

MEDICINAL PLANT RAW MATERIALS FOR INDIAN DRUG AND PHARMACEUTICAL INDUSTRY II. PROBLEMS AND PROSPECTS OF DEVELOPMENT OF RESOURCES

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Introduction

Assessment of resources of medicinal plant raw materials required by Indian drug and pharmaceutical industry discussed in the first part of this paper (Sarin, 2003) indicates a high potential of further development through a comprehensive approach. However, there are a number of problems which are to be tackled to obtain desired results. The country with a rich plant diversity, wide spectrum of agro-ecological conditions and advanced scientific and managerial expertise and infrastructure, lags behind many countries in this sphere. A serious and in-depth study of problems and potentials is needed to identify weakness and strength in this regard. The issues requiring immediate attentions are discussed here.

Systematic census and inventorisation

There is no inventorisation of medicinal plants at national level. The flora of India has been worked out in detail and inventories of plants occurring in most parts of the country are available in various floras, compendiums and manuals. The country is dotted with a large number of herbaria housing well preserved and

identified plant specimens, most of which carry notes on distribution pattern, flowering and fruiting period, local uses and other useful information. A lot of work has also been carried out on medico-ethno botany by research councils working under the Department of Indian Systems of Medicine (ISM) and through certain projects sponsored by the Ministry of Environment & Forests. A number of Non-Government Organizations (NGOs) working on medicinal plants and folk medicine in different parts of India have collected a lot of data while useful information has also been collected by students working for doctorate in some universities. Systematic retrieval of relevant information from these sources and its consolidation at a single place is highly desirable in making a proper assessment of medicinal plant resources of the country.

Identity of botanical source

Botanical identity of a majority of plants mentioned in the pharmacopoeia of 'Ayurvedic', 'Unani' and other traditional systems of medicine practiced in India, has been located since the introduction of modern system of plant classification in the country. There, however, are a number of crude drugs where the identity of plant

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source has not been finally established. The identity of the botanical source of the components of 'Ashtavarga', 'Murva', 'Granthiparni', 'Gajpippli' and many others is still unknown or highly debated. In other cases, more than one plant, sometimes with widely different taxonomical and morphological characters, is considered as the source of the same crude drug. A few examples in this category are *Bergenia ciliata forma ligulata*, and *Didymocarpus pedicellatus* (Fig. 1A and B) variously considered as the source of 'Pashanbheda'; *Boerhavia diffusa* and *Trianthema portulacastrum* as source of 'Punarnava' and *Hemidesmus indicus*, *Cryptolepis buchananii*, *Ichnocarpus frutescence* and *Decalepis hamiltonii* as the source of 'Sariva' (Sarin, 1996). The true source of the crude drug in these cases can be established only after detailed chemical and pharmacological investigations are carried out. Such studies conducted in a number of cases have yielded very interesting results. Detailed investigations have been carried out by various workers on *Bacopa monnieri* and *Centella asiatica* (Fig 2 A and B) variously ascribed the name 'Brahmi', an Ayurvedic drug considered to have marked effect on brain function differ chemically. *Bacopa monnieri* contains Bacosides A and B (Singh and Dhawan, 1985), while *Centella asiatica* contains medicassoside and asiaticoside, as the major constituents. The former has sedative and anti-epileptic action, though found to increase learning performance also while the latter produces significant intellectual improvement and also possesses tranquillizing, sedative and anti-anxiety properties (Shah and Chauhan, 1996). Similarly, the crude drug 'Nirvisi' or 'Jadwar' which is considered to be derived from *Delphinium denudatum*, was found to be the root of a species of

Aconitum. The two main alkaloids isolated from drug obtained from the market were identified as denudatine and denudatinine which belong to atisine group. The roots collected from the plants of *Delphinium denudatum*, on the other hand were found to contain conedelphine and isotalatizidine (Pelletier *et al.*, 1967). The physiological activity of the alkaloids from the two sources do not conform to those ascribed to the drug in Ayurvedic and Unani pharmacopoeia and thus requires further investigation.

Among the crude drug materials having more than one botanical source, those belonging to the species of the same genera and family do not pose much of a problem. In most of such cases, chemical composition is similar, though concentration of major constituents may differ. Thus, the three species of genus *Berberis*, sold in the market by the name of 'Daruharidra' have berberine as major alkaloid. Its concentration is highest in the roots of *Berberis chitria* (syn. *Berberis aristata* var. *chitria*) and *B. asiatica* and low in *B. lycium*. Similarly plumbagin considered to be the main physiologically active compound in the drug 'Chitraka' is present in both *Plumbago indica* and *P. zeylanica* named 'Raktachiraka' and 'Shwetachitraka' respectively, while *Embelia ribes* and *E. tsjeriam-cottam* fruits of which constitute the drug 'Vidanga' contain embelin and embelic acid in different concentrations (Sarin, 1993). While dealing with this subject, one must keep in mind that 'Ayurvedic' and 'Unani' names of herbal drugs came into being long before Linnean concept of binomial nomenclature was adopted for naming plants. Thus a group of plant species, having some common morphological characters and belonging to same genus

were considered as the source of a drug. In cases where a plant species belonging to different genera or even families were identified as the source of a particular drug, the plants found to have curative properties similar to those attributed to it in classical literature were given the identical name. This, perhaps became necessary due to non-availability of the original plant source in different parts of Indian sub-continent having a large geographical expanse (Sarin, 1995). Thus we find that botanical source of many plant drugs differ from region to region. A few prominent examples in this regard are : 'Rasna' - having *Pluchea lanceolata* as the plant source in North and North-West India; *Vanda tessellata* in eastern and central India and *Alpinia galanga* in the southern States. Similarly *Ephemerantha macraei* is the source of the drug 'Jeevanti' in the central and eastern parts of the country, *Leptadenia reticulata* constitutes the plant source in western regions while *Holostemma ada-kodien* is considered to be the true source in Karnataka, Tamil Nadu and Kerala.

The raw material used by drug and pharmaceutical industry is generally procured through market channels and are sometimes found adulterated. Pharmacognostic studies have been done for a number of important crude drug materials to distinguish the genuine material from the adulterant. Such information has been recorded in various pharmacopoeias. Under the present pattern of utilization, however, the material is obtained and processed in large quantities and use of such information is generally found impractical. The efficient way to determine adulteration is through morphological and organoleptic studies. Another method used for this purpose is

thin layer chromatography (TLC) and high pressure liquid chromatography (HPLC) which is employed for the analysis of extractives of the samples of the crude drug, collected at random. On account of its rapidity and ease of visual evaluation, TLC finger- printing has become popular for identification of the plant source of the crude drug under use. This method can however, be employed only by large manufacturers of drugs who are able to establish these facilities. For others, the use of morphological and organoleptic characters will be the right tool for authentication purposes. The author has carried out studies on about 200 crude drug materials largely and regularly employed by the Indian drug and pharmaceutical industry (Sarin, 1996). There is a need for further work in this area to cover all the crude drug materials used in the production of drugs, pharmaceuticals cosmetic and other over the counter products.

Techno-economic evaluation

The information required for this purpose is about the source from where the raw material is available; present production if cultivated or range and pattern of natural distribution and areas with rich population if originating from the wild. The study of growth parameters in relation to ecological conditions prevailing in the areas where the plant grows, mode of multiplication/regeneration and quality, preferably based on active chemical constituents is also necessary. This type of study, though laborious and time consuming, is nevertheless very useful. It not only provides information on availability of the raw material but also yields data on topographic, climatic, edaphic and

hydrological conditions under which the plant grows and flourishes in nature. This study also provides leads to evolve efficient methods for *in-situ* and *ex-situ* conservation as well as for domestication and cultivation. The work also includes market studies such as procurement, channels of supply etc. Presently, the work on these lines is limited to a very few medicinal plants raw materials. Notable among these are *Dioscorea deltoidea* rhizome (Sarin, 1970), *Rauvolfia serpentina* root (Sarin, 1974), Indian *Datura* species (Sarin 1976), *Costus speciosus* (Sarin *et al.*, 1981), *Adhatoda vasica* (Atal *et al.*, 1986), *Holarrhena antidysenterica* (Kaul and Atal, 1983), *Picrorhiza kurroa* (Kapahi *et al.*, 1993) and *Coleus forskohlii* (Shah, 1996). There is a great need of continuing this type of studies on plant raw materials under large scale use in the industry.

Quantitative assessment of availability of the raw material from natural sources

Assessment of the quantities of medicinal plant materials available from cultivated sources pose no difficulty. The estimation of the material available from the wild on the other hand, is laborious, time consuming and expensive. There is no set pattern of growth and distribution of plants associated with different types of plant communities except under forest ecosystem. One has therefore to depend on ocular estimates, past records of extraction and enquiries with local collectors and traders to arrive at some estimates of annual availability of a particular raw material obtained from plants associated with a vegetation other than the forest. Estimation of population of a medicinal plant can be made in a

forest on the basis of its association with a particular forest type or sub-type. Procedures, however, have to be developed for the purpose of estimating yield of the raw material. Determination of availability in terms of quantity of a medicinal raw material from forest area is not easy. The conventional managerial methods can not be used for this purpose. The study is not confined to a small area or a particular forest type but spreads over a large area having a variety of vegetation types which may include scrub and grasslands. A complete survey of the area is out of question because of the prohibitive cost and enormous time it may consume. Sampling which is essentially based on phyto-sociological methods employed for analysis of vegetation is suggested for this work. The object of this method will be to obtain an estimate of the value of some characteristics of a population of medicinal plant from a small number of sampling units selected and examined as representative of the whole. One of the methods suggested is triple sampling procedure (Bhatia, 1982). This includes :

- (1) *Reconnaissance* to find out the occurrence, density and other phyto-sociological attributes, recorded visually and preparation of stock maps depicting occurrence and recording rough density and frequency classes.
- (2) *Probability sampling* to obtain ocular estimates of the proportion of area under the medicinal plant and making a rough estimate of the area covered by it.
- (3) *Estimation of availability* by laying down at least two quadrates of appropriate size on line transects drawn at random and in zigzag fashion. The size of the sampling plot for this purpose is kept at 0.4 hectare

in each compartment where the plant occurs.

A somewhat similar procedure is adopted by the Australian Department of Agriculture where the plots for study are laid down either in zigzag or checkerboard fashion depending upon frequency and density of the plant (Cain and Castro, 1959).

Another method for making an assessment of raw material from under a forest community is the multiple chain system used by the foresters in pre-investment survey of growing timber stock. The author used this method in assessment of rhizome resources of *Dioscorea deltoidea* rhizome in the temperate forests after incorporating certain modifications to suit the studies of ground flora (Sarin and Gupta, 1968). Line transects were laid down in nine forest types and sub-types found to have the presence of the plant in the herb stratum. The length of the transect and the size of the quadrat was determined after working out the minimal area as described by Oosting (1956) The per cent frequency and density of the plant was worked out as per multiple quadrat method (Curtis and McIntosh, 1950) and the number of plants per unit area under a particular forest type calculated. Underground part (rhizome) was obtained from 25 plants selected at random and the average yield of rhizome per plant was calculated. The studies gave a fair idea of the availability of the fresh rhizome, based on average yield per unit area under a particular forest type (Sarin and Chopra, 1985). The quantification of availability of the raw material can, however, be done only in a small area and the data generated in these studies is applied to larger area. This type of study, therefore, gives only

approximate figures as chances of variability in the occurrence and distribution pattern of a plant species are quite normal in the forest ecosystem. This exercise is nevertheless important and concerted efforts are necessary to develop quick and efficient procedures in this regard.

Quality of a medicinal plant raw material originating from different localities

Effect of physical and agro-ecological conditions and locality factors on the therapeutic properties and composition of physiologically active constituents of a crude drug is well known. This fact is recognized in Ayurveda and other traditional systems of medicine. The case of 'Haritaki' (fruits of *Terminalia chebula*) can be cited as an example where seven varieties originating from different parts of India have been attributed with different types of therapeutic properties (Pandey and Chuneekar, 1995). In an all-India survey carried out for qualitative evaluation of 'Sarpagandha' (roots of *Rauvolfia serpentina*), chemical analysis of samples collected from different localities revealed an average content of 2.35 per cent of total alkaloids in the material originating from sub-Himalayan tract against an average content of 1.7 per cent in the roots collected from other parts of the country (Sarin, 1986). In similar studies conducted on *Datura metel* for utilization for production of tropane alkaloids, dried leaves and flowering tops of the plant collected from the lower catchments of river Godawari in Orissa and Andhra Pradesh were found to contain 0.36 to 0.4 per cent of alkaloids against an all-India average of 0.18 per cent (Sarin, 1976). In yet another study, rhizome

samples of *Costus speciosus* revealed a high concentration of diosgenin – a precursor of steroidal hormones – in the foothill regions and adjoining plains of North-West Himalayas against a low content in plains and coastal regions (Sarin *et al.*, 1981). Similar findings have been obtained in the case of *Holarrhena anti-dysenterica* (Bhutani *et al.*, 1984) and *Coleus forskohlii* (Shah, 1996). Determination of the physiologically active chemical constituents responsible for the therapeutic action of a plant drug will be an appropriate yardstick to evaluate the quality of the raw material. This type of study is necessary, especially in the case of raw materials under large and regular use by the drug and pharmaceutical industry. This may also help in obtaining high yielding planting material and selection of suitable localities for cultivation of the medicinal plant.

Collection, drying and storage

Therapeutic quality of a crude drug also depends on the age of the plant source and the vegetative stage when the required part of the plant is collected. Great importance is attached to it in Ayurvedic, Unani and other systems of traditional medicine as well as modern pharmacopoeia. For example fruits of *Terminalia chebula* should be harvested at a stage when these attain full size but are still unripe; the fruits of *Aegle marmelos* yielding the drug 'Belgiri' are harvested when raw; anthers of *Mesua ferrea* constituting the drug 'Nagkesar' are separated from flowers when still in bud stage; 'Ashwagandha' (root of cultivated *Withania somnifera*) is harvested from 6 to 7 months old plants (Atal *et al.*, 1975); 'Sarpagandha' (root of *Rauvolfia*

serpentina) is collected when the rootbark constitutes one-fourth of the total biomass of the root while 'Giloi' (stem of *Tinospora cordifolia*) should consist of mature stems collected at the time when the climber is leafless.

The variation in the active chemical content of a medicinal plant raw material collected during different seasons and phenological conditions of the plant from which it is obtained has been reported by various workers. The resin content of *Podophyllum hexandrum* roots was found to be maximum when the plant flowers in the month of May. On the other hand the percentage of podophyllotoxin, the chemical compound responsible for anti tumour activity of the drug, is highest during the months of September-October when the fruits are fully mature (Kapoor and Sarin, 1962). A study of total alkaloid content of the leaves of *Adhatoda zeylanica* (which constitute the drug 'Vasaca') during different seasons and phenological conditions of the plant revealed (Atal *et al.*, 1980) that highest yield of total alkaloids is obtained during the months of July to October when the flowering is over and the fruits are at different stages of maturation. Similar studies in the case of 'Kutaja' (bark of *Holarrhena anti-dysenterica*) revealed maximum alkaloidal content at a stage when the plants are in full bloom (Dutta *et al.*, 1950). There is exhaustive literature on this subject and should be used while standardizing harvest techniques.

Post-harvest processing which requires reduction in bulk through cutting, chipping, removal of moisture and storage is very important to maintain the therapeutic efficacy of the raw material. A quick drying is necessary under



Plate 1A. *Bergenia ciliata* (Haw.) Sternb forma *ligulata*



Plate 1B. *Didymocarpus pedicellatus* as source of "Pashanbheda"



Plate 2A. *Centella asiatica* herb as source of "Brahmi"



Plate 2B. *Bacopa monnieri* herb as source of Brahmi

temperature and exposure conditions which differ from material to material. The crude drugs containing glycosides, flavanoids and essential oils are to be dried under low temperatures within a short time after harvest. For example 'Tagar' (root of *Valeriana jatamansi*) if dried at temperatures above 25 °C, loses much of its valpotriate content, which is the main chemical constituent responsible for sedative and tranquillizing properties of the drug; *Colchicum luteum* corms and *Gloriosa superba* tubers show higher concentration of the alkaloid colchicine if dried quickly under high temperature while Anvla (fruit of *Emblica officinalis*) is to be used fresh to obtain maximum concentration of ascorbic acid, the source of Vitamin C. Methods for collection and post-harvest handling have been developed for only a small number of raw materials majority of which are used for bulk production of phyto-pharmaceuticals. There is a great need for developing similar methods in the case of crude drugs employed for the manufacture of drugs based on Indian systems of medicine. The methods evolved for this purpose should be simple which could be easily understood and adopted by the common collectors. This may help in avoiding indiscriminate removal of plant, supply of good quality material to the consumer and enabling the collector in getting a better price for his produce.

Conservation of endangered and threatened medicinal plants

Medicinal plants which have acquired endangered and threatened status, require urgent damage control measures. These are the only source to provide understanding of reproductive biology, genetic architecture, relationships with the

environmental factors, with their growth and natural distribution. Basic approaches for conservation are (a) *ex-situ* preservation which requires maintenance of germplasm out side their original habitat and (b) *in-situ* conservation by protective maintenance of a natural plant population (Singh and Gautam, 1997). The former approach, however, lacks the normal evolution process which is always operative in nature. The latter approach, on the other hand, allows for continued dynamic adaptation of plants to the environmental conditions prevailing in the natural habitat. The distribution pattern of a wild plant in different phyto-geographical regions and its area of concentration, where it still continues to perpetuate is of special significance for taking up *in-situ* conservation. The critical factors to be incorporated in all conservation oriented programmes include prevention of destruction of the population and its habitat; maintenance and enhancement of the population level and prevention of excessive exploitation.

Initiatives have already been taken by various agencies involved in conservation activities. A National Board of Medicinal Plants has been set up, one of whose activities is conservation. The Ministry of Environment and Forests is funding an All-India coordinated project on conservation of endangered plant species (Raghupathy, 2001). The Botanical Survey of India which has compiled the Red Data Book, undertakes a periodic updating of plants under threat. Work in this area is also being carried by many other institutions and non-government organizations. Mention in this regard may be made to recent compilation of such data by Foundation for Revitalization of Local

Health Traditions, Bangalore (Ravikumar and Ved, 2000), G.B. Pant Institute of Himalayan Environment, Almora, (Samant *et al.*, 1998) and Regional Research Laboratory, Jammu (Srivastava *et al.*, 2000). It is essential that the outcome of such findings are taken out of print in order to achieve the objectives. Certain rich pockets with natural population of certain medicinal plants considered endangered, have been located and the findings have been published by various workers, since the Red Data Book was first published. However, no sincere efforts to preserve these pockets were made. An example in this regard is the report on pockets of rich population of *Aconitum deinorrhizum* Stapf. (a critically endangered medicinal plant) in the sub-alpine localities of Chattardhar and Bhalesh hill ranges of Bhadarwah Tehsil in Jammu and Kashmir. It was published in 1967 (Sarin and Gupta, 1967) but no steps to preserve the plant were made and the latest visit to the area revealed that the plant has almost disappeared from the place. Similar has been the case of *Panax pseudoginseng*, a number of varieties of which occur wild in eastern Himalayas. Extensive chemical and pharmacological investigation on the roots of the plant (Kapil *et al.*, 1996) found the adaptogenic properties of Himalayan Ginseng similar to those of Korean and American Ginseng. The plant, though included in the threatened list did not receive due attention of conservationists and large quantities of roots are being collected from forest areas of Nagaland and Meghalaya.

Development of agro-technologies & cultivation

Agro-technologies for cultivation of a

number of plants have been developed but a majority of these have remained unutilized.. Some of the reasons for this state of affairs are : inability of the farmer to adopt to high tech methodology; unsuitability of agro-climate and site conditions of the area where cultivation has been taken up; high cost of production which cannot compete with the raw materials collected from wild sources; absence of any interest on the part of drug and pharmaceutical industry in purchasing the cultivated produce at reasonable price even if the quality of the material is better than that procured from wild sources; lack of publicity regarding the cultivation practices developed by specialists and research workers, especially among the farmers and small cultivators and above all, absence of any comprehensive approach to the problem among the stakeholders. This calls for development of appropriate technologies which should be more or less in line with the agricultural practices used by the farmer and reduction in the cost of cultivated produce. Cultivation of a desired plant may be taken up in the land and area where the crop can perform well. It has been noticed that plants suitable for cultivation in a particular region are suggested for cultivation any where in the country. Selection for this purpose may be made by taking into account the performance of the crop with regards to production of biomass of the part of the plant used as raw material and its therapeutic quality. Availability of suitable planting material is also a big problem. Priorities in selecting medicinal plants to be cultivated on large scale should be considered on the basis of demand and to avoid competition with a produce from the wild which may be freely available at lower prices.

Conclusions

There is a growing demand for plant-based medicines, pharmaceuticals, health and body care products, and cosmetics, etc., in the national and international market. India has great potential in this area. The country is already a major producer of herbal medicines, phyto-pharmaceuticals, cosmetics and other products. It has abundant raw material resources which are not being properly harnessed to obtain maximum benefits. Technologies for conservation and augmentation of resources and maintaining or even enhancing their quality have already been developed in many of cases. The fate of a majority of such technologies developed at

considerable cost in terms of time, money and expertise has been uncertain. The institutions engaged in this work feel frustrated that agricultural and related technologies developed by them are hardly ever used. Reports are now available of the fate of some medicinal plants cultivated by the farmers. Such cultivation failed largely on account of absence of market demand. While the developed technologies, thus, lie unused or cultivation of the plants given up, the Indian drug and pharmaceutical industry continues to get almost 90 per cent of its supplies from the collections made from the wild. A proper and comprehensive approach to the problems is therefore necessary for gainful utilization of medicinal plant resources.

SUMMARY

Proper utilization of medicinal plant resources of India requires a comprehensive approach. There are many issues concerning this area of activity. These include inventorisation, quantitative and techno-economic evaluation, standardization in terms of therapeutic efficacy and augmentation of resources through conservation, domestication and large scale cultivation. The country has been engaged in research and development in this area since long and a lot of information on different aspects is available. There is a need for retrieval and documentation of this information at national level, developing appropriate technologies and creating conditions for gainful utilization of available and developed resources. Such an exercise may go a long way for proper utilization of the resources and taking up further work to fill in the gaps.

भारतीय औषधियां और औषध-निर्माण उद्योग के लिए औषधीय कच्चा-माल

II – संसाधन विकास की समस्याएं और संभावनाएं

वाई.के.०. सीन

सारांश

भारत के औषध पादों का समुचित उपयोग करने के लिए सर्वसमावेशी दृष्टि अपनाना आवश्यक है। क्रियाशीलता के इस क्षेत्र के साथ कितनी ही समस्याएं जुड़ी हुई हैं। इनमें तालिकानिर्माण, मात्रात्मक और प्राविधि-आर्थिक मूल्यांकन, रोगनिवारण क्षमता के विचार से प्रतिमानीकरण तथा संरक्षण, घरेलूकरण और बृहत् परिमाण पर कृषिकरण द्वारा संसाधनों का अभिवर्धन करना सम्मिलित हैं। हमारा देश इस क्षेत्र में अनुसंधान और विकास कार्य करने में काफी समय से लगा हुआ है और इसके विविध पक्षों के बारे में ढेर-सारी जानकारी उपलब्ध है। इस जानकारी का राष्ट्रीय स्तर पर पुनः प्राप्त और उसका प्रलेखन करने, समुचित प्रौद्योगिकियां विकसित करने तथा उपलब्ध और विकसित किए संसाधनों का लाभप्रद उपयोग करने की दशाएं उत्पन्न करने की बहुत आवश्यकता है। ऐसा करना संसाधनों का उपयोग करने तथा बीच में छूटे रह गए स्थानों को भरने के लिए आगे कार्य आरम्भ करने का मार्ग काफी दूरी तक प्रशस्त बनाएगा।

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