REVIEW ARTICLE ON HERBAL MEDICINES

Ms. Yogita A. Sangale 1, Ms. Vrushali S. Shinde 2, and Dr. Sachin B. Somwanshi 3

1. Research Scholar, Department of Pharmaceutics, P.R.E.S's, College of Pharmacy (For Women), Chincholi, Nashik, MH, India – 422102
Email : yogitasangale22@gmail.com
Email : vrushali681@gmail.com

2. Associate Professor, Department of Pharmaceutics, P.R.E.S's, College of Pharmacy (For Women), Chincholi, Nashik, MH, India – 422102
Email : sachinsomwanshi27@gmail.com

Abstract -

Herbal medicines it is a medical system that has its origin in ancient cultures and that involves the medicinal use of plants and its extract to treat illness and to assist bodily functions. It has been around since prehistoric times. Herbal medicines is still the main stay of about 75% of the world population, especially in the under developed and developing countries, for primary healthcare because of better cultural acceptability, better compatibility with the human body and lesser side effects. However, in the last few years there has been a major increase in their use in the developed world. Recent findings indicate that all herbal medicines may not be safe as severe consequences are reported for some herbal drugs. Herbal medicines are most popular form of traditional medicines and are highly lucrative in international market. The medicinal plant contribute to 80% of the raw materials used in the preparation of drugs. It can be taken orally or applied locally. 200 years ago first pharmacological compound morphine, was produced from opium extracted from the seeds of poppy flower. Today plants are being used to treat a number of health issues, proving that food is medicine. For the preservation of medicinal plants, establishment of community gardens and kitchen gardens is necessary. This will ensure sustainable supply of safe, effective, and affordable medicinal herbs. This article presents a systemic review on herbal medicine including safety, efficacy, quality control, clinical trials, bioavailability, herbal drug interaction, intellectual property rights marketing and regulatory aspects.

Key Words - Herbal medicines, Traditional medicines, Drug interaction.

Introduction -

The word medicine is derived from the Latin *arsmedicina* , meaning *the art of healing*. Herbal drugs referred as plants materials or herbalism, involves the use of whole plants or parts of plants, to treat injuries or illnesses. Herbal drugs referred as plants materials or herbalism, involves the use of whole

plants or parts of plants, to treat injuries or illnesses(1).
Herbal medicine is the use of plants, plant parts, their water or solvent extracts, essential oils, gums, resins, exudates, or other form of advanced products made from plant parts used therapeutically to provide proactive support of various physiological systems; or, in more conventional medical sense, to treat, cure, or prevent a disease in animals and in humans(2).
World health organization (WHO) has distinct herbal drugs complete, labeled medicinal products that have vigorous ingredients, aerial or secretive parts of the plants or other plant materials or combinations world health organization has set precise guidelines for the evaluation of safety, efficacy, and quality of herbal medicines(3).
Herbal drugs is a chief constituent in traditional medicine and a common constituent in Ayurvedic, homeopathic, naturopathic, and other medicine systems(4).
Herbs are usually considered as safe because of they belong to natural sources(5).
Herbal products have reach extensive adequacy as beneficial agents like antimicrobial, anti-diabetic, antifertility, anti-ageing, anti-arthritic, sedative, antidepressant, antianxiety, antispasmodic, analgesic, anti-inflammatory, anti HIV, vasodilatory, hepatoprotective, treatment of cirrhosis, gallstones, acne, asthma, menopause, migraine, impotence, Alzheimer's disease, chronic fatigue and memory enhancing activities(6).

Advantages -

1) Fewer side effects.

2) More protection.

3) Low cost.

4) Potency and efficiency.

5) Enhanced tolerance.

6) Complete accessibility.

7) Recyclability.

Disadvantages -

1) Risk with self-doing.

2) Complexity in standardization.

3) Not able to cure rapid sickness and accidents.

Difference of Herbal and Conventional Drugs -

Compared with well-defined synthetic drugs, herbal medicines exhibit some marked difference, namely ;

1) The active principles are frequently unknown

2) Standardization stability and quality control are feasible but not easy;

3) The availability and quality of raw materials are frequently problematic;

4) Well controlled double blind clinical and toxicological studies to prove their efficacy and safety are rare;

5) Empirical use in folk medicine is a very important characteristics;

6) They have a wide range of therapeutic use and are suitable for chronic treatments;

7) The occurrence of undesirable side effects seems to be less frequent with herbal medicines , but well controlled randomized clinical trials have revealed that they also exist;

8) They usually cost less than synthetic drugs(7).

Relationship between Ayurveda and modern medicines -

Ayurveda is one of the major traditional forms of medical practice in India, has produced many useful leads in developing medications for chronic diseases.

Sources of toxic chemicals and contaminations in herbal products -

1) Herbal medicine include the use crude or raw herbs which are collected from the wild or from cultivated fields and their prepared or ready made (formulated mixture of herbal or other natural materials) products. Toxic contamination may come from;

2) Environments and conditions in which medicinal plants are grown or collected.

3) The conditions under which they are dried and processed.

4) The storage conditions and conditions during transport.

5) The manufacturing processes when the ready made medicinal products are produced.

It has been reported that the stored drug samples herbal mycotoxin producing fungi in high frequency(8,9). WHO has paid serious attention on mycotoxin contamination in herbal drugs, considering it as a global problem. Some of the powdered drugs breaing trademarks of std. Indian herbal firms have been reported to contain high concentration of aflatoxin B1. Detection of mycotoxins (Aflatoxin B1, Ochratoxin, Citrinin, and Zearalenone) is certainly a matter of great concern in stored drugs of important medicinal plants, roots / rhizomes of Asparagus racemosus (0.16mg/g), Atropa belladonna (0.27mg/g), etc.(10). Such herbal drugs containing mycotoxins above the relevance limit fixed by WHO for human consumption, will be certainly rejected in the global market(11).

Another major issue is concerns with the harvest of medicinal plants in appropriate seasons. The medicinal properties of plants vary with respect to different seasons. The age of the plant decides its medicinal potency. Hence, the authentic part of medicinal plants of a particular age should be harvested in a particular season before processing for drug manufacture, to avoid any alteration in its medicinal

potency. With the implementation of good agriculture practice (GAP) and Good Manufacturing Practice (GMP) and the introduction of advanced analytical technologies(12,13), quality control of herbs will be improved during the next few years(14).

Active principle identification and standardization -

The variability in the content and concentrations of constituents of plant material, together with the range of extraction techniques and processing steps used by different manufacturers, results in marked variability in the content and quality of commercially available herbal products. Standardization is an important step in which active constituents are known. However, for many herbs the active constituents not known. In these cases, products may be standardized on content of certain `marker` compounds (chemicals characteristic of the herb or present in large quantities) However, this approach makes assumptions about the relationship between the quantity of marker compounds and that of the unknown active constituents(15).
Further there should be a quality control test for the entire preparation to ensure the quality of the drug(1).
Standardization of herbal drugs is not just an analytical operation for identification and assay of active principles; rather, it comprises total information and controls to necessarily guarantee consistent composition of all herbals ex. (Aertex) it a polyherbal formulation which is designed for the treatment of arthritis in which contains four botanicals. The formulation standardized using modern scientific tools and with known markers, has been granted a US patent(16).

Bioavailability of herbal drugs -

The bioavailability of the active constituents of the herb is another area of considerable importance. Before a compound can act systemically it must pass from the gastrointestinal tract into the blood stream. This is an area in which surprisingly little is known for herbal constituents(17).
Cinnabar has been for a long time in traditional medicine. The toxic effects of inorganic mercury are well recognized, but because of its insolubility it has been assumed that this compound would not be significantly absorbed from the gastrointestinal tract. However, investigation of on the oral absorption of cinnabar in mice found a significant increase in mercury concentration in the liver and kidney(18).

QC of herbal medicine -

Consistency in composition and biological activity are essential requirements for the safe and effective use of therapeutic agents. Quality is the critical determinant of safety and efficacy of botanical medicines; however, botanical preparations rarely meet the standards of quality, which refers to procedures and makers for assessing and verifying the strength of botanical raw materials or extracts or formulations there of(19).
Methods for quality control of herbal medicine involve sensory inspection (macroscopic and microscopic examinations). Macroscopic identity of botanical materials is based on parameters like shape, color, size, characteristics, texture, surface, fracture characteristics, odour, taste, and such organoleptic properties

which are compared to standard reference material. Microscopy involve comparative microscopic inspection of broken as well as powdered crude, botanical materials(20) and analytical inspection using instrumental techniques such as thin layer chromatography, HPLC, GC-MS,LC-MS, near infrared (NIR) and spectrophotometer, etc.(21).

In any herbal medicine and its extract, there are hundreds of unknown components and many of them are in low amount. Moreover, there usually exists variability within the same herbal materials. Consequently, to obtain reliable chromatographic fingerprints which represents pharmacologically active and chemically characteristic components is not an easy or trivial work. Fortunately, chromatography offers very powerful separation ability, such that the complex chemical components in herbal medicine extracts can be separated into many relatively simple subtractions. Furthermore, the recent approaches of applying hyphenated chromatography and spectrometry such as high performance liquid chromatography diode array detection (HPLC-DAD), gas chromatography mass spectroscopy (GS-MS), capillary electrophoresis diode array detection (CE-DAD), HPLC-MS and HPLC-NMR, could provide the additional spectral information, which will be very helpful for the qualitative analysis and even for the online structural elucidation. With the help of the spectral information the hyphenated instruments show greatly improved performances in terms of the elimination of instrumental interferences, retention time shift correction, selectivity, chromatographic separation abilities, and measurement precision. If hyphenated chromatography is further combined with chemometric approaches, clear pictures might be developed for chromatographic fingerprints obtained. A chemical fingerprint obtained by hyphenated chromatography, out of question, will become the primary tool for quality control of herbal medicines. However, using the chemical fingerprints for the purpose of quality control of herbal medicines can only address to the problem of comparing the integrated sameness and difference and controlling their stability of the available herbal products. The complex relationship between the chromatographic fingerprints and efficacy of the herbal medicines (QRFE) is not taken into account yet, which seems to be the most important aspect for the quality control of herbal medicines. In fact, the research field of quality control of herbal medicines is really an interdisciplinary research. It needs crossover of chemistry, pharmacology, medicine and even statistics to provide a platform for the quality control of traditional herbal medicines and further to discover the novel therapeutics composed of multiple chemical compounds(22).

Clinical trials -

Clinical studies are necessary to confirm the pharmacological effects of medicinal plants before they can be integrated into conventional medical practice. This would be especially true in case of some unrelated effects of therapy contributing to efficacy that may be difficult to measure preclinically, well recorded case reports can contribute towards useful information of such times and stimulate further study(23).

Endpoints measured should include specific modern parameters, other associated indices and general improvement (i.e. quality of life or accumulated scores of symptoms)(24).

Despite its difficulties, conforming to both traditional diagnostic and therapeutic systems and modern methodological demands is achievable (25).

Quantitative standardization of pattern diagnosis is also a good method to reevaluate the efficacy of herbal formulae. The methods and guidelines used for clinical validation of modern medicines must be applied to herbal products even though the latter fees a holistic approaches to treatment. However, conventional concepts of clinical research design may be difficult to apply when using clinical research to evaluate various systems and practices of traditional medicines. This could be due to the fact that

herbal remedies are individualized (each person has certain predispositions to disease and susceptible to factors like environment, genetics, dietary and lifestyle) therapies. The number of patients required for undertaking clinical trial of medicinal plants is large not only since the study design needs to be adequate and statistically appropriate but also to cater to the control, confounders and placebo groups to provide sufficient evidence for judging efficacy of the plant under study(26).
Recent meta-analysis of reviews published in important medical journals, such as the Annals of Internal Medicine, the Journal of the American Medical Association (JAMA), the British Medical Journal, the Lancet, and the British Journal of Clinical Pharmacology, among others, confirms this assumption.
Several factors might contribute to the explanation of such discrepancies, for example:
1) Lack of standardization and quality control of the herbal drugs used in clinical trials
2) Use of different dosages of herbal medicines
3) Inadequate randomization in most studies, and patients not properly selected
4) Numbers of patients in most trials insufficient for the attainment of statistical significance
5) Difficulties in establishing appropriate placebos because of the tastes, aromas, etc.
6) Wide variations in the duration of treatments using herbal medicines(27).

Herbal drug interaction -

Many medicinal herbs and pharmaceutical drugs are therapeutic at one dose and toxic at another. Interactions between herbs and drugs may increase or decrease the pharmacological or toxicological effects of either component. Synergistic therapeutic effects may complicate the dosing of long term medications ex. Herbs traditionally used to decrease glucose concentrations in diabetics could theoretically precipitate hypoglycemia if taken in combination with conventional drugs(28).
Patients enhancing 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. Gingko is used for Alzheimer's disease and causes increase bleeding with aspirin. Ginseng has multiple uses and causing synergism with monoamine oxidase inhibitors. Kava is used as anxiolytic and shows synergism with benzodiazepines 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 reactions(29-32).

Regulation of herbal medicine -

Many herbal products fall between the far ends of this regulatory range: unlicensed preparations are thought to account for over 80% of herbal sales. Many medicine like products on the British herbal market remain unregistered for two reasons: acceptable data on efficacy, safety, and quality may not be available, and the licensing fee is high(33).
The main registering and regulating body for western herbal practitioner is the National Institute of Medical Herbalist, situated in Exeter U.K. Only graduates of approved courses are accepted on to the register, and a strict code of ethics is maintained. The European Herbal Practitioner Association, an

umbrella body with about 1000 members, has been set up to encourage greater unity among herbalists. However, it has no formal criteria for screening membership and no published code of ethics as yet(34).

Current status of herbal medicine -

Currently more than 80% of the world population depends on traditional and plant derived medicine because plants are important sources of medicines and presently about 25% of pharmaceutical prescriptions in the United States contain at least one plant derived ingredient. In the last century, roughly 121 pharmaceutical products were. Formulated based on the traditional knowledge obtained from various sources(35). In fact it is now believed that nature contributes up to 90% to the new drug molecule. Nature has provided many of the effective agent such as dactinomycin, bleomycin, and etoposide (anticancer), mefloquine, chloroquine, and artether (antimalarial), harunganin, cryptolepine (antidiabetic), curcumin, phenoxidol (anti HIV drugs), etc.(36,37).

India has around 25,000 effective plant based formulation used traditionally with over 1.5 million practitioner of traditional medicinal system and 7800 medicinal drug manufacturing units in India, which consume about 2000 tons of herbs annually(38).

In 1978, WHO officially recognized the potential of herbal medicine and traditional health practitioners. A series of resolutions concerning policy, objectives and activities on herbal medicine have been issued by the world health assembly(39).

In 1991 WHO developed guidelines for the assessment of herbal medicine and the sixth International Conference of Drug Regulatory Authorities held at Ottawa in the same year ratified the same. The silent features of WHO guidelines are Quality assessment (crude plant materials or plant extracts and finished product) stability (shelf life) safety assessment (documentation of safety based on experience and toxicological studies) assessment of efficacy (documented evidence of traditional use and preclinical and clinical(40). Significant and steady progress in implementing, regulating and managing traditional medicine in most regions of the world takes place after WHO Traditional Medicine strategy 2002-2005, state member also developed their own documentation and safety concern(41).

Indian herbal market is nearly 50 billion rupees with 14% annual growth. 1 billion rupees worth of herbal product are being exported. The demand for medicinal plants is increasing everyday and WHO has projected that global herbal market will grow up to $5 trillion in 2050 from the current level of $62 billion. India and China produce more than 70% of the global diversity. The significant global herbal export market include EU, USA, Canada, Australia, Singapore, and Japan while Brazil, Argentina, Mexico, China, and Indonesia are New emerging market(42).

Research in herbal medicine -

In the past, drug discovery of bioactive compounds from plants was time consuming, and the process of isolation and identifying the chemical structures of bioactive compounds from an extract could take several months or years. Now a days techniques like HPLC oupled to mass spectrometry ,NMR and robotics have minimize time significantly(43). In larger countries becoming the parties to the convention on biological diversity the process of accessing the basic lead resource benefit sharing during commercial phase. These processes tend to impede the pace of discovery process at various phases irrespective of the concerns leading to such processes(44).

Conclusion -

Herbs are staging a comeback and in the present days herbal products represents safety and security as compare to synthetic drug which leads toward research in herbal medicines. The traditional knowledge play important role if a holistic approach and involvement and participation of documentation, preservation and use for the benefit of humankind before it is lost forever.

Reference -

1.Winslow, L; Kroll, DJ (1998), “Herbs as Medicines, Archives of Internal Medicine”, 158, 2192-2199.

2. Weiss RF, Fintelmann V. Herbal Medicine. 2nd English edition. New York: Thieme, 2000.

3.WHO technical report series (1996),“Guidelines for the Assessment of Herbal Medicines”, 863, 178-184.

4. 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.

5.Harish, P (2001), “Herbal drugs”, Current Science, 81(1), 15.

6.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.

7. Calixto JB. Efficacy, safety, quality control,marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents).Braz J Med Biol Res 2000; 33: 179-189.

8.Horie Y, Yamazaki M, Itokawa H and Kinoshita H. On the toxigenic fungi contaminating herbal drugs as raw materials in pharmaceutical industries. Trans. Mycol. Soc. Jpn. 1979; 23: 435ñ 447.

9. Roy AK. and Chaurasia HK. Aflatoxin problems in some medicinal plants under storage. Int. J. Crude Drug Res 1989; 27:156ñ160.

10. Roy AK. Threat to medicinal plants and drugs by fungi. J. Indian Bot. Soc 1989; 68: 149ñ 153.

11. Dubey NK, Rajesh Kumar and Pramila Tripathi. Global promotion of herbal medicine: Indiaís opportunity. Current Science 2004; 86 (1):37-41.

12. De Smet PAGM. Health risks of herbal remedies: an update. Clin. Pharmacol. Ther 2004; 76: 1ñ17.

13. Cheng Y. An approach to comparative analysis of chromatographic fingerprints for assuring the quality of botanical drugs. J.Chem. Inf. Comput. Sci 2003; 43: 1068ñ1076.

14. Zhang H. Identification and determination of the major constituents in traditional Chinese medicine Si-Wu-Tang by HPLC coupled with DAD and ESI-MS. J. Pharm. Biomed. Anal 2004; 34: 705ñ713.

15. Schulz V, H‰nsel R and Tyler VE. Rational Phytotherapy. A Physiciansí Guide to Herbal Medicine, Fourth edition. Berlin: Springer,2000.

16. Patwardhan B. A method of treating musculoskeletal disease and a novel composition there of. US Patent 5494668,1996.

17. Tyler VE. Phytomedicine: Back to the Future.Journal of Natural Products 1999; 62: 1589-1592.

18. Sanjoy Kumar Pal and Yogeshwer Shukla.Herbal Medicine: Current Status and the Future. Asian Pacific J Cancer Prev 2003; 4: 281-288.

19. Cardellina JH. Challenges and opportunities confronting the botanical dietary supplement industry. J Nat Prod 2002; 65: 1073ñ84.

20. Quality Control Methods for Medicinal Plant Materials, WHO, Geneva, 1998.

21. Choi DW, Kim JH, Cho SY, Kim DH, Chang SY. Toxicology 181/182. 2002; 581.

22. Yi-Zeng Liang, Peishan Xie and Kelvin Chan Quality control of herbal medicines. Journal of Chromatography B 2004; 812: 53ñ70.

23. Morris BA. Importance of case reports. Can Med Assoc J. 1989; 141: 875-876.

24. Critchley JA. Alternative therapies and medical science: designing clinical trials of alternative/complementary medicinesñis evidence-based traditional Chinese medicine attainable? J. Clin. Pharmacol 2000; 40: 462ñ467.

25. Nahin RL and Straus SE. Research into complementary and alternative medicine: problems and potential. Br. Med. J 2001; 322: 161ñ164.

26. WHO. General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine. 2000.

27.Raghvendra HL, Yogesh HS, Gopalkrishn B, Chandrashekhar VM, Satishkumar BP, An overview of Herbal Medicine, Inf – J.Ph.Sci May - Aug. 2009; 1(1) :1-20.

28. Bailey CJ and Day C. Traditional plant medicines as treatments for diabetes. Diabetes Care 1989; 12: 553ñ64.

29. Hussin, AH (2001), “Adverse effects of herbs and drug herbal interactions”,Malaysian Journal of Pharmacy, 1, 39-44.

30. Kuhn, MA (2002), “Herbal remedies: drugherb interactions”, Critical Care Nurse”, 22, 22-32.

31. Aiyer, MN; Namboodiri, AN and Kolammal, M (1957), “Pharmacognosy of Ayurvedic Drugs, Trivandrum, 5, 49-55.

32. Basu, NK and Lamsal, P (1947),“Investigation on Indian medicinal Plants II: Hydrocotyle asiatica”, Quart.J. Pharm., 20,137.

33. De Smet PAGM (1995). Should herbal medicines-like product be licensed as medicines? BMJ, 310, 1023-4.

34. Vickers A and Zollman C (1999). ABC of complementary medicine: herbal medicine. BMJ, 319, 1050 - 3.

35. Verma S and Singh SP, Current and future status of herbal medicines, Veterinary World, 2008; 1(11): 347-350.

36. Moshi MJ, Current and future prospects of integrating traditional and alternative medicine in the management of diseases in Tanzania, Tanzania Health Research Bulletin, 2005; 7(3):159-166.

37. Maria Russo, Carmela Spagnuolo, Idolo Tedesco and Gian Luigi Russo, Phytochemicals in Cancer prevention and therapy: Truth or Dare, Toxins, 2010; 2(4): 517-551.

38. Kokate CK, Purohit AP and Gokhale S B. Pharmacognosy. 49th edition. Pune: Nirali Prakashan; 2014.

39. Agarwal P, Amreen Fatima and Singh PP, Herbal medicine scenario in India and European countries, Journal of Pharmacognosy and Phytochemistry, 2012; 1(4): 88-93.

40. Hasan SZ, Misra V, Singh S, Arora G, Sharma S and Sarika Sharma, Current status of herbal drugs and their future perspectives, Biological Forum - An International Journal, 2009;1(1): 12 -17.

41.QAZI MAJAJ A, MOLVI KHURSHID, Herbal Medicine : A Comprehensive Review, International Journal Of Pharmaceutical Research, Apr - June 2016, Vol - 8, Issue – 2.

43. Salim AA,Chin YW and Kinghorn AD.Drug discovery from plants.Ramawat KG,Merillon JM,editors.Bioactive molecules and medicinal plants.Berlin:Springer; 2008.

44. KatiyarC,Gupta A,Kanjilal S,Katiyar S,Drug discovery from plant sources: An integrated approach, An International Quarterly Journal of Research in Ayurveda, 2012; 33 (1): 10-19.