International Journal of Multidisciplinary Research and Development

IJMRD 2014; 1(6): 258-262
www.allsubjectjournal.com
Received: 23-10-2014
Accepted: 26-11-2014
E-ISSN: 2349-4182
P-ISSN: 2349-5979

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Technique in herbal drug standardization, modernization and integration of Indian traditional herbal medicine in clinical practice: Importance, challenges and future

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Abstract
In spite of incredible advances in modern science, technology and allopathic medicine a large we are unable to provide quality healthcare to all. Traditional medicine particularly herbal medicine considered as a major healthcare provider around the globe particularly in rural and remote areas. A large section of people depends on such medicine for their primary healthcare mainly in underdeveloped or developing countries. Indian traditional medicinal system like Ayurveda, Siddha and Unani has a very rich history of their effectiveness; modern research also acknowledged the importance of such medicine. Indian traditional medicine or medicinal plants are also considered as a vital source of new drug. Mainstreaming of such medicine is important for the people. The modernization of herbal medicine is the need of hour to cater the global demand by means of patient compatibility. The omic technique can also play an important role for the conservation of knowledge of ancient plant species.

Keywords: herbal drug, standardization, modernization, integration, ayurveda

Introduction
Herbal medicines are the synthesis of therapeutic experiences of generations of practicing physicians of indigenous systems of medicine for over hundreds of years and they are known to be the oldest health care products that have been used by mankind all over the world in the form of folklore medicines or traditional medicines or ethnic medicines. The therapeutic use of herbal medicine is gaining considerable momentum in the world. The World Health Organization (WHO) estimates that herbal medicine is still the mainstay of about 75-80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side-effects. Standardization of herbal plant is a critical issue to ensure the quality of the research process for safety and efficacy of the research products, which are critical to scientists and regulators for ensuring the quality and interoperability of herbal products.

Herbal medicine and its importance
Plants are always the key source of drug or treatment strategy in different traditional medicinal systems. In recent years, many people are choosing to plant based medicines or products to improve their health conditions or as curative substance either alone or in combination with others. According to the WHO, herbs or herbal products are used by the large number of populations for basic healthcare needs. Herbal medicine includes herbs, herbal materials (plant parts) or preparations, processed and finished herbal products, active ingredient.In recent years, a huge resurgence of the use of herbal product due to the side effects of modern drugs, failure of modern therapies for against chronic diseases, and microbial resistance. It is estimated that nearly 75% of the plant based therapeutic entities used worldwide were included from traditional/folk medicine. In India, approximately 70% of modern drug are discovered from natural resources andnumber of other synthetic analogues have been prepared from prototype compounds isolated from plants.

Promotion of herbal medicine – problems need to be addressed
In spite of global reorganization and very sound history of traditional uses, promotion of herbal medicine faces number of challenges around the glove mainly in developed nations. Following problems need to be overcome before the promotion of traditional herbal

knowledge around the world.

- Quality issues: Adulteration, misidentification of plant, faulty collection and preparation, incorrect formulation process are the main problems that reduces the effectiveness of herbal preparation and can be considered as key factors affecting quality and purity of herbal medicines.
- Processing and harvesting issues: Indiscriminate harvesting, poor agriculture and propagation method, poor pre and postharvest practices, lack of processing techniques leads to the substandard quality of herbal drugs.
- Quality control related issues: Standardization, poor quality control procedure and lack of Good Manufacturing Practices (GMP) are the main hurdle to maintain the quality of herbal drugs. Lack of awareness regarding the guideline among growers and manufacturers, lack of implementation and regulation of the guideline are also frequent in small and medium scale industries.
- Administrative issues: Lack of regulation and controlling authority in herbal sector, lack of proper monitoring and controlling are absolute need for the quality of drugs.
- Infrastructure related issue: Lack of processing technique, trained personal, sophisticated instrument, utilization of modern techniques, facility to fabricate instrument locally are the major problems.
- Pharmacovigilance: Proper pharmacovigilance in herbal sector is the need of time to find the toxicological data and adverse drug reaction of herbal drugs. Adverse reactions, contraindications, interactions with other drug, food and existing orthodox pharmaceuticals need to be monitor properly.
- Clinical trial: Since the safety continues to be a foremost issue with the use of herbal remedies therefore, clinical trials are necessary to understand the safety and efficacy of these drugs before introduced them in global market.
- IPR and bio-piracy: Bio-piracy is the major difficulty in promotion of herbal traditional medicine. Documentation of folk knowledge thus important for our future.
- Irrational use: It is believed that herbal products don't have any side effects, interaction, but unfortunately is not true. Thus, irrational practice of these drugs can lead to various problems which can hinder the promotion of such drugs.
- R&D: Research and development on dosage, processing, techniques are the key need for any drug, but in herbal sector it is quite less compare to allopathic medicine. Although in recent years, the trend is changing. Research to understand the mode of action and pharmacokinetics phenomenon, improvement/creation of monographs and reference standards for marker-based analysis are necessary of time. Decisive gap in current ethno pharmacological and modern medicinal plant research is another problem for sustainable, socio-culturally equitable and safe supply of herbal medicines.
- Other issues: Unethical practice of herbal medicine, lack of qualified physician, exposure of unreliable and misleading information, lack of sufficient fund, absence of focused marketing and branding, lack of knowledge sharing also hold back the global promotion of herbal medicine. Lack of protection of biodiversity and protecting the traditional medicinal plants are also a big challenge.

Modernization & integration of herbal medicine in clinical practice – experience from India

In spite of number of hurdles, the traditional medicine of India in acknowledged widely around the world and the demand is increasing continuously. Combined effort of public and government sector is essential for the promotion of herbal medicine.

Pharmacopeias and formularies

Both traditional and modern parameters are used to test the quality and to standardize the raw and finished products. Several methods like organoleptic standardization of drugs, chemical investigation, and bioassay are used. Pharmacognostical, chemical and standards of the plant drugs used in ISM are mentioned in such publications. These pharmacopoeias and formularies contain information about the biological source, synonyms, description, TLC, important formulation, therapeutic indication, and details related to identity, purity, strength. Recently, chromatographic fingerprint profile as a supplementary to Ayurvedic Pharmacopoeia was also published. Identification and estimation of active therapeutic ingredients and marker compounds with reference to which drugs of Ayurveda, Siddha and Unani can be standardized are still developing and all these parameters are being added to pharmacopoeias. Inclusion of monograph on herbal drug in Indian Pharmacopeia and formulation of Herbal Pharmacopeia are also a major step to achieve the goal. Along with pharmacopoeias and formularies other publications like 'Production of ISM Drugs with Current Good Manufacturing Practices', 'Quality Standards of Indian Medicinal Plants' could also be useful to maintain the standard and quality of ISM.

Research, industry, education and practice

Several research works are going on the ASU drugs. Basic research to preclinical or clinical study, investigation on standardization and formulation on ISM are a hot area of research in current time. Central Council for Research in Ayurvedic Sciences, Central Council for Research in Unani Medicine, Central Council for Research in Siddha, Central Council for Research in Yoga & Naturopathy, CSIR, Central Drug Research Institute (CDRI), several private research centre, institution and universities are actively engaged in research, development and promotion of traditional herbal medicine.

Development of use OMIC technique in herbal medicine

With the advancement in omic technique, the use of omic science is originating nearly in all biomedical fields. Omic techniques provide simultaneous assessment of classes of molecule, which are the main experimental spree for such an approach. Potential for application of omic analytical technologies and bioinformatics studies involving herbal medicine have higher cost and the range of multidisciplinary expertise is required for their application which initially constrained their application.

Omic technique is mainly used for identification of biomedical resources such as genomic technique in DNA

sequencing and fingerprinting or DNA microarrays. All the research works mainly related to biological issue mostly addressing the corroboration and quality control of herbal products. With the increase in pharmacological studies, the newer trends are established for the use of omic technique in the field of herbal plant related to pharmacological experiment. Proteomic technique have been applied for the treatment of cardiovascular diseases, epilepsy cancer etc. with the herbal medicine.

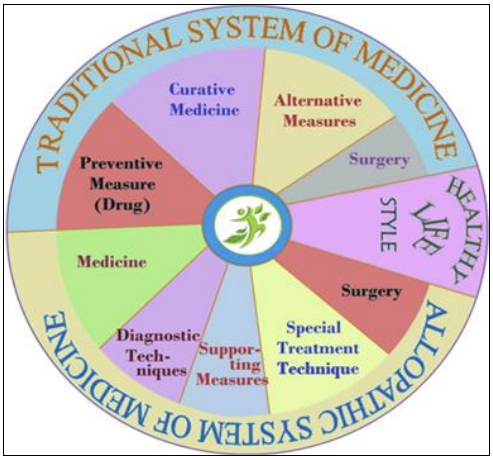

Fig 1

Typical Examples of Drug Discovery from Herbal Medicine

Antimalarial drugs developed from Artemisia annua and therapeutic agents for the treatment of hepatitis developed from the fruit of Fructus schisandrae chinensis (FSC) are the examples of successful drug discovery from herbal medicines. These remarkable achievements in research and development of THM have received worldwide acceptance.

Antimalarial Drugs

Malaria, which is currently the most prevalent and devastating infectious diseases, is a mosquito-borne infectious disease of humans caused by eukaryotic protists of the genus Plasmodium. Malaria causes more than one million deaths worldwide each year. Cerebral malaria has a mortality rate as high as 20%, which can rise to 50% in pregnancy, and severe malarial anemia can have a mortality rate of over 13%. Surviving patients with cerebral malariahave an increased risk of neurological and cognitive deficits, behavioral difficulties, and epilepsy [82]. Currently, chemotherapy remains the mainstay of interventional strategy in malaria control.

Archaeological findings from Mawangdui Han Dynasty Tombs from 200 BC indicated that the herb Qing-Hao derived from Artemisia annua has been used in herbal remedies for “lingering heat in joints and bones” and “exhaustion due to heat/fevers” in China for over two thousand years. The use of Qing-Hao for treating malaria dates back to the fourth century.

Hepatitis, an inflammatory disease of the liver, is commonly caused by drug intoxication or viral infection, with the latter being classified into types A, B, C, D, and E. According to WHO, 2 billion people worldwide have been infected by the hepatitis B virus (HBV), and among them 350–400 million are chronic HBV carriers, and about 1 million deaths are caused by HBV infection every year. It is estimated that around 1.2 million and 3.2 million people in the USA are battling chronic hepatitis B and C, respectively, and more than 85,000 new cases of hepatitis are diagnosed each year. In China, there are 93 million HBV carriers, and among them 30 million are patients with chronic hepatitis B.

Bicyclol, which was approved in 2001 as a therapeutic agent for hepatitis in China, has obtained patent protection in 15 countries and regions. The development of bicyclol highlights drug discovery from THM. FSC, Chinese magnolia vine fruit or orange magnolia vine fruit in English, is a commonly used THM. According to TCM theory, FSC possesses five kinds of flavors, namely, pungent, sweet, sour, bitter, and salty, which bespeak much of its therapeutic potential.

Problems of Drug Discovery from Herbal Medicine

Strategies of drug discovery from nature resources are greatly different from those of synthetics. It involves two key issues, ecological ethics and resource-dependent sustainable development. The current development of herbal medicines involves both modern ethics and technologies. In this section, ecological ethics on the drug discovery from herbal medicine are discussed. Ecological ethics are moral principles governing human attitudes towards the environment and rules of conduct for care and preservation of the environment. On our planet, no species, including humans, can evolve independently of its coevolution with other species. By the same token, no species can live independently of other species. As the ecological environment on earth deteriorates, the number of existing species has drastically decreased over the last five decades, with the exception of the rapidly growing humans. In fact, the imbalance between humans and other species has become a threat to the survival of humans, thereby ecosystem or plant ecology should be firstly considered in the herbal development. Plants including medicinal plants have incredible biological diversity, showing extreme flexibility in ecomorphology. It is undoubtedly that plants play an important role in ecosystems by providing essential services. Without plants there would be no human, animals, and insects, no life as we understand it on earth without plants. In any case vegetation always acts as indicator of general ecosystem health. Unfortunately, many species have disappeared even before they could be identified. Ten years ago, biologists warned that 25% of all species could become extinct over the next 20 to 30 years. Over the past two decades, pharmaceutical companies have shown an increased interest in exploring new compounds from plants for drug development. However, the lack of a rational approach in many aspects of this undertaking, including drug discovery from herbal medicine, has limited the success of these endeavors. In 2004, the World Wildlife Fund pointed out that due to the overexploitation of human consumption, 20% of medicinal plants in the world are facing extinction. These include popular medicinal plants such as Cypripedium pubescens, Trillium erectum, Aletris farinose, Chamaelirium luteum syn. Heloniaslutea (dioica), Hydrastis Canadensis, and Panaxquinquefolius, as well as many plants used in traditional herbal medicine. There are about 250,000 higher plant species on Earth and over 80,000 have good medicinal values. The past experience told us that once a plant species had been identified for its commercial potential, it may face a risk of extinction. In China, for instance, there are about thousand endangered

plants, of which 60–70% are medicinal plants. There are nearly 12,000 species of medicinal plants used in TCM, and more than 6,000 species have disappeared over a period of less than 20 years. At present, out of 400 kinds of commonly used herbs, the supply of more than 20% of them has become depleted from natural sources. For example, the annual sales of Isatistinctoria L., Ban-Lan-Gen in Chinese, were increased from 3,000 tons in 1970s to 60,000 tons during the period from 2006 to 2008; the over consumption of Ban-Lan-Gen has depleted its supply from natural source. Therefore, the preservation of endangered and rare medicinal plants has been an area of immense interest. Due to the market-driven overexploitation of herbal or plant resources in recent years, many herbs have been listed as endangered species. China, where herbal preparations account for 30–50% of the total medicinal consumption, has a number of herbs listed in the China Plant Red Data Book, in which the category of "Rare and Endangered Plants" includes *Acanthopanax senticosus*, *Fritillaria ussuriensis*, *Aquilaria sinensis*, Fritillaria Walujew, *Astragalus membranaceus*, *Gastrodia elata*, A. membranaceus. var. mongolicus, Ginkgo biloba, *Changium smyrnioides*, *Glehnia littoralis*, *Cistanche deserticola*, *Illicium difengpi*, *Coptis teeta*, *Juglans regia*, *Coptis chinensis*, Magnolia officinalis, *Dalbergia odorifera* M. o. var. biloba, *Dendrobium* candidum, *Morinda officinalis*, *Dimocarpus longan*, *Panax ginseng*, *Eucommia ulmoides*, *Phellodendron amurense*, Ferula sinkiangensis, *Picrorhiza scrophulariiflora*, *Fritillaria pallidiflora*, and Rosa rugosa. Many herbs from Arabian herbal medicine, including *Anchusa Negevensis*, Anchusa ovata, *Eryngium barrelieri*, *Eryngium maritimum*, *Eryngium maritimum*, Euphorbia hirsute, *Ophioglossum lusitanicum*, *Ophioglossum polyphyllum*, Teucrium procerum, *Teucrium scordium*, and *Teucrium scordium*, have also been designated rare or endangered species. Drug development from herbal medicine should take into account the diversity of species and ecological ethics. Ideally, during the drug development, one first isolates and identifies target compounds from herbs or plants, which is followed by total chemical synthesis of the compound(s), as was the case for aspirin. When a bioactive compound has been isolated, modification of the chemical structure may be performed in order to reduce the toxicity and increase the efficacy and solubility of the drug candidate. Acetylsalicylic acid, also called aspirin, is an acetyl derivative of salicylic acid, which is derived from the metabolism of salicin, a naturally occurring compound found in the bark of Willow and Spiraea plant 150 years ago. However, commercially available salicylic acid and aspirin are synthetics. Interestingly, aspirin causes a lesser degree of digestive upset than salicylic acid. Semisynthetic derivatives of artemisinin isolated from the plant Artemisia annua, such as dihydroartemisinin, artemether, and artesunate, were found to be more bioavailable and have greater activity than artemisinin itself. However, it is well known that the modification of the chemical structure of compounds derived from herbs does not always yield results with positive impact on the societies such as heroin (diamorphine) and "Bing-Du" (methamphetamine). The ethical principles should be conformed during the development and exploitation of herbal medicine. After all, humans should not fulfill their own needs at the expense of other species on earth. On the other hand, in less developed countries herbal medicine is the primary source of health care. When these herbs are seized by big Pharma, the resulting drugs will not be available to the people because of the costs. This is also an ethical issue in drug discovery from herbal medicines. Generally, the herbal medicines that are traditionally used on their value are less expensive than the new single-component drugs from them.

In order to meet the escalating demand for medicinal plants, herbal agriculture or farming of these plants is imperative—and the development of agrotechnology related to herbal production has become an area of intensive research. Farming medicinal plants (Yao-Nong in Chinese) for herb production has provided a number of jobs in China. During 2005–2010, central and local governments as well as enterprises in China invested 115.56 million RMB for the cultivation of herbs. Currently, there are 250 kinds of medical plants being cultivated or grown in China, encompassing 33.3 million hectares of farmland.Cell and bacterial cultures as well as transgenic plants are also available for supplying source materials for drug discovery from herbal medicine. For instance, Artemisia annua is the commercial source of artemisinin, but the concentration of artemisinin in this herb is low, ranging from 0.01 to 0.8% of the dry weight of the plant. To meet the increasing demand in the market, transgenic plants containing a higher content of artemisinin were developed. Although the use of transgenic plants is a disputable means of preserving biodiversity, genetic engineering will play an important role in saving the medicinal plants which are rare, endangered, or threatened with extinction. If the precursor (mevalonic acid lactone) and elicitor (methyl jasmonate) were added to the cell cultures, the production of artemisinin was increased by about 6 times relative to control cultures. In addition, Escherichia coli can produce terpene amorpha-4, 11-diene, a precursor of artemisinin. Generally, drug discovery from herbs should mainly involve synthesis and cultivation of medicinal plants, not just exploiting the wild plants in nature. Furthermore, to the largest possible extent, all parts of a medicinal plant should be utilized. For example, ginsenosides, the active ingredients of Radix Ginseng, are also found in the leaves and stems of Panax ginseng, therefore, leaves are also of medicinal values like stems. We can only harvest the leaves of Panax ginseng and let it grow back next year.

Conclusion

As ancient humans adopted a plant-based (i.e., herbivorous) diet, the body function of humans may have been primed by a large number of secondary metabolites derived from plants. Considering the extremely high cost and longtime of new drug development, as well as the high drug attrition rate, an imminent task for pharmaceutical companies is to explore new ways for drug R&D. Therefore, more and more attention in the field of drug discovery has been focused on the herbal medicine. Herbal medicine as a source of new compounds for drugs is going to become a global trend in the pharmaceutical industry.

References

1. Medicinal plants Chinese, www.hm160.cn/121/1211108.htm.
2. Zhang B, Peng Y, Zhang Z, *et al*., GAP production of TCM herbs in China, Planta Medica. 2010;

76(10):1948-1955.
3. Heuberger H, Bauer R, Friedl F, *et al*., Cultivation and breeding of Chinese medicinal plants in Germany, Planta Medica. 2010; 76(17):1956-1962.
4. Zhang L, Jing F, Li F, *et al*., Development of transgenic Artemisia annua (Chinese worm-wood) plants with an enhanced content of artemisinin, an effective anti-malarial drug, by hairpin-RNA-mediated gene silencing, Biotechnology and Applied Biochemistry. 2009; 52(3):199-207.
5. Baldi A, Dixit VK. Yield enhancement strategies for artemisinin production by suspension cultures of Artemisia annua, Bioresource Technology. 2008; 99(11):4609-4614.
6. Newman JD, Marshall J, Chang M, *et al*., High-level production of amorpha-4,11-diene in a two-phase partitioning bioreactor of metabolically engineered Escherichia coli, Biotechnology and Bioengineering. 2006; 95(4):684-691.
7. Wang JH, Lia W, Sha Y, Tezuka Y, Kadota S, Li X. Triterpenoid saponins from leaves and stems of Panaxquinquefolium L, Journal of Asian Natural Products Research. 2001; 3(2):123-130.
8. Chen J, Zhao R, Zeng YM, *et al*., Three new triterpenoid saponins from the leaves and stems of Panaxquinquefolium, Journal of Asian Natural Products Research. 2009; 11(3):195-201.
9. Epstein RS, Moyer TP, Aubert RE, Kane DJ, Xia F. Warfarin genotyping reduces hospitalization rates results from the MM-WES (Medco-Mayo Warfarin Effectiveness study). J Am CollCardiol. 2010; 55(25):2804-12.
10. Caraco Y, Blotnick S, Muszkat M. CYP2C9 genotype-guided warfarin prescribing enhances the efficacy and safety of anticoagulation: a prospective randomized controlled study. Clin Pharmacol Ther. 2008; 83(3):460-70.
11. Calvel P, Antoine DR, Bernard J, Charles P. Testicular postgenomics: targeting the regulation of spermatogenesis. Phil Trans R Soc. B. 2010; 365(1546):1481-500.
12. Altelaar AM, Heck AJ. Trends in ultrasensitive proteomics. Curr Opin Chem Biol. 2012; (2):205-10.