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REVIEWS

ANTIMICROBIAL ACTIVITY OF SELECTED ESSENTIAL OILS FROM THE MYRTACEAE FAMILY

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ABSTRACT

INTRODUCTION: Antimicrobial resistance (AMR) is an important global problem affecting health care and leading to the inability to treat infections caused by pathogens. The increasing resistance and limitations of the number of antimicrobials increases the demand for new potential drugs from various sources.

AIM: The purpose of the review article is to present knowledge about essential oils of the *Myrtaceae* family as possible alternatives to address AMR.

MATERIALS AND METHODS: The literature in PubMed, Google Scholar and ScienceDirect was searched and analyzed.

RESULTS: Essential oils are natural products and because of their multi-component chemical composition, there is no evidence of emerging resistance of bacterial strains to them. They are a promising alternative to address AMR.

CONCLUSION: The increase in resistance to almost all classes of antibiotics, combined with a limited number of new antimicrobial agents, leads to the need to search for and implement new therapeutic agents. Analysis of literature data from a scientific database shows promising antimicrobial effects of essential oils, proven mostly in experimental studies. A larger number of studies that investigate the activity of the multi-component blend of essential oils, targeting the most abundant components they contain, are needed.

Keywords: *eucalyptus, clove, tea tree, AMR, eucalyptol, eugenol*

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INTRODUCTION

Antimicrobial Resistance

Antimicrobial resistance (AMR) is a serious global problem affecting health and the economy. Misuse, incorrect and excessive use of antibiotics are leading causes of the development of resistant bacterial strains, which lead to difficulties in the treatment of nosocomial infections (1). Globally, the deaths due to infection by resistant microorganisms amount to

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about 700,000 people per year. By 2050, it is estimated that 10 million lives could be at risk if AMR is not managed (2). In 2017, the World Health Organization published a list of priority pathogens, including microbes such as *Staphyloccocus aureus, Acinetobacter baumannii, Streptococcus pneumoniae, Escherichia coli, Klebsiella sp., Enterobacter sp.,* and others that demonstrate resistance to almost all classes of antibiotics (including penicillin, vancomycin, carbapenem, ampicillin, azithromycin, ceftriaxone) (3). A significant number of bacteria from the genera *Staphylococcus, Escherichia, Pseudomonas, Salmonella, Bacillus, Pasteurella*, etc. have the ability to form biofilms and present a challenge when treating infections (4). Biofilms are the cause of over 60% of microbial infections (5) and 2/3 of all human bacterial infections (6).

Increased resistance to antimicrobial drug therapy, combined with a limited number of new antimicrobial agents, leads to the need to search for and implement new therapeutic agents. Plants and their products are of interest to science, thanks to their biodiversity and potential for discovering new molecules with a wide spectrum of action. Many drugs, including antimicrobials, contain one or more plant components or are synthetically derived from them (7).

Essential oils (EOs) are the basis of various studies. They are extracted from aromatic plants and demonstrate a wide spectrum of antimicrobial activity against human pathogens (expressed in planktonic and sessile form). The potential of EOs as antimicrobial agents is known and has long been studied. A wealth of data is also available on the phytoconstituents responsible for the mode of action and activity (7).

Medicinal products derived from aromatic plants are widely used in traditional medicine for the treatment of bacterial infections (8). Numerous scientific studies have demonstrated that EOs can be effective in controlling antibiotic-resistant strains (9). These oils possess distinctive physicochemical properties such as high volatility, hydrophobicity, and lipophilicity, which contribute to their biological activity and pharmacological effects (10).

AIM

The purpose of a review article is to present knowledge about EOs of the *Myrtaceae* family as possible alternatives to address antimicrobial resistance.

MATERIALS AND METHODS

Databases such as PubMed, ScienceDirect, and Google Scholar were used to collect and analyze scientific data by the following keywords: eucalyptus, clove, tea tree, AMR, eucalyptol, eugenol.

RESULTS

Myrtaceae Family

Certain plant families produce aromatic plants rich in EOs—*Myrtaceae, Apiaceae (Umbelliferae), Hypericaceae, Poaceae, Asteraceae (Compositae), Lamiaceae (Labiatae), Zingiberaceae, Cupressaceae, Lauraceae, Pinaceae, Piperaceae,* and *Rutaceae* (11). *Myrtaceae* is one of the most important EO families, including plants distributed throughout the world. It is considered to be eighth in size (12). It consists of 145 genera and 5970 species, including eucalyptus, cloves, and tea tree (13). Many members of this family are the source of EOs used in pharmaceutical and medical practice.

The pharmacological profile of this family includes antibacterial (Gram-positive and Gram-negative bacteria), fungicidal, acaricidal, antiviral, anti-inflammatory, anti-tumour, antioxidant, and anti-diabetic effects (14). Due to their antimicrobial activity, the clove, eucalyptus, and tea tree EOs are investigated with the aim of discovering new antimicrobial drugs.

Eucalyptus

Eucalyptus was introduced to Algeria in 1854 by Ramel (15) and is one of the most important and widespread species in the world. Due to their biological and pharmacological properties, eucalyptus species are well-known as medicinal plants. The main representative from which EOs are extracted is *Eucalyptus globulus* (*E. globulus*). The oil obtained from it is widely used in the world for the purposes of pharmacy, medicine, perfumery, cosmetics, and the food industry. The oil has shown antibacterial, anti-inflammatory, and antioxidant properties (16–18).

The oil exhibits a broad range of therapeutic properties and is utilized as a preventive agent, anesthetic, antiseptic, analgesic, antipyretic, expectorant,

astringent, disinfectant, insect repellent, diaphoretic, hemostat, inhalant, sedative, stimulant, anti-inflammatory, and for treating numerous conditions, including bronchitis, laryngitis, laryngalgia, pharyngitis, influenza, inflammation, fever, sore throat-asthma, tuberculosis, sores, rhinitis, cramps, boils, abscesses, dysentery, burns, diabetes, enteritis, diarrhea, diphtheria, encephalitis, erysipelas, arthritis, leprosy, malaria, mastitis, worms, and cancer (19).

The antibacterial activity of eucalyptus EOs is due to the components eucalyptol, linalool, citronellol, p-cymene, limonene, citronellal, citronellyl acetate, eucamalol, α-terpineol, β-pinene, γ-terpinene, allocymene, and aromadendrene (19). Essential oil obtained from the shoots, buds, and fruits of *Eucalyptus globulus* contains between 15 and 75% eugenol, and that obtained between the leaves contains from 70 and 95% (20). Eucalyptol (1,8-cineole) is the active compound in eucalyptus oil responsible for its antibacterial activity. According to pharmacopoeial standards, dried eucalyptus leaves must contain at least 2.0% v/w volatile oil, which is primarily composed of 1,8-cineole. (18).

Eucalyptus oil exhibits a very strong inhibitory effect against pathogens causing respiratory tract infections, *Staphylococcus* aureus (MIC_{50} = 64 mg/L, MIC_{90} = 128 mg/L, MBC = 512 mg/L), *Streptococcus pyogenes* (MIC_{50} = 32 mg/L, MIC_{90} = 64 mg/L, MBC = 128 mg/L), *S. pneumoniae* (MIC_{50} = 16 mg/L, MIC_{90} = 32 mg/L, MBC = 64 mg/L), and *Haemophilus influenzae* (MIC_{50} = 16 mg/L ,MIC_{90} = 32 mg/L, MBC = 64 mg/L) (18,21,22), and is used in the treatment of respiratory infections. At a low concentration, it inhibits the growth of Gram-negative bacilli (from the genus *Bacterioides sp., Prevotella sp., Fusobacterium sp.*) and Gram-positive cocci (from the genus *Micromonas sp.* and *Anerococcus*). Antibacterial properties are demonstrated even against vancomycin-resistant streptococci and methicillin-resistant staphylococci. Eucalyptus is also useful in the treatment of urinary tract infection caused by antibiotic-resistant strains of *Escherichia coli,* which are however sensitive to EOs (15).

Tea Tree

Tea tree EO is obtained from the leaves of *Melaleuca alternifolia* (M. and B.) Ch., *Melaleuca dissitiflora* F. Muell, and *Melaleuca linariifolia* Smith., the low-cineole chemotype being of greatest practical utility. The predominant component of this EO is terpinen-4-ol, which is a monoterpene alcohol and is in the 29–45% range. In smaller amounts they contain: eugenol, limonene, -terpinene, -pinene, -terpineol, -terpinene, and p-cymene (20).

The antimicrobial activity of tea tree oil is primarily attributed to terpinen-4-ol, its major component. To enhance its antimicrobial effectiveness, Carson et al. (2006) established a minimum threshold of 30% for terpinen-4-ol content, without specifying an upper limit. In contrast, a maximum limit of 15% was set for 1,8-cineole. The composition of tea tree oil can undergo significant changes during storage, with levels of ρ-cymene increasing while α- and γ-terpinene levels decrease. Factors such as light, heat, exposure to air, and moisture can impact the stability of tea tree oil, making it essential to store it in a cool, dry, and dark environment, preferably in a container with minimal air exposure (23).

Tea tree oil is considered the most powerful aromatherapy antimicrobial. It is used in dermatology, as well as in the treatment of persistent gynecological infections and respiratory diseases (23,24). It exhibits its antibacterial effects against both aerobic and anaerobic bacteria and has the ability to inhibit the proliferation of Gram-positive and Gram-negative bacteria, including those such as *Pseudomonas aeruginosa*, which are partially resistant to antibiotics. The inhibitory activity of the oil against Gram-positive bacteria isolated from the surface of the skin, such as the following staphylococci: *Staphylococcus aureus, S. capitis, S. epidermidis, S. haemolyticus, S. hominis, S. saprophyticus, S. warneri, S. xylosus,* and micrococci such as: *Micrococcus luteus, M. varianus,* and *Corynebacterium sp.*, has been proven. Gram-negative bacteria isolated from the skin (*Escherichia coli, Klebsiella pneumoniae, Serratia marcescens, Pseudomonas aeruginosa, Acinetobacter baumanii*) show a lower sensitivity to this oil, which is why application in a higher concentration is necessary (18). After the addition of *Melaleuca alternifolia* EO, a deficiency of bacteria was observed in the nasopharynx, characterized by clinical symptoms, such as increased granulocyte chemiluminescence activity, and an overall reduction in the frequency of bacterial respiratory infections (20).

A study on tea tree oil revealed that it exhibits antimicrobial properties by inhibiting the growth of Gram-positive bacteria (*Staphylococcus aureus, Staphylococcus haemolyticus, Staphylococcus epidermidis, Corynebacterium ulcerans, Streptococcus pyogenes, Streptococcus viridans, Streptococcus pneumoniae*) and Gram-negative bacteria (*Escherichia coli, Pseudomonas aeruginosa, Enterobacter georginosa, Haemophilus parainfluenzae, Acinetobacter calcoaceticus var Lwoffi, Xanthomonas maltophilia, Neisseria polysaccharea, Neisseria mucosa, Branhamella catharalis*) isolated from chronic urinary tract infection. As a result of research, it was found that the use of EO in a dilution of 1:200 inhibits the growth of all bacteria isolated from the upper respiratory tract (25).

Clinical studies have proven that tea tree and lavender oils exhibit not only a strong antibacterial, but also an immunostimulating effect.

In addition, tea tree essential oils exhibit activity against the viral agent of herpes labialis (herpes simplex, HSV). It is also used to treat human melanoma, respiratory infections, in the treatment of methicillin-resistant *Staphylococcus aureus*, oral and genital candidiasis, subcutaneous infections, skin infections, insect bites (14).

Clove

Syzygium aromaticum, commonly called clove (*Myrtaceae* family) is indigenous to the islands of Indonesia. It is now cultivated worldwide as a flavoring agent, for medicinal purposes, and for use in perfumes (26). It is widely used as a food preservative due to its antimicrobial properties (27). Apart from its antimicrobial properties, antioxidant, analgesic, anti-inflammatory, anesthetic, and insecticidal activity have been reported (28). It is also used for preventing degenerative diseases because of its antioxidant effects (29).

Essential oil of *S. aromaticum* contains 50% eugenol 50%, along with β-caryophyllene, eugenyl acetate, α-humulene, 2-(octadecyloxy)-ethanol, pinene (α and β), neral, geranial, γ-terpinene, cis-ocimene, allo-ocimene, 1,8-cineole, linalool, borneol, myrcene, pinen-2-ol, levomenthol, and other components present in smaller amounts (26,30,31). The phenolic compounds eugenol demonstrate highly pronounced antimicrobial activity and a wide spectrum of action. Plants that provide an EO containing up to 90% eugenol are: clove (*Syzygium aromaticum*), cinnamon (*Cinnamomum zeylanicum* Blume), bay leaf (*Laurus nobilis* L.), nutmeg (*Myristica fragilis* Hott.), and several types of basil such as: *Ocimum basilicum* L., *O. gratissimum* L., and *Ocimum sanctum* (20,32). Caryophyllene is another compound associated with both the antibacterial and wound-healing properties of EOs (33,34). In addition to clove, it is found in various plants, including basil (*Ocimum* spp.), cannabis (*Cannabis* spp.), lavender (*Lavandula angustifolia*), and black pepper (*Piper nigrum*) (35). Other compounds, such as levomenthol, are commonly used in mouthwashes for their antimicrobial effects (36). While levomenthol is the primary constituent of *Mentha piperita* (37), it is present in smaller amounts in clove. Another important bioactive compound is humulene, which has been shown to exhibit antibacterial activity (38). Moreover, secondary components of EOs may significantly contribute to their antimicrobial effects by interacting with primary compounds to inhibit microbial growth. The hydrophobic nature of EOs further facilitates their ability to disrupt the outer cytoplasmic membrane of pathogens, affecting membrane integrity and function (39).

The composition of EOs is influenced by various factors, including climate, distillation method, and plant variety (40). Studies have shown that clove EO exhibits strong inhibitory activity against a range of Gram-positive (*Staphylococcus aureus, Listeria monocytogenes, Enterococcus faecalis, Streptococcus pyogenes, Bacillus cereus, Bacillus subtilis, Bacillus brevis*) and Gram-negative bacteria (*Escherichia coli, Yersinia enterocolitica, Salmonella choleraesuis, Salmonella typhi, Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa*) (41,42). Given its high eugenol content, clove oil is considered a promising candidate for antimicrobial therapy. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant global health concern due to its resistance to multiple antibiotics, including amoxicillin/clavulanic acid (43), amikacin (44), ampicillin (45), ciprofloxacin (46), ceftaroline (47), erythromycin (48), tetracycline (49), clindamycin (50), gentamicin (51), levofloxacin (52), oxacillin (53), and trimethoprim/sulfamethoxazole (54). Previous studies have demonstrated that clove oil is effective against MRSA,

with a reported minimum inhibitory concentration (MIC) of 2.5 µL/mL and a minimum bactericidal concentration (MBC) of 5 µL/mL (39). A 2022 in vitro study by Alanazi et al. confirmed these values, further supporting the potential of clove oil in combating MRSA. Additionally, eugenol and its derivatives have been reported to exhibit antiviral activity against herpes simplex virus and various strains of influenza, as well as to reduce the replication of human immunodeficiency virus-1 (HIV-1) (30).

CONCLUSION

The increase in resistance to almost all classes of antibiotics, combined with a limited number of new antimicrobial agents, leads to the need to search for and implement new therapeutic agents. The analysis of literature data from scientific databases shows that, in experimental conditions, EOs and their biologically active substances represent a promising alternative for the development of new drugs that are useful in the fight against AMR. However, the number of scientific studies is insufficient and further experimental experiments are needed to determine their effect in clinical practice. Also, more studies that examine the activity of the multicomponent blend of EOs, targeting the components in the highest amount they contain, are needed. It is important to establish whether the oil should be administered as a mixture of all its biologically active substances, or whether individual components of the formulation can be administered and still obtain a biological effect.

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