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THE ROLE OF MEDICINAL PLANTS IN THE RACE AGAINST ANTIMICROBIAL RESISTANCE IN NIGERIA.

Adelegan, Ayokunmi Joseph[1]; Chukundah, Uchechi Doris, Ph.D ; Kolawole, Alex Ayodele[1]
[1]Department of Microbiology, Federal university, Otuoke, Bayelsa State.

ABSTRACT
Antimicrobial resistance to human pathogens has proven to be a hurdle for clinicians in Nigeria. This review article was aimed at examining the role of medicinal plants in the race against antimicrobial resistance in Nigeria. This study was undertaken using a qualitative design approach. The search for qualitative and qualitative studies concentrated on the phytochemical constituents of medicinal plants, and evidence of their antimicrobial activity in published in reputable journals. The results of this study shows different medicinal plants have been used for their antimicrobial properties such as Zigiber officinale, Caspicum Chinese, and Vernonia amygdalina. These plants contain phytochemicals such as; glycosides, alkaloids, lignans, lignins, phenolic compounds, cyanogenic compounds, flavonoids, tannins, and saponins. The presence of these bioactive compounds in plants form the basis for their bioactive compounds. The antimicrobial activity of medicinal plants used in the various studies synthesized were determined using the disk diffusion methods and the broth dilution method. Zigiber officinale, Caspicum Chinese, and Vernonia amygdalina have been shown to exhibit antimicrobial activity against; Staphylococcus aureus, Klebsiella pneumonia, Escherichia coli, and Pseudomonas aeruginosa, Aeromonas hydrophila, Salmonella typhi, and Candida albicans. These findings suggest that these medicinal plants can serve as effective alternatives to synthetic drugs, and can help reduce the healthcare burden associated with drug resistance pathogens. Therefore, the search for more medicinal plants, and their application should be promoted globally. .

INTRODUCTION

The use of medicinal plants dates back to the medieval era. It served as a reliable source of medicine for curing ailments of various kinds. The use of medicinal plants down to this day is pivotal in the success of the primary health care systems in most nations. Lee *et al.,* (2007) stated that over 25% of the total prescribed drugs globally, and the ones found in modern pharmacopeias originate from plants. More so, about 121 active plant compounds are in use currently. In fact, the World Health Organization (WHO) has asserted that 11% of the 252 essential and basic drugs used globally are sorely from plant sources (Lee *et al.,* 2007).

Olgica*et al.*, (2012) reaffirmed that plant active ingredients/substances are the source of almost one-quarter of the total synthetic drugs such as; quinine which is used as an antimalarial agent. Estimates reveal that over 60% of the anti-infectious and anti-tumor drugs that are in the market already or under the clinical trial phase are from plant sources (Olgica*et al.,* 2012).

The medicinal properties of plants are based on the chemical constituents they contain. Plants exhibit anti-oxidant properties, anti-tumor, antimicrobial, and antipyretic properties due to the presence of the plants' phytochemicals, also known as secondary metabolites(Lee *et al.,* 2007).

Currently, we are witnessing the rekindling of interest in the application of medicinal plants due to various reasons such as; reduced efficiency of commonly used antibiotics, severe side effects from synthetic drugs due to abuse and incorrect intake, and difficulty in assessing synthetic drugs in some parts of the world, especially in developing countries. In contrast, medicinal plants are available in almost all parts of the world and are safer to use when compared to synthetic drugs (Nikaido, 2009).

One of the biggest problems with employing synthetic antimicrobial medications is without a doubt the problem of antibiotic resistance. The necessity to find new antimicrobial agents has grown over time due to the growth in microorganism resistance to many commercially produced synthetic antimicrobial agents. (Kraus, 2008). The demand for alternative antimicrobial agents has sparked

interest in researching plant extracts with proven therapeutic properties for use in the production of herbal antimicrobials by pharmaceutical companies. The hunt for novel raw materials to employ in creating new antimicrobial agents to counter the harmful microorganisms' rising resistance has resulted from this.Pharmaceutical companies have long utilized extracts from medicinal plants in the production of herbal antibacterial agents. However, over time, some pathogens have developed resistance to some of the herbal antimicrobials that are commercially produced. This has made it necessary to enhance the antibacterial properties of both synthetic/conventional antimicrobial agents and commercially generated herbal antimicrobial agents. Evaluation of the interaction between herbal extracts and commercially available antimicrobial agents and the creation of concoctions from herbal extracts as a means of creating novel and more effective antimicrobial agents (Sommer andDantas, 2011).
It is becoming more and more popular to use medicinal plant extracts with therapeutic properties in the creation of antibacterial agents. This is because there is a need to expand the pool of currently accessible, commercially produced antibacterial agents. Additionally, other components of the same medicinal plants have been employed to create antimicrobial medicines with varying antimicrobial efficacy against pathogenic microbes. (Sommer andDantas, 2011). This review will outline the use of antibiotics as a solution to microbial infections. Emphasis will be placed on medicinal plants and their phytochemical constituents. We will also review a few medicinal plants in relation to their antimicrobial activities. Methods of screening medicinal plants and assessing their antimicrobial potency will also be discussed.

Medicinal plants
Throughout human history, there has been extensive usage of medicinal plants (Lichterman, 2004). In non-industrialized communities, the use of medicinal plants to heal illnesses is almost universal and frequently less expensive than using pricey conventional medications (Fabricant and Farnsworth, 2001). According to estimates from the World Health Organization (WHO), primary healthcare is provided in some way by herbal medicine for 80% of the world's population, particularly in Asian and African nations. Eighty percent of the more than 120 active chemicals already extracted from higher plants are employed in modern medicine and show a favorable link with the traditional uses of the plants from whence they were derived. (Fabricant and Farnsworth, 2001).

Phytochemicals in medicinal plants
Secondary plant metabolites known as phytochemicals have drawn a lot of attention as possible sources for medicines. (Krishnaraju, 2005). Plants can produce and store a wide range of phytochemicals, including glycosides, alkaloids, lignans, lignins, phenolic compounds, cyanogenic compounds, flavonoids, tannins, and saponins. (Okwu, 2004). Plants also possess strong antibacterial properties since they contain phenolic chemicals and essential oils (Aboaba andEfuwape, 2001). Alkaloids, tannins, flavonoids, and phenolic compounds are the most bioactive components of medicinal plants. Medicinal plants have been known to produce a variety of phytochemicals with a known antibacterial activity that belongs to chemical structural classes: terpenoids, phenolic, alkaloids, lectins, polypeptides, and polyacetylenes (Afolayan, 2003).
Higher plants are a possible source of novel antibiotic prototypes (Afolayan, 2003). Studies have found a number of chemicals in medicinal plants that are potent antibiotics (Afolayan, 2003). Traditional treatments that are frequently used have already yielded substances that are efficient against bacterial strains that are resistant to antibiotics (Kone *et al.*, 2004).
Tannins
Astringent plant material known as tannin can be found in a variety of plant parts, including leaves, fruits, seeds, roots, and bark (Ramakrishnan, 2006). They are water-soluble phenolic compounds that naturally occur in plants and have larger molecular weights of 500–3000. They also contain

phenolic hydroxyl groups, which enable them to cross-link with various proteins and macromolecules in an efficient manner (Ramakrishnan, 2006).
The majority of plants contain tannins, which are hypothesized to serve as chemical defenses against infections and herbivores (Gedir*et al.,* 2005). They have mostly been utilized commercially to preserve leather by creating glue stains and mordants (Kanth*et al.,* 2009). It has also been applied in various concentrations in the pickling process for vegetables to confer a measure of protection against yeasts, molds, and bacteria (Andrade *et al.,* 2005).
Tannins' antimicrobial activity has been investigated in a number of medical sectors with promising results for their antioxidant, anticarcinogenic, and antimutagenic qualities. Tannins have been used to stop a variety of fungi, yeasts, bacteria, and viruses from growing. Studies have demonstrated that tannins have antimicrobial properties (Akiyama *et al.,* 2001). Vegetable tannins contain certain bioactive tannins that have been discovered to be hazardous to microbes, including catechin and pyrogallol (Akiyama *et al.,* 2001). Tannins have been discovered to be highly valuable as a cytotoxic and antitumor agent in addition to being effective against pathogenic microorganisms (Josh *et al.,* 2013).

Flavonoids
Flavonoids, also known as bioflavonoids, are secondary metabolites of plants with a 15-carbon skeleton, two phenyl rings, and one heterocyclic ring. According to their chemical makeup, about 500 families of flavonoids from diverse plants have been identified (Ververidis*et al.,* 2007). Anthocyanidin, flavans, flavanols, flavanones, and anthoxanthins are the typical subgroups (Zhao *et al.,* 2012). They are responsible for the coloring of flowers, the filtering of UV rays in higher plants, and symbiotic nitrogen fixation in plants (Galoetti*et al.,* 2008). Additionally, they are known to have inhibitory effects on plant disease-causing pathogens like Fusarium oxysporum (Galoetti*et al.,* 2008).
Flavonoids are recognized to have antibacterial properties that are effective against bacterial, fungal, and viral pathogens. They are typically recognized for their antibacterial action, which interferes with the cytoplasmic membrane's ability to function properly, the production of nucleic acids, and the process of metabolizing energy (Cushnie and Lamb, 2005). It has been discovered that several medicinal plants' flavonoids prevent the synthesis of nucleic acids, increase the permeability of the inner bacterial membrane, and reduce the membrane potential of both Gram-positive and Gram-negative bacteria (Cushnie and Lamb, 2005). Flavonoids have been revealed to include certain bioactive constituents that have antifungal, antibacterial, and insecticidal properties (Abdel *et al.,* 2013).
Numerous in vitro and in vivo investigations conducted in the past have demonstrated that when combined with antibiotics, they exhibit synergistic effect and reduce many harmful bacteria (Cushnie and Lamb, 2011; Manner *et al.,* 2013). Additional in vivo investigations have demonstrated the potential of flavonoids as pharmaceutical treatments for bacterial illnesses or as a means of infection prevention through food intake (Zamora *et al.,* 2012).

Alkaloids
They are a class of nitrogen-containing natural substances with either neutral or mildly acidic characteristics. They may also occasionally contain oxygen, sulfur, and less frequently, other substances like phosphorus, chlorine, and bromine (Schardl*et al.,* 2007). Although mostly created by plants, they can also be made by a wide range of other species, such as bacteria, fungi, and mammals (Kittakoop*et al.,* 2014). They don't dissolve well in water but do in organic solvents (Shi *et al.,* 2104). They are categorized into five main classes, including cyclopeptide and peptide, pseudo-alkaloids and alkaloids, polyamine alkaloids and proto-alkaloids (Faulkner *et al.,* 2006). Asthma, malaria, analgesic, antiamyhyrithic, anti-cancer, and vasodilatory properties are only a few of the pharmacological effects they have (Cushnie and Lamb, 2014). Some alkaloids have been utilized in entheogenic rituals and as recreational drugs because they have psychotropic and

stimulating properties (Blankenship *et al.,* 2005). With regard to bacterial pathogens like *Staphylococcus aureus, Klebsiella pneumonia, Escherichia coli,* and *Pseudomonas aeruginosa*, alkaloids exhibit strong antibacterial action (Maatalah*et al.,* 2012).
It has been discovered that certain of the bioactive elements of alkaloids, including morphine and cordine, are effective against trypanosomes and plasmodia in addition to bacteria and fungi (Maatalah*et al.,* 2012). In the small intestines, where they have the capacity to intercalate with microbial genetic material.Certain of the alkaloids included in dietary food components have also been discovered to possess microbiocidal and antidiarrheal effects (Maatalah*et al.,* 2012; Garba andOkeniyi, 2012).

Saponins
Because they contain lipophilic triterpene and one or more hydrophilic glycoside moieties, they are a class of chemical compounds found in a range of plant species and are referred to as amphipathic glycosides. In plants, saponins are recognized to provide defense against bacteria and fungi. Saponins have been used as a component in numerous commercial therapeutic claims for natural goods that assist people or other living things (Skene and Phillip, 2006). Saponin is another naturally occurring antimicrobial element of plant defense mechanisms, some of which are beneficial rather than harmful to animals (Rupasighe*et al.,* 2003; Hubert et al., 2005).
There is proof that oral traditional medicine preparations containing saponins are likely to result in terpenoid glycoside hydrolysis (Asl*et al.,* 2008). Studies have shown that extracts from medicinal plants rich in saponins are effective against a range of bacteria, including; *Aeromonas hydrophila, Salmonella typhi, Escherichia coli,* and *Candida albicans* (Deshpande *et al.,* 2013). The main factor causing saponins' antibacterial action is their ability to lyse bacterial membranes rather than the surface tension of the extracellular medium (Asl, 2008). In addition to their antibacterial properties, saponins have shown biological properties, the most notable of which are their lethal effects on malignant or tumor cells (Yokosuka andMimaki, 2009).In addition to cytotoxicity, antifungal, and antibacterial capabilities, and in vivo anticancer activity, other plants are well known for generating steroidal saponins. (Li *et al.,* 2012).

Assessment of Antimicrobial activity of medicinal plants
The examination of bioactivity is crucial for determining how well a plant can treat bacterial infections and how susceptible a pathogen is to the plant. Pathologists use antimicrobial susceptibility testing to identify which microbial strains are resistant to certain antimicrobials, and pharmacologists use it to assess the effectiveness of novel antimicrobials derived from biological extracts against various microbes. Numerous techniques, including turbidity measurement, turbidity, direct microscopic counts, and viable counts are used to measure bacterial growth. The broth micro-dilution and disk diffusion methods are two of the common antimicrobial susceptibility methods used to assess the impact of plant extracts or any other antibacterial on pathogens. The "minimum inhibitory concentration" (MIC) of plant extracts is determined using the broth microdilution method, whereas the zones of inhibition displayed by the extracts are determined using the disk diffusion method. When compared to the disk diffusion approach, this method is less time-consuming, less expensive, and quite reproducible. Bacterial growth could be determined spectrophotometrically by measuring the optical density, or more accurately visually by grading turbidity (Esemone*et al.,* 2010). Visual evaluation of bacterial growth has the drawback of lacking objectivity and precision, whereas spectrophotometric measurements may be less accurate due to additives or antibacterial compounds that impact on the spectral characteristics of growth media, (ii) bacterial aggregation, or (iii) bacterial pigments (Grare*et al.,* 2008).

Antimicrobial activities of indigenous medicinal plants
Ginger (*Zingiber officinale*)

In a study published in 2019, Shuaibu*et al,* (2019). sought to identify the phytochemical components of *Z. officinale* extracts from various parts of Kaduna State, Nigeria, and assess their antibacterial efficacy against a variety of clinical bacteria isolates. Three zones in Kaduna State provided samples of Z. officinale. The clinical isolates from the Garkuwa Specialist Hospital in Kaduna included *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The antibacterial activity of the phytochemicals was assessed using qualitative analysis of the phytochemicals and tube dilution and agar well diffusion test techniques.Steroids, glycosides, tannins, flavonoids, alkaloids, saponins, and phlobotannins were among the phytochemicals that the study found in the extracts. The methanolic extract of *Z. officinale* from zone 3 at a concentration of 50 mg/ml showed the greatest efficacy against *P. aeruginosa* (31.6 mm). Additionally, the zone 3 methanolic extract of *Z. officinale* had the highest MIC (12.5 mg/ml) against *P. aeruginosa*. The MBC values of the methanolic crude extract of Z. officinale from all three zones, however, are similar (50 mg/ml). The research demonstrates *Z. officinale's* potential for treating bacterial illnesses.
Zingiber officinale ethanolic extracts were screened for phytochemicals and antibacterial activity as part of the Suleiman*et al.,* (2019), investigation. Fresh *Zingiber officinale* (Ginger) rhizomes were procured from the Kachia Local Government Area in the Nigerian state of Kaduna (Kaduna South). While phytochemical screening was done to ascertain the phytochemical makeup of the ginger rhizomes, the antibacterial activity was assessed using the agar well diffusion method. Alkaloids and saponins were absent from all of the extracts, according to the phytochemical screening results, while flavonoids, tannins, and steroids were present.The bioassay result showed diversity in the extracts' biological activity. With zones of inhibition ranging in diameter from 7.31 to 18.67 mm.All of the extracts demonstrated antibacterial activity against all of the tested microorganisms. *Staphylococcus epidermidis* extracts in chloroform were found to have the highest zone of inhibition at 100 mg/ml, while *Pseudomonas aeruginosa* extracts in n-hexane were found to have the lowest zone at 25 mg/ml. However, n-hexane extracts at a concentration of 25 mg/ml were ineffective against *Klebsiella pneumoniae*and*Pseudomonas aeruginosa*.

Capsicum chinense

Jharna*et al.,* (2018) conducted a study to ascertain the impact of various *Capsicum chinense* extract concentrations on particular bacteria (*Staphylococcus aureus, Escherichia coli*). Extracts were discovered to be successful in combating the test microorganisms. In comparison to *Capsicum chinense* var. *Roja Bhut*, the extract from *Capsicum chinense var. Noga Bhut* had greater antibacterial activity against *Staphylococcus aureus*. In comparison to *Capsicum chinense var. Noga Bhut,* the extract from *Capsicum chinense var. Roja Bhut* had greater antibacterial activity against *Escherichia coli*. With a 12 mm zone of inhibition, 75% extract of the *Capsicum chinense* variety CA1 showed greater antibacterial activity against Escherichia coli. against *Staphylococcus aureus*, the 75% extract of *Capsicum chinense* variety CC2 demonstrated a maximal 11 mm zone. Stronger antibacterial effects were associated with higher extract concentrations. Gayathri *et al.,* (2016) conducted research on the extraction, quantitation, phytochemical, and antibacterial activity of capsaicin from extracts of *Capsicum chinense* in acetone and acetonitrile. According to phytochemical investigation, the callus, leaf, stalk, fruit, and seed extracts contain high concentrations of alkaloids, flavonoids, phenols, saponins, and other phytochemicals. Through the use of the agar well diffusion method, the acetone and acetonitrile extracts demonstrated the highest zone of inhibition of *Klebsiella pneumonia* and *Staphylococcus aureus* against the gram positive and gram negative bacteria, respectively. At various concentrations, it was discovered that the acetone and acetonitrile extracts were more efficient against all the tested bacteria and fungus. In a rat model of an infected wound, Steve *et al.,* (2021) assessed the antibacterial and therapeutic characteristics of an extract of *Capsicum annuum* L. (Solanaceae) and its antibacterial action mechanisms. Maceration in methanol was used to make the fruit extract. The methanol extract of *C. annuum* fruits was tested for its antibacterial properties using the broth microdilution technique. Using a rat model, the therapeutic effectiveness of the extract gel was tested on an excision wound

infected with *Staphylococcus aureus*. Using spectrophotometric techniques, the extract's total phenol, flavonoid, and tannin concentrations as well as its antibacterial modes of action were identified.
The total phenolic, flavonoid and tannin contents of the C. annuum fruit extract have been connected to its antibacterial activity. The prevention of biofilm formation, the ATPases/H+ proton pump, and dehydrogenase activity, as well as the modification of the bacterial cell membrane through the leaking of nucleic acids, reducing sugars, and proteins, are what cause the antibacterial activity. The percentage of wound closure increased significantly (p 0:05) after applying the extracted gel, and *S. aureus* was completely eliminated from the infection site.

Vernonia amygdalina

Using the agar well diffusion method, Evbuomwan*et al.,* (2018) carried out a study to examine the phytochemical and bactericidal activity of *Vernonia amygdalina* leaf extract against clinical isolates taken from the University of Benin Teaching Hospital. There were phytochemicals such flavonoids, cardiac glycosides, reducing sugar, terpenoids, and saponins in *Vernonia amygdalina*. Inhibition zones for ethanol extract against *E. coli* ranged from 7.0 mm at 25 mg/ml to 14.5 mm at 200 mg/ml, for S. aureus from 6.5 mm at 100 mg/ml to 9.0 mm at 200 mg/ml, from 11.0 mm at 50 mg/ml to 16.5 mm at 200 mg/ml, and for staph from 7.5 mm at 25 mg/ml to 11.5 mm. For *Pseudomonas aeruginosa*, the inhibition zones in aqueous extract ranged from 8.0 mm to 2.0 mm at 25 mg/ml to 12.5 mm to 1.5 mm at 200 mg/ml, and for S. aureus, from 9.0 mm to 1.0 mm at 50 mg/ml to 15.0 mm to 1.5 mm at 200 mg/ml.
In *S. aureus, P. aeruginosa, B. subtilis,* and *K. pneumoniae*, the minimum inhibitory concentration of ethanolic extract ranged from 25mg/ml to 50mg/ml, whereas in *E. coli* it was 25mg/ml. For *Pseudomonas aeruginosa* and *K. pneumonia*, the minimum bactericidal concentration of the ethanol extract was 50 mg/ml, while it was 100 mg/ml for *E. coli, S. aureus*, and *B. subtilis*. In the aqueous fraction of the plant, MBC of 200mg/ml for B. subtilis, *S. aureus,* and *P. aeruginosa* were noted. *S. aureus* was the bacterial strain that was most resistant to antibiotics (80%), while *P. aeruginosa* was the least resistant (10%). S. aureus had the highest level of resistance (80%), while *P. aeruginosa* had the lowest level of resistance (10%). The most effective antibiotics were ciprofloxacin, septrin, chloramphenicol, and pefloxacin. The potency of *Vernonia amygdalina* extract was found to be higher than conventional antibiotics.
A study by Audu*et al.,* (2018) examined the phytochemicals in *V. amygdalina*, which was obtained from Lapai, Niger State, Nigeria, in order to confirm the plant's purported antibacterial efficacy. Agar-well diffusion assay was used to conduct phytochemical analysis and research on the antibacterial activity of *V. amygdalina* stem bark and root extract against *Aspergillus niger, Staphylococcus aureus, Candida albicans,* and *Pseudomonas aeruginosa*. The stem bark and roots extract contained phenolics, phlobatannins, saponins, tannins, flavonoids, glycosides, steroids, and alkaloids according to preliminary phytochemical screening. With regard to S*. aureus* and *P. aeruginosa*, the acetone extract of stem bark's inhibitory zone had the maximum diameter (16 mm) (16 mm). With the exception of *S. aureus*, which showed inhibitory activity with a 7 mm diameter of inhibition zone on stem bark extract, all the pathogens showed resistance to the water extract of stem bark and root. The findings of this study point to the presence of substances in the extracts that are pharmacologically active and have antibacterial action against pathogenic strains, which supports their use as an ethnomedicinal.

CONCLUSION

The emergence of antimicrobial-resistant pathogens has resulted to severe complications in treating infections as they render synthetic antibiotics ineffective. This situation has increased the attention given to medicinal plants as effective alternatives. The use of medicinal plants for therapeutic purposes stems from the chemical constituents they possess. These chemical compounds/phytochemicals have been demonstrated to possess bioactive activity against several pathogens, even multi-drug resistant strains. The three medicinal plants examined; *Zingiber officinale, Capsicum chinense*, and *Vernonia amygdalina* have been reported to show antimicrobial activity in several studies. Thus, they offer effective alternatives to synthetic drugs.

RECOMMENDATIONS

The use of medicinal plants is received with mixed perceptions as a big part of urban dwellers lack trust in their potential due to the dearth of scientific evidence of their efficacy against pathogens. Thus, there is a need to further strengthen the use of medicinal plants by undertaking more research on the antimicrobial potentials of medicinal plants.

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