REVIEW ARTICLE

International market scenario of traditional Indian herbal drugs – India declining….

Aneesh T. P., Mohamed Hisham, Sonal Sekhar M., Manjusree Madhu, Deepa T. V.
Amrita School of Pharmacy, Amrita Vishwavidyapeetham University, Kochi-682026, Kerala, India

In the present article, an endeavor has been made to present an overview of the comparison of Indian traditional herbal medicine in the international market. This article intends to contribute to this knowledge by giving a survey of published data regarding the microbial contamination of herbal plants, by dealing with methodological aspects and by considering the influence of different commonly used pharmaceutical preparation techniques on the microbiological status of the products. It also highlights heavy metal poisoning of these herbal products and the need for India to follow the Good Agriculture Practice (GAP) guidelines. As herbal medicinal products are complex mixtures, which originate from biological sources, great efforts are necessary to guarantee a constant and adequate quality. By carefully selecting the plant material and a standardized manufacturing process, the pattern and concentration of constituents should be kept as constant as possible, as this is a prerequisite for reproducible therapeutic results. China has successfully overcome such difficulties by modernizing its traditional medicine profession with government-sponsored GAPs. The cultivation practices offer Standard Operating Procedures for use of fertilizers, irrigation systems and disease management allied with insects and pest prevention and cure. GAPs also establish standards for noxious and harmful contaminants like heavy metals, pesticide residues and microbes in plants.

Key words: Ayurveda, traditional Indian medicine, traditional Chinese medicine, herbal products, microbial loading, heavy metal poisoning, good agricultural practices, traditional drugs, complementary and alternative medicines

INTRODUCTION

Herbal medicine has been used in India for thousands of years and is increasingly been used worldwide during the last few decades as evidenced by rapidly growing global and national markets of herbal drugs. The global pharmaceutical market was worth US $550 billion in 2004 and is expected to exceed US $900 billion by the year 2009. According to WHO estimates, the present demand for medicinal plants is ~US $14 billion a year and by the year 2050 it would be ~US $5 trillion. Due to high prices and harmful side effects of synthetic drugs, people rely more on herbal drugs and this trend is growing, not only in developing countries but in developed countries too. India has 2.4% of world's area with 8% of global biodiversity. The forests of India are estimated to harbour 90% of India's medicinal plants diversity in the wide range of forest types that occur. In India, around 25,000 effective plant-based formulations are used in traditional and folk medicine. More than 1.5 million practitioners are using the traditional medicinal system for health care in India. It is estimated that more than 7800 manufacturing units are involved in the production of natural health products and traditional plant-based formulations in India, which requires more than 2000 Tones of a medicinal plant raw material annually.[1,2]

Unfortunately, the number of reports of people experiencing negative effects, caused by the use of herbal drugs, has also been increasing. There may be various reasons for such problems, poor quality of herbal medicines due to insufficient attention being paid to the quality assurance and control of these products. Although WHO has developed guidelines for the quality control of herbal drugs which provide a detailed description of the techniques and measures required for the appropriate cultivation and collection of medicinal plants, there is still a lacuna between this available knowledge and implementation, because farmers and other relevant persons like producers, handlers and processors of herbal drugs are not much aware of WHO's guidelines and they continue their work as before without any quality control measures which results in inferior quality of herbal drugs with lots of contaminants like heavy metals, pesticides and microbes. Hence, training for farmers and other relevant persons is an important measure to be taken to ensure good quality of raw herbal drugs. Contamination with excessive banned pesticides, microbial contaminants, heavy metals and chemical toxins causes various deformities like congenital paralysis, sensory neural defects, liver and kidney damage etc. These

Address for correspondence: Prof. Aneesh T. P., Amrita School of Pharmacy, Amrita Vishwavidyapeetham University, Kochi-682041, Kerala, India.
E-mail: aneesh21atp@gmail.com
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contaminants may be related to the source of herbal drugs, if these are grown under contaminated environment. Chemical toxins may come from unfavourable post harvest techniques, wrong storage conditions or chemical treatment during the storage period etc. Some of these environmental factors may be controlled by implementing good source, good agricultural practices (GAPs) and standard operating procedures (SOP) for producing good quality herbal products.[3,4,5,6]

Herbal medicines may be associated with a broad variety of microbial loading and exert an important impact on the overall quality of herbal products and preparations. Generally, herbs are valued for their distinctive aroma, colour and flavour. Unfortunately, they are often contaminated with high levels of bacteria, molds and yeasts; if untreated, the herbs will result in rapid spoilage of the foods and can also result in serious food-borne illness. Post harvest and post-processing, herbs are always contaminated with microorganisms from the plants themselves, soil, water, air and dust. A wide spectrum of microorganisms and microbial loads has been previously reported in medicinal plants. Risk assessment of the microbial load of medicinal plants has therefore become an important subject in the establishment of modern Hazard Analysis and Critical Control Point (HACCP) schemes or International Standards Organization (ISO) standards. Most countries set maximum dose regulatory limits and these higher limits allow for higher levels of microbial control. Gamma irradiation in the range of 3–10 kGy reduces the total aerobic viable cell counts in highly contaminated spices and dry herbs to 103–104 CFU/g. Gamma irradiations is better than ethylene dioxide treatment (Food and Environmental Protection

Section Joint FAO/IAEA Division Nuclear Techniques in Food and Agriculture International Atomic Energy Agency, 1999).[4,7] According to microbiological criteria for spices that have been recommended by the International Commission on Microbiological Specifications for Foods (ICMSF, 1974), spices are of an unacceptable quality when the bacterial counts exceed 106 CFU/g and the numbers of molds are higher than 104 CFU/g. The herbs could be contaminated by human handlers during harvesting or processing. Coliform bacteria were also detected in all herbs, at levels varying with the season. The highest levels were found in herbs harvested in the summer due to high temperatures which enhanced bacterial growth, even in dried powdered herbs. The presence of coliforms implied the possibility of faecal contamination and inadequate sanitation management, while the herbs were being grown. According to WHO and European Pharmacopoeia, herbal drugs must meet the modern hygienic standards, which aim at low microbial load or the absence of pathogenic microorganisms. WHO, USFDA, European Scientific Cooperative on Phytomedicine (ESCOP) have published standard sets of guidelines to address the concerns.[8,9,10]

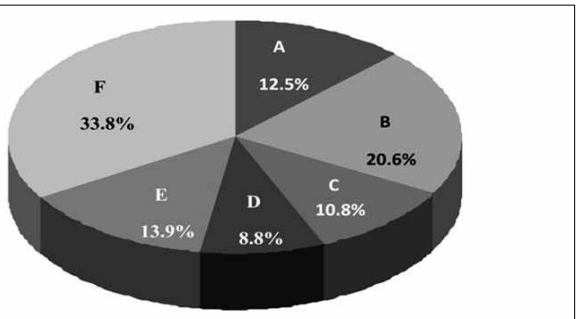
Contamination of herbal drugs with heavy metals is also of prime concern. The poor quality control of these products causes health hazard, as some products may have unusually high concentration of potent and poisonous ingredients that may be fatal if consumed unknowingly. Herbal medicine products can be sold as dietary supplements, which are not required to undergo rigorous testing before entering the marketplace. Indeed, the Dietary Supplement Health and Education Act (DSHEA) do not require proof of safety or efficacy. This leads to heavy metal poisoning, so it is required to have a mandatory test of all imported dietary supplements for toxic heavy metals. The sorts of problems that could arise from toxicity include seizures, high blood pressure, kidney damage and developmental delay in children. The reasons for the heavy metals could be contamination from groundwater or the addition might be intentional as Ayurvedic medical texts do argue that heavy metals are good for health. The main cause is the lack of good agricultural practices (GAP). Arsenic poisoning could manifest as nausea, abdominal pain, vomiting, muscle cramps, heart abnormalities, liver damage, anaemia and reduced motor nerve function, while lead poisoning can cause weight loss, insomnia, dizziness, swelling of the brain and paralysis. Mercury poisoning could be associated with tremors, insomnia, memory loss, slowed sensory and motor nerve function and reduced mental function.[11,12,13]

INTERNATIONAL MARKET SCENARIO OF TRADITIONAL HERBAL PRODUCTS

Traditional Chinese Medicine (TCM) uses over ~5000 plant species, while India uses about ~7000. But still in the international market, TCM is well established when compared to Indian Ayurvedic medicine, which is in such a tenuous condition, and the way they have grown to be accepted and developed have been haphazard and informal. It is for these reasons why the Indian herbal medicines market is reputedly worth around ~US $1 billion worldwide, as against the global market for herbal medicines which is in the region of US $62 billion, with the Chinese herbal medical market said to be worth ~ US $19 billion. A huge opportunity awaits the ingenious Indian pharmaceuticals, to be availed through innovation, patents and trademarks [Figure 1]. India has enormous resources of medicinal and herbal plants. The pre-historic knowledge of Ayurveda and its applications to cure illnesses effectively has not been explored fully by India. If this happens successfully, India could gain a very significant competitive edge in the global market, especially in the pharma, beauty care and healthcare segments. There is a lot of scope for India to achieve global leadership through export of quality produce and products from medicinal and

aromatic plants. But India seems to be lagging behind and is ranked third in the herbal medicine category, with less than 2% of global market share, while China occupies nearly 30% of the market [Figures 2 and 3]. According to an Ayurveda expert, Chinese herbal medicines, which rarely contain 10% scientific base when compared with the Indian Ayurvedic system, are doing better than India by 50-fold.[14,15] The major reasons may be:

1. There have been a very large number of Chinese people immigrating into the USA and they support Chinese culture. There are only few Indians in America and only five colleges that provide training in Ayurveda. Globally, Chinese herbs are more preferred probably because of the research which the western countries are conducting on these herbs. As in India, the medicinal herbs hardly undergo 'double blind trials' to establish their real usefulness. The scientific base for Indian herbal medicines is lacking.[16,17,18]
2. China has been willing to actively export its medical system. Under government sponsorship, China produced translated books and sent them to America. The crude herbs and finished herbal products have been imported by Chinese immigrants and made available to anyone who wanted them. By contrast, the Indian government is not involved in export of Ayurveda and few Indian writers have made an effort to have their books published for an American audience.[19,20]
3. The Chinese medical system's basic concepts of yin and yang and five elements, the unusual practice of acupuncture, TUI NA (therapeutic massage) have attracted attention from a diverse group of people. In contrast, the three doshas, the emphasis on dietary restrictions and the importance of such methods as oil massage and various purification procedures, has attracted a much smaller audience. The most heavily promoted traditional Ayurvedic practice is Panchakarma (a purification procedure). In the USA, it is offered as a several day event (requiring the person to make a major change in their normal schedule and habits) that has a high expense leaving it open only to the wealthy. In contrast, an acupuncture session usually lasts about half an hour and can be fit into most schedules, and it has a modest cost per session.[21,22,23]
4. Further, the quality of herbal materials from China has been better than those from India in many instances (due to differences in quality control procedures). Quality control, standardization, scientific methods of production and evaluation were completely missing in India. China has successfully overcome such difficulties by modernizing its traditional medicine profession with government-sponsored GAPs and Good Manufacturing Practices (GMPs). GAPs stress selection of the correct germplasm with a high content of stable active components. The cultivation practices offer SOPs for use of fertilizers, irrigation systems and disease management allied with insects and pest prevention and cure. GAPs also establish standards for noxious and harmful contaminants like heavy metals, pesticide residues and microbes in plants. All manufactures of TCM are mandated to comply with guidelines laid down by China's State Drug Administration (SDA) by



A *Emblica officinalis* Gaertn (Amla); B. *Asparagus racemouse* Willd (Shatawar), *Withanta somnifera* Dunal (Aswagandha), *Terninalia chebula* Retz (Harar), *Saraca asoca* [Roxb.] (Ashoka); C. *Aegle marmelos* Corr. (Bel), *Cassia angustifolia* Vahl (Sonapaatri/Sana), *Adhatoda vasica* Nees. (Adusa/Arusa); D. *Piper longum* Linn (Pippali), *Bacopa monnieri* [Linn.] (Brahmi), *Sida cordifolta* Linn (Kanghi), *Ocimum sanctum* Linn. (Tulsi); E. *Bambusa bambos* Druce. (Vansalochan), *Boerhaavia diffusa* Linn (Punarnava), *Azadirachta indica* A. Juss. (Neem), *Solanum nigrum* Linn (Mokoya), *Woodfordia fruticosa* Kurz *(Dhataki), Andrographis paniculata* Nees (Kalmegh), *Syzygium aromaticum* (Linn.) (Ling/lavang), *Tinospora cordfolia* [Wild] (Giloe, Guduchi); F. Others.

Figure 1: Percentage demand of few major herbal plants in export market of India

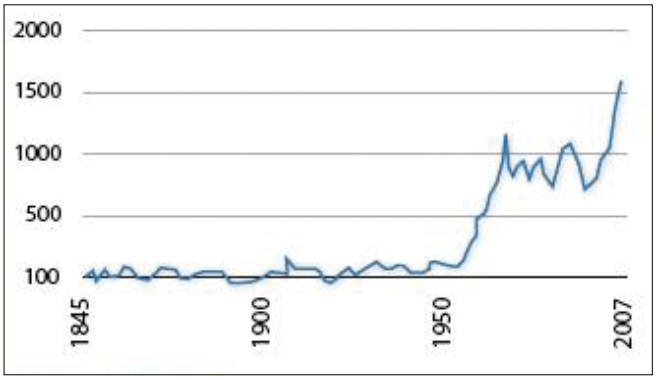


Figure 3: Increase of export of traditional Indian herbs every year (in crores) (Source: The Economist)

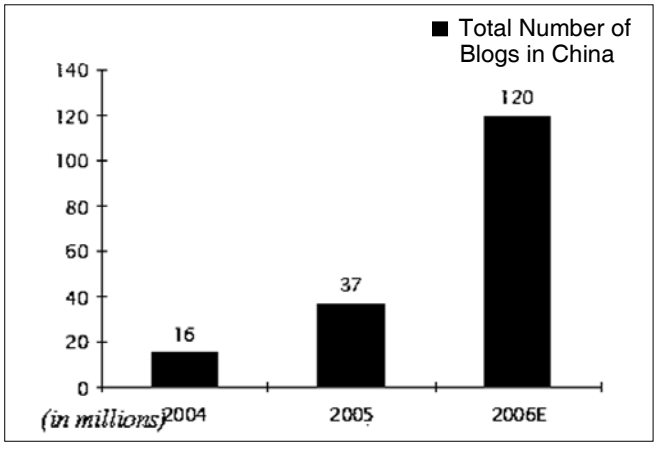


Figure 2: Increase of export of traditional Chinese herbs every year (in millions)

2004 and farms producing raw ingredients must comply with SDA-imposed standards by 2007.[24,25,26]

Although Chinese medicine has gained considerable ground, it cannot be compared with the most significant import of India so far in the international arena that is Yoga which is a part of the Ayurvedic medical system. A well-directed effort could result in Ayurveda having a standing somewhat similar to that of Chinese medicine, while continuation of the laissez-faire approach that seems to have marked this field up to now could mean that bits and pieces of Ayurveda will simply be subsumed into the general arena of Complementary and Alternative Medicine (CAM). Nevertheless, the Indian herbal medicine market is growing at a steady pace of between 15% and 20% every year. Indian and Chinese medicines have a lot in common. Some Chinese herbs that were imported into India include green tea and cinnamon and some essential oils such as oil of bergamot, citronella oil, essential oils of geranium, spearmint oil, essential oil of vetiver, anise oil, cinnamon bark oil, eucalyptus oil and ginger oil.[27,28]

Examples of successful companies, such as Himalaya Drug Company (HDC), Emami, Aswini, Ayur, Dabur, Cholayil Pharma, etc., that have patented their herbal and ayurvedic products in India and abroad.[29]

DETERMINANTS OF SUCCESS

Government of India also has expressed support and encouragement for the Traditional Indian Medicine (TIM). A separate department for Indian Systems of Medicine and Homeopathy now known as AYUSH (Ayurveda, Yoga, Unani, Siddha, Homoeopathy) was established in March 1995 to promote indigenous systems. Priorities include education, standardization of drugs, enhancement of availability of raw materials, research and development, information, communication and larger involvement in the national system for delivering health care. The Central Council of Indian Medicine oversees teaching and training institutes, while Central Council for Research in Ayurveda and Siddha deals with interdisciplinary research.[30,31]

India has world-class expertise and facilities for organic synthesis, isolation and structure elucidation, biological screening, toxicological testing and pharmacokinetics. This is supplemented by the expertise for the development of agro-technology for the cultivation of medicinal plants. Industry participation to ensure successful upscaling and implementation of technology is increasing. India has progressive research institutes like Central Drug Research Institute (CDRI), Central Institute of Medicinal and Aromatic Plants and National Botanical Research Institute, at Lucknow, Regional Research Laboratories (RRL), at Jammu, and Bhubaneshwar, North East Institute of Science and Technology (NEIST), Jorhat, National Chemical Laboratory, at Pune, which routinely undertake research on medicinal plants. Most of them are involved in standardizing the herbal medicines and isolating active compounds, quality planting materials for farmers, conservation of endangered species and to prevent exploitation of the natural resources.[32,33]

Analysis of most frequently used plant-based therapies in the Ayurvedic system revealed that 43% of them have been tested on humans, while 62% have been the subject of one or more animal studies. Among these, drugs having sufficient clinical data are guggul, brahmi, ashwagandha, amlaki, guduchi, kutki, shatavari and shunthi Pharmacopoeia of India (1996) covers few botanical monographs like clove, guggul, opium, mentha, senna and ashwagandha. The Ayurvedic Pharmacopoeia of India gives monographs for 258 different Ayurvedic drugs.[34]

Presently, Indian systems of medicine use more than 1100 medicinal plants of which most are collected from the wild. More than 60 species are in great demand. The tribal belt of India is rich in these plants and the tribes mainly depend on this trade for livelihood. There are ample of opportunities for adulteration and contamination in the process. Thus, the adequate availability of quality raw materials free from adulterants at reasonable prices has become a big problem for industry, and the demand is increasing every year. However, very few efforts have been made either by government or by industry to seriously study the supply and demand.

India needs to follow GAPs to ensure the use of correct raw materials and cover the entire life cycle including the harvesting, processing, transportation and storage. The selection of the correct germplasm using modern DNA fingerprinting and chemoprofiling techniques is also a priority.[35] The domestic herbal market has now crossed the Rs.5000 crore mark, and is set to reach further heights this year. Herbal exports from India are worth Rs.450 crore, whereas even a decade back the amount was barely Rs.100 crore. This may not be a huge sum when compared to the Chinese herbal exports market which is worth Rs.2000 crore, but the sheer potential of the Indian herbal companies should make people sit up and take notice. The biggest stumbling block facing the Indian herbal care segment is still the lack of trust it generates in the developed markets like Europe and USA. It is widely believed that Indian herbal extracts do not undergo rigorous toxicity tests. Indian firms would have to be better in promoting themselves internationally, especially in regulated markets. Indian herbal extracts will have to undergo stricter toxicity tests to win the confidence of the developed world.[36,37,38]

Numerous drugs have entered the international pharmacopoeia via the study of ethnopharmacology and traditional medicine. For traditional medicines, newer guidelines of standardization, manufacture and quality control and scientifically rigorous research on the scientific basis for traditional treatments will be required. Traditional medical practices can offer a more holistic approach to drug design and myriad of possible targets for scientific analysis. Powerful new technologies such as automated separation techniques, high-throughput screening and combinatorial chemistry are revolutionizing drug discovery and this will help to rediscover the drug discovery process.[39,40,41]

STATISTICS WHICH SHOW CONTAMINATION OF INDIAN HERBAL PRODUCTS

1. Researchers at Boston University School of Medicine (BUSM) have found that one-fifth of Indian-manufactured Ayurvedic medicines purchased via the Internet contain lead, mercury or arsenic. Using an Internet search, the researchers identified 25 websites featuring 673 Ayurvedic medicines. They randomly selected and purchased 193 products made by 37 different manufacturers for analyses. Overall, 20.7% of Ayurvedic medicines contained detectable lead, mercury and arsenic [Figure 4]. Among products containing metals, 75% claimed GMPs or testing for heavy metals.[42,43]

2. Current study was of a patient admitted in Boston hospital with intractable seizures. Tests showed his blood lead level to be 89 (the normal level for adults is less than 2). Interviews with the family revealed that the man, an Indian born professional in his 50s, had been taking Guggulu, an Ayurvedic arthritis medicine, for the past 6 years. The product was then analysed and found to have very high levels of lead, mercury and arsenic.[45,46]

3. Between April and October 2003, U.S. Food and Drug Administration officials visited stores in Boston and purchased ayurvedic products intended for oral consumption and then tested at the New England Environmental Protection Agency lab. Overall, of the 70 products purchased, 13 products contained lead (median concentration, 40 μg/g), 6 contained mercury (median concentration, 20,225 μg/g) and 6 contained arsenic (median concentration, 430 μg/g) and these had labels recommending their use for infants and children. The contamination issue is a result of poor manufacturing practices.[47,48]

4. Consultant Clinical Toxicologist, Dr Paul Dargan, of Guy's and St Thomas' NHS Foundation Trust, London, with colleagues there and Dr Indika Gawarammana of the Faculty of Medicine and South Asian Clinical Toxicology Research at the University of Peradeniya, Sri Lanka, have investigated to prove that many Ayurvedic medicines contain dangerous quantities of heavy metals, including lead, mercury, thallium and arsenic.[49]

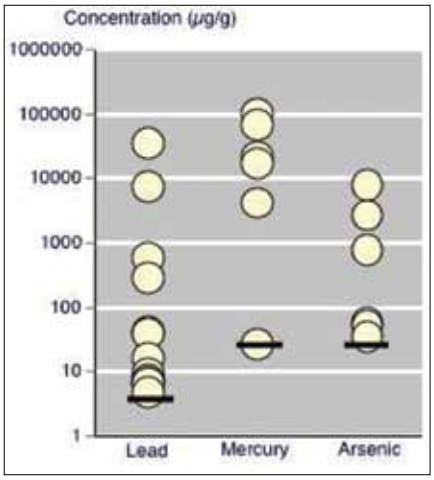


Figure 4: Concentration (logarithmic scale) of lead, mercury and arsenic in Ayurvedic medicines (μg/g) in those medicines where it was detected. The horizontal black bars approximate maximum recommended levels of oral intake[44]

5. The products banned for consumption in the UK market include Karela tables (made by Shriji Herbal Products), Karela capsules (Himalaya Drug Co), Yograi Guggal and Sudarshan tablets (both Zandu Pharmaceuticals), Shilajit capsules (Darbur India), SAFI liquid (Hamdard-WAKF) and Maha Sudarshan Churna Powder (supplied by Zandu Pharmaceuticals, D and K Pharmacy, Chhatrisha and Dabur, India).[50,51]

6. Recently, a study conducted by Harvard Medical School on Indian ayurvedic medicines found potentially harmful levels of lead, mercury and arsenic in the products like 'Bal Guti', 'Mahayograj Guggulu', 'Mahalaxmi vilas Ras', 'Safi', 'Shilajit' etc. of some of the leading companies within ayurvedic communities.[52]

The microbial quality and antibacterial properties of two Indian herbal remedies with such claimed efficacy of curing all manners of microbial diseases were assessed. The herbal remedies were discovered to be contaminated with a total of four fungi (Basidiobotrytis sp, Oedocephalum sp, Varicosporium sp and *Articulospora inflata*) and three bacteria (*Bacillus subtilis, Bacillus coagulans* and *Bacillus cereus*) [Table 1].[53]

PREVENTION

1. Microbial load was reduced under permissible level of irradiation which is already a well-known

Table 1: Microorganism isolated from two Indian herbal preparation

Microbial isolates	Herbal preparation A	Herbal preparation B
Basidiotrytis sp	+	-
Oedocephalum sp	+	-
Varicosporium sp	+	-
Articulospora inflata	-	+
Bacillus cereus	+	+
Bacillus subtilis	+	-
Bacillus coagulans	-	+

+: present. -: absent

decontamination method, but it has received less attention for medicinal plants, especially on fresh herbs. Microbial load behavior, antioxidant activity, and enzymatic inhibition activity were measured for doses up to 50 kGy.[7,53]

2. In the 55 people tested for the heavy metals, pesticides and herbicide toxins, initially 801 toxins were found in the subjects' livers, 825 toxins in the breasts and 824 toxins in the brain. Studies proved that natural cellular defence removes heavy metals, pesticides toxic chemicals from body.[54]

CONCLUSION

Numerous drugs have entered the international market through exploration of ethnopharmacology and traditional medicine. Progress in genomics and proteomics has opened new gateways in therapeutics and drug discovery and development. Better understanding of the human genome has helped in understanding scientific basis of individual variation. TIM and TCM, carry many generations' observations that have well-organized and documented data. China has successfully promoted its own therapies and drugs like ginseng, ma huang and gingko with scientific evidences acceptable for the global community. The approach of integrative medicine by selective incorporation of elements of TCM alongside the modern methods of diagnosis has achieved a great success in China. It is no exaggeration to say that an 'Herbal Revolution' by India is just waiting to happen. India could truly become a global leader in the herbal medicine category by inventing and patenting medicines for several ailments by using a combination or mixture of herbal formulations.[12,34]

Although herbal medicines have been used for thousands of years, basic research programmes need to be focused on the quality assurance. To overcome contaminations from pesticide residues and heavy metals, there should be control measures to implement necessary SOP at source. Good laboratory practices (GLP) and GMPs are also needed to produce good quality medicinal products. Without all these measures, it is impossible to realize the dream of having a major share of a herbal drug industry despite having gold mine of well documented and well-practiced knowledge of traditional herbal medicines. TCM examples would help India at various levels including policies, quality standards, integration practices, research models and the complementary integration where public health is kept at the central position. Both TIM and TCM are great traditions with strong philosophical basis and could play an important role in new therapies, drug discovery and development processes.

Be careful of what you are sticking in your tummy herbally. Unfortunately, you cannot necessarily rely on regulators making sure they are safe. There is an urgent need for studies to quantify the frequency and potential risk of heavy metal poisoning from Ayurvedic medicines. Also needed is 'culturally appropriate education' that can inform the public of the potential for toxicity associated with the many different products associated with this practice.[36,37]

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