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# A review on Herbal Medicines and Herbal Drug Technology

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**ABSTRACT**

Natural products are gaining increased applications in drug discovery and development. Being chemically diverse they are able to modulate several targets simultaneously in a complex system. During the past decade, there have been significant advances in herbal drug technology. The traditional system of medicines dating ancient civilizations could reveal the safety of herbal drugs. It is the right time to decide upon the issues of safety and efficacy of herbal drug products. The legal status and approval mechanism of herbal medicine also vary from country to country. World Health Organization (WHO) has set specific guidelines for the assessment of the safety, efficacy and quality of herbal medicines as a prerequisite for global harmonization. The advancement of science and technology invades the herbal drug products in a broad manner. In keeping with these advances, a plethora of review article on this subject has been prepared to have a smooth platform for the beginners in this vast field.

## INTRODUCTION

Herbal medicines are the oldest remedies known to mankind. Herbs have been used by all cultures throughout history but India has one of the oldest, richest and most diverse cultural living traditions associated with the use of medicinal plants. In the present scenario, the demand for herbal products is growing exponentially throughout the world and major pharmaceutical companies are currently conducting extensive research on plant materials for their potential medicinal value. Herbal drug technology is used for converting botanical materials into medicines, where standardization and quality control with proper integration of modern scientific techniques and traditional knowledge is important. Herbal formulations have reached widespread acceptability as therapeutic agents for diabetics, arthritics, liver diseases, cough and cold, and memory enhancement throughout the world. Herbals are traditionally considered harmless and increasingly being consumed by people without prescription. The traditional medicine is increasingly solicited through the traditional practitioners and herbalists in the treatment of infectious diseases. The household remedies mostly consist of regular kitchen ingredients and are generally used as over the counter (OTC) medicines.[1-7]

The major drawback of modern medicines is their side effects which may lead to life threatening of patients. Herbal medicines also have their list of side effects like any other synthetic drug. Thus it is essential to evaluate their clinical safety and efficacy. Current focus on chemotype-driven finger printing and related techniques requires integration with genotype-driven molecular techniques so that an optimal characterization of botanical materials is possible. The role of natural products, herbal medicine, tribal and traditional medicines is being increasingly appreciated in recent years for the prevention and cure of human elements. Being chemically diverse they are able to modulate several targets simultaneously in a complex system.

Natural product research is often based on ethnobotanical information and many of the drugs used today were employed in indigenous societies. One of the aims of ethnopharmaceutical research is better understanding of the pharmacological effects of different medicinal plants traditionally used in healthcare. Plants are regarded as a promising source of novel therapeutic agents due to their higher structural diversity as compared to standard synthetic chemistry. Plants have applications in the development of therapeutic agents and act as a source of bioactive compounds for possible use as drugs[8-10] Three approaches to natural product-based drug discovery are as follows:

- Screening of crude extracts
- Screening of pre-fractionated extracts
- Screening of pure compounds

## Standardization of Herbal Drugs

Quality control of herbal medicines is a tedious and difficult job. Commercialization of the manufacture of these medicines to meet their increasing demand has resulted in a decline in their quality and also primarily due to a lack of adequate regulations pertaining to this sector of medicine. The need of the hour is to evolve a systematic approach and to develop well-designed methodologies for the standardization of herbal raw materials and herbal formulations.[11-15]

India can emerge as the major country and play the lead role in production of standardized, therapeutically effective ayurvedic formulation. India needs to explore the medicinally important plants. This can be achieved only if the herbal products are evaluated and analyzed using sophisticated modern techniques of standardization such as UV-Visible, TLC, HPLC, HPTLC, GC-MS, spectrofluorimetric and other methods.

Herbal medicines differ from that of the conventional drugs and many innovative methods are coming into being for the sake of quality assessment of herbal drugs. Fingerprint analysis approach using chromatography has become the most potent tools for quality control of herbal medicines because of its simplicity and reliability. It can serve as a tool for identification, authentication and quality control of herbal drugs. Now a days newer and advanced methods are available for the standardization of herbal drugs like fluorescence quenching, combination of chromatographic and spectrophotometric methods, biological assays, use of biomarkers in fingerprinting etc. Bioassay can play an important role in the standardization of herbal drugs and can also become an important quality control method as well as for proper stability testing of the product.

Quality, efficacy and safety studies are essentials for Drug Registration. These studies must be performed in compliance with current international guidelines, which cover not only synthetic chemical entities but also phytopharmaceuticals. Thus, there arises the need to identify appropriate active principle or marker compounds (biomarker/active marker) to characterize the extracts.[16-20]

Scientifically validated and technologically standardized herbal medicines may be derived using a safe path of reverse pharmacological approach based on traditional knowledge database. This may play a vital role in drug discovery, development and therapeutics. Herbal medicinal products may vary in composition and properties, unlike conventional pharmaceutical products, which are usually prepared from synthetic, chemically pure materials by means of reproducible manufacturing techniques and procedures. Correct identification and quality assurance of the starting material is, therefore, an essential prerequisite to ensure reproducible quality of herbal medicine, which contributes to its safety and efficacy.

## Pharmacovigilance of Herbal Medicines

Pharmacovigilance means the science and activities relating to the detection, assessment, understanding and prevention of the adverse effects or any other possible drug-related problems, related to herbal, traditional and complementary medicines. Systematic data on the incidence of traditional medicine-associated adverse effects are not available due to products with multiple ingredients, poor standardization, lack of clinical trials,

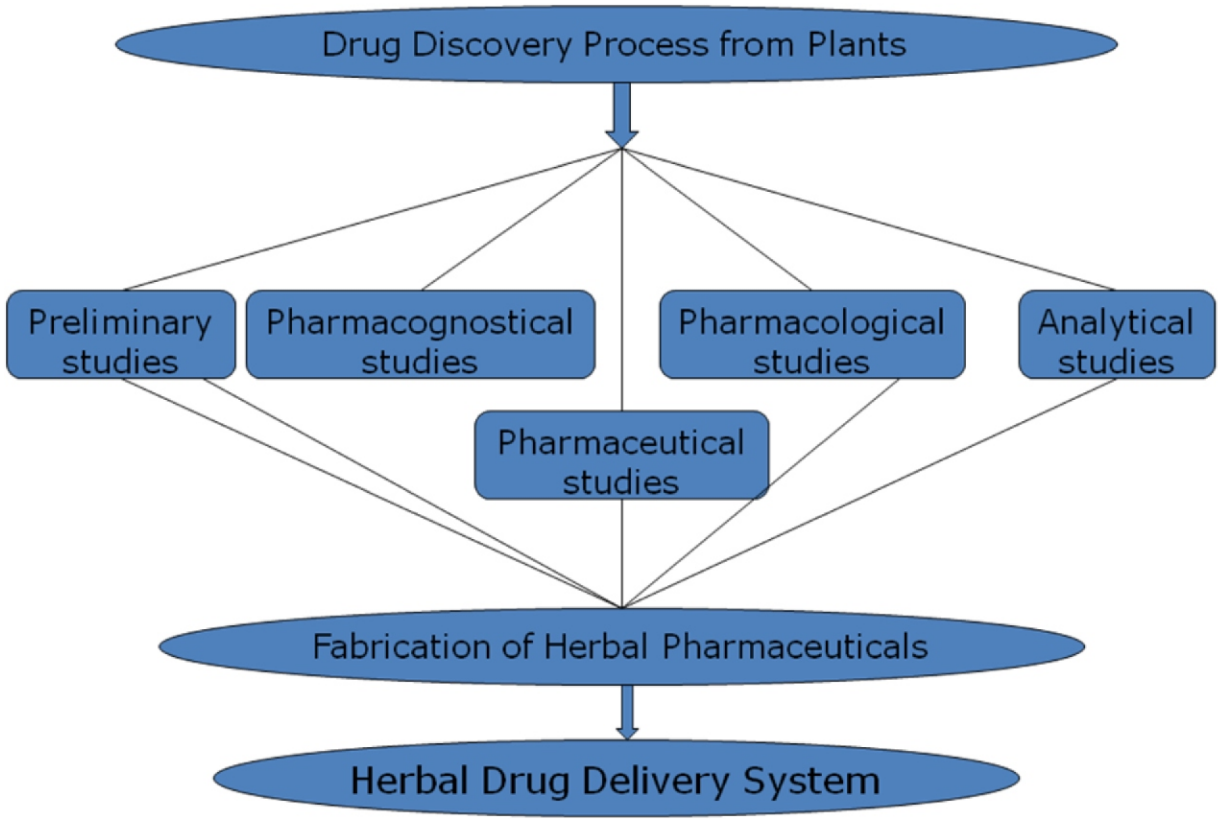


**Fig. 1.** Design and Development of Herbal Drug Delivery System

variation in manufacturing processes, contamination, adulteration and misidentification of herbs etc. Pharmacovigilance for herbal medicines is in its infancy and monitoring the safety of herbal medicines presents unique challenges as such preparations are available from a wide range of outlets where no healthcare professionals are available. It aims to achieve the ultimate goal of safer and more effective treatment available to patients. The Medicines and Healthcare Products Regulatory Agency's, UK has launched 'yellow card' scheme for ADR reporting for monitoring the safety of herbal medicines. Indian drug regulation has not yet fully integrated traditional herbal medicine into all aspects of health care system. Herbal pharmacovigilance should be implemented in Indian herbal regulatory system to access various aspects of ADR associated with single herb and/or polyherbal formulation. Modified spontaneous reporting forms are to be designed following WHO template to collect information on suspected ADRs of herbal medicines.[21,22]

**Table 1 :** List of Herbal Plants and their Biological Activity

| S.No | Category | Herbal Plants | |
|---|---|---|---|
| | | Botanical Source | Principle Constituents |
| 1. | Anti-inflammatory natural products | Berberis aristata<br>Boswellia serrata<br>Commiphora mukul<br>Curcuma longa | Berberine<br>Boswellic acid<br>Guggulsterone<br>Curcumin |
| 2. | Cardiovascular natural products | Coleus sp.<br>Rauwolfia serpentine<br>Terminalia arjuna<br>Thevetia neriifolia | Coleonol<br>Reserpine<br>Arjunolic acid<br>Thevitin A & B |
| 3. | Anti-diabetic natural products | Eugenia jambolena<br>Momordica charantia<br>Pterocarpus marsupium | Anthocyanins<br>Charantin<br>Liquiritigenin & Isoliquiritigenin |
| 4. | Anti-obesity natural products | Alpinia officinarum<br>Areca catechu<br>Commiphora mukul | 3-Methyletherganglin<br>Tannins<br>Guggulipid |
| 5. | Anti-malarial natural products | Selaginella bryopteris | Bilobetin & Heveaflavone |
| 6. | Anti-leishmanial natural products | Diospyros spp.<br>Plumbago spp. | Diospyrin<br>Plumbagin |
| 7. | Anti-viral natural products | Terminalia belerica | Termilignan Thannilignan & Anolignan B |
| 8. | Anti-neoplastic natural products | Arnebia nobilis<br>Roylea calycina | Arnebin-I<br>Precalyone |
| 9. | Immunomodulatory natural products | Tinospora cordifolia | Tinosporic acid & Cordifolioside |
| 10. | Fertility enhancer | Embelia ribes | Embelia |

### Global Status and Regulation of Herbal Medicines

Herbal products are well established as phytomedicines in some countries, whereas in others their therapeutic claims are not allowed and regarded as foods. The World Health Organization (WHO) has reviewed the regulatory control of herbal medicines in 50 countries. The Drugs Directorate has provided guidelines for the manufacture and sale of botanical products which fall into three categories:

I. Food supplements (no DIN required, no therapeutic claims)

II. Phytopharmaceuticals with full drug status (approved therapeutic indications, approved dosage, efficacy supported by scientific evidence, DIN required)

III. Traditional herbal medicines (selfmedication only, efficacy supported from the herbal literature, approved therapeutic indications and dosage) (Leung, 1980).

In India, the first National Health Policy 1983, mentions that India's rich tradition of health care should be included in national programmes. The department of AYUSH, which was started in 1995, regulates traditional medicine (TM) programmes. The government of India has an explicit and separate policy for TM since 2002 and is also governed by the Drugs and Cosmetics Act, 1940. GMPs are mandatory since 2002, although not exactly as recommended by WHO, but still they are based on them. Central and State governments are impressing upon manufacturing units to comply with GMP norms and to ensure quality standards. The world market for herbal medicine, including herbal products and raw materials has been estimated to have an annual growth rate between 5 and 15%. Total global herbal drug market is estimated as US $62 billion and is expected to grow US $1 to 5 trillion by the year 2050. The value of medicinal plants-related trade in India is estimated at Rs 5000 crores per annum. Global trend leading to increased demands of medicinal plants for pharmaceuticals, phytochemicals, nutraceuticals, cosmetics and other products is an opportunity sector for Indian trade and commerce.[23-25]

## APPLICATIONS

### ➢ Herbal Remedies for Psoriasis Diseases

Psoriasis is undoubtedly distressing and topical treatments using herbal remedies can able to overcome the adverse and antagonistic effects and also improve the bioavailability of drug. Herbals drugs like Aloe, Cayenne, Chamomile, Dong Quai, Emu oil, Evening prime rose oil, Fish oil, Tea tree oil, Turmeric, Slippery elm, Wintergreen, Shark cartilage, Milk thistle, Glucosamine, Flexseed oil are generally used for the treatment of psoriasis.

### ➢ Herbal drugs for disorders caused by "cellphones"

Radiation from cell phones and telephone towers can cause health problems such as brain tumors, cancer, infertility, memory loss, depression, sleep and behavior problems. Long-term exposure to cell phone radiation affects the body, particularly the electrical organ, brain. Now-a-days *herbal drugs* are widely used in the curing of disorders caused by cellphones. Drugs like *Radix Curcume, Herba Agrimonia* and *Fructus Aurantii* are collectively marketed under the tradename "Canelim Capsules" which are used in Brain Cancer. Other drugs viz. *Hypericum perforatum, Passiflora incamata,* Valerian, Lemon balm tea, etc are used in curing insomnia.

### ➢ Polyherbal Therapies

In the past decade there has been a paradigm shift from single-target drugs to multi-target drugs. Multi-target approaches are directed towards the activation of defense, protective and repair mechanisms of the body rather than destruction of the damage-causing agent. This may be achieved by the use of a combination of drugs. The concept of multi-targeted therapy exists in traditional medical treatments that employ multi-component extracts of natural products which simultaneously act on multiple targets. They have the synergistic, potentiative, agonistic/antagonistic pharmacological agents within themselves that work together in a dynamic way to produce therapeutic efficacy with minimum side effects.[26-34]

### ➢ Phytosomes A Novel Herbal Drug Delivery System

Phytosomes are a new concept in herbal delivery systems. Complexing the polyphenolic phytoconstituents in molar ratio with phosphatidylcholine results into a new herbal drug delivery system- "Phytosome". The term "phyto" means plant while "some" means cell-like. Phytosomes are advanced forms of herbal products that are better absorbed, utilized, and as a result produce better pharmacokinetic and therapeutic profile than conventional herbal extracts. Clinical trials of phytosomes have shown increase in bioavailability of herbal extracts. Phytosomal drug delivery system is mainly used to deliver systemic antioxidants (mainly flavonoid and terpenoid component) and also used to treat the disease like blood pressure, liver disease, cancer, skin disease and to protect the brain lining.[35]

### ➢ Use of Herbal Excipients in Novel Drug Delivery

The use of natural excipients to deliver the bioactive agents has been hampered by the synthetic materials. However advantages offered by these natural excipients are non-toxic, less expensive and freely available. Natural polysaccharides (Pectins, starch, guar gum, amylase and karaya gum) are extensively used for the development of solid dosage forms. Bioadhesive sodium alginate microspheres of metoprolol tartrate for intranasal systemic delivery are prepared to avoid the first-pass effect, as an alternative therapy to injection, and to obtain improved therapeutic efficacy in the treatment of hypertension and angina pectoris.

### ➢ Use of Molecular Biomarkers in Herbal Technology

DNA-based techniques have been widely used for authentication of plant species of medicinal importance. Also DNA-based molecular markers have proved their utility in various fields viz. taxonomy, physiology, embryology and genetics. A number of constituents from the herbs can be used as biomarker which exhibits diverse pharmacological activity. Molecular biomarkers are widely used in producing genetic variation/genotyping many medicinal plants, in the determination of adulteration/substitution, in medicinal plant breeding, in food and neutraceuticals application such as identification of disease resistant genes, diversity analysis of exotic germplasms, sex identification of dioeceous plant and in phylogenetic analysis. These markers together with DNA are useful in various *invitro* and *invivo* herbal technology.[36,37]

### Examples:

***i. Genetic variation/genotyping :*** Random amplified polymorphic DNA (RAPD)28,29 RAPD-based molecular markers have been found to be useful in differentiating different accessions of *Taxus wallichiana*38, neem39, *Juniperus*

*communis* L.40, *Codonopsis pilosula*41, *Allium schoenoprasum* L.42, *Andrographis paniculata*43 collected from different geographical regions.

***ii. Authentication of medicinal plant :*** Dried fruit samples of *Lycium barbarum* were differentiated from its related species using RAPD markers68.

***iii. Detection of adulteration/substitution :*** RAPD technique was adopted to identify eight types of dried *Coptis* rhizomes and one type of *Picrorrhiza* rhizome, a substitute for the former in the Chinese herbal market80 .

### ➢ DNA Microarrays in Herbal Drug Technology and Research

The DNA Microarray (DNA arrays, gene chips or biochips) is an orderly arrangement of thousands of oligonucleotides or identified sequenced genes printed on an impermeable solid support, usually glass, silicon chips or nylon membrane. DNA microarrays provide a revolutionary approach to the investigation of gene expression, serve as suitable high throughput tool for simultaneous analysis of multiple genes and thus play an essential role in quality control of herbal drugs and extracts. In natural products a broad report are of chemical entities act together on multiple targets that makes it necessary to study the changes in expression of multiple genes simultaneously. Three main applications of DNA microarrays are as follows:

❖ In pharmacodynamics: For discovery of new diagnostic and prognostic indicators and biomarkers of therapeutic response; elucidation of molecular mechanism of action of a herb, its formulations or its phytochemical components and identification and validation of new molecular targets for herbal drug development.

❖ In pharmacogenomics: For prediction of potential side-effects of the herbal drug during preclinical activity and safety studies; identification of genes involved in conferring drug sensitivity or resistance and prediction of patients most likely to benefit from the drug and use in general pharmacogenomic studies.

❖ In pharmacognosy: For correct botanical identification and authentication of crude plant materials as part of standardization and quality control.

Other applications of DNA microarrays include toxicogenomics and quality control of herbal drugs and extracts.[38-43]

### ➢ Herbal Cosmeceuticals

The term cosmeceuticals is used to describe the OTC skin care products that claim therapeutic benefits by the addition of plant based active ingredients such as a-hydroxy acids, retinoic acid, ascorbic acid and co-enzymes to increase the skin elasticity, delay skin ageing by reducing the wrinkles, antioxidant property as protective against UV radiation and to check the degradation of the collagen respectively. These are applied topically in the form of creams, powders, lotions etc and also used in soaps, shampoos and perfumes for skin care, acne and hair growth and care. The herbs which are commonly used now-a-days are Aloe, Almond oil, Mehandi, Neem, Sandalwood oil, Coconut oil etc. Also *Thuja Occidentalis* (helps in UV absorption and used in whitening of skin) and *Gaultheria Fragmatisma* are used as natural skin care agent.

### Safer Use of Herbal Drugs

Herbs have a medicinal effect, but the effect is usually not nearly as strong as that of pharmaceutical drugs. This is because prescription drugs have been synthesized and manufactured in a laboratory by taking the "active ingredient" found in plant based or some other form. Sometimes even after processing, the most active ingredients have not been separated from the parts of herbal plants. Sufficient data does not exist for most plants to guarantee their quality, efficacy and safety. Plants contain hundreds of constituents and some of them are very toxic, such as the most cytotoxic anti-cancer plant-derived drugs, digitalis and the pyrrolizidine alkaloids, etc. However, the adverse effects of phytotherapeutic agents are less frequent compared with synthetic drugs, but well-controlled clinical trials have now confirmed that such effects really exist. The most important thing to remember is that if you want to use herbal medicines it is always safest to be under the care and control of a qualified herbalist [44-49]

## CONCLUSION

In India more than 70% of the population uses herbal drugs for their health. There is a vast experience-based evidence for many of these drugs. For better understanding of molecular mechanisms, analysis of gene expression is necessary. It may provide a suitable high-throughput platform for research and development of drugs from natural products. Instead of using the wild plants, domestic production, biotechnological studies and genetic improvement of medicinal plants will offer great advantages, since it will be possible to obtain uniform and high quality raw materials which are fundamental to the efficacy and safety of herbal drugs. Harmonization and improvement in the processes of regulation is needed. Newer approaches utilizing collaborative research and modern herbal drug technology in combination with traditional health principles will reveal the hidden secrets to unburden mankind from dreadful diseases.

## REFERENCES


1. Heinrich M. Ethnobotany and natural products: the search for new molecules, new treatments of old diseases or a better understanding of indigenous cultures. Curr Top Med Chem. 2003:3:141154.
2. Vuorela P, Leinonen M, Saikku P, Tammela P, Rauha JP, Wennberg T. Natural products in the process of finding new drug candidates. Curr Med Chem. 2004:11:13751389.
3. Patwardhan B. Ethnopharmacology and drug discovery. J Ethnopharmacol. 2005:100:5052.
4. Schmidt B, Ribnicky D. M, Poulev A, Logendra S, Cefalu W. T, Raskin I. A natural history of botanical therapeutics. Metabolism. 2008:57:S39.
5. Brower V. Back to nature: Extinction of medicinal plants threatens drug discovery. J Natl Cancer Inst. 2008: 100:838839.
6. Calapai G. European legislation on herbal medicines: A look into the future. Drug Saf. 2008:31: 428431.
7. Ribnicky D. M, Poulev A, Schmidt B, Cefalu W. T, Raskin I. The science of botanical supplements for human health: A view from the NIH botanical research centers: Evaluation of botanicals for improving human health. Am J Clin Nutr. 2008:87:472S475S.

8. Li J. W. H, Vederas J. C. Drug discovery and natural products: End of an era or an endless frontier? Science. 2009:325:161165.
9. Xutian S, Zhang J, Louise W. New exploration and understanding of traditional Chinese medicine. Am J Chin Med. 2009:37:411426.
10. Evans M, Shaw A, Thompson E. A, Falk S, Turton P, Thompson T, Sharp D. Decisions to use complementary and alternative medicine (CAM) by male cancer patients: Information-seeking roles and types of evidence used. BMC Complement Altern Med. 2007:7:25.
11. Bent S. Herbal medicine in the United States: Review of the Efficacy, Safety, and Regulation. J Gen Intern Med. 2008:23(6):854-859.
12. Sahoo N, Choudhury K, Manchikanti P. Manufacturing of biodrugs: Need for harmonization in regulatory standards. BioDrugs. 2009:23(4):217229.
13. Sahoo N, Manchikanti P, Dey S. Herbal drugs: Standards and regulation. Fitoterapia. 2010:81(6):462471.
14. Kantor M. The role of rigorous scientific evaluation in the use and practice of complementary and alternative medicine. J Am Coll Radiol. 2009:6:254262.
15. Li W. F, Jiang J. G, Chen J. Chinese medicine and its modernization demands. Arch Med Res. 2008:39:246251.
16. De Smet P. Herbal medicine in Europe: Relaxing regulatory standards. N Engl J Med. 2005:352:11761178.
17. Vlietinck A, Pieters L, Apers S. Legal requirements for the quality of herbal substances and herbal preparations for the manufacturing of herbal medicinal products in the European Union. Planta Med. 2009:75:683688.
18. Agarwal SS, Paridhavi M. Screening methods used for herbal drugs. Herbal Drug Technology, 1st edn, Universities Press; Hyderabad,2007.p.490-624.
19. Ye F, Wang H, Jiang S, Wu J, Shao J, Cheng X. Quality evaluation of commercial extracts of *Scutellaria baicalensis*. Nutr Cancer. 2004:49:21722.
20. Saper RB, Phillips RS, Sehgal A, Khouri N, Davis RB, Paquin J. Lead, mercury, and arsenic in US- and Indian manufactured Ayurvedic medicines sold via the Internet. JAMA. 2008:300:915-923.
21. Pipasha B. Setting standards for proactive Pharmacovigilance in India: The way forward. Indian J Pharmacol. 2007:39:124-128.
22. Tilburt J. C, Kaptchuk T. J. J. Herbal medicine research and global health: An ethical analysis. Bull World Health Organ. 2008:86(8):594599.
23. Vaidya ADB, Devasagayam TPA. Current status of herbal drugs in India: An overview. J Clin Biochem Nutr. 2007:41(1):1-11.
24. Singh J, Singh AK, Khanuja SP. Medicinal Plants: India's Opportunities. Pharma Bioworld. 2003:1:59-66.
25. Aneesh TP, Hisham M, Sekhar MS, Madhu M, Deepa TV. International Market Scenario of Traditional Indian Herbal Drugs- India Declining. Int J Green Phar. 2009:3(3):184-190.
26. Ernst E. Herbal medicine in the treatment of rheumatic diseases. Rheum Dis Clin N Am. 2011:37:95-102.
27. Andreescu C, Mulsant BH, Emanuel JE. Complementary and alternative medicine in the treatment of bipolar disorder-A review of the evidence. Journal of Affective Disorders. 2008:110:16-26.
28. May BH, Xue CC, Yang AW. Herbal medicine for dementia: A systematic review. Phytotherapy Research. 2009:23:447-459.
29. Freeman MP, Fava M, Lake J et al. Complementary and alternative medicine in major depressive disorder: The American Psychiatric Association Task Force report. J Clinical Psychiatry. 2010:71(6):669-681.
30. Balsano C, Alisi A. Antioxidant effects of natural bioactive compounds. Curr Pharm Des. 2009:15:30633073.
31. Niv N, Shatkin JP, Hamilton AB, Unutzer J, Klap R, Young AS. The use of herbal medications and dietary supplements by people with mental illness. Community Mental Health J. 2010:46:563-569.
32. Sarris J. Herbal medicines in the treatment of psychiatric disorders: A systematic review. Phytotherapy Research. 2007:21:703-716.
33. Tang S. Y, Halliwell B. Medicinal plants and antioxidants: What do we learn from cell culture and Caenorhabditis elegans studies? Biochem Biophys Res Commun. 2010:394:15.
34. Ramnath V, Kuttan G, Kuttan R. Immunopotentiating activity of abrin, a lectin from Abrus precatorius L. Ind J Exp Biol. 2002:40:910-913.
35. Rishton G. M. Natural products as a robust source of new drugs and drug leads: Past successes and present day issues. Am J Cardiol. 2008:101:43D49D.
36. Benzie I. F. F, Wachtel-Galor S. Biomarkers in long-term vegetarian diets. Adv Clin Chem. 2009:47:170208.
37. Benzie I. F, Wachtel-Galor S. Vegetarian diets and public health: Biomarker and redox connections. Antioxid Redox Signal. 2010:13(10):15751591.
38. Csermely P, Agoston V, Pongor S. The efficiency of multi-target drugs: the network approach might help drug design. Trends Pharmacol Sci. 2005:26:178182.
39. Wagner H, Steinke B, Allescher HD. Multitarget Therapy in Functional Dyspepsia. Phytomedicine. 2006:13(V):1-130.
40. Williamson EM. Synergy and other interactions in phytomedicines. Phytomedicine. 2001:8:400-409.
41. Imming P, Sinning Ch, Meyer A. Drugs, their targets and the nature and number of drug targets. Drug Discovery. 2006:5:821-834.
42. Roy S, Khanna S, Shah H, Rink C, Phillips C, Preuss H, et al. Human genome screen to identify the genetic basis of the anti-inflammatory effects of Boswellia in microvascular endothelial cells. DNA Cell Biol. 2005:24:244255.
43. Boyer J, Allen WL, McLean EG, Wilson PM, McCulla A, Moore S. Pharmacogenomic identification of novel determinants of response to chemotherapy in colon cancer. Cancer Res. 2006:66:27652777.

44. Cohen P. A, Ernst E. Safety of herbal supplements: A guide for cardiologists. Cardiovasc Ther. 2010:28:246253.

45. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs. Drugs. 2009:69(13):1777-1798.

46. Fugh Berman A. Herbdrug interactions. Lancet. 2000:355:134138.

47. Coxeter PD, McLachlan AJ, Duke CC, Roufogalis BD. Herbdrug interactions: an evidence based approach. Curr Med Chem. 2004:11:15131525.

48. Ernst E, Schmidt K, Wider B. CAM research in Britain: The last 10 years. Complement Ther Clin Pract. 2005:11:1720.

49. Conboy L, Kaptchuk T. J, Eisenberg D. M, Gottlieb B, Acevedo-Garcia D. The relationship between social factors and attitudes toward conventional and CAM practitioners. Complement Ther Clin Pract. 2007:13:146157.