

REVIEW ARTICLE

Phytochemical constituents of *Cymbopogon citratus* and their antimicrobial, antioxidant, and cytoprotective effects: Mechanistic insights and biomedical relevanceBeena Pal¹, Amar P. Garg^{2*}, and Damodar Gupta³¹Department of Biotechnology, School of Biotechnology and Life Sciences, Shobhit Institute of Engineering and Technology (NAAC Accredited Grade "A" Deemed to-be-University), Meerut, Uttar Pradesh, India²Department of Research, Centre for Multidisciplinary Studies and Research, Swami Vivekanand Subharti University, Meerut, Uttar Pradesh, India³Department of Nutraceuticals, Institute of Nuclear Medicine and Allied Sciences, Defence Research and Development Organization, Delhi, India

Abstract

Cymbopogon citratus (lemongrass) is a widely utilized medicinal and aromatic plant with a long history of traditional applications across Asia, Africa, and South America. In recent decades, scientific attention has increasingly focused on elucidating its phytochemical composition and validating its therapeutic properties through experimental and molecular studies. The present review critically synthesizes current evidence on the phytochemical constituents of *C. citratus* and their antimicrobial, antioxidant, and cytoprotective effects, with particular emphasis on underlying biological mechanisms and emerging biomedical relevance. Major bioactive compounds, including citral, flavonoids, phenolic acids, terpenoids, and essential oils, are discussed in relation to their roles in inhibiting pathogenic microorganisms, neutralizing oxidative stress, and maintaining cellular integrity. The review further highlights mechanistic pathways such as membrane disruption, enzyme inhibition, reactive oxygen species modulation, mitochondrial protection, and anti-inflammatory signaling. Recent advances in nanotechnology-based formulations and functional therapeutic applications are also examined. Collectively, the evidence positions *C. citratus* as a promising natural source for the development of antimicrobial and cytoprotective agents, supporting further translational and clinical investigations. This review synthesizes evidence from experimental, mechanistic, and translational studies published over the last two decades.

Keywords: Antimicrobial activity; Antioxidant mechanisms; Biomedical applications; *Cymbopogon citratus*; Cytoprotection; Phytochemistry

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1. Introduction

The growing global burden of infectious diseases, oxidative stress-related disorders, and chronic degenerative conditions has intensified the demand for safe, effective, and naturally derived therapeutic agents.¹ Antimicrobial resistance has emerged as a critical

public health challenge, significantly compromising the efficacy of conventional antibiotics and increasing morbidity, mortality, and healthcare costs worldwide. At the same time, oxidative stress—resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defenses—plays a pivotal role in the pathogenesis of numerous diseases, including cancer, cardiovascular disorders, neurodegenerative diseases, diabetes, and inflammatory conditions.² These interlinked challenges have redirected scientific interest toward medicinal plants as reservoirs of structurally diverse bioactive compounds with multi-target therapeutic potential.

Cymbopogon citratus, commonly known as lemongrass, is a perennial aromatic herb belonging to the family Poaceae. It is widely cultivated in tropical and subtropical regions and has been extensively used in traditional medicine systems such as Ayurveda, Unani, and folk medicine for centuries.³ Traditionally, *C. citratus* has been employed for the treatment of fever, infections, gastrointestinal disturbances, inflammation, pain, and respiratory ailments, as well as for its calming and detoxifying effects. Its widespread use as a herbal infusion, culinary ingredient, and source of essential oil underscores its cultural, nutritional, and medicinal significance.⁴

Recent phytochemical and pharmacological studies have validated many of the traditional claims associated with *C. citratus*. Scientific investigations have revealed that the plant is rich in essential oils, phenolic compounds, flavonoids, terpenoids, tannins, and other secondary metabolites that collectively contribute to its broad spectrum of biological activities.⁵ Among these, citral—comprising the isomeric forms geranial and neral—has been identified as the principal bioactive constituent responsible for the characteristic aroma and a major proportion of its antimicrobial and antioxidant activities. In addition to volatile components, non-volatile phytochemicals such as flavonoids and phenolic acids play a crucial role in free-radical scavenging, metal chelation, and cellular protection.⁶

The antimicrobial activity of *C. citratus* has been demonstrated against a wide array of pathogenic bacteria and fungi, including both Gram-positive and Gram-negative organisms. These effects are mediated through multiple mechanisms, such as disruption of microbial cell membranes, inhibition of enzymatic activity, interference with energy metabolism, and impairment of microbial virulence factors. Importantly, the multi-target actions exhibited by plant-derived compounds offer a strategic advantage in addressing antimicrobial resistance, as they reduce the likelihood of rapid resistance development

compared to single-target synthetic drugs.⁷

In parallel, the antioxidant and cytoprotective properties of *C. citratus* have gained increasing attention. Oxidative stress-induced cellular damage is a common pathological denominator in numerous diseases, and plant-based antioxidants have emerged as promising agents for mitigating such damage. Phytochemicals present in *C. citratus* have been shown to neutralize ROS and reactive nitrogen species (RNS), inhibit lipid peroxidation, enhance endogenous antioxidant enzyme systems, and preserve mitochondrial function. These actions collectively contribute to cytoprotection, maintenance of cellular homeostasis, and prevention of tissue injury under pathological conditions. The quality and quantity of phytochemicals (mainly polyphenols, flavonoids, and terpenes) in *C. citratus* vary significantly depending on rainfall, soil type and composition, pH, harvesting time, and plant age, which greatly influence its biological and biomedical properties—including anticancer, antimicrobial, anti-filarial, anti-amoebic, antiseptic, analgesic, unesthetic, and anti-inflammatory.⁸

Beyond conventional pharmacological applications, contemporary research has expanded the biomedical relevance of *C. citratus* through its integration into nanotechnology, functional foods, and nutraceutical formulations. Green synthesis of nanoparticles using *C. citratus* extracts has demonstrated enhanced antimicrobial efficacy, improved bioavailability, and reduced cytotoxicity, highlighting its potential in next-generation therapeutic strategies. Such interdisciplinary applications further reinforce the significance of *C. citratus* as a versatile and sustainable natural resource in modern medicine (Figure 1).⁹

Despite the growing body of literature, a comprehensive and mechanistically oriented synthesis of the phytochemical constituents of *C. citratus* and their antimicrobial, antioxidant, and cytoprotective effects remains limited. Therefore, this review synthesizes existing experimental and mechanistic evidence, elucidating the molecular pathways underlying these biological activities and discussing their translational and biomedical implications. By integrating traditional knowledge with contemporary scientific insights, this review provides a coherent framework supporting the therapeutic potential of *C. citratus* and identifying future research directions necessary for its clinical advancement.

2. Phytochemical profile of *Cymbopogon citratus*

The therapeutic versatility of *C. citratus* is fundamentally linked to its rich and diverse phytochemical composition.

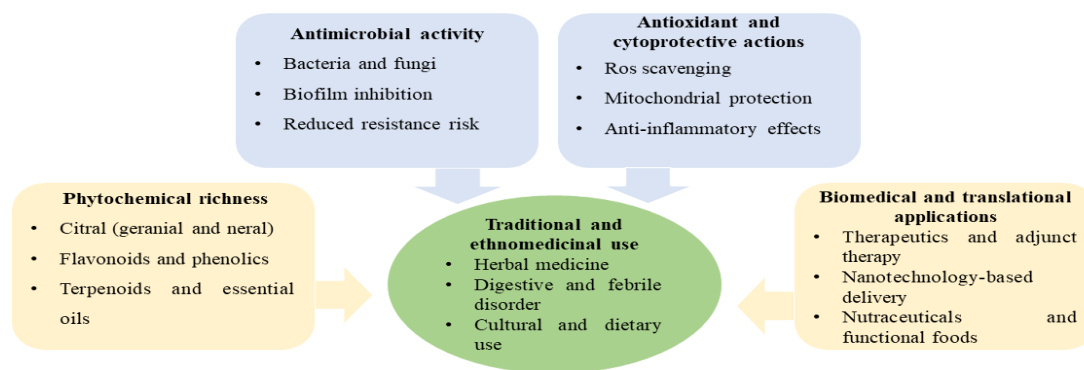


Figure 1. Schematic overview of the traditional use, phytochemical composition, and key biological activities of *Cymbopogon citratus*, highlighting its antimicrobial, antioxidant, cytoprotective, and biomedical applications. Image created by the authors.
Abbreviation: ROS: Reactive oxygen species.

Extensive phytochemical investigations have demonstrated that the plant contains both volatile and non-volatile bioactive constituents, each contributing distinctly to its antimicrobial, antioxidant, and cytoprotective properties (Figure 1). The qualitative and quantitative composition of these phytochemicals is influenced by factors such as geographical origin, cultivation conditions, plant maturity, and processing methods (particularly drying and extraction)¹⁰, as well as environmental factors such as locality, soil pH, temperature, rainfall, and plant age.⁸ The biomedical applications of *C. citratus* essential oil depend largely on its major components, including polyphenols, flavonoids, and terpenes.

Broadly, the phytochemical constituents of *C. citratus* can be classified into essential oil constituents, phenolic compounds, flavonoids, terpenoids, tannins, saponins, and minor alkaloids. The synergistic interaction among these compounds underlies the plant's broad spectrum of biological activities.

2.1. Essential oil constituents

The essential oil of *C. citratus* is the most extensively studied phytochemical fraction and represents a major contributor to its biological activity. It is primarily composed of monoterpenes and oxygenated monoterpenes, with citral—a mixture of the geometric isomers geranial (α -citral) and neral (β -citral)—constituting the dominant component (Figure 2). Citral is responsible for the characteristic lemon aroma of the plant and plays a central role in its antimicrobial and antioxidant functions.¹¹

In addition to citral, the essential oil contains other bioactive compounds, such as myrcene, limonene, geraniol, citronellal, and linalool. These constituents exhibit strong lipophilic properties, enabling effective

interaction with microbial membranes and contributing to membrane destabilization and enzyme inhibition. The relative abundance of these components varies depending on seasonal harvesting and extraction conditions, which in turn influences the pharmacological potency of the oil.^{11,12}

2.2. Phenolic compounds

Phenolic compounds represent an important group of non-volatile phytochemicals (Figure 3) in *C. citratus* and are largely responsible for its antioxidant potential. These compounds include simple phenolics and phenolic acids such as caffeic acid, ferulic acid, chlorogenic acid, and gallic acid. Their chemical structure, characterized by hydroxyl groups attached to aromatic rings, enables efficient scavenging of ROS and inhibition of lipid peroxidation.¹³

Phenolic compounds also exhibit metal-chelating properties, reducing the availability of transition metals involved in free radical generation. Through these mechanisms, phenolics contribute to cellular redox balance and protect against oxidative stress-induced damage.¹⁴

2.3. Flavonoids

Flavonoids constitute another major class of bioactive compounds identified in *C. citratus* (Figure 3). Commonly reported flavonoids include quercetin, luteolin, apigenin, and kaempferol, which are known for their strong antioxidant, anti-inflammatory, and cytoprotective activities. These compounds exert their effects by modulating intracellular signaling pathways, regulating antioxidant enzyme expression, and inhibiting pro-oxidant enzymes.¹⁵

Flavonoids also play a supportive role in antimicrobial activity by interfering with microbial adhesion, biofilm

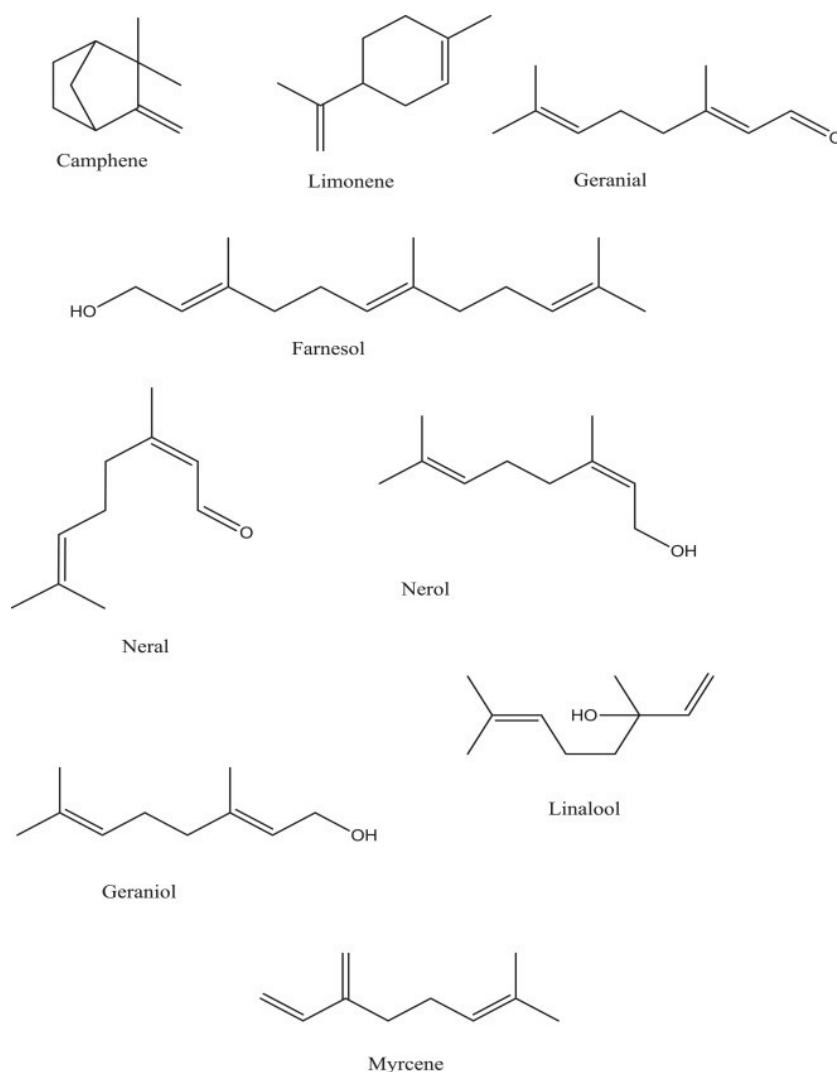


Figure 2. Chemical structure of a major component of the essential oil of *Cymbopogon citratus*. Adapted from Oladeji *et al.*¹¹

formation, and nucleic acid synthesis. Their multifunctional nature further enhances the overall therapeutic efficacy of *C. citratus* extracts.¹⁶

2.4. Terpenoids, tannins, and other secondary metabolites

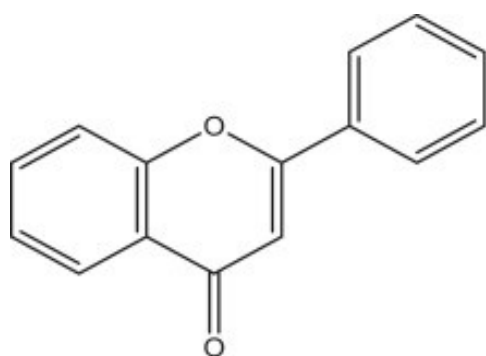
Beyond essential oils and polyphenols, *C. citratus* contains various terpenoids, tannins, saponins, and trace alkaloids that contribute to its biological activity. Terpenoids exhibit antimicrobial and anti-inflammatory properties, while tannins are known for their protein-precipitating ability, which can inhibit microbial growth and toxin production.¹⁷

Saponins present in *C. citratus* possess membrane-active properties that may enhance antimicrobial efficacy

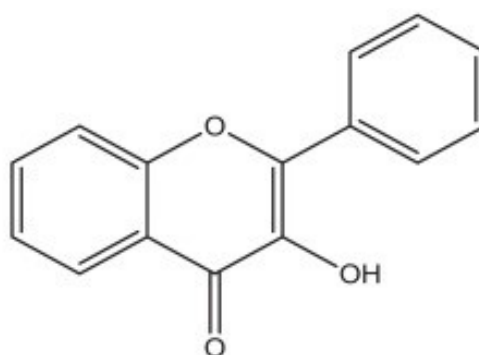
and improve the bioavailability of other phytochemicals. Although alkaloids occur in relatively low concentrations, they may contribute synergistically to the plant's pharmacological profile.¹⁸

2.5. Influence of extraction and processing on phytochemical composition

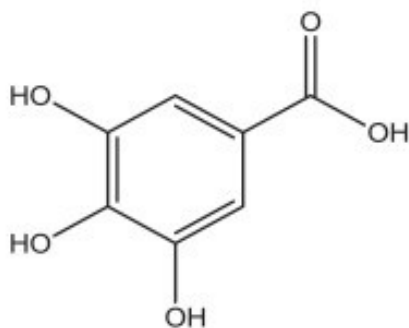
The phytochemical yield and biological activity of *C. citratus* are significantly affected by extraction methods and processing conditions. Solvent polarity plays a crucial role in determining the type and concentration of extracted compounds, with ethanolic extracts generally yielding higher levels of phenolics and flavonoids, while steam distillation or hydrodistillation is preferred for essential oil extraction.¹⁹



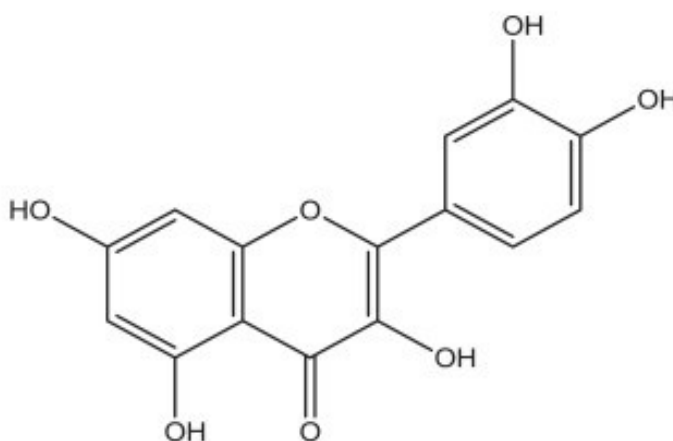
flavone



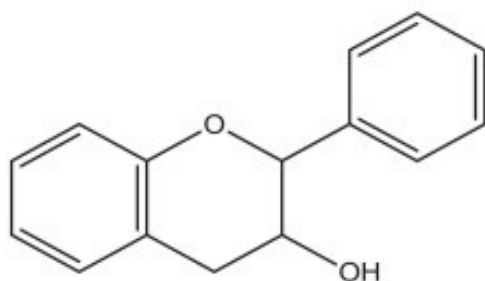
flavonol



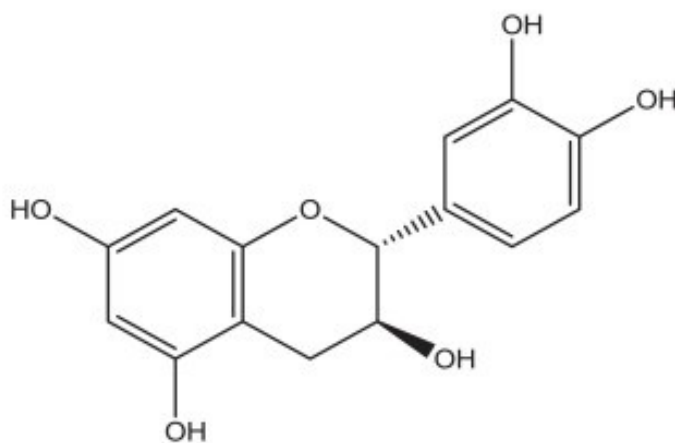
Gallic acid



Quercetin



Flavan-3-ol



catechin

Figure 3. Chemical structures of representative phenolic compounds and flavonoids in *Cymbopogon citratus*. Adapted from Oladeji *et al.*¹¹

Drying methods, including oven drying, shade drying, and sun drying, also influence phytochemical stability. Controlled drying conditions are particularly important for preserving volatile constituents and preventing degradation of heat-sensitive compounds. These variations highlight the need for standardized processing protocols to ensure consistency and reproducibility in therapeutic applications.²⁰

2.6. Phytochemical synergy and therapeutic relevance

Rather than acting in isolation, the phytochemicals of

C. citratus function synergistically to produce enhanced biological effects. The combined action of essential oil constituents, phenolic compounds, and flavonoids results in a multi-target therapeutic profile encompassing antimicrobial defense, oxidative stress modulation, and cellular protection (Table 1). This synergism is a defining feature of plant-based therapeutics and represents a key advantage over single-compound synthetic drugs.²¹

3. Antimicrobial effects

The antimicrobial potential of *C. citratus* has been widely documented against a broad spectrum of pathogenic

Table 1. Major phytochemicals of *Cymbopogon citratus* and their associated biological activities

Phytochemical/ compound	Chemical class	Major biological activities	Key mechanisms of action	Biomedical relevance
Citral (geranial and neral)	Monoterpene aldehyde (essential oil)	Antibacterial, antifungal, and antioxidant	Disruption of microbial cell membranes, inhibition of ergosterol synthesis, and induction of oxidative stress in pathogens	Natural antimicrobial agent; potential alternative to synthetic antibiotics
Geraniol	Monoterpene alcohol	Antimicrobial and anti- inflammatory	Increased membrane permeability, enzyme inhibition, and suppression of microbial growth	Topical antimicrobial formulations; supportive therapy
Myrcene	Monoterpene hydrocarbon	Antimicrobial and antioxidant	Interaction with lipid bilayers and modulation of oxidative pathways	Adjunct antimicrobial and antioxidant agent
Limonene	Monoterpene	Antioxidant and antimicrobial	Free radical scavenging and membrane destabilization	Functional food and nutraceutical applications
Flavonoids (quercetin, luteolin, apigenin, and kaempferol)	Polyphenolic compounds	Antioxidant, cytoprotective, anti- inflammatory, and antimicrobial	ROS scavenging, metal chelation, modulation of antioxidant enzymes, and inhibition of biofilm formation	Prevention of oxidative stress- related disorders; cellular protection
Phenolic acids (caffeic acid, ferulic acid, chlorogenic acid, and gallic acid)	Phenolic compounds	Antioxidant and cytoprotective	Free radical neutralization, inhibition of lipid peroxidation, and metal ion chelation	Protection against oxidative damage; nutraceutical formulations
Terpenoids	Isoprenoid compounds	Antimicrobial and anti- inflammatory	Disruption of microbial metabolism and interference with membrane integrity	Broad-spectrum antimicrobial support
Tannins	Polyphenolic compounds	Antimicrobial and antioxidant	Protein precipitation, enzyme inhibition, and microbial growth suppression	Natural antimicrobial and preservative agent
Saponins	Glycosidic compounds	Antimicrobial and cytoprotective	Membrane interaction, enhanced permeability, and synergistic effects	Enhanced bioavailability of phytochemicals
Trace alkaloids	Nitrogen-containing compounds	Supportive antimicrobial activity	Enzyme inhibition, metabolic interference	Synergistic contribution to therapeutic effects

Note: Adapted from Swamy *et al.*²²

microorganisms, including Gram-positive bacteria, Gram-negative bacteria, and fungi. This activity is primarily attributed to its rich phytochemical composition, particularly citral-rich essential oils, flavonoids, phenolic acids, and terpenoids. Unlike conventional antimicrobials that often act on a single molecular target, *C. citratus* exerts its antimicrobial effects through multiple complementary mechanisms, thereby reducing the likelihood of rapid resistance development. These mechanisms collectively explain the broad-spectrum and resistance-modulating effects of *C. citratus*.²³

3.1. Antibacterial activity

Numerous *in vitro* studies have demonstrated that essential oils and solvent extracts of *C. citratus* effectively inhibit clinically relevant bacterial pathogens such as *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, *Salmonella enterica*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, and *Bacillus subtilis* (Table 2). The antibacterial efficacy varies with extract type, concentration, and bacterial strain, with essential oil fractions generally exhibiting stronger activity due to their high content of lipophilic terpenoids.^{24–27}

Aqueous extracts of *C. citratus* leaves exhibit significant antimicrobial effects against pathogenic species (*Salmonella* sp. and *E. coli*), while supporting beneficial gut bacteria (e.g., *Lactobacillus* sp.), indicating safety for intestinal microbiota essential for host health.²⁸

Flavonoids act on multiple bacterial targets, including DNA gyrase, fatty acid synthesis type II, dihydrofolate reductase–epigallocatechin gallate helicase, and virulence enzymes.^{29,30} Moreover, luteolin, a flavonoid in *C. citratus*, exhibits strong antimicrobial activity by disrupting the membranes of *S. aureus* and *Listeria monocytogenes* and inhibiting biofilm formation.^{31,32}

In a previous study, Pal *et al.*²⁰ reported that phytochemicals from microwave-dried *C. citratus* leaf extracts exhibit selective antimicrobial activity against human pathogens (*S. aureus*, *K. pneumoniae*, *Shigella flexneri*, and *Salmonella typhi*) while protecting beneficial gut bacteria, including *Streptococcus thermophilus*, *Lactobacillus fermentum*, *Lactobacillus sporogenes*, and *E. coli*.

The primary antibacterial mechanism involves disruption of the bacterial cell membrane. Lipophilic constituents—such as citral and geraniol—penetrate the phospholipid bilayer, increasing membrane permeability and causing leakage of intracellular components, including ions, proteins, and nucleic acids. This loss of membrane integrity compromises bacterial viability and ultimately

leads to cell death.³³

In addition to membrane disruption, *C. citratus* phytochemicals interfere with bacterial enzyme systems and metabolic pathways. Inhibition of enzymes involved in energy production, protein synthesis, and cell wall biosynthesis further suppresses bacterial growth and replication. Phenolic compounds also inhibit bacterial quorum sensing and biofilm formation, thereby reducing bacterial virulence and persistence.³⁴

3.2. Antifungal activity

C. citratus has demonstrated notable antifungal activity against pathogenic fungi, particularly *Candida albicans*, *Candida tropicalis*, *Aspergillus niger*, and *Aspergillus fumigatus*. The antifungal effects are predominantly associated with citral and other monoterpenes present in the essential oil.^{35,36}

A key antifungal mechanism is the inhibition of ergosterol biosynthesis, an essential component of fungal cell membranes. Disruption of ergosterol synthesis alters membrane fluidity and permeability, leading to impaired nutrient transport and fungal cell lysis. Additionally, oxidative stress induced within fungal cells contributes to mitochondrial dysfunction and apoptosis-like cell death.³⁷

3.3. Antimalarial activity

Leaf extracts of *C. citratus* have demonstrated promising antimalarial activity against *Plasmodium* species (e.g., *Plasmodium falciparum*), targeting circumsporozoite protein, merozoite surface protein 1, and erythrocyte membrane protein 1 of *P. falciparum*, which are involved in malaria pathogenesis. Moreover, *in silico* studies demonstrated that swertiajaponin, a compound from *C. citratus*, forms strong hydrogen bond interactions with LYS29, CYS30, TYR34, ASN52, GLY55, and CYS58 amino acid residues, exhibiting strong binding affinity to merozoite surface protein 1 of *P. falciparum*, comparable to the standard treatment (Artesunate–Amodiaquine). Additionally, another compound, quercetin, exhibits binding energies of 6.8 kcal/mol with *P. falciparum* circumsporozoite protein (6.8 kcal/mol) and 8.3 kcal/mol with *P. falciparum* erythrocyte membrane protein 1, which are slightly lower than those of the standard drug.³⁸

3.4. Antiviral activity

In silico studies also confirmed that phytosterol compounds from *C. citratus* and *Curcuma longa* exhibit antiviral activities. The study indicated that phytosterol compounds inhibited the 3CL^{pro} SARS-CoV-2 protease, an enzyme that plays a critical role in coronavirus replication.³⁹

Table 2. Antimicrobial spectrum of *Cymbopogon citratus* and target microorganisms

Microbial category	Target microorganisms	Type of extract/ component	Observed antimicrobial effect	Primary mechanism(s)
Gram-positive bacteria	<i>Staphylococcus aureus</i> , <i>Streptococcus pyogenes</i> , and <i>Enterococcus faecalis</i>	Essential oil; ethanolic extract	Strong growth inhibition; bactericidal at higher concentrations	Cell membrane disruption; enzyme inhibition
Gram-negative bacteria	<i>Escherichia coli</i> , <i>Salmonella</i> <i>enterica</i> , <i>Klebsiella</i> <i>pneumoniae</i> , and <i>Pseudomonas aeruginosa</i>	Essential oil; hydroalcoholic extract	Moderate to strong inhibition depending on strain	Increased membrane permeability; metabolic interference
Yeasts	<i>Candida albicans</i> and <i>Candida tropicalis</i>	Essential oil (citrals-rich)	Significant antifungal activity	Ergosterol biosynthesis inhibition; membrane destabilization
Filamentous fungi	<i>Aspergillus niger</i> and <i>Aspergillus fumigatus</i>	Essential oil; solvent extracts	Growth suppression; fungistatic to fungicidal effects	Oxidative stress induction; mitochondrial dysfunction
Biofilm-forming bacteria	<i>Staphylococcus aureus</i> and <i>Pseudomonas aeruginosa</i>	Phenolic-rich extracts	Inhibition of biofilm formation	Quorum-sensing interference; adhesion suppression
Multidrug-resistant strains	MDR <i>Escherichia coli</i> and MDR <i>Staphylococcus aureus</i> (reported models)	Essential oil; nanoparticle formulations	Enhanced antimicrobial efficacy	Multi-target mechanisms; synergistic action

Note: Adapted from Liguori *et al.*⁴⁰

Abbreviation: MDR: Multi-drug resistant.

3.5. Mechanistic insights into antimicrobial action

The antimicrobial activity of *C. citratus* is characterized by a multi-target mode of action, which includes:⁴¹

- Disruption of microbial cell membranes and cell walls.
- Inhibition of intracellular enzymes and metabolic pathways.
- Interference with nucleic acid synthesis.
- Suppression of biofilm formation and quorum sensing.
- Induction of oxidative stress within microbial cells.

This multi-mechanistic approach is particularly advantageous in combating multidrug-resistant microorganisms, as it reduces selective pressure on a single microbial target and thereby limits resistance development.

3.6. Synergistic interactions and combination effects

The antimicrobial efficacy of *C. citratus* is enhanced by synergistic interactions among its phytochemical constituents. For example, citral may increase membrane permeability, facilitating the intracellular penetration of flavonoids and phenolic acids that further inhibit enzymatic and genetic processes. Such synergism has also been observed when *C. citratus* leaf extracts are used in combination with conventional antibiotics, resulting in enhanced antibacterial activity and reduced effective doses of synthetic drugs.⁴²

3.7. Emerging applications in antimicrobial strategies

Recent advances have explored the incorporation of *C. citratus* leaf extracts into nanoparticle-based systems, food packaging materials, and topical formulations to enhance antimicrobial efficacy and stability. Green-synthesized nanoparticles using *C. citratus* leaf extracts have demonstrated superior antimicrobial performance compared to crude extracts, highlighting the potential of nanotechnology-assisted applications. Furthermore, its utilization as a natural antimicrobial agent in food preservation and healthcare products underscores its translational relevance.⁴³

4. Antioxidant mechanisms

Oxidative stress represents a central molecular event in the development and progression of a wide spectrum of pathological conditions, including cardiovascular diseases, neurodegenerative disorders, metabolic syndromes, cancer, and inflammatory diseases. It arises when the production of ROS and RNS exceeds the capacity of endogenous antioxidant defense systems. In recent years, plant-derived antioxidants have emerged as promising alternatives to synthetic antioxidants due to their multifunctional actions and favorable safety profiles. *C. citratus* exhibits

potent antioxidant activity mediated through multiple complementary biochemical and cellular mechanisms.⁴⁴ Additionally, bioactive compounds of *C. citratus* such as rutin,⁴⁵ quercetin,⁴⁶ kaempferol,⁴⁷ luteolin,⁴⁸ apigenin,⁴⁹ and isoorientin⁵⁰ have demonstrated promising antioxidant potential.

4.1. Direct scavenging of reactive oxygen species and reactive nitrogen species

A primary antioxidant mechanism of *C. citratus* involves the direct neutralization of ROS and RNS. Phenolic acids and flavonoids present in the plant possess redox-active hydroxyl groups capable of donating electrons or hydrogen atoms to unstable free radicals, thereby inhibiting radical chain reactions. This direct scavenging activity reduces the accumulation of superoxide anions, hydroxyl radicals, hydrogen peroxide, and nitric oxide derivatives, protecting cellular macromolecules from oxidative damage.⁵¹

In vitro antioxidant assays consistently demonstrate the strong radical scavenging capacity of *C. citratus* extracts, confirming their effectiveness as primary antioxidants. These activities are particularly pronounced in hydroalcoholic and ethanolic extracts, which efficiently solubilize phenolic and flavonoid compounds.⁵²

4.2. Inhibition of lipid peroxidation

Lipid peroxidation is a critical downstream consequence of oxidative stress and leads to loss of membrane integrity, altered membrane fluidity, and formation of cytotoxic aldehydes. Bioactive constituents of *C. citratus* inhibit lipid peroxidation by interrupting the propagation phase of oxidative chain reactions. By neutralizing lipid peroxyl radicals, these phytochemicals prevent the oxidative degradation of polyunsaturated fatty acids within cellular and subcellular membranes.⁵³

This mechanism is particularly relevant in tissues with high lipid content, such as neural and hepatic tissues, where oxidative damage can result in irreversible functional impairment.

4.3. Metal ion chelation and suppression of reactive oxygen species generation

Transition metals such as iron and copper catalyze the formation of highly reactive hydroxyl radicals through Fenton and Haber–Weiss reactions. Phenolic compounds in *C. citratus* exhibit strong metal-chelating properties, binding these redox-active ions and reducing their participation in radical-generating reactions. This indirect antioxidant mechanism limits ROS production at its source, complementing direct free radical scavenging.⁵⁴

By suppressing metal-mediated oxidative reactions,

C. citratus contributes to long-term redox stability within biological systems.

4.4. Enhancement of endogenous antioxidant defense systems

Beyond direct antioxidant actions, *C. citratus* phytochemicals modulate intracellular antioxidant defense pathways. Experimental studies indicate that exposure to components of *C. citratus* extracts enhances the activity and expression of key endogenous antioxidant enzymes, including superoxide dismutase, catalase, and glutathione peroxidase. These enzymes constitute the first line of cellular defense against oxidative stress by catalyzing the detoxification of superoxide radicals and hydrogen peroxide.⁵⁵

The upregulation of endogenous antioxidant systems contributes to sustained cytoprotection and enhances cellular resilience against repeated or chronic oxidative insults.

4.5. Mitochondrial protection and maintenance of redox homeostasis

Mitochondria are both a primary source and a major target of oxidative stress. Excessive ROS generation within mitochondria disrupts electron transport, damages mitochondrial DNA, and triggers apoptotic signaling pathways. Bioactive compounds in *C. citratus* have been shown to preserve mitochondrial membrane potential and reduce mitochondrial ROS accumulation. By stabilizing mitochondrial function, these phytochemicals maintain cellular energy metabolism and prevent oxidative stress-induced apoptosis.⁵⁶ This mitochondrial protection is a critical component of the cytoprotective profile of *C. citratus* and underlies its potential role in preventing degenerative and metabolic disorders.

4.6. Synergistic antioxidant interactions

The antioxidant efficacy of *C. citratus* does not arise from a single compound but rather from the synergistic interaction of multiple phytochemical classes. Essential oil constituents provide rapid radical-quenching effects, whereas phenolic acids and flavonoids offer sustained antioxidant activity and regulatory control over cellular defense pathways. This synergism enhances overall biological effectiveness and distinguishes *C. citratus* from isolated single-compound antioxidants.⁵⁷

5. Cytoprotective effects

Cytoprotection refers to the ability of bioactive compounds to preserve cellular integrity, functionality, and survival under conditions of physiological stress or pathological

insult. Increasing evidence indicates that *C. citratus* exhibits pronounced cytoprotective effects, which are closely linked to its antioxidant, anti-inflammatory, and mitochondrial-stabilizing properties. These effects collectively mitigate cellular damage induced by oxidative stress, inflammation, xenobiotics, and metabolic imbalance, thereby supporting tissue homeostasis and cellular resilience.⁵⁸

5.1. Protection against oxidative stress-induced cellular damage

Oxidative stress is a primary driver of cellular injury, leading to DNA damage, protein oxidation, lipid peroxidation, and disruption of membrane integrity. Phytochemicals present in *C. citratus*, particularly flavonoids and phenolic acids, protect cells by reducing intracellular ROS accumulation and stabilizing redox balance. By limiting oxidative injury at the molecular level, these compounds prevent downstream activation of stress-sensitive signaling pathways that culminate in cellular dysfunction and death.⁵⁹

Experimental studies have demonstrated that *C. citratus* leaf extracts significantly reduce markers of oxidative damage while enhancing cell viability in normal cell lines exposed to oxidative insults, underscoring their cytoprotective capacity.

5.2. Mitochondrial stabilization and energy homeostasis

Mitochondria play a central role in cellular survival by regulating energy production, redox signaling, and apoptotic pathways. Oxidative damage to mitochondrial membranes and mitochondrial DNA can impair ATP synthesis and trigger intrinsic apoptotic cascades. Bioactive constituents of *C. citratus* have been shown to preserve mitochondrial membrane potential, reduce mitochondrial ROS generation, and maintain electron transport chain efficiency.⁶⁰

By stabilizing mitochondrial function, *C. citratus* supports cellular energy homeostasis and prevents the release of pro-apoptotic factors such as cytochrome c, thereby enhancing cell survival under stress conditions.

5.3. Modulation of apoptotic pathways

Apoptosis is a tightly regulated process that eliminates damaged or dysfunctional cells; however, excessive or inappropriate activation contributes to tissue degeneration and disease progression. Phytochemicals from *C. citratus* modulate key apoptotic signaling pathways by regulating the balance between pro-apoptotic and anti-apoptotic proteins. These compounds suppress caspase activation and reduce mitochondrial-mediated apoptotic signaling under oxidative or inflammatory stress.⁶¹

This anti-apoptotic effect is particularly relevant for protecting normal cells from secondary damage during exposure to toxins, environmental stressors, or therapeutic agents.

5.4. Anti-inflammatory contributions to cytoprotection

Inflammation and oxidative stress are closely interconnected processes that amplify cellular injury. *C. citratus* exhibits notable anti-inflammatory properties that contribute indirectly to its cytoprotective effects. Its phytochemicals downregulate the production of pro-inflammatory cytokines and mediators, thereby reducing inflammatory stress on cells and tissues.⁶²

By attenuating chronic low-grade inflammation, *C. citratus* helps maintain cellular homeostasis and prevents inflammation-driven cytotoxicity, particularly in tissues prone to oxidative and metabolic stress.

5.5. Selective cytoprotection and safety profile

An important aspect of cytoprotection is selectivity—the ability to protect normal cells without promoting the survival of damaged or malignant cells. Available evidence suggests that *C. citratus* exhibits a favorable safety profile, with low cytotoxicity toward normal cells at biologically active concentrations. This selective cytoprotective effect enhances its potential utility as a supportive therapeutic agent, particularly in contexts where oxidative or inflammatory stress compromises healthy tissues.⁶³

6. In vivo applications

Numerous *in vivo* studies have been conducted to assess the therapeutic effects of *C. citratus* (Table 3). Leaves of *C. citratus* are traditionally used in the management of different types of diabetes and related metabolic disorders.^{64,65} Additionally, *C. citratus* tea has been reported to be effective in reducing blood glucose and lipid levels, improving insulin levels, enhancing β -cell function, and increasing liver glycogen content.⁶⁶

7. Biomedical and translational applications

The expanding body of experimental evidence supporting the antimicrobial, antioxidant, and cytoprotective properties of *C. citratus* has catalyzed its transition from traditional medicinal use to contemporary biomedical applications. Advances in phytochemistry, formulation science, and translational research have positioned *C. citratus* as a promising candidate for integration into therapeutic, preventive, and supportive healthcare strategies.⁷¹ Its broad biological activity spectrum, coupled

Table 3. Summary of *in vivo* studies on *Cymbopogon citratus*

Study type	Participants	Intervention	Outcome
Randomized controlled trial	60 adults with mild anxiety	Inhalation of lemongrass oil (5 min/day for six days)	Reduced cortisol and improved mood scores
Double-blind randomized controlled trial	40 hypertensive adults	Lemongrass tea (daily for four weeks)	Decrease in systolic and diastolic blood pressure
Controlled human study	72 orthodontic patients	Lemongrass mouthwash vs. chlorhexidine	Comparable antimicrobial activity; reduced gingival inflammation
Comparative aromatherapy study	45 students (stress model)	Lemongrass vs. Lavender inhalation	Significantly reduced stress and blood pressure with lemongrass
Clinical trial	90 dental patients	Lemongrass gel for gingivitis	Effective in reducing plaque and bleeding indices

Note: Adapted from Refs.^{67–70}

with a favorable safety profile, underscores its relevance in modern biomedical research. However, issues related to long-term safety and regulatory approval of such formulations warrant further investigation.

7.1. Therapeutic applications in infectious diseases

The broad-spectrum antimicrobial activity of *C. citratus* has significant implications for the management of infectious diseases, particularly in the context of rising antimicrobial resistance. Essential oil constituents and standardized extracts have demonstrated efficacy against bacterial and fungal pathogens commonly associated with skin, respiratory, gastrointestinal, and urogenital infections. The multi-target mechanisms of action—encompassing membrane disruption, enzyme inhibition, and suppression of microbial virulence—support its potential use as an alternative or adjunct to conventional antimicrobial agents.⁷²

In translational settings, *C. citratus*-based formulations may contribute to reducing antibiotic dosage requirements, thereby limiting adverse effects and slowing the development of drug resistance. Topical preparations, oral formulations, and inhalable systems represent potential delivery routes currently under investigation.

7.2. Role in oxidative stress-related disorders

Given its robust antioxidant and cytoprotective properties, *C. citratus* holds promise in the prevention and management of oxidative stress-related diseases. These include cardiovascular disorders, metabolic syndrome, neurodegenerative diseases, and inflammatory conditions. By restoring redox balance and preserving cellular integrity, *C. citratus* phytochemicals may mitigate disease progression and support tissue function.⁷³

Functional foods and nutraceuticals incorporating

C. citratus extracts are being explored as preventive interventions aimed at enhancing antioxidant defenses and reducing chronic oxidative burden in at-risk populations.

7.3. Cytoprotective and supportive therapeutic applications

The cytoprotective effects of *C. citratus* extend its translational relevance beyond disease treatment to supportive care. Protection of normal cells against oxidative and inflammatory damage has important implications in conditions such as environmental toxin exposure, metabolic stress, and therapeutic interventions that induce collateral cellular injury. Its selective cytoprotection suggests its potential use as an adjunct in therapies where preservation of healthy tissue is essential.⁷⁴

7.4. Nanotechnology-based and advanced formulations

Recent advances in nanotechnology have expanded the biomedical applications of *C. citratus*. Plant-mediated green synthesis of metallic nanoparticles using *C. citratus* extracts has demonstrated enhanced antimicrobial efficacy, improved stability, and reduced cytotoxicity compared to conventional formulations. These nanoconjugates offer improved bioavailability and targeted delivery, thereby addressing limitations associated with poor solubility and stability of phytochemicals.⁷⁵

Nanotechnology-based systems also open avenues for controlled release and site-specific delivery, further strengthening the translational potential of *C. citratus* in clinical settings.

7.5. Applications in functional foods and nutraceuticals

The incorporation of *C. citratus* into functional foods,

herbal beverages, and nutraceutical formulations reflects growing consumer interest in plant-based health-promoting products. Its antioxidant and antimicrobial properties support food preservation, shelf-life extension, and potential enhancement of nutritional value. Regular dietary consumption of *C. citratus*-based products may contribute to immunomodulation and overall health maintenance.⁷⁶

7.6. Safety, standardization, and clinical translation

For successful clinical translation, issues related to safety, standardization, and dosage optimization must be addressed. Although *C. citratus* is generally regarded as safe when consumed at traditional doses, rigorous toxicological evaluations and clinical studies are necessary to establish standardized formulations and evidence-based therapeutic guidelines. Harmonization of extraction protocols and quality control measures is critical for ensuring reproducibility and regulatory acceptance.⁷⁷

8. Limitations and research gaps

Despite substantial experimental evidence supporting the antimicrobial, antioxidant, and cytoprotective properties of *C. citratus*, several limitations constrain its translational and clinical applicability. A major challenge lies in the lack of standardization of extraction methods, phytochemical profiling, and dosage reporting across studies. Variations in plant source, harvesting season, drying conditions, and solvent systems lead to significant heterogeneity in phytochemical composition, thereby making cross-study comparisons difficult and limiting reproducibility.

In addition, most available data are derived from *in vitro* investigations, with comparatively fewer *in vivo* studies and a notable scarcity of well-designed human clinical trials. Consequently, the pharmacokinetics, bioavailability, optimal dosing regimens, and long-term safety of *C. citratus* phytochemicals remain insufficiently characterized. This gap hinders the development of evidence-based therapeutic guidelines required for clinical translation.

Another limitation is the incomplete mechanistic understanding at the molecular level. While multiple biological effects have been reported, detailed insights into gene expression modulation, signaling pathway regulation, and target-specific interactions are limited. Advanced omics-based approaches, including transcriptomics, proteomics, and metabolomics, remain underutilized and represent an important avenue for future research.

Additionally, toxicological and interaction studies are limited, particularly regarding long-term exposure and

potential interactions with conventional drugs. Given the increasing interest in using *C. citratus* as an adjunct therapy, systematic evaluation of herb–drug interactions is essential to ensure safety.

Finally, although nanotechnology-based formulations and functional applications show promise, scalability, regulatory compliance, and cost-effectiveness have not been adequately addressed. Translational research, bridging laboratory findings with industrial and clinical implementation, remains a critical gap in knowledge.

9. Future perspectives and conclusion

The growing scientific evidence surrounding *C. citratus* highlights its considerable potential as a multifunctional medicinal plant with broad biomedical relevance. The convergence of its antimicrobial, antioxidant, and cytoprotective properties positions *C. citratus* as a promising natural candidate for addressing contemporary health challenges, including antimicrobial resistance, oxidative stress-mediated disorders, and cellular injury associated with chronic diseases. However, the successful translation of these properties into clinically relevant applications requires a strategic and evidence-informed research framework.

9.1. Future perspectives

Future research on *C. citratus* should prioritize the standardization of phytochemical profiles to ensure reproducibility and consistency across studies. Variability arising from differences in geographical origin, cultivation practices, harvesting time, and extraction methods remains a major limitation in current research. Establishing standardized extraction protocols and phytochemical benchmarks will be essential for regulatory approval and clinical acceptance.

Another critical area for future investigation is the elucidation of molecular mechanisms at the genomic, proteomic, and metabolomic levels. While multiple studies have demonstrated biological activity, deeper insights into intracellular signaling pathways, gene expression modulation, and long-term cellular responses are required to strengthen mechanistic understanding. Such studies will enhance the rational design of *C. citratus*-based therapeutics and improve targeted specificity.

The integration of nanotechnology and advanced drug delivery systems represents a promising avenue for enhancing the bioavailability, stability, and targeted action of *C. citratus* phytochemicals. Green-synthesized nanoconjugates and controlled-release formulations may overcome current pharmacokinetic limitations and

facilitate clinical translation. Additionally, combining *C. citratus* extracts with existing therapeutic agents warrants further exploration, particularly for synergistic antimicrobial and cytoprotective effects.

From a translational perspective, well-designed preclinical and clinical studies are urgently needed. Toxicological evaluations, pharmacokinetic profiling, and dose–response assessments are critical to establish safety margins and therapeutic windows. Human clinical trials, although limited to date, will ultimately determine the clinical efficacy and practical applicability of *C. citratus*-based interventions.

9.2. Conclusion

Cymbopogon citratus emerges as a biologically versatile plant endowed with a rich phytochemical composition that underpins its antimicrobial, antioxidant, and cytoprotective activities. Through multi-target mechanisms involving microbial membrane disruption, free radical scavenging, enhancement of endogenous antioxidant defenses, mitochondrial stabilization, and modulation of apoptotic and inflammatory pathways, *C. citratus* demonstrates significant potential for biomedical and therapeutic applications.

This review consolidates current experimental and mechanistic evidence, emphasizing the integrative nature of *C. citratus* bioactivities and their relevance to modern healthcare. While traditional usage has long supported its medicinal value, contemporary scientific validation provides a robust foundation for its development into standardized therapeutics, functional foods, and evidence-based supportive healthcare formulations.

In conclusion, *C. citratus* represents a promising bridge between traditional medicine and modern biomedical innovation. Future interdisciplinary research, coupled with rigorous clinical validation, is essential to fully realize its therapeutic potential and to translate its bioactive properties into safe, effective, and clinically relevant applications for global health benefit.

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