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Chapter

Pharmacognosy: Importance and Drawbacks

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Abstract

In many nations of the world, a great number of deaths and morbidity arising from illnesses are witnessed due to lack of basic health care. Phytotherapy has continued to play a significant role in the prevention and treatment of diseases (communicable and noncommunicable). Interestingly, more than 80% of the global populations now adopt phytotherapy as a basic source of maintaining good healthy conditions, owing to the pronounced side effects, nonavailability, and expensive nature of conventional treatment options. While this review looked at the prospects and downsides of phytomedicine as it relates to the national health care system, it established the fact that although a number of medicinal plants had been resourceful (effective) against a range of diseases, with few developed into drugs based on the available phytotherapeutics, quite a large number of them are yet to scale through clinical trials to determine their safety and efficacy. It is believed that until this is done, we hope phytomedicine to be adopted or integrated into the national health care system in many countries.

Keywords: medicinal plants, traditional medicine, secondary metabolites, drug discovery, phytotherapy

1. Introduction

1

1.1 History of medicinal plant use

The origin of medicinal plants use had been since time immemorial and traced back to Europe, Egypt, etc. many centuries ago [1]. The first records of knowledge documentation were, however, produced by Shen Nung (a Chinese emperor) 2500 BC ago, describing different recipes of drug preparation from more than 300 medicinal plants for the management of numerous human diseases. Records had it that the use of plants (herbs) as medicine started gaining momentum around 500 BC, though prior to this period, their use was not limited to healing but believed to possess spiritual (ritual) power as well until the advent of scientific era particularly around 1960s when much relevance was played on development of synthetic products based on assumption that they are safer and come with

little side effects [2]. Despite the aforementioned, the last two decades witnessed a drastic revival in the use and acceptance of phytomedicine by a majority of the people from developing nations (70–90%) as a major source of primary health care. This was also buttressed by WHO's submission, encouraging the discovery and development of lead drugs from plant-based formulations and/or medicines which are believed to be effective and safe [2]. In fact, the development of morphine, quinine, reserpine, ephedrine, etc., from *Papaver somniferum*, *Cinchona* spp., and *Rauwolfia serpentina* as first set of drugs from medicinal plants brought much popularity and attested to their acceptance and potential use across different parts of the globe especially from Europe and Egypt, with records of well over 900 drugs compiled in history by chain of scientists such as Discorides and Galen [3]. Moreover, it suffices to submit that China is the only country with complete catalog of phytomedicine [2].

Mankind relies on plants and/or its extract, an integral part of traditional medicine (TM) which as a matter of fact is the origin for medical medicine. The knowledge of TM particularly in issues relating to the health of both humans and animals has continued to emerge in many nations of the world. Despite the unproven quality, safety, and efficacy, they are becoming the major source of health care for 80% of the entire population in both developed and developing countries (such as USA, China, India) in disease control, prevention, and management [4]. Interestingly, TM or phytotherapy (traditional system of health care) in the last two decades is being adopted by every region based on the specific sociocultural context illustrating the way medicinal plants (MP) or the inherent secondary metabolites are used, as well as their disparity in the approach to health and diseases. This TM varies from one community to another and notable among them are Acupuncture (Chinese), Ayurveda (Indian), Kampo (Japanese), Unani (Arabian), Basotho (among Africans), etc., some or majority of which had been in existence many centuries even before the advent of modern medicine.

Similarly, the reliance on plants by humankind is not only limited to medicine but also to other basic needs such as food, clothing, and shelter, all produced or manufactured from plant matrices (leaves, woods, and fibers) and storage parts (fruits and tubers) [5]. Medicinally, plant harbors chemicals referred to as the secondary metabolites, which are derived biosynthetically from plant primary metabolites (e.g., carbohydrates, amino acids, and lipids) though might not be directly involved in the growth, development, or reproduction of plants [6]. These secondary metabolites can be classified into several groups depending on their chemical classes [7].

2. Plant secondary metabolite and their therapeutic significance

Secondary metabolites are organic compound produced and found in all plant tissues to drive metabolic activities, as well as providing self-defense against herbivore and any form of environmental toxicity [8]. Plant is a well-known source of medicinal product for both traditional and modern medicines for the treatment and management of human illnesses. The usage of the plant in this regard is attributed to the presence of secondary metabolites [9]. Apart from the fact that they are widely used in medicine, they are also employed industrially in the production and manufacturing of dyes, drugs, polymers, waxes, glues, fibers, antibiotics, herbicides, insecticides, cosmetics, etc. [10]. In general, secondary metabolites found in plants can be categorized into three major groups including terpenes (cardiac glycosides, carotenoids, and sterols), phenolics (flavonoids and nonflavonoids), and nitrogen-based compounds (alkaloids and glucosinolates).

Terpenes are the largest and highly diversified class of secondary metabolites derived as a result of polymerization of isoprenoid unit of five carbon compounds [11]. Based on the five carbon compound used as its building block, it can be subdivided into monoterpenes, sesquiterpenes, diterpenes, triterpenes, tetraterpenes, polyterpenes, and steroids whose precursor is triterpenes. The therapeutic significance of terpenoids from different plants has been reported, e.g., terpenes from eucalyptus oil is known for its antidiabetic property [11], ursolic acid from *Rosmarinus officinalis* and β -sesquiphellandrene from *Piper guineense* are known to be psychoprotective [12]. Antibacterial and antifungal potential of terpenoids derived from *Pilgerodendron uviferum*, *Picea abies* and other plant sources have also been reported [13–15]. Furthermore, a steroidal terpenoids called glycyrrhizic acid elicited anti-inflammatory activity [8].

The phenolics are secondary metabolites that are produced in the shikimic acid pathway of plants involving pentose phosphate through phenylpropanoid metabolization of at least one aromatic ring of hydrocarbon attached to one or more hydroxyl groups [10, 16]. Phenolics are generally categorized into two based on their structure, namely, flavonoids and nonflavonoids. Structurally, flavonoids are derived from two aromatic rings linked to a bridge consisting of three carbons $(C_6-C_3-C_6)$ and are sub-divided into six main categories, including flavonols, flavones, flavanones, flavan-3-ols, isoflavones, and anthocyanins. However, the nonflavonoids are subdivided into five main categories, including hydroxybenzoates, hydroxycinnamates, lignans, and stilbenes [17]. Compellingly, wide arrays of pharmacological potentials, such as antidiabetic, antioxidant, antiviral, antimicrobial, anticancer, and anti-inflammatory, have been credited to plant-based phenolic compounds. For example, cyanidin 3-sambubioside and 5-caffeoyl quinic acid derived from the fruit of Viburnum dilatatum Thumb. had been found to elicit significant antioxidant and radical scavenging activities while also inhibiting the syndrome-linked complications of postprandial hyperglycemia [16]. Furthermore, plant-based phenolic acids such as garcinone E, kaempferol, resveratrol, syringaresinol, and quercetin are known to be potent anticancer agents [18]. The antiinflammatory, antiviral, and antibacterial potential of phenolics in the management of skin disorder have also been reported [17, 19–21].

Alkaloids are structurally diversified secondary metabolites derived from nitrogen-based amino acid with nitrogen atom in the heterocyclic ring. Based on the nature of their heterocyclic and building block, alkaloids are classified into different subgroups such as indole, tropane, piperidine, purine, imidazole, pyrrolizidine, pyrrolidine, quinolizidine, and isoquinoline alkaloids [22]. Noteworthy, therapeutic effects have been credited to a wide range of alkaloids from plants. Typical examples from alkaloids are *Callistemon citrinus* and *Vernonia adoensis* reported to elicit antibacterial effects on *Staphylococcus aureus* and *Pseudomonas aeruginosa* [23]. Additionally, alkaloids originating from *Aerva lanata* roots were able to mitigate postprandial hyperglycemia in diabetic rats [24]. The *in vitro* antioxidant activity of *Phoebe declinata* leaves extract has also been attributed to its alkaloid. It was found to inhibit 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical while consequently reducing ferric chloride to ferrous [25]. Furthermore, plant-based alkaloidal compounds such as reserpiline, α-yohimbine, methylaplysinopsin, isoquinoline, physostigmine, and pilocarpine are good psychoprotective agents [12].

3. Medicinal plants as therapeutic agents

Healing with medicinal plants is as old as mankind itself. The link between man and his quest for medicines in nature dates back to ancient times, when there were

convincing proofs from written documents, monuments, and even original plant medicines [26]. Specifically, the oldest written evidence of usage of medicinal plants for preparation of drugs was found on a Sumerian clay slab from Nagpur, approximately 5000 years old. It comprised 12 recipes for drug preparation referring to over 250 plants [27]. Awareness of medicinal plants usage is a result of the many years of struggles against illnesses, which has prompted man to seek medicines in leaves, roots, barks, and other parts of plants [28]. The knowledge of the development of ideas related to the usage of medicinal plants, as well as the evolution of awareness, has increased the ability of health providers to respond to the challenges that have emerged with the spreading of professional services in the enhancement of man's life. Until the advent of iatrochemistry in sixteenth century, plants had been the source of treatment and prophylaxis for many diseases [27]. This is well exemplified globally where medicinal plants have always being an integral part of the health care system since time immemorial.

During the last decades, it has become evident that there exists a plethora of plants with medicinal potential, and it is increasingly being accepted that medicinal plants are offering potential lead compounds in the drug discovery process. In fact, the developed world has also witnessed an ascending trend in the utilization of complementary or alternative medicine (CAM) particularly herbal remedies [29]. While over 80% of the population in Sub-Saharan African countries like Nigeria and South Africa use herbal remedies for their primary health care, reports from developed countries such as Canada, Germany, and the US revealed that more than 70% of their populations have tried CAM at least once [29]. The most common traditional medicine in common practice across the globe is the use of medicinal plants. In most of the countries, medicinal plants are the most easily accessible health resource available to the community. In addition, they are most often the preferred option for the patients. For most of these people, traditional healers offer information, counseling, and treatment to patients and their families in a personal manner, as well as having an understanding of their patient's environment [30].

Indeed, modern allopathic medicine has its roots in traditional medicine, and it is likely that many important new remedies will be developed and commercialized in the future from plant biodiversity, as it has been till now, by following the leads provided by traditional knowledge and experiences. The extensive use of traditional medicine, composed mainly of medicinal plants, has been argued to be linked to cultural and economic reasons. This is why the WHO encourages member states to promote and integrate traditional medical practices in their health system [31]. While a good number of plants (with only selected representatives listed here) have elicited significant therapeutic and pharmacological effects against well-known debilitating and degenerating diseases such as diabetes (Artemisia afra, Chilianthus olearaceus, Vernonia amygdalina [32], Dicoma anomala [33], Psidium guajava [34], and Solanum incanum [35]), cancer (Taxus brevifolia, Podophyllum peltatum [36], and Catharanthus roseus [37]), malaria (Plumbago indica, Garcinia mangostana, Dioscorea membranacea, Artemisia annua, Piper chaba, Myristica fragrans, and Kaempferia galangal) [38], HIV/AIDS (Geranium phaeum, Sambucus racemosa [39], Tuberaria lignosa, and Sanguisorba minor magnolia [40]), schizophrenia (Abrus precatorius, Acacia ataxacantha, Adansonia digitata, Datura innoxia, Ficus sycomorus, Parkia biglobosa, and Ximenia Americana) [41], tuberculosis (Adhatoda vasica, Alpinia galangal, and Ocimum sanctum) [42], microvascular and macrovascular disorders (Anisodus tanguticus, Salvia miltiorrhiza [43], Camellia sinensis, Castanospermum australe, Curcuma longa, Ocimum santum [44], Stigma maydis [45], Spondias mombin [46], and Gazania krebsiana [47]), etc., studies are also in the forefront on the evaluation of plants against the neglected tropical diseases (NTD). **Table 1** presents some of the medicinal plants with reported significant efficacy against the NTDs.

Disease/infection	Selected plants for treatment	Reference
Buruli ulcer Acacia nilotica, Ageratum conyzoides, Albizia zygia, Allium sativum, Capsicum annuum, Cassia alata, Chalcas exotica, Carica papaya, Dysphania ambrosioides, Moringa oleifera, Nauclea latifolia, Pergularia daemia, Psidium guajava, Spondias mombin, Zingiber officinale		[66, 67]
Chagas disease	Argemone ochroleuca, Capparis spinosa, Commicarpus grandiflorus, Cucumis prophetarum, Euphorbia ammak, Hypoestes forskaolii, Kleinia odora, Marrubium vulgare, Peganum harmala, Psiadia punctulata, Ricinus communis, Solanum villosum, Tribulus macropterus, Withania somnifera	[68]
Dengue and chikungunya	Aloysia gratissima, Andrographis paniculata, Artemisia douglasiana, Citrus limon, Cymbopogon citratus, Cleome aculeata, Eupatorium catarium, Heterotheca latifolia, Hyptis mutabilis, Lantana grisebachii, Momordica charantia, Ocimum sanctum, Pelargonium citrosum, Senna angustifolia, Tridax procumbers, Vernonia cinerea	[69–71]
Dracunculiasis	Moringa oleifera	[72]
Echinococcosis	Azadirachta indica	[73]
Foodborne trematodiasis	Artemisia annua	[74]
Helminthiasis	Aloe ferox, Cassinopsis ilicifolia, Coddia rudis, Combretum molle, Elephantorrhiza elephantina, Gazania krebsiana, Hypoxis colchicifolia, Leonotis leonurus, Markhamia obtusifolia, Tulbaghia violacea	[75–81]
Leishmaniasis	Aloe vera, Chenopodium ambrosioides, Hyptis pectinata, Pfaffia glomerata, Ruta graveolens	[82]
Leprosy	Achyranthes aspera, Amaranthus spinosus, Aristolochia indica, Azadirachta indica, Calotropis gigantea, Eclipta alba, Ficus benghalensis, Jasminum grandiflorum, Michelia champaca, Piper betle, Thespesia populnea, Trichodesma indicum	[83]
Lymphatic filariasis	Acacia auriculiformis, Aegle marmelos, Centratherum anthelminticum, Ficus racemosa, Hibiscus mutabilis, Mallotus philippensis, Moringa oleifera, Sphaeranthus indicus, Zingiber officinale, Vitex negundo	[84–90]
Mycetoma	Acacia nilotica, Acacia nubica, Boswellia papyrifera, Citrullus colocynthis, Cuminum cyminum, Moringa oleifera, Nigella sativa	[91, 92]
Onchocerciasis	Annona senegalensis, Anogeissus leiocarpus, Polyalthia suaveolens, Discoglypremna caloneura, Homalium africanum, Khaya senegalensis, Margaritaria discoidea, Parquetina nigrescens	[93–96]
Rabies	Amarantheus spinosus, Croton macrostachyus, Phytolacca dodecandra	[97, 98]
Scabies	Abelmoschus esculentus, Aegle marmelos, Boerhavia diffusa, Clerodendrum infortunatum, Heliotropium indicum, Pongamia pinnata, Phyllanthus emblica, Schleichera oleosa	[99, 100]
Schistosomiasis	Abrus precatorius, Allium sativum, Citrus reticulata, Pterocarpus angolensis, Ozoroa insignis, Vernonia amygdalina	[101–104]
Snakebite envenoming	Allium cepa, Areca catechu, Aristolochia shimadai, Byrsonima crassa, Casearia sylvestris, Davilla elliptica, Delonix elata, Eclipta prostrata, Emblica officinalis, Hemidesmus indicus, Schumanniophyton magnificum, Vitis negundo	[105–107]
Taeniasis	Capillipedium foetidum, Cymbopogon nardus, Cyperus rotundus, Gardenia lucida, Hedychium coronarium, Hedychium spicatum, Inula racemosa, Litsea chinensis, Pistacia integerrima, Randia dumetorum	[108–111]
Trachoma	Abrus precatorius, Aloe marlothii, Calpurnia aurea, Dodonaea viscosa, Erythrina abyssinica, Eucomis pallidiflora, Gethyllis namaquensis, Hypoxis obtusa, Kleinia longiflora, Primula auriculata, Protea caffra, Terfezia claveryi, Tinospora smilacina, Tribulus terrestris, Ziziphus mucronata	[112–118]

Disease/infection	Selected plants for treatment	Reference(s)
Trypanosomiasis	Acacia nilotica, Allium sativum, Albizia gummifera, Bombax buonopozense, Heterotis rotundifolia, Morinda lucida, Pterocarpus erinaceus, Securinega virosa, Terminalia avicennioides, Vernonia subuligera, Ximenia americana, Zanthoxylum zanthoxyloides	[119–125]
Yaws	Alafia multiflora, Boerhavia diffusa, Commicarpus plubaginieus, Dioscorea hispida, Hibiscus diversifolius, Indigofera hirsuta, Spondias mombin, Strychnos ignatii	[126]

Table 1.Some selected medicinal plants used against neglected tropical diseases.

4. Drugs (medicine) discovered from natural sources and development

The development of new drug is a complex, time-consuming, and expensive process (**Figure 1**). The time taken from discovery of a new drug to its reaching the clinic is approximately 12 years, involving more than 1 billion US dollars of investments in today's context [48]. Essentially, the new drug discovery involves the

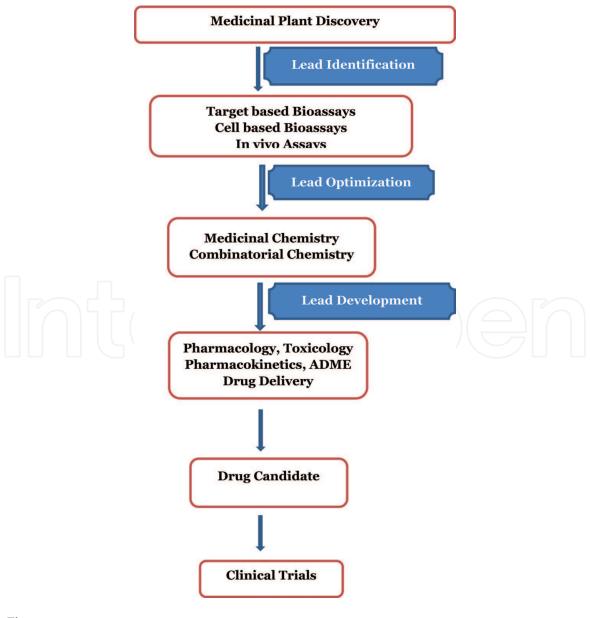


Figure 1.Modern drug discovery and development processes from the medicinal plant [127].

identification of new chemical entities (NCEs), having the required characteristic of drug ability and medicinal chemistry. These NCEs can be sourced either through chemical synthesis or through isolation from natural products. Initial success stories in new drug discovery came from medicinal chemistry inventions, which led to the need of development of higher number of chemical libraries through combinatorial chemistry. This approach, however, was proven to be less effective in terms of overall success rate. The second source of NCEs for potential use as drug molecules has been the natural products. Before the advent of high throughput screening and the post genomic era, more than 80% of drug substances were purely natural products or were inspired by the molecules derived from natural sources (including semisynthetic analogs) [49]. There are various examples of development of new drugs from the plant sources. Morphine was isolated from opium produced from cut seed pods of the poppy plant (Papaver somniferum) approximately 200 years ago [50]. Pharmaceutical research expanded after the Second World War to include massive screening of microorganisms for new antibiotics, inspired by the discovery of penicillin [50]. Few drugs developed from natural sources have undoubtedly revolutionized medicine like antibiotics (e.g., penicillin, tetracycline, erythromycin), antiparasitics (e.g., avermectin), antimalarials (e.g., quinine, artemisinin), lipid control agents (e.g., lovastatin and analogs), immune-suppressants for organ transplants (e.g., cyclosporine, rapamycins), and anticancer drugs (e.g., paclitaxel, irinotecan) [51].

The WHO has estimated that the majority of the populations in Africa, Asia, and Latin America still use TM for their primary health care needs [52]. In industrialized countries, plant-based TM or phytotherapeuticals are often termed complementary or alternative medicine (CAM), and their use has increased steadily over the last 10 years [53]. In the USA alone, the total estimated "herbal" sale for 2005 was \$4.4 billion, a significant increase from \$2.5 billion in 1995 [54] while also accounting for an estimated 1 billion Malaysia ringgit annually [55]. However, such "botanical dietary supplements" are regulated as foods rather than drugs by the United States Food and Drug Administration (US FDA) [54].

5. Recent developments of plant-derived active compounds in drug development

With the recent interest in molecular modeling, combinatorial chemistry, and other synthetic chemistry techniques by pharmaceutical companies and funding organizations, natural products, and particularly medicinal plants, remains an important source of new drugs, new drug leads, and NCEs [56]. In both 2001 and 2002, approximately one quarter of the bestselling drugs worldwide were natural products or derived from natural products. Some of the plant-derived drugs and their significance are listed in the **Table 2**. Many plant-derived compounds have been used as drugs, either in their original or semisynthetic form. Recent developments in drug discovery from plants, including information on approved drugs and

S/N	Compound	Plant name	Classification	Biological function
1	Aescin	Aesculus hippocastanum	saponins	Anti-inflammatory, vasoconstrictor and vasoprotective effects
2	Ajmalicine	Rauwolfia spp., Catharanthus roseus, and Mitragyna speciosa	alkaloid	Antihypertensive drug used in the treatment of high blood pressure

S/N	Compound	Plant name	Classification	Biological function
3	Berberine	Berberis vulgaris	alkaloid	Treatment for bacillary dysentery
4	Colchicine	Colchicum autumnale	alkaloid	Antitumor agent
5	Curcumin	Zingiberaceae	phenols	dietary supplement
6	Emetine	Cephaelis ipecacuanha	alkaloid	Amoebicide, emetic
7	Hesperidin	Citrus species	Flavonoid	Treatment for capillary fragility
8	Lapachol	Handroanthus impetiginosus	phenols	Anticancer, antitumor
9	Nordihydroguaiaretic acid	Larrea tridentata	phenols	Antioxidant activity
10	Quinine	Cinchona officinalis	alkaloid	Antimalarial drug

Table 2.Selected compounds derived from medicinal plants.

plant extracts or compounds now in clinical trials, are available [57]. It is anticipated that in the future, plant-derived compounds will still be an essential aspect of the therapeutic array of medicines available to the physician [57].

6. Importance of phytotherapy (for diseases control) within the global health care system

Phyto (plants in the form of leaves, flowers and roots) therapy (treatment) has continued to reflect a great deal of significance in health care around the world in curing diseases while also ensuring a good state of health and/or conditions is maintained. In fact, a significant proportion of the entire global populace had found solace in phytomedicine, embracing it as a major source for their health care system as maintained by WHO in one of their submissions; hence, presenting the impact or relevance of herbal therapy in this chapter cannot be out of context with regard to medicine or medicinal products emanating from these MPs such as Papaver somniferum, Cinchona, Hibiscus sabdariffa, Rosmarinus officinalis, Nigella sativa, Artemisia afra, Vatica rassak, etc., some (about 5000 out over 250,000) had either being developed (as drugs or vaccines) and commercialized (morphine, quinine, ephedrine, etc.) and many others in the final process of drug development [2] for confirmation of safety and efficacy (clinical trials) against avalanches of illnesses including but not limited to hypertension, asthma, malaria, pain, hemorrhage, psychosis, cancer, migraine, etc. [58, 59]. This makes herbal medicine to become a basic health service to people of diverse culture irrespective of their status (poor or rich) and location (remote or urban), and this acceptance (in use either singly or combination with orthodox medicine) has continued to escalate in recent times [60], thereby complementing or reducing the use of modern medicine (despite its availability) probably due to inadequacies in providing holistic healing where behavioral, emotional, and/or spiritual factors are the underlying causes of the diseases [61]. In view of the foregoing, continents such as Asia, Africa, and Latin America with countries such as China, India, etc., had embraced the adoption of the two systems (phytotherapy and modern medicine) for their national health care needs. Although issues of safety, efficacy, and quality of herbal medicines have undermined their integration into national health care policy in some countries, this had not prevented, in any big amount, the popular use by the citizenry. Interestingly too, because MPs are core sources for pharmaceutical manufacturing, they in addition to herbal medicines play an important role in pharmaceutical market (PM). In fact, in a reported submission, in 1995, they occupied 33.1% of the total PMs [55].

7. Shortcomings (if available) of phytomedicine to the conventional or modern medicine

Globally, the high demand of use for herbal medicine for the treatment of illnesses is undisputable, and one begs to ask or wonder whether these products are actually of good quality, safe, and effective. There are assumptions and/or claims that despite general usage, few of them have been attributed to illnesses and fatalities as some of them have reported to cause liver and kidney damage [62–64]. In fact, this was also attributed to why they have not been globally accepted as par with conventional medicine within the national health care policy of many countries. The reason for this was not far-fetched. A lot of people believed that many herbal formulations lacked safety evaluations such as clinical trials as to why they cannot be placed in the same pedigree with modern medicine, but this was somehow disagreed by some researchers and/or policy makers who opined that clinical trials may be conducted only when large batches are intended. Additionally, in clinical practice, the failure to integrate phytotherapy as one of the courses or modules in medical school was seen in some quarters as the reason why it became somehow extremely difficult for medical practitioners to prescribe it, hence, the advantage convention medicine enjoys nowadays. Other problems include but not limited to storage conditions, inexplicit dosage, wrong labeling information, individualization of prescription with numerous active ingredients and other components, lack of information on the industrial use of MPs, little or no fact on the market benefit and business potentials, etc. [65]. It is worthy of mention that despite these limitations, phytotherapy had the potentials in salvaging numerous human diseases.

8. Conclusion

The use of phytotherapy in preventing or curing ill-effects faced by mankind was established by the great roles played by natural products obtained from MP. With continued efforts in research and utilization of HM on daily basis, it is envisioned that it would attain its rightful place and be embraced as efficient system worthy of acceptance within the global health care practice.



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