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Use of Medicinal Plants as Antimicrobial Agents: A Review of the Successes Story

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Abstract: *The use of plants as natural alternative medicines dated back to prehistoric period. Different cultures and beliefs in the world have one history or the other of using plant or its derivatives as a remedy for many diseases. Phytomedicine usually have multiple effects on the body either therapeutic or side effects, the former out-weighs the latter. Their actions often go beyond the symptomatic treatment of diseases caused by microorganisms to formulation of products for daily use. Most medicinal plants are rich in secondary metabolites possessing numerous biological activities such as antioxidant, anticancer, antimalarial, anti-inflammatory, analgesics antimicrobial, among others. There is still a great interest in medicinal herbs all over world. The main reason for this is that herbs contain compounds of therapeutic efficacy, and they are derived from natural sources which are tolerated to patient's body physiologies than the synthetic drugs. Though there was an initial decline in use of medicinal plants, yet the last decade has seen resurgence both in the study and use of phytomedicines in treatment of numerous ailments. These benefits derived from medicinal plants especially as antimicrobial agents necessitated the need for this present review.*

Keywords: *Medicinal plants; antimicrobial agents; synthetic drugs; phytomedicines; alternative medicine.*

1.1. The Nature of Phytomedicine

Phytomedicine or herbal medicine is also known as ethnomedicine. It refers to the use of any plant's parts like leaves, stembarks, roots, flowers, fruits, seeds, berries, latex or exudates for medicinal purpose (Iwu, 2014). Herbal plants may be annuals, biennials and perennials. Annual herbaceous plants life period is half-one year only. That is, the plant dies completely at the end of the growing season or when they have flowered and fruited. Biennial herbal plants complete their life cycle within two seasons. Perennial herbal on the other hand, plants grow for many years and these includes many trees, shrubs and herbs (Burkhill, 2004). The stems die at the end of the growing seasons, but parts of the plant may survive under or close to the ground or root part from season to season. The new growth of plant develops from living tissues remaining on the roots (Krishnan, 2018; Sofowora, 2006).

Traditional medicine practitioners used plant's parts in most cases as crude extracts. These crude plant extracts contain many phytoconstituents that act synergistically to achieve a common goal of restoring normal health. They claim that these constituents worked together synergistically to exert therapeutic effects on a particular disease is greater than the total effect of the individual plant constituents. The toxic effects of herbal drugs are also reduced when a whole herb is used instead of isolated bioactive ingredients (Andrew *et al.*, 1999; Iwu, 2014).

1.2. Reason for Reconsidering Plant as Antimicrobial Agent

The introduction of new antimicrobials comes with an immediate response to the development of antimicrobial resistance by targeted microorganisms which employed several documented mechanisms

to evade the effects of chemotherapeutic agents like antibiotics (Munita and Arias, 2016). A prominent example is the methicillin resistant *Staphylococcus aureus* that has developed resistance to almost all classes of drugs. Antibiotic resistance is usually a consequence of the misuse and overuse of antimicrobial agents. This development of antibiotic resistance among microorganisms necessitating continous drug discovery coupled with mild to severe negative side effects of synthetic drug use on patients has given rise to the need for alternatives such as probiotics and phytomedicine (Munita and Arias, 2016).

The rapid increase in the consumption of herbal remedies worldwide have been stimulated by several factors, including the notion that all herbal products are safe and efficacious (Bashar *et al*., 2005). The use of phytomedicine is on the increase daily in both developed, developing and under-developed nations of the world. For instance, in the United States of America, products such as Ginkgo (*Ginkgo biloba*), Echinacea species (commonly called cone flower), Garlic and many others are advertised widely as safer, more natural and healthier alternatives to conventional medicines. More than 15 million people in the United States consume herbal remedies or high-dose vitamins, and the total number of visits to complementary and alternative medicine (CAM) providers far exceeds those to primary physicians, amounting to more than $34 billion out-of-pocket costs for CAM annually (Eisenberg *et al*., 1998). Approximately 70% of German physicians prescribed plant-based medicines to the patients for arrays of ailments.

1.3. Plants: An Alternative Source for Antimicrobial Agent

Plants are one of the most important sources of medicines. Historically, the ancient civilizations considered plants as the main source of new leads for antimicrobial remedies and pharmaceutical development (McChesney *et al.,* 2007). The first ancient record written on hundreds of Sumerian clay tablets in Cuneiform, are from Mesopotamia (Iraq) dated from about 2600 BC. Egyptian medicine dates from about 2900 BC while, her pharmaceutical record "*Ebers Papyrus*" dating from 1500 BC documented over 700 drugs which are mostly plants (Newman *et al*., 1999). There are about 45,000 medicinal plant species which possess medicinal properties (Grover *et al.,* 2002). In ancient cultures, people collected information about herbal drugs, and documented in herbal pharmacopoeias (Soumya *et al.,* 2009). In the modern pharmacopoeias, it was recorded that more than 25% drugs are derived from plants some of which are of synthetic analogues. Until 1990's, approximately 80% of all remedies were produced from roots, barks and leaves of plants (McChesney *et al*., 2007), and many have been evaluated for their antimicrobial activities.

In India, the collection and processing of medicinal plants and plant-derived products contributes a major part in each year to the national economy, as a source of both full and part time employment. Medicinal plants are extensively utilized throughout the world in two distinct areas of health management viz: traditional system of medicine and modern system of medicine Mohd *et al*., 2012). A number of recent drugs contained active ingredient that have been isolated from plants for thousands of years. Humans were totally reliant on plant-based medicines for their primary health care before the discovery of synthetic drugs (Singh *et al.,* 2008). The Nigerian traditional medicine system has shown many medicinal plants as potent antimicrobial agents against multi-drug resistant pathogens such as *E. coli*, vancomycin-resistant enterococci (VRE), and *Candida albican* as well as other pathogens in clinical manifestation (Iwu, 2014).

1.4. Importance of Plants as Antimicrobial Agents

Hong-Xi and Song (2001), examined thirty-eight plant-derived flavonoids representing seven different structural groups for activities against antibiotic-resistant bacteria using the disc-diffusion and broth dilution assays. Among the flavonoids examined, five flavonoids (flavanonol, myricetin datiscetin, kaempferol and quercetin) and two flavones (apigenin and luteolin) exhibited inhibitory activity against methicillin-resistant *Staphylococcus aureus* (MRSA). Flavanonol was also found to inhibit the growth of multidrug-resistant *Burkholderia cepacia*, VRE, and other medically important organisms such as *Klebsiella pneumoniae* and *Staphylococcus epidermidis*. Similarly, myricetin was bactericidal to *B. cepacia*. The results of the radiolabel incorporation assay showed that myricetin inhibited protein synthesis by *B. cepacia.* (Ortega-Ramirez *et al*., 2014). Also, Seow *et al*. (2014), proposed medicinal plants traditionally used to treat health disorders and to prevent diseases, as a source of bioactive compounds having food additive properties. Medicinal plants are rich in terpenes and phenolic compounds that possessed antimicrobial and antioxidant properties. The essential oils derived from

plants exhibited several biological activities such as antioxidant, anticancer, anti-venom, anti-inflammatory and antimicrobial activities. Nautiyala *et al.* (2007) observed that an hour treatment with medicinal smoke, released by burning wood and mixture of odoriferous and medicinal herbs, lead to 94% reduction in bacterial counts. Absence of pathogenic bacteria (*Corynebacterium urealyticum, Enterobacter aerogenes, Enterobacter aerogenes, Klebsiella mobilis, Kocuria rosea, Pseudomonas syringae pv. persicae, Staphylococcus lentus)* in the open room even after 30 days is indicative of the bactericidal potential of the medicinal smoke treatment. Medicinal smoke from natural herbal products has a potential for use as a smoke/inhalational form of drug delivery. Similarly, Savant *et al*. (2014) reported that Plant based antimicrobials represent a vast untapped source for medicines. Continued and further exploration of plant antimicrobials needs to occur.

Plants based antimicrobials have enormous therapeutic potentials. They are effective in the treatment of infectious diseases, while simultaneously mitigating many of the side effects that are often associated with synthetic antimicrobial agents. They are effective, yet gentle. Many plants have tropisms to specific organs or systems in the body. Phyto-medicines usually have multiple effects on the body. Their actions often act beyond the symptomatic treatment of disease. An example of this is *Hydrastis canadensis*. *Hydrastis* not only has antimicrobial activity, but also increases blood supply to the spleen promoting optimal activity of the spleen to release mediating compounds as reported by Savant *et al*. (2014).

1.5. Benefits of Medicinal Plants

Since time immemorial, man all over the globe depended on plant kingdom to meet all their needs of medicines: for alleviating ailments, search for eternal health, longevity and to seek remedy for pain relief and discomfort, fragrance, favours and foods. It had prompted the early man to explore his immediate natural surrounding and try many plant, animal products, mineral and develop a variety of therapeutic agents. Medicinal plants still play an important role in emerging and developing countries of Asia, both in preventive and curative treatments, despite advances in modern conventional medicines (Shah and Seth, 2010). They also generate income to the people of many countries of the world, who earn their livelihood from selling collected materials (leaves, roots, barks and stems) from the wild or by cultivating on their farms. Thus, the medicinal plants constitute a very important national resource. For examples, people in India and China are famously known to have used plants in organized health care regime for over 5,000 years. European herbal medicines blossomed in the Graeco-Roman era and remained in mainstream until six decades ago. The ancient civilization of India, China, Greece, Arab and other countries of the world developed their own systems of medicine independent of each other, but all of them were predominantly plant based.

One of the oldest repositories of human knowledge, the *Rig Veda* (4500–4600 B.C.) mentioned the use of medicinal. plants for the treatment of one or many diseases. In the long run to overcome the powerful forces of nature, human beings have always turned towards plants. There are available records about the local communities in the Asian, African and Latin American countries having a long history of dependence on traditional remedies, largely based on plants, for immediate access to relatively safe, cost-effective, efficacious and culturally acceptable solutions to primary health care. In Nigeria, the use of medicinal plants to treat certain diseases is gradually overtaking the orthodox medicines because of the aforementioned benefits endowed in plants.

The World Health Organization had estimated that 80% of the population of developing countries relied on traditional medicines, mostly plant drugs for their primary health care needs. Even the modern pharmacopoeia still contains at least 25% drugs derived from plants and many others, which are semisynthetic, built on prototype compounds isolated from plants. Medicinal plants are the major components of all indigenous or alternative systems of medicine. For example, they are common elements in Ayurveda, homoeopathy, naturopathy, Oriental and Native American Indian medicine. The demand for herbal drugs is increasing worldwide due to growing recognition of natural plant-based products, being nontoxic, having no side effects, easily available at affordable prices and sometimes the only source of health care available to the poor (Sofowora, 2006; Iwu, 2014). Hence, medicinal plant sector has traditionally occupied an important position in the socio-cultural, spiritual, economic values of rural and tribal lives of both developing and developed countries. Millions of rural households are using medicinal plants in self-help mode (Sofowora, 2006; Shah and Seth, 2010).

1.6. Plants Contributions to the Management and Treatment of Some Common Diseases

1.6.1. Medicinal Plants in Cancer Therapy

Medicinal plants are an essential source of arrays of chemical compounds that have been used for the past many years in the treatment of different types of cancers. Cancers are the third disease in the ranking of diseases treated successfully with medicinal plants. It is on record that about 25% of drugs in the modern pharmacopoeia are derived from plants, including several anticancer drugs currently in clinical use like vincristine, vinblastine, paclitaxel, podophyllotoxin, camptothecin and combretastatin. These plant-derived compounds, their derivatives as well as analogues based on these drugs constitute an arsenal against various types of neoplasms. The traditional use of plants provides a lead for cancer chemo-preventive molecules. The development of new derivatives from bioactive compounds of food origin has been a viable way to reduce toxicity and increase their effectiveness against cancer. The combined efforts of pharmacognocists, botanists, pharmacologists, plant chemists and biologists are required to discover new effective drugs to fight cancer. (Ramawat, 2009).

1.6.2. Medicinal Plants as Antimalarial Agents in Malaria Fever

The use of medicinal plants to treat malaria fever as antipyretic agents ranked first. The use of plants from various plant families such as Meliaceae, Asteraceae, Poaceae and Fabaceae have contributed immensely towards the successful eradication of Plasmodium species from the blood of humans (Iwu, 2014; Ramawat, 2009). Antimalarial drug resistance has spread and intensified in recent years, and has become a great world challenge. It is estimated that about 300 to 500 million human beings are infected each year with malaria while, between 1.5 to 2.5 million individuals die yearly (Ramawat, 2009). The development of artemisinin and its derivatives from *Artemisia annua* from plant had helped to reduced resistance posed by *Plasmodium spp.* in order to ease the malaria burden globally. Drug combinations based on artemisinin offer an effective therapy to counteract malaria drug resistance in many synthetic drugs.

1.6.3. Medicinal Plants Used in Microbial Infections

The plant constituents with antibacterial action are tentatively grouped according to their main chemical groups as follows:

Phenols: In *Anacardium occidental* the aromatic phenols cardol and anacardol are not only bactericidal and antifungal but also vermicidal and protozoicidal. The phenol chloropherin in *Chlorophora excelsa* is antibacterial and antifungal and in *Ocimum viride*, the thymol and eugenol are antimicrobial.

Quinones: The naphthoquinone plumbagin, found in *Plumbago zeylanica* and also in *Diospyros mespiliformis* and *Drosera indica*, is antibacterial, antifungal, antiprotozoal and anthelmintic, and the benzoquinone from *Embelia schimperi* is slightly antibacterial but mainly anthelmintic.

Acids: Citric acid in *Bryophyllum pinnatum*, is antibacterial and the fatty acids with acyclopentene nucleus (chaulmoogric and gorlicacids) in *Caloncoba echinata* act on the lepra bacillus. The acidic phenols gallic acid (and ethyl gallate) are reported to be antibacterial in *Bombax* spp. and antibacterial and anthelmintic in *Acacia farnesiana* and *Mangifera indica*.

Alkaloids: Berberine in *Argemone mexicana* (also found in *Chasmanthera dependens*) is said to be antimicrobial and antiprotozoal; sanguinarine acts as a lipolytic pro-drug and is antifungal. Cryptolepine in *Cryptolepis sanguinolenta* and *Sida spp.* and solanine in *Solanum nodiflorum* are all antibacterial and this also applies to the indole alkaloids of *Strychnos afzeli* and funiferine from *Tiliacora funifera*.

Flavonoids: Ageratum conyzoides contains an antibacterial flavone (the plant extract is also anthelmintic in vitro). *Combretum micranthum* and *C. racemosum* are antibacterial; they contain flavonoids, alkaloids (combretines) and catechuic tannins. *Canscora decussta* inhibits *Mycobacterium tuberculosis* and is also antiviral, whilst *Psidium guaijava* has three flavonoids with a strong antibacterial effect on *M. tuberculosis*. The flavonoids of *Uvaria chamae* act on *M. smegmatis*, they are also reported to be larvicidal.

Sulphur heterosides: Allicinin *Allium spp.* is antibacterial and antifungal and this is also the case for the isothiocyanate glucosides in *Capparis decidua* (glucocapparin), *Lepidium sativum* (glucotropeolin), *Moringa oleifera* (rhamnosyl-oxybenzyl-isothiocyanate); and *Carica papaya* seeds(tropaeolin). Cleomin from *Ritchiea longipedicillata* is antibacterial and anthelmintic(mainly). Hydrogen cyanide (HCN) found in *Acalypha wilkesiana* may account for the antibacterial action of this plant.

Terpenoids: Antibacterial activity is reported for *Borreria verticillata* (sesquiterpenic lactone), *Xylopia aethiopica* (diterpene, xylopic acid), *Azadirachta indica* (seeds, triterpenoids, also antiviral) and *Ekebergia senegalensis* (stembark, meliacins). The leaves of *Azadirachta* are insecticidal and those of *Ekebergia* are ichthyotoxic.

Proteolytic enzymes: Papain from *Carica papaya*, calotropine from *Calotropis procera* and bromelain from *Ananas comosus* are able to digest bacterial and parasitic cells and bromelain even digests worms. Polyacetylenes and phenylheptatriene from *Eclipta prostrata* and *Bidens pilosa* (leaves) respectively, have a strong UV-mediated toxicity to bacteria and *Candida albicans* and are also toxic to insects and

CONCLUSION

Plants based antimicrobials have enormous therapeutic potentials. They are effective in the treatment of infectious diseases, while simultaneously mitigating many of the side effects that are often associated with synthetic antimicrobial agents. The demand for herbal drugs is increasing worldwide due to growing recognition of natural plant-based products, being nontoxic, having no side effects, easily available at affordable prices and sometimes the only source of health care available to the poor (Sofowora, 2006; Iwu, 2014). There is the need for intensified research in phytomedicine as a complimentary partner in the race to conquer disease causing organisms and all forms of ailments for a safer world.

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