Review Article

Exploring Guava and Neem Extracts as Therapeutic Options for Methicillin-resistant *Staphylococcus aureus* (MRSA) inAfrica

ABSTRACT

MRSA is a virulent strain of antibiotic-resistant *Staphylococcus aureus* and a Principal cause of disease prevalence and death rates. MRSA's resistance to traditional antibiotics makes it a rather crucial threat to public health. Plants with traditional medicinal uses, including *A. indica* and *P. guajava*, may provide an alternate means of treatment.This review explores the antibacterial capabilities of *Psidium guajava* (guava) and *Azadirachta indica* (neem) against MRSA by evaluating data from multiple investigations carried out in Africa. Study shows that *A. indica* and *P. guajava* extracts may have strong antibacterial action; multiple studies show that they can prevent growth of MRSA and stop formation of biofilms. Despite the extracts' lower efficacy when compared to modern antibiotics, reports suggest that plant extracts could serve as a novel approach to effectively tackle antimicrobial resistance due to their enhanced synergistic efficacy when combined with other extracts. This is all achieved with low toxicity, hence the call for more research to investigate this thoroughly. Moreover, the socio-economic consequences of applying these easily accessible and reasonably priced plant-based remedies in environments with limited resources were determined to be advantageous to Africa. The review highlights the necessity of conducting more thorough clinical trials and standardizing procedures to validate the therapeutic potential of these plants against MRSA.

Keywords: MRSA. herbal plant, Antibacterial activity, *Azadirachta indica,Psidium guajava*

1.0 INTRODUCTION

MRSA, an alarming Gram-positive bacterium closely linked with the emergence of antimicrobial resistance (AMR) was initially identified in 1960. Just before the identification in 1960, Methicillin was

approved and introduced to treat *Staphylococcus aureus* infections that were resistant to penicillin [1] [2]. *Staphylococcus aureus* is responsible for several bacterial infections in the human population and is capable of developing resistance to several antibiotics, posing the world's health at risk while rendering treatment more challenging.S. aureus was reported in 1961 as having developed resistance to recently introduced methicillin in the United Kingdom [3]. One major global health concern that is contributing to the rising prevalence in healthcare and the community is the rise of MRSA. To worsen matters, there are few effective therapeutic options available to treat individuals with MRSA infections. The resistance facilitates MRSA survival and multiplication in the presence of antibiotics, accelerating its explosive growth [4]. The gene responsible for methicillin resistance mecA gene, and has an SCCmec element, was horizontally transmitted to a sensitive *S. aureus* strain, according to epidemiological research [4]. The resistance of re S. aureus to methicillin is caused by expression of penicillin-binding protein 2a (PBP2a), which makes it resistant to β-lactam drugs like methicillin. Bacteriophages allow S. aureus organisms to exchange this kind of resistance. This is among the rare instances of chromosome-mediated medication resistance by phage transduction that have medicinal significance [5] It is very important that surveillance is accurate and reliable because major economic and societal costs, as well as increase in death rate, have been linked to MRSA [6].

The production of protective biofilms by *S. aureus* and constant change in resistance mechanisms has made treatment of MRSA infections become difficult. All these distinct resistance mechanisms work together to render conventional treatment modalities ineffective [7]. Researchers are now driven to concentrate on novel antimicrobial therapeutics that are different from conventional antibiotics since the problem of antibiotic resistance is increasing due to the delay in the discovery of new antibiotics [8].

Medicines from plants prove to be better antimicrobial agents even though their antibacterial activity is milder than conventional antibiotics [9]. Historically, therapeutic compounds for various kinds of illnesses have been derived from plants. It has been discovered that several kinds of leaves, stems, and their extracts have antimicrobial and antioxidant properties [10]. Many medicinal plants contain bioactive compounds such as tannins, terpenoids, alkaloids, steroids, coumarins, and flavonoids that have been proven to have antimicrobial properties in vitro, These compounds make them effective in the treatment of infectious diseases [11]. Over 20,000 plant species have been identified by the World Health Organization (WHO) for their medicinal properties. Because of these plants' accessibility, affordability, demonstrated specificity, biodegradability, low toxicity, and minimal residual toxicity, their use is becoming feasible and gaining attention. These characteristics make them a preferred option for use.

Psidium guajava (guava) and *Azadirachta indica* (neem) are the primary focus of this study because of their antimicrobial qualities, ease of growth, maintenance, and quick environmental adaptation.The neem and guava plant extract has been reported to have potential antimicrobial effect[12]. This review will eventually provide in-depth information about these plants.Due to the global threat posed by Methicillin *Staphylococcus aureus*, this review aims to present the antibacterial activity of some African indigenous medicinal plants (*Psidium guajava* and *Azadirachta indica*) and the effects of their active ingredients on MRSA using available evidence to determine their viability as alternative or complementary therapies in the fight against antibiotic-resistant infection.

2.0 PREVALENCE AND INCIDENCE OF MRSA

2.1 Overview of Tropical and Systemic Infections Caused by MRSA in Africa

MRSA is a global health threat, causing a spectrum of illnesses from minor skin infections to severe septicemia [13]. MRSA infections are a primary cause of hospital-acquired infections, often leading to extended hospitalizations, increased mortality rates, and severe health complications. Children, elderly and immunocompromised individuals (including those with genetic factors affecting their body's immune system activation), people with long-term diseases like diabetes, hepatitis, or HIV, and residents of developed countries are more likely to carry *S. aureus*. [14-16]. Individuals with a history of extended hospital stays, intensive care unit treatment, or recent hospitalizations, especially those who used antibiotics in recent times, are more susceptible to MRSA infections.

A systematic review conducted in 2014 [17] found MRSA prevalence rates varied across African and Middle Eastern countries. The Arabian Peninsula had the highest rates (66.4%), followed by North Africa (48.6%), Middle East (47.5%), sub-Saharan and central Africa (40.4%), and South Africa (24.4%).

2.1.1 Common infections associated with MRSA

MRSA infections are grouped as either community associated (CA-MRSA), hospital associated (HA-MRSA) and Livestock associated (LA-MRSA) [18]. MRSA can lead to infections in various organs, with the skin and under-skin tissues being the most common. It could cause severe infections such as bone infections (osteomyelitis), brain infections (meningitis), lung infections (pneumonia, lung abscess), and pus-filled lung infections (empyema).

2.1.1.1 Skin and soft tissue infections (SSTI): Community-acquired MRSA (CA-MRSA) is the primary bacterial culprit behind skin and soft tissue infections(SSTIs) such as diabetic foot ulcers, cellulitis and necrotizing fasciitis. This often leads to multi- drug resistant infections, resulting in recurrent infections, increased hospitalizations, and higher mortality rates[19,20]. Africa carries a disproportionately high burden of SSTIs, as evidenced by the fact that these infections drive 16.2% of all adult inpatient antibiotic prescriptions for systemic use, a percentage unmatched anywhere else in the world [21,22]. Between 2015 and 2016, global epidemic monitoring found the rate of MRSA in Africa as 60.1% [23] .

2.1.1.2 Bone infection: MRSA are the primary pathogens responsible for Osteomyelitis (infection of the bone) and Septic arthritis (infection of the joint) [18].

2.1.1.3 Pneumonia: In the wake of rampant antibiotic prescription and use, pneumonia caused by *Staphylococcus aureus* has become less aggressive and is not always linked to influenza. However, it remains a severe condition associated with other factors that increase the risk of *S. aureus* infections, resulting in a mortality rate of 30-40%. Notably, community-acquired MRSA (CA-MRSA) can cause a particularly dangerous case of pneumonia called necrotizing pneumonia. [18]. Other MRSA infections include Bacteremia and Endocarditis.

2.1.2 Current treatments available for MRSA

Several factors influence the antibiotic treatment selected for MRSA infections, including the specific type of infection, the local prevalence of antibiotic-resistant *S. aureus* strains, drug availability, potential side effects, and the patient's overall health.

Vancomycin is regarded as one of the only remaining therapeutic options for MRSA infections; a study showed that MRSA isolates from nasal swabs were 86.67% susceptible to Vancomycin [24].

Ceftobiprole treats infections caused by diverse bacteria encompassing Gram-positive and Gram-negative organisms. Notably, it can treat MRSA infections due to its ability to target specific bacterial proteins (penicillin-binding proteins or PBPs) that other antibiotics cannot. Laboratory studies show that ceftobiprole is highly effective against nearly all MRSA strains tested. However, strains with very high levels of resistance (MIC values of 4 mg/L or higher) can develop resistance to CEF [25,26]. For most uncomplicated cutaneous infections potentially caused by MRSA, initial treatment often involves oral antibiotics such as minocycline, trimethoprim-sulfamethoxazole, doxycycline, or clindamycin [26].

Vancomycin has been the standard treatment for MRSA infections. However, the emergence of S. aureus strains with diminishing susceptibility to the antibiotic has curtailed its effectiveness [27], drastically reducing therapeutic options for infections caused by MRSA to a limited number of costly drugs [28]. Teicoplanin, daptomycin, and linezolid are some expensive viable alternatives whose high cost pose significant challenges in clinical practice [29]. Recent studies have shown that many plant extracts possess antibacterial properties effective against MRSA. This suggests that these plants could be a potential source of new treatments for this challenging infection [28].

2.2 Resistance Patterns; Overview of Antimicrobial Resistance Trends in Africa

The gradual increase in MRSA cases, particularly within hospital settings, facilitated the identification of patients likely to experience treatment complications [30].

MRSA prevalence rates in Africa vary widely [31], with the epidemiological landscape showing a diverse range of clonal types across different geographic locations. A comprehensive analysis of MRSA strains across Africa identified dominant "pandemic" clones, including ST5 and ST239/241, widely distributed throughout the continent. However, some MRSA strains were more geographically restricted, with ST612 prevalent in Southern Africa and ST80 common in Northern Africa. Notably, community-acquired MRSA strains (ST8 and ST88) were found in both hospital and social environments [32].

With recognition of the inconsistency of data surveillance systems in various African communities; A 2024 study found lower MRSA prevalence rates in clinical infections such as wounds, skin, soft tissues, and surgical site in Western Africa (23%, confidence interval 9-41%; six studies) in relation to Eastern Africa (58%, confidence interval 41-73%; 23 studies) [21].

MRSA prevalence in Africa varies significantly, ranging from 12% to 80% across nine countries studied. East African nations have reported particularly high rates. For instance, Uganda has recorded MRSA rates between 31.5% and 42% among patients and healthcare workers [33], while Rwanda's prevalence falls between 31% and 82% [34]. Research reports from Tanzania have shown MRSA rates ranging from 10% to 50% [35.36].

Table 1: MRSA Prevalence in African Countries

Reference	Location	Research Period	Sample type	%MRSA

[37]	Algeria	2015-2016	nasal swab from animals	5.08
[38]	Algeria	2014-2015	raw milk (cow)	15.9
[39]	Benin	2019-2020	clinical samples	42.7
[40]	Burkina faso	2016	nasal swab	3.9
[41]	Cameroon	2019	nasal swab	45.4
[42]	DR Congo	2013-2014	clinical samples	29.6
[43]	Ghana	2010-2013	clinical samples	100
[44]	Ghana	2014-2015	nasal swab	0.2
[45]	Kenya	NR	clinical samples	34.4
[46]	Nigeria	NR	nasal swab	16.5
[46]	Nigeria	NR	nasal swab	16.5
[47]	Nigeria	2014-2015	nasal swab; wound swab	15.8
[32]	South Africa	2015-2017	blood samples	27.1
[48]	Rwanda	2013-2014	clinical samples	28.3
[49]	South Africa	2010-2017	blood culture	34.6

[50]	Tanzania	2015	raw milk	0.6

2.3 Economic Burden of MRSA on Healthcare systems and communities

African healthcare systems face significant challenges, including underfunding, insufficient infrastructure, equipment shortages, limited medication supplies, and a dearth of qualified healthcare professionals due in part to emigration to developed countries. MRSA has spread globally, affecting countries across Africa such as Nigeria, Cameroon, Tanzania, Eritrea, Senegal, Ethiopia, and Madagascar. Many MRSA infections occur within hospitals and disproportionately affect individuals with HIV/AIDS, other chronic illnesses like diabetes, and healthcare workers themselves [51].

MRSA infections can significantly increase the length of hospital stays and direct medical costs.The cost of implementing preventive measures can also vary depending on the specific interventions used.

3.0*Azadirachta indica* AND *Psidium guajava L.*

3.1 *Azadirachta indica*

Azadirachta indica, a large tropical evergreen tree, is known to be a traditional remedy for several ailments in humans and has been recognized for its extensive antimicrobial activities [52]. It is one of the medicinal herbs with a range of therapeutic properties, including antibacterial [53], antiviral [54], anticancer, antioxidant, antiulcer [55], hepatoprotective [56] and wound healing effects. Neem exhibits broad spectrum antibacterial activity. Presently,It offers products such as tea, oils, pills, powders, and other kinds of creams and lotions. There are therapeutic properties in every component of the neem tree. Alkaloids, oils, fluoride, tannins, saponins, calcium, sterols, and flavonoids are abundant in its twigs. Its seeds are an excellent source of proteins and fatty acids[57]

3.1.1 Methods of extraction Phytochemicals present and Mechanism of Action of *Azadirachta indica* on MRSA

To maximize the extract yield, the most efficient solvent needs to be investigated.Soxhlet and immersion techniques are suitable methods that give higher neem extract [58]. It is generally preferable to extract neem oil using a solvent-based soxhlet extraction technique. This is due to the very high oil yield and less turbid oil obtained from mechanical pressing [59].

Different active components can be extracted using different extraction mediums such as water, ethanol, methanol, chloroform, hexane, ethyl acetate and ether. The research reported maximum yield using ethanol and minimum yield using distilled water. The leaf and stem bark extracts contained saponins, anthranoids, anthraquinones, alkaloids, phenols, tannins, phlobatannins, and cardiac glycosides and wide range of bioactive substances, including epicatechin, gallic acid, nimonol, nimocinol, nimocinolide, azadirachtin, nimbin, salannin, epoxyazadiradione, etc. Neem contains over 300 different phytochemicals[60].

The bacterial cell membrane is one of the potential targets of novel antibiotics that could prove effective against resistant bacteria [61]. *Azadirachtaindica* damages and lyses the cell membrane of MRSA.Nimbolide, a compound found in neem (Azadirachta indica), effectively targets bacteria within cells, disrupts bacterial communities (biofilms), and damages bacterial cell membranes. This makes it a promising candidate for treating severe infections caused by drug-resistant strains of Staphylococcus aureus, such as MRSA. [62]. The study found that exposing Staphylococcus aureus to nimbolide at the lowest concentration needed to kill all bacteria resulted in severe damage to the bacterial cell wall. This damage caused the cells to rupture and burst open. The greater absorption of propidium iodide in the nimbolide-treated S. aureus cells was the cause of the permeability barrier breakdown and cell membrane structure in microbial membrane structures. Nimbolidide clearly damages the cytoplasmic membranes of bacteria [62].

3.2 Review of *Psidium guajava* L.

Guava (Psidium guajava L.), which is mostly grown in tropical and subtropical locations throughout many countries, possesses antibacterial properties.Several phytochemical components have been considered to be responsible for the antimicrobial properties of guava extracts [63,64]. The leaves, fruits, bark/stems, and roots are parts of guava plant used for medicinal purposes [65]. The distinct bioactive qualities of guava are attributed to the distinct compositions of its leaves, fruits, barks/stems, and roots. Guava leaves have long been used as a remedy for numerous ailments which as a result of the phenolics and flavonoids produced by guava.In particular, guava leaves and bark have been utilized for many years across different countries [66].

3.2.1 Methods of extraction, phytochemicals present and mechanism of action of *Psidium guajava* L. on Methicillin-resistant *Staphylococcus aureus*

A variety of solvents, including ethanol, water, methanol, dimethyl sulfoxide, ethyl acetate, and hexane, can be employed to extract phytochemicals from guava leaves. A particular study utilized four solvents with escalating polarity—hexane,methanol, ethanol, and water—to extract compounds from guava leaves. The results of the antibacterial assay showed that the guava leaf extracts in methanol and ethanol had inhibitory activity against gram-positive bacteria. [67].

The phytochemicals present in the extracts of guava leaf are rich in a wide range of polyphenols. According to a study, guava leaves are high in tannins, phenols, and flavonoids while they are relatively low in alkaloids, triterpenes, saponins, and flavonoids. Given the potent antibacterial effects of polyphenols, it is likely that guava leaves' abundance in phenols, flavonoids, and tannins are the probable cause of their antimicrobial qualities. The antimicrobial activity of the studied extract was due to its greater content of total phenolics. [68] The plant's various parts each contain a different bioactive component. Phenols, terpenes, tannins, alkaloids, and flavonoids are all found in the leaves and stems. However,phenols, terpenes, and flavonoids are absent from the fruits [65]. The concentration of the tannin in guava leaves influences the effectiveness of antibacterial compounds present in the leaves. The higher levels of tannin antibacterial activity will increase [68].

The production of phytochemicals by guava plants offers defense against disease invasion, including bacteria, fungus, and viruses. By mechanism, when a pathogen invades, a supply of nutrients and amino acids will be used up to produce the phytochemicals needed to defend against the disease from the outside[65]. There is more and enough resources on the efficacy of *Psidium guajava* on Methicillin-resistant *Staphylococcus aureus* but limited work on the mechanism

Plant-derived chemicals typically combat antibiotic-resistant bacteria using various strategies. These include weakening the bacteria's protective outer layer, preventing the bacteria from expelling antibiotics, altering the bacteria's target sites for antibiotics, inactivating bacterial enzymes, and modifying the bacteria's enzyme function 69].

4.0 EFFICACY STUDIES OF *Azadirachta indica* AND *Psidium guajava L.*

4.1 Summary of evidence of *Azadirachta indica* antimicrobial activity.

In vivo experiments are often carried out to better imitate infections that occur in humans. One of such experiments was done by administering drug from neem extracts orally or gastrically in mice, rats, guinea pigs, and rabbits, as well as intraperitoneal or intravenous injection. A full examination of this subject can be found in [70], where the published animal trials revealed that the level of neem toxicity was highly dependent on the plant part used and extraction solvent, and the treatment method and type used. To elaborate, it showed that mice did not die when given an ethanolic neem leaf extract orally at a dose of less than 2000 mg/kg body weight [71]. On the other hand, rats administered 50–200 mg/kg of an ethanolic extract of neem stem bark experienced changes in biochemical indicators of toxicity, which could potentially impact organ function [72]. On the other hand, a small human trial found no discernible effects on blood parameters indicating organ toxicity when adults with gastric hypersecretion and gastro-oesophageal or gastroduodenal ulcers took lyophilised powdered aqueous neem bark extract twice daily for 10 weeks [55]. Furthermore, 156 adults and 110 children who applied 1% neem oil externally for a year did not exhibit any notable side effects [73]. It's interesting to note that [74] discovered that neem leaf and seed extracts prepared with alcohol (ethanol) were more toxic than those extracted with water. Despite the fact that these results validate neem's antibacterial qualities, more investigation is required to establish the lowest inhibitory concentration of extracts in order to avoid overly harmful effects.

4.1.1 Determination of the antimicrobial efficacy of *Azadirachta indica extracts* against MRSA

A 2019 study investigated the antibacterial effectiveness of ethanolic extracts from the leaves of green tea (*Camellia sinensis*) and neem (*Azadirachta indica*) against MRSA and Shiga toxin-producing *E. coli* (STEC) [75]. A highly concentrated alcohol solution (99% ethanol) was first used to extract compounds from the leaves and then diluted with a less concentrated alcohol solution (50% ethanol) for testing. The antibacterial potency of these extracts was evaluated by measuring the zone diameter of inhibition (ZDI) and determining the lowest concentration needed to prevent bacterial growth (minimum inhibitory concentration) using broth microdilution and disc diffusion methods. The lowest concentration required to kill bacteria (minimum bactericidal concentration) was also determined using nutrient agar plates.

The results showed that green tea exhibited the highest ZDI against MRSA at 7.5 mm, while neem had the lowest at 4.9 mm. For STEC, green tea and a green tea-neem combination produced the highest ZDI of 4.5 mm. The MIC values for neem were 125 mg/ml against MRSA and 31.25 mg/ml against STEC, while green tea extract showed MIC values of 15.625 mg/ml and 31.25 mg/ml for MRSA and STEC, respectively. The combined extract had an MIC of 46.87 mg/ml for both bacteria. Green tea also had the lowest MBC values, 31.25 mg/ml for MRSA and 62.5 mg/ml for STEC, whereas neem's MBC values were higher, exceeding 250 mg/ml and 500 mg/ml for STEC, and 93.75 mg/ml and 375 mg/ml for MRSA [76]. The findings suggest that neem and green tea leaves possess significant antibacterial properties, which could be further explored for developing new antimicrobial agents against STEC and MRSA.

4.2 Summary of Evidence of *Psidium guajava L.* Antimicrobial Activity.

In the case of *Psidium guajava L.,* their extracts from research have shown they have strong antibacterial properties that can stop *S. aureus* from growing. *P. guajava* methanolic extracts from plant leaves and bark have the ability to inhibit *Salmonella* and *Bacillus* bacteria because it contains active flavonoid components [77]. It also has anti-plaque properties. It is possible to separate the flavonoid components and their derivatives from the guava and apply them in stopping the growth of certain bacteria at various dilutions. The plant's leaf aqueous extract contains pinene and terpinene, which have antibacterial properties. Owing to its bacteriostatic properties towards harmful germs, it is also utilized as a medication for cough, diarrhea, mouth ulcer and some wounds with swollen gum [78]. While methanol extract exhibits high MIC, water-based and alcohol-based demonstrate limited antibacterial activity. The most effective extract is methanolic due to its high activity. Given that it exhibits efficacy against haemolysis, this extract also demonstrates antihemolytic potential. Guava strongly inhibits the growth of gram-positive bacteria and moderately, gram-negative bacterial pathogens. They are also known to have antiviral properties; able to manage viral infections like influenza [79]. The viral resistance can be occupied and held by them. The guava extract's capacity to degrade proteins is what actually gives guava their antiviral properties. Additionally guava has antioxidant and anticancer properties as well. The peels, seeds, and pulp of guavas contain a variety of chemicals, including cyanidin 3-glucoside, kaempferol, and gallic acid [80]. However, it is unexpected that the seeds and skin contain more of these substances than the pulp. Guava becomes quite important as a food because of these chemicals. It is abundantly evident that guava leaf extracts, both aqueous and methanolic, may create an amazing zone of inhibition by preventing bacterial growth. When the antifungal activity of the ethanol extract is at its lowest, the extracts in methanol and water have the highest MIC [76]. In conclusion, guava leaves, seeds, skin, and pulp all have remarkably strong antimicrobial properties.

4.2.1 Determination of the antimicrobial efficacy of *Psidium guajava L.* against MRSA

MRSA is a well-known pathogen due to its resistance to conventional antibiotics. Research has shown promising results for the effectiveness of guava and neem oil against MRSA. A 2012 study explored the antibacterial properties of both aqueous and methanolic extracts from the stem bark of *Psidium guajava* against eight MRSA strains [81]. The plant material underwent standard extraction and phytochemical analysis, followed by testing the extracts' antibacterial effectiveness using agar diffusion and agar dilution methods. The study revealed that *Psidium guajava* contains key phytochemicals like proteins, carbohydrates, glycosides, and tannins. Both the methanolic and aqueous stem bark extracts demonstrated antibacterial activity against MRSA, with methanol extracts showing minimum inhibitory concentrations (MIC) between 62.5 and 250 µg/ml, and aqueous extracts with MICs and MBCs ranging from 125 to 500 µg/ml.

A recent study conducted in Ugbokolo, Nigeria, in 2022 investigated the chemical composition and antibacterial properties of extracts from guava leaves and stem bark. These extracts, prepared using alcohol (methanol) and water, were tested against common bacteria such as *E. coli*, *Salmonella typhi, S. aureus, and Proteus sp.* [82]. Conducted from July to December 2019, this study involved phytochemical screening using standard laboratory techniques, followed by column chromatography to refine the extracts. The bacterial isolates were identified using various microbiological and biochemical methods, and their susceptibility to the extracts was tested using agar well diffusion and broth dilution methods. The study confirmed the presence of bioactive compounds like tannins, flavonoids, phenols, and saponins, and found significant differences ($P < 0.05$) in the antibacterial sensitivity of the isolates to the different extracts. Notably, *Staphylococcus aureus* was most sensitive to the stem bark extract at 200 mg/ml concentration, while *Proteus sp.* was the least sensitive. The study concluded that *Psidium guajava* extracts, particularly the methanolic extract of the stem bark, showed significant antibacterial activity, suggesting potential advantages over the tested bacteria and the need for further research.

4.3 Comparison of the Efficacy of *Psidium guajava* and*Azadirachta indica* with Conventional Antibiotics on MRSA

Currently, seven antibiotics are commonly used to treat MRSA: vancomycin, diphospicine, linezolid, trimethoprim and sulfamethoxazole (TMP-SMZ), quinupristin-dalfopristin, clindamycin, and tigecycline. However, MRSA strains are increasingly developing resistance to these drugs, reducing their overall effectiveness. As a result, there are limited treatment options available for infections caused by MRSA and *S. aureus* strains that show decreasing sensitivity to vancomycin [83]. This situation underscores the urgent need for new medications capable of effectively treating *S. aureus*, particularly as the pathogen becomes resistant to multiple drugs.

Vancomycin works by disrupting the construction of the bacterial cell wall. It attaches to a specific part of the cell wall building blocks (D-alanyl-D-alanine terminus of cell wall precursors) preventing them from linking together and forming a stable wall. This ultimately leads to the bacteria's death. This inhibition causes an accumulation of UDP-linked MurNAc-pentapeptide precursors within the bacterial cell [84]. The effectiveness of vancomycin relies on multiple hydrogen bonds formed between its peptide components and the D-Ala-D-Ala residues in the cell wall. Any factor that interferes with vancomycin's ability to bind to these residues will reduce its efficacy.

The widespread use of vancomycin to treat MRSA has led to the development of vancomycin-intermediate and vancomycin-resistant *S. aureus* strains, known as VISA and VRSA, respectively. The ability of *S. aureus* to cause potentially fatal infections both in hospitals and in the community has raised significant concern within the medical field. Globally, three types of vancomycin-resistant *S. aureus* have emerged: vancomycin-intermediate *S. aureus* (VISA), heterogeneous vancomycin-intermediate *S. aureus* (hVISA), and vancomycin-resistant *S. aureus* (VRSA) [85].

A 2017 study [86] compared the antibacterial efficacy of *Azadirachta indica* (neem) and *Psidium guajava* extracts against MRSA and vancomycin-resistant *S. aureus* (VRSA), in relation to traditional antibiotics. The MRSA and VRSA strains were obtained from a tertiary hospital in Nigeria, and their susceptibility to plant extracts and common antibiotics was assessed using standard microbiological methods. The study found that both neem and guava extracts displayed some antibacterial activity against MRSA and VRSA at concentrations of 100 mg/ml and 50 mg/ml, though the standard antibiotics were more effective. These results highlight the potential of *A. indica* and *P. guajava* extracts in combating drug-resistant bacteria, while also emphasizing the ongoing need for the discovery of new antibacterial compounds from plants.

5. RECOMMENDATIONS AND CONCLUSION

There is a pressing need for more research on plant-derived antimicrobials today. Numerous synthetic drugs currently available induce a range of side effects. Consequently, developing plant-based compounds could be useful in fulfilling the need for new drugs with fewer side effects. This review investigated the potential of Neem and Guava extracts as therapeutic treatments for MRSA infections. In the course of this review, it was discovered that the exact mechanism of actions of these plants remain unexplored but their efficacy is widely researched. Also, there is suggested inconsistency in the quality of extract (antibacterial chemicals) obtained from these plants based on the location they were grown, the specific part of the plant the extract was recovered from (leaf, bark) and the kind of solvent used for the extraction process. To this effect, more investigation should be done on the optimum conditions (soil, weather) required to obtain the antibacterial chemicals present in these extracts at their full range of activity [87].

Furthermore, lack of clinical trials for drugs based on these extracts make it difficult for the adoption of these extracts as alternatives to synthetic antibiotics. Also with the resilience and availability of these plants, their extracts may prove to be cheaper alternatives which can be easily sustained by Africa in its fight against MRSA. Research on the in vitro antibacterial evaluation of particular plants, however, lays the groundwork for upcoming phytochemical and pharmacological studies targeted at discovering new antibacterial drugs to counteract antibiotic resistance.

In conclusion, extracts from guava and neem show great promise as alternative treatments for the fight against antibiotic resistance. With their broad-spectrum activity, lower susceptibility to resistance, and synergistic interactions with traditional antibiotics, they have the potential to improve upon the antimicrobial techniques currently in use.

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