PROSPECTS AND CHALLENGES IN DEVELOPMENT OF HERBAL MEDICINES

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Introduction

Herbal medicine is becoming popular and gaining importance with greater number of people seeking natural remedies. Medicinal plants have an advantage over their synthetic counter part based on their long term use by humans. Around fifty percent of the drugs under prescription segment are derived from natural sources. Terrestrial plants offer a unique and renewable resource for the discovery of potential new drugs and biological entities because of the structural and biological diversity of their constituents. However, as of now only 6% of the world's approximately 250,000 flowering plants have been analyzed so far for their possible medicinal uses. India ranks as 8th largest country in its natural resources having around 47000 plant species, out of which 7500 species are cited as medicinal plants. Among these cited medicinal plants only 800 species are claimed to be in use and in that around 120 species are used in large quantities, constituting only about 1.6% of the total number of medicinal plants and around 0.25% of the total number of plant species in India. The task force constituted by planning commission expects that the export market for natural products will go up to 10,000 crores by 2010. There are about 7000 manufacturing units in Indian system of medicine (ISM) and 5,64,000 ISM practitioners with an addition of 8000 new practitioners every year. About 284 academic and training institutions exist and over 2 crore people are involved in collection of medicinal plants.

According to a recent survey, around 120 plant derived chemical compounds are being currently used as drugs. Many of these were extracted and purified directly from plants[1]. The study of natural products as a source of novel active compounds reached its peak during 1970-80 and of the 877 small molecules (new chemical entity; NCE's) introduced between 1981 and 2002 roughly half (49%) were derived from natural products and semi-synthetic natural product analogues[2].

Natural resources are of great importance as reservoir of chemical diversity aimed at new drug discovery and are explored for antimicrobial, cardiovascular, immunomodulator and anticancer properties. Around 80% of all such products are of plant origin and their sales exceeded 65 million US dollar in 2003. Few examples of such products and derivatives used by pharmaceutical industry include paclitaxel, vincristine, vinblastine, artimisine, camptothecin and podophylotoxin. The nutraceutical market in Europe and US were estimated to be 9 and 10-12 billion US dollar in 2003 and is predicted to expand at a compounded rate of more than 20% per year. The introduction of Dietary Supplement Health and Education Act (DSHEA) in 1994 by US Congress has fuelled the rapid growth in this segment.[3]

This scenario indicates a huge potential in herbal market. India is possessing a gold mine of well recorded and traditionally well practiced knowledge of herbal medicines, as medicinal herbs have been in use under indigenous system of medicine like Ayurveda, Siddha and Unani. Inspite of having immense resources, India has not yet globalized its traditional resources.

In order to promote Indian Herbal products, there is an urgent need to evaluate the therapeutic potential as per the World Health Organization (WHO) guidelines. Ironically not many Indian products are available in the standard form, which is the minimum market requirement for introducing a product in western market.

Challenges and bottle necks

Medicinal products from natural sources especially plants face many challenges starting from raw

materials to commercialization and export. Some of the major bottlenecks faced by herbal drug industry are discussed below.

Identification and authentication

Crude drugs are known differently by various names in different parts of the country .The irony here is that, the same crude drug may be attributed to more than one plant and several plants may be sold under a single name. For example the popular Ayurvedic drug "Sariva" is known to be confused with *Ichnocarpus frutescens. Decalepis hamiltonii, Hemidesmus indicus* and *Cryptolepis buchanina*. Apart from this kind of problem, several other challenges like adulteration, substitution, (example Chincona species used for the antimalarial purpose adulterated and substituted by *Adabsonia digitata, Momordica charantia*.) nonavailability/ irregular supply and substandard quality of the plant material.

Collection

Many medicinal plants show variation in their chemical constituents depending upon the season, for example the alkaloid content in the leaves of *Adhatoda vesica* varies from 0.2% to 2% w/w of total alkaloids. Most of the people involved in cultivation and collection of the plants are not aware of such informations.

Drying

The method of drying affects the chemical content of medicinal herbs, for example the glycosides content in digitalis depletes on sun drying and also shade drying has not been found suitable due to enzymatic degradation. Improperly dried plant material (moisture not less than 10% w/w) often catches fungus and gets adversely contaminated as deadly mycotoxins secreted by fungus renders the material completely useless.

Residues

In India several pesticides like Dichlorodiphenyltrichloro ethane (DDT) and Lindane are still in rampant use which results in increased pesticide residue, and few plants have tendency to hyper accumulate heavy metals leading to rejection of crude material for safety reasons. Recently World Health Organization has published guidelines for maintaining international permissible limits for pesticides, mycotoxins and heavy metal residues.

Proven agro-industrial technologies have to be applied to the cultivation and processing of medicinal plants and the manufacture of herbal medicines. The single most important factor which stands in the way of wider acceptance of herbal medicines is the non-availability or inadequacy of standards checking their quality by chemical and/or bioassay techniques.

Pharmacognostic and phytochemical standardization

In order to standardize the raw material the following points have to be considered such as authentication, presence of foreign matter, organoleptic evaluation, macro and microscopic examination, volatile oil contents, ash value, extractive value, pesticide and heavy metal residues, microbial load, radioactive contaminants and chromatographic profile. The difficulty in developing quality control standards is that most of these products use whole herbs, or plants or their total extracts and in some cases even mixture of a number of plants. These often contain varied number and quantity of chemical constituents. It is challenging to develop suitable standards because a crude drug or a preparation there of is regarded as one active entity in its entirety. Standardization of a herbal medicine and/or a preparation there of is not just an analytical operation in that it does not end with the identification and assay of an active principle but it embodies total information and controls which are necessary to guarantee the consistency of composition.[4]

Research and development

The main challenges of working with traditionally used medicinal plants are standardization, bioactivity guided fractionation, elucidation of the molecular mechanism of action and generating proof of efficacy preferably through clinical trials and safety studies since ISM has not given much emphasis to the evaluation of adverse side effects[5].

The western concept of standardization of a herbal medicine means clear knowledge of active compound(s) and their quantification. Such information is almost absent and one approach which can be used to find active chemical constituents of medicinal plants is bioactivity guided fractionation. To identify the active fraction/principle, there is a need for *in vitro* bioassays which are rapid, reproducible and economical. There are several contractual research laboratories in India which offer clinical services. However there is not a single contractual research laboratory in our country which is offering the complete spectrum of these assays. In such a scenario mechanism based research and bioactivity guided fractionation of the medicinal plants continues to be ignored. New compounds isolated from plants are elucidated, results are rushed to publication and the compounds then lie dormant and decomposing

for years in one of the phytochemist shelves. The goal of most of the phytochemist is simply to isolate, characterize and publish plethora of novel natural structures.

There are few hurdles which need to be sorted out to hasten bio-activity guided fractionation such as solubilisation of extracts, availability of insufficient number of assays, need for separation to enhance the concentration of active moieties and prevention of loss of activity due to separation.

Excipients

Excipient is required for the making of complete dosage form. Excipients which are already approved as pharmaceutical aids in GRAS pharmaceuticals in modern medicine industry and standard monographs are available in various pharmacopoeias like Indian pharmacopoeia, British pharmacopoeia, United states pharmacopoeia etc., should be permitted for use as long as the manufacturer provide the rationality of their use[6].

Regulatory status

In many countries herbal medicines are not regulated by law and the registered products are not controlled by regulatory bodies. A special licensing system needs to be considered which offers opportunities to screen the constituents to demand a proof of quality, safety and efficacy before marketing and to ensure a correct and appropriate use, and also to oblige license holder to report suspected reactions with a post marketing surveillance[3].

Lack of proper awareness about Intellectual Property Rights (IPR) and their implementation is a major concern. This unawareness about IPR is common not only among ordinary people, but also among academicians, scientific professionals and herbal industry too[7].

One of the major problems faced by the Indian exporter is that most of the popular Indian medicinal plants are not listed and/or approved for export in developed countries. Some common plants like *Commiphora mukul, Garcinia indica, Asparagus racemosus, Berberis aristata* are not listed with the Therapeutic Goods Administration (TGA) which is the health authority of Australia and the export of these plants becomes impossible. The process by which TGA under takes addition of new substance in Australian Register for Therapeutic Goods (ARTG) is expensive and time consuming.

The need of the hour is that Indian government should initiate discussions with such countries with the aim to convince them on safety and efficacy of such herbs. The task should be taken up by some government bodies (mainly collecting, compiling and disseminating information-generating the required data only wherever necessary) with the help of the government of India.

Conclusion

The prevalence of a variety of climatic condition 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 and research and development of phytomedicines. Now, the time has come to compile and document available knowledge on our valuable plant resources and to prove their utility by employing modern scientific tools. In order to make India as a significant player in the global herbal market, timely inception of appropriate policies, coupled with sincere and coordinated efforts by cultivator of medicinal plants, scientist and exporter is required.

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INFO MANIA

ANSWERS

1. **Alopecia at the junction of nose and muzzle**
2. **Ruminal drinkers.**
3. **Coprophagy, as exhibited by rabbits**
4. **Gavage**
5. **False. Reverse is true.**
6. **Airway,Breathing,Circulation**
7. **Feline Infectious Peritonitis.**
8. **Biological Application.**
9. **Lactic Acidosis**
10. **Fryers**

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