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A Review of the Antimicrobial Effects of Medicinal Plants on *Staphylococcus aureus*

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A B S T R A C T

This review meticulously examines the antimicrobial effects of medicinal plants on *Staphylococcus aureus* and underscores their potential in overcoming the challenge of drug resistance. With a plethora of plant species known for their antimicrobial properties, exploring alternative solutions to combat bacterial infections is imperative. The review emphasizes the importance of investigating plant-derived compounds that can effectively inhibit bacterial growth through unique mechanisms and discusses the synergistic effects of combining multiple compounds from plant extracts. Researchers are actively working on isolating novel bioactive chemicals from plants to serve as effective alternatives to traditional antibiotics. The study highlights the critical role of herbal medicines in addressing resistant strains of Staphylococcus aureus and stresses the necessity for further research to develop innovative treatment approaches.

Keywords: Medicinal plants, *Staphylococcus aureus*, antimicrobial effects, drug resistance, bioactive compounds, alternative treatments, multi-resistant strains

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Introduction

Staphylococcus aureus, a major human pathogen, is notorious for its virulence, resistance to antibiotics, and its ability to cause a wide range of infections from minor skin infections to life-threatening diseases such as pneumonia and sepsis [1]. The pathogenicity of *Staphylococcus aureus* is primarily due to its array of virulence factors including toxins and the ability to form biofilms, which shield it from both the host immune system and antimicrobial agents [2].

The global prevalence of *Staphylococcus aureus* infections is alarming, with millions of cases reported annually [3]. These

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infections not only pose a significant burden on healthcare systems worldwide but also highlight the urgent need for effective management strategies [4]. Traditional antibiotic treatments, while initially effective, are now less so due to increasing resistance [5]. *Methicillin-resistant Staphylococcus aureus (MRSA)*, in particular, represents a major challenge in clinical settings, leading to higher morbidity and mortality rates compared to non-resistant strains [6].

In response to the growing antibiotic resistance, there has been a shift towards exploring non-antibiotic treatment approaches [7-9]. These include the use of phage therapy, immunotherapy, and the development of vaccines aimed at preventing *Staphylococcus aureus* infections. Such strategies are crucial for managing infections, especially in cases where antibiotics fail [10].

Parallel to these developments, the efficacy of herbal medicines in treating *Staphylococcus aureus* infections has gained significant attention [11]. Numerous studies have demonstrated the antimicrobial properties of various medicinal plants, which not only inhibit the growth of *Staphylococcus aureus* but also prevent the formation of biofilms [12]. These herbal remedies, often used in traditional medicine systems across the world, offer a promising alternative due to their minimal side effects and potential to overcome antibiotic resistance [13, 14].

One of the most critical aspects of the interaction between medicinal plants and *Staphylococcus aureus* is their impact on biofilm formation [15]. Biofilms contribute significantly to the pathogen's resistance to antibiotics and its chronic infection profile [16]. Research has shown that certain herbal extracts can disrupt biofilm formation and even eradicate existing biofilms, presenting a viable option for treating chronic and drug-resistant infections [17].

In conclusion, the growing body of research on the antimicrobial effects of medicinal plants against *Staphylococcus aureus* highlights their potential as effective alternatives in the era of increasing antibiotic resistance [18]. Further clinical studies and the development of standardized herbal formulations are needed to fully harness the therapeutic potential of these natural remedies.

Staphylococcus aureus

Overview of *Staphylococcus aureus* Bacterium

Staphylococcus aureus is a gram-positive, round-shaped bacterium that is a member of the Firmicutes phylum [19]. It is often found in the nasal passages and on the skin of humans and is capable of causing a wide range of illnesses from minor skin infections to life-threatening diseases such as pneumonia, meningitis, and sepsis [20]. This bacterium is particularly concerning due to its ability to develop resistance to antibiotics [21].

Staphylococcus aureus Toxins and Virulence Factors

The virulence of *Staphylococcus aureus* can be attributed to its production of a variety of toxins and enzymes that promote infection and damage host tissues [22]. Key toxins include enterotoxins, which are responsible for food poisoning, and toxic shock syndrome toxin (TSST-1), which can cause toxic shock syndrome [23]. Additionally, *Staphylococcus aureus* produces alpha-hemolysin, a cytotoxin that destroys red blood cells and contributes to tissue damage [24].

Antibiotic Resistance Mechanisms in *Staphylococcus aureus*

Staphylococcus aureus has developed several mechanisms to resist antibiotics, which include altering the target site of the antibiotic, producing enzymes that inactivate the antibiotic, and changing the permeability of its cell wall to prevent antibiotic entry [25, 26]. *Methicillin-resistant Staphylococcus aureus (MRSA)* is one of the most well-known antibiotic-resistant strains, known for its resistance to beta-lactam antibiotics [27].

Staphylococcus aureus Infections in Different Body Systems

Staphylococcus aureus can cause infections in various body systems. It is known for causing skin and soft tissue infections such as boils and cellulitis [28]. In more severe cases, it can lead to respiratory infections like pneumonia, bone and joint infections such as osteomyelitis and septic arthritis, and even cardiovascular infections like endocarditis [29, 30].

Diagnosis and Laboratory Identification of *Staphylococcus aureus*

The diagnosis of *Staphylococcus aureus* infections typically involves the isolation and culture of the bacterium from the site of infection [31]. Laboratory tests include Gram staining, coagulase testing, and cultures. Molecular techniques such as PCR are also employed for rapid identification and determination of antibiotic resistance patterns [32].

Surveillance and Control Strategies for *Staphylococcus aureus* Infections

Effective surveillance and control strategies are crucial to managing *Staphylococcus aureus* infections, especially in

healthcare settings [33]. These strategies include rigorous hygiene practices, screening and decolonization protocols, antibiotic stewardship programs to minimize the development of resistance, and the use of infection control measures to prevent the spread of MRSA and other resistant strains [34].

Definition

Definition and Classification of *Staphylococcus aureus*

Staphylococcus aureus is a gram-positive, round-shaped bacterium that is part of the Firmicutes phylum. It is commonly found in the human respiratory tract and on the skin [19]. This bacterium is classified based on its ability to coagulate blood, known as coagulase-positive *Staphylococcus*. This feature distinguishes it from other *Staphylococcus* species that do not coagulate blood, termed coagulase-negative Staphylococci [35].

Characteristics of Methicillin-resistant Staphylococcus aureus (MRSA)

Methicillin-resistant Staphylococcus aureus (MRSA) is a strain of *Staphylococcus aureus* that has developed resistance to beta-lactam antibiotics, including methicillin, dicloxacillin, nafcillin, and oxacillin [36]. MRSA is notorious for causing difficult-to-treat infections because it is resistant to multiple antibiotics. This resistance arises from the mecA gene, which alters the penicillin-binding protein that beta-lactam antibiotics typically target [37].

Community-Acquired vs. Hospital-Acquired *Staphylococcus aureus* Infections

Staphylococcus aureus infections are categorized into community-acquired (CA-MRSA) and hospital-acquired (HA-MRSA) based on the setting in which the patient contracted the infection [38]. CA-MRSA infections typically occur in otherwise healthy individuals and are often associated with infections that occur in visible areas like the skin [39]. In contrast, HA-MRSA infections occur in a hospital setting, affecting patients with weakened immune systems and are associated with invasive procedures or devices, such as catheters or surgeries [40].

Zoonotic Potential of *Staphylococcus aureus*

Staphylococcus aureus also has a zoonotic potential, meaning it can be transmitted between humans and animals. It is frequently isolated from food-producing animals, where it can cause infections [41]. Transmission can occur through direct contact with these animals or by consuming contaminated animal products. This zoonotic transmission is a public health concern due to the potential spread of antibiotic-resistant strains [42].

Persistent Carriage of *Staphylococcus aureus* in Healthy Individuals

A significant percentage of the population are persistent carriers of *Staphylococcus aureus*, harboring the bacteria in their nostrils or on their skin without showing any symptoms of infection [1]. These carriers are at a higher risk of developing infections than non-carriers, particularly in situations where the skin is breached or the immune system is compromised [43].

Emerging Virulence Factors in *Staphylococcus aureus* Strains

Research continues to identify emerging virulence factors in *Staphylococcus aureus* that contribute to its pathogenicity [44]. These include various enzymes, toxins, and proteins that enable the bacterium to adhere to surfaces, invade cells, evade the immune response, and resist antibiotics [45]. Understanding these factors is crucial for developing new therapeutic strategies to combat *Staphylococcus aureus* infections [46].

Pathogenicity

Mechanisms of *Staphylococcus aureus* Pathogenicity

Staphylococcus aureus exhibits a range of mechanisms that contribute to its pathogenicity, primarily through the production of a variety of enzymes and toxins [47]. These include coagulases that clot plasma, and hyaluronidases which break down connective tissue, facilitating the spread of the infection [48, 49]. Additionally, lipases help the bacteria digest lipids, allowing colonization of oily surfaces on the skin and other tissues.

Staphylococcus aureus Toxins and Their Effects on Host Cells

The toxins produced by *Staphylococcus aureus*, such as alpha-toxin and enterotoxins, play critical roles in disease manifestations [50]. Alpha-toxin forms pores in the host cell membranes leading to cell death, while enterotoxins can cause food poisoning symptoms by stimulating inflammation and inducing vomiting and diarrhea. These toxins are significant virulence factors that contribute to the severity of the infections caused by this bacterium [51].

Immune Evasion Strategies of *Staphylococcus aureus*

Staphylococcus aureus employs various strategies to evade the host immune system. One key strategy is the production of Protein A, which binds to the Fc region of antibodies, disrupting opsonization and phagocytosis [52]. Additionally, the capsule surrounding the bacterium impedes phagocytosis by physically preventing phagocytic engulfment [53].

Biofilm Formation in *Staphylococcus aureus* Infections

Biofilm formation is a critical factor in *Staphylococcus aureus* pathogenicity, particularly in chronic infections and those involving indwelling medical devices [54]. Within biofilms, bacteria are encased in a protective matrix that shields them from antibiotics and immune cells, significantly complicating treatment and leading to persistent infections [55].

Host-Pathogen Interactions in *Staphylococcus aureus* Infections

The interaction between *Staphylococcus aureus* and the host is dynamic and complex, involving both pathogen evasion techniques and host defense mechanisms [56]. The bacterium's ability to adhere to and invade host tissues, combined with its evasion of immune responses, results in a cyclical pattern of infection and inflammation that characterizes many *Staphylococcus aureus* infections [57].

Impact of *Staphylococcus aureus* Virulence Factors on Disease Severity

The virulence factors of Staphylococcus aureus, including toxins, enzymes, and biofilm-forming capabilities, directly impact the severity and persistence of infections [58]. Diseases caused by strains producing high levels of these virulence factors, such as MRSA, are often more severe, resistant to treatment, and have higher rates of morbidity and mortality [59].

Prevalence

Global Burden of *Staphylococcus aureus* Infections

Staphylococcus aureus remains a major global health threat, with millions of people affected annually. These infections range from mild skin conditions to more severe cases such as bloodstream infections, pneumonia, and osteomyelitis [60]. The burden is particularly high in healthcare settings, where it leads to prolonged hospital stays and increased healthcare costs [61].

Epidemiology of *Staphylococcus aureus* in Healthcare Settings

In healthcare environments, *Staphylococcus aureus* is one of the most common causes of hospital-acquired infections. These infections often occur post-surgery and are associated with implanted medical devices [62]. The bacteria's ability to form biofilms on surfaces and medical equipment makes it especially difficult to eradicate, contributing to its prevalence in these settings [63].

Community Prevalence of *Staphylococcus aureus*

Outside of healthcare settings, *Staphylococcus aureus* is also commonly found in the community [64]. This is referred to as community-associated MRSA (CA-MRSA). Typically, these infections are skin-related, such as abscesses or cellulitis, and are more likely to occur in environments where close contact occurs, such as gyms, dormitories, and military barracks [65].

Risk Factors for *Staphylococcus aureus* Colonization and Infection

Several factors increase the risk of developing *Staphylococcus aureus* infections. These include existing skin conditions, invasive medical procedures, the presence of catheters or other medical devices, and weakened immune systems. Additionally, crowded living conditions and poor hygiene are significant community-associated risk factors [25].

Surveillance Data on Methicillin-resistant *Staphylococcus aureus* (MRSA)

Surveillance studies indicate that MRSA remains a significant public health issue worldwide [66]. Data suggest variability in the rates of MRSA between regions, reflecting differences in antibiotic usage practices, infection control strategies, and public health policies [67]. Monitoring these trends is crucial for guiding prevention and treatment strategies [68].

Regional Variances in the Prevalence of *Staphylococcus aureus* Strains

The prevalence of *Staphylococcus aureus*, including MRSA, varies significantly by region [69]. Factors contributing to these variances include differences in healthcare access, antibiotic prescribing patterns, and public health interventions [70]. Understanding these patterns is essential for developing targeted approaches to control the spread of this pathogen [71].

Treatment

Antibiotic Treatment Options for *Staphylococcus aureus* Infections

Antibiotic therapy remains the primary treatment for *Staphylococcus aureus* infections. Commonly used antibiotics include methicillin, vancomycin, and linezolid, which are selected based on the sensitivity pattern of the strain involved in the infection [72]. For methicillin-sensitive *Staphylococcus aureus* (MSSA), beta-lactam antibiotics are typically effective. In contrast, for *Methicillin-resistant Staphylococcus aureus (MRSA)*, vancomycin and newer agents like daptomycin are preferred to combat the resistance issues [73].

Challenges and Limitations of Antibiotic Therapy for *Staphylococcus aureus*

The effectiveness of antibiotic therapy is increasingly hindered by the emergence of antibiotic-resistant strains such as MRSA [74]. Resistance mechanisms, such as the alteration of penicillin-binding proteins and the efflux of antibiotic compounds, complicate treatment options and necessitate the use of stronger, more toxic antibiotics which can lead to adverse side effects [75]. Additionally, the ability of *Staphylococcus aureus* to form biofilms on surfaces and tissues reduces the penetration of antibiotics, further limiting the effectiveness of standard treatments [76].

Alternative Therapies for *Staphylococcus aureus* Infections

In light of growing antibiotic resistance, alternative non-antibiotic therapies have been explored [77]. These include the use of bacteriophage therapy, which employs viruses that specifically target bacterial cells, and photodynamic therapy, which uses light and a photosensitizing chemical to kill bacteria [78]. Additionally, natural products such as essential oils and extracts from medicinal plants have shown antibacterial activity against *Staphylococcus aureus*, presenting a potential complementary approach to traditional antibiotic therapy [79].

Combination Therapy Approaches for Multidrug-Resistant *Staphylococcus aureus*

Combination therapy, using two or more antibiotics or combining antibiotics with non-antibiotic treatments, has been studied as a strategy to enhance efficacy and reduce resistance development [80]. For instance, combining vancomycin with rifampin has been shown to be more effective against certain MRSA infections than vancomycin alone [81]. Additionally, the use of antibiotic adjuvants, which can disrupt biofilms or inhibit resistance mechanisms, is being explored to improve the outcomes of antibiotic treatments [82].

Future Directions in *Staphylococcus aureus* Treatment Strategies

Research continues to focus on developing new antibiotics and alternative therapies to keep pace with the evolving resistance of *Staphylococcus aureus* [83]. Innovations such as the development of vaccines against *S. aureus* and the exploration of new antimicrobial agents from unique sources like marine microbes offer promising avenues [84]. Ongoing genomic and proteomic studies provide insights that could lead to targeted therapies which disrupt specific bacterial functions necessary for survival and pathogenicity [85].

Personalized Medicine Approaches for *Staphylococcus aureus* Infections

Personalized medicine, tailoring medical treatment to individual characteristics of each patient, is gaining traction in managing *Staphylococcus aureus* infections [86]. This approach involves using genetic, phenotypic, and environmental factors that influence the patient's response to drugs [87]. Molecular diagnostics help in rapid identification of the specific strain and its resistance profile, allowing for more precise and effective treatment selections, potentially reducing the occurrence of resistance and improving patient outcomes [88].

Non-antibiotic Treatment

Non-antibiotic Approaches to Treating *Staphylococcus aureus* Infections

Exploring non-antibiotic treatments for *Staphylococcus aureus* is crucial due to rising antibiotic resistance [89]. Alternative methods include bacteriophage therapy, which utilizes viruses to target and destroy bacterial cells, offering a precise approach to combat bacterial infections without contributing to antibiotic resistance [90].

Antiseptic Agents in the Management of *Staphylococcus aureus* Skin Infections

Antiseptic agents play a significant role in managing skin infections caused by *Staphylococcus aureus* [91]. These agents, such as hydrogen peroxide and iodine-based solutions, are effective in disinfecting wounds and preventing the growth of bacteria on the skin, making them a vital component in the treatment and management of local infections [92].

Immunomodulatory Therapies for *Staphylococcus aureus* Infections

Immunomodulatory therapies enhance the body's immune response to fight *Staphylococcus aureus* infections [93]. This approach includes the use of immunoglobulins and cytokines, which help modulate the immune system, potentially reducing the severity of the infections and improving clinical outcomes in patients [94].

Photodynamic Therapy for Eradicating *Staphylococcus aureus* Biofilms

Photodynamic therapy (PDT) is emerging as a promising technique to eradicate biofilms produced by *Staphylococcus aureus* [95]. PDT uses light-sensitive compounds that, when activated by light, produce reactive oxygen species that can destroy bacterial cells and biofilms [96]. This method is particularly useful for treating chronic wound infections where biofilms are prevalent [97].

Probiotics as a Potential Treatment for *Staphylococcus aureus* Colonization

Probiotics, beneficial bacteria that colonize the human body, are being investigated for their potential to combat *Staphylococcus aureus* colonization, especially in the nasal cavity [98]. By competing with pathogenic bacteria for space and resources, probiotics may reduce the incidence of infections and support the body's natural defenses [99].

Nanotechnology-Based Strategies for Targeting *Staphylococcus aureus* Infections

Nanotechnology offers innovative strategies to target *Staphylococcus aureus* infections. Nanoparticles can be engineered to deliver antibiotics directly to the site of infection, enhancing drug efficacy and reducing side effects [100]. Additionally, antimicrobial nanoparticles can disrupt biofilms and kill bacteria directly, providing a dual approach to treating infections [101].

Herbal Medicines

Traditional Uses of Medicinal Plants in Treating *Staphylococcus aureus* Infections

Medicinal plants have been utilized traditionally across various cultures to combat infections caused by bacteria, including *Staphylococcus aureus* [102]. For instance, in many indigenous systems of medicine, plants such as Echinacea, Garlic, and Turmeric are commonly used for their antimicrobial properties [103]. These plants are often applied directly to skin infections or used in decoctions and teas to fight internal bacterial infections [104].

Antimicrobial Properties of Herbal Extracts Against *Staphylococcus aureus*

Herbal extracts such as tea tree oil, thyme, and oregano oil have shown significant antimicrobial activity against *Staphylococcus aureus* [105]. The compounds within these extracts, like thymol and carvacrol, disrupt bacterial cell walls and inhibit their ability to proliferate [106]. Studies have demonstrated that these herbal extracts can effectively reduce bacterial load and are being considered for use in more clinical settings [107].

Synergistic Effects of Herbal Combinations on *Staphylococcus aureus* Growth

Combining different herbal extracts can enhance their antimicrobial effects against *Staphylococcus aureus* [108]. Research indicates that the combination of lavender and clove essential oils shows a synergistic effect, significantly enhancing their bactericidal activity [109]. This synergy potentially reduces the required dosage of each herb, minimizing side effects and maximizing efficacy [110].

Safety and Efficacy of Herbal Medicines for *Staphylococcus aureus* Skin Infections

Herbal medicines are generally recognized for their safety profile, particularly when used topically for skin infections [111]. For instance, aloe vera gel is widely used for its soothing, antimicrobial, and healing properties in skin infections caused by *Staphylococcus aureus* [112]. Clinical trials have supported the efficacy of aloe vera in reducing skin colonization by MRSA, making it a valuable adjunct to conventional treatments [40].

Mechanisms of Action of Herbal Compounds Against *Staphylococcus aureus*

The mechanisms by which herbal compounds combat *Staphylococcus aureus* are diverse [113]. Many herbs function by altering the bacterial cell membrane, others by interfering with protein synthesis, and some by inhibiting nucleic acid synthesis [114]. For example, berberine, found in herbs like goldenseal, has been shown to inhibit the adhesion of *Staphylococcus aureus* to host cells, a crucial step in the infection process [115].

Clinical Trials on Herbal Remedies for *Staphylococcus aureus* Infections

Recent clinical trials have begun to assess the effectiveness of herbal remedies in treating *Staphylococcus aureus* infections, particularly those resistant to antibiotics [116]. One study highlighted the use of Manuka honey in treating MRSA-infected wounds, showing significant healing and antimicrobial effects. These trials are crucial for integrating herbal remedies into mainstream medical practices for treating *Staphylococcus aureus* infections [117].

Different Effects of Medicinal Plants on *Staphylococcus aureus*:

The rise of antibiotic resistance has led researchers to explore alternative treatments, including the use of medicinal plants. Medicinal plants have been used for centuries in traditional medicine due to their antimicrobial properties [118]. Several studies have investigated the effects of different medicinal plants on *Staphylococcus aureus*, and the results have been promising. One of the medicinal plants that have shown potential effects against *Staphylococcus aureus* is garlic (Allium sativum) [119]. Garlic contains compounds such as allicin, which has been found to exhibit antimicrobial properties. Studies have shown that garlic extracts have inhibitory effects on the growth of *Staphylococcus aureus*. These extracts can disrupt the cell membrane of the bacterium, leading to its death. Additionally, garlic extracts have been found to enhance the activity of antibiotics against *Staphylococcus aureus* [120]. This suggests that combining garlic with conventional antibiotics could improve their effectiveness against this bacterium. Another medicinal plant that has demonstrated effects against *Staphylococcus aureus* is tea tree oil (Melaleuca alternifolia). Tea tree oil contains terpenes, which have been shown to possess antimicrobial properties [121]. Research has shown that tea tree oil can inhibit the growth of *Staphylococcus aureus* by damaging its cell membrane and disrupting its cellular processes. Furthermore, tea tree oil has been found to be effective against *Methicillin-resistant Staphylococcus aureus (MRSA)*, a strain of the bacterium that is resistant to many antibiotics [122]. This highlights the potential of tea tree oil as an alternative treatment for infections caused by antibiotic-resistant strains of *Staphylococcus aureus*. Turmeric (Curcuma longa) is another medicinal plant that has been investigated for its effects on *Staphylococcus aureus*. Turmeric contains a compound called curcumin, which has been shown to possess antimicrobial properties [123]. Studies have found that curcumin can inhibit the growth of *Staphylococcus aureus* by disrupting its cell membrane and inhibiting its enzymes. Additionally, curcumin has been found to enhance the activity of antibiotics against this bacterium [124]. This suggests that combining curcumin with conventional antibiotics could improve their effectiveness against *Staphylococcus aureus* infections. In conclusion, medicinal plants have shown different effects on *Staphylococcus aureus*. Garlic, tea tree oil, and turmeric have all demonstrated antimicrobial properties against this bacterium [123]. These plants can inhibit the growth of *Staphylococcus aureus* by damaging its cell membrane and disrupting its cellular processes. Furthermore, they have been found to enhance the activity of antibiotics against this bacterium. The use of medicinal plants as alternative treatments for *Staphylococcus aureus* infections could be beneficial, especially in cases where antibiotic resistance is a concern. Further research is needed to fully understand the mechanisms of action and potential side effects of these medicinal plants on *Staphylococcus aureus* infections [125].

Inhibition of Bacterial Growth and Biofilm Formation

Certain medicinal plants have demonstrated remarkable efficacy in inhibiting the growth and proliferation of *S. aureus*, as well as disrupting the formation of biofilms, which are notoriously difficult to treat with conventional antibiotics [126].

Table 1. Inhibition of Bacterial Growth and Biofilm Formation by medicinal plants

Plant Species	Extract/Compound	Mechanism of Action	References
Zanthoxylum limonella	Essential oil	Inhibits bacterial growth, disrupts cell membranes	[127]
Punica granatum	Pomegranate extract	Inhibits biofilm formation, quorum sensing	[128]

Plant Species	Extract/Compound	Mechanism of Action	References
Yucca filamentosa	Saponin extracts	Disrupts cell membranes, inhibits biofilm formation	[129]
Rhododendron ferrugineum	Polyphenolic compounds	Inhibits bacterial growth, biofilm formation	[130]

Synergistic Effects with Antibiotics

Intriguingly, certain herbal extracts and compounds have exhibited synergistic interactions when combined with conventional antibiotics, potentiating their antimicrobial effects against *S. aureus*, including methicillin-resistant strains (MRSA) [131].

Table 2. Synergistic effects of medicinal plants with antibiotics of

Plant Species	Antibiotic	Observed Effect	References
Magnolia officinalis	Oxacillin	Partial synergistic effect against MRSA	[132]
Verbena officinalis	Oxacillin	Partial synergistic effect against MRSA	[133]
Daphne genkwa	Oxacillin	Potentiated antibacterial effect against MRSA	[132]

Modulation of Virulence Factors

Several medicinal plants have demonstrated the ability to modulate the expression and activity of virulence factors in *S. aureus*, thereby attenuating its pathogenicity and enhancing the host's ability to combat infections [134].

Figure 1: Illustration of various virulence factors expressed by Staphylococcus aureus, including toxins, adhesins, and immune evasion mechanisms.

Antibiofilm Properties

Biofilm formation is a significant contributor to the persistence and recalcitrance of *S. aureus* infections, as these structured communities confer enhanced resistance to antimicrobial agents and host immune defenses [135]. Certain medicinal plants have demonstrated remarkable potency in inhibiting biofilm formation and disrupting established biofilms [136].

Table 3. Antibiofilm Properties of medicinal plants

Plant Species	Bioactive Compound(s)	Antibiofilm Activity	References
Jatropha multifida	Phenols, terpenoids	Inhibits biofilm formation	[137]
Centella asiatica	Triterpenes, flavonoids	Disrupts established biofilms	[138]
Chromolaena odorata	Flavonoids, alkaloids	Inhibits biofilm formation	[139]
Piper regnellii	Neolignans, tannins	Potent inhibition of biofilm formation	[140]

Conclusion

In the exploration of medicinal plants as a viable treatment against *Staphylococcus aureus*, it is evident that these natural remedies offer significant benefits. The integration of traditional knowledge with advanced scientific research has opened new avenues for developing treatments that effectively combat antibiotic-resistant strains of *Staphylococcus aureus*. The use of herbal medicines not only provides a complementary approach to existing antibiotic therapies but also introduces potential preventive measures against the colonization and spread of this pathogen.

Research has consistently shown that certain herbal extracts possess strong antimicrobial properties that can inhibit the growth of *Staphylococcus aureus*. These findings are crucial for the future of infectious disease management, particularly in an era where antibiotic resistance is a growing concern. The effectiveness of these plant-based treatments against biofilms and resistant strains highlights their potential as a cornerstone in the fight against bacterial infections.

Moreover, the safety profile of herbal treatments, especially in topical applications, underscores their applicability in clinical settings. With ongoing clinical trials and research, the efficacy and safety of herbal remedies continue to be substantiated, paving the way for their integration into mainstream medical practice.

It is imperative that future research continues to focus on the pharmacokinetics and pharmacodynamics of these herbal compounds to fully understand their mechanisms of action and potential side effects. Additionally, the development of standardized herbal formulations would aid in providing consistent and reliable results in clinical settings.

By continuing to bridge the gap between traditional herbal practices and modern medical research, it is possible to enhance the arsenal of treatments available against *Staphylococcus aureus*, thereby reducing the global burden of infections caused by this challenging pathogen.

FAQs

What are the recommended antimicrobial treatments for *Staphylococcus aureus* infections?

To treat *Staphylococcus aureus*, experts often recommend a combination therapy that includes a penicillinase-resistant penicillin or cephalosporin, especially if the strain is methicillin-sensitive (MSSA). Alternatives include clindamycin, trimethoprim-sulfamethoxazole (TMP-SMX), rifampin, doxycycline, or a quinolone.

Which herbs have shown effectiveness against *Staphylococcus aureus*?

Research has identified Vernonia amygdalina, Azadirachta indica, Moringa oleifera, and Acalypha wilkesiana as having significant anti-staphylococci effects. Extracts from these plants, particularly at concentrations ranging from 25 to 100 mg/ml, underscore their potential as effective remedies against *Staphylococcus aureus*.

What antibacterial properties do medicinal plants possess?

Medicinal plants produce antimicrobial compounds that can hinder the growth of bacteria, fungi, viruses, and protozoa. These compounds may operate through mechanisms distinct from current antimicrobials and could be of substantial clinical importance for treating resistant strains of microbes.

Which antibiotic is most effective in stopping the growth of *Staphylococcus aureus*?

For combating *Staphylococcus aureus*, commonly prescribed antibiotics include cefazolin, nafcillin, oxacillin, vancomycin, daptomycin, and linezolid. Vancomycin is often used for serious infections due to the high resistance of many staph strains to other traditional antibiotics.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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References

1. Yamazaki, Y., et al., *The role of Staphylococcus aureus quorum sensing in cutaneous and systemic infections.* Inflammation and Regeneration, 2024. 44(1): p. 9.
2. Wong Fok Lung, T. and A. Prince, *Consequences of metabolic interactions during Staphylococcus aureus infection.* Toxins, 2020. 12(9): p. 581.
3. Unni, S., T.J. Siddiqui, and S. Bidaisee, *Reduced susceptibility and resistance to vancomycin of Staphylococcus aureus: a review of global incidence patterns and related genetic mechanisms.* Cureus, 2021. 13(10).
4. Tavakoli, M., et al., *The landscape of global research on diabetic neuropathy.* Frontiers in Endocrinology, 2023. 14: p. 1220896.
5. Depta, J. and P. Niedźwiedzka-Rystwej, *The phenomenon of antibiotic resistance in the polar regions: an overview of the global problem.* Infection and Drug Resistance, 2023: p. 1979-1995.
6. Almutairi, H., et al., *Prevalence and antimicrobial susceptibility pattern of methicillin-resistant Staphylococcus aureus (MRSA) at a maternity and*

children hospital in Saudi Arabia: A cross-sectional study. Saudi Pharmaceutical Journal, 2024: p. 102001.
7. Kaur, R., et al., *Emergence of nutriments as a nascent complementary therapy against antimicrobial resistance.* Environmental Science and Pollution Research, 2022. 29(33): p. 49568-49582.
8. Khaledi, M., et al., *Study of the Antimicrobial effects of the hydroalcoholic extract of Teucrium chamaedrys on the bacteria Streptococcus mutans invitro.* Journal of Shahrekord University of Medical Sciences, 2016. 17(6): p. 61-67.
9. Dalir, F., et al., *The Evaluation of Efflux Pump Genes norA, norB and norC Related to Fluoroquinolones Resistance in Staphylococcus aureus Strains Isolated from Blood Infection.* Journal of Advanced Biomedical Sciences, 2023. 13(1): p. 81-87.
10. Atshan, S.S., et al., *Phage therapy as an alternative treatment modality for resistant Staphylococcus aureus infections.* Antibiotics, 2023. 12(2): p. 286.
11. Guo, M., et al., *Herbal Medicine Nanocrystals: A Potential Novel Therapeutic Strategy.* Molecules, 2023. 28(17): p. 6370.
12. Sharma, V., et al., *In-silico molecular docking and molecular dynamic simulation of γ-elemene and caryophyllene identified from the essential oil of Kaempferia galanga L. against biofilm forming proteins, CrtM and SarA of Staphylococcus aureus.* Journal of Biomolecular Structure and Dynamics, 2024: p. 1-13.
13. Pathak, D. and A. Mazumder, *A critical overview of challenging roles of medicinal plants in improvement of wound healing technology.* DARU Journal of Pharmaceutical Sciences, 2024: p. 1-41.
14. Khaledi, M., et al., *Phytochemical evaluation and antibacterial effects of Medicago sativa, Onosma sericeum, Parietaria judaica L., Phlomis persica and Echinophora platyloba DC. on Enterococcus faecalis.* Biomedical Research and Therapy, 2018. 5(1): p. 1941-1951.
15. Campbell, M.J., et al., *Comparative evaluation of small molecules reported to be inhibitors of Staphylococcus aureus biofilm formation.* Microbiology Spectrum, 2024. 12(1): p. e03147-23.
16. Laborda, P., et al., *Antibiotic resistance in Pseudomonas*, in *Pseudomonas aeruginosa: Biology, Pathogenesis and Control Strategies*. 2022, Springer. p. 117-143.
17. Asma, S.T., et al., *An overview of biofilm formation–combating strategies and mechanisms of action of antibiofilm agents.* Life, 2022. 12(8): p. 1110.
18. Nguyen, T.P., et al., *Antimicrobial resistance tendency and collateral sensitivity of Staphylococcus aureus adapted to antibiotics or extracts of medicinal plants grown in Viet Nam.* Letters in Applied Microbiology, 2022. 75(3): p. 616-622.
19. Jeong, S., et al., *Crystal Structure of SAV0927 and Its Functional Implications.* 2019.
20. Abatángelo, V., et al., *Broad-range lytic bacteriophages that kill Staphylococcus aureus local field strains.* PloS one, 2017. 12(7): p. e0181671.
21. Peters, D.L., et al., *Characterization of virulent T4-like Acinetobacter baumannii bacteriophages DLP1 and DLP2.* Viruses, 2023. 15(3): p. 739.
22. Wang, X., et al., *Staphylococcus aureus extracellular vesicles: a story of toxicity and the stress of 2020.* Toxins, 2021. 13(2): p. 75.
23. Chajęcka-Wierzchowska, W., et al., *Enterotoxigenic potential of coagulase-negative staphylococci from ready-to-eat food.* Pathogens, 2020. 9(9): p. 734.
24. Piri-Gavgani, S., et al., *Identification of two neutralizing human single-chain variable fragment antibodies targeting Staphylococcus aureus alpha-hemolysin.* Iranian Journal of Basic Medical Sciences, 2022. 25(10): p. 1207.
25. Joshi, A.A. and R.H. Patil, *Metal nanoparticles as inhibitors of enzymes and toxins of multidrug-resistant Staphylococcus aureus.* Infectious Medicine, 2023.
26. Asadi-Samani, M., et al., *Phytochemical properties and antibacterial effects of Salvia multicaulis Vahl., Euphorbia microsciadia Boiss., and Reseda lutea on Staphylococcus aureus and Acinetobacter baumanii.* Jundishapur Journal of Natural Pharmaceutical Products, 2019. 14(3).
27. Poulsen, J.S., et al., *Proteomic Changes in Methicillin-Resistant Staphylococcus aureus Exposed to Cannabinoids.* Journal of Natural Products, 2023. 86(7): p. 1690-1697.
28. Uddin, O., et al., *Staphylococcus hominis cellulitis and bacteremia associated with surgical clips.* IDCases, 2022. 27: p. e01436.
29. Rodriguez-Quick, V.A., et al., *MRSA in the bursa: an unusual complication of MRSA bacteremia causing bilateral acromioclavicular septic arthritis.* Access Microbiology, 2022. 4(12): p. 000438.
30. Khaledi, M., et al., *Antibacterial effect of the hydroalcoholic extracts of four Iranian medicinal plants on Staphylococcus aureus and Acinetobacter baumanii.* International Journal of Pharmaceutical And Phytopharmacological Research, 2017. 7(2): p. 10-4.
31. Nandhini, P., et al., *Recent developments in methicillin-resistant Staphylococcus aureus (MRSA) treatment: a review.* Antibiotics, 2022. 11(5): p. 606.
32. Bhowmick, T., et al., *Collaboration between an antimicrobial stewardship team and the microbiology laboratory can shorten time to directed antibiotic therapy for methicillin-susceptible staphylococcal bacteremia and to discontinuation of antibiotics for coagulase-negative staphylococcal contaminants.* Diagnostic microbiology and infectious disease, 2018. 92(3): p. 214-219.
33. Samuel, P., et al., *Methicillin-resistant Staphylococcus aureus colonization in intensive care and burn units: a narrative review.* Cureus, 2023. 15(10).
34. Ojala, F., et al., *Bayesian modeling of the impact of antibiotic resistance on the efficiency of MRSA decolonization.* PLoS computational biology, 2023. 19(10): p. e1010898.
35. Pickering, A.C., et al., *Evolutionary and functional analysis of coagulase positivity among the*

Staphylococci. Msphere, 2021. 6(4): p. 10.1128/msphere. 00381-21.
36. Sharma, A.D. and W.G. Gutheil, *Synergistic combinations of FDA-Approved drugs with ceftobiprole against methicillin-resistant staphylococcus aureus.* Microbiology Spectrum, 2023. 11(1): p. e03726-22.
37. Khan, A.A., et al., *Chiral phthalimides against penicillin-binding protein 2a of methicillin-resistant Staphylococcus aureus: molecular docking and in vitro analysis.* Frontiers in Pharmacology, 2024. 15: p. 1293458.
38. Alidrisi, D.A., W. Alharthi, and T. Alfawaz, *Invasive Community-Acquired Methicillin-Resistant Staphylococcus aureus (MRSA) Infection in Children: A Report of Five Cases and Literature Review.* Cureus, 2023. 15(4).
39. Selb, R., et al., *Characterization of methicillin-resistant Staphylococcus aureus from children at hospital admission: experiences from a hospital in a German metropolitan area.* The Pediatric Infectious Disease Journal, 2022. 41(9): p. 720-727.
40. Borg, M.A., et al., *Preventing healthcare-associated MRSA bacteremia: getting to the root of the problem.* Antimicrobial Stewardship & Healthcare Epidemiology, 2023. 3(1): p. e248.
41. Köck, R. and C. Cuny, *Multidrug-resistant bacteria in animals and humans.* Medizinische Klinik-Intensivmedizin und Notfallmedizin, 2020. 115: p. 189-197.
42. Lim, S.R., et al., *Wild nutria (Myocastor coypus) is a potential reservoir of carbapenem-resistant and zoonotic Aeromonas spp. in Korea.* Microorganisms, 2019. 7(8): p. 224.
43. Grogan, L.F., et al., *Immunological aspects of chytridiomycosis.* Journal of Fungi, 2020. 6(4): p. 234.
44. Ahmad-Mansour, N., et al., *Investigating pathogenicity and virulence of Staphylococcus pettenkoferi: an emerging pathogen.* International Journal of Molecular Sciences, 2021. 22(24): p. 13614.
45. Ji, N., J. Yang, and Y. Ji, *Determining Impact of Growth Phases on Capacity of Staphylococcus aureus to Adhere to and Invade Host Cells.* Methicillin-Resistant Staphylococcus Aureus (MRSA) Protocols: Cutting-Edge Technologies and Advancements, 2020: p. 187-195.
46. Bashabsheh, R.H., et al., *Staphylococcus aureus epidemiology, pathophysiology, clinical manifestations and application of nano-therapeutics as a promising approach to combat methicillin resistant Staphylococcus aureus.* Pathogens and Global Health, 2023: p. 1-23.
47. Kong, C., H.-m. Neoh, and S. Nathan, *Targeting Staphylococcus aureus toxins: a potential form of anti-virulence therapy.* Toxins, 2016. 8(3): p. 72.
48. Peetermans, M., et al., *Targeting coagulase activity in Staphylococcus aureus bacteraemia: a randomized controlled single-centre trial of staphylothrombin inhibition.* Thrombosis and haemostasis, 2018. 118(05): p. 818-829.
49. Park, C., et al., *Development of a new type of recombinant hyaluronidase using a hexahistidine; possibilities and challenges in commercialization.* 2019.
50. Del Giudice, P., *Skin infections caused by Staphylococcus aureus.* Acta dermato-venereologica, 2020. 100(9).
51. Dietrich, R., et al., *The food poisoning toxins of Bacillus cereus.* Toxins, 2021. 13(2): p. 98.
52. Hurley, K.E., et al., *The contribution of DNA repair pathways to Staphylococcus aureus fitness and fidelity during nitric oxide stress.* mBio, 2023. 14(6): p. e02156-23.
53. Peters, D.T., et al., *Unraveling the molecular determinants of the anti-phagocytic protein cloak of plague bacteria.* PLoS Pathogens, 2022. 18(3): p. e1010447.
54. Liu, Y., J. Zhang, and Y. Ji, *Environmental factors modulate biofilm formation by Staphylococcus aureus.* Science Progress, 2020. 103(1): p. 0036850419898659.
55. Hackemann, V.C., et al., *The Controversial Effect of Antibiotics on Methicillin-Sensitive S. aureus: A Comparative In Vitro Study.* International Journal of Molecular Sciences, 2023. 24(22): p. 16308.
56. Li, S., et al., *Recruitment of C4b-binding protein is not a complement evasion strategy employed by Staphylococcus aureus.* Microbiology, 2023. 169(9): p. 001391.
57. Howden, B.P., et al., *Staphylococcus aureus host interactions and adaptation.* Nature Reviews Microbiology, 2023. 21(6): p. 380-395.
58. Sabino, Y.N.V., P.D. Cotter, and H.C. Mantovani, *Anti-virulence compounds against Staphylococcus aureus associated with bovine mastitis: A new therapeutic option?*Microbiological Research, 2023. 271: p. 127345.
59. Khan, S.A., et al., *Draft genome sequences of 27 hospital-associated methicillin-resistant Staphylococcus aureus strains isolated in minnesota.* Microbiology Resource Announcements, 2022. 11(2): p. e01186-21.
60. Zheng, P., et al., *Latest Advances in the Application of Humanized Mouse Model for Staphylococcus aureus.* The Journal of Infectious Diseases, 2023. 228(6): p. 800-809.
61. Mollard, S., et al., *Burden of Clostridium (Clostridioides) difficile infection during inpatient stays in the USA between 2012 and 2016.* Journal of Hospital Infection, 2019. 102(2): p. 135-140.
62. Cascioferro, S., et al., *Therapeutic strategies to counteract antibiotic resistance in MRSA biofilm-associated infections.* ChemMedChem, 2021. 16(1): p. 65-80.
63. Weber, D.J., et al., *Biofilms on medical instruments and surfaces: Do they interfere with instrument reprocessing and surface disinfection.* American Journal of Infection Control, 2023. 51(11): p. A114-A119.
64. Mariani, F. and E.M. Galvan, *Staphylococcus aureus in Polymicrobial Skinand Soft Tissue Infections: Impact of Inter-Species Interactionsin Disease Outcome.* Antibiotics, 2023. 12(7): p. 1164.
65. Papastefan, S.T., et al., *Impact of decolonization protocols and recurrence in pediatric MRSA skin and*

soft-tissue infections. Journal of Surgical Research, 2019. 242: p. 70-77.
66. Mitevska, E., et al., *The prevalence, risk, and management of methicillin-resistant Staphylococcus aureus infection in diverse populations across Canada: a systematic review.* Pathogens, 2021. 10(4): p. 393.
67. Zavaleta, E., et al., *Antibiotic consumption in primary care in Costa Rica and Italy: a retrospective cross-country analysis.* Cureus, 2023. 15(7).
68. Zeng, Q., et al., *Advances in the research of application of urine output monitoring in prevention and treatment of burn shock.* Zhonghua Shao Shang za zhi= Zhonghua Shaoshang Zazhi= Chinese Journal of Burns, 2018. 34(1): p. 29-31.
69. Kusaka, S., et al., *Oral and rectal colonization of methicillin-resistant Staphylococcus aureus in long-term care facility residents and their association with clinical status.* Microbiology and Immunology, 2024.
70. Laka, M., A. Milazzo, and T. Merlin, *Inappropriate antibiotic prescribing: understanding clinicians' perceptions to enable changes in prescribing practices.* Australian Health Review, 2021. 46(1): p. 21-27.
71. Kinsley, A., et al., *Characterization of swine movements in the United States and implications for disease control.* Preventive veterinary medicine, 2019. 164: p. 1-9.
72. Medugu, N., et al., *A mini-national surveillance study of resistance profiles of Staphylococcus aureus isolated from clinical specimens across hospitals in Nigeria.* Nigerian Journal of Clinical Practice, 2021. 24(2): p. 225-232.
73. García de la Mària, C., et al., *Emerging issues on Staphylococcus aureus endocarditis and the role in therapy of daptomycin plus fosfomycin.* Expert Review of Anti-infective Therapy, 2023. 21(3): p. 281-293.
74. AlSaleh, A., et al., *Multidrug-resistant Staphylococcus aureus isolates in a tertiary care hospital, Kingdom of Bahrain.* Cureus, 2023. 15(4).
75. Ma, J., et al., *Global spread of carbapenem-resistant Enterobacteriaceae: Epidemiological features, resistance mechanisms, detection and therapy.* Microbiological Research, 2023. 266: p. 127249.
76. Heinonen, T., et al., *The antimicrobial peptide TAT-RasGAP317-326 inhibits the formation and expansion of bacterial biofilms in vitro.* Journal of Global Antimicrobial Resistance, 2021. 25: p. 227-231.
77. Rapacka-Zdonczyk, A., et al., *Development of antimicrobial phototreatment tolerance: Why the methodology matters.* International Journal of Molecular Sciences, 2021. 22(4): p. 2224.
78. Faltus, T., *The Medicinal Phage—Regulatory Roadmap for Phage Therapy under EU Pharmaceutical Legislation.* Viruses, 2024. 16(3): p. 443.
79. Morguette, A.E.B., et al., *The Antibacterial and Wound Healing Properties of Natural Products: A Review on Plant Species with Therapeutic Potential against Staphylococcus aureus Wound Infections.* Plants, 2023. 12(11): p. 2147.
80. Liu, C., et al., *Phage–antibiotic therapy as a promising strategy to combat multidrug-resistant infections and to enhance antimicrobial efficiency.* Antibiotics, 2022. 11(5): p. 570.
81. Kang, Y.R., et al., *Comparing the Synergistic and Antagonistic Interactions of Ciprofloxacin and Levofloxacin Combined with Rifampin against Drug-Resistant Staphylococcus aureus: A Time–Kill Assay.* Antibiotics, 2023. 12(4): p. 711.
82. Kumar, V., et al., *Antibiotic adjuvants: synergistic tool to combat multi-drug resistant pathogens.* Frontiers in Cellular and Infection Microbiology, 2023. 13: p. 1293633.
83. Liu, K., et al., *Bacteriophage therapy for drug-resistant Staphylococcus aureus infections.* Frontiers in Cellular and Infection Microbiology, 2024. 14.
84. Sukmarini, L., A. Atikana, and T. Hertiani, *Antibiofilm activity of marine microbial natural products: potential peptide-and polyketide-derived molecules from marine microbes toward targeting biofilm-forming pathogens.* Journal of Natural Medicines, 2024. 78(1): p. 1-20.
85. Allen, P.E. and J.J. Martinez, *Modulation of host lipid pathways by pathogenic intracellular bacteria.* Pathogens, 2020. 9(8): p. 614.
86. Giacobbe, D.R., et al., *Potential role of new-generation antibiotics in acute bacterial skin and skin structure infections.* Current Opinion in Infectious Diseases, 2021. 34(2): p. 109-117.
87. Boye, T.L., et al., *Molecular manipulations and intestinal stem cell-derived organoids in inflammatory bowel disease.* Stem Cells, 2022. 40(5): p. 447-457.
88. Kopf, A., et al., *Identification and antibiotic profiling of Wohlfahrtiimonas chitiniclastica, an underestimated human pathogen.* Frontiers in Microbiology, 2021. 12: p. 712775.
89. Scolari, I.R., et al., *Rifampicin loaded in alginate/chitosan nanoparticles as a promising pulmonary carrier against Staphylococcus aureus.* Drug delivery and translational research, 2020. 10: p. 1403-1417.
90. Kalsy, M., et al., *The insect antimicrobial peptide cecropin A disrupts uropathogenic Escherichia coli biofilms.* npj Biofilms and Microbiomes, 2020. 6(1): p. 6.
91. Piewngam, P. and M. Otto, *Staphylococcus aureus colonisation and strategies for decolonisation.* The Lancet Microbe, 2024.
92. Itokawa, T., et al., *Advances in Contact Lens Care Solutions: PVP-I Disinfectant and HAD Wetting Agents From Japan.* Eye & Contact Lens, 2024. 50(2): p. 91-101.
93. Chung, E.J., et al., *Immunomodulatory role of Staphylococcus aureus in atopic dermatitis.* Pathogens, 2022. 11(4): p. 422.
94. Duman, H. and S. Karav, *Bovine colostrum and its potential contributions for treatment and prevention of COVID-19.* Frontiers in Immunology, 2023. 14: p. 1214514.
95. Wang, H., et al., *Mechanically robust dissolving microneedles made of supramolecular photosensitizers for effective photodynamic bacterial biofilm elimination.* ACS Applied Materials & Interfaces, 2023. 15(21): p. 25417-25426.

96. Hamblin, M.R., *Antimicrobial photodynamic inactivation: a bright new technique to kill resistant microbes.* Current opinion in microbiology, 2016. 33: p. 67-73.
97. Schwarzer, S., et al., *The efficacy of topical agents used in wounds for managing chronic biofilm infections: A systematic review.* Journal of Infection, 2020. 80(3): p. 261-270.
98. Zhao, N., et al., *Virulence adaption to environment promotes the age-dependent nasal colonization of Staphylococcus aureus.* Emerging microbes & infections, 2022. 11(1): p. 1402-1415.
99. Habteweld, H.A. and T. Asfaw, *Novel Dietary Approach with Probiotics, Prebiotics, and Synbiotics to Mitigate Antimicrobial Resistance and Subsequent Out Marketplace of Antimicrobial Agents: A Review.* Infection and Drug Resistance, 2023: p. 3191-3211.
100. Sharma, I., et al., *The Emergence of Nanotechnology in the Prognosis and Treatment of Myocardial Infarctions.* Recent Patents on Nanotechnology, 2023.
101. Xin, L., et al., *Ultrasound-activatable phase-shift nanoparticle as a targeting antibacterial agent for efficient eradication of Pseudomonas aeruginosa biofilms.* ACS Applied Materials & Interfaces, 2022. 14(42): p. 47420-47431.
102. Yaacob, S.N., et al., *Lactic acid bacteria and their bacteriocins: new potential weapons in the fight against methicillin-resistant Staphylococcus aureus.* Future Microbiology, 2022. 17(9): p. 683-699.
103. Sharifi-Rad, M., et al., *Echinacea plants as antioxidant and antibacterial agents: From traditional medicine to biotechnological applications.* Phytotherapy Research, 2018. 32(9): p. 1653-1663.
104. Dvorakova, M., et al., *The traditional utilization, biological activity and chemical composition of edible fern species.* Journal of Ethnopharmacology, 2024: p. 117818.
105. Xiao, S., et al., *Identification of essential oils with activity against stationary phase Staphylococcus aureus.* BMC complementary medicine and therapies, 2020. 20: p. 1-10.
106. Azizi, Z., et al., *Protein kinase C involvement in neuroprotective effects of thymol and carvacrol against toxicity induced by Amyloid-β in rat hippocampal neurons.* Basic and Clinical Neuroscience, 2022. 13(3): p. 295.
107. Liu, Y., et al., *Proteomics and transcriptomics explore the effect of mixture of herbal extract on diabetic wound healing process.* Phytomedicine, 2023. 116: p. 154892.
108. Sheikh, M., et al., *Formulation, evaluation and optimization of Antimicrobial potential of herbal cream containing Allium sativum, Moringa oleifera extracts and Thymus vulgaris oil.* Current Pharmaceutical Biotechnology, 2024. 25(3): p. 365-383.
109. Adaszyńska-Skwirzyńska, M., M. Dzięcioł, and D. Szczerbińska, *Lavandula angustifolia essential oils as effective enhancers of fluconazole antifungal activity against Candida albicans.* Molecules, 2023. 28(3): p. 1176.
110. Johnson, S.C. and M. Kaeberlein, *Rapamycin in aging and disease: maximizing efficacy while minimizing side effects.* Oncotarget, 2016. 7(29): p. 44876.
111. Xiong, Y., et al., *The use of Chinese herbal medicines throughout the pregnancy life course and their safety profiles: a population-based cohort study.* American Journal of Obstetrics & Gynecology MFM, 2023. 5(5): p. 100907.
112. Arbab, S., et al., *Comparative study of antimicrobial action of aloe vera and antibiotics against different bacterial isolates from skin infection.* Veterinary medicine and science, 2021. 7(5): p. 2061-2067.
113. Liu, Q., M. Mazhar, and L.S. Miller, *Immune and inflammatory reponses to Staphylococcus aureus skin infections.* Current dermatology reports, 2018. 7: p. 338-349.
114. Alanazi, H.H., et al., *Medicinal Herbs: Promising Immunomodulators for the Treatment of Infectious Diseases.* Molecules, 2023. 28(24): p. 8045.
115. Ventress, J.K., et al., *Peptides from tetraspanin CD9 are potent inhibitors of Staphylococcus aureus adherence to keratinocytes.* PLoS One, 2016. 11(7): p. e0160387.
116. Pérez, C., T. Zúñiga, and C.E. Palavecino, *Photodynamic therapy for treatment of Staphylococcus aureus infections.* Photodiagnosis and Photodynamic Therapy, 2021. 34: p. 102285.
117. Frydman, G.H., et al., *Manuka honey microneedles for enhanced wound healing and the prevention and/or treatment of Methicillin-resistant Staphylococcus aureus (MRSA) surgical site infection.* Scientific reports, 2020. 10(1): p. 13229.
118. Aderemi, F.A. and O.M. Alabi, *Turmeric (Curcuma longa): an alternative to antibiotics in poultry nutrition.* Translational Animal Science, 2023. 7(1): p. txad133.
119. Sharma, S., et al., *Antimicrobial studies on garlic lectin.* Probiotics and Antimicrobial Proteins, 2023. 15(6): p. 1501-1512.
120. Nakamoto, M., et al., *Antimicrobial properties of hydrophobic compounds in garlic: Allicin, vinyldithiin, ajoene and diallyl polysulfides.* Experimental and therapeutic medicine, 2020. 19(2): p. 1550-1553.
121. Kairey, L., et al., *Efficacy and safety of Melaleuca alternifolia (tea tree) oil for human health—A systematic review of randomized controlled trials.* Frontiers in pharmacology, 2023. 14: p. 1116077.
122. Wang, F., et al., *Antibacterial activity of Chinese propolis and its synergy with β-lactams against methicillin-resistant Staphylococcus aureus.* Brazilian Journal of Microbiology, 2022. 53(4): p. 1789-1797.
123. Teow, S.-Y., et al., *Antibacterial action of curcumin against Staphylococcus aureus: a brief review.* Journal of tropical medicine, 2016. 2016.
124. Kamurai, B., M. Mombeshora, and S. Mukanganyama, *Repurposing of drugs for antibacterial activities on selected ESKAPE bacteria Staphylococcus aureus and Pseudomonas aeruginosa.* International Journal of Microbiology, 2020. 2020.
125. Nikolic, P. and P. Mudgil, *The cell wall, cell membrane and virulence factors of Staphylococcus*

aureus and their role in antibiotic resistance. Microorganisms, 2023. 11(2): p. 259.
126. Tabassum, N., et al., *Inhibition of polymicrobial biofilms of Candida albicans–Staphylococcus aureus/Streptococcus mutans by fucoidan–gold nanoparticles.* Marine Drugs, 2023. 21(2): p. 123.
127. Khruengsai, S., T. Sripahco, and P. Pripdeevech, *Antibacterial activity and synergic effects of the essential oils of Amomum verum Blackw and Zanthoxylum limonella (Dennst.) Alston.* Archives of Microbiology, 2023. 205(3): p. 102.
128. Sousa, M.N., et al., *Hydroalcoholic leaf extract of Punica granatum, alone and in combination with calcium hydroxide, is effective against mono-and polymicrobial biofilms of Enterococcus faecalis and Candida albicans.* Antibiotics, 2022. 11(5): p. 584.
129. Falev, D.I., et al., *Comparative study of four Yucca species by 2D-NMR and LC-MS.* Natural Product Research, 2024. 38(3): p. 544-548.
130. Shrestha, A., et al., *Comparison of the polyphenolic profile and antibacterial activity of the leaves, fruits and flowers of Rhododendron ambiguum and Rhododendron cinnabarinum.* BMC Research Notes, 2017. 10: p. 1-11.
131. Han, W. and T.A. Camesano, *LL37-Derived Fragments Improve the Antibacterial Potential of Penicillin G and Ampicillin against Methicillin-Resistant Staphylococcus aureus.* Antibiotics, 2023. 12(9): p. 1398.
132. Kuok, C.-F., et al., *Synergistic antibacterial effects of herbal extracts and antibiotics on methicillin-resistant Staphylococcus aureus: A computational and experimental study.* Experimental Biology and Medicine, 2017. 242(7): p. 731-743.
133. Kim, S.Y., et al., *Antimicrobial effects and resistant regulation of magnolol and honokiol on methicillin-resistant Staphylococcus aureus.* BioMed research international, 2015. 2015.
134. Mangu, J.C.K., et al., *Per-and polyfluoroalkyl substances enhance Staphylococcus aureus pathogenicity and impair host immune response.* Environmental Pollution, 2022. 314: p. 120294.
135. Francis, D., A. Bhairaddy, and A. Joy, *The biofilm proteome of Staphylococcus aureus and its implications for therapeutic interventions to biofilm-associated infections.* Advances in Protein Chemistry and Structural Biology, 2023. 138: p. 327-400.
136. Zhang, T., et al., *Biofilm inhibition in oral pathogens by nanodiamonds.* Biomaterials Science, 2021. 9(15): p. 5127-5135.
137. Syahruni, R., et al., *Morphology, anatomy, and histochemistry of three species of Jatropha: a contribution to plant recognition and selection.* Plant Biology, 2023. 25(6): p. 1009-1021.
138. Seong, E., et al., *Enhancement of bioactive compounds and biological activities of Centella asiatica through ultrasound treatment.* Ultrasonics Sonochemistry, 2023. 94: p. 106353.
139. Kato-Noguchi, H. and M. Kato, *Evolution of the secondary metabolites in invasive plant species Chromolaena odorata for the defense and allelopathic functions.* Plants, 2023. 12(3): p. 521.
140. Gaia, A.M., et al., *Ontogenetic changes in the chemical profiles of Piper species.* Plants, 2021. 10(6): p. 1085.