and dental applications for flavouring, fragrance, antibacterial, and anaesthetic effects. Eugenol is classified as generally recognised as safe (GRAS) and non-mutagenic by the World Health Organisation (WHO) ^[2].



EUGENOL

Antioxidant, Anti-Inflammatory, Analgesic, and Antimicrobial Properties: Eugenol's antioxidant, anti-inflammatory, analgesic, and antibacterial properties have been highlighted in a large body of research [2]. Its use in high-value industries such as medicines, dentistry, flavouring agents, agriculture, and cosmeceuticals is a result of its pharmacological spectrum [2].

In terms of antibacterial action, eugenol works well against a variety of bacteria, both Gram-positive and Gram-negative, fungi (*Candida* species), and some viruses, including strains that are resistant to drugs [3]. Additionally, formulations like micro- and nanoemulsions greatly improve its aqueous solubility and activity, which is especially useful for antibacterial and food preservation applications [3]. Through the inhibition of microbial adhesion, survival, and virulence factor expression, it has demonstrated efficacy against biofilm formation, a significant problem in healthcare settings. *E. coli* and other pathogens' metabolic activities and genes linked to biofilms are disrupted by hydrophilic copolymers and sol-gel coatings containing eugenol [4-5]. Notably, ROS-induced bacterial membrane rupture mediates the eugenol breakdown of carbapenem-resistant *Klebsiella pneumoniae* biofilms [6].

Prevention of Biofilm Development on Medical equipment: The increasing risk of biofilm-mediated infections on medical equipment necessitates the use of efficient intervention techniques. By decreasing bacterial viability, dispersing biofilm matrices, and downregulating

biofilm-associated gene expression (such as *pgaA*) in *E. coli*, eugenol exhibits biofilm inhibitory effect through a variety of mechanisms [4]. It has the potential to reduce microbial colonisation of implanted biomaterials when added to antibacterial coatings and copolymers [5]. Eugenol efficiently breaks down carbapenem-resistant *K. pneumoniae* biofilms in multidrug-resistant environments by causing ROS production and membrane disruption [7].

Alzheimer's disease and Neuroprotective Effects: Eugenol has strong neuroprotective qualities that are especially pertinent to neurodegenerative illnesses like Alzheimer's. It reduces neuroinflammation, scavenges free radicals, reduces oxidative stress, and alters the NF- κ B and calcium signalling pathways [8]. Through anti-apoptotic and anti-necroptotic pathways, eugenol preserves neuronal integrity, improves cognitive impairments, and decreases amyloid- β formation in preclinical models [9]. Eugenol, when included in a diet, offers protection against a number of brain conditions, such as anxiety, stress, Parkinson's disease, and Alzheimer's disease [10].

Despite **neuroprotection**, eugenol has **vasorelaxant, antiplatelet, and antihyperglycemic** properties. It may also have cardiovascular advantages. Through the cPLA₂-NF- κ B-Ca²⁺ signalling axis, it regulates platelet activation, which lowers platelet aggregation and thrombus formation in vivo [11]. Eugenol is thus positioned as a potentially effective anti-thrombotic and cardiovascular protective medication. Eugenol also has the ability to lower blood sugar levels, most likely as a result of its antioxidative and metabolic control mechanisms [12].

Gastrointestinal Protective Effects and IBS-Like Dysfunction: Using antioxidative and cytoprotective pathways, eugenol has gastroprotective activity, which includes the decrease of stomach mucosal lesions [13]. Although there are few direct researches on eugenol specifically, its overall stress-modulating, anti-inflammatory, and motility-regulating qualities imply potential therapeutic efficacy in functional GI disorders in the mitigation of restraint stress (RS)-induced IBS-like gastrointestinal dysfunction [14].

Rheumatoid Arthritis and Anti-Inflammatory Actions: Eugenol has anti-inflammatory properties in rheumatoid arthritis models by inhibiting pro-inflammatory cytokines such as

VEGF, IL-6, and IL-8 as well as NF- κ B signalling ^[15]. Its potential in treating chronic inflammatory joint illnesses is highlighted by its ability to reduce synovial inflammation and induce apoptosis in activated immune cells.

Anticancer, Cytotoxic, Chemopreventive Actions: By interfering with cell viability, inducing apoptosis, encouraging the production of reactive oxygen species, and destroying mitochondrial membrane potential, eugenol exhibits cytotoxicity against HeLa cells and other cancer types. Eugenol specifically kills HeLa cells at 500 μ M and works in concert with chemotherapeutics like gemcitabine and cisplatin to increase the potency of cytotoxicity and make cells more sensitive to radiation ^[16].

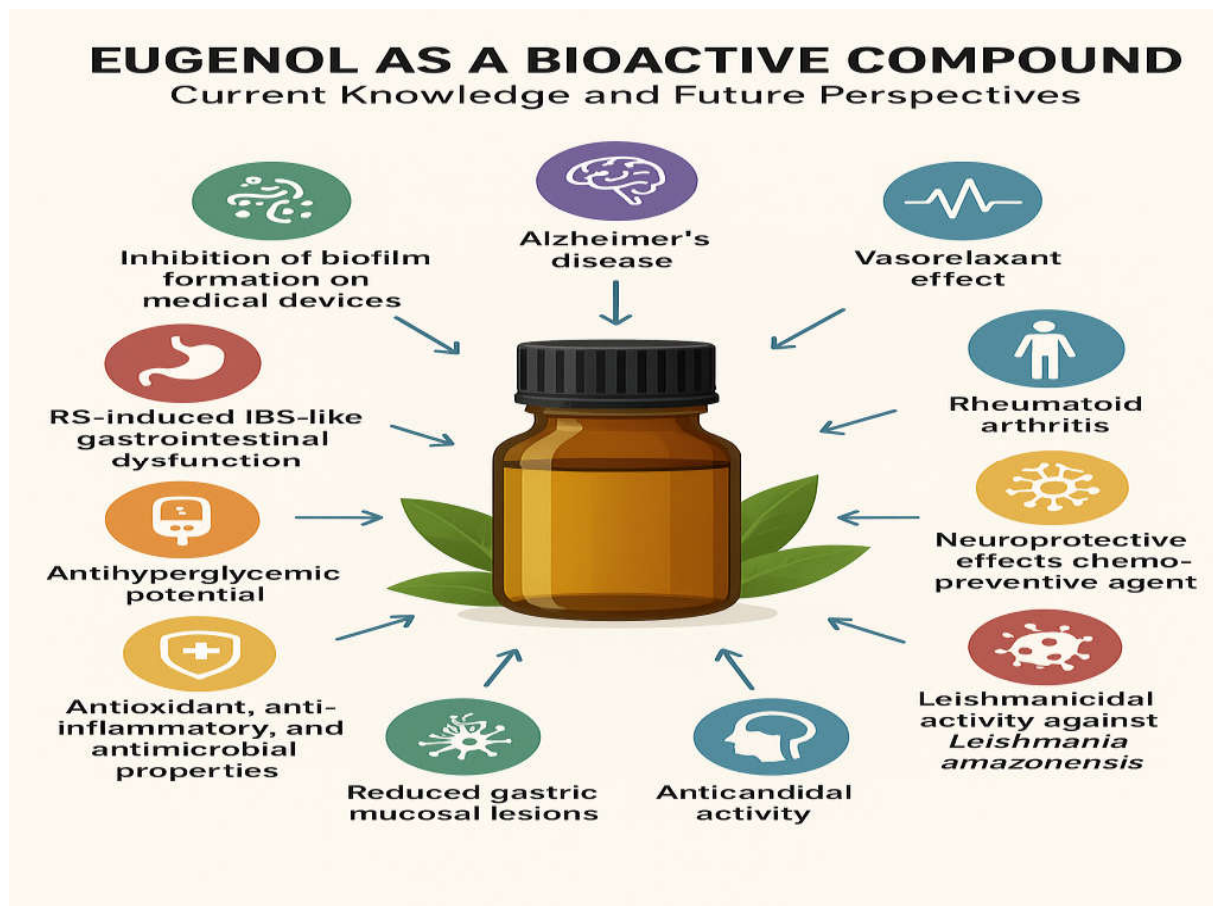
Antidepressant and Antipyretic Effects: Eugenol has antidepressant and antipyretic properties, most likely due to its central action, which involves neurotransmitter pathway modification and MAO-A/MAO-B inhibition ^[17]. Its therapeutic application is further expanded by these neuropsychiatric effects.

Antiparasitic: Eugenol has leishmanicidal activity; when prepared as oil-in-water emulsions, it efficiently targets *Leishmania donovani* promastigotes and intracellular amastigotes ^[18]. Despite the lack of studies on *Leishmania amazonensis*, this demonstrates the broad range of antiparasitic properties of eugenol.

Eugenol has anticandidal activity against *Candida albicans* by preventing filamentation, adhesion, and biofilm formation. It exhibits synergistic effect against resistant strains of *Candida* when used with antifungals such as fluconazole ^[19].

Challenges with Safety, Toxicity, and Formulation: Eugenol can cause hepatotoxicity, neurotoxicity, contact dermatitis, sedation, and, in rare cases, mutagenesis consequences at high exposures, although being generally harmless at moderate dosages ^[20]. Its low water solubility and volatility make formulation and distribution more difficult. However, by enhancing

bioavailability and targeted administration, nanotechnology-based vehicles (nanoemulsions, inclusion complexes) [21].



2. DISCUSSION

Eugenol's strong antibacterial, anti-inflammatory, and antioxidant qualities make it a useful multipurpose bioactive agent. Notable antibiofilm activity is part of its antimicrobial range, and this activity is very important for preventing infections on medical devices. While eugenol efficiently reduces colonisation in a rat otitis media model, it also dramatically inhibits the formation of biofilms by MRSA and MSSA in vitro, destroying existing biofilms, damaging bacterial membranes, and lowering enterotoxin and biofilm-related gene expression [22].

Eugenol-loaded chitosan coatings, especially those that include mesoporous silica nanoparticles (MSNs), provide a viable method for preventing biofilm formation on medical equipment, according to parallel findings [23]. By decreasing extracellular polymeric substances (EPS), motility, extracellular DNA, and quorum sensing activity, eugenol nanoemulsions prevent *Listeria monocytogenes* biofilms on stainless steel [24]. All things considered, these findings support eugenol's extensive antibiofilm properties and prospective application in infection prevention settings.

In stress-induced models, eugenol, which targets gastrointestinal health, shows considerable therapeutic benefit. Oral treatment at 50 mg/kg reduced plasma corticosterone levels and decreased faecal output increases caused by restraint stress in rats by around 80%. Additionally, eugenol improved antioxidant defences and altered serotonergic activity in important brain areas [25]. These results indicate its promise for treating IBS-like dysfunctions by highlighting its essential control of the HPA axis and monoaminergic neurotransmission.

Eugenol successfully reduced oxidative damage and neuropathy in rats exposed to acrylamide from a neuroprotective and anti-stress standpoint, lowering indicators including ROS, MDA, and acetylcholinesterase activity while also enhancing behavioural results [26]. Its potential usefulness in neurodegenerative diseases is increased by such antioxidant-based neuroprotection. The vasorelaxant properties of eugenol support cardiovascular health. According to earlier research, it partially depends on endothelium-derived NO to relax vascular smooth muscle by blocking voltage-dependent and receptor-operated calcium channels [27–28]. These results highlight the potential use of eugenol in the treatment of hypertension and vascular tone. In experimental models of rheumatoid arthritis eugenol has shown anti-inflammatory potential by lowering serum pro-inflammatory cytokines and reducing joint oedema [29]. These findings imply that eugenol may be used as a supplement to reduce persistent joint inflammation.

In diabetic animals, eugenol also has antihyperglycemic actions by lowering oxidative stress and regulating glucose homeostasis [30]. It may provide comprehensive advantages in cardio-

metabolic illnesses by bridging neuroprotective and vascular benefits through its impact on metabolic pathways. Additionally, the chemical has anticancer characteristics. It inhibits the growth of HeLa and other cancer cells, causes apoptosis, and produces ROS. Eugenol increases cytotoxicity when used with chemotherapeutic drugs, which could lead to better treatment results [31]. Its potential in chemo preventive techniques is highlighted by this context-dependent modification of oxidative equilibrium.

Eugenol exhibits antipyretic and antidepressant-like activity in relation to its neuropsychiatric effects, which are probably mediated via the augmentation of neurotransmitter systems and the inhibition of monoamine oxidase (MAO-A/B) [32]. It shows promise for supporting mood and cognition because of these qualities as well as its neuroprotective and stress-modulating abilities. When used in combination with fluconazole, eugenol exhibits synergistic antifungal potential by inhibiting *Candida albicans* biofilms and interfering with adhesion and filamentation. Although there is currently little information on *Leishmania amazonensis* specifically, its leishmanicidal action broadens its antimicrobial spectrum and demonstrates effectiveness against *Leishmania* species [33].

Challenges and Formulation Techniques: Eugenol has a number of translational issues in spite of its broad range of bioactivity. Particularly in dental settings, high dosages can cause toxicity, such as hepatotoxicity, sedation, nephrotoxicity, and allergic contact reactions [34]. Stability and efficient delivery are further restricted by its volatile nature and limited water solubility. Recent developments in formulation, however, provide encouraging answers. Medical device surfaces with eugenol-embedded sol-gel coatings have the potential to be antibacterial [35]. Eugenol is positioned for safer and more efficient therapeutic applications thanks to nanoemulsions and other carriers that improve absorption provide controlled release, and lower toxicity.

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3. CONCLUSION

The primary component in clove oil, eugenol, has a wide range of pharmacological actions, which makes it a promising bioactive substance for a variety of medicinal uses. Its strong antibacterial, anti-inflammatory, and antioxidant qualities support its capacity to prevent infections and stop biofilm formation on medical equipment. Its relevance in neurological and psychiatric illnesses is highlighted by its neuroprotective effects, which include prospective benefits in Alzheimer's disease, stress-induced gastrointestinal dysfunction, and antidepressant and antipyretic actions. In addition to its significant cytotoxicity towards HeLa cells, eugenol has vasorelaxant, antihyperglycemic, and chemopreventive properties, indicating potential in cancer, metabolic, and cardiovascular treatments.

In addition, it has anticandidal efficacy, leishmanicidal action against *Leishmania amazonensis*, and decreases stomach mucosal ulcers. Notwithstanding these advantages, issues including low solubility, volatility, and dose-dependent toxicity call for safety assessments and optimised administration methods. Eugenol has great potential as a multipurpose therapeutic agent with improvements in nanoformulations and targeted delivery; more in vivo and clinical research is necessary to convert its wide range of bioactivity into secure, efficient medical uses.

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