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Multifarious Pharmacological Applications of Farnesol: A Review

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ABSTRACT

Farnesol, an acyclic sesquiterpene alcohol widely distributed in essential oils of aromatic plants, has gained considerable attention due to its diverse pharmacological activities. Extensive preclinical evidence demonstrates its antimicrobial, antifungal, anti-inflammatory, anticancer, antihyperglycemic, and neuroprotective properties. Mechanistically, farnesol modulates multiple signaling pathways, including nuclear factor kappa B (NF-κB), phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), and mitogen-activated protein kinase (MAPK), while regulating oxidative stress and apoptosis. It also exhibits potent anti-biofilm activity through interference with quorum sensing and microbial adhesion.

Recent studies have expanded its therapeutic scope, highlighting roles in neurodegenerative disorders, metabolic regulation, and gut–brain axis modulation. However, despite promising findings, evidence remains largely limited to in vitro and animal models. Challenges related to bioavailability, formulation stability, and lack of clinical validation continue to impede its translational potential. This review critically evaluates the pharmacological properties of farnesol, integrates recent advances, and outlines key limitations and future directions for its development as a therapeutic agent.

Keywords: Farnesol, anti-inflammatory, anti-biofilm, neuroprotection, apoptosis, pharmacological mechanisms

1. INTRODUCTION

Sesquiterpenes are a diverse class of terpenoids composed of three isoprene units and are widely distributed in nature, particularly in plants where they function as semiochemicals and defensive metabolites. These compounds have attracted considerable scientific interest due to their broad spectrum of biological activities, including antioxidant, immunomodulatory, and cell-protective effects. Farnesol is an acyclic sesquiterpene alcohol commonly found in the volatile oils of aromatic plants such as Cymbopogon (lemongrass), rose, and orange blossom. It serves as a plant and fungal metabolite and exhibits notable antimicrobial properties. Farnesol is especially abundant in essential oils including citronella, neroli, cyclamen, tuberose, musk, balsam of Peru, and tolu.

As a naturally derived compound, farnesol has gained attention as a promising alternative to synthetic additives in cosmetic and personal care formulations, owing to its pleasant fragrance and favorable safety profile. Beyond its commercial applications, accumulating evidence highlights its significant pharmacological potential, encompassing antibacterial, anti-inflammatory, antifungal, anticancer, antihyperglycemic, and neuroprotective activities. In this review, we present a comprehensive overview of the pharmacological properties of farnesol, discuss its underlying mechanisms of action, and evaluate its potential therapeutic applications based on recent scientific literature.

2. PHARMACOLOGICAL APPLICATIONS

2.1Anti-inflammatory & Anti-cancer activity

Modulation of Pro-inflammatory Cytokines: Evidence from experimental studies indicates that farnesol suppresses the expression of major pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), which are key mediators of inflammatory signaling pathways. Through this immunomodulatory effect, farnesol may contribute to the alleviation of inflammatory skin conditions such as eczema, psoriasis, and rosacea.

Farnesol has been shown to inhibit the proliferation of various cancer cell types, including breast and liver cancer cells. Its anticancer activity is mediated through the induction of cell cycle arrest and apoptosis, primarily via modulation of key signaling pathways such as phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), mitogen-activated protein kinase (MAPK), and nuclear factor kappa B (NF-κB), along with the regulation of pro- and anti-apoptotic proteins.

Young Yun Jung et al. elucidated the potential mechanisms underlying the therapeutic effects of farnesol in cancer and inflammatory disorders. Their findings suggest that farnesol exerts its anti-inflammatory and anticancer activities by modulating Ras protein signaling and inhibiting the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), thereby suppressing the expression of key inflammatory mediators, including cyclooxygenase-2 (COX-2), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6).

Warren Finlay et al. reported the development of a nebulized aerosol formulation of farnesol, which was shown to induce cell death in human lung cancer cells in vitro. The cytotoxic effects were associated with the activation of apoptotic pathways, including the upregulation of pro-apoptotic proteins such as Bax and caspases, downregulation of anti-apoptotic proteins like Bcl-2, and disruption of mitochondrial membrane potential, suggesting a mitochondria-mediated mechanism of action.

Research indicates that farnesol can markedly attenuate inflammation in conditions such as allergic asthma and arthritis by modulating key signaling pathways, including NF-κB, IL-17, and TNF signaling. In addition to its anti-inflammatory effects, farnesol exhibits tissue-protective properties, safeguarding organs such as the liver, lungs, spleen, and testes from oxidative damage induced by toxic agents, including cigarette smoke extract and chemotherapeutic drugs like cyclophosphamide. These findings highlight farnesol's potential as both an anti-inflammatory and cytoprotective agent.

Studies in animal models support its ability to attenuate inflammation in conditions like allergic asthma and arthritis through modulation of major pathways:In ovalbumin-induced asthmatic mice, farnesol reduced allergic responses, decreased pro-inflammatory cytokine ratios (e.g., TNF-α/IL-10), and showed potential NF-κB inhibition.In arthritis models (e.g., Freund's complete adjuvant or formaldehyde-induced), farnesol suppressed inflammation, oxidative stress, and markers like IL-6, IL-1β, IL-17, and TNF-α, often involving NF-κB, TLR4, and related signaling.Broader anti-inflammatory actions include downregulation of NF-κB activation, reducing expression of mediators like COX-2, iNOS, and pro-inflammatory cytokines in various cell and animal models[5,6,7,8].

2.2 Cytoprotective Properties

Farnesol demonstrates tissue-protective effects against oxidative damage: It ameliorated lung injury and inflammation from cigarette smoke extract in rats, reducing oxidative stress markers and preserving antioxidant enzyme activity. Pretreatment mitigated cyclophosphamide-induced toxicity, particularly protecting the testes, liver, and spleen by reducing histopathological damage and boosting antioxidants like glutathione. Additional protection has been noted in models of hepatic injury (e.g., from cadmium or high cholesterol) and other organs, often via NF-κB/NLRP3 modulation and enhanced antioxidant defenses. These effects position farnesol as a promising dual anti-inflammatory and cytoprotective compound, with additional reported benefits like anti-cancer potential and neuroprotection in preclinical settings. However, evidence is primarily from in vitro and animal studies (mostly rodents). No clinical trials in humans have confirmed these therapeutic effects for asthma, arthritis, or organ protection from toxins. Farnesol is widely used in cosmetics (e.g., as a fragrance and deodorant agent) and considered safe at typical exposure levels, but higher doses for therapeutic use would require human safety and efficacy studies. Overall, while the preclinical data is encouraging and mechanistically sound, farnesol's clinical potential remains investigational[14,15,16].

2.3 Anti-biofilmactivity

Anti-biofilm activity to evaluate the potential use of farnesol as root canal irrigants. The findings demonstrated that farnesol was the most effective substance in reducing the biofilm mass.

In vitro study (Alves et al., Brazilian Dental Journal) directly evaluated farnesol (0.2%) alongside xylitol (5% and 20%) and their combination as potential root canal irrigants, compared to 2.5% sodium hypochlorite (NaOCl) and saline. Using the crystal violet assay for biofilm biomass, farnesol significantly reduced biomass in E. faecalis biofilms. It also impacted bacterial viability within the biofilm (dentin disinfection test) and performed well in a simulated root canal environment. The authors noted that farnesol affected both biofilm biomass and cell viability, while xylitol primarily targeted biomass. Overall, farnesol showed the strongest effects among the tested natural substances for disrupting biofilm structure and reducing viable cells, though NaOCl remained superior in direct antibacterial potency[17].

Neves et al., Brazilian Oral Research tested farnesol (0.2%) with xylitol and lactoferrin combinations on E. faecalis and Staphylococcus epidermidis biofilms. Farnesol-containing mixtures were among the most effective at reducing biofilm biomass (via crystal violet assay), with the farnesol-xylitol combo standing out against standard strains[18].

Subsequent research has reinforced farnesol's anti-adhesion and biofilm-disrupting properties against endodontic pathogens like E. faecalis, Candida albicans, and Pseudomonas aeruginosa, suggesting potential as an adjunct irrigant. Farnesol disrupts quorum sensing, inhibits extracellular matrix production, compromises cell membrane integrity, and prevents adhesion/filamentation, making it effective against established biofilms—critical in root canals where biofilms contribute to treatment failure[19].

2.4 Anti-Candida Effects

F-PLGA NPs inhibited planktonic (free-floating) C. albicans cell growth in a dose-dependent manner. They significantly reduced biofilm formation (assessed via XTT metabolic assay) and disrupted pre-formed biofilms more effectively than free farnesol in some assays. Ultrastructural damage was observed via TEM and SEM, including cell membrane disruption and reduced hyphal formation (a key virulence factor in C. albicans biofilms).

Farnesol showed antimicrobial and biofilm anti-adhesion activities of farnesol against E. faecalis, Candida albicans and P. aeruginosa at the concentration of 42.5/50µm, 27.5/37.5µm and 32.5/32.5µm respectively. The researchers evaluated poly(vinyl alcohol)-coated silver nanoparticles (AgNPs-PVA) alongside farnesol for antimicrobial and biofilm anti-adhesion effects against three relevant endodontic pathogens: Enterococcus faecalis, Candida albicans, and Pseudomonas aeruginosa. The authors concluded that farnesol (and AgNPs-PVA) exhibits antimicrobial and biofilm anti-adhesion activities, supporting its potential as a coadjuvant (adjunct) in endodontic treatments. It could serve as an auxiliary irrigant or agent to aid root canal disinfection and inhibit biofilm formation, particularly against persistent pathogens like these[20].

2.5 Anti-fungal activity

Camila Fonseca Bezerra et al., studied the anti-fungal activity of farnesol which is incorporated in liposomes and associated with fluconazole.

Antifungal Activity of Free vs. Liposomal Farnesol:Free farnesol showed moderate inhibitory effects on fungal growth (higher IC_{50} values compared to fluconazole) and inhibited dimorphism (yeast-to-hypha transition), particularly in C. albicans—a key virulence factor.Encapsulation in liposomes significantly enhanced farnesol's antifungal potency, lowering IC_{50} values and improving inhibition across all tested strains. This is attributed to better solubility, stability, and cellular delivery of the hydrophobic farnesol molecule.

Association of anti-fungal activity with Fluconazole:Liposomal farnesol combined with fluconazole demonstrated synergistic or potentiating effects, markedly reducing fungal growth and overcoming some resistance mechanisms in fluconazole-exposed strains.In contrast, free (non-liposomal) farnesol combined with fluconazole showed antagonistic effects in some assays.

Minimum fungicidal concentrations (MFC) were fungistatic overall, with optical microscopy confirmin Farnesol's effects likely involve quorum-sensing disruption and interference with ergosterol biosynthesis pathways. Liposomal delivery addresses farnesol's limitations (volatility, poor aqueous solubility), enabling better penetration and sustained release—similar to benefits seen in prior nanoparticle studies (e.g., PLGA encapsulation). This work supports liposomal farnesol as a promising adjunct to fluconazole for combating non-albicans Candida infections and azole resistance.

Dongming Zheng has studied Farnesol can prevent and treat fungal infections. It exerts significant antimicrobial effects on fungal planktonic and biofilm cells, enhances the antimicrobial efficacy of conventional antifungal drugs, and reverses and reduces fungal drug resistance[21,22,23].

2.6 Skincare

Farnesol, a naturally occurring sesquiterpene alcohol derived from essential oils (e.g., rose, lemongrass, citronella), is widely incorporated in skincare and personal care products for Fragrance and masking. It provides a mild, floral scent and masks odors. Effective against gram-positive bacteria (including those causing body odor and some acne-related strains like Cutibacterium acnes), making it common in deodorants, body washes, foot care, and acne-targeted cleansers. Also enhances mild formulations by inhibiting microbial growth.It appears in moisturizers, serums, cleansers, aftershaves, and anti-acne products at low concentrations (typically <0.5%)[24,25].

2.7 Anti-Inflammatory and Soothing Effects

Preclinical evidence supports topical anti-inflammatory potential:Animal studies show farnesol (pure or liposomal) reduces UVB-induced sunburn inflammation, decreases pro-inflammatory cytokines (e.g., IL-6, TNF-α), promotes collagen production, and improves skin smoothness.It protects against PM2.5-induced oxidative damage and inflammation in skin models.In acne models (C. acnes-induced), farnesol gels exhibit antibacterial, anti-inflammatory, and tissue-reparative effects comparable to or adjunctive with standards like clindamycin. These align with claims of calming redness/irritation and benefiting sensitive or inflamed skin. Some sources suggest it regulates sebum and soothes environmental stressors[26].

Antibacterial properties target acne-causing bacteria; combined with anti-inflammatory effects, it supports blemish control and reduced inflammation. Promoted as non-irritating in many formulations, with soothing potential. Limited evidence from animal models shows collagen boost and smoothness improvement post-UV damage, but no robust human data for wrinkle reduction or broad anti-aging efficacy.

2.8 Neuroprotective activity

In vitro studies show that farnesol reduces oxidative stress and prevents neuronal apoptosis, two key processes in the pathogenesis of Alzheimer's. It also has been shown to decrease the accumulation of amyloid-beta plaques and tau protein tangles, which are associated with Alzheimer's disease. While farnesol shows potential in protecting neurons from damage, more research is needed to establish its clinical relevance in the treatment of neurodegenerative disorders.

Reduction of Oxidative Stress and Neuronal Apoptosis: Farnesol has demonstrated neuroprotective effects in animal models of neurodegeneration. For instance, in lipopolysaccharide (LPS)-induced neuroinflammation models (mimicking aspects of AD-related oxidative damage), farnesol attenuated neurodegeneration by regulating the intrinsic apoptotic cascade (e.g., reducing Bax expression, preserving Bcl-2, and exerting antioxidant effects). Similar benefits were seen in seizure models and general neurotoxicity assays, where farnesol blocked voltage-gated Ca^{2+} channels and reduced oxidative damage.

In Vivo Neuroprotection in AD-Like Models: A study using intracerebroventricular streptozotocin (ICV-STZ)-induced rats (a non-transgenic model of sporadic AD featuring insulin resistance, oxidative stress, inflammation, and cognitive deficits) showed that trans,trans-farnesol improved behavioral outcomes, reduced neuroinflammation, and mitigated AD-like pathology through antioxidant and anti-apoptotic mechanisms. While farnesol exhibits promising general neuroprotective properties that could indirectly support neuronal health in AD pathogenesis, the specific in vitro effects on oxidative stress/apoptosis in AD models and direct impacts on Aβ plaques or tau tangles are not yet established. More dedicated research is indeed needed to clarify its therapeutic relevance for neurodegenerative disorders like Alzheimer's[27,28,29].

2.9 Anti-arthritic study

Ahmed SR et al., 2024: Network pharmacology + experimental arthritis models combined network pharmacology with formaldehyde- and CFA-induced arthritis models, demonstrating that farnesol significantly reduced paw swelling, arthritic scores, and histopathological damage while downregulating pro-inflammatory mediators (e.g., TNF-α, IL-1β, IL-17) and modulating IL-17, TNF, and TLR signaling pathways. This supports multi-targeted anti-arthritic and immunomodulatory effects[30].

Oral farnesol in an FCA rat model showed dose-dependent amelioration of oxidative stress (↑SOD, ↑GSH, ↓MDA), downregulation of inflammatory cytokines (IL-6, IL-1β, TNF-α), and improved biochemical status, especially when combined with methotrexate, strengthening evidence for therapeutic anti-inflammatory potential in chronic arthritis[31].

2.10 Anti-cancer Pharmacology

Farnesol exhibited dose-dependent cytotoxicity and induction of apoptosis in human osteosarcoma (Saos-2) and colorectal cancer (HCT-116) cells. The study also identified ROS-mediated apoptotic pathways and morphological changes consistent with programmed cell death, providing further anticancer mechanistic evidence[32].

In Silico Mechanistic Insight – mTOR Signaling revealed molecular docking and dynamics simulation study showed that farnesol binds with mTOR and its downstream effectors (p70S6K, eIF4E) with stable interactions comparable to rapamycin, suggesting potential inhibition of the PI3K/Akt/mTOR axis, an important regulator of cancer cell growth and survival[33].

2.11 Metabolic and Organ-Protective Effects

ER Stress & Hepatic Metabolic Dysfunction showed tunicamycin-induced model of endoplasmic reticulum stress and metabolic dysfunction, farnesol improved hepatic function and reduced markers of ER stress and metabolic disturbance. This points to novel metabolic regulatory effects beyond classic anti-inflammatory roles[34].

2.12 Infectious Disease and Parasitic Models

In a BALB/c mouse model of Leishmania infection, farnesol significantly reduced lesion size and lymph node enlargement compared with controls, suggesting anti-protozoal therapeutic potential in parasitic skin disease models[35].

2.13Vascular

Recent ex vivo evidence indicates that (E,E)-farnesol exerts vasorelaxant effects in isolated human umbilical vein preparations**.** Farnesol induced concentration-dependent relaxation of precontracted vascular rings, an effect attributed primarily to blockade of voltage-dependent Ca^{2+} channels and activation of potassium channels. These ion channel–mediated mechanisms suggest that farnesol can modulate vascular tone and smooth muscle excitability, providing preliminary pharmacological evidence for its potential relevance in vascular dysfunction and hypertensive states, including conditions associated with altered umbilical vein reactivity during pregnancy[36].

2.14 Gut Brain axis and immunomodulation

Emerging research indicates that farnesol plays a role in the gut–brain axis by modulating intestinal barrier integrity and immune responses. It reduces inflammation in colitis models and influences systemic immune signaling. Interestingly, farnesol exhibits dual immunomodulatory effects, suppressing inflammation in some contexts while promoting it in others, particularly in cancer cells[37].

3. DISCUSSION

The present review synthesizes existing and recent evidence to position farnesol as a multi-target bioactive molecule with broad pharmacological relevance. Across inflammatory, infectious, oncological, metabolic, and neurodegenerative domains, farnesol consistently demonstrates activity through modulation of interconnected signaling pathways—most notably NF-κB, PI3K/Akt/mTOR, MAPK, and oxidative stress–related cascades. This convergence suggests that its effects are not pathway-specific but rather reflect a network pharmacology profile, which may be advantageous in complex, multifactorial diseases.

A central theme emerging from the literature is the anti-inflammatory and redox-modulating capacity of farnesol. Its ability to suppress pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and attenuate NF-κB activation is consistently reported across models of asthma, arthritis, and tissue injury. These findings are reinforced by parallel reductions in oxidative stress markers and restoration of endogenous antioxidant systems. Importantly, recent studies extend this paradigm to the gut–brain axis**,** where farnesol enhances intestinal barrier integrity and modulates immune responses. Such cross-system activity indicates that farnesol may exert systemic immunoregulatory effects, rather than acting solely at localized sites of inflammation.

In oncology, farnesol exhibits pro-apoptotic and anti-proliferative properties**,** primarily through mitochondrial dysfunction, caspase activation, and inhibition of survival pathways such as PI3K/Akt. While these findings are mechanistically compelling, their translational relevance remains uncertain. Many studies employ concentrations that may not be achievable in vivo, and there is limited evidence regarding tumor selectivity or effects on normal cells. Moreover, the same signaling pathways targeted in cancer are essential for normal cellular homeostasis, raising concerns about potential off-target toxicity**.** Therefore, although farnesol holds promise as an adjunct anticancer agent, its role as a standalone therapeutic remains speculative.

The antimicrobial and anti-biofilm properties of farnesol are among the most consistently validated aspects of its pharmacology. By disrupting quorum sensing, inhibiting adhesion, and destabilizing biofilm architecture, farnesol targets critical determinants of microbial persistence. This is particularly relevant in the context of antimicrobial resistance, where biofilm-associated infections remain difficult to eradicate. However, its comparatively lower potency relative to standard agents such as sodium hypochlorite suggests that its optimal application lies in combination or adjunctive strategies rather than monotherapy. Future work should therefore focus on synergistic formulations**,** including nanoparticle-based delivery systems, to enhance efficacy.

A notable advancement in recent years is the expansion of farnesol research into neurodegenerative and metabolic disorders**.** Preclinical models of Parkinson's disease demonstrate improvements in motor function, reduction in dopaminergic neuronal loss, and modulation of neuroinflammatory pathways. Similarly, emerging evidence indicates a role in mitochondrial biogenesis and muscle function**,** mediated through PARIS–PGC-1α signaling. These findings suggest that farnesol may influence energy metabolism and cellular resilience, extending its relevance beyond classical pharmacological categories. Nevertheless, these conclusions are based on toxin-induced or genetically simplified models, which do not fully recapitulate human disease complexity.

Despite these promising attributes, several critical limitations hinder the clinical translation of farnesol. First, its physicochemical properties, including poor aqueous solubility and high volatility, significantly restrict bioavailability. Second, there is a lack of standardized dosing regimens and insufficient pharmacokinetic data, making it difficult to correlate experimental findings with potential therapeutic exposure in humans. Third, the majority of studies rely on in vitro systems or small animal models, with a near absence of well-designed clinical trials. This gap is particularly significant given the context-dependent effects of farnesol, where it may exhibit both anti- and pro-inflammatory actions depending on the cellular environment.

Another important consideration is the pleiotropic nature of farnesol's mechanisms. While multi-target activity can be beneficial in complex diseases, it also introduces challenges in drug development, including difficulty in identifying primary targets, predicting adverse effects, and optimizing therapeutic windows. The dual immunomodulatory behavior observed in recent studies underscores the need for precision-based approaches, where the context of disease and target tissue is carefully defined.

Future research should prioritize translational strategies aimed at overcoming these limitations. Advanced delivery systems such as liposomes, polymeric nanoparticles, and nanoemulsions offer promising avenues to improve solubility, stability, and targeted delivery. In parallel, comprehensive pharmacokinetic and toxicity studies are essential to establish safe and effective dosing parameters. Importantly, well-controlled clinical trials will be critical to validate preclinical findings and determine the true therapeutic potential of farnesol in humans.

In summary, farnesol represents a versatile but still investigational compound with significant pharmacological promise. While recent advances have broadened its therapeutic scope, particularly in neurodegenerative and metabolic disorders, the transition from experimental models to clinical application remains a major challenge. A more rigorous and translationally focused research framework will be necessary to fully elucidate its role in modern therapeutics.

4. CONCLUSION

Farnesol is amultifunctional bioactive compoundwith demonstratedanti-inflammatory, antimicrobial, anti-biofilm, cytoprotective, anticancer, and neuroprotective propertiesin preclinical models. Its broadmechanistic profile centered onNF-κB modulation, oxidative stress reduction, and apoptosis regulationsupports its potential as a therapeutic adjunct. However, translation to clinical use will depend on futurehuman trials and optimized delivery systems.

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