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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

The review 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 of remedies throughout the five continents of the world. Majority of the views have been based on ethno practices. Topical issues and an overview cover medicinal plants, past and their present uses, use of antibiotics in allopathic medicine and development of antimicrobial and antifungal resistances to the drugs currently in 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. An overview of the medicinal plants past and present uses/Introduction

A global review of phytomedicine in relation to ethnology reveals that the science of plants in the early days was based on the utilitarian approach^[1]. This is evident in the many because there are several records of highly prized plant species which have been mentioned several times in literature. An example is found in the Chinese civilization where there are records of one plant, *Artemisia annua* L. whose records are available in the tomb of Mawangdui Han dating back to 168 BC^[2]. It is known to have treated over 52 kinds of diseases^[3]. The plant is further mentioned in Zhou Hou Bei Ji Fang^[4] which was written in 340 AD. The realisation of its potential in the mid-1960s led to its commercialisation. It is therefore not new to South East Asians since the Chinese have used it for over the last 2,000 years against fever and other related ailments. In such a rich culture, records indicates other plant species that were and are still being used for curative purposes^[5]. Against such a rich cultural background embedded in the traditions, there has been gradual but dynamic penetration of the traditional Chinese medicine to other regions of the world like Japan via Korea^[6]. Chinese medicine influenced Koreans which in turn influenced the Japanese during the reign of Emperor Ingyo (411-453AD). Medical envoys continued to arrive from Korea throughout the next century and also during the time of the Emperor Suiko (592-628AD); Japanese envoys were sent directly to China to study medicine referred to as Kambo. Later in history, the Japanese evolved their traditional oriental medicine. Since culture is dynamic, the Chinese medicine was gradually integrated into Kambo and simplified^[3]. People still use the same practice in modern Japan to date. Chinese and Kambo have remained the most ancient forms of treatment with philosophical and experimental approaches^[9]. Such scientific development is rather gradual, systematic and more reliable compared to the allopathic approach. Because of little or no side effects, it is forecast that the Western world will have turned to alternative medicine by the year 2010^[10]. Use of plant or plant related preparations are also common in India and their surrounding communities. The reason is that Ayurvedic medicine practice has conserved most of their traditions^[9]. Beginning with Pakistan and India, which have only political boundaries, but are culturally identical, previous and current efforts have been made to elucidate effective compounds from plants in this region for pharmacological uses with little success^[11]. For example, bio-assay guided fractionation of the ethanolic extracts of *Polyalthia longifolia* var *pendula* stem, showed promising antibacterial activity against thirteen Gram negative and nine Gram positive bacteria.

However, pure compounds obtained from fractionations only showed some activities against fungi, *Mycobacterium stegmatis* and *M. fortuitum* [12]. Elucidation of the structures of ethanolic extracts of the above plants revealed the presence of: [13] trihydroxypentanoic acid as the active principle and a rich source of antibacterial agents. The compounds are safe, more potent, life saving and may be used for a long period of time particularly in light of frequent emergence of multi-drug resistant micro-organisms [14]. Although most countries prefer allopathic medicine, such practices are only sustainable before chronic cases arise [15]. It is, therefore, a request by other intending users that Chinese and Indian art are made more accessible. It is imperative that the governments of both countries India and China provide both moral and material support for the traditional industries to thrive globally [16].

In the Middle East, the scenario of herbal and art of medicine was knowledge learned from Greco-Roman period emanating from remote places [17]. The Arab inhabitants introduced to the West the Chinese technique of preparing minerals chemical [9]. These works are mainly recorded in the *-Materia Medica* of Jami of Ibn Baiar who died in 1248. His work had more than 2000 substances including many plant products [6]. This entire body of knowledge was further introduced to Western Europe by Christian doctors travelling with crusaders, and in the medieval ages, herbs became an important source of remedy and vast international commodity of commerce [18].

In the ancient Greek Empire, there are records of taxonomy of useful plants particularly those that were used by humans as food, for building, tools and medicines [19]. Such records are found in the works of Diocles, one of the first *Materia Medica*, the Rhizotomikon who was a Greek philosopher and a student of Aristotle [20].

Unfortunately, his work is now lost, but he gave an insight into plant taxonomy. With the Roman Empire succeeding the Greek Empire, a Roman soldier-physician by the name Diokorediodes (1STAD) wrote the "*De Materia Medica*" which was the compendium containing only useful plants in the world of medicine [22]. The work had 950 curative substances of which 600 were plant products, the rest are of animal and mineral origin [23]. Each document has botanical illustrations, medicinal qualities, method of preparation and warnings about undesirable effects. If any tradition exists that has withstood the test of time, it is in the traditional use of plants for curative purposes. East India which is incidentally sandwiched between some major influential cultures of China and the West, also underwent a similar process in development of medicine just like China and Japan. Prior to the emergence of Ayurvedic medicine, during the rise of philosophies of the Upanishads, Buddhism and other schools of thought that relied on nature were also developed [24]. The practices in the preceding paragraphs employed Ethnobotany which is a

multidisciplinary endeavour and encompasses several disciplines seeking to analyse how humans interact with plants in their environs. It means that it would combine anthropology, linguistics and botany as independent disciplines that are combined to form a solid background against which interpretations can be made [25].

There has been massive universal degradation of vegetation and that has led to a decline on the floral diversity all over the world [26]. Such unfortunate happenings are being witnessed in majority of areas with high floral diversity. Suggestions for urgent need of universal conservation whereby organized methods of management of land resources are used to maintain a balance between natural resources and evolutionary changes is imperative [27].

To achieve such goals, ethnobotany may be used to carry out many investigations in plant studies which are not possible without anthropological studies. Certain phytoscientists have taken advantage of ethnology and made outstanding scientific researches some of which have been used for therapeutic purposes [25].

In the Nilgiri Hills, the blue hills of South India, has tropical, sub-tropical and temperate climate and is inhabited by conservative tribal people, numbering about six tribes [28]. Over 80 indigenous and endemic plants have been studied by several scientists, and in a review of their findings, it is recorded that different plant species are used by different minority groups in the area. The same plants are put to similar or different uses as detected from cross cultural relationships in other studies. Such uses of the same plants by different groups may be a predictable indicator of their therapeutic efficacy [28]. The work further reaffirms that heterogeneity of the knowledge of medicinal plants by any indigenous community or communities explores the diverse knowledge about medicinal plants in their surroundings [29].

The surveys carried out, in most of the cases, took note of endangered species in which proper preservation is an urgent requirement. Some few selected plants used in Ethnomedicine by the people in Nilgiri Hills were noted including their phytochemical and pharmacological principles. They were *Adhatoda vasica* (Nees) C.B.Cl. and *Alstonia schloraris* (R. Br) (Asclepiadaceae). The above plants contained; echiternie and ditamine inositol which are active as antitumors, anticancer and thrombopoietic. Other plant species with active principles like *Artemisia nilagrica* CB Clarke Pamp (Asteraceae) has alkaloids that have antimalarial activities. *Embelia ribes* Burm. f. (Myrsinaceae) has embelin that functions as antifungal/antibacterial and *Mormodica charantia* L. (Cucurbitaceae) which contains Momoridine that works as antidiabetic and antifertility are also part of the flora. Such knowledge may be useful for furthering pharmaceutical studies and thus synthesis of medically important compounds.

Anthropology, ethno-biology and aspects related to the

presence of so many medicinal plant species as well as traditional significance of these plants have been used to draw comprehensive medico-ethno biological studies [28]. Such a study formed the basis for establishing the potential of the flora in any locality that might be generating interest. The approach through the studies of traditional plant usage when based on the indigenous population and their medicinal value revealed that Euphorbiaceae family, amongst many families led to the evolution of certain substances which have proved to be anticancer, antitumor, cardiac stimulants, and central nervous system drugs. It is important to deviate and make a treatise consideration of individual plants used in folklore medicine in Asia and elsewhere. Currently, lot of interests has been generated as pertains to phytomedicine. Basing the facts on ethnobotany, selective and advanced studies are presently carried out to augment the use of certain plants in allopathic medicine [30]. The genera *Uncaria* which are pantropical plants have found widespread use in traditional medicine [31]. Based on ethnological information, a few species from the family have been selected and elucidated to understand their chemistry by one worker and are available in the public domain. Some species of the genus *Uncaria* have been subjected to chemical and their ethnomedicinal values verified. They include *U. ianosa* var *glabrata* (Bl) (Rihsd) that was studied in west Sumatra where it is used in traditional medicine as a remedy for food poisoning, *U. rynchophylla* Miq. the plant extracts are used in Phytomedicine in China against epilepsy *U. guianensis* (Aub) dried and powdered leaves are used in the treatment of dysentery and the healing of wounds. Water extracts of the latter are used for the osteoarthritis treatment. In Peru, *U. hirsute* Havil. water extracts with its hooks in combination with other drugs are used as “thang-kau- tin” which, on testing exhibited liver protection activity and it also exhibited activity as an antihypertension drug. *U. macrophylla* (Wall) is commonly found in the Chinese pharmacopoeia and was found to be useful in the treatment of hypnosis [31]. *U. sinensis* (Oliv) Havil is used in Japan as a herbal sedative and analgesic and is important in the treatment of vascular dementia. In Peru, *U. tomentosa* Wild DC. is commonly used in traditional medicine against blood disorders and for the treatment of arthritis. In East Africa, *U. africana* G. Don. is used by the Ogiek community against stomach disorders and as tonic [32].

Ayuverda traditional India medicine and traditional Chinese medicine remain the most ancient form of medicine yet they are practical living traditions in medicine. This is because they both possess great philosophical and experimental basis. Their attributes are based solely on patience and cultural values of the two traditions [6]. This has made them more popular and preferred. Elsewhere, the majority of patients are turning to Phytomedicine due to several reasons as stated earlier namely; increased side effects and; lack

of curative treatment for several chronic diseases. High costs of new drugs have been realized because of microbial resistance to new drugs and emerging diseases [33]. It has, therefore, been postulated that, by 2010, at least two thirds for example, of the United States population will be using one or more of the alternative therapeutic treatments. There is a fast growing market for botanicals at a rate of between 5 to 15% annually [10]. Most of the knowledge and usage of the raw materials are largely dependent on the traditional knowledge [6].

In the majority of cultural medical practices, plants remain the bulk source of medicaments employed in folklore medicine. Many hundreds of plants are used in Asian Chinese, Indian and Japanese medical practices [6]. Comparatively, Unani practised by the Muslims is derived from many herbs and its final preparations include pills, syrups, confections and alcoholic extracts. Minerals, metals and metalloids such as gold, mercury silver, tin or arsenic were also employed, although some of these metals are very toxic [19]. The Unani medicine originated from ancient Greece and has been influenced by Persian, Egyptian and African medicine. The other fundamental difference between Ayurvedic and *Unani* is that the Unani had hospitals where patients could be treated with any of the drugs but Ayurvedic was carried out within family households. Now the opium and mercury used in Ayurvedic are not recorded in the ancient traditional Ayurvedic texts but sneaked into the system through the interaction with its Muslim counterpart [19]. That implies that *Unani* employs more metallic use as compared to Ayurvedic.

Hundreds of plants were used in Asian medicine by the Hakims or the healers of Unani medicine [6]. For example in one ailment, at least 88 species belonging to about 44 families are used in the control of high blood pressure. Modern research has upheld the pharmacological aspects such as hypoglycaemic effect of many of these traditional drugs. The task that remains is to establish their efficacy and safety to humans. Some of these plant species used in the past and present by the Hakims to treat diabetes are from the families: *Curcubitaceae*. *Mormodica charantia*, *Cucumis sativus*, *Curcubita pepo* (seeds) and *Citrullus vulgaris*. They are all herbalist armamentarium for the control of diabetes, although; their efficacies have not been established. Another ancient plant which the Hakims have used for centuries against run down conditions and depression is *Hypericum perforatum* A. Rich (Lusaciaceae). To date, the plants remain the most prescribed placebo herbal drug preparation for depression in the USA [34].

The Unani and Ayurvedic medicines include *Melia* and *Azadiracta indica* (Meliaceae) and *Abrus precatorius* (Fabaceae) which have been used from antiquity to date. There are many more which were in use, but the fact that they have not been mentioned does not mean that they are less important. The mentioned only underscore the ones important role of ethnobotany in

the current medical systems all over the world [35]. In trying to conserve the use of Phytomedicine and further support folklore medicine, the World Health Organization redefined traditional medical practice (TM) recently, as comprising therapeutic practices that have been in existence, often for hundreds of years, before the spread of modern scientific medicine and are still in use today [10]. The practices are variable and contain considerable mysticism and secrecy. The previous definition which took into account the sociological environment, whether living or dead and the metaphysical forces of the universe are still valid [5]. This validity arises from the sociological aspect which confirms its sustainability.

In the whole world, China traditional knowledge of medicine has been used in selecting and evaluating the efficacy of plant extracts against current and recently emerging viral infections. In the Mediterranean and the Near East areas, the family Clusiaceae the genus *Hyperacid* has generated lots of interests due to its variety of compounds with the ability for different biological activities and use in folklore medicine. They demonstrated antimicrobial, antifungal and antiviral activities [11].

2. Current studies of plants as medicine

Bangladesh is a country with rich flora. Some of this flora has been screened for their anti-bacterial cytotoxicity. Ethyl acetate and chloroform extracts of dried leaves of *Sida rhombifolia* demonstrated activity against selected Gram-positive and Gram-negative bacteria [19]. It was also suggested that the lethality of brine shrimps could demonstrate the presence of some antitumour compounds. Its active principles could lead to development of cheaper and dependable antibiotics instead of the synthetic ones. However, this would require studies on their efficacies and safety including clinical trials. In the same regional location, that is, in Japan, further quest for compounds which could assist in alternative natural antibiotics, has been carried out. It emerged that several compounds found in *Erythrina poeppigiana* possessed antimicrobial agents with anti-candidial and anti-MRSA (Methicillin resistant *Staphylococcus aureus*) [36]. It is rare to find such drug combinations in allopathic systems, though in demand, particularly in cases of immuno-compromised and immuno-suppressed conditions.

Nigella sativa (Ranunculaceae), commonly referred to as black cumin, is used traditionally in the Indian sub-continent, Arabian countries and Europe for culinary and medicine as a natural remedy for a number of ailments [37]. The diseases it cures are even described in the *Melanthion* of Hippocrates and Dioscorides and, as the Gith of Pliny [38]. Many of the claimed folklore medicinal values of the plant have been tested and scientifically verified [37]. The pharmacological tests in animal models have revealed that the oil has strong antinociceptive depressing properties on the central nervous system, anticarcinogenic and mutagenic, antihepatic and nephrotoxic, and antidiabetic mellitus

effects. It is also effective in reducing ulcer index, antihypertensive, immuno-potentiating properties in human T cells. The oil also has strong activities against human pathogenic Gram-positive Gram-negative bacteria, and fungi. More bioactivity was also detected in cestoda and nematode. At the levels that are comparable to those of piperazine in *Schistosoma mansoni*. Lastly, it was reported that the administration of the plant extracts intraperitoneally or otherwise in rats consecutively for a period of 5 days did not significantly affect the activities of several enzymes and metabolites indicative of hepatic and renal function. In other words, the plant has low toxicity in mammals. In this review, special credit and recognition is given to over 40 authors whose works have been enumerated without being quoted as they have been quoted by [39] in their extensive review.

Uses similar to those of *Nigella sativa* was extended to cover black pepper, black cummin and revealed similar results showing that tested essential oils and acetone extracts exhibited broad spectrum antimicrobial and antioxidants. A conventional method involving ultrasound assisted and solvent extraction method showed that the extracts of Ginger (*Z. officinale*) fingerroot (*B. pandurata*) and tumericin (*C. longal*) have high antimicrobial activities against *L. monocytogenes* and *S. typhimurium* [40].

With ever emerging resistance of bacteria to various antibiotics, it is empirical that new methods of combating the problem are invented. *Helicobacter pylori* which causes gastrointestinal infections in adults and children is often treated with antibiotics. However, the antibiotic therapy requires a cocktail of more than three drugs [41]. Studies of various organic solvents of six Iranian plants, *Juglans regia*, *Xanthium brasilicum*, *Ligustrum vulgare*, *Thymus kotschyanus* and *Trachyspermum copticum* indicated that all the plants contain bioactive principles which have inhibitory growth principles against bacteria. This gave hope to use them as substitute antibiotics. There have been studies of Gram-negative bacteria, *H. pylori*, and its problem to human and there are possibilities to link it to gastric cancer and adenocarcinoma. Studies on one single plant, *Plumbago zeylanica* L. on its non-polar extracts exhibited reasonable bacterial activity at pH ranges of 1-7 [42, 43].

Anti-microbial and cytotoxic studies of three Neoligans were isolated from *Magnolia officinalis* Rehd et Wils. (Magnoliaceae) [44]. Further studies *in vitro* on enterobacteriaceae produced promising results. This was necessitated by the observation that a number of strains of Enterococci ssp pose resistance to Vancomycin while *Staphylococcus aureus* has more often demonstrated resistance to Methicillin. It was confirmed that certain neoligans extracted from the plant exhibited reasonable anti-microbial activities up to the minimal bactericidal concentration (MBC) levels [45].

Pseudomonas ssp. is an opportunistic pathogenic organism that may exhibits multi- drug resistance

characteristics ^[46]. Recent studies in Australia cite 30 isolates of *Pseudomonas aeruginosa*, 11 isolates of *P. fluorescens* and 15 isolates of *P. putida* using oil and components of *Melaleuca alternifolia* L. tests indicated that *Pseudomonas* ssp are susceptible to the extract ^[46]. It was concluded that many oil products from the test plant could be employed in wound management or hand washing and contain 5-10% (w/v) oil. Given that MBC of the oil for *P. aeruginosa* was 4%, it is possible that the use of such topical agents in both treatment of wounds and other skin washing situations could be of benefit in preventing or reducing infection and transmission. However, clinical trials are currently on the same extracts ^[47, 48].

Studies of the activities of ten traditional plant extracts against 35 clinical isolates of Methicillin resistant *Staphylococcus aureus* also indicated that ethanolic extracts of the plants, 9 of the study species exhibited activity against all isolates tested ^[49]. Some of the native traditional plants whose extracts were used included *Garcinia mangostana*, *Punica granatum* and *Quercus infectoria*. They were found to be effective. It was concluded that these plants, which showed significant activity against MRSA isolates, could possess metabolic toxins or broad spectrum antimicrobial compounds. Further analysis of the extracts could yield inexpensive alternative drugs to conventional treatment of the bacteria. Traditional herbal medicine has been used for a long time in the treatment of infectious diseases in many countries and in China *in vitro* studies of plant extracts have shown activities against HIV ^[50]. Some of the families screened include Asteraceae, Rutaceae, Rosaceae, Acanthaceae Lamiaceae, and Araliaceae among others. It was noticed that they give reasonable and promising results. Preliminary results of the evaluation of *Garcinia mangostana* L. (Clausiaceae) have significant anti-microbial activity against MRSA isolates. The plant is known to possess compounds such as tannins metabolites whose antimicrobial activity is well-known ^[49].

Further studies to evaluate the efficacy of Thai basil oils and their micro emulsions *in vitro* activities against *Propionibacterium acnes* revealed promising results ^[51]. The essential oils were obtained from: *Ocimum basilicum* L., *O. sanctum* L. and *O. americanum* L. using disc diffusion and tube dilution methods to obtain areas of inhibition and minimal bacteriostatic concentration (MIC), respectively. *Ocimum basilicum* and *O. sanctum* also showed 2 and 3% v/v MIC. However, *O. americanum* did not exhibit growth inhibition even at the highest concentration levels although it had initially inhibited the growth of the test organism. It was further demonstrated that *P. acnes*, which is a common teenage problem, could be managed effectively by incorporating the oils from *O. basilicum* and *O. sanctum* in common facial creams ^[51]. Several bacterial strains and plant species were used *in vitro* studies in the laboratory, in which various parts of plants used in folklore medicine were selected. The

plants included: *Lantana camara*, *Hymenaea courbaril*, *Myroxylon balsamum*, *Aristolochia cymbifera*, *Chondrodendron platyphyllum*, *Drimys winteri* and *Xyanthoxylum tingoassuoba*. It was established that several of these plant extracts had efficacies against both the Gram-positive and Gram-negative bacteria such as, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. They could in future prove to be alternative agents for therapy of infections caused by the micro-organisms. The use of solvents such as ethanol, ethyl acetate and hexane, and further phytochemical screening revealed the presence of various classes of compounds like, flavonoids, tannins, alkaloids and glycosocoles all of which have been known to possess anti-microbial activities ^[52].

Many hundreds of plants around the world are used in the management of bacterial infections ^[53]. Conventional drugs usually provide effective therapeutic results. However, this benefit is limited by development of resistance; hence a need for drug discovery. Plant products have been found to be safer than synthetic products ^[6]. Therefore, many patients often prefer to use plant sourced medicines. There is therefore need to have trained human power on the use of herbal/plant in the management of diseases. The evidence summarized in the above chapters suggests possible benefits from some plant preparations with antimicrobial activity. *Micromeria cristata* (Lamiaceae) and subsp. *Phrygia* was studied and the results were that; essential oils and components of extracts of the plant leaves used as herbal tea, has profound activity against *Proteus vulgaris*, *Salmonella typhimurium* and *Candida albicans* ^[54].

3. Viral infections still elusive

The search for affordable anti- HIV and AIDS drug is not necessarily of academic curiosity but a necessity. Natural products are important sources of new drugs but may also lead to tailored synthesis ^[53]. Flavonoids and other related polyphenols possess good anti HIV properties since they inhibit reverse transcriptase induced interferons and inactivate viral protease ^[55]. Plants which are capable of providing anti HIV flavonoid components are: *Scutellaria baicalensis*, *Thevatia peruviana*, *Desmos* ssp, *Maytenus senegalensis*, *Juglans mandshurica* and *Camellia sinensis*. A few of these plants yield flavonoids which act as enzyme inhibitors and immuno toxins in their own ways ^[56]. There are other plants which yield classes of compounds like coumarins which are a distinct subgroup of non-nucleotide reverse transcriptase inhibitors which have received special attention as antiretroviral ^[50]. Coumarins have been isolated from plants such as *Fraxinus tschunganica*, and *Ferula sumbul*. Terpenoids and triterpenoids from these two plants have been found to exhibit antiretroviral activity with different mechanisms of action such as replication in HIV-1 ^[57]. *Clausena exacanta* showed anti HIV activity with very low cytotoxicity ^[57].

Globalisation has resulted in a massive increase in trade and human mobility. This has facilitated the rapid spread of human infectious agents such as *Staphylococcus aureus* and other pathogens, including those that are drug resistant [58]. A particularly serious threat to human health is posed by methicillin resistant *staphylococcal* strains which have acquired molecular mechanisms to evade the action of β -lactam antibiotics (BLAS). Studies by [59] revealed that, classical studies of the species *H. triquetrifolium* Turra. which has been used in ethnomedicine in parts of Turkey as sedative and antiseptic were effective in the treatment of burns in which *S. aureus* is common in secondary infections [60]. However, an all-out and exhaustive study was not possible since the plant is not used independently. It was, therefore, necessary to make a collective study of the whole genus and species available. The species included: *H. triquetrifolium*, *H. scabrum* and *H. scabroides*. The studies involved their essential oils which had been extracted using steam distillation [61]. The oils extracted proved to be of variable broad spectrum activities against both Gram positive and negative bacteria as well as *Candida albicans* [61]. Their efficacies validated their traditional use against diseases caused by these organisms.

In North America, early explorers traded knowledge with the indigenous American Indians [26]. The indigenous Indians taught them the type of plant herbs used to sharpen their senses for hunting, to build endurance and to bait their traps. Some of these plant species were so potent that they became articles of trade in the old and the new worlds [63]. Ginseng (*Panax quinquefolius* L.) growing in the Iroquois territory in the new world was dug up plentifully by Jesuits and sold to the Chinese. The money generated from this commercial concern was used to build schools. To date ginseng remains a sizeable crude phytomedicinal product exported from the USA. The red Indians of the American continent have been using it as an oral stimulant since the prehistoric civilisations to date [26]. In Central America, the search for plant active compounds against infectious agents has been noted [64]. Certain Guatemalan plants such as *Guazuma ulmifolia* Lam., *Acalypha guatemalensis* Pax. Haffm., *Smilax spinosa* Kill, *Ocimum micranthum* Wild and *Piper auritum* were screened to ascertain their antibacterial, antiprotozoal and antioxidant activities. The aforementioned study was targeted at ascertaining their activities against infectious agents to correlate the oxidant potential of their different extracts in order to validate their popular use in traditional medicine by the local population. It was established that all classes of active compounds were present included flavonoids, anthroquinones, condensed tannins and sugars. Such compounds have been synthetically incorporated into allopathic therapy. Furthermore, the trials revealed that compounds found in them confirm the traditional ways in which they are used in the area.

In a whole America, herbal drugs have been used in vogue by Indians. Some crude extracts have even been

incorporated into Brazilian pharmaceuticals for the treatment of infectious diseases [65]. A list of such plants is also available [66]. Some of these plants, as indicated in the previous chapters, have been known to be able to combat nosocomial bacterial, Gram negative and Gram-positive pathogens.

Plants are forever emigrants either through nature or by humans to satisfy human needs and desires. With such human behaviour, plants have been translocated into different continents of the world where they naturalized to assume the status of being indigenous [65]. *Thuja occidentalis* L. commonly referred to as white cedar, is indigenous to Eastern North America and is grown in Europe as an ornamental tree. To native Indians in Canada, during 16th century expedition, it was found as a source of remedy for scurvy. It was later established to be adjuvant to antibiotics in severe bacterial infections such as bronchitis, angina pharyngitis, otitis media and sinusitis [67]. An up-to-date review of the various uses of the plant which are evidence based for the plant has established such uses. The essential oil extracted from *T. occidentalis* that is α -thujone and β -thujone, were the major constituents. The other useful metabolites included; flavonoids tannins and coumarins. The immunopharmacological potential of *Thuja* spp has been investigated in various *in vitro* and *in vivo* test models [67].

Further studies found in the review of studies which were done *in vivo* indicated that, in mice, the leukocyte count was dose dependent and the percentage of segmented granulocytes decreased from 36 to 9% and stab granulocytes from 15 to 3%. The number of lymphocytes in the control mice also decreased from 89 to 48%. There was also stimulation of cytokine production in the mice treated with the extracts. There was also increase in response in the number of splenic plaque- forming cells and titers of specific antibodies in sera from mice treated with the extracts. After long-term treatment of mice with ethanolic mixture of *Thuja occidentalis* Hera, *Baptisia tinctoriae*, *Echinacea purpureae* and *Echinacea pallidae*, it emerged that there was increase in the plaque forming cells in the mice. The immune stimulation went on without necessarily affecting the weight of the spleen. Separate studies on the influenza virus type, an infection in mice indicate that there was an increase in the survival rate after the mice were treated to the aforementioned mixture from ethanolic extracts [67].

4. Plants as a major source of medicines

The search for plants with biological and therapeutic activities has been a continuous process the world over [68]. In Mexico, several field surveys have been carried out to isolate and elucidate active compounds in plants. Laboratory tests of the undermentioned plants' ethanol extracts against Gram-positive bacteria have revealed that: *Bursera microphylla* (Bursaceae), *Wislizenia refracta* (Capparidaceae), *Baccharis glutinosa* (Asteraceae), *Pithecellobium dulce* (Mimosaceae),

Fraximum uhlei (Olacaceae), *Ludwigia octovalvis* (Onagraceae), *Solanum nigrum* L (Solanaceae) *Asclepias subulata* (Asclepiadiaceae) had high antibacterial activities. The selections were based on the ethnobotanical survey, which was carried out on the local populations over a period of time. Most of the plant preparations were known to treat notorious and chronic diseases that were caused by non-bacterial pathogens.

5. Conclusion

With all the above surveyed and discussed scenarios, it would be logical to do a documentation of the local medicinal flora for future reference. It is also imperative that a thorough pharmacological profiling be done if a scientific selection and discovery of the new products is to be achieved. Finally, it is important that; the pharmacognosy of such drugs is carried out to assist in the selection of the new products for commercial development.

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