

Global promotion of herbal medicine: India's opportunity

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Due to side effects of synthetic products, herbal products are gaining popularity in the world market. In spite of well-practised knowledge of herbal medicine and occurrence of a large number of medicinal plants, the share of India in the global market is not up to the mark. The present article deals with the measures to be adopted for global promotion of Indian herbal products.

MEDICINAL herbs are moving from fringe to mainstream use with a greater number of people seeking remedies and health approaches free from side effects caused by synthetic chemicals. Recently, considerable attention has been paid to utilize eco-friendly and biofriendly plant-based products for the prevention and cure of different human diseases. Considering the adverse effects of synthetic drugs^{1,2}, the Western population is looking for natural remedies which are safe and effective. It is documented that 80% of the world's population has faith in traditional medicine, particularly plant drugs for their primary healthcare.

India is sitting on a gold mine of well-recorded and traditionally well-practised knowledge of herbal medicine. This country is perhaps the largest producer of medicinal herbs and is rightly called the botanical garden of the world. There are very few medicinal herbs of commercial importance which are not found in this country. India officially recognizes over 3000 plants for their medicinal value. It is generally estimated that over 6000 plants in India are in use in traditional, folk and herbal medicine, representing about 75% of the medicinal needs of the Third World countries³. Three of the ten most widely selling herbal medicines in the developed countries, namely preparations of *Allium sativum*, *Aloe barbedensis* and *Panax* sp. are available in India. There are about 7000 firms manufacturing traditional medicines with or without standardization.

Medicinal herbs have been in use in one form or another, under indigenous systems of medicine like Ayurveda, Sidha and Unani. India, with its traditional background, needs to increase its share in the world market. But unlike China, India has not been able to capitalize on this herbal wealth by promoting its use in the developed world, despite their renewed interest in herbal medicines. This can be achieved by judicious product identification based on diseases prevalent in the developed world for which no medicine or palliative therapy is available. Such herbal medicines will find speedy access into those countries.

Undoubtedly, the plant kingdom still holds many species of plants containing substances of medicinal value which have yet to be discovered. India is a land of immense biodiversity in which two out of eighteen hot spots of the world are located. India is also one of the twelve mega biodiversity countries in the world. The total number of plant species of all groups recorded from India is 45,000 (the total number may be even close to 60,000, as several parts of India are yet to be botanically explored). Of these, seed-bearing plants account for nearly 15,000–18,000. India enjoys the benefits of varied climate, from alpine in the Himalaya to tropical wet in the south and arid in Rajasthan. Such climatic conditions have given rise to rich and varied flora in the Indian subcontinent.

In order to promote Indian herbal drugs, there is an urgent need to evaluate the therapeutic potentials of the drugs as per WHO guidelines⁴. Ironically, not many Indian products are available in standardized form, which is the minimum requirement for introducing a product in the Western market.

Are pharmaceutical firms responsible for low market?

Adulteration in market samples is one of the greatest drawbacks in promotion of herbal products from India. Plant samples in the market are stored under undesirable conditions over the years, and often contain a mixture of other plant species⁵, thus adversely affecting their bioefficacy. The efficacy of many of drugs is fading because of the adulterated, dried raw materials profusely available in the indigenous market⁶. Due to this adulteration and altered efficacy, the faith in crude drug promotion has declined⁷. Desire for quick returns by some of the pharmaceutical firms by not processing the herbal materials in a proper way, is the major cause of decline of Ayurveda in India. It also adversely affects the global promotion of Indian herbal products. Workers in these firms frequently lack the knowledge and skill required in processing. The common examples which are well known are substitution of the bark of *Holarrhena antidysentrica* by *Wrightia tictoria*, and *Saraca indica* by *Trema orientalis*⁸.

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Mycotoxin elaboration in stored drug samples

It has been reported that the stored drug samples harbour mycotoxin-producing fungi in high frequency⁹⁻¹¹. Degradation of alkaloids and medicinally valuable secondary metabolites of stored plant drugs due to fungal infestations has been reported. WHO has also paid serious attention on mycotoxin contamination in herbal drugs, considering it as a global problem. However, its incidence is higher in tropical and subtropical countries as the harvesting practices and high temperature and moisture contents are conducive to fungal invasion and mycotoxin elaboration¹². Some of the powdered drugs bearing trademarks of standard Indian herbal firms have been reported to contain high concentration of aflatoxin B₁. Detection of mycotoxins (aflatoxin B₁, ochratoxin, citrinin and zearalenone) is certainly a matter of great concern in stored drugs of important medicinal plants, e.g. roots/rhizomes of *Asparagus racemosus* (0.16 µg/g), *Atropa belladonna* (0.27 µg/g), *Withania somnifera* (0.68 µg/g) *Plumbago zelanica* (1.13 µg/g); fruits of *Emblica officinalis* (up to 1.51 µg/g), *Terminalia chebula* (1.19 µg/g); seeds of *Macuna puriens* (1.16 µg/g)¹³. Such herbal drugs containing mycotoxins above the tolerance limit fixed by WHO for human consumption, will be certainly rejected in the global market. This is because of improper storage and processing of herbal drugs by Indian firms. The situation is alarming and appropriate quality-control measures have to be taken urgently. It would be, therefore, advisable to treat plant drugs with nontoxic chemicals at various stages of storage and processing.

Improper harvestation

Another major issue requiring immediate attention concerns the harvest of medicinal plants in appropriate seasons. The medicinal properties of plants vary with respect to different seasons. These properties may be restricted to one particular part of the plant. The age of the plant also decides its medicinal potency. Therefore, the authentic part of medicinal plants of a particular age should be harvested in a particular season before processing for drug manufacture, to avoid any alteration in its medicinal potency. The medicinal potency of an angiospermic taxon also varies among its populations occurring in different geographical localities. Besides, the period of storage in sun or shade conditions also affects medicinal properties of the plants. Precautions during harvestation of medicinal plants are not observed by most of the firms and it ultimately results in decline in efficacy of the herbal drugs.

Responsibility of research organizations and universities

Research needs to be enhanced to identify plants with potential medicinal value and to isolate compounds of medicinal importance. Every plant-based product should

be documented properly with regard to the identification of species and utilization of specific parts of the plant. Some of the common medicinal plants are known in different parts of the country by different names. 'Shankhpuspi' is an important medicinal plant. Different plants, viz. *Clitoria ternatea* Linn. in Kerala, *Canscora decussata* Schult. in Bengal, and *Convolvulus pluricaulis* Chois. and *Evolvulus alsinoides* Linn. in other parts of India are known as Shankhpuspi¹⁴. This type of confusion is also met with other medicinal plants. There is an urgent need of taxonomic databases of ethnomedicinal plants prepared in joint collaboration by Ayurvedic practitioners and experienced plant taxonomists. Correct taxonomic identification of medicinal plants before their processing for drug manufacture is an important aspect. Wrong identification of herbs has led to many cases of poisoning. *Boerhaavia diffusa* is used widely as a 'quality of life enhancer' in the traditional system of medicine. However, both *B. diffusa* and the plant *Trianthema portulacastrum* are known as 'Punarva', and so both the plants may be collected at the same time¹⁵ (see ref. 8, p. 163).

Most of earlier plant scientists attracted towards huge Indian flora, made extensive surveys and proposed their systems of classification. But in the present scenario of newly born modern disciplines in botany; taxonomy is treated as a neglected discipline. Even in most of the botany departments of Central Universities, no facilities are provided for herbaria of regional medicinal plants. There is a lack of trained personnel for both proper identification of plants and to teach plant taxonomy. So every university where botany is taught as a subject should have a well-maintained medicinal plant garden. Also, it should be their responsibility to conserve the rare medicinal plants of the area. Training the youth of the country in taxonomy of ethnomedicinal plants would help in developing such databases.

Safety profile assessment

Ayurvedic practitioners have not given much emphasis to the evaluation of adverse side reactions. The efficacy of some herbal products is beyond doubt. However, mutagenic and carcinogenic effects have been identified in some of these drugs. Although herbal medicines are widely used, cases of toxicity reported seem to be less. A commonly used drug, Licorice is reported to cause oedema and hypertension if used for a long time. Likewise Ginseng, one of the most widely used herbal drugs causes hypertension, gynaecomastia and vaginal bleeding¹⁵. Toxic materials like arsenic, mercury, lead, etc. have been detected from time to time in some herbs. The Food and Drug Administration, USA has banned utilization of many plants by human beings on this ground. Hepatotoxicity, nephrotoxicity and most critically, drug interactions with synthetic medicines are common in some of the herbal practices. One of the popular plants, *Acorus calamus*, has

been banned due to the presence of B-asarone, which has shown carcinogenic properties¹⁶. This plant is popular among Ayurvedic practitioners. The toxic effects of herbal drugs may also be because of adulteration, contamination by pesticides and their diseased state. WHO has laid down guidelines for determination of adverse reactions as essential requirements for human application. Keeping these facts in view, the safety limit profile of the herbal drugs should be recorded in order to popularize Indian pharma in the global market. The government and drug industry must come forward in funding and undertaking this task, so that good quality and safe herbal preparations are a reality.

Active principle identification and standardization

The identification of biologically active compounds is an essential requirement for quality control and dose determination of plant-based drugs. A medicinal herb can be viewed as a synthetic laboratory as it produces and contains a number of chemical compounds. These compounds, responsible for medical activity of the herb, are secondary metabolites. For example, alkaloids which are nitrogenous principles of organic compounds combine with acids to form crystalline salts. In addition, herbs may contain saponins, resins, oleoresins, lactones and volatile oils. Complete phytochemical investigations of most of the medicinally important herbs of India have not been carried out so far. This would be beneficial in standardization and dose determination of herbal drugs. Further, there should be a quality control test for the entire preparation to ensure the quality of the drug.

Bioprospecting of indigenous medicinal flora

Gene technology has given unlimited powers to developed countries to exploit the genetic resources of poor nations, leading to a situation of 'biopiracy' and 'gene robbing'. A number of herbs, viz. neem, haldi and ashwagandha and plant drugs of India have been patented by outsiders on the basis of secondary researches.

In such a putative situation, it is extremely important for the biodiversity-rich nations to build capabilities at least to know their biodiversity and prevent biopiracy. To achieve such a capability, it is a prerequisite to inventorize and document the bioresources, putting a price tag to them. More recently, the term bioprospecting has been widely used to assess the economic potential of different plant species. It would involve economics of sustainable utilization of our biodiversity. It can throw light on new classes of materials. Bioprospecting would be one of the challenging areas for future research in the 21st Century. It would enable us to make use of our rich biological heritage. Bioprospecting can enhance the conservation value of Indian medicinal plants. In addition, this would check illegal exploitation of such indigenous plants through

biopiracy or gene robbing by biotechnologically developed countries and would be helpful in many fold enhancement of Indian herbal medicine in the global market. If quick and urgent steps are not taken in bioprospecting our ethnomedicinal plants, the fate of some of the valuable Indian plants will be like that of neem and haldi.

Synergy in relation to pharmacological action of phytomedicines

There is no doubt that most herbs exhibit their effects on a variety of constituents and the idea of synergy within and between them is also gaining acceptance¹⁷. It is not well-documented in most of the herbal medicines whether they are acting truly in a synergistic way or by additive effects. Clinical evaluation is also difficult, without knowing the extent to which synergy occurs within the herbal preparations. Some of the components of the crude drugs may not have any biological activity, but may be the enhancers of potency of the active components. St. John's wort (*Hypericum perforatum*, family Hypericaceae) is one of the most important herbs of proven clinical efficacy as an antidepressant. Its activity is due to hypericins which are naphthodianthrone. It has also been suggested that pure hypericins are very weak and the positive results are due to impurities in the fraction used, which would suggest some polyvalent action as well as synergy. St John's wort thus represents a good example of a herb which may exhibit synergism and polyvalent action¹⁸. Ginger (*Zingiber officinale*) is another example of a chemically unstable range of compounds being responsible for the activity and probably acting synergistically¹⁹.

Synergism or enhancement of activity of herbal drugs is also possible using combinations of herbs. In case of multiple herb extracts, some of the herbs enhance the potency of the real effective herb. Besides, in some cases, herbs or their constituents reduce the toxic effects of the main medicinal herb, making the herbal combination safe for the human system²⁰. Our ancient Ayurvedic system relies on this principle. In order to promote Indian herb preparations in the global market, care should be taken during drug standardization. Appropriate proportions of each herb used in the formulation of more efficacious drugs should be taken, so as to get effective chemotherapeutic response. Synergism between herbal drugs may be also beneficial in the treatment of a disease caused due to multiple factors. Synergy in herbal medicine may lead to improved products and it would be better if new and improved drug formulations are prepared with some of the globally demanded drugs of Indian medicinal plants so that India may occupy a leading position in the world market of herbal drugs.

Conservation and sustainable exploitation

The unscrupulous collection of medicinal plants from wild habitats by traders has threatened the very existence of

valuable medicinal plant resources. Due to biopiracy and over exploitation, some of the ethnomedicinal plants are becoming rare. Reserves of medicinal plants are diminishing and are in danger of extinction due to unfriendly harvesting techniques, loss of growth habitat and their unmonitored trades. *Coleus forskohlii*, an Indian species is now listed as vulnerable to extinction in the wild as a result of indiscriminate collection for the isolation of forskolin, a diterpenoid used in the treatment of glaucoma and heart disease²¹. Some important species that need immediate attention for conservation in India are *Aconitum deinorrhizum*, *A. heterophyllum*, *Angelica glauca*, *Arnebia benthemii*, *Artemisia brevifolia*, *A. maritime*, *Atropa acuminata*, *Berberis aristata*, *Colchicum luteum*, *Corydalis govaniana*, *Dactylorhiza hatagirica*, *Dioscorea deltoidea*, *Ephedra gerardiana*, *Ferula jaeschkeana*, *Gentiana kurroa*, *Hedychium spicatum*, *Jurinea dolomi-aeae*, *Nardostachys jatamansi*, *Orchis latifolia*, *Picrorrhiza kurroa*, *Podophyllum hexandrum*, *Rheum emodi*, *Swertia chirata*, *Valeriana wallichii* and *Zanthoxylum alatum*²². These are important medicinal plants and their conservation in sustainable environment is urgently needed, keeping in view the demand of their drugs in the global market.

Cultivation of wild medicinal plants

Both wild and cultivated plants are used for drug formulation. However, in many cases cultivation is advisable because of the improved quality of the drug. The efficacy of medicinal herbs is affected by different environmental factors. Temperature, rainfall, day length and soil characteristics are some of the factors which affect the potency of the medicinal plants. A plant may grow well in different situations, but fail to produce the same constituents (e.g. *Cinchonas* growing at altitudes and in plains). The cultivation of some medicinal plants in demand under appropriate environmental conditions will provide (i) better development of plants owing to improved conditions of the soil, pruning, and control of insect pests, and (ii) better facilities for treatment after collection. For example, drying at a correct temperature in the case of colchicum, belladonna and valerian.

For success in cultivation it is necessary to study the conditions under which the plants flourish in the wild state and reproduce these conditions or improve on them. India is satisfactorily cultivating some wild medicinal herbs. Several research institutes have undertaken studies on the cultivation practices of medicinal plants, which were found suitable and remunerative for commercial cultivation. The agronomic practices for growing poppy, senna, cinchona, belladonna and a few other plants have been developed. One should start cultivation of some more globally important medicinal herbs which are endemic to India or comparatively grow more luxuriantly in this country. India has a huge unused saline land in its sea

coast and it should develop agrotechnological procedures to use such land for cultivation of medicinal plants.

Quality control during collection and processing

The season at which each drug is collected is a matter of considerable importance. The amount and nature of active constituents is not constant throughout the year. The age of the plant is also of considerable importance and governs not only the total quantity of the active constituents produced, but also the relative proportions of the active principles. Duration of the drying conditions of the harvested medicinal herb also varies from a few hours to many weeks^{21,23}. If enzyme action is to be encouraged, slow drying at moderate temperatures is necessary. Storage of the harvested plant parts under hygienic conditions is another important factor to be considered during processing of the drug. Drugs such as Indian hemp and sarsaparilla deteriorate even when carefully stored. It has been reported that the content of taxol in *Taxus baccata* leaves and extracts stored at room temperature for one year decreased by 30–40% and 70–80% respectively, while storage in a freezer and out of direct sunlight produced no adverse deterioration²⁴. Such information regarding suitable conditions for storage of most of our medicinal herbs, is not available. Careless processing of medicinal drugs without considering these points is a major reason for ineffectiveness of some of our traditional medicines. Such deteriorated drugs will definitely not be accepted in the global market. The drug-manufacturing firms in India should take care during processing of medicinal herbs like some firms in other Asian countries which are our real competitors in the global market.

Plant cell and tissue culture, biochemical conversions and clonal propagation in indigenous medicinal plants

Low seed set, poor seed viability, high dormancy and low percentage of seed germination are some of the problems in propagation of some medicinal plants. Seed set is extremely poor in safed musli. Seed germination is poor in *Swertia*. Although, tissue culture protocols in safed musli, guggul and some other medicinal plants have been reported, none of them has been commercially adopted so far²⁵. The production of crude drugs is subject to the vagaries of the climate, to crop disease, to varying methods of collection and drying which influence quality, and to the inherent variation of active constituents arising from plants of the same species having different genetic characteristics. To overcome this problem, recently, one of the rapidly expanding areas of pharmacognosy has involved the application of tissue culture of plant cells, tissues and organs in the study of medicinal plants. This includes development of commercial production of expensive bio-

medicaments, discovery of new metabolites, selection of superior strains of medicinal plants and improvement of medicinal plant species by genetic engineering. In some laboratories of India like the Regional Research Laboratories Bhubneshwar, research work is in progress on the enhancement of valuable secondary metabolites of some medicinally important aromatic plants (e.g. geraniol content in *Cymbopogon martinii* oil) which are produced in plants in low levels. This would definitely attract foreign firms towards such indigenous medicinal plants. Some of the plant tissue-culture laboratories in India have published their research findings in this aspect. However, looking into the number of medicinal plant species in this country, coordinated research projects should be launched on this aspect, which would not only have high industrial significance but also lead to improvement of medicinal potency of traditional medicinal herbs by producing their different chemical races or 'chemodemes'. A clone of *A. annua* giving a high yield of the important antimalarial artemisinin, has recently been reported²¹. Medicinal plants growing in varied geographical regions of India may exhibit geographic chemotypes. The chemical races of our indigenous medicinal plants, whether they be of natural origin or produced by plant breeding, can offer considerable scope for the improvement of therapeutic value of the drug, either by adjustment of individual constituents or by increase in overall yield. Such biotechnological approaches would be beneficial in providing standardized drugs of Indian pharma in bulk for commercial availability in the global market.

Conclusion

The prevalence of a variety of climatic conditions puts India in a supreme position with respect to richness of medicinal flora. As such, India should occupy a significant position in the world trade of botanical drugs. India should focus on agrotechnology, process technology, standardization, quality control, research and development of herbal drugs. Now, the time has come to compile and document available knowledge on our valuable plant resources and to prove their utility scientifically through detailed phytochemical, biological and pharmacological investigations at selected centres in different regions of the country. India should adopt organized cultivation of medicinal plants that have export potential and import substitutions. Efforts should be made to cultivate potential medicinal plants as field crops. Their conservation should be done in appropriate ecological conditions. In order to push India as a significant player in the global herbal product market, herbal products should be standardized as per WHO guidelines.

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