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Review Article

RECENT TRENDS IN HERBAL DRUGS: A REVIEW

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ABSTRACT

Herbal medicines make up a significant constituent of the tendency toward alternative medicine. Herbal medicine is becoming ever more popular in today's world as people seek out natural remedies. Herbal medicines have been used since the dawn of civilization to maintain health and to treat various diseases. To compete with the growing pharmaceutical market, there is an importance to use and scientifically authenticate more medicinally useful herbal products. This article provides a general idea of herbal medicines and intended to explain the therapeutic effectiveness of various herbal medicines, adverse drug reactions, drug interactions, standardization and stability testing of herbal medicines, pharmacovigilance and regulatory status of herbal medicines.

Keywords: Herbal drugs, Standardization, Stability testing, Efficiency.

INTRODUCTION

Herbal drugs referred as plants materials or herbalism, involves the use of whole plants or parts of plants, to treat injuries or illnesses¹. Herbal drugs are use of therapeutic herbs to prevent and treat diseases and ailments or to support health and healing². These are drugs or preparations made from a plant or plants and used for any of such purposes. Herbal drugs are the oldest form of health care known to mankind³. There are many herbal products offered that assert to treat the symptoms of a broad range of problems, from depression to cold and flu. World Health Organization⁴ (WHO) has distinct herbal drugs as complete, labeled medicinal products that have vigorous ingredients, aerial or secretive parts of the plant or other plant material or combinations. World Health Organization has set

precise guidelines for the evaluation of the safety, efficacy, and quality of herbal medicines. WHO estimates that 80% of the world populations currently use herbal drugs for major healthcare. Exceptionally, in some countries herbal drugs may also enclose by tradition, natural organic or inorganic active constituents which are not of plant source. Herbal drug is a chief constituent in traditional medicine and a common constituent in ayurvedic, homeopathic, naturopathic and other medicine systems⁵. Herbs are usually considered as safe since they belong to natural sources⁶. The use of herbal drugs due to toxicity and side effects of allopathic medicines, has led to rapid increase in the number of herbal drug manufacturers. For the past few decades, herbal drugs have been more and more consumed by the people with no prescription.

Seeds, leaves, stems, bark, roots, flowers, and extracts of all of these have been used in herbal drugs over the millennia of their use. Herbal products have reached extensive adequacy as beneficial agents like antimicrobial, antidiabetic, antifertility, antiageing, antiarthritic, sedative, antidepressant, antianxiety, antispasmodic, analgesic, anti-inflammatory, anti-HIV, vasodilatory, hepatoprotective, treatment of cirrhosis, asthma, acne, impotence, menopause, migraine, gall stones, chronic fatigue, alzheimer's disease and memory enhancing activities⁷. Herbal drugs have been recognized for approximately 4000 years. These drugs have survived real world testing and thousands of years of human testing. Some drugs have been discontinued due to their toxicity, while others have been modified or combined with additional herbs to counterbalance side effects.

Advantages of Herbal Drugs

- Low/Minimum cost
- potency and efficiency
- enhanced tolerance
- More protection
- fewer side-effects
- complete accessibility
- recyclable

Disadvantages of Herbal Drugs

- Not able to cure rapid sickness and accidents
- Risk with self dosing
- Complexity in standardizations

Usage and Preparation of Herbal Drugs

The use of herbal drugs in the correct way provides effectual and safe treatment for many ailments. The efficiency of the herbal drugs is typically subjective to the patient⁸. The strength of

the herbal drugs varies based on the genetic distinction, growing conditions, timing and method of harvesting, revelation of the herbs to air, light and dampness, and type of conservation of the herbs. Some of the plants that make up herbal drugs are cultured and processed in the country and others

are imported from around the world. Raw materials for herbal drugs may be derived from carefully cultivated plants or collected in the wild⁹. Herbal drugs are accessible in several forms and often require preparation before their use. They can be normally purchased in mass form as dried plants, plant parts or insecurely packed for herbal teas and decoctions. Decoctions are made by boiling the herb in water, then straining out of the plant material. More intense forms of herbal drugs are available in the form of hydro alcoholic tinctures and fluid extracts. Methods of preparation may differ because of the nature of the plants active chemical constituents¹⁰.

Pharmacological Actions of Herbal Drugs

Anti-inflammatory activity

The extracts of *Achillea millefolium*, *Artemisia vulgaris*, *Bauhinia tarapotensis*, *Curcuma longa*, *Forsythia suspense*, *Houttuynia cordata*, *Glycyrrhiza uralensis*, *Lonicera japonica*, *Ruta graveolens*, *Securidaca longipedunculata* and *Valeriana wallichii* have shown anti-inflammatory activity¹⁰.

Antidiabetic activity

From earliest period, peoples are using herbal plants as home remedies for the treatment of diabetes¹¹. The a variety of herbal plants with antidiabetic activity are *Abroma augusta*, *Acacia melanoxylon*, *Acacia modesta*, *Acacia nilotica*, *Aconitum ferox*, *Adhatoda vasika*, *Adiantum capillus*, *Adiantum incisum*, *Agrimonia eupatoria*, *Allium sativum*, *Aloe barbadensis*, *Althaea officinalis*, *Apium graveolens*, *Arctium lappa*, *Commiphora abyssinca*, *Embilica officinalis*, *Eucalyptus globules*, *Ginseng panax*, *Gymnema sylvestre*, *Inula helenium*, *Juniperus communis*, *Medicago sativa*, *Nigella sativa*, *Orthosiphon stamineus*, *Panax quinquefolius*, *Polygala senega*, *Plantago ovata*, *Punica granatum*, *Salvia officinalis*, *Scoparia dulcis*, *Tanacetum vulgare*, *Taraxacum officinale*, *Tecoma stans*, *Trifolium alexandrinum*, *Trigonella foenum*, *Turnera diffusa*,

Urtica, dioica, Xanthium strumarium, Zea mays and *Zingiber officinale*¹²⁻¹⁵.

Analgesic activity

The extracts of *Bougainvillea spectabilis, Chelidonium majus, Ficus glomerata, Dalbergia lanceolaria, Glaucium grandiflorum, Glaucium paucilobum, Nepeta italic, Polyalthia longifolia, Sida acuta, Stylosanthes fruticosa, Toona ciliate, Zataria multiflora* and *Zingiber zerumbet* are used as analgesic agents¹⁶.

Anticancer activity

Medicinal plant products exhibiting anticancer activity continue to be the subject of extensive research aimed at the development of drugs for the treatment of different human tumors. The medicinal plants used for the treatment of cancer are, *Acalypha fruticosa, Alangium lamarki, Catharanthus roseus, Celastrus paniculatus, Embelia ribes, Ficus glomerata, Ficus racemosa, Ocimum basilicum, Plumbago zeylanica, Terminalia chebula, Tylophora indica, Wrightia tinctoria*. The extracts used for the treatment of breast cancer is *Buthus martensi, Colla cornu, Herba epimedii, Fructus lycii, Radix angelicae, Radix bupleuri, Rhizoma corydalis, Rhizoma curculiginis, Radix paeoniae, Radix glycyrrhizae, Scolopendra subspinipes, Squama manitis, Tuber curcumae*. The herbal drugs used for treatment of pancreatic cancer are *Emblica officinalis, Nigella sativa* and *Terminalia belleric*¹⁷⁻¹⁹.

Antiageing activity

Cell membranes are particularly susceptible to the hostility of free radicals. When the nucleus is injured, the cell loses its ability to replicate itself. The impaired cell replication results in the destabilized immune system, skin ageing and many age related disorders. Various antioxidants neutralize the free radicals and prevent oxidation on a cellular level. The most effectual antioxidants include pine bark extract, grape seed extract, and blue berries were effectual against the hostility of free radicals. Some commonly used herbs as antiageing agents are *Allium sativum, Arnica*

montana, Cucumis sativum, Curcuma longa, Ficus bengalensis, Lycium barbarum, Ocimum sanctum, Panax ginseng, Prunus amygdalus, Santalum album, Rosa damascene and *Withania somnifera*^{20, 21}.

Antifertility activity

Plant drugs have involved in the concentration of many scientists as a primary source of naturally occurring fertility regulating agents because of their little or no side effects. The plants that have been reported to have antifertility activity are *Amaranthus retroflexus, Artabotrys odoratissimus, Barberis vulgaris, Carica papaya, Dieffenbachia seguine, Evodia rutacapra, Fatsia horrid, Ferula assafoetida, Hibiscus rosasinensis, Lonicera ciliosa, Magnolia virginiana, Mardenia cundurango, Pisum sativum, Podophyllum peltatum, Punica granatum, Raphanus sativus, Rehmannia glutinosa, Semecarpus anacardium, Sesbania sesban, Stemona japonica, Thuja occidentalis, Taxus baccata* and *Verbena officinalis*²².

Antipsoriasis activity

A variety of natural proprietary formulas and preparations containing plant materials have been used to provide symptomatic relief in psoriasis. The different herbal remedies for psoriasis are, turmeric, curcumin, shark cartilage extract, oregano oil, milk thistle. Various antimicrobial agents *Azadirachta indica, Calendula officinalis, Cassia tora, Wrightia tinctoria* have been used in the management of psoriasis^{23, 24}.

Antidepressive activity

A number of nutritional and herbal supplements have shown promise as alternative treatments for depression. A large number of plants have potential functions to treat depression which are described as, *Bacopa monniera, Panax quinquefolius, Piper methysticum, Rhodiola rosea, Valeriana officinalis* and *Hypericum perforatum*²⁵.

Antivitaligo Activity

Antivitaligo oil is a herbal remedy manufactured with potent herbs and is produced with traditional methods and is also a complete traditional herbal formulation. The plants which can be used in the treatment of vitiligo are *Acorus calamus*, *Adiantum capillus*, *Boswellia serrata*, *Cassia angustifolia*, *Cassia tora*, *Cinnamomum cassia*, *Fumaria officinalis*, *Glycyhizza glabra*, *Lavandula stoechas*, *Psoralea cordyfolia*, *Pterocarpus santalinus*, *Rosa damascene*, *Sphaeranthus indicus*, *Tephrosia purpuria*, *Vitis vinifera*, *Zingiber officinale* and *Zizyphus sativa*²⁶.

Treatment of dental diseases

The plants having the dental care properties are *Acacia catechu*, *Acacia arabica*, *Althea officinalis*, *Anacyclus pyrethrum*, *Azadirachta indica*, *Barleria prionitis*, *Cinnamomum camphora*, *Cuminum cyminum*, *Eucalyptus globules*, *gardenia gummifera*, *Holarrhenia antidysenterica*, *Jasminum grandiflorum*, *Juglans regia*, *Mimusops elengi*, *Myrica sapida*, *Myroxylon balsamum*, *Ochrocarpus longifolius*, *Ocimum sanctum*, *Origanum vulgare*, *Piper longum*, *Piper nigrum*, *Pistacia lentiscus*, *Pterocarpus marsupium*, *Punica granatum*, *Salvadora persica*, *Salvia officinalis*, *Solanum xanthocarpum*, *Symplocos racemosa*, *Syzygium aromaticum*,

Thalictrum foliolosum and *Zanthoxylum alatum*. All these regimens play an important role in suppressing the dental problems^{27, 28}.

Adverse Drug Reactions

Herbal drugs are not completely free of adverse drug reactions. Some adverse drug reactions of typically used herbs are, impulsive bleeding by *Gingo biloba*, gastrointestinal disturbances, allergic reactions, fatigue, dizziness, photosensitivity, confusion *Hypericum perforatum*, hypertension, cardiac arrhythmias, myocardial infarction, anxiety by ephedrine, headache by Paprika, diarrhea by Chast tree fruit and liver toxicity by *Piper methysticum*^{29, 30}.

Herbal Drug Interactions

Patients enchanting drugs with a narrow therapeutic index like cyclosporine, digoxin, phenytoin, procainamide, theophylline, warfarin etc. should be dispirited from using herbal products. All drugs with narrow therapeutic index may either have increased adverse effects or be less effective when used in combination with herbal drugs. Ginko is used for Alzheimer's disease and causes increased bleeding with aspirin. Ginseng has multiple uses and causing synergism with monoamine oxidase inhibitors. Kava is used as anxiolytic and shows synergism with benzodiazepines. St. Use of heavy metals is permitted in traditional medicines but in specific concentrations, which were mentioned by ancient physicians. There are now many examples of the toxicity caused by the use of heavy metals in the preparations of traditional drugs. Lead, copper, mercury, arsenic, silver and gold that are commonly added to these preparations, have caused toxicity on many occasions. Patients should not use herbal drugs arbitrarily with modern medicines, as there are potential of drug interactions and increased risk of adverse drug reactions³¹⁻³⁴.

Standardization of Herbal Drugs

Herbal drugs imply knowledge and practice of herbal healing for the prevention, diagnosis, and elimination of physical, mental, or social imbalance³⁵. The costs for health care are rising at an alarming rate throughout the world. At the same time, the world market for phytopharmaceuticals is growing progressively. The World Bank estimates that trade in medicinal plants, botanical drug products, and raw materials are growing at an annual rate of between 5 and 15 %^{36, 37}. It is a common observation that people diagnosed with incurable chronic disease states such as diabetes, arthritis, and AIDS turned to herbal therapies for a sense of control and mental comfort from taking action³⁸. Herbal product studies cannot be considered scientifically valid if the product tested has not been authenticated and characterized in order to ensure reproducibility in the manufacturing of the product in question. Several studies have indicated quantitative variations in marker

constituents in herbal preparations. Moreover, many dangerous and lethal side effects have recently been reported, including direct toxic effects, allergic reactions, effects from contaminants, and interactions with drugs and other herbs. The 10 most commonly used herbs in the United States, systematic reviews have concluded that only 4 are likely to be effective and there is very limited evidence to evaluate the efficacy of the approximately 20000 other available herbal products³⁹. Standardized herbal products of consistent quality and containing well-defined constituents are required for reliable clinical trials and to provide consistent beneficial therapeutic effects. Pharmacological properties of an herbal formulation depend on phytochemical constituents present therein. Development of authentic analytical methods which can reliably profile the phytochemical composition, including quantitative analyses of marker/bioactive compounds and other major constituents, is a major challenge to scientists. Without consistent quality of a phytochemical mixture, a consistent pharmacological effect is not expected. Resurgence of interest and the growing market of herbal medicinal products necessitate strong commitment by the stakeholders to safeguard the consumer and the industry. Standardization is the first step for the establishment of a consistent biological activity, a consistent chemical profile, or simply a quality assurance program for production and manufacturing. Therefore, the EU has defined three categories of herbal products:

- Those containing constituents (single compounds or families of compounds) with known and experienced therapeutic activity that are deemed solely responsible for clinical efficacy.
- Those containing chemically defined constituents possessing relevant pharmacological properties which are likely to contribute to the clinical efficacy.

- Those in which no constituents have been identified as being responsible for the therapeutic activity.

Standardization as defined in the text for guidance on the quality of herbal medicinal products means adjusting the herbal drug preparation to a defined content of a constituent or group of substances with known therapeutic activity. The European Medicines Agency (EMA) makes the distinction between constituents with known therapeutic activity which can be used to standardize a biological effect and marker compounds which allow standardization on a set amount of the chosen compound. The EMA defines marker compounds as chemically defined constituents of a herbal drug which are of interest for control purposes, independent of whether they have any therapeutic activity or not. Examples of markers are the valerianic acids in *Valeriana officinalis* L., ginkgolides and flavonoids in *Ginkgo biloba* L. and hypericin and hyperforin in *Hypericum perforatum* L.^{40, 41}.

Stability testing of Herbal Drugs

Stability testing of herbal drugs is a challenging risk, because the entire herb or herbal product is regarded as the active matter, regardless of whether constituents with defined therapeutic activity are known⁴². The purpose of a stability testing is to provide proof on how the quality of the herbal products varies with the time under the influence of environmental factors such as temperature, light, oxygen, moisture, other ingredient or excipients in the dosage form, particle size of drug, microbial contamination, trace metal contamination, leaching from the container and to establish a recommended storage condition and shelf-life. Stability testing is necessary to ensure that the product is of satisfactory quality throughout its entire storage period. Stability studies should be performed on at least three production batches of the herbal products for the proposed shelf-life, which is normally denoted as long term stability and is performed under natural atmospheric conditions. Stability data can also be generated under

accelerated atmospheric conditions of temperature, humidity and light, which is referred to as short term stability and the data so obtained is used for predicting shelf-life of the product. Stability testing should be conducted on the dosage form packaged in the container closure system proposed for marketing. With the help of modern analytical techniques like spectrophotometry, HPLC, HPTLC and by employing proper guidelines it is possible to generate a sound stability data of herbal products and predict their shelf-life, which will help in improving global acceptability of herbal products⁴³.

Pharmacovigilance of Herbal Drugs

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects of drugs or any other possible drug-related problems. Recently, its concerns have been widened to include: herbals, traditional and complementary medicines, blood products, biological, medical devices and vaccines⁴⁴. The aims of pharmacovigilance is to protect patients from unnecessary harm by identifying previously unrecognized drug hazards, elucidating pre-disposing factors and quantifying risk in relation to benefits⁴⁵. The purpose of pharmacovigilance is to detect, assess and understand to prevent the adverse effects or any other possible drug-related problems, related to herbal, traditionally and complementary medicines⁴⁶. Herbal drugs are broadly used in both developed and developing countries however, in current years, there are several high-profile herbal safety concerns having an impact on the public health. Herbal drugs are traditionally considered as harmless but as medicinal products they require drug observation in order to identify their risks. Published data shows that the risk is due either to a contaminant or to an added drug. Tremendously limited knowledge about the constituents of herbal drugs and their effects in humans, the lack of rigorous quality control and the heterogeneous nature of herbal drugs necessitates the continuous monitoring of the safety of these products. WHO has increased its efforts to promote herbal safety

monitoring within the background of the WHO International Drug Monitoring Programme. The WHO guidelines aim to propose the member states of a frame work for facilitating the regulation of herbal medicines used in traditional medicine covering issues like classification, assessment of safety, assessment of the efficacy, quality assurance, pharmacovigilance and control of advertisements of herbal drugs products. The pharmacovigilance of herbal medicines exhibits particular challenges because such preparations are available from a wide range of outlets typically where there is no health care professional available, most purchases are in conventional OTC environment. Various methods in pharmacovigilance are passive observation includes impulsive reporting and stimulated reporting, active surveillance by sentinel sites, drug event monitoring, registries, comparative observational studies by survey study, case control study, targeted clinical investigations by investigate drug-drug interactions and food-drug interactions⁴⁷. The importance of genetic factors in determining an individual vulnerability to adverse drug reactions is well documented and this implies to herbal medicines as well as to conventional drugs. Pharmacovigilance is therefore one of the important post-marketing safety tools in ensuring the safety of pharmaceutical and related health products⁴⁸.

Regulatory Status of Herbal Drugs

The lawful situation of herbal drugs varies from country to country. Developing countries have folk knowledge of herbs and their use in traditional medicine is wide spread. But, these countries do not have any lawmaking criteria to include these traditionally used herbal drugs in drug legislation⁴⁹. Endorsement of herbal drugs in most countries is based on traditional herbal references, provided they are not known to be unsafe when used to treat slight illnesses. But, now-a-days claims are being made to treat more serious illnesses with herbal drugs for which no traditional knowledge is present⁵⁰. Therefore, narrow requirements for herbal drugs are necessary to ensure the safety,

efficacy and quality and to support specific indications; scientific and clinical evidence must be acquired. Depending upon the nature of herbs and market availability, different requirements exist for submission of clinical trial data and toxicity data. The regulatory requirements of herbal drugs is varies from one country to other country. Some countries accept traditional, experience based evidence while some consider herbal remedies as dangerous or of questionable value⁵¹.

CONCLUSION

Medicinal herbs as potential source of therapeutics aids has attained a significant role in health care system all over the world for human beings not only in the diseased condition but also as potential material for maintaining proper health⁵². It is clear that the herbal industry can make great strides in the world. With the increased use of herbal products, the future worldwide labeling practice should adequately address quality aspects. Standardization of methods and quality control data on safety and efficacy are required for understanding of the use of herbal drugs. A major factor impeding the development of the medicinal plant based industries in developing countries has been the lack of information on the social and economic benefits that could be derived from the industrial utilization of medicinal plants. Further research is required to exploit the compounds responsible for the observed biological activity⁵³.

REFERENCES

1. Winslow, L; Kroll, DJ (1998), "**Herbs as Medicines, Archives of Internal Medicine**", 158, 2192-2199.
2. Gossell, M; Simon, OR; West, ME (2006), "The past and the present use of plants for medicines", **West Indian Medical Journal**, 55,217.
3. De-Smet, PGAM (1997), "The role of plant derived drugs and herbal medicines in healthcare drugs, 54, 801-840.

4. WHO technical report series (1996), "**Guidelines for the Assessment of Herbal Medicines**", 863, 178-184.
5. Abhishek, K; Ashutosh, M and Sinha, BN (2006), "Herbal drugs- present status and efforts to promote and regulate cultivation", **The Pharma Review**, 6, 73-77.
6. Harish, P (2001), "Herbal drugs", **Current Science**, 81(1), 15.
7. Coleman, LM and Fowler, LL and Williams ME (1995), "Use of unproven therapies by people with alzheimer's disease", **Journal of the American Geriatrics Society**, 43,747-750.
8. Sutherland, LR and Verhoef, MJ (1994), "Why do patients seek a second opinion or alternative medicine", **Clinical Gastroenterology**", 19,194-197.
9. Catherine, C; Crone, MD; Thomas, N and Wise, MD (1998), "Use of herbal medicines among consultation-liaison populations", **The Academy of Psychosomatic Medicine**", 39(1), 3-13.
10. **The Indian Pharmacopoeia** (1996), Govt. of India, Ministry of Health and Family Welfare, The Controller of Publication, A-53, 54, 89.
11. Mukherjee, PK; Maiti, K; Mukherjee, K and Houghton, PJ (2006), "Leads from Indian medicinal plants with hypoglycemic potentials", **Journal of Ethnopharmacology**, 106, 1-28.
12. Jia, W; Gao, Wa and Tang, L (2003), "Antidiabetic Herbal Drugs Officially Approved in China", **Phytother. Res.**, 17, 1127-1134.
13. An SM; Chen, W and Feng, XL (1998), "The treatment of 30 type II diabetic patients with Yu-san-xiao", **J Pract Trad Chin Med**, 14, 44-45.
14. Al-Awadi, FM and Gumaa, KA (1987), "Studies on the activity of individual plants of an antidiabetic plant mixture", **Acta Diabetologica Latina**", 24, 37-41.

15. Shang, MF (2000), "Status of the development of antidiabetic TCM in China", *Chin J TCM Inform*, 7, 78-81.
16. Sehgal, A (2003), "Herbal medicines-harmless or harmful", *Anesthesia*; 57,947-948.
17. Feng, Y; Wang, N; Zhu, M; Feng, Y; Li H and Tsao, S (2011), "Recent Progress on Anticancer Candidates in Patents of Herbal Medicinal Products; Recent Patents on Food", *Nutrition & Agriculture*, 3 30-48.
18. Rodeiro, I; Magarino, Y; Ocejo, O; Garrido, G and Delgado, R (2008), "Use of natural products in anti-cancer alternative therapy: risk of interactions with conventional anti-cancer drugs; Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas, 7 (6), 332-344.
19. Lalla, JK (2005), "Herbal medicines revisited", *The Pharma Review*, 12, 101-105.
20. Khan, I; Alam, S; Akhter, S; Shahin, N and Ansari, FZ (2007), "Ageing and its herbal treatment", *The Pharma Review*, 12,131-134.
21. Chang, RC and So, KF (2008), "Use of anti-ageing herbal medicine *Lycium barbarum* against aging-associated diseases", *Cell and Molecular Neurobiology*, 28(5), 643-652.
22. Nandakishore, D; Shubhangi, G; Prakash, I; Pallavi, S; Parimal, K and Shishupal, B (2007), "Herbal plants with antifertility activity", *The Pharma Review*, 8, 131-135.
23. Raman, D., Sabitha, JS and Shivanand, BG (2005), "Anti-microbial activity of herbs used in psoriasis" *The Pharma Review*, 8, 71-72.
24. Ben, E; Ziv, M and Frenkel, M (2004), "Complementary medicine and psoriasis: linking the patient's outlook with evidence-based medicine", *Int J Dermatol*, 43(7) 552.
25. Jeyaprakash, K (2007), "Herbal therapy for depression", *Herbal Tech Industry*, 3(7), 19-25.
26. Ansari, FZ; Alam, S; Jain, P; Akhter, S and Ansari, MZH (2008), "Vitiligo and its herbal treatment", *The Pharma Review*, 12, 137-13.
27. Schie, AAA (1989), "Modes of action of currently known chemical antiplaque agents otherthan chlorohexidine", *Journal of Dental Research*, 68, 1609.
28. Akhtar, N; Ali, M and Alam, MS (2005), "Herbal drugs used in dental care", *The Pharma Review*, 10, 61-68.
29. Chauhan, VS (2006), "Standardizing herbs and intermediates-newer approaches", *The Pharma Review*, 2, 37-44.
30. Raina, MK (2003), "Quality control of herbal and herbo-mineral formulations", *Indian Journal of Natural Products*, 19,11-15.
31. Hussin, AH (2001), "Adverse effects of herbs and drug herbal interactions", *Malaysian Journal of Pharmacy*, 1, 39-44.
32. Kuhn, MA (2002), "Herbal remedies: drug-herb interactions", *Critical Care Nurse*", 22, 22-32.
33. Aiyer, MN; Namboodiri, AN and Kolammal, M (1957), "*Pharmacognosy of Ayurvedic Drugs*, Trivandrum, 5, 49-55.
34. Basu, NK and Lamsal, P (1947), "Investigation on Indian medicinal Plants II: *Hydrocotyle asiatica*", *Quart.J. Pharm.*, 20,137.
35. Akerele, O (1993), *Herbalgram*, 28,13.
36. Benedum, J (1998), "*In Phytopharmaka IV*", Rietbrock, 3.
37. Patwardhan, B; Warude, D; Pushpangadan, P and Bhatt, N (2005), "*Evidence-Based Complem. Altern. Med*, 2, 465.
38. Nortier, JL; Martinez, MCM; Schmeiser, HH; Arlt, VM and Bieler, A *et. al.* (2000), *Engl. J. Medicine*, 342, 1686.
39. Bent, S and Ko, R (2004), "Standardization of herbal medicines", *Am. J. Med.*, 116, 478.
40. EMEA (2000), "Position paper on the risks associated with the use of herbal products

- containing *Aristolochia* species”, **EMEA/HMPWP**, 23.
41. Ernst, E (2000), “Evidence-Based Herbal Medicine”, **Eur. J. Clin. Pharmacol**, 56, 523.
 42. Thakur, AK; Prasad, NAV and Ladha, KS (2008), “Stability testing of herbal products”, **The Pharma Review**, 4, 109-112.
 43. Kathrin, K; Eike, R and Anne, B (2003), “Validation of standardized high performance thin layer chromatographic methods for quality and stability testing of medicines”, **Journal of AOAC International**, 86(5), 909-915.
 44. Manoj, S *et al.* (2006), “Pharmacovigilance of herbal medicines”, **The Pharma Review**, 12, 119-124.
 45. Kshirsagar, N (2005), “The pharmacovigilance system in India”, **Drug Safety**, 28,647-650.
 46. Routledge, P (1998), “150 Years of pharmacovigilance”, **The Lancet**, 351, 1200-1201.
 47. Bigoniya, P (2009), “Pharmacovigilance of herbal medicines: current status and future strategies”, **The Pharma Review**, 5, 77-88.
 48. Chan, TYK (1997), “Monitoring the safety of herbal medicines”, **Drug Safety**, 17, 209-215.
 49. Sukhdev, S; Arun, N and Kalia, AN (2008), “Patentability of herbal products: A review”, **The Pharma Review**, 4,118-124.
 50. Raskin, L *et al.* (2002), “Plants and human health in the twenty first century”, **Trends in Biotechnology**, 20 (12), 522-531.
 51. Calixto, JB (2000), “Efficacy, safety, quality control, marketing, and regulatory guidelines for herbal medicines”, **Brazilian Journal of Medical and Biological Research**, 33,179-189.
 52. Verma, S and Singh, SP (2008), “Current and future status of herbal medicines”, **Veterinary World**, 1(11), 347-350.
 53. Alam, S *et al.* (2007), “Role of herbals in drug delivery system”, **The Pharma Review**, 6 106-107.