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The role of phytomedicine in the challenges of emerging, re-emerging diseases; and pathogens resistance to antibiotics

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Abstract
This article reviews literature related to the study. It focuses on the historical use of plants as medicine by human. The approach taken is based on the geographical location of various civilizations in which the plants are/were used as source remedies throughout the five continents of the world. Topical issues and a**n** overview cover on medicinal plants, past and their present uses, use of antibiotics in allopathic medicine and development of antimicrobial and antifungal resistance drugs to the currently use. In addition, issues on the emergence and reemergence of new and old diseases have also been covered.

Keywords: Antibiotics; Re-Emerging Diseases; Pathogens Resistance.

1. Fungal infections and their challenges

Perhaps the most stubborn disease causing micro-organisms are the fungi. All the way from oomycetes to *fungi imperfecti*, they are known to inflict suffering both to plants and animals [6] and [8]. The cost implications and losses caused by them are enormous. At the moment, the remedies remain elusive. However, it has been proved that higher plants have the potential to provide solutions to these problems because they have active principles, which are antifungal[7]. The bark of *Butea monosperma* (Ceacelpiniaceae) extracted with petroleum and ethyl acetate yielded biologically active compounds against *Cladosporum cladosporioides*. Due to the upsurge in the number of immuno-suppressed and immuno-compromised infections in many parts of the world, it has become imperative to develop new antifungal drugs, which can be of benefit to humans [7]. Although most of the plant extracts from native plants from North America had antifungal activities on various parasitic fungi; they were only slightly active against the more susceptible dermatophytes like *Microsporum cookerii*, *Microsporum gypserum* and *Trichophyton mentagrophyte*.

There are better prospects of obtaining dermofungicides from the tropics, which have a larger biodiversity as compared to that of the northern temperate regions. This holds true because most of the species like *Rhus glabra* (Anacardiaceae), *Opuntia fraglis* (Cactaceae) and *Achillea millofolium* ssp *pubens* have a wider and diversified genus representation in the tropics [8]. From South America in Surinam, it also emerged that certain family members of the Apocynaceae and Logiaceae yielded indole alkaloids, which were active against Gram negative bacteria [9]. Some of the tests on the organisms individually included *E. coli*, which is a mild pathogen, *B. subtilis* that causes food poisoning, *S. aureus,* and *C. albicans* which could be disease causing organisms and are difficult to deal with particularly when they have turned infectious. The local populations used selected plants from the aforementioned families of plants in traditional medicine and had their activities verified by the scientists through *in vitro* and animal studies. Studies in other regions as in the case of Indians living in the Amazonia by other scholars like Spruce and Martins concluded that the communities had limited vegetal pharmacopoeia [10]. Later workers disapproved this fact and actually proved that numerous collections of the plants were of high medicinal value [11].

It is true that plants manufacture secondary, tertiary and quaternary metabolites which are used as a source of protection against adverse ambient conditions. Such conditions are hot and arid,

cold and arid, cold and humid. These conditions may occur once throughout the year or alternately in a year in the tropical areas. Whereas the adverse dry and arid environments, humid tropics, and temperate conditions have been well-investigated; the altitudes modify tropics to give afronomontane climates which have not been documented.

Since the invasion of North America by settlers, Phytomedicine has evolved and the knowledge was passed from physician to physician and through generations [12] and [10]. During this period, there was partnership between home folk medicine and family doctors [13]. It is therefore clear that all the common ills were treated by physicians using preparations from plants. This fact is supported by the earlier pharmacopoeias [13]. However, with the technological advances in the 20th century, simple plant and water remedies were gradually discarded. Today, several Americans have lost touch with herbal preparations. This fact notwithstanding, the re-emergence of Native Indian American culture has increased interest in Native Indian herbal medicines. Some reasons for these resurgences of the popularity of traditional medicines are because pharmaceutical drugs are seen increasingly as oversubscribed, expensive and dangerous, yet herbal remedies are seen as less expensive and less toxic. Second, people are increasingly willing to self treat their medical needs by investigating and using herbs and herbal preparations particularly those with chronic illness such as arthritis, diabetes, cancer and AIDS. Successful management of such ailments is elusive. People who suffer such maladies are turning to herbs as adjuncts for treatments [14]. This has also led to enhancement of regulations status of herbal medicine throughout the world thereby. Thus further re -enforcing the role of such medicine in enhancing provision of health.

2. Role of plants in traditional medical practices

The World Health Organisation (WHO) estimates that 80% of the 4 billion people in the world depend on plants or plant related products for primary health care [15]. The sophistication of herbal remedies around the world varies with the technological advancement of the countries that make and use them [16]. These remedies range from medicinal teas and crude tablets used in traditional medicine to concentrated, standardised extracts produced in modern pharmaceutical facilities and used in modern medical systems under a physician's supervision [17]. Diseases caused by infectious microbes are some of the outstanding maladies of human race and livestock [18]. From time immemorial, the use and search for antimicrobials has and will always occupy centre stage for research activities. There is therefore need for research and innovation to combat new opportunistic infections as a result of the HIV pandemic. *Candida* species are some of the commonest micro-organisms, which are responsible for nosocomial blood stream infection with mortality rates of almost 50%. Risk groups are dilapidated persons or patients with compromised immune systems including infants, pregnant women, and diabetics, cancer, and AIDS patients treated previously with antibiotics [19]. Most antifungal drugs which have been licensed have therapeutic limitations in that there is fungal drug resistance, drug related toxicity, hazardous drug interactions or insufficient bio-availability. This explains why it is tricky to overcome or manage fungal problems that are encountered in life [18]. Since the beginning of scientific researches in medicinal plants, these plants have been a subject of investigations. Such studies have led to structure elucidation, which has caused an increase in publications dealing with pharmacological examinations of individual compounds of plant origin [18].

3. Pharmaceutical product development from plants

To obtain information about the usefulness of such natural resources for development of anticandidal/antifungal drugs, the identities of isolated compounds and their described properties have been compiled and are aiding scholars towards finding solutions against such complications that have been mentioned. With regard to pharmaceutical drugs discovery, it is evident that over the past two decades, interest in drugs derived from higher plants, especially the therapeutic ones, has increased remarkably [20]. Currently, the major pharmaceutical companies have demonstrated renewed interest in investigating higher plants as sources of new lead structures and source of new drugs. The evaluation of such new compounds against nosocomial pathogens that have proved resistant to conventional antibiotics is a common phenomenon [21]. With this in mind, about seven plants from Brazil were selected for screening against *Pseudomonas aeruginosa, Enteroccocus faecalis, Enteroccocus coli, Staphylococcus aureus, A. calcoaceticus* and *P. microbilis*. These organisms are known to cause both surgical and post-surgical ailments as well as medical complications in human [18]. Quite a number of them were extracted with various solvents and found to have antimicrobial activities against the above listed microbes [21].

4. Role of ethnobotany in drug development

Traditional systems all over the world are in the provision of primary health using the art they have inherited from ancient times [22]. The use of medicinal plants in the management of bacterial and fungal maladies is not a new phenomenon or art but a carryover from such antique periods as in the cases of traditional use of essential oils from medicinal plants. The Indian physician, Sushruta reported in 600 BC the medicinal use of essential oils. Oils from plants were used for the treatment of infections of the mouth, jaw and teeth [23]. Going through other literature, it is possible to compile a list of plant families from which essential oils that possess antimicrobial activity are found. They include families such as Asteraceae, Apiaceae, Lamiaceae, Fabaceae, Rutaceae, Zingiberaceae, Myrtaceae, Lauraceae, Cuperaceae among. Approximately 20% of the extracts are consumed as fragrances in perfumery and cosmetics, 5% in pharmacy and 15% are used for the isolation of components respectively [24]. Such compounds have been extracted from plants such as *Larrea divirata* Cav [25]. It is reported that the plant has *in vitro* fungal toxic activities which is safe to the non-targeted cells and gives results which are comparable to Ketoconazole. The

elucidation of compounds from antifungal activities is desired particularly from tropical plants [26]. A further reason for such desires is that the side effects of such extracts are minimal and therefore considered safe. Ethnobotany is and remains an integral part of human life and through folklore, compounds extracted from plants and specific plant parts are worthy of further investigations for their use as potent sources of antimicrobial and antihelmintic agents. Herbal and plant medicines have become a popular form of healthcare. Even though several differences exist between herbal and
pharmacological treatments, herbal medicine can be tested for efficacy using conventional trial methodologies [27]. Moreover, many of today's synthetic drugs originated from the plant kingdom, and only 200 years ago our pharmacopoeia was dominated by herbal medicines. The non-complexity of herbal products in their physical structures, methods of preparations and investigations of their efficacy makes them desirable, particularly considered against their popularity. For some but by no means all herbal medicines, efficacy data are now emerging [28]. Most of the herbal drugs reviewed are efficacious for certain conditions. Generally speaking, research into phyto-medicines is much less active than research into conventional drugs [21]. In most countries, Phytomedicine is considered or given as dietary supplements and thus lacks legal status to prove their efficacy and safety. Based on the data available todate, it is impossible to draw general conclusions about the therapeutic value of Phytomedicine, more so herbal ones for that matter. However, many of the plants presented in the reviews show promising activity in various antimicrobial agents and the efforts to regularise their therapeutic exploitation should not be relaxed [21]. Ethnomedicine has been used in selecting and justifying continued use of certain traditional plants [29]. In combating methicillin resistant *Staphylococcus aureus* certain plant crude ethanol extracts were used. It was evident in the scientific records that water and ethanol extracts of certain traditional plants like *Acalypha wilkesiana, Ocimum gratissimum, Ageratum conyzoides, Briddellia ferruginea, Terminalia avicennoides* and *Phyllanthus discoideus* were ineffective [30].

Antimicrobially active alkaloids have also been isolated from alcohol extract of certain wild plants like *Tabernaemontana chippi* L. which are found along the tropical rainforest, in Ivory Coast, Liberia and Ghana [30]. The extractions yielded several alkaloids, which are active against both Gram positive and Gram-negative bacteria [31]. Ethno medical survey also showed that they were used against various ailments, the majority of which are bacterial in nature extracts but were ineffective *in vitro* in the study in that their efficacies were too low to be recommended for traditional use [29]. Elsewhere and in Africa, traditional medicine is well recognized and is of great value. Based on fact and faith, many potent drugs have been purified from traditional medicinal plants by persistent research [32]. They include: anticancer, antimalaria, antibacterial and antidiabetic compounds [33]. In South Africa, there has been a trend to treat gastrointestinal complaints with traditional herbal preparations. Based on this traditional information, about fourteen traditionally used medicinal plants by the Venda rural communities were selected for clinical bacterial screening. Two plants, *Warburgia salutaris* and *Maerua edulis* showed antimicrobial activities that were higher than synthetic and conventional antibiotics. Further screening of other plants; *Piper capense, Lippia javanica, Berchemia discolor, Cassine tranvaalensis* and *Pseudlastylis marouneifolia* not only possess antimicrobial efficacy but also fungicidal effects on *Candida albicans, C. brusei* and *Cryptococcus neoformas* [33]. It is now evident that indigenous knowledge can be employed in the development of today's pharmaceutical industry. Some of the success in pharmaceutical industries is attributed to ethno-biological information obtained from local people [35]. Plants have remained a major source of medicine for humans. For purposes of review, only a few families have been selected in this chapter. There are certain families which are relatively small as compared to the others though being included in studies. Araliaceae are tropical plants which are trees, shrubs or some are climbers that have been taken into account during the reviews. Some genera in this family are traditional drug yielders. The best known drug which has been used for centuries from the family is *Panax schinseng* [36]. Oleaceae is important because *Olea hochstetteri*, which is found in the BIBLE as olive plant yields high herbal drugs quality used both in pharmaceutical industries and culinary [37]. Asclepadiaceae too is important and has been used in folk medicine although currently they do not yield any medicine [36]. The Convolvuliaceae, Boraginaceae, Verbenaceae, Lamiaceae, Solanaceae, Acanthaceae, Scrophulariaceae and Pedaliaceae families majority of which yield avariety of drugs like: hypotensive, expectorant and carminative. The plant species have been used in cooking since the advent of human time to date. They are also important constituents of perfumery because of their essential oils. Some selected genera are *Lavandula, Ajuga, Origanum, Mentha, Basils* and *Salvia*. Solanaceae family is best known for its alkaloids and has been used in medicine, both in the new and the old worlds. It also has those important vegetables like *Lycopersicum* spp, *Solanum tuberosum, Capsicum annum* and *Solanum melongena* to mention but a few. Some of the aforementioned species have been used in folklore and allopathic medicine. The genus *Datura* comprising; *D. stromanium, D. metel, D. inoxia* and *Duboisia* spp., *Solanum dulcamara, Atropa belladonna* and, *N. tobaccum* which are used as tobacco, currently provide source of modern drugs (Dev, 1989). Most of the plants found in Solanaceae family are important because they yield important alkaloids which are used as a base for the manufacture of various drugs in today's pharmaceutical industries. Adopting them in Western medicine depended largely on ethnological observation by European explorers and missionaries who visited the new Worlds and Asia [21]. Considering the gradual and steady developments in Ethnomedicine, herbs may be a cheaper option for medical problems in the provision of therapy in that their efficacy and acceptance are growing and that they have very few side effects [38]. Herbs grow everywhere and are inexpensive to collect and prepare. In view of the current crisis in the provision of healthcare in most African countries, there is every reason to promote knowledge of

understanding which type of herb is used for treating which ailment in the various communities. Some health planners have given ways through which the aforementioned justification can be used to achieve the provision of primary healthcare [16]. In many areas where these plants are found, they are subjected to destructive harvesting by greedy traders. Second, majority of the rural and urban poor have strong attachment to herbal medicine and third, there are traditional healers who rely on herbs where they combine spiritual beliefs with therapeutic efficacy. Birth attendants and bone setters also use a lot of herbal medicine. It is a strong belief that all these categories of traditional healers acquire their skill through oral inheritance [39]. The facts reinforce the warning given by [16] and [49] that African authorities can only afford to ignore herbal medicine at their own peril. Moreover, African healthcare has never been and probably will never be, adequately and equitably availed. This is because there is uncontrollable rapid population growth, poor economic performance and political instability to mention but a few [41]. In West Africa, *Garcinia cola* has been used as a chewing stick and to treat stomach problems. When its ethanolic extract was screened against *E. feacalis* and *S. aureus*, the result showed high level of efficacy in the *in vitro* studies [30].

5. Missing data in Phytomedicine

The shortcomings with regard to medicinal plant studies and its use in the sub-Saharan Africa and the rest of the new world is that most of the knowledge were derived through oral traditions. Subsequently; there were no written records prior to the advent of colonial epoch [42]. But this fact does not infantilise the art and use of plants for treatments amongst African. The foregoing facts on Africa were later fortified in the quest for solutions to several maladies like malaria, asthma and later HIV or AIDS. Practitioners of traditional medicine (TM) in Africa include herbalists, plants and plant products sellers, traditional birth attendants, bonesetters, diviners, faith healers, traditional surgeons, spiritualists and others. There is a period and method through which such skills are mastered. The training for these practitioners is still by apprenticeship for a minimum of 7 years. During this period, the apprentice is expected to master all the ethno-practices which encompass all the botanicals and zoological which are used in the practices and their methods of use. There are specializations and the practitioners also refer patients to one another appropriately [43]. The use of medicinal plants all over the world predates the introduction of antibiotics and other modern drugs in the African continent [16]. Herbal medicine has been widely used and it formed an integral part of primary healthcare Universally [29]. Traditional healers in Kenyan communities use herbal and phytotherapy to treat different kinds of ailments. The reputed efficacies of these medicinal plants have been experienced and passed on from one generation to the other. Apparently, of scientific proof of efficiencies of the medicinal plants as claimed by traditional healers in the Ogiek communities is lacking. Further, medicinal plants constitute an effective source of both traditional and modern medicine. It is estimated that about 80% of rural population depends on plants [5]. Scientific screening of various plant extracts against microbes; bacteria, viruses and fungi is one sure way through which the continued use of such plant preparations could be justified. In the same vein, a lot of plants have been used in culinary art and this has also led to testing of their extracts for medicinal uses for example, the antimicrobial screening of *Decalepis hamiltonic* against food-related pathogenic micro-organisms [45] and [46]. It has also been demonstrated that plants possess metabolites which are biologically active against pathogenic micro-organisms [46]. This explains why such plants have the capability of prolonging shelf lives of foodstuff. It further demonstrated the usefulness of plant extracts in food preservation management and against contamination. In sub-tropical Africa, bacterial and fungal infections represent an ever-increasing problem, more so in patients and people who are immunocompromised [47]. It is imperative to establish the efficacy of the plants since majority of the local population are rural and over 70% of them depend on plants as therapeutic sources [48]. However, most of the previous studies have been descriptive and exploratory. Biological, pharmacological and phytochemical data are lacking [30]. Attempts have been made to highlight the potential and verify the continued use of medicinal plants from West Africa with tests ranging from antibacterial to antifungal properties [47]. Other infectious diseases like diarrhea have threatened the lives of millions of people around the world. It is estimated that 20% of infants in developing countries die before their fifth birthday due to diarrhea [49]. The problem is more compounded by antimicrobial resistance to antibiotics. The alternative antibiotics are too exorbitant and beyond the affordability of the rural people [50] and [33]. Traditional setups had means of treatment. For example, in South Africa, majority of the people have well organized traditional curative practices. In an attempt to document such practices of antibacterial screening of medicinal plants from South Africa; some workers have investigated certain aromatic plants by extracting their essential oils and using them against some enteropathogens. They achieved comparable results, >40% of the tested plants that showed justified and continued use in traditional medicine [33]. There are also cases of comparing indigenous plant species with commercial species as in the case of *Tulbaghia alliacea* with *Allium cepa* in the management of candidiasis in South Africa [49a]. It emerged that the *T. alliancea* extracts had comparable results to *A. sativum*, which is known to be a traditional commercial preparation and source of treatment in case of *Candida* spp. However, the commercial preparation is too expensive for the rural poor. This problem is further complicated by the fact that most people who are affected by modern maladies in the developing world have limited access to conventional drugs due to prohibitive costs. [48]. This is the commonest scenario particularly in the light of near epidemic AIDS deaths which reach 2500 daily and 10-20% having fatal results [49]. The use of medicinal plants all over the world predates the introduction of antibiotics and other modern drugs on the African continent [50]. Herbal medicine has been widely used and formed an integral part of primary healthcare all over the world [51] The screening therefore, justifies continued traditional use of several plant species against

opportunistic fungal bacterial infections due to immuno suppressed conditions. Some screenings have been carried out elsewhere on indigenous plants in other continents and have however naturalized in other places where their potentials have been identified to possess other uses such as cosmetics, antiseptic agents' germicides and carminatives [49]. In Egypt, it emerged that the species; *M. armillaris, M. alternifolia, M. leucadendron,* and *M. stypheloides* each yielded essential oils from the leaves that possessed bioactivity against Gram positive bacteria, *Aspergillus* spp, viral conjunctivitis disease and represent a detoxicant in first line of defence against peroxidation of polyunsaturated fatty acids and phospholipids [52]. *Shigella dysenteriae*, type A, is a common problem in the world and its scientific importance was recognized in Japan in 1893. However, to date, there is no known vaccine for it [53a]. Certain African Savannah medicinal flora for example, *Mallotus oppositifollium* extracts are currently used in the management of diarrhea and dysentery. *In vitro* hexane extracts have been demonstrated to have antimicrobial activity against *Shigella* spp. [48, 46] and [53]. Across Africa, typhoid fever, caused by *Salmonella typhi* remains a major problem in rural areas where there is poor sanitation [53a]. To manage and overcome the malady *Cleistropholis patens* Benth (Anonaceae) is traditionally used in Nsukka, Nigeria to manage the disease [43] and [43]. There are certain botanicals which possess multiple uses in life [51]. In Ethiopian livestock with mastitis, the herb *Persicaria senegalense* is used as a remedy as well as topical antiseptic by women after delivery. In addition, for veterinary trials, it showed that the inflammation subsided within five to seven days of substituting animal cabbage fodder with herbs.

6. Role of aromatic plants in medicine in African traditional medicine

For centuries, the antimicrobial properties of essential oils from medicinal plants have been recognized, but scientifically studied only recently. It has been confirmed that some of them have antibacterial activities against food borne bacteria thus extending shelf lives of processed food [52]. Several species of the genus *Thymus* covering *T. pectinatus, T. capitatus* and *T. herba-barona* all of which are wild were collected and steam distilled then the volatile oil extracts subjected to some Gram-negative and Gram-positive bacteria to ascertain the efficacy of the extracts; it emerged that the extracts were active against the bacteria and could be effectively employed in the preservation of food [53]. African traditional treatments use holistic approach [15]. The point demonstrates the uniqueness of African medicine. Such types of treatments are variable and indicative of the specializations. The medicines include vegetable organs such as leaves, barks, roots, seeds, flowers, resins, latex or whole part of plant and/or together with parts of animals and/or some minerals like alum salts. African medicines may contain just one active ingredient but, flavourings, preservatives or colouring agents are also incorporated into the mixture [20]. Such colourings may act but are not necessarily synergists. The African TM also has ingredients comprising several preparations which have ingredients for all ailments that need to be managed to restore the patient's balance. These make the African (TM) fundamentally different from allopathic ones whereby several prescriptions may be made for reported case illness [20]. In Africa (TM) is administered through liquid, solid, semi-solid or gas formulation, although intravenous or other forms of injections are absent. Other specialised forms of treatment used in Africa (TM) include obstetrics and gynecology, dry heat therapy, hydrotherapy, treatment of burns, fasting and dieting spinal manipulation, psychotherapy, spiritual healing, occultism and massage. Africans have their form of surgeries which include male circumcision, female genital mutilation, tribal marks, cutting of the umbilical cord, tooth abstraction, piercing of the ear lobes uvulectomy, whitlow operation, trephination and abdominal surgery. However, there is no x-ray or anaethesia used in Africa. After the surgeries, the patients are treated with herbal preparations to heal the wounds [54]. Such practices are mainly dependent on a plant uses that have evolved over centuries and therefore, still remain part and parcel of rural cultures. The *A. conyzoides* collected are heated over fire and the resultant sap squeezed into palm oil expressed from the mesocarp of *Elais guiniensis*. The concoction is used to rub the whole body. *A. conyzoides* has been used in vogue by Africans in dressing wounds and treatment of ulcers [50]. It is used as a styptic in East Africa [35]. The common uses is due to its antimicrobial activities which have been demonstrated scientifically but the occult power it is claimed to possess when collected at night cannot easily be rationalized on scientific basis, especially when there is no precise diagnosis of the disease. Some other examples are: in many African homes, chewing sticks are used to clean the teeth. The chewed ends are used to clean the teeth thoroughly. The sticks impart varying sensations, a tingling, peppery taste and numbing is provided by *Zanthoxylum zanthoxloides* Waterman, a strong bitter taste and frothing by *Masularia acuminata* (G. Don) and initial bitterness becoming sweeter later by *Vernonia amygdalina* Del. Buffered extracts of most of these sticks showed varying antimicrobial activities [41]. The other practices in African (TM) such as; the collecting of medicinal plants is only done at a certain season, using cold extraction as opposed to boiling, using young leaves instead of old ones, using fallen dead leaves instead of young ones and using fresh ones, have been rationalized as being due to seasonal, diurnal or age variations in accumulation of active constituent of plants or the thermolability of active ingredients of certain plants [50]. In Malawi, *Polygala nyikensis* which is used to treat skin conditions, proved both *in vitro* and *in vivo* to contain xanthones which have high antifungal activities [41]. Further researches by [39] to ascertain the efficacy of African medicinal plants showed that the use had very positive sides. For example, the use of *Rauwolfia vomitoria*, roots to treat mentally ill patients; *Plumbago zeylenica*, roots for treatment of various fungal skin diseases, *Ocimum gratissimum* leaves which has essential oils to treat diarrhea are all justifiable [41]. Such plants like *Combretum mucroriatum* and *Mitragyna stipulosa* have proved effective as antihelminths but active ingredients have not been elucidated [41]. There are a lot more plants which are currently being used in folklore medicine but their characterization is yet to be done.

7. Challenges from antibiotic resistance by pathogens

Two pathways may be used by the organisms in acquiring the resistance. One is by modification of their own genes and, two, by acquisition of resistant genes from other bacteria. The resistant genes that encode systems to either expel or inactivate antibiotics occur naturally because many antibiotic producing organisms need them to avoid self-destruction [16]. Thus, we can say that antibiotic usage boosts the frequent development of resistant organisms [16]. Mutation occurs even during the single treatment and therefore, their target can be modified to confer resistance in a very short time after the introduction of new drugs as was in the case of penicillin and more recently in linezolid, an oxazolidinone that interacts with the peptidyl - +RNA binding P site at the 50s submit [16]. The emergence of resistant micro-organisms has even preceded the clinical use of some antibiotics [57]. It can therefore dbe said with certainty that the development of new classes of antibiotics and their introduction into medical use has been met by further development in antibiotic resistance such that multi-drug resistant bacterial pathogens are now common [58]. Bacterial resistance to conventional antibiotic treatment is most critical in hospital environments than anywhere else [59]. The spread of antibiotic resistance in clinical and community settings is therefore, a pragmatic phenomenon [60]. In Industrialized, countries bacterial multi-resistance to drugs is responsible for over 50% of infections. The problem of resistance is related to the degree of exposure to antibiotics and is exacerbated by inappropriate use, both in developed and developing countries. In a nutshell, antibiotic resistance poses one of the greatest challenges face public health officials since it increases healthcare costs [26]. A good example is the reemergence of tuberculosis especially *M. tuberculosis* that is multi-drug resistant and whose treatment is a hundred times more costly than that of the normal therapy [62]. The cost implications in the provision of healthcare may, therefore, be a major component in antibiotic therapy compliance. Those victims who cannot afford combination therapy or other costly prescribed drugs may altogether assume that they have recovered hence they default the treatment. Methicillin resistance involves a complex network of molecules and primarily depends on sufficient expression of penicillin binding protein with low sensitivity towards BLAS [59]. It further requires that other factors include the fine-tuned regulation of autolytic activity of cell wall components, as well as optimal rate of peptidoglycan precursor formation and highly specific peptidoglycan precursor structure. Regarding the evolution of various resistances, studies show that the resistance of bacteria to antibiotics has been a progressive one [60]. However, β-lactamase production evolved rapidly in *S. aureus* and > 50% of hospitals acquired *S. aureus* isolates were penicillin G. resistant by 1948. This proportion has reached between 80-90% to date [63]. The resistance is due to the introduction of various broad spectrum antibiotics including Methicillin which was introduced in 1960 [58]. It is unfortunate that Methicillin resistant strains of *S. aureus* have spread with speed to unknown proportions in many countries thereby rendering it ineffective. Most countries have since then ceased to use the drug as an ultimate drug of choice. There have been genetic studies of the vancomycin resistant strains of *S. aureus* which reveal that *Van* A gene is the one that has mutated to lead to this resistance [64]. In *P. aeruginosa*, about 116 rectal swabs over a period of time revealed that: 78% the test organisms were resistant to penicillin. Of these, five strains were resistant to penicillin G and to other antibiotics in the following order: erythromycin, clindamycin (one strain), erythromycin A and tetracycline (one), erythromycin A (one), tetracycline (one) and fusidic acid (one) [65]. It finally emerged that antibiotics did not seem to impede the survival fitness of *S. aureus* in intestinal commensal microflora. Strains that have acquired resistance e host may, therefore, spread to other hosts unhindered by their resistance phenotype [65]. There is indication that *S. aureus* exists in variant colonies. Such as colonies referred to as small variant have been implicated in persistence and spread of chronic infections [66]. Data may lead to the understanding of the methicillin resistance of the *S. aureus* and the ways through which such complications could help in assisting the design of new therapeutic strategies. This loaded statement does not resolve the mystery of the current antibiotic resistances [67]. Epidemiology in human communities may present challenges in that certain diseases could remain pandemic, re-emerging and endemic. Respiratory tract infections are commonly caused by bacteria [68]. *P. aeruginosa, K. pneumoniae, S. pneumoniae, S. aureus, H. influenzae* and *Legionella* ssp. *S. pneumoniae* is one of the commonest causative organism in common respiratory tract infections (RTI) [68]. Currently, antibiotic resistant *S. pneumoniae* has emerged and this threatens successful treatment of the disease which is common in urban communities [69]. To consolidate future antibiotic therapy, 649,552 patients: on treatment with selected macrolides, *ß-lactams* like amoxicillin, amoxicillin/clavulanate, azithromycin, cephalexin and levofloxacillin produced interesting results [70]. Out of the 649,552 available patients of RTI and 7,252 susceptibility tests performed on *S. pneumoniae* isolates, there were no statistically significant trends in resistance for resolution proportion following treatment by either *ß-lactams* or macrolides among any of the RTI'S. Further, to this, there was no positive significant association between *S. pneumoniae* susceptibility and RTI treatment results apart from significant positive association between erythromycin. Also, there was non-susceptibility in ear isolates and macrolides treatment resolution for supportive acuter otitis media. It was concluded that on the population level *in vitro S. pneumoniae* nonsusceptibility to macrolide or *β-lactam* antibiotics were not associated with treatment failure conditions of probable *S. pneumoniae* etiology [68]. With the foregoing revelations in mind, it has been noticed that there are prospects and challenges in developing new agents for tough Gram-negatives like *P. aeruginosa* and *K. pneumoniae* which are all known pathogens [71]. There is emphasis on the mechanisms through which the resistance is developed against floroquinolones and aminoglycoside through the development of extended spectrum β–lactamase which is capable of inactivating both amino glycoside and flouroquinoione [71]. The other reason of the development of resistance to *P. aeruginosa* is due to reduction in the cell permeability and efflux of the drug,

which occurs as cell mobilization [72]. The tendency of mutation to occur and the Mutator cells persisting is a very common phenomenon which leads to resistance to β-lactam and amino glycosides. There occurs a mismatch which is common in *P. aeruginosa* [72] multi-drug efflux transport may also cause high resistance in pathogenic bacteria to amino glycoside in the case of *Acetiobacter* ssp [73]. In prostates and mid-ear infections there is a tendency of multi-drug resistance development which is attributed to microfilm colony development [75]. After such development, there is a tendency of reduction of the cell permeability with the interior of the colony recruiting more cells to behave in that manner by the bacteria using quorum sensing mechanism [71]. The prospects of the discovery of new antibacterial agents given the seriousness of hospital acquired infections which are frequently becoming multi-drug resistant; is to carry out empirical therapy [68]. This may be achieved by delaying the treatment until culture and susceptibility data for a particular infection are available. These resistances of the organisms to new antibiotics paint rather bleak pictures for new antibiotics [71]. Scientists work round the clock to ensure that they keep pace with pathogens to counter newly emerging strains [76]. Antibiotic use exerts influence on the resistance to several pathogens which were previously controlled by vancomycin as the drug of choice. This implies, for example, that Enterococci have certain strains which are vancomycin resistant (VRE). In such situations, the first drugs of choice are ampicillin and aminogycosides in nosocomial environments. However, in the event that resistance to aminoglycoside and ampicillin is experienced, certain glycopeptides are employed [77]. Further, it was revealed that in order to curb VRE, it is empirical not only to control infection but to regulate and have careful administration of antibiotics like cephalosporin. The reason for this desire of restrictions is because such complicated antibiotics lead to the emergence of VRE's and a tendency to colonization pressure from within the communities. Food is another conduit through which transmission of antibiotic resistance occurs [77] this is why resistant pathogens are continually emerging rapidly. The emergence of these resistant pathogens, poses a real threat to public health. Unfortunately, most of such foodstuffs such as milk products, shrimps and groceries are bought from traders and eaten raw [78]. Such foodstuff could provide a time bomb and challenge to the fight against antibiotic resistance by microbes in human. Although it would be a long and tedious effort to clean up AR gene pool from the environment, interrupting the transmission of AR bacteria into humans by focusing efforts on the food chains could be an effective strategy to combat the AR challenge in humans. This effort, however, remains a pipe dream.

8. Conclusion

There are several maladies which are emerging. The surer way of dealing with them is to turn to Mother Nature with plants presenting a quicker solution.

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