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REVIEW ARTICLE

PLANT BASED MEDICINES: CURRENT TRENDS

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ABSTRACT

Medicinal systems in India when traced back to 5000 BC coincide with the emergence of the Indus Valley civilization around 4500 BC, where agriculture was given much importance. As per the ancient traditions, local communities in every ecosystem starting from the Himalayas down to the coastal plains have discovered the medical uses of thousands of plants found locally in their respective ecosystem. India has one of the richest medical plant cultures in the world. It is a culture that is of tremendous contemporary relevance because it can on one hand ensure health security to millions of people and on the other hand it can provide new and safe herbal drugs to the entire world. It is estimated that there are around 25000 effective plant based formulations used in folk (rural) medicine and known to rural communities all over India and around 10000 designed formulations are available in the indigenous medical texts. Ayurved and Siddha System are probably more than 4000 years old. Charak Samhita (500 BC) the classical, ancient *Pharmacopeias* were complied on the basis of knowledge obtained from Atharveda. It is estimated that as many as 3226 communities out of 4775 communities in India (70%) are dependent on plant based medicines. The main reasons for wide spread use of plant based medicines in AYUSH (Ayurvedic, Yoga, Unani, Siddha and Homeopathy) of ISM include: Efficacy and Safety of the medicine, cultural acceptability, availability, lesser side effects, high sensitivity to disease causing entities (bacteria, fungi, viruses, worms etc.) and above all, the cost effectiveness as compared to allopathic medicines and western system of medicines. In spite of extensive use ofMedicinal and Aromatic Plants(MAPs) in AYUSH and obvious advantages over allopathic medicines, the turnover of Indian herbal medicinal industries is a meagre sum of about Rs. 2300 Crores as against that of allopathic pharmaceutical industry of Rs. 14500 Crores, with a 15% per annum growth rate for ISM.

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INTRODUCTION

Nature made human and bestowed countless favours. Paradoxically, illness, diseases, complications, inconsistencies and disorders grew slowly. The creator has not made any disease without any cure for it and graced the earth with numerous plants, especially for healing. It has been the necessity of man, which made him trace out the cure from the nature itself. Due to the safe status of plant based medicines, they are in great demand in the developing as well as developed countries for primary and/or daily health care. Majority of Indian population have access to or practice various traditional medicines to maintain health or treat diseases. These include herbs that can be used either as mono-therapy or as add-on therapy. But the most important challenge faced by these formulations arises due to lack of standardization, identification and pharmacopoeial standards (Ali *et al*., 2009). It is thus prudent to undertake the standardization of plant based medicines used in various healthcare systems. Moreover, plant based medicines are prepared from materials of natural origin which are prone to contamination, detoriation and variation in composition. There is a pressing need for evaluation and analysis of plant based drugs using sophisticated techniques (Chopra and Doiphode, 2002). Medicinal plants constitute an effective source of traditional (Ayurvedic, Chinese, Homeopathic and Unani) and modern medicine. Germany and France, together represent 39% of the $14 billion global retail market. Today, approximately 70% of synthetic medicines are derived from plants. India's herbal and traditional medicine industries have annual turnover of about Rs. 4000-6000 crore markets and have big export potential. For export to western countries, America and Canada, their strict quality parameters and quality controls and safety and efficacy are required (Waxler *et al*., 1988). India is one of the most important countries in the world in term of floristic diversity. About 54% of the country's land is under cultivation for food, ornamental and medicinal plant crops and

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approximately 19% area has varying degree of forest vegetation cover. Land based developmental activities provide means of livelihood, health and opportunity for employment. India has global position in the field of traditional medicines. About 90% herbal raw drugs used in the manufacture of vegetable drugs are obtained from the wild source which is limited. There are about 45,000 plants species in India which are in abundant in the regions of eastern Himalaya, Western sea coaste and Andman and Nicobar Islands. The rich heritage of flora is due to diversified and varied agro-climatic conditions. The official documented plants with medicinal potential are 3,000 but traditional practitioner use about 8,000 vegetable drugs. India is the largest producer of medicinal herbs and approximately called the botanical garden of the world (Patwardhan *et al*., 2004). In Indian medicinal systems the most practitioners formulate and dispense their own recipes; hence, this requires proper documentation and research. There are currently about 2, 50,000 registered medical practitioners of the Ayurvedic system; the total for all traditional systems being nearly 2,91,000 as comparable to 7,00,000 of the modern medicines. In rural India, 70% of the population is dependent on the traditional system of medicine. In western world also the practitioner of herbal medicines is steadily growing and approximately 40% of the population is taking herbs to treat diseases (Akerele *et al*., 1993). Plant based drugs can be used directly, i.e., they may be collected, dried and used as therapeutic agents (crude drug), or their constituents/active principles separated by various chemical processes, which are employed as medicines. The active principle or compounds with similar structure and activity are manufactured chemically to produce the synthetic drugs used in allopathic or modern system of medicine (Gadre *et al*., 2001). Intensive phytochemical and pharmacological research efforts are underway worldwide to screen plants for active compounds and to develop new pharmaceutical products. These developments raised a number of important, controversial, ethical and legal issues related to intellectual property rights. Today, and in the decades to come, there is an urgent need to find out an equitable resolution, if future development of plant based drugs, be they traditional, modern or more likely a hybrid of the two, is ever to serve the diverse health care needs of our global society (Grabley *et al*., 1999; Clark *et al*., 1996).

Importance of plants and plant derived products

About 130 pure chemical substances extracted from some 100 species of higher plants are used in medicines throughout the world. According to a 1994 United Nations Development Project (UNDP) report, the annual value of medicinal plants derived from developing countries is about $32 billion (Rs.3200,000 crore). Theoretically, there is the possibility of discovering 328 new modern drugs lying hidden in nearly 3, 25,000 species found in tropical rain forests. There are 47 major modern plant based drugs in the world market and the predicted 328 more potential drugs have an estimated value of $147 billion. There is massive wealth available in these collections, but what is coming in the way is the lack of standardized products, lack of reliable production technologies and the absence of pharmacological profile of drugs (Chaudhary *et al*., 1996). The importance of plants in Eastern Europe, Africa, South America, southern and central Asia countries have amalgamated the modern medicine with traditional medicine and at least 60% of the prescriptions issued in such countries contain one or more plant products (Hamburger *et al*., 1991). Plant secondary metabolites are not only useful as potential drugs in their natural unmodified form but are also suitable as synthetic intermediate substances for the production of useful drugs.

The readily available plant steroid, diosgenin, from several species of yams (Dioscorea) and hecogenin from Sisal leaves (*Agave sisalana*) may be synthetically converted to steroids with anabolic, anti-inflammatory and oral contraceptive activities (Balandrin *et al*., 1985). Secondary metabolites tend to be biosynthesized in specialized cell types, at only some of the life stages of the plant and are usually accumulated in much lower quantities than primary metabolites (Balandrin *et al*., 1988). Among the secondary metabolites used as therapeutic agents are alkaloids, anthraquinone glycosides, cardiac glycosides and lignans whose biosynthetic precursors are amino acids, polypetides, isoprenoids and shikimate derived compounds, respectively (Tyler *et al*., 1988; Fransworth *et al*., 1985).

Current and future prospects of plant based drugs

The interest in Nature as a source of potential chemotherapeutic agents continues. Natural products and their derivatives represent more than 50% of all the drugs in clinical use in the world. Higher plants contribute no less than 25% of the total. During the last 40 years, at least a dozen potent drugs have been derived from flowering plants including *Dioscorea*species derived diosgenin from which all anovulatory contraceptive agents have been derived; reserpine and other anti-hypertensive and tranquilizing alkaloids from *Rauwolfia* species; pilocarpine to treat glaucoma and dry mouth, derived from a group of South American trees (*Pilocarpus species*) in the Citrus family; two powerful anti-cancer agents from the Rosy Periwinkle (*Catharanthusroseus*); laxative agents from Cassia species and as a cardiotonic agent to treat heart failure from Digitalis species. Approximately half (125,000) of the world's flowering plant species live in the tropical forests (Ameenah *et al*., 2006). Tropical rain forests continue to support a vast reservoir of potential drug species. They continue to provide natural product chemists with invaluable compounds of starting points for the development of new drugs. The potential for finding more compounds is enormous as at date only about 1% of tropical species have been studied for their pharmaceutical potential. This proportion is even lower for species confined to the tropical rain forests. To date about 50 drugs have come from tropical plants. The existence of undiscovered pharmaceuticals for modern medicine has often been cited as one of the most important reasons for protecting tropical forests, so the high annual extinction rate is a matter for concern, to say the least (Abdin *et al*., 2003).

There is a growing interest in herbal drugs, and as an example of this, the consumption of medicinal plants has doubled in the last ten years in Western Europe. Use of medicinal plants is expected to raise globally, due to increasing trend towards self-medication, reduction in costs of subsidized health care,

various international and national organizations improving the status of plant based medicine industry and renewed interest of companies in isolating useful compounds from the plants. It implies increasing pressure on wild plant resources and, therefore, the need for serious conservation efforts including development of cultivation techniques has never been greater. Serious over-exploitation of many medicinal plants such as *Rauwolfia*, *Dioscorea, Swertiachirata, Valeriana, Orchis* and *Harpagophytumprocumbens* has already occurred (Wagner *et al*., 1990).

This traditional role of international organization and universities is one that has considerable potential for expansion, so far as medicinal plants are concerned. There are some aspects of particular relevance for the rational utilization of medicinal plants and other natural products. Significant progress over the next few years will depend on the imagination and determination, which can be brought to bear on the subject (Hamberger *et al*., 1991). Modern instrumentation and biological assay methods provide the possibility of developing suitable quality control criteria for plant based drugs. The structural determination of novel plant constituents can be performed with minimal delay by using a combinationof sophisticated spectroscopic (UV, FT-IR, ^{1}H NMR, ^{13}C NMR, Mass spectroscopy) and X-ray crystallographic techniques. High-throughput automated bioassays are widely available, so that a detailed biological profile can be obtained easily on just a few milligrams of a natural product. Thus, there is every indication that the direct utility and promise of plants for the improvement of human health will continue well into the 21st century (Kinghorn *et al*., 1993).

Quality control and quality assurance of plant based drugs

Plant materials and herbal remedies derived from them represent substantial portion of global market and in this respect internationally recognized guidelines for their quality control are necessary. WHO has recognized the need to ensure quality control of medicinal plant products by using modern techniques and by applying suitable standards. Several Pharmacopoeias including Indian Pharmacopoeia, British Pharmacopoeia, Pharmacopoeia of Republic of China, Japanese Pharmacopoeia and United State Pharmacopoeia do cover monograph and quality control test for few of medicinal plants used in the respective countries but basically these pharmacopoeia are designed to cater to chemical based medicine and pharmaceutical necessities by giving their standards and test methods. For pharmaceutical purpose, the quality of medicinal plant materials must be as high as that of other medicinal preparations.

However, it is impossible to assay for specific chemical entity, when the bioactive ingredient is not known. Further problem is posed by those preparations, which contain heterogeneous mixtures. Directive on the analytical control of vegetable drug must take account of the fact that material to be examined has complex and inconsistent composition. Therefore, the analytical limits cannot be as precise as for the pure chemical compound (Gruenwald *et al*., 2008). Vegetable drugs are inevitably inconsistent because of their composition and hence the standardization may be influenced by several factors such as age and origins, harvesting period, method of drying and so on. To eliminate some of the causes of inconsistency, one should use cultivated rather than wild plant, which are often heterogeneous in respect of the factors and consequently in their content of active principles (Gupta *et al*., 2003).

Challenges in drug discovery from medicinal plants

In spite of the success of drug discovery programmes from plants in the past 2-3 decades, future endeavours face many challenges. Natural products scientists and pharmaceutical industries will need to continuously improve the quality and quantity of compounds that enter the drug development phase to keep pace with other drug discovery efforts. The process of drug discovery has been estimated to take an average period of 10 years and cost more than 800 million dollars (Dickson *et al*., 2004). Much of this time and money is spent on the numerous leads that are discarded during the drug discovery process. It is estimated that only one in 5000 lead compounds will successfully advance through clinical trials and be approved for use. In the drug discovery process, lead identification is the first step. Lead optimization (involving medicinal and combinatorial chemistry), lead development (including pharmacology, toxicology, pharmacokinetics, ADME and drug delivery), and clinical trials all take considerable time (Jachak, *et al*., 2007).

The objective of the research approach is the targeted isolation of new bioactive plant products, i.e., lead substances with novel structures and novel mechanisms of action. This approach has provided a few classical examples, but the problem most often encountered here is not enough availability. The problem of availability can be overcome by semi-synthesis/synthesis or using tissue-culture techniques (by genetically modifying the biosynthetic pathway of the compound of interest). As drug discovery from plants has traditionally been time-consuming, faster and better methodologies for plant collection, bioassay screening, compound isolation and its development must be employed (Koehn *et al*., 2005). The design, determination and implementation of appropriate, clinically relevant, high-throughput bioassays are difficult processes for all drug discovery programmes (Knowles *et al*., 2003; Kramer *et al*., 2004). Although the design of high-throughput screening assays can be challenging, once a screening assay is in place, compound and extract libraries can be tested for biological activity (Walters *et al*., 2003). Challenges in bioassay screening remain an important issue in the future of drug discovery from medicinal plants. Natural products, in general, are typically isolated in small quantities that are insufficient for lead optimization, lead development and clinical trials. Thus, there is a need to develop collaborations with synthetic and medicinal chemists to explore the possibilities of its semi-synthesis or total synthesis (Federsel, 2003; Ley and Baxendale, 2002; Lombardino and Lowe, 2004). One can also improve the natural products compound development by creating natural products libraries that combine the features of natural products with combinatorial chemistry (Federsel *et al*., 2003).

Worldwide trade of plant based drugs

The global market for herbal medicines currently stands at over $ 60 billion annually. The sale of herbal medicines is expected to get higher at 6.4% an average annual growth rate (Inamdar *et al*., 2008). Due to the contribution of numerous significant factors, the market of herbal medicines has grown at an expressive rate worldwide. Since millions of people all over the world have been using herbal medicines for thousands of years; great interest in alternative medicines; preference of populations for preventive medicine due to increasing population age; the belief that herbal medicines might be of effective benefit in the treatment of certain diseases where conventional therapies and medicines have proven to be inadequate; tendency towards self-medication; improvement in quality, proof of efficacy and safety of herbal medicines and high cost of synthetic medicines (Inamdar *et al*., 2000). According to World Health Organization, herbal medicines are lucrative globally and they represent a market value of about US $ 43 billion a year (Christie *et al*., 2001).

According to an estimate in 1991, the plant based medicine market in the European countries was about $ 6 billion, with Germany accounting for $ 3 billion, France $ 1.6 billion and Italy $ 0.6 billion while in other countries was 0.8 billion. In 1996, the plant based medicine market in the European countries was about $ 10 billion, in USA about $ 4 million, in India about $ 1.0 billion and in other countries was $ 5.0 billion (Prajapti *et al*., 2003). In 1997, the European mark*et al*one reached about $ 7.0 billion. The German market corresponds to about 50% of the European market, about $ 3.5 billion. This market is followed by France, $ 1.8 billion; Italy, $ 700 million; the United Kingdom, $ 400 million; Spain, $ 300 million; the Netherlands, about $ 100 million (Pushpangadan *et al*., 2005).

Current status of complementary and alternative medicine (CAM) utilization

Botanicals and natural supplements now a days considered in various disease ailments. Natural compounds in the treatment of arthritis may also be regarded as a part of CAM (Complementary and Alternative Medicine) and these are now widely accepted worldwide. CAM therapies includes diet modification, Ayurveda, homoeopathy, chiropractic, acupuncture, wearing of copper bracelets, magnetotherapy, use of botanical herbs, and vitamins/mineral supplements, based on the belief that modern medicines have no cure for RA and adverse reactions are rare with CAM. Because of these and other limitations the use of CAM therapies such as acupuncture and extracts of medicinal herbals is on the rise and according to reports ~60-90% of dissatisfied arthritis patients are likely to seek the option of CAM therapy (Jubie *et al*., 2008). Herbal medicines are the root of various traditional medicines systems around the world. An increasing number of people in US as many as 42% use CAM approaches to help meet their personal health problems (Volluri *et al*., 2011). Many plants and plant products are under scientific exploration novel therapeutic agent. Arthritis is one of the foremost disease for which patient seeks the CAM option worldwide. In Australia the figure is 20-48% Canada has a figure of CAM utilization which is around 11-32%. Then comes India, amongst next CAM users i.e. somewhere around 33%. Israel is reported to bear the least figure of CAM users i.e. 6% only. Netherlands comparatively has a good CAM utilization figure of 16%. UK shows the CAM utilization about 25-73%. Then France has 36% CAM utilization and South Africa shows 38% CAM utilization figure. In India 43-72% people use CAM and in US 18-94% people are using CAM. Australian rheumatic patients use 40-82% CAM. In Germany CAM users are 72% and in Canada 62% (Viji *et al*., 2011).

Conclusion

In recent years, there has been a phenomenal rise in the interest of scientific community to explore the pharmacological actions of herbs or to confirm the claims made about them in the official books of herbal traditional medicine (Nadkarni *et al*., 1996). The emerging importance of biologically active medicinal plants and their constituents as possible therapeutic measures has become a subject of active scientific investigation. It is likely that in future safe and effective medicines will be developed from medicinal plants to treat various degenerative diseases.

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