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Review Article

Antimicrobial Activity of Essential Oils and Their Mechanism of Action Against Bacterial and Fungal Infections

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Abstract

The development of resistance to various antimicrobial agents by bacteria, fungi, viruses, and parasites poses a major challenge to the medical field in treating the infections they cause. Consequently, there is an urgent need to explore new and innovative antimicrobials. A promising solution lies in the use of natural products, such as essential oils, as antimicrobial agents. Herbs and essential oils have been used since ancient times in various aspects of life, including perfumes, cosmetics, agriculture, and industry. In medicine, these essential oils have demonstrated numerous applications, such as analgesic, anti-inflammatory, antioxidant, fungicidal, and antitumor activities. Essential oils present a viable alternative to synthetic chemicals due to the presence of biologically active compounds, such as phenols and terpenes, that inhibit or prevent pathogen growth. This review paper aims to explore the importance of essential oils, their components, and the mechanisms they use to combat pathogens. It will also highlight their role as a potential solution to multidrug resistance and discuss future prospects.

Keywords: Essential oils; Antibiotics; Antimicrobial resistance; bacterial infection; Fungal infection; Terpenes; Terpenoids.

1. INTRODUCTION

Essential oils contain a complex mixture of bioactive compounds, such as terpenes, phenols, and aldehydes, which contribute to their antimicrobial activity (Carpena *et al.,* 2021). These bioactive constituents have been able to exhibit a range of antimicrobial effects, including inhibiting the growth of bacteria and fungi, disrupting their cell membranes, and interfering with their metabolic processes (Tariq *et al.,* 2019). Understanding the specific mechanisms by which essential oils exert their antimicrobial effects is crucial for harnessing their potential in the development of new antimicrobial therapies. The use of essential oils as a natural and alternative approach to combating bacterial and fungal infections has gained significant attention in recent years. Essential oils, derived from various plants, have exhibited promising antimicrobial properties, making them a subject of interest for researchers and healthcare professionals alike (Bassolé and Juliani, 2012). Through understanding the properties and modes of action of essential oils, we can gain valuable insights into their potential use as effective antimicrobial agents (Yang *et al.,* 2021a).

There has been increasing interest in the investigation of different species of plants to identify their potential therapeutic applications as medicines (Nik Mohamad Nek Rahimi *et al.,* 2022). Natural products such as essential oils are secondary metabolites that can be obtained from either plant or animal sources or produced by microorganisms (Moo *et al.,* 2020a). Several essential oils been used to treat infections caused by a variety of infectious agents, including bacteria, viruses, and parasites, as a result of their lipophilic character, together with their phenolic components (García-Salinas *et al.,* 2018).

Over the past decade, highly potent oils with a broad spectrum of inhibitory and destructive activities towards different microorganisms, due to direct effects of their main elements or some synergitic effects with established treatments, have been identified. The chemical structure of the compounds present in essential oils is generally related to their antiseptic properties. Together with their lipophilic properties, the chemical properities of phenols and phenolic ethers contribute to the disruption and subsequent disintegration of the lipophilic microbial envelope. Since many studies have demonstrated such results, interest in the antioxidant and antimicrobial activities of essential oils in the augmentation of established therapeutics has been increasing. The beneficial effects of essential oils in oil-in-water emulsions used as foodstuffs are related to their potential to safely eliminate dangerous microorganisms. The antimicrobial potency of various essential oils is the main determinant of their potential use in specific clinical applications. Some of the major current and future antibacterial, and antifungal applications of essential oils have therefore been collected in the sections below. According to International Organization for Standardization (ISO), essential oil is a 'product obtained from a natural raw material of plant origin, by steam distillation, by mechanical processes from the epicarp of citrus fruits, or by dry distillation, after separation of the aqueous phase if any by physical processes' and it can also be treated physically without changing its composition (Sharma *et al.,* 2021).

1.1. Overview of Antimicrobial Resistance:

Antimicrobial resistance (AMR) occurs naturally but is accelerated by the misuse of antimicrobial agents in humans, animals, and the environment. The misuse of antibiotics and resistance resulting from over consumption in humans and animals is a factor in the emergence and spread of resistance. Patients not completing antibiotic courses, the use of low-quality medicines, inappropriate prescribing, or abuse when used without medical prescriptions thgether with verinary use to enhancen food utilization and growth rates in animals, all contribute to long-term effects at the population level, often leading to disease management problems. Prescriptions from human or veterinary clinics, are often not regulated to avoid inappropriate prescription, such as prescribing antibiotics for viral infections in humans and animals. This is especially the case when demanding patients expect to leave the clinic for some kind of treatment for their ailment (Salam *et al.,* 2023).

Antimicrobials have generated significant health gains for humans and domestic animals, as well as crop plant protection in agriculture. The rapid spread of AMR through bacterial populations cannot be attributed to a single mechanism. It is often the result of complex processes. It is therefore necessary to subdivide antibiotics into groups based on the different mechanism of action before analyzing the factors that affect resistance to these molecules (Mancuso *et al.,* 2021). The World Health Organization has reported that resistance to major human pathogens has reached alarming levels in many parts of the world. In 2019, bacterial antimicrobial resistance was linked to approximately 5 million deaths, and without effective intervention, this figure is expected to rise significantly by 2050, highlighting the critical need for immediate action. (Ho *et al.,* 2025) As a result, the world urgently needs to change how it prescribes and uses antibiotics. The emergence of AMR is a reflection of the diverse mechanisms by which microbes adapt to changes in their environment and resist the potent actions of different types of antimicrobial agents, including antibiotics, antivirals, antifungals, and antiparasitics.

1.2. Importance of Essential Oils:

The subject of bacterial resistance to essential oils has been reviewed previously, although not to the same extent as resistance to the most commonly prescribed antibiotics which garnered intense public discussion in recent years. As consumers are becoming more and more informed about issues of food safety, health, and nutrition, they are also becoming more aware of the benefits and potential applications of medicinal and aromatic plants and their metabolites. These plants produce a large variety of secondary metabolites with diverse potential applications; among them, essential oils (Dhifi *et al.,* 2016). Essential oils derived from plants contain a wide range of bioactive compounds such as terpenes, phenols, aldehydes, ketones, alcohols, and esters that contribute to their therapeutic effects. Before incorporating these oils into drug delivery systems, it is essential to understand both traditional and modern methods used for their extraction from various botanical sources (Sultana *et al.,* 2025). Essential oils from dill, rosewood, thyme, oregano, cinnamon, lemongrass, spearmint, clove, and tea tree oils have been widely studied, along with a few of their main chemical components. The antimicrobial activities of essential oils have been correlated with non-specific hydrophobic interactions in which water is a competing solvent and structural lipids are solubilized and displaced from the cellular membrane. Some essential oils, such as those from Melaleuca alternifolia, Thymus moroderi, and T. camphoratus, destroy bacteria or yeast through a combination of cell lysis and ultrastructural changes. The lipophilic nature of the phenylpropanoids, which are present in many essential oils, accounts for their interaction with bacterial membranes. These compounds can accumulate in hydrophobic protones, competing with structural lipids, such as phospholipids and fatty acids. This accounts for one of the major concerns surrounding the use of essential oils in food applications linked to their toxicity, with some essential oil constituents such as puleqone and thujone being toxic when consumed in large amounts (Mukurumbira *et al.,* 2022).

1.3. Essential Oils composition:

Essential oils are in general a very complex mixture of 60–300 of nonpolar and semipolar lipophilic components of low molecular weight, at different concentrations with two or three appearing to be major constituents: (i)terpenoids, straight-chain compounds not containing any side chain, (ii) aromatic and phenolic components and (iii) Sulfured derivatives. The difference in taste and odor of essential oils highly depends on the plant type, season of harvesting, geographical location, methods of drying and the techniques involved in extraction(Wani *et al.,* 2021). As Goodarzi and his partners conducted an analysis of the components of the *Astrodaucus persicus* plant using Gas Chromatography-Mass Spectrometry (GC-MS). Their study revealed the presence of α-thujene, β-pinene, and α-pinene in abundance in the essential oils of the blue flowers and fruits. In contrast, the primary components found in the essential oil of the blue leaves and stems were α-thujene, α-pinene, and α-fenchene. Additionally, β-pinene, α-thujene, and α-pinene were identified in the essential oils of the ripe fruits(Goodarzi *et al.,* 2016).

Essential oils are concentrated liquids of complex mixtures of aromatic hydrophobic oily volatile compounds and can be extracted from different parts of plants such as bark, buds, flowers, fruits, leaves, peels, roots, seeds, twigs, or whole plant from a single botanical source to give a spectrum of different activities (Masyita *et al.,* 2022). Terpenoids play several physiological and ecological functions in plant life through direct and indirect plant defenses and also in human society.It is worth noting that the effectiveness of essential oils against a wide range of pathogens is largely due to their chemical composition, which includes compounds such as phenols, terpenoids, aldehydes, ketones, ethers, epoxides, and others (Wani *et al.,* 2021). For example, each type of terpene imparts unique aromatic and biological properties to the essential oil. Alcohols, on the other hand, are known for their antimicrobial and anti-inflammatory properties, making them valuable components of essential oils with potential medicinal benefits. Esters contribute to the fruity and floral aromas of essential oils, while phenols exhibit strong antibacterial and antifungal activities (Jilo, 2021).

In general, their antimicrobial activity is related to the interaction of some secondary metabolites present in essential oils with the bacterial cell structure. The main mechanism of action of EOs against microorganisms involves the interaction of their hydrophobic components with the lipids of the cell membrane.(da Silva *et al.,* 2021). This various variability gives rise to the diverse range of essential oils available, each with its own unique composition and properties. Understanding the chemical composition of EOs is crucial for harnessing their therapeutic potential and developing effective antimicrobial agents. The interaction of the active components with the bacterial membrane results in the loss of membrane integrity, which damages the membrane and alters how the electron transport chain functions, how nutrients are absorbed into the cell, how proteins and nucleic acids are synthesized, how cellular content organizes, and how enzymes necessary for energy metabolism retain activity, all of which ultimately lead to cell death. The diverse range of chemicals found in EOs make different contributions to the biological activity. Each type of terpene imparts unique aromatic and biological properties to the EO. Alcohols, on the other hand, are known for their antimicrobial and anti-inflammatory properties, making them valuable components of EOs with potential medicinal benefits. Esters contribute to the fruity and floral aromas of EOs, while phenols exhibit strong antibacterial and antifungal activities.

1.4. Terpenes and terpenoids:

Studies have been performed on plant secondary metabolites such as EOs in the hope of discovering an theraputic alternatives that can alleviate the current challenge of antibiotic resistance. EO is a concentrated plant secondary metabolite composed of a mixture of chemical compounds ranging from terpenes and terpenoids to aromatic compounds that gives fragrance to a plant. Numerous studies have established the antimicrobial potential of essential oils against bacteria, fungi, and viruses(Yang *et al.,* 2021a). Terpenes are made up of isoprene units and constitute one of the largest and most structurally diverse families of natural products. Still more numerous than terpenes is a class of compounds named "terpenoids" (or isoprenoids). Terpenes are hydrocarbons, while terpenoids are a modified class of terpenes that present oxygen-containing functional groups, such as ketone, hydroxy, aldehyde, ether, or carboxylic moieties(de Sousa *et al.,* 2023).

Furthermore, terpenes are known for their antimicrobial effects on both antibiotic-susceptible and antibiotic-resistant bacteria, primarily through mechanisms such as inducing cell rupture and inhibiting the synthesis of proteins and DNA. Building on this evidence, terpenes like carvacrol, carvone, eugenol, geraniol, and thymol have exhibited significant antibacterial properties against *Staphylococcus aureus (Masyita et al., 2022).* In addition to their antibacterial properties, terpenes and terpenoids play a crucial role in supporting and enhancing human health. Studies conducted in recent decades have demonstrated their use as anticancer, anti-inflammatory, antioxidant, anti-allergic, antineuropathic, antiaggregative, anticoagulant, sedative, and analgesic agents, facilitated by the activity of monoterpenes, sesquiterpenes, diterpenes, triterpenes, tetraterpenes, and glycosides (Zhao *et al.,* 2016). Their applications extend beyond these therapeutic benefits, encompassing pharmaceutical products, nutritional supplements, food and beverages, cosmetics, perfumes, synthetic chemicals, flavor and aroma additives, rubber products, and the biofuel industry(Tetali, 2019).

These subtle structural differences between terpenoids and phenylpropanoids generate disparity between their antimicrobial activities and the diversity of observable cellular effects, leading us to believe that more than one mechanism of action is involved. They are classified as hemiterpenes (one isoprenoid unit);

monoterpenes (two isoprenoid unites); sesquiterpenes (three isoprenoid unites); diterpenes (four isoprenoid unites); sesteterpenes (five isoprenoid unites); triterpenes (six isoprenoid unites) and tetraterpenes (eight isoprenoid unites) (Cappiello *et al.,* 2020). It is counterintuitive to propose a single mechanism for EO action, in view of the complex mixture of chemical compounds in EOs that exhibits synergistic or antagonistic effects on their combined over all biological activity (Andrade-Ochoa *et al.,* 2021) (Boncan *et al.,* 2020).

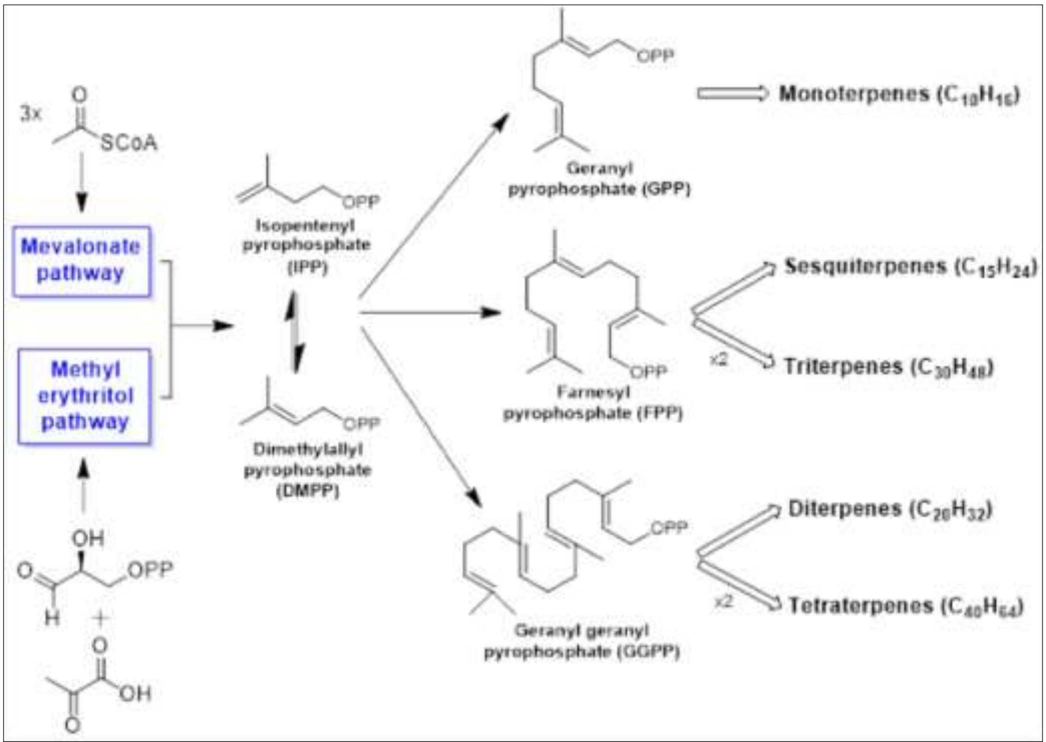

Figure 1: General scheme for the biosynthesis of terpenoids (de Sousa *et al.,* 2023). Classifying the terpenes into several categories according to the number of C5 building blocks in their core structure: hemiterpenes (C_5H_8), monoterpenes ($C_{10}H_{16}$), sesquiterpenes ($C_{15}H_{24}$), diterpenes ($C_{20}H_{32}$), triterpenes ($C_{30}H_{48}$), tetraterpenes or carotenoids ($C_{40}H_{64}$), and polyterpenes [$(C_5H_8)_n$]. Among the terpenic constituents, the mono- and sesquiterpenes are the most volatile and abundant in essential oils (de Sousa *et al.,* 2023)

2. Essential Oils acting Suppressing Bacterial and Fungal Infections:

Based on current research and available studies, essential oils offer a promising alternative to synthetic compounds due to the resistance pathogenic microorganisms have developed against many commercial antibiotics (Wińska *et al.,* 2019). Additionally, essential oils contain a diverse range of secondary metabolites that can inhibit or slow the growth of bacteria, yeast, and mold by targeting various bacterial components, particularly the membrane and cytoplasm. In some cases, they can even alter cell morphology (Chorianopoulos *et al.,* 2008)(Burt and Reinders, 2003). On the other hand, confirming the presence of a fungal infection and selecting the appropriate treatment can be challenging, as fungi are eukaryotic organisms. Nevertheless, the fungal cell wall presents an ideal target for antifungal agents due to its chitin structure, which is absent in human cells and thus reduces toxicity (Cortés *et al.,* 2019)(Kalemba and Kunicka, 2003) (Hyldgaard *et al.,* 2012) . Classified by the Food and Drug Administration (FDA) as 'Generally Recognized as Safe' (GRAS), essential oils are considered safe due to their natural origin (Edris, 2007).

For example, tea tree oil has been shown to exhibit strong antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, as well as antifungal activity against *Candida* species. Similarly, thyme oil has demonstrated potential antibacterial activity against a variety of bacteria, including those that cause foodborne diseases. The antimicrobial impact of essential oils can be credited with a variety of causes, including disrupting microbial cell membranes, decreasing enzyme function, and interfering with cellular processes. Furthermore, essential oils frequently have synergistic effects when coupled with conventional antibiotics, potentially increasing their efficacy and lowering the chance of resistance development. The exploration of the invention from sources of plant metabolites gives sustenance against the concern of the development of resistant pathogens(Alam *et al.,* 2022).

Despite these hopeful findings, further research is needed to fully understand the therapeutic potential of essential oils in clinical settings, including their safety, efficacy, and best ways of delivery. Nonetheless, the increased interest in natural therapies emphasizes the significance of researching alternate ways towards treating bacterial and fungal diseases, especially in light of rising antibiotic resistance.

2.1. Effect of EO on the Bacterial membrane:

The discovery of antimicrobial activities in plants through recent research has shown positive outcomes in eliminating difficult to treat bacterial infections (Nik Mohamad Nek Rahimi *et al.,* 2022). The antibacterial activity of essential oils derives from their ability to inhibit bacterial replication in combination with the suppression of bacterial metabolic activity. Several studies have reported that some plants and specifically their essential oils such as clove, thyme, rosemary, oregano, cinnamon, and pimento showed potent inhibitory effects against various bacterial pathogens (Aljaafari *et al.,* 2021).

In general, essential oil antimicrobial activity is related to the interaction of specific secondary metabolites with components of the bacterial cell structure. The main mechanism of action of essential oils against microorganisms involves the interaction of their hydrophobic components with the lipids of the cell membrane (da Silva *et al.,* 2021). The variability in composition gives rise to the diverse range of essential oils available, each with specific activities and properties. Understanding the chemical composition of essential oils is crucial for harnessing their therapeutic potential and developing them as effective antimicrobial agents. The interaction of the active components with the bacterial membrane results in the loss of membrane integrity, which damages the membrane and alters how the electron transport chain functions, how nutrients are absorbed into the cell, how proteins and nucleic acids are synthesized, how the cellular content organizes, and how enzymes necessary for energy metabolism retain activity, all of which ultimately lead to cell death. The diverse range of chemicals found inessential oilsmake different contributions to their biological activity (Aljaafari *et al.,* 2021).

It is important to evaluate molecules which themselves appear to exhibit only a weak or immeasurable effect. This is because they may facilitate the activity of other essential oil components to increase activity. The interaction of essential oil constituents with the bacterium at different stages of the lifecycle may impact efficacy, for example interaction with spores or newly germinated may increase the time required to kill them. Minor components in the oils may circumvent this barrier. Using less active compounds found in essential oils could derive novel benefits in treatment (Tavares *et al.,* 2020) (Antunes Filho *et al.,* 2023) (Sharmeen *et al.,* 2021). Essential oils frequently have synergistic effects when used in combination with conventional antibiotics, potentially increasing antibacterial efficacy and lowering the risk of antibiotic resistance.

Existing antimicrobial peptides and natural or synthetic alternatives to antimicrobials face some limitations in their ability to solve the AMR public health concern. Essential oils have been used for hundreds of years, and they may be an under exploited resource to help address AMR. A plethora of scientific literature exists on the antimicrobial activity of essential oils and plant extracts. Although the major potential side effects of essential oils appear to be dose reversible, the assessment of bacterial resistance to these natural antimicrobial agents is generally incomplete or non-existent (Aljaafari *et al.,* 2021).

2.1.1. EO on the bacterial membrane protein and phospholipids and their mechanism:

The most essential oils intensively studied are cinnamon *(Cinnamomum zeylanicum),* lemongrass *(Cymbopogon citratus),* tea tree *(Melaleuca alternifolia)*, and rosemary *(Rosmarinus officinalis)*. Multiple studies have shown synergistic effects between various essential oils and antibiotics, potentially providing a possible resolution to the antibiotic resistance issue in the clinical setting (Kong *et al.,* 2022). Essential oils have been widely investigated for their interactions with bacterial membranes, proteins, and phospholipids, which has shed information on their antibacterial mechanisms. Essential oils primarily target the bacterial cell membrane, a critical barrier that isolates the cell's interior from its external environment (Zengin and Baysal, 2014). This disturbance eventually undermines the membrane's ability to maintain ion gradients and control nutrient intake, leading to cell lysis and death. Furthermore, essential oils can target bacterial membrane proteins, including important membrane proteins that play critical roles in cellular activities such as nutrition transport, energy synthesis, and cell signalling (Gao *et al.,* 2023). Essential oil constituents can disrupt important physiological processes by attaching to or interfering with these proteins, preventing bacterial growth and survival. Moreover, essential oils were able to interact with bacterial phospholipids, which are important components of the cell membrane. Certain essential oil components, such as phenolic compounds like thymol and carvacrol, have a strong attraction for phospholipid bilayers, where they can penetrate and disturb membrane structure and function. This disruption can cause membrane depolarization, release of intracellular contents, and, eventually, bacterial cell death.

Essential oils may have antibacterial activity through processes other than membrane disruption. For example, some essential oil constituents impede bacterial enzyme activity, impair DNA replication or protein synthesis, and alter cellular signalling pathways. For instance, the activity of two essential oil components was evaluated against multidrug-resistant *Pseudomonas aeruginosa*. Hibicuslide C, a component derived from the essential oil of *Abutilon theophrasti*, was able to to fragmentation of *P. aeruginosa* DNA (Lee *et al.,* 2016). Additionally, quercetin was observed to inhibit the FabZ enzyme in *P. aeruginosa (Geethalakshmi et al., 2018).*

These complex actions help to explain why many essential oils have broad-spectrum antibacterial activity against a variety of bacterial infections. Further studies are needed to validate protein expression differences elicited by essential oil treatment (Barbosa *et al.,* 2020). Although the biological membrane is a bilayer, it is believed that many important phenomena which take place in bilayer membrane can be investigated experimentally at the monolayer interface. The Langmuir monolayer technique has been successfully employed to study the characteristics of membrane structure and interaction between lipid and protein molecules, by mimicking both the mammalian and bacterial cell membranes. Monolayers have also been used to evaluate antibacterial peptides, proteins, and more recently chitosan, whose antimicrobial properties were extensively reviewed. However, the study of low molecular weight compounds using Langmuir monolayers has not been extensively reported (Nowotarska *et al.,* 2014). Langmuir monolayers composed of bacterial phospholipids have been used as model membranes to study interactions of the five naturally occurring phenolic compounds (Nowotarska *et al.,* 2014).

Table 1: Essential Oils efficacy as antimicrobials

Essential Oil/ Essential Oil Constituents	**Antibacterial**	**Ref.**	**Antifungal**	**Ref.**
Cinnamon bark	*Escherichia coli* Klebsiella pneumoniae Staphylococcus aureus Pseudomonas aeruginosa	(Yang *et al.,* 2021a)	*Aspergillus niger* *Candida albicans* *Cryptococcus neoformans*	(Yang *et al.,* 2021a)
Tea tree	*E. coli* *Propionibacterium acnes* S. aureus	(Yang *et al.,* 2021a)(Hammer *et al.,* 2004)	*C. albicans* *Candida glabrata* *Saccharomyces cerevisiae* *Trichophyton rubrum* *Trichophyton mentagrophytes*	(Yang *et al.,* 2021a)
Rosemary	*E. coli* Enterococcus faecalis S. aureus	(Yang *et al.,* 2021a)	*Aspergillus flavus* *C. albicans*	(Yang *et al.,* 2021a)
Lavender	*K. pneumoniae* *Proteus mirabilis* *P. aeruginosa* *Salmonella enterica*	(Yang *et al.,* 2021a)	*Alternaria alternate* *Aspergillus fumigatus* *C. albicans* *Chaetomium globosum* *Cladosporium cladosporoides* *Penicillium chrysogenum*	(Yang *et al.,* 2021a)
lemongrass	*P. aeruginosa* *Staphylococcus aureus* *Bacillus subtilis* *Salmonella enterica typhimurium* *Klebsiella pneumoniae*	(Mukarram *et al.,* 2022)	*C. albicans* *Fusarium moniliforme* *Aspergillus fumigatus* *Candida tropicalis* *Cochliobolus lunatus* *Drosera indica*	(Mukarram *et al.,* 2022)
Carvacrol	*Enterobacter cloacae* *E. coli* *Listeria monocytogenes* *Pseudomonas fluorescens* *Pseudomonas putida* *S. aureus*	(Mączka *et al.,* 2023)	*C. glabrata* *Candida krusei* *Candida tropicalis* *Candida parapsilosis* *C. albicans*	(Kong *et al.,* 2022)
Peppermint	*L. monocytogenes* *S. aureus* *Enterobacteriaceae* *Pseudomonas aeruginosa* *Rhodococcus equi* *Salmonella choleraesuis*	(Robu *et al.,* 2022) (Yang *et al.,* 2021a)6/13/2025 9:37:00 AM	*A. niger* *Aspergillus oryzae* *Aspergillus ochraceus* *C. albicans* *Cryptococcus neoformans*	(Yang *et al.,* 2021a)

	Micrococcus luteus *Staphylococcus epidermidis*			
Eucalyptus	*E. coli* *Edwardsiella tarda* *Lactococcus garviae* *Streptococcus iniae* *Streptococcus parauberis* *S. aureus*	(Yang *et al.,* 2021a)	*Fusarium sp.* *Aspergillus sp.* *Ulocladium sp.* *Coprinellus sp.* *Penicillium sp.*	(Yang *et al.,* 2021a)
Oregano	*Acinetobacter baumannii* *Aeromonas veronii* *Bacillus subtilis* *E. coli* *Listeria monocytogenes* *Enterococcus faecalis* *K. pneumoniae* *P. aeruginosa* *S. enterica* *S. aureus*	(Gurtler and Garner, 2022)	*Rhizoctonia solani* *Sclerotinia sclerotiorum* *Botrytis cinerea* *Phytophthora capsici* *Rhizopus stolonifera*	(Wu *et al.,* 2023)
Thyme	*Aeromonas hydrophila* *Brochothrix thermosphacta* *E. coli* lactic acid bacteria *L. monocytogenes* *S. enterica* *Shigella flexneri* *S. aureus* *Yersinia enterocolitica* *Aspergillus species*	(Pinto *et al.,* 2020) (Gurtler and Garner, 2022)13/06/2025 09:37:00	*Rhizoctonia solani* *Rhizopus stolonifer* *Botrytis cinerea* *Phytophthora capsici* *Sclerotinia sclerotiorum*	(Wu *et al.,* 2023)

2.2. Efficacy of Essential Oils in Treating Fungal infections:

It is more difficult to develop treatments for fungal infections than the bacterial infections, because human and fungal cells share the commonality of being eukaryotic (Pathakumari *et al.,* 2020). Treating human fungal infections mainly involve the use of oral tablets or topicals creams. If the fungal treatment targets and acts against a common structure in eukaryotic cells, this may also lead to excessive toxicity for the human cells, compromising host safety (Aljaafari *et al.,* 2021). None the less the intrinsic antibacterial characteristics of essential oils have made them promising targets for investigation as alternative treatments for fungal infections. Fungal infections caused by pathogenic fungi can affect many regions of the body, including the skin, nails, mucous membranes, and internal organs (Petrović *et al.,* 2025). A study has reported the fungicidal properties of clove, cinnamon, and oregano essential oils and also the capacity of purified constituents to suppress viable cell count, mycelia growth, and mycotoxin production by pathogenic fungi (Aljaafari *et al.,* 2021). Several essential oils have been tested for their effectiveness against fungal infections such as dermatophytes, yeasts, and moulds. Tea tree oil, extracted from the leaves of the *M. alternifolia* plant, has been shown to have significant antifungal properties against a variety of fungi, including *Candida* species responsible for oral and vaginal yeast infections, as well as dermatophytes implicated in athlete's foot and nail fungus (Ganaie and Wani, 2021).

An essential oil with strong public awareness is oregano oil, which contains significant levels of phenolic chemicals such as carvacrol and thymol. These chemicals have strong antifungal action against a variety of fungal species, including *Candida albicans*, *Aspergillus* species, and *Cryptococcus neoformans*. Cinnamon oil, clove oil, and lavender oil have antifungal activity against fungal pathogens usually associated with skin and nail infections. The antifungal effects of essential oils are mediated by a variety of mechanisms, including disruption of fungal cell membranes, inhibition of fungal enzyme activity, and interference with critical cellular processes such as cell wall formation and ergosterol biosynthesis (Hammoudi Halat *et al.,* 2022). Essential oil components can penetrate fungal cells, impair membrane integrity, and modify membrane permeability, resulting in intracellular leakage and, eventually, fungal cell death. Furthermore, essential oils frequently have synergistic effects when coupled with traditional antifungal medicines, potentially increasing efficacy and lowering the likelihood of treatment resistance. This synergy may be due to complimentary modes of action and increased permeability of fungal cell membranes to traditional antifungal drugs. Despite their promising antifungal characteristics, there are still hurdles to realizing the full medicinal potential of essential oils for fungal disease treatment. Variability in oil content, limited solubility, and potential skin irritation or sensitization all require additional research to optimize formulations, doses, and administration routes. Essential oils provide a natural and possibly safer method to treating fungal infections, serving as an alternative or complementary therapy to traditional antifungal medications. Further studies on the antifungal mechanisms and therapeutic applications of essential oils are required to provide evidence-based guidelines for their usage in clinical practice (Mandras *et al.,* 2021).

Although some progress has been made in this field, the molecular mechanism of the synergistic antifungal effect of essential oils is still unclear. In particular, it is rare to analyze the synergistic antifungal mechanism of the effective components of essential oils at the molecular level (Ju *et al.,* 2022).

2.3. Pathways involved in development of EO and potential antimicrobials agents:

Antimicrobials are useful compounds intended to eradicate or stop the growth of harmful microorganisms. However, in the race towards developing alternative approaches to combat AMR, it appears that the scientific community is falling behind when pitched against the evolutionary capacity of multi-drug resistant (MDR) bacteria (Moo *et al.,* 2020). Antimicrobial agents used to kill or inhibit the growth of pathogenic or food spoilage bacteria can exist in natural or synthetic forms. The use of synthetic antimicrobial compounds in food preservation has raised consumers' concerns, since they present numerous toxicological questions over long term exposure. This uncertainty has resulted in the differences in permissible food additives in the US and Europe. Researchers have now diverted their attention to antimicrobial mining from the traditional microorganism towards the plant kingdom. This is because individual plants produce a highly diverse range of complex secondary metabolites that have potential applications as novel antimicrobials (Yang *et al.,* 2021b). Essential oils are secondary plant metabolites and are essential for plant survival mechanisms in complex ecosystems populated by parasites, pathogens, competitors and predators. Consequently each essential oil has a broad range of specific antibacterial and antifungal activities evolved for the environment which that plant inhabits (Hou *et al.,* 2022). Therefore, greater attention is now being paid to the screening of this immense resource for novel antimicrobial activities (Chouhan *et al.,* 2017). Multidrug-resistant bacteria harbour various molecular and cellular mechanisms for AMR. These AMR mechanisms include active antimicrobial efflux pumps, reduced drug entry into cells of pathogens, enzymatic metabolism of antimicrobial agents to inactive products, biofilm formation, altered drug targets, and protection of antimicrobial targets (Varela *et al.,* 2021).

Antimicrobial producing microbes frequently acquire resistance genes to protect themselves against their own naturally occurring antimicrobial agents. Antibiotic resistance in bacteria may arise either through the inheritance or acquisition of resistant genes. While antimicrobials are natural compounds that aid survival, from a human view point they are useful compounds adapted to eradicate or stop the growth of harmful microorganisms (Moo *et al.,* 2020). Membrane permeability can also be altered by antibiotics; preventing the entry of more antibiotics into the cells, which when coupled to the other mechanisms of drug export or inactivation, enables resistance against higher concentrations of antibiotics (Yang *et al.,* 2019).

Out of all essential oils evaluated oregano and cinnamon oils are the most effective antimicrobials (Andrade-Ochoa *et al.,* 2021). This is supported by a more recent study where extracts from various parts often different plants were tested such as the fruit peel of Citrus bergamia (Risso & Poit.) and Citrus limon (L.) Osbeck, the flower, leaf, and terminal branches of Clinopodium nepeta (L.) Kuntze, Foeniculum vulgare subsp. piperitum (Ucria) Beg., Myrtus communis L., Origanum vulgare L. subsp. viridulum (Martrin-Donos) Nyman, Salvia officinalis L. and Salvia rosmarinus Spenn, while for Citrus reticulata (Blanco) and Laurus nobilis L. only the leaf and terminal branches were used. The most effective inhibitors of bacterial growth were essential oils from Clinopodium nepeta, Origanum vulgare, and Foeniculum vulgare (D'Aquila *et al.,* 2022) (Hou *et al.,* 2022) (Mukurumbira *et al.,* 2022).

3. Mode of action of EOs, both proteomic and genomic methodologies:

Recent advances in genomics and proteomics have deepened our knowledge of how essential oils act as antimicrobials and how they modulate microbial genes (Aljaafari *et al.,* 2021). The availability of complete genome sequences for many pathogenic microorganisms has facilitated the identification of potential antimicrobial targets, making it a valuable resource for researching and developing new antimicrobial drugs. Furthermore, genomic technologies offer insights into the genetic changes in pathogens that lead to the emergence of resistance genes (Fields *et al.,* 2017). In addition, proteomic analysis techniques enable effective evaluation and modification of protein profiles, significantly aiding in the separation, identification, and quantification of the various components of essential oils (Pérez-Llarena and Bou, 2016).

The comparative analysis of gene expression between essential oil-treated and nontreated cells is the main strategy used to assess genomic changes in the target pathogens induced by treatment. Several investigations determined that thyme essential oil had anti-quorum sensing and anti-biofilm formation action against the opportunistic pathogen, *P. aeruginosa* (Yang *et al.,* 2021a). The gene expression profile of peppermint essential oil-treated and nontreated *Campylobacter jejuni* was compared using comparative real-time polymerase chain reaction (PCR) (Mayr *et al.,* 2010). A panel of genes related to pathogenesis, stress response, basic metabolism, and transcription regulation were screened and increased expression of oxidative stress response genes was found in the essential oil-treated *C. jejuni*. The effect of lavender essential oil against *E. coli* was evaluated with comparative microarray analysis (Coşeriu *et al.,* 2023).

Genomic methods also include techniques for studying the three-dimensional structure of the genome, as well as the interactions between different regions of the genetic material (Mohanta *et al.,* 2021).These methods have opened-up new avenues for understanding the complexity of gene regulation and the role of non-coding DNA in various biological processes. Genomic methods play a crucial role in biological research, providing scientists with the tools to study the entire genetic material of an organism. These techniques allow researchers to analyze the structure, function, and regulation of genes, as well as their interaction with the environment. The use of genomic methods in biological research has revolutionized the way scientists approach complex biological questions, leading to significant advancements in various fields, including medicine, agriculture, and biotechnology (Hamdan *et al.,* 2022).In the field of biological research, genomic techniques play a crucial role in studying the mode of action of essential oils. Genomic techniques encompass a wide range of methods that are used to analyze the structure and function of genomes, including DNA sequencing, gene expression analysis, and genome editing (Jerković and Cavalli, 2021).

One of the key goals of proteomic methods is to identify and quantify the complete set of proteins present in a biological sample, known as the proteome. This can involve the use of gel electrophoresis to separate proteins based on their size and charge, followed by mass spectrometry to identify and characterize individual protein components. Moreover, proteomic methods also enable the identification of protein-protein interactions and the mapping of protein pathways and signaling networks. By shedding light on the dynamics of protein expression and function, proteomics has the potential to uncover novel biomarkers for disease, as well as new drug targets for therapeutic intervention. By applying proteomics, researchers can uncover the specific proteins and pathways affected by essential oils in biological systems, providing mechanistic insights into their therapeutic properties. This systematic analysis of protein expression and modifications can help unravel the molecular targets of essential oils and their impact on cellular function, paving the way for the development of novel therapeutic interventions. The proteomic analysis involves an analysis of the proteome profile of untreated andessential oil-treated cells to identify and quantify differentially expressed proteins signals.

Studies have shown an increased expression of oxidative stress-related proteins such as *dps, sodB*, and *katA* following treatment with peppermint essential oil (Kovács *et al.,* 2019). In a similar approach, the effect of oregano essential oil on *Salmonella enteritidis* was investigated (Yang *et al.,* 2021a). Similar oxidative stress induction was observed by comparing the proteome profile of untreated and cinnamon bark essential oil-treated clinical-relevant strains of *K. pneumoniae* using nanoscale liquid chromatography coupled to tandem mass spectrometry (nano LC-MS/MS). This group has previously performed biochemical studies on the mode of action of cinnamon bark essential oil against the same clinically relevant strains of *K. pneumoniae*, revealing that essential oil disrupts bacterial membrane using zeta potential measurement, outer membrane permeability assay, and electron microscopy. The follow-up study using nano LC-MS/MS showed an increase in the abundance of oxidative stress-sensitive proteins such as glycyl radical cofactor, catalase peroxidase and DNA mismatch repair protein, which indicates the presence of oxidative stress during cinnamon bark essential oil treatment (Yang *et al.,* 2021a). Mass spectrometry is another powerful proteomic technique that can be used to identify and quantify the proteins present in a sample. By coupling mass spectrometry with techniques such as liquid chromatography, researchers can gain a deeper understanding of the proteome changes induced by essential oils. Protein microarray technology allows for the high-throughput analysis of protein-protein interactions, which can be used to elucidate the impact of essential oils on various signalling pathways within cells. Overall, proteomic techniques provide a detailed and holistic view of the cellular response to essential oils, shedding light on their mode of action at the molecular level. These methods provide a comprehensive analysis of the proteins present in a biological sample, allowing researchers to gain insight into the molecular mechanisms underlying the effects of essential oils. One commonly used proteomic technique is two-dimensional gel electrophoresis, which separates proteins based on their isoelectric point and molecular weight. This method can be used to compare the protein profiles of cells or tissues before and after treatment with essential oils, identifying specific proteins that are up- or down-regulated in response to the treatment.

3.1. Synergism in Essential Oils Constituent Actions:

A number of studies found that several essential oil constituents can enhance efficacy and potency of conventional antibiotics when used in combination (Aljaafari *et al.,* 2021). For many years, this synergism has been the primary focus of combinatory therapy with different antibiotics since it significantly reduces the effective dosage of an antimicrobial drugs needed to treat a specific disease. The impact of additivity, which can reduce the minimum effective dosage of two antimicrobial agents used in combination, is an important consideration and the molecular basis of this effect must be understood. Many compounds with biological activity have an aromatic ring structure, such as the phenolic monoterpenes thymol and carvacrol or the phenyl propenes (cinnamaldehyde and eugenol). Besides the functional groups present in essential oils which may interact with antibiotics, synergistic interactions among the components in the essential oil may also contribute to overall activity (Milagres de Almeida *et al.,* 2023).

The antimicrobial properties of essential oils, primarily depend on their chemical constituents, such as the quantity of the dominant compounds, and whether direct or vapor phase is utilized for activity (Mani-López *et al.,* 2021). The interaction between antimicrobial compounds can result in three different outcomes: (i) synergistic, (ii) additive, or (iii) antagonistic. Synergy occurs when two antimicrobial compounds combine to produce antibacterial activity that exceeds the sum of their individual effects. An additive effect is produced by combining antimicrobials producing an antimicrobial effect that is equal to the sum of the individual compounds. An antagonistic effect results in a decreased antimicrobial activity of two compounds in combination as compared with their individual antimicrobial activity (Chouhan *et al.,* 2017). Antimicrobial activity of a given essential oil may depend on one or two of the major constituents only that make up the entire oil. In accordance with the increasing level of evidence, the ratio in which the main active constituents are present may not be the only factor responsible for the inherent activity of essential oils, but the interactions between these and minor constituents in the oils are also important. The combination of eugenol with linalool or menthol exhibited the highest synergy, suggesting that combination of a monoterpenoid phenol with a monoterpenoid alcohol is effective. When tested in binary or ternary combinations, various synergistic antimicrobial activities have been reported for constituents or fractions of essential oils.

3.2. Mechanisms of antimicrobial action in the disruption of plasma membranes:

Research into the discovery of antimicrobial phytochemicals, their mechanisms of action, and their inclusion in possible treatments and therapies is progressing rapidly (Álvarez-Martínez *et al.,* 2021). To penetrate the plasma membrane, antimicrobial peptides must first cross the glycocalix layer to establish an interaction with the plasma membrane. The bacterial plasma membrane is the semipermeable barrier between the inside of the bacterial cell and the environment, in addition it serves as the site for crucial cellular processes, such as energy production and maintaining cell shape. One of the key antimicrobial mechanisms involves the formation of pores in the membrane, which can be induced by certain antimicrobial peptides and lipopeptides. These molecules can insert themselves into the lipid bilayer, causing the formation of pores that compromise the integrity of the membrane and disrupt essential cellular processes. Another membrane-targeting antimicrobial mechanism involves interference with membrane potential and permeability, which can be achieved through the inhibition of specific ion channels or transporters, leading to the disruption of cellular homeostasis. Additionally, some antimicrobial agents can directly alter the lipid bilayer structure, affecting the fluidity and stability of the membrane (Gray and Wenzel, 2020) (Huang, 2020) (Segovia *et al.,* 2021).

Integral membrane proteins are embedded within the phospholipid bilayer, playing various roles in transport, signalling, and cell stability. The membrane is also involved in the synthesis of essential molecules and the regulation of intracellular processes.

(Ackermann and Stanislas, 2020). The latest technologies allow the efficient identification and characterization of new antimicrobial agents through membrane interaction (Bogdanov *et al.,* 2020).

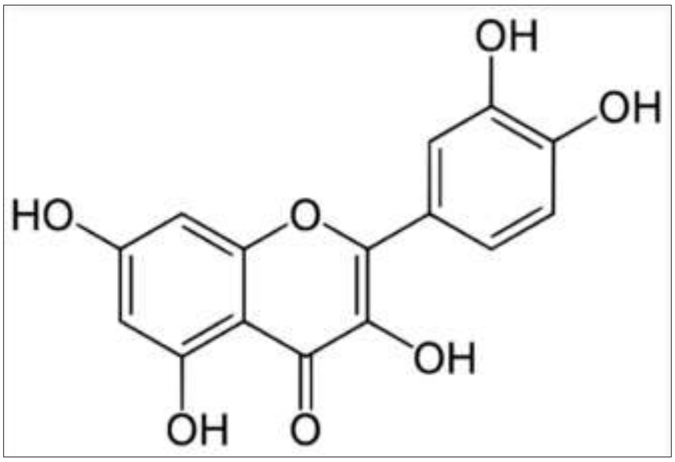

Figure 2: Molecular structure of quercetin

The development of omics techniques, computational techniques and other new approaches beyond the classical ligand-target paradigm, such as network pharmacology and systems biology, has promoted the discovery and clarification of the mechanism of action of many plant compounds with remarkable antimicrobial potential (Álvarez-Martínez *et al.,* 2021). The format and route of administration of the antimicrobial agent is a crucial element in designing antimicrobial therapies. Lots of technologies and methods are used to investigate the action mechanisms of antimicrobials (Li *et al.,* 2021). Among the most active phytochemicals studied, polyphenols and terpenes stand out, either alone or as part of plant extracts or essential oils in treatment studies. The most common mechanisms of antimicrobial action are those related to the disruption of plasma membranes. The specific mechanisms of the polyphenols and terpenes that produce membrane effects appear to be related to the alteration of the membrane potential produced by ion transport and binding to other molecules such as membrane proteins. Quercetin for example is one of the most abundant flavonoids and is antibacterial against a wide range of bacterial strains, particularly those affecting the gastrointestinal, respiratory, urinary, and integumentary systems (Nguyen and Bhattacharya, 2022). Quercetin acts by damaging both the cell wall and cell membrane of bacteria. Quercetin possesses many pharmacological activities such as antioxidant, anticancer, antiviral, antimicrobial, neuroprotection, anti-inflammatory, cardiovascular and anti-obesity.

Recently, quercetin has also achieved GRAS (Generally Recognized As Safe) status by the United States Food and Drug Organization. The antimicrobial activity of quercetin has been widely studied by many researchers and has been considered as a potential therapy against different pathogenic microorganisms. In addition, multidrug resistance (MDR) in bacteria has become a major problem worldwide due to the continuous use of antibiotics against bacterial infections. Treatment of these MDR strains has posed a major challenge to the pharmaceutical industry (Nguyen and Bhattacharya, 2022).

Peptide antimicrobials act through charge and hydrophobicity interaction to generate pharmacophores to produce their activity at the cell membrane. The experimental use of these peptides in quality-of-membrane assays provides significant support for the idea that both the nonselective hydrophobic and the characteristic cationic amphiphilic mechanisms synergize to result in a disrupted architecture to undermine normal functioning of the plasma membrane(Ponti *et al.,* 2021). There is also data in favour of a different, more delicate class of pharmacological antibacterial actions that preferentially target bilateral variations in microbe composition relative to host mammalian cells, conferring greater specificity (Svenson *et al.,* 2022) (Yuan *et al.,* 2023). The specific target of an antimicrobial agent is crucial to its effectiveness as an agent. Peptide and nonpeptidic medicines that target membrane cationic characteristics are frequently active against a wide range of bacteria, exerting both quick and potent inhibitory effects. Polyunsaturated fatty acids, particularly in membrane phospholipids, appear to have a role in the beneficial influence of fish oil-based diets and supplements on host defence modulators of the immune system (Browne *et al.,* 2020) (Benfield and Henriques, 2020) (Ayoub Moubareck, 2020).

4. Importance of EO for reducing antimicrobial resistance:

AMR nderstanding the processes and driving factors of AMR is critical for effectively combating this growing threat. AMR develops when microorganisms such as bacteria, viruses, fungi, and parasites evolve to no longer respond to the treatments that are intended to kill them. This renders routine therapies ineffective, increasing the risk of infections, prolonging sickness, and raising mortality rates. Poor infection prevention and control measures, a lack of clean water, inadequate sanitation, and subpar healthcare systems all contribute to the problem. Ethnopharmacology, with its focus on traditional medicine and indigenous knowledge, plays a crucial role in providing alternative sources of antimicrobial compounds and novel treatment approaches (Salam *et al.,* 2023). Current regulatory measures seek to establish a consistent and coordinated approach to combating AMR, involving a wide range of stakeholders, including government agencies, healthcare institutions, pharmaceutical corporations, and the public. But it is the development of new effective treatments against a spectrum of pathogens that may be the most effective approach.

The discovery and subsequent widespread use of antibiotics were one of the most important medical advances in the treatment of infectious diseases. AMR is not only a problem in terms of protection from infectious diseases but also in terms of the treatment of immune suppression patients within oncology and transplantation units. It is important to emphasize that AMR is a natural outcome of bacterial evolution and will arise as long as pathogens are exposed to antimicrobials as a selective pressure (Janotto *et al.,* 2023).

4.1. Resistant genes and the use of antimicrobial agents:

Even after the establishment of antibiotics as a treatment, pathogenic bacteria take a huge toll on humanity in terms of morbidity and mortality outcomes (Varela *et al.,* 2021). The antibiotics used for decades to treat bacterial diseases are declining in their efficacy due to AMR. Today scientists continue to study new ways to synthesize and modify natural antibiotics to fight more stubborn types of microbes. Bacteria can survive antibiotic stress by means of varied mechanism. Different antibiotics work on different facets of the pathogen's biology to suppress growth, targeting a wide range of cellular components including the genetic material, proteins, the cytoplasmic membrane, and other cell wall components (Koch *et al.,* 2021). The genetic basis of AMR refers to the genes and mutations that allow microbes to withstand antimicrobial agents. These genes can arise by mutation and inheritance or be acquired through horizontal gene transfer through processes like conjugation. One typical route of AMR is the creation of enzymes that deactivate antimicrobial drugs, such as beta-lactamases, which degrade beta-lactam antibiotics like penicillin. Another process involves changes in the antimicrobial agent's microbial target structure, which reduce its potency. Additionally, microorganisms can develop efflux pumps that actively remove antimicrobial agents from the cell before their growth suppressive action can take effect.

Understanding the genetic basis of AMR is essential for the development of new antimicrobial agents, as well as strategies to combat the spread of resistance (Varela *et al.,* 2021). Such AMR systems involve the engagement of bacterial molecular and cellular-based machinery (Varela *et al.,* 2021). Mechanisms of AMR include the active export systems within the membranes of bacteria, prevention of antimicrobial entrance into cells of pathogenic bacteria, enzymatic destruction of antimicrobial agents, production of thick biofilms, modified targets of antimicrobials, and bacterial sites of action that are protected from antimicrobials (Varela *et al.,* 2021). Additionally, bacteria that are resistant to multiple drugs have developed mechanisms to transfer genetic resistance factors between pathogenic species in the clinical environment, the food production industry, the human gut, and agriculture. It is worth noting that since the early twentieth century, β-lactamases have played a role in combating infections. However, the emergence of the β-lactamase family, which now includes more than 2,800 enzymes, has enabled the enzymatic destruction of β-lactams. As a result, Enterobacteriaceae have developed resistance to β-lactams by producing β-lactamases through genes such as CMY-2 and FOX (Klein *et al.,* 2018). On the other hand, Enterococci developed resistance to vancomycin through glycopeptide resistance genes, such as the *vanA* gene. This resistance is achieved by employing a mechanism that reduces the affinity of the antibiotic for its cellular target, thereby preventing the entry of antimicrobials into the bacterial cells (Binda *et al.,* 2014).

The resistance mechanism of Gram-positive bacteria can occur through two major strategies: enzymatic degradation of antibiotic by the production of β-lactamases (Jubeh *et al.,* 2020). The discovery of more β-lactams was a result of penicillin resistance, but unfortunately, the emergence of resistance was always followed by it. The decline in treatment options for patients resulted in an increase in morbidity and mortality due to the increasing resistance to antibiotics. The World Health Organization (WHO) published a global priority pathogens list and categorized them as critical, high, and medium antibiotic-resistant bacteria that urgently need research and development of new treatments (Jubeh *et al.,* 2020). Antibiotic resistance is generally caused by spontaneous mutations in resistance genes. Bacterial drug resistance mechanisms are more complex than they appear. The major crisis of drug resistance is associated with rapid and broad transfer of resistance gene(s) among bacteria, ultimately leading to high levels of resistance (Shin *et al.,* 2018). By enhancing data collection and analysis, healthcare systems can better understand the prevalence and patterns of AMR e, allowing for the early detection of emerging threats and the implementation of targeted interventions.

International collaboration and coordination are essential to address AMR on a global scale, as resistant genes can easily spread across borders. By working together, countries can share knowledge, resources, and best practices to combat AMR effectively (Mattar *et al.,* 2020). Another strategy focuses on the development of new antimicrobial agents and alternative treatments. This involves investing in research and development to discover and produce novel antibiotics, as well as exploring non-antibiotic therapies such as phage therapy and antibody-based treatments. One approach involves promoting the appropriate use of antimicrobial agents, which includes educating healthcare professionals and the public about the proper prescription and use of antibiotics.

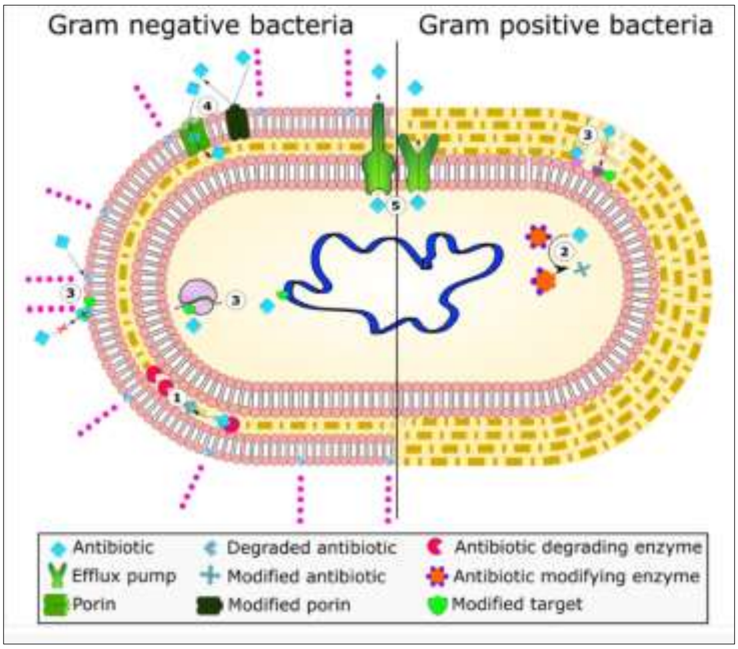

Figure 3: Bacterial mechanisms of resistance to antimicrobial agents. The common mechanisms of antibiotic resistance in bacteria are enzymatic hydrolysis, enzymatic modifications of antibiotics by group transfer and redox process, modifications of antibiotic targets, reduced permeability to antibiotics by modifications of porins, and active extrusion of antibiotics by membrane efflux pumps (Varela *et al.*, 2021). To prevent bacteria from becoming resistant to antimicrobial agents, new strategies must be developed. Understanding the resistance systems at the molecular and cellular levels is necessary for discovering novel approaches to address multiple AMR in these microbial pathogens. Our introductory overview of these diverse bacteria resistance mechanisms is available to both young and new investigators

4.2. Determination of Compounds Responsible for Antimicrobial Activity in Complex Mixtures:

Biological and pharmacological tests using essential oils and their chemical constituents performed via experimental models at the molecular, cellular, and animal levels have generated promising results in several areas of science (de Sousa *et al.,* 2023). Their pharmacological profile includes antimicrobial, anti-inflammatory, antitumor, and antioxidant activities. The chemical complexity and variability of the medicinal plant extracts/bioactive compounds can make study difficult, particularly when identifying active compounds. Recent studies to elucidate the mechanisms of action of traditionally used medicinal plant extracts have found a complex mixture of bioactive compounds may act at multiple targets to produce the biological effect (Vaou *et al.,* 2022). Most of the studies presenting the antimicrobial properties of medicinal plant extracts and bioactive compounds make use of unfractionated extracts that usually show weak *in vitro* antimicrobial activity. These studies were infrequently confirmed by means of *in vivo* assays. Thus, the precise mechanisms of action of the vast majority of such bioactive compounds are unknown (Vaou *et al.,* 2022).

There is the potential to develop an antimicrobial regimen that is more potent than a single antibiotic by combining different modes of action. Chemically complex treatments may have great therapeutic potential as they have fewer side effects compared to synthetic drugs due to the lower concentration of individual components and also less chance of developing resistance (Vaou *et al.,* 2021). Research has demonstrated that antimicrobials produced from plants frequently do not cause resistance. Considerable evidence exists that the combination effects within medicinal plant extracts can alter the antimicrobial activity. Nevertheless, the vast majority of complex medicinal plant-derived extracts still await detailed research to understand the combined effect of the compounds present whether it be synergistic or antagonistic (Vaou *et al.,* 2022). The synergism between essential oils and conventional antibiotics has been investigated in a study of five essential oils with seven antibiotics. The combined effect of peppermint, cinnamon bark, and lavender essential oil with piperacillin and meropenem showed significant synergy against different *E. coli* strains (Vaou *et al.,* 2022). Since the antibiotic and the essential oil are using completely different modes of attack, for example blocking cell wall synthesis and disrupting electron transfer, the synergistic interactions can result in several fold reductions in the required doses of the combined agents (Sharma *et al.,* 2020). Again this reduction in required dose can diminish the risk of side effects from the treatment.

5. CONCLUSION AND FUTURE PRESPECTIVES

Bacterial pathogens can cause severe disease and death. Over the past century much effort has gone into the development of treatments, centred around antibiotics. This has gone hand in hand with improvements in personal hygiene, food handling and preparation, hand washing, public sanitation, and education across all levels. In medical healthcare and treatment centres, antimicrobial stewardship is still an important approach, with improvements in prescription practice and control of antibiotic access. The development of multidrug resistant in bacteria in veterinary medicine and agriculture are going to pose a continued threat to human health. Ethical oversight is crucial in addressing AMR, by promoting responsible use of antibiotics, implementing strict regulations, and promoting research and development of new antimicrobial agents. Incentives to discover new antibacterial agents with novel modes of action are few, and progress on this front is slow. However, it is critical to develop new antimicrobials to counter emerging AMR threats. It is important to understand the constantly evolving resistance profile of environmental organisms; this gives insight into risks that are likely to arise in pathogenic microbes.

A promising avenue in the battle against multidrug-resistant pathogens entails the clinical investigation of non-antibiotic agents as anti-bacterial agents, such as non-steroidal anti-inflammatory drugs, anaesthetics, and statins. Recently, a series of new and well-developed anti-infective strategies for the circumvention of multidrug-resistant pathogens were describe(Shanmugaraj *et al.,* 2021)(Scoffone *et al.,* 2024).These and other strategic approaches for reducing the conditions that foster the spread of bacterial infections are important candidates for investigation. An in-depth understanding of the underlying mechanisms of resistance is critical for developing new prevention methods against the growing trend of antibiotic resistance. To obtain more cost-efficient results and implement them more quickly, it is necessary to use more affordable technology. Future directions should focus on enhancing surveillance and monitoring of antimicrobial use, as well as investing in public education and awareness campaigns to promote responsible antibiotic usage.

By emphasizing the importance of ethical oversight and implementing proactive measures, we can work towards reducing AMR and safeguarding the effectiveness of antibiotics for future generations. While the antibacterial properties of essential oils are well recognized, research on antifungal and anti-mycotoxigenic actions is relatively limited. From a health and economic standpoint, it is critical to identify effective, safe, and cost-effective antifungal medicines to reduce fungal pathogen growth and mycotoxin generation. However, variable findings have been observed in different studies due to differences in fungal cultures used during activity analysis, geographical origin, harvesting time, part of the plant from which the essential oil was derived, and extracting and screening approaches. In whatever context t is critical to consider these parameters when working with essential oils because they affect their composition, profile, and biological functions. The molecular targets of many essential oil components have yet to be identified and their effect on proteins embedded in the cytoplasmic membrane and phospholipids in the membrane are the main focus for future research.

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