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REVIEW ARTICLE

Ocimum-derived bioactive metabolites as next-generation antimicrobials targeting drug-resistant pathogens

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Abstract

Antimicrobial resistance (AMR) is rapidly growing worldwide and becoming a well-being threat. It challenges the consumption of antibiotics and eventually jeopardises the management of diseases. Excessive use of antibiotics led to the development of pathogens that are resistant towards multiple drugs. *Ocimum* species (Tulsi) is known for their potent antimicrobial efficacy and for traditional pharmaceutical applications. It also holds a revered status in Ayurveda and was used to treat various diseases like respiratory, digestive issues, skin infections and stress-related disorders due to its rich phytochemical content that includes ursolic acid, flavonoids, eugenol, rosmarinic acid and essential oils. These bioactive compounds exhibit antimicrobial efficacy against pathogenic microbes. Mechanistically, its metabolites disrupt the microbial cell membranes, inhibit quorum sensing (QS), suppress the production of critical enzymes like β-lactamases, inhibit the formation of biofilm, thus making pathogens more susceptible to antibiotics. Notably, eugenol has been demonstrated to be effective against methicillin-resistant *Staphylococcus aureus* (MRSA), whereas linalool and thymol show efficacy against extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*. The main objective of this study is to seek and elucidate the possible mechanism of action and potential of *Ocimum* as sustainable next-generation antimicrobial agents, where *Ocimum*-based treatments represents "One Health" approach that could provide safe and natural ways to fight against AMR in humans and animals.

Keywords: AMR; essential oils; drug resistance; *Ocimum*; synergistic

Introduction

Antimicrobial resistance (AMR) is usually responsible for an estimated 1.27 million deaths worldwide each year, with projections indicating a rise (WHO/CDC reports). The discovery of antibiotics led to a shift in medication, significantly reducing deaths from bacterial infections and continues to play a crucial role in advanced healthcare systems (1). Initially celebrated as wonder drugs, antibiotics have saved many lives and are still widely relied upon. Beyond human medicine, these have also been used in livestock and poultry farming in developing countries as preventive measures to support the health system and enhance production (2). Unfortunately, antibiotics have enhanced a worldwide health threat and given rise to AMR against all micro-organisms, where they develop the ability to survive exposure to drugs that were designed to eliminate them. As these microorganisms adapt to withstand therapies and once-controllable infections grow progressively harder to eliminate, that frequently results in serious complications or fatal outcomes. This escalating global burden needs an urgent need to explore plant based sustainable antimicrobials.

Antibiotics are chemical substances produced by bacteria and are specifically targeted at bacterial infections. They are among the most used antimicrobials around the globe. Resistance to antibiotics has been rising exponentially, especially in areas where access to and regulation of these drugs are less controlled (3). When these medicines are taken very frequently or too much, it makes it easier for germs to change, survive and spread their ability to resist. Microbes also experience DNA mutations that are against those drugs that are used for their survival, making the treatment ineffective (4). The continuous increase in AMR in pathogens is known as "superbugs" that ultimately poses an alarming problem threating the medical progress. Microbial infections are not only difficult to treat but also result in higher mortality rates (5). The factors contributing to AMR are extremely complex and should involve sectors far beyond medicine. In this era, AMR is becoming a silently escalating crisis that affects everyone irrespective of age, gender, or location. The primary aim of this review is to investigate and clarify the potential mechanisms of action and efficacy of Tulsi as sustainable next-generation antimicrobial agents. The review also gives a detailed overview of taxonomy, ethnobotany, phytochemistry and pharmacology of Tulsi with special emphasis on antimicrobial properties. Efforts have also been made to delve into the mechanistic aspects of antimicrobial properties of this plant.

Effectiveness of natural products in combating AMR

In response to the increasing threat of AMR, many researchers are focusing on plant-based natural substances as an effective alternative to conventional medicines. These naturally derived plant or animal-based products can be obtained from plants, microbes, marine life and any other organisms. These products offer promising, effective therapeutic properties due to their structural diversity and unique biological activities. Many of the antibiotics widely used today, such as aminoglycosides, penicillin and tetracyclines, were originally derived from natural sources. Their chemical compositions, which are often difficult to reproduce synthetically, significantly contribute to their powerful antimicrobial properties, making them valuable in the search for new drugs. As AMR continues to degrade the effectiveness of standard treatments, the identification of nature's vast chemical library has become more advantageous nowadays. These bioactive compounds represent a largely untapped source of potential antibiotics that could work through novel and diverse mechanisms, addressing resistant strains more effectively (6). A key strength of many natural antimicrobial agents lies in their ability to target multiple pathways within a microbial cell. In contrast to many synthetic antibiotics that typically act on a single bacterial function, natural compounds often interfere with multiple cellular processes simultaneously. This multi-targeted strategy makes it more difficult for bacteria to adapt, as it would require simultaneous genetic changes at multiple sites to overcome the drug's effects.

Rationale for focusing on *Ocimum*

Ocimum sanctum, commonly known as Tulsi, has been held in high regard for centuries, particularly across the Indian subcontinent, due to its diverse healing properties (Fig. 1) (7). Its long-standing use in traditional medicine includes treatment for various bacterial, viral, fungal and vector-borne illnesses. Tulsi, like many other medicinal plants, has not only broad therapeutic potential but also a safe usage profile, with no significant toxic effects reported with regular consumption. The effective uses of Tulsi lie in its therapeutic efficacy and accessibility. Its abundance with no side effects has made it a great option for researchers who are looking for plant-based antimicrobial solutions (8). Many studies have proved that Tulsi leaf extracts and essential oils can act as effective curative agents against a wide range of pathogens, which makes it a strong option for replacing different synthetic medications in the medical industry. The linoleic acid present in oil which are derived from Tulsi, contributes to its antibacterial activity, particularly against microbes such as *Staphylococcus aureus, Bacillus pumilus* and *Pseudomonas aeruginosa* (9–11). Many reports suggested that the antibacterial properties of Tulsi are more effective when they are freshly plucked as compared to dried leaf preparations (12–14). The essential oil of Tulsi has also been studied for its anti-tubercular potential. It demonstrated notable activity against *Mycobacterium tuberculosis*, showing roughly one-tenth the potency of streptomycin and a quarter of the efficacy of isoniazid-two widely used anti-TB drugs (15).

Fig. 1. *Ocimum* sp.

Background of *Ocimum*

Taxonomy and species diversity

Ocimum sanctum, commonly known as Tulsi or Holy Basil, holds a central place in traditional medicine and spiritual practices, particularly in India (16). Taxonomically, it belongs to the family: Lamiaceae, Kingdom: Plantae, Division: Magnoliophyta, Class: Magnoliopsida, Order: Lamiales, Genus: *Ocimum* and Species: *Ocimum sanctum*. The genus *Ocimum* is known for its rich diversity, comprising approximately 35 to 65 aromatic plant species distributed across tropical and subtropical regions (17). These include economically and medicinally valuable species such as *Ocimum basilicum, Ocimum gratissimum* (often associated with Vana Tulsi), *Ocimum campechianum* and *Ocimum citriodorum* (lemon basil) (18, 19). *Ocimum sanctum* shows its prominent role in Ayurveda and it is also associated with religious and cultural traditions (16). *Ocimum sanctum* also depicts various significant intraspecific diversity, which are supplemented with several chemotypes and are different in their phytochemical profiles, oil composition and therapeutic uses (20). The main varieties of Tulsi include Rama Tulsi (with bright green leaves), Krishna or Shyam Tulsi (known for its purplish foliage) and Vana Tulsi, which is often identified as *O. gratissimum* (21). These varieties vary in appearance and habitat preference, organoleptic taste, aroma and medicinal properties, which contribute to the biodiversity and adaptive potential of the species.

Traditional and ethnomedicinal uses

Being an effective adaptogen and therapeutic herb, Tulsi, also called Holy Basil, is highly valued in Ayurveda. It has historically been used to support respiratory health (for colds, coughs and asthma), enhance immunity, lessen stress and improve digestion (22). Tulsi leaves are chewed fresh or ingested as a herbal tea regularly for overall health in several regions of Tamil Nadu, Gujarat, Maharashtra and North India. Tulsi, which is frequently made as remedies or pastes, is used in daily life by tribal and ethnic tribes, including the Bhil of Rajasthan and Madhya Pradesh, the Santhal of Jharkhand and West Bengal and the Toda of the Nilgiri Hills in Tamil Nadu to treat fevers, skin diseases and bug bites (23). The leaves extract, when combined with products like honey, ginger, or cloves, provides relief from influenza, bronchitis, cough and other respiratory diseases (24–26). Regular consumption of its leaves can boost immunity, enhance digestion, stimulate appetite and also support detoxification by purifying the blood (27). Cardiovascular support is another very important benefit from Tulsi, which can help to reduce cholesterol and strengthen the heart muscle (28). Tulsi also supports the nervous system and its calming nature is effective in managing stress-related problems (29). For getting relief from migraines and heat-induced discomfort the paste of Tulsi leaves mixed with sandalwood can be applied to the forehead. Tulsi also provides oral health, as chewing its leaves helps treat mouth ulcers and other bacterial infections (30).

Phytochemical profile

Tulsi is known for its therapeutic and nutritional benefits and contains a wide array of bioactive phytochemicals. The levels and makeup of these compounds are strongly shaped by multiple environmental factors, including soil characteristics, weather conditions (like humidity, rainfall and temperature) and, along with the stage of harvesting and the methods of post-harvest handling, processing and storage. Preliminary phytochemical analyses have shown the presence of both primary and secondary metabolites in the plant. These include carbohydrates, proteins, lipids, flavonoids, saponins, tannins, glycosides, alkaloids and volatile oils. In addition to its pharmacological uses, Tulsi holds considerable nutritional importance (Table 1). The fresh leaves contain approximately 3 % proteins and amino acids, 27 % carbohydrates, 25 % lipids and fatty acids, 10 % mineral content and 1 % vitamins. Elemental analysis of the leaf matter reveals a composition of about 42 % carbon, 51 % oxygen, 9.4 % hydrogen, 7.4 % nitrogen and 0.7 % sulfur (31).

A distinctive feature of Tulsi is its essential oil content, which contributes to its characteristic aroma. These volatile oils make up around 0.7 % (v/w) of the leaf content and are composed of several key constituents, including eugenol (ranging between 67.4 % to 72.8 %), 1,8-cineole, estragole, β-caryophyllene, β-pinene, (E)-β-ocimene and β-bisabolene. Other significant compounds found in the volatile oil include camphene, (Z)-α-bisabolene, germacrene D, methyl eugenol, α-caryophyllene, chavicol and (E)-α-bergamotene. Additionally, less common phytochemicals such as borneocamphor, beta-caryophyllene epoxide, humulene oxide, rosmarinic acid, calamine, farnesene, eicosane, (+)-germacrene A, β-guaiene, α-murolene and 5-isopropyl-2-methylphenol have also been detected (32) Ocimum species exhibit broad-spectrum antimicrobial activity (Table 2), with *O. sanctum* and *O. tenuiflorum* showing strong antibacterial effects against both Gram-negative and Gram-positive bacteria, alongside antifungal (Table 3) and antiviral potential (Table 4). Major phytochemicals such as eugenol, ursolic acid, rosmarinic acid, flavonoids and essential oils are largely responsible for these bioactivities. Other species, including *O. basilicum*, *O. gratissimum* and *O. kilimandscharicum*, also demonstrate variable antibacterial, antifungal and limited antiviral effects, highlighting the therapeutic versatility of the genus.

Tulsi leaves also serve as an important mineral source, containing essential elements like calcium (Ca), potassium (K), sodium (Na), magnesium (Mg), phosphorus (P), iron (Fe), and zinc (Zn). Additionally, trace amounts of heavy metals, including manganese (Mn), copper (Cu), molybdenum (Mo), nickel (Ni), chromium (Cr), arsenic (As), lead (Pb), mercury (Hg), have been reported. The fixed oil derived from Tulsi seeds comprises a range of fatty acids. The omega-3 and omega-6 fatty acids, derived from α-linolenic acid (18:3, n-3) and linoleic acid (18:2, n-6) respectively, play essential roles in cell membrane integrity and are key precursors in the biosynthesis of eicosanoids like prostaglandins, leukotrienes and thromboxanes. Tulsi is nutritionally fortified with different vitamins, including Vitamin A, Vitamin B-complex group,

Table 1. Phytochemical constituents of *Ocimum* metabolites

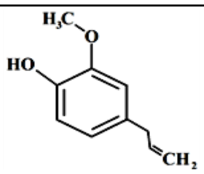
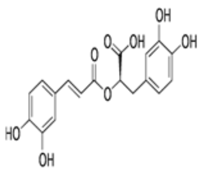
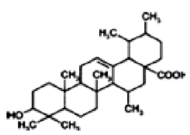
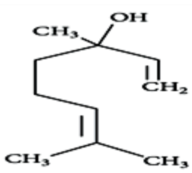
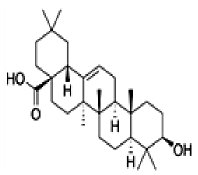
Metabolite	Molecular structure	Chemical class	Structural characteristics	Primary uses and benefits
Eugenol		Phenylpropene	Allyl chain-substituted guaiacol, contains a phenolic ring with a methoxy group	Potent antimicrobial, analgesic (used in dental care) and antioxidant
Rosmarinic acid		Polyphenol	An ester of caffeic acid and 3,4-dihydroxy phenyllactic acid	Anti-inflammatory, antiviral and used for neuroprotection
Ursolic acid		Pentacyclic triterpenoid	A five-rind structure with a carboxylic acid group at one end	Signicicant anti-tumor, hepatoprotective and skin-healing properties
Linalool		Terpene alcohol	A linear monoterpene with a hydroxyl group and two double bonds	Provides the floral scent used for stress reduction and as an anticonvulsant
Oleanolic acid		Pentacyclic triterpenoid	Isomer of ursolic acid, differs in the position of the methyl groups	Antiviral (HIV / Hepatitis), anti-inflammatory and protects the liver

Table 2. *Ocimum* possessing antibacterial properties

***Ocimum* Sp.**	**Antibacterial Activity**	**References**
Ocimum sanctum (Tulsi)	Strong activity against *E. coli*, *Salmonella enterica*, *Listeria monocytogenes*; more effective against Gram-negative bacteria	(74)
Ocimum basilicum (Sweet Basil)	Active against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E. coli*	(75)
Ocimum gratissimum	Exhibits antibacterial activity against *Staphylococcus aureus*, *E. coli*, *Salmonella* spp.	(76)
Ocimum kilimandscharicum	Antibacterial effects primarily against *Staphylococcus aureus* and *Bacillus subtilis*	(77)
Ocimum basilicum (Sweet Basil)	Antibacterial effects against *E. coli*, *Salmonella*, *Pseudomonas* spp.	(78)

Table 3. *Ocimum* sp. possessing antifungal properties

***Ocimum* Sp.**	**Antifungal Activity**	**References**
Ocimum sanctum (Tulsi)	Effective against *Candida albicans* and *Aspergillus niger*	(79)
Ocimum basilicum (Sweet Basil)	Shows antifungal effects against *Candida* species and dermatophytes	(80)
Ocimum gratissimum	Effective against *Candida albicans* and *Aspergillus* species	(81)
Ocimum kilimandscharicum	Limited but notable antifungal activity reported	(82)
Ocimum basilicum (Sweet Basil)	Antifungal against *Candida* spp. and other fungi	(83)

Table 4. *Ocimum sp*. possessing antiviral properties

***Ocimum* Sp.**	**Antifungal Activity**	**References**
Ocimum sanctum (Tulsi)	Exhibits inhibitory effects against herpes simplex virus (HSV) and influenza virus	(84)
Ocimum basilicum (Sweet Basil)	Demonstrated Antiviral activity against human immunodeficiency virus (HIV) and dengue virus	(85)
Ocimum gratissimum	Shown Antiviral effects against some respiratory viruses	(86)
Ocimum basilicum (Sweet Basil)	Potential Antiviral activity reported against herpes viruses	(87)

Vitamin C, Vitamin D, Vitamin E and Vitamin K, which offer antioxidant protection against cellular damage and oxidative stress and support immune function**.** Phenolic compounds and flavonoids are another significant class of phytochemicals that are present in Tulsi. These include vanillin, orientin, vicenin, ursolic acid, gallic acid, vanillic acid, luteolin, apigenin, apigenin-7-O-glucuronide and molludistin (33). Complex glycosides and their methoxy derivative have also been identified from Tulsi extract. The alcoholic extract of Tulsi from the aerial parts of the plant contains an even broader phytochemical diversity, including stigmast-5-en-3β-ol (stigmasterol), triacontanol ferulate, isovitexin, vicenin-2, aesculectin, chlorogenic acid, gallotannins like gallic acid methyl and ethyl esters, caffeic acid derivatives such as protocatechuic acid and vanillic acid.

Antimicrobial properties of *Ocimum*

Tulsi extracts have demonstrated significant antibacterial effects against a broad spectrum of foodborne pathogens. In several studies, *Ocimum* extracts exhibited pronounced inhibitory activity, particularly against Gram-negative bacteria such as *Salmonella enteritica*, *Vibrio parahaemolyticus* and *Escherichia coli* (34–36). In comparison, the antibacterial activity against Gram-positive bacteria such as *Listeria monocytogenes,* was generally found to be weaker, which suggests a selective effectiveness toward Gram-negative strains (34, 37). It has been observed that Gram-negative bacteria exhibit higher sensitivity due to their outer membrane permeability barrier, where it inhibit growth of *Escherichia coli*, *Salmonella typhi* and *P.aeruginosa* under *in vitro* conditions, as demonstrated by significant zones of inhibition in agar diffusion assays (13, 33, 34). The leaves of Tulsi contain bioactive chemical compounds such as eugenol, ursolic acid, flavonoids and essential oils, which also contribute to their antimicrobial potential against various foodborne microbial pathogens. For phytochemical extraction, the chloroform-based extraction method has emerged as particularly effective in isolating phytochemicals responsible for antimicrobial activity (7). The essential oils derived from Tulsi leaves also possess notable antibacterial properties, which further enhance the herb's potential as a natural preservative (11, 38). A systematic comparison of minimum inhibitory concentration (MIC) values was found to exhibit MICs in the range of 50–500 µg/mL against common bacterial pathogens, depending on the extract type and target organism (39). In contrast, conventional antibiotics such as ciprofloxacin, ampicillin, or gentamicin typically show much lower MICs (0.1–10 µg/mL). Essential oils rich in eugenol or linalool often demonstrate comparatively lower MICs (25–100 µg/mL) than crude extracts (40). While *Ocimum* metabolites are less potent on a per-mass basis, their multi-target mechanisms and reduced resistance pressure offer complementary advantages. These comparisons highlight the need to position *Ocimum* compounds as adjuncts or leads for optimisation, rather than direct antibiotic replacements (41).

Due to antibiotic resistance and food safety, the antimicrobial properties of Tulsi have promising applications. Its extracts serve as natural preservatives in food systems, which reduces the reliance on synthetic additives. Additionally, the bioactive compounds in Tulsi also offer the development of novel antibacterial agents to reduce foodborne infections (13). Tulsi extracts possess antibacterial activity against pathogenic bacteria isolated, which underscores their value not only in traditional medicine but in modern food preservation and pharmaceutical development.

Mechanisms of action against microbes

Disruption of cell membranes

Eugenol, as well as thymol extracted from Tulsi, are highly lipophilic compounds that can easily enter bacterial membranes and disturb their mechanical integrity (42, 43). Disturbance within the lipid bilayer causes breakdown of the cellular membrane, which leads to an increase in permeability and results in the leakage of essential ions, like potassium (K^+) and calcium (Ca^{2+}) (44). The loss of

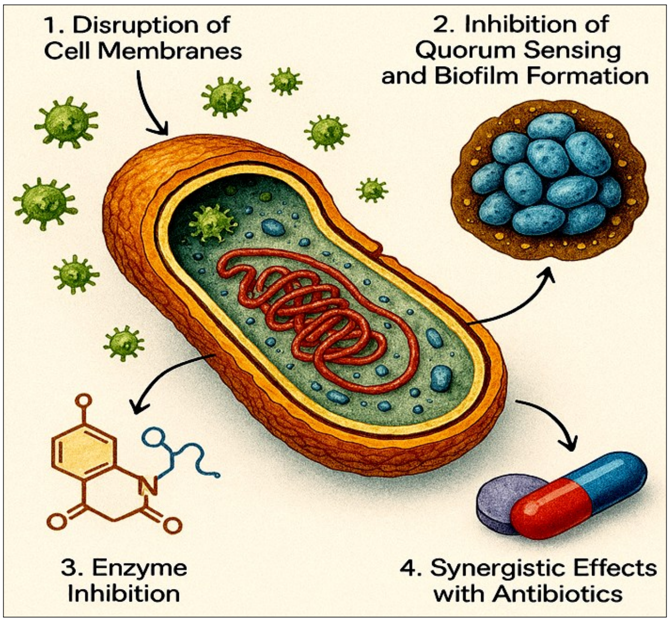


Fig. 2. Mechanisms of action against pathogenic microbes.

intracellular proteins and nucleotides again starts to destabilise the cell integrity, leading to shrinkage of cytoplasm and ultimately to cell lysis (Ca^{2+}) (45). In the case of fungi, these metabolites specifically interact with the cell membrane and impair its fluidity and hamper its overall membrane stability, thereby inhibiting growth and survival (46) (Fig. 2).

Inhibition of quorum sensing and biofilm formation

Many pathogenic bacteria performs quorum sensing (QS) for communication and regulation of virulence factors making it crucial for antimicrobial action (47). *Ocimum* chemical metabolites such as eugenol and linalool, disrupt QS by interfering with signalling molecules like acyl-homoserine lactones in Gram-negative bacteria and peptide-based signals in Gram-positive bacteria (48). Disruption of QS interferes with the synchronised production of toxins, enzymes and other virulence determinants, thereby markedly diminishing pathogenic potential (49). Moreover, these bioactive compounds restrict biofilm development by hindering microbial attachment, clumping and the synthesis of extracellular polymeric substances (EPS), as demonstrated in *P. aeruginosa* (50, 51). Through suppression of QS and inhibition of biofilm formation, these metabolites of *Ocimum* increase microbial vulnerability to both antibiotics and the host's immune response.

Enzyme inhibition

In its antimicrobial action Tulsi also inhibits key microbial enzymes, DNA Gyrase Topoisomerase II, β-lactamase, Proteases, Transpeptidase and Lipases, which are essential for survival and resistance (11, 52–55). Compounds like eugenol from Tulsi are found to inhibit β-lactamases, which reestablishes the efficiency of β-lactam antibiotics against resistant bacteria. Other metabolites from Tulsi target efflux pumps and also reduce the ability of bacteria to expel antibiotics, ultimately leading to higher intracellular drug concentrations and improved bactericidal effects (56). Furthermore, inhibition of enzymes such as ATPases and proteases disrupts vital metabolic pathways, which also impairs energy production and protein turnover. *Ocimum* compounds also interfere with ergosterol biosynthetic enzymes, further weakening cell membranes and reducing fungal growth (56).

Synergistic effects with antibiotics

One of the most fascinating aspects of Tulsi metabolites is their synergistic interaction with conventional antibiotics. Biochemicals such as eugenol help to enhance the activity of aminoglycosides and tetracyclines, while linalool helps in increasing the potency of fluoroquinolones, which strengthens the effect of macrolides by suppressing efflux mechanisms (57). These synergistic interactions lower the MIC of antibiotics, effectively overcoming drug resistance in many pathogens (41). Using combination therapy reduces the required antibiotic dose, thereby reducing toxicity and adverse effects, while simultaneously delivering a twofold mode of action by interfering with multiple microbial pathways. This synergistic effect underscores the promise of Tulsi metabolites as supportive agents in antimicrobial treatment, presenting a natural and sustainable approach to tackling multidrug-resistant infections.

However, *Ocimum*-derived metabolites exhibit antimicrobial efficacy *in vitro* by disrupting microbial cellular membranes, inhibiting enzymes and interfering with biofilm production (58). *In vivo* studies using animal models have demonstrated a reduction in pathogen load and modulation of the host immune response, while in silico analyses reveal strong binding affinities of key metabolites to microbial target proteins, thereby supporting their mechanistic potential (59, 60). Altogether, these approaches provide complementary evidence for their efficacy as next-generation antimicrobials.

Ocimum and antimicrobial resistance (AMR)

Antimicrobial resistance depicts a critical threat, with the increase of multiple drug-resistant (MDR) pathogens such as *Pseudomonas aeruginosa*, *E. coli* and *Klebsiella pneumoniae*, which show resistance towards multiple antibiotics and pose major treatment challenges. *Ocimum* species, including *O. sanctum* and *O. basilicum*, have acquired significant attention as sources of natural metabolites with activity against resistant strains. Eugenol exhibits inhibitory activity against methicillin-resistant *Staphylococcus aureus* (MRSA), whereas linalool and thymol have been shown to be effective against extended-spectrum β-lactamase (ESBL)-producing *E. coli* (61, 62). Phytochemicals such as eugenol, thymol, carvacrol, rosmarinic acid and ursolic acid demonstrate effective antimicrobial effects that extend to MDR bacteria and fungi (63–64) (Fig. 3). These metabolites act through multiple mechanisms, making them less susceptible to resistance development. Compared to conventional drugs, microbes often develop resistance. Their lipophilic properties allow them to penetrate and disrupt microbial membranes, a process that bypasses common resistance determinants (65). Additionally,

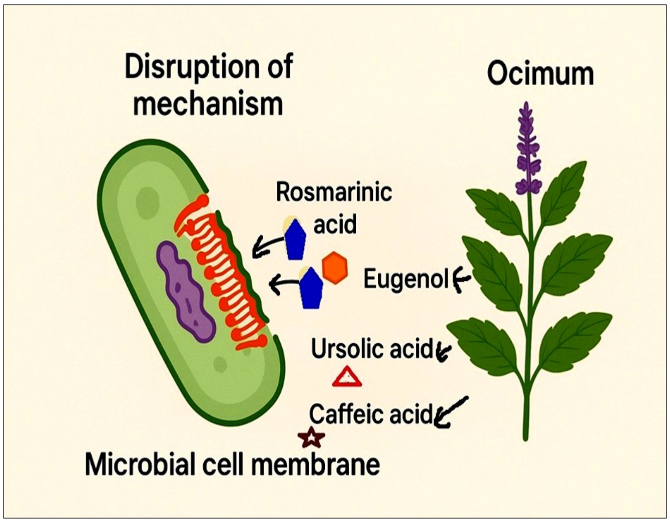


Fig. 3. Phytochemicals disrupting the cellular membrane of pathogenic microbes.

several *Ocimum*-derived compounds function as resistance modulators: eugenol has been reported to inhibit β-lactamases, thereby restoring the effectiveness of β-lactam antibiotics, while linalool and thymol suppress bacterial efflux pump activity, increasing intracellular drug accumulation and enhancing the bactericidal effects of antibiotics (66). Beyond this, *Ocimum* metabolites interfere with QS and inhibit biofilm formation in resistant pathogens, reducing virulence and persistence; for instance, eugenol has demonstrated anti-biofilm activity against MDR *Pseudomonas* and *Klebsiella*. Rosmarinic acid and other compounds also show synergistic effects with antibiotics, lowering minimum inhibitory concentrations (MICs), reducing required doses and minimising toxicity risks (67, 68). This dual action, combining direct antimicrobial effects with resistance-modulating properties, highlights the potential of *Ocimum* metabolites to serve as effective adjuvants in antibiotic therapy (69). Their multi-targeted mechanisms not only make it harder for microbes to evolve resistance but also help reduce selective pressure when used alongside conventional drugs. Collectively, the evidence positions *Ocimum* as a promising natural resource in the fight against AMR, offering both stand-alone antimicrobial activity and the ability to restore or enhance the effectiveness of existing antibiotics.

Compared to non-*Ocimum* plant-derived antimicrobials such as curcumin (*Curcuma longa*), allicin (*Allium sativum*) and neem limonoids (*Azadirachta indica*), *Ocimum* metabolites generally show moderate antimicrobial potency but broader multi-target activity. While compounds like allicin often exhibit lower MIC values, *Ocimum* phytochemicals such as eugenol and rosmarinic acid offer better safety profiles and antioxidant–immunomodulatory benefits. These features position *Ocimum* metabolites as promising adjuncts or synergistic agents rather than direct replacements for highly potent plant antimicrobials (70).

Limitations and challenges

Despite the various antimicrobial potential of *Ocimum* metabolites, there are several limitations and challenges that hinder their clinical translation. One major issue associated with the variability in phytochemical composition is that some of the factors, like plant species, cultivation conditions, soil type, climate and harvest time, significantly influence the quantity and quality of bioactive compounds. Moreover, the absence of uniform extraction and purification techniques frequently results in variations in the concentration, purity and biological activity of extracts reported across different studies (71). In terms of bioavailability and pharmacokinetics, it possesses poor water solubility and rapid metabolism, which can reduce its absorption and therapeutic efficacy *in vivo*. Due to differences in metabolism, distribution and clearance among individuals or animal models, the consistency and predictability of their antimicrobial effects can be affected. Developing stable and effective formulations for oral or topical delivery is also becoming difficult due to compound instability and degradation. Another critical concern is achieving sufficient concentrations at infection sites without causing toxicity. A major limitation lies in the limited knowledge of safety and toxicity profiles; although *Ocimum* has long been considered safe in traditional use, elevated levels of certain metabolites, such as eugenol, may exert cytotoxic or irritant effects, highlighting the need for precise dosage regulation. Standardising extracts, ensuring safety and scaling production for clinical use are complex and resource-intensive and are also major concerns.

Prospects

Research on *Ocimum* appears to be highly encouraging and diverse, particularly in the domain of antimicrobial management, novel drug development and clinical validation. Its wide spectrum of phyto-constituents-including ursolic acid, eugenol and rosmarinic acid-demonstrates substantial promise as precursor molecules that can be used for designing new therapeutic agents aimed to possess anti-cancer, anti-inflammatory and anti-neurological disorders (72). Progress in integrative molecular docking and omics approaches can lead to the discovery and refinement of these phyto-metabolites (Fig. 4). Its phytochemicals can act synergistically with conventional drugs, prevent microbial resistance mechanisms like quorum sensing and thus serve as natural antimicrobials in agriculture and livestock management. However, despite inspiring preclinical data, the conversion to clinical application remains a serious challenge. Standardised extraction protocols, severe metabolite profiling and well-designed human trials are important to validate efficacy and safety (73). *Ocimum* metabolites as antimicrobials include standardising extract composition and optimising active compound concentrations for consistent efficacy. Preclinical studies should focus on pharmacokinetics, bioavailability and toxicity profiling in relevant animal models. Clinical trials can be designed to evaluate safety, dosing and synergistic effects with conventional antibiotics. Additionally, regulatory pathways should be addressed early to facilitate translation into therapeutics and integration into AMR management strategies. Associations with regulatory bodies such as AYUSH and incorporation into global pharmacopoeias could pave the way for broader acceptance and application of *Ocimum*-based therapeutics.

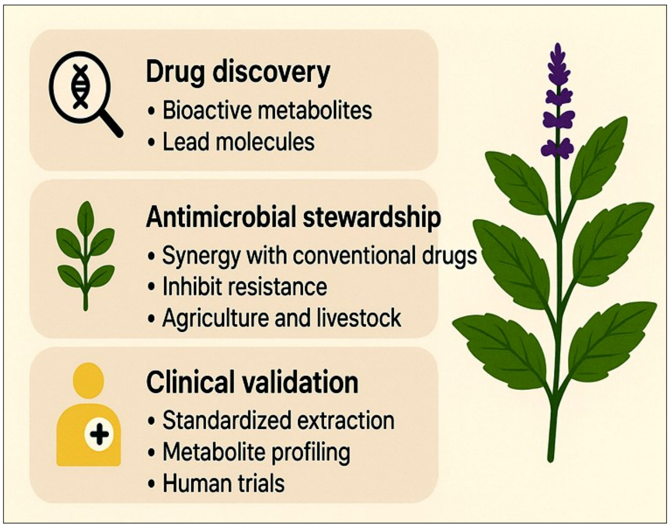


Fig. 4. Prospects of *Ocimum* phytochemicals.

Conclusion

Antimicrobial resistance is a worldwide health threat produced largely by the over-consumption of antibiotics, leading to evolvement of multidrug-resistant pathogens. *Ocimum* species (Tulsi), valued in Ayurveda, own rich phytochemicals such as eugenol, ursolic acid, flavonoids and crucial oils with strong antimicrobial efficacy. These components can disrupt cellular microbial membranes, inhibit quorum sensing, suppress enzymes β-lactamases and stop biofilm formation, enhancing pathogenic susceptibility towards antibiotics. Eugenol proved to be efficient against MRSA, while linalool and thymol were found to be prominent antibacterials against ESBL-producing *E. coli*. *Ocimum*-derived metabolites hold significant promise as next-generation antimicrobials, with potential applications spanning human health, veterinary medicine, agriculture and environmental control of antimicrobial resistance. Their integration into these sectors could reduce reliance on conventional antibiotics, mitigate the spread of drug-resistant pathogens and support sustainable practices, highlighting the need for targeted research, policy support and translational development. Thus, *Ocimum* metabolites also synergise with antibiotics by lowering the MICs. Modern tools like genomics, molecular docking and metabolomics can deepen understanding of these effects. Integrating *Ocimum*-based strategies into a "One Health" framework proposes sustainable solutions towards AMR.

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Authors' contributions

PB conceptualised the study. FF wrote the original draft of the manuscript. PS reviewed and edited the manuscript. MHS conducted the formal analysis and undertook the investigation. SG developed the methodology. SS supervised the project and handled project administration.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interest to declare.

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