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Invited commentary

Medicinal plants and phytomedicines

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1. Medicinal plants

Plants have been one of the important sources of medicines ever since the dawn of human civilization. Chemically, medicinal plants may have secondary metabolites like alkaloids, glycosides, steroids or other groups of compounds which have marked pharmaceutical action as anticancer, antimalarial, antidiabetic, antidysenteric, *etc*. In spite of tremendous developments in the field of allopathy during the 20th century, plants still remain as one of the major sources of drugs in modern as well as traditional system of medicine throughout the world.

India has 15 agroclimatic zones and 17000-18000 species of flowering plants of which 6000-7000 are estimated to have medicinal usage in folk and documented systems of medicine, like Ayurveda, Siddha, Unani and Homoeopathy. About 960 species of medicinal plants are estimated to be in trade of which 178 species have annual consumption levels in excess of 100 metric tons. Medicinal plants are not only a major resource base for the traditional medicine and herbal industry but also provide livelihood and health security to a large segment of Indian population. The domestic trade of the AYUSH industry is of the order of Rs. 80 to 90 billion. There is global resurgence in traditional and alternative healthcare systems, resulting in world herbal trade which stands at US$ 120 billion and is expected to reach US$ 7 trillion by 2050. Indian share in the world trade, at present, however, is quite low (1-2%).

The World Health Organisation (WHO) estimated that 80% of the population of developing countries rely on traditional medicines, mostly plant based drugs, for their primary healthcare needs. Also, modern pharmacopoeia still contain at least 25% drugs derived from plants and many others which are synthetic analogues built on prototype compounds isolated from plants. Demand for medicinal plants is increasing in both developing and developed countries due to growing recognition of natural products, being non-narcotic, having no side-effects, easily available at affordable prices and sometimes the only source of healthcare available to the poor. Medicinal plant sector has traditionally occupied an important position in the socio-cultural, spiritual and medicinal arena of rural and tribal lives of India. Millions of rural households use medicinal plants in a self-help mode. Over one and a half million practitioners of the Indian System of Medicine in the oral and codified streams use medicinal plants in preventive, promotive and curative applications. There are estimated to be over 7800 manufacturing units in India. In recent years, the growing demand for herbal products has led to a quantum jump in volume of plant materials traded within and across the countries. Though India has a rich biodiversity, the growing demand is putting a heavy strain on the existing resources. While the demand for medicinal plants is growing, some of them are increasingly being threatened in their natural habitat. For meeting the future needs, cultivation of medicinal plants has to be encouraged.

It is evident that the Indian people have tremendous passion for medicinal plants and use them for wide range of health related applications from a common cold to memory improvement and treatment of poisonous snake bites to a cure for muscular dystrophy and the enhancement of body's general immunity. In the oral traditions local communities in every ecosystem from the trans himalayas down to the coastal plains have discovered the medical uses of thousands of plants found locally in their ecosystem. India has one of the richest plant medical 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. There are estimated to be around 25000 effective plant based formulations used in folk medicine and known to rural communities all over India and around 10000 designed formulations are available in the indigenous medical texts.

Distribution of medicinal plants macro analysis show that they are distributed across diverse habitats and landscape elements. Around 70% of India's medicinal plants are found in tropical areas, mostly in the various forest types, spread across the Western and Eastern ghats, the Vindhyas, Chotta Nagpur plateau, Aravalis and Himalayas. Although less than 30% of the medicinal plants are found in the temperate and alpine areas and higher altitudes they include species of high medicinal value. Macro studies show that a larger percentage of the known medicinal plants occur in the dry and moist deciduous vegetation as compared to the evergreen or temperate habitats. Analysis of habits of medicinal plants indicate that they are distributed across various habitats. One third are trees and an equal portion shrubs and the remaining one third herbs, grasses and climbers. A very small proportion of the medicinal plants are lower plants like lichens, fern, algae, *etc.* Majority of the medicinal plants are higher flowering plants. Of the 386 families and 2200 genera in which medicinal plants are recorded, the families Asteraceae, Euphorbiaceae, Lamiaceae, Fabaceae, Rubiaceae, Poaceae, Acanthaceae, Rosaceae and Apiaceae share the larger proportion of medicinal plant species with the highest number of species (419) falling under Asteraceae. About 90% of medicinal plants used by the industries are collected from the wild. While

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over 800 species are used by industry, less than 20 species of plants are under commercial cultivation. Over 70% of the plant collections involve destructive harvesting because of the use of parts like roots, bark, wood, stem and the whole plant in case of herbs. This poses a definite threat to the genetic stocks and to the diversity of medicinal plants, if biodiversity is not sustainably used. Crude drugs are usually the dried parts of medicinal plants (roots, stem, bark, leaves, flowers, seeds, fruits and whole plants, *etc*.) that form the essential raw materials for the production of traditional remedies of Ayurveda, Siddha, Unani, Homeopathy, Tibetan and other systems of medicine including the folk, ethno or tribal medicines. The crude drugs are also used to obtain therapeutically active chemical constituents by specialised methods of extraction, isolation, fractionation and purification and are used as phytochemicals for the production of modern allopathic medicines or herbal/phytomedicines.

Medicinal plants are living resource, exhaustible if overused and sustainable if used with care and wisdom. Current practices of harvesting are unsustainable and many studies have highlighted depletion of resource base. Medicinal plants based industries although old and vast are still being managed on traditional practices and lack a proactive and socially responsible image. There is a vast, secretive and largely unregulated trade in medicinal plants, mainly from the wild which continues to grow dramatically in the absence of serious policy attention with environmental planning.

Confusion also exists in the identification of plant materials where the origin of a particular drug is assigned to more than one plant, sometimes having vastly different morphological and taxonomical characters. There are few others, where the identity of plant sources is doubtful or still unknown, therefore, adulteration is common in such cases. The true source of the crude drug in such cases can be located only after detailed chemical and pharmacological studies. Detailed chemical investigation on *Bacopa monnieri* and *Centella asiatica*, the two plants variously described by the name "Brahmi" has revealed entirely different phytochemical composition. The former contains alkaloids brahmine, herpestine, gama amino butyric acid and bacoside A & B which have been found to have important action on brain function, while *Centella asiatica* contains asiaticoside, brahmoside, hydrocotyline, *etc*. which have hardly common relationship with the properties ascribed to the drug "Brahmi" in the text. The quality of medicinal plants depends on the geographical origin, time and stage of growth when collection has been done and post harvest handling. The collections in most cases are done by villagers and tribal people residing in the vicinity of forest in their spare time. The plant part is collected without paying attention to the stage of maturity, dried haphazardly and stored for long periods under unsuitable conditions. The quality of collected material, as such is often degraded. Trade in medicinal plants at all levels in India is marked by secrecy and opacity in working. There has been little attempt at external regulation by Government and self-regulation by traders and herbal medicine company. However, it is in the best interest of the industry to develop a long term "social contract" with the collectors or growers and buyers. Collection of Non Timber Forest Product (NTFP), which includes most of the medicinal plants, is a way of life with tribal and rural communities in and around the forest. As the prices paid to the gatherers tend to be very low they often mine the natural resources as their main objective is to generate an income. A critical factor in the wild harvesting is the availability of cheap labour to undertake the very labour intensive work of gathering. As in many cases, income from such sources represents the only form of paid employment for rural and tribal people, there is an eagerness to undertake such work. Several medicinal plants have been assessed as endangered, vulnerable and threatened due to over harvesting or unskillful harvesting in the wild. Habitat destruction in the form of deforestation is an added danger. The Government of India has put 29 species in the negative list of export which are believed to be threatened in the wild.

1.1 Cultivation of medicinal plants

Presently over 90% of the medicinal plants and their products are being collected from the wild. Some of the medicinal plants like Sarpagandha, Guggal, *Saraca asoca* are endangered and being unscrupulously collected from the wild, leading to extinct of such species. Hence, there is an urgent need of the conservation and cultivation of these valuable medicinal plants for future use. The cultivation of medicinal plants in the farmers' fields has several unique advantages. Firstly, the World Health Organisation (WHO) has emphasized the need for better utilization of the indigenous system of medicine, based on the locally available medicinal plants in the developing countries. Secondly, owing to the realization of the toxicity associated with the use of synthetic drugs, western countries are increasingly aware of the fact that drugs from natural sources are safer. Therefore, an upsurge in the use of products based on plants is expected. Vast range of agroclimatic conditions in India make almost all medicinal plants' cultivation feasible. Indian System of Medicine (ISM) *viz*., Ayurveda, Siddha and Unani mainly gives plant based remedies for most of the diseases. It offers most appropriate cure against many diseases like jaundice, asthma, arthritis, diabetes, *etc.* where there is no complete cure in allopathy. Besides, India has a good resource of cheap labour and skilled man power.

Cultivated material is infinitely more appropriate for use in the production of drugs. Indeed, standardisation whether for pure products, extracts or crude drugs are critical and while become increasingly so, as quality requirements continue to become more stringent. Given the higher cost of cultivated material, cultivation is often done under contract. In the majority of cases, companies would cultivate only those plant species which they use in large quantity or in the production of derivatives and isolates, for which standardisation is essential and quality is critical. More recently growers have set up cooperatives or collaborative ventures in an attempt to improve their negotiating power and achieve higher price. Some of the constraints associated with the processing of medicinal plants which may result in reducing their competitiveness in global markets and which have to be addressed are poor agricultural practices, poor harvesting (indiscriminate) and post-harvest treatment practices, lack of research on development of high-yielding varieties, domestication, *etc*. Poor propagation methods, inefficient processing techniques leading to low yields and poor quality products, poor quality control procedures, lack of good manufacturing practices, lack of R&D on product and process development, difficulties in marketing, lack of local market for primary processed products and lack of trained personnel and equipments.

1.2 Marketing

Marketing is an insurmountable problem besetting the development of the plant-based industry in developing countries and marketability will be a crucial factor in determining the failure or success of these industries. The market outlets can be for local use and for export. For local use, some products could reach the consumer directly while others have to be either further processed or used as secondary components in other industrial products. Hence, user industries have to be promoted so that locally produce extracts can be used to save foreign exchange, needed for importation of such additives. Further, processing to yield value added products will be limited by the local demand situation unless they could be produced at prices to be competitive in the world market. Even if the cost of production is low and quality of the products is good, substantial market promotion has to be undertaken in order to penetrate the world market. A clear understanding of both the supply-side issues and the factors driving the demand and size of the medicinal plant market is a vital step towards planning for both the conservation and sustainable use of the habitats of these plants as well as for ensuring continued availability of the basic ingredients used to address the health needs of the majority of the world's population.

2. Phytomedicines and drugs

Once the medicinal plants are collected from the wild or cultivated and raw material is available aplenty, the next course of action would be to develop herbal medicines/phytomedicines. Numerous methods have been utilized to acquire compounds for drug discovery including isolation from plants and other natural sources. Natural products have played an important role as new chemical entities (NCEs). About 20% of NCEs were considered natural product mimics, meaning that the synthetic compound was derived from the study of natural products. Drugs derived from medicinal plants, can serve not only as new drugs themselves but also as drug leads. Even when new chemical structures are not found during drug discovery from medicinal plants, known compounds with new biological activity can provide important drug leads.

2.1 Few drugs developed from medicinal plants

An array of medicinal plants has been explored to synthesise drugs. Few of the drugs have been listed below. Arteether (trade name Artemotil®) is a potent antimalarial drug and is derived from artemisinin, isolated from *Artemisia annua* L. (Asteraceae). Good work has been done by CIMAP (Central Institute for Medicinal and Aromatic Plants, Lucknow) on this herb in India. Tiotropium (trade name Spiriva®) has recently been released in the United States market for treatment of chronic obstructive pulmonary disease (COPD). A derivative of atropine that has been isolated from *Atropa belladonna* L. (Solanaceae). M6G or morphine-6-glucuronide is a metabolite of morphine from Opium (*Papaver somniferum* L.) from Papaveraceae and used as an alternative pain medication with fewer side effects than morphine. Vinflunine is a modification of vinblastine from *Catharanthus roseus* (Apocynaceae) for use as an anticancer agent with improved efficacy. Exatecan is an analog of camptothecin from *Camptotheca acuminata* Decne. (Nyssaceae) and is being developed as an anticancer agent. Forskolin, for the treatment of glaucoma, is developed from *Coleus forskohlii.* Reserpine, ajmaline, serpentine from *Rauvolfia serpentina* are being used for hypertension and as pain killer. Withanine, somniferine from Ashwagandha (*Withania somnifera*) are for general debility or as immuno- modulator. Andrographolides from Kalmegh (*Andrographis paniculata*) are extracted for malarial and other fevers. Sennosides from senna (*Cassia ungustifolia*) for laxative purpose are some of the examples.

2.2 Phytochemicals for disease management

Using phytomedicines is one part of the efforts of man to combat diseases. The other part of managing diseases is preventing them. It is well said that prevention is better than cure. But the question is can we prevent some diseases by taking plant based phytochemicals? Probably the answer is difficult, however, phytochemicals have been used to prevent certain types of cancers and heart diseases.

The recent past has witnessed a tremendous resurgence in the interest and use of medicinal plant products. Once the domain of health-food and speciality stores, phytomedicines have clearly re-emerged into the mainstream as evidenced by their availability for sale at a wide range of retail outlets, the extent of their advertisement in the popular media, and the recent entrance of several major pharmaceutical companies into the business of producing phytomedicinal products. No doubt, a major contributing factor to this great increase in phytomedicinal use in the United States has been the passing of federal legislation in 1994 (Dietary Supplement Health and Education Act or "DSHEA") that facilitated the production and marketing of phytomedicinal products. The past few years have also witnessed intense interest in "nutraceuticals" (or "functional foods") in which phytochemical constituents can have long-term health promoting qualities. The nutraceuticals have a nutritional role in the diet and the benefits to health may arise from long-term use as foods (*i.e.*, chemoprevention). In contrast, many medicinal plants exert specific medicinal actions without serving a nutritional role in the human diet and may be used in response to specific health problems over short- or long-term intervals.

Some of the phytochemicals which are commonly available in fruits and vegetables are carotenoids, flavonoids, isoflavones, isothiocyanates, phytosterols, anthocyanins, polyphenols, organosulfides, *etc.* which comprise caffeine (coffee); theobromine, theophylline (tea); lycopene (tomato); quercetin (onion); allicin (onion and garlic); capsaicin (chilli), *etc.* There is some evidence that a diet rich in fruits, vegetables and whole grains reduces the risk of certain types of cancer, heart disease, *etc.* In advanced countries including the USA, phytochemicals are available as dietary supplements**.** In these countries, the diet is rich in fat and protein and very poor in dietary fibre which is one of the major reasons for colon cancer.

However, evidence suggests that these single supplements are not as beneficial as the foods from which they are derived. That means dietary supplements are not as helpful as consuming directly the fresh fruits and vegetables. Till that period until conclusive research findings emerge, healthcare professionals advise a balanced diet with an overweight on fruits, vegetables, legumes and whole grains.

2.3 Organic farming

Organic farming in general features cultural, biological and mechanical practices that aim at cycling of resources, promote ecological balance and conserve biodiversity. Synthetic chemicals and fertilizers are not allowed, although certain organically approved pesticides may be used under limited conditions.

Organic farming systems rely on crop rotation, animal and plant manures, some hand weeding and biological pest control. Although the organic farming movement in the UK dates back to the Second World War, there has been a marked increase in the demand for organic foods over the past few years, with consequent growth of this niche market. Atleast in part, this demand appears to reflect consumer concern regarding the safety of food produced under intensive farming systems. Consumer concern regarding possible adverse health effects of foods produced using intensive farming methods has led to considerable interest in the health benefits of organically-produced crops and animal products. There appears to be widespread perception amongst consumers that such methods result in foods of higher nutritional quality.

One study indicated that organically grown crops had 17% higher concentrations of polyphenols comparing to conventionally grown crops. Another analysis revealed that conventionally grown produce was four times more likely to have pesticide residue than organically grown crops. With respect to chemical differences in the composition of organically grown food compared with conventionally grown food, studies have examined differences in nutrients, antinutrients and pesticide residues. It is difficult to generalize due to differences in the methods of testing, the practices of agriculture affect the chemical composition of food, variations in weather, inputs applied, soil composition, the cultivar used, *etc*. Claims that organic food tastes better are generally not supported by evidence. Public believes that organic food is safer, more nutritious and tastes better than conventional food. These beliefs have increased the demand for organic food despite higher prices. A 2012 meta-analysis noted that there have been no long-term studies of health outcomes of populations consuming predominantly organic versus conventionally produced food controlling for socioeconomic factors and such studies would be expensive to conduct. However, farmers have to be trained in all aspects of organic farming of medicinal plants including obtaining certification from associations that do the monitoring starting from cultivation to final harvesting. Organic farming which is labour-intensive gives the developing countries the comparative advantage to be competitive.

3. Conclusion

Plants have been one of the important sources of medicines ever since the dawn of human civilization. In spite of tremendous developments in the field of allopathy, plants still remain as one of the major sources of drugs in modern as well as traditional system of medicine throughout the world. The use of plants as medicines has involved the isolation of active compounds, beginning with the isolation of morphine from opium in the early 19th century. Later, isolation of drugs such as cocaine, codeine, digitoxin and quinine, in addition to morphine, of which some are still in use.

Prevention is better than cure. But the question is can we prevent some diseases by taking plant based phytochemicals? Probably the answer is difficult, however, phytochemicals have been used to prevent certain types of cancers and heart diseases. In advanced countries including USA, phytochemicals are available as dietary supplements**.** In these countries, the diet is rich in fat and protein and very poor in dietary fibre which is one of the major reasons for colon cancer.

The probable remedy lies in practicing organic farming or vigilant practice of integrated management of pests and diseases thereby such healthy food can be produced. Man should continue to find newer, more effective drugs either synthetic or plant based to cure diseases. Focus should be given to possibly prevent diseases by eating healthy, nutritive food with better life styles. Organic farming may give solutions to get pesticide free, nutritive, quality food. And finally, let us keep away from junk food and switch back to our rich traditional food!

The journals publishing literature on medicinal plants, phyto-medicines and related aspects are doing a yeoman service to the mankind. These journals also serve as a source of inspiration to the researchers to involve themselves in quality research. In the light of this, **International Journal-Annals of Phytomedicine** is already on its way to reach its mission and achieve greater heights in publishing innovative research outcomes.

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Biography

Born on July 21, 1960 in Vijayapura district of Karnataka, completed initial schooling in his native district, and studied in College of Agriculture, Dharwad and secured B.Sc. (Agri.) in 1982 with first rank and seven gold medals and M.Sc. (Agri.) in 1986 with distinctions from University of Agricultural Sciences, Dharwad. Completed Ph.D in 1993 from the University of Illinois (Urbana-Champaign) in Agronomy and secured three prestigious Post Doctoral Programmes [University of Illinois-Urbana-Champaign, USA (1993-95); J.W. Goethe University, Frankfurt, Germany with Alexander Von Humboldt Fellowship (1999) and Rothamsted Research Station, England (2004) with Commonwealth Fellowship]. During his thirty years of service, he has served in teaching, research, outreach and managerial positions with proven academic, technical and administrative skills. He started service as Instructor in Agronomy at College of Agriculture, Dharwad (UAS, Bangalore) in 1984; and served as Assistant Professor of Agronomy (1988 to 1995), Associate Professor of Agronomy (1995 to 1999) and later as Professor of Agronomy from 1999 in UAS, Dharwad. Later, he worked as Associate Director of Research, Regional Agricultural Research Station, Vijayapura until 2006 and served as Editor, Publication Centre UAS, Dharwad until 2012. He served as the Registrar, University of Agricultural Sciences, Raichur during the period from 2012 to 2014.

He is the recipient of several national and international awards/distinctions *viz*., Dewang Mehta Business School Award for Outstanding Contribution to Education (2014); Outstanding Achievement Award (2013) and Leadership Award (2011) from Society for Applied Biotechnology; Dr. A. P. J. Abdul Kalam National Award (2008); Sir C.V. Raman Award for Young Scientist from Government of Karnataka (2004); and also received three Incentive Awards from University of Agricultural Sciences, Dharwad for bringing highest amount of external funding for the research projects worth of Rs.300 lakhs. He is a Fellow of Society for Plant Research (2012); Society for Applied Biotechnology (2010); International Benevolent Research Forum (2009); Indian Society of Agronomy (2009), National Academy of Biological Sciences (2007) and National Environmental Science Academy (2005). He also worked as a Member of QRT for CICR and AICCIP, Nagpur. Presently, serving as President of Cotton Research and Development Association and Executive Council Member of Indian Society of Agricultural Information Technology and in various committees of ICAR and PPV&FRA.

He has guided seven Ph.D and nine M.Sc (Agri.) students of Department of Agronomy as Chairman and served as member of the advisory committees of 42 post graduate students of different faculties of the University. Published 120 research papers in peer-reviewed journals and presented about 112 research papers in National and International conferences/seminars. He has written and published twenty eight books and hundreds of articles in regional language for the benefit of farming community. Served on editorial Boards of - Karnataka Journal of Agricultural Sciences, Journal of Farming Systems Research and Development, Pesticide Research Journal, The Bulletin on Agricultural Sciences, International Journal on Agricultural Sciences, Biotechnology, Bioinformatics and Bioengineering and American-Eurasian Journal of Agronomy. He served as President of UAS Teacher's Association and served for welfare of the teaching community. As a student leader, he took active part in the movement for establishment of UAS Dharwad.