



INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES (Int. J. of Pharm. Life Sci.)

Herbal Medicine and Pharmacovigilance: A Future Prospective

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Abstract

World Health Organization (WHO) has defined herbal medicines as finished, labelled medicinal products that contain active ingredients, aerial or underground parts of the plant or other plant material or combinations. World Health Organization has set specific guidelines for the assessment of the safety, efficacy, and quality of herbal medicines. As the use of herbal medicines has increased, so too have the reports of suspected toxicity and adverse events. Safety and efficacy are the two major concerns about any drug, while efficacy can be detected with relative ease; the same cannot be said about safety because the adverse effect of a drug may be uncommon but very serious. This gave a birth to a new branch of pharmacology called pharmacovigilance. As many herbal products on the market have not been thoroughly tested for their pharmacology and toxicology, pharmacovigilance has paramount importance in detecting unwanted reactions. It is clear that the herbal industry can make great strides in the world. With the increased use of herbal products, the future worldwide labelling practise 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 medicines. There is the need of more research and reporting to be done to understand the adverse effects associated with the herbal drugs beside their vast health benefits to ensure the proper well being of humans.

Key-Words: WHO, Herbal Medicine, Pharmacovigilance

Introduction

Herbal medicines consist of plant or its part to treat injuries, disease or illnesses and are used to prevent and treat diseases and ailments or to promote health and healing. It is a drug or preparation made from a plant or plants and used for any of such purposes. Herbal medicines are the oldest form of health care known to mankind. (1, 2, 3)

World Health Organization (WHO) has defined herbal medicines as finished, labelled medicinal products that contain active ingredients, aerial or underground parts of the plant or other plant material or combinations. World Health Organization has set specific guidelines for the assessment of the safety, efficacy, and quality of herbal medicines. WHO estimates that approx 81% of the world populations presently use herbal medicine for primary health care. (4)

Herbal medicines are traditionally considered harmless since these belong to natural sources. However, this is not true as there is several case reports of adverse reactions of herbal drugs mentioned in published literature. Although most traditional therapies are presumed to be safe, there is still the problem of how to assess and quantify the possibility of very rare adverse events. (5)

As the use of herbal medicines has increased, so too have the reports of suspected toxicity and adverse events. Such unwanted reactions can be due to 1) side effects ; 2) reactions occurring as a result of overdose, over duration, tolerance, dependence-addiction, 3) hypersensitivity, allergic and idiosyncratic reactions, 4) mid term and long term toxic effects including liver, renal, cardiac and neurotoxicity also genotoxicity and teratogenicity. As many herbal products on the market have not been thoroughly tested for their pharmacology and toxicology, pharmacovigilance has paramount importance in detecting unwanted reactions. (6)

WHO definition of Pharmacovigilance

WHO define the Pharmacovigilance (PV) as the pharmacological science relating to the detection,

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evaluation, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines.(7)

In common words, pharmacovigilance is the knowledge of amassing, observing, examining, assessing and estimating evidence from health care workers and patients on the contrary effects of drugs, natural products, herbal and traditional medicines with a emphasis view to:

- Finding new risk associated with remedies.
- Prevention and control of infectious diseases in patients.
- Reporting requirements in special situations.(8)

Herbal Drugs and its importance

The World Health organisation (WHO) has recently defined traditional medicine (including herbal drug) as comprising therapeutic practices that have been in existence, often for hundreds of years, before and development and spread of modern medicine and are still in use today. (9)

An herb is defined as a plant part used for its aromatic, savoury, medicinal or cosmetic properties. Generally, the whole plant or plant parts are used singly or in combination with more than one plant for the purpose of treatment. It has been estimated that 80% of the world population use some form of herbal medicine. There is little doubt that the use of herbal medicines is growing. Worldwide, the usage increases at a rate of 10-20% annually. The first reason for the use of herbals is that it is part of the culture and belief of some people for maintenance of health or to treat certain ailments. The second reason for the increased use of herbals is the relatively cheaper cost of herbal products and hence affordability to the lower income group. The third reason is that the public has the impression of herbals being natural and that anything natural is safe. (10)

Ancient literature also mentions herbal medicines for age related diseases namely memory loss, osteoporosis, diabetic wounds, immune and liver disorders etc. for which no modern medicine or only palliative therapy is available. These drugs are made from renewable resources of raw materials by ecofriendly processes and will bring economic prosperity to the masses growing these raw materials.

Adverse drug reaction associated with herbal medicines

An adverse reaction (ADR) is defined as a noxious and unintended response to a marketed health product, which occurs at doses normally used or tested for the diagnosis, treatment, or prevention of a disease or the modification of an organic function. (11) The

evaluation of ADRs is most critical in the field of pharmacovigilance. Concerning marketed remedies, a suitable definition of an adverse drug reaction is as follows:

“In patient at normal doses harmful and unpleasant reaction of drug for treatment and medication of diseases or for changes of biological utility.” (12)

It is undeniable that plants have an important role in the development of modern medicines. More than 60-70% of modern medicines in the world market are directly or indirectly derived from plant products. The number of reports of adverse effects of herbal medicines is now increasing due to increased use and also probably due to increased awareness among the consumers and clinical practitioners. (13)

Herbal remedies are not entirely free of adverse drug reactions. Some adverse drug reactions of commonly used herbs are, Ginkgo biloba cause spontaneous bleeding, St. John's Wort (*Hypericum perforatum*) cause gastrointestinal disturbances, allergic reactions, fatigue, dizziness, photosensitivity, confusion, *Capsicum annuum* cause hypertension, cardiac arrhythmias, myocardial infraction, *Ephedra* cause anxiety, *Vitex agnus* (Chast tree fruit) cause headache, diarrhoea and *Piper methysticum* cause liver toxicity.(14)

Mostly patients taking drugs with a narrow therapeutic index like Cyclosporin, Digoxin, Phenytoin, Procainamide, Theophylline, Warfarin etc. should be discouraged from using herbal products. (15)

All drugs with narrow therapeutic index may either have increased adverse effects or be less effective when used in conjunction with herbal products. Ginkgo is used for Alzheimer's disease and causes increased bleeding with aspirin. Ginseng has multiple uses and causing synergism with monoamine oxidase inhibitors. Kaa is used as anxiolytic and shows synergism with benzodiazepines. St. John's Wort is used as antidepressant and causes reduced plasma levels of warfarin, cyclosporine, oral contraceptives, theophylline etc. (16)

Pharmacovigilance and Herbal Medicines

Pharmacovigilance, a French term referring to identify side effects of drugs, their treatment, documentation, reportage and regulatory decisions based on them, is a well established science in the developed world. (17)

Pharmacovigilance is a discipline involving detection, evaluation and prevention of undesirable effects of medicines. It involves monitoring the safety of drug over a period of time, identification of adverse drug reactions in humans, access risk-benefit ratio. (18) Safety and efficacy are the two major concerns about

any drug, while efficacy can be detected with relative ease; the same cannot be said about safety because the adverse effect of a drug may be uncommon but very serious. This gave a birth to a new branch of pharmacology called pharmacovigilance. (19) The aim of pharmacovigilance is to protect patients from unnecessary harm by identifying previously unrecognised drug hazards, elucidating predisposing factors and quantifying risk in relation to benefits. (20) Herbal medicines are widely used in both developed and developing countries however, in recent years, there are several high profile herbal safety concerns having an impact on the public health. Herbal medicines are traditionally considered as harmless but as medicinal products they require drug surveillance in order to identify their risks. Published data shows that the risk is due to either to a contaminant or to an added drug. WHO has increased its efforts to promote herbal safety monitoring within the context of the WHO International Drug Monitoring Programme. The WHO guidelines aims 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 efficacy, quality assurance, pharmacovigilance and control of advertisements of herbal medicinal 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. (21) Various methods in pharmacovigilance are passive surveillance includes spontaneous 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 interactions. (22) The importance of genetic factors in determining an individual susceptibility 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 products. (23)

Regulatory Requirement of Herbal Medicines

The legal situation of herbal medicines 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 legislative criteria to include these traditionally used herbal medicines in drug legislation.

(24) Approval of herbal medicines in most countries is based on traditional herbal references, provided they are not known to be unsafe when used to treat minor illnesses. But, now-a-days claims are being made to treat more serious illnesses with herbal medicines for which no traditional knowledge is present. (25)

Therefore, regulatory requirements for herbal medicines are necessary to ensure the safety, efficacy and quality and to support specific indications; scientific and clinical evidence must be acquired. (26) 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 medicines is varies from one country to other country. (27)

Benefit OF Pharmacovigilance in Herbal Medicines

In order to provide consistency in the naming of herbs in adverse reaction (AR) reports, the WHO Collaboration Centre for International Drug Monitoring has recommended the use of proper scientific binomial names for herbs used in medicine, including the use of such names (where this information is available) in the coding of AR reports. (28) This would ensure comparability between reports from various international pharmacovigilance databases. It is equally important for the authors of published AR case reports to identify the specific product(s) involved, including label and manufacturer information, specific ingredients, and dose employed. Published case reports would also benefit from analysis of the suspect product used, for contamination and adulteration, or species identification, where possible. A lack of, or incorrect, herbal identification has been noted as a potential source of confusion in published case reports of herbal medicinal product toxicity. (29)

Ways to provoke Pharmacovigilance in Herbals

- Introduce pharmacovigilance concepts into the curriculum of herbals at the undergraduate and postgraduate level.
- Make reporting of adverse reactions to regulatory mandatory for herbal formulations.
- Human resource of development is a key feature for the success of this enterprise. It will be necessary to train herbal experts in the science of pharmacovigilance and include them not only in reporting but also in assessment of the adverse reactions.
- Healthcare professionals should remain vigilant for potential interactions between herbals and prescription medications, especially when it involves medications with narrow therapeutic indices. Due to the wide use

and easy availability of herbal medicines, herbal toxicity has become an issue of concern. The safety and quality of herbal medicine should be ensured through greater research, pharmacovigilance, greater regulatory control, and better communication between patients and health professionals. The recommended approach is to include herbal medicines in existing national pharmacovigilance systems which incorporate coverage of herbal medicines. Pharmacovigilance in herbal medicine in India is perhaps an untaught of concept as yet; we do not need “Herbal thalidomide” to wake the pharmacovigilance community to the need of the hour.(30)

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 health.(31) It is clear that the herbal industry can make great strides in the world. With the increased use of herbal products, the future worldwide labelling practise should adequately address quality aspects. Standardisation of methods and quality control data on safety and efficacy are required for understanding of the use of herbal medicines. (32) 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. (33) There is the need of more research and reporting to be done to understand the adverse effects associated with the herbal drugs beside their vast health benefits to ensure the proper well being of humans. The myth of “if it’s herbal it is safe” has to be removed and the norms and requirements should be followed for manufacture and marketing of herbal products, and medical information’s should be provided in general. Pharmacovigilance report should be developed and shared for future reference to medicinal products to avoid any case of severe adverse reaction, since these are traditional medicinal products and are used widely.

References

1. Winslow LC, Kroll DJ, Herbs as medicines, Archives of Internal Medicine, 158, 1998, 2192-2199.
2. Gossell M, Simon OR, West ME, The past and the present use of plants for medicines, West Indian Medical Journal, 55, 2006, 217.
3. De-Smet PGAM, The role of plant derived drugs and herbal medicines in health care, Drugs, 54, 1997, 801-840.
4. WHO technical report series, Guidelines for the assessment of herbal medicines, 863, 1996, 178-184. (EMERGING ISSUES IN PHARMACOVIGILANCE OF HERBAL MEDICINES IN INDIA. By RAJA CHAKRAVERTY, Int. J. Pharm. Sci. Rev. Res., 20(1), May – Jun 2013; 08, 40-42).
5. Pharmacovigilance of herbal medicine
 - Debbie Shawa, Ladds Graemeb,
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6. Journal of Ethnopharmacology, Volume 140, Issue 3, 10 April 2012, Pages 513–518, Good Practice in Traditional Chinese Medicine Research in the Post-genomic Era. Gunasakarn S, satheesh K R. a Practical guide on Pharmacovigilance for beginners, First Edition.
7. Pharmacovigilance: A Review, Avani Patel, D.Giles, Vidhya Thomas, G Urubasavarajaswamy PM, Riddhi Patel, Acharya & B.M. Reddy college of Pharmacy, Dept of Pharmaceutical chemistry, Bangalore-560090, Karnataka, India.
8. Ganseer, A., Geology of the Himalayas, Interscience, New York, 1964, page. 289.
9. Malaysian Journal of Pharmacy 2001; 1(2):39-44 Continuing Pharmacy Education, Adverse effects Of Herbs and Drug-Herbal interactions, Abash j Hussin, School of pharmaceutical sciences, university Sains Malaysia, 11800 Pulau pinang, Malaysia.
10. Health Canada, Release of the guidance document for industry- reporting adverse reactions to marketed health products, 2009 [last accessed on March 17 2011].
11. Pharmacovigilance: a Review, Avani Patel, D.Giles, Vidhya Thomas, G Urubasavarajaswamy PM, Riddhi Patel, Acharya & B.M. Reddy college of Pharmacy, Dept of Pharmaceutical chemistry, Bangalore-560090, Karnataka, India.

12. S.S. College of Pharmacy, Haala, Gujarat, India Received 13 Aug 2011; Revised 14 Oct 2011; Accepted 24 Oct 2011
13. Malaysian Journal of Pharmacy 2001; 1(2):39-4. Continuing Pharmacy Education Adverse effects Of Herbs and Drug-Herbal interactions, Abash j Hussain, School of pharmaceutical sciences, University Sains Malaysia, 11800 Pulau pinang, Malaysia.
14. Kuhn MA, Herbal remedies: drug-herb interactions, Critical Care Nurse, 22, 2002, 22-32.
15. Hussin AH, Adverse effects of herbs and drug herbal interactions, Malaysian Journal Of pharmacy, 2001, 39-44.
16. Chauhan VS, Standardising herbs and intermediates newer approaches, The Pharma review, 2, 2006, 37-44.
17. Evans SJW, Pharmacovigilance: a science or fielding emergencies, Statistics in medicine, 19, 2000, 3199-3209.
18. Chan TY, Monitoring the safety of herbal medicines, Drug Safety, 17, 1997, 209-215.
19. Ponnusankar S, Venkatesh P, Venkatesh M, Mandal SC, Mukherjee PK, Herbal drug require pharmacovigilance study- need and reality, The Pharma review, 12, 2007, 113-120.
20. Kshirsagar N, The pharmacovigilance system in India, Drug Safety, 28, 2005, 647-650.
21. Nainwal, IJPSR, 2010; Vol. 1(11): 60-65, IJPSR (2010), vol.1, issue 11, Pharmacovigilance of Herbal Medicines: An Intangible Approach, Dev Bhoomi Institute of Pharmacy and Research, Dehradun, Uttarakhand, India
22. Bigoniya P, Pharmacovigilance of herbal medicines: current status and future strategies, The Pharma Review, 5, 2009, 77-88.
23. Chan TYK, Monitoring the safety of herbal medicines, Drug Safety, 17, 1997, 209-215.
24. Sukhdev S, Arun N, Kaila AN, Patentibility of herbal products: a review, The Pharma Review, 4, 2008, 118-124.
25. Raskin L, Ribnicky DN, Komarnytsky S, Lic N, Poulev A, Borisjuk N, plants and human health in the twenty first century, Trends in Biotechnology, 20(12), 2002, 522-531.
26. Mukherjee PK, exploring botanicals in Indian systems of medicine regulatory perspectives, Clinical Research and Regulatory Affairs, 20, 2003, 249-264.
27. Calixto JB, Efficacy, safety, quality control, marketing, and regulatory guidelines for herbal medicines, Brazilian Journal of Medical and Biological Research, 33, 2000, 179-189.
28. Jordan SA, Cunningham DG, Marles RJ. Assessment of herbal medicinal products: Challenges, and opportunities to increase the knowledge base for safety assessment. Toxicol Appl Pharmacol 2010; 243: 198-216.
29. But PP, Atherton DJ, Rustin MH, Brostoff J. Need for correct identification of herbs in herbal poisoning. Lancet 1993; 341:637-8.
30. General Pharmacy, Year : 2011 Volume : 3 Issue : 3 Page : 25-258, Pharmacovigilance of herbal products in India, P Wal, A Wal, S Gupta, G Sharma, AK Rai, Department of Pharmacognosy, Pranveer Singh Institute of Technology, Kanpur, Uttar Pradesh, India.
31. Verma S, Singh SP, Current and future status of herbal medicines, Veterinary world, 1(11), 2008, 347-350.
32. Alam S, Ali R, Akhter S, Haque A, Ansari Sh, Role of herbals in drug delivery systems, The Pharma Review, 6, 207,106-107.
33. Bhanu PS, Sagar TK, Zafer R, Failure and Successes of Herbal Medicines, the Indian Pharmacist, 54(2), 2000, 221-235.

How to cite this article

Verma A., Sharma A. and Garg K. (2014). Herbal medicine and pharmacovigilance: A future prospective. *Int. J. Pharm. Life Sci.*, 5(3):3413-3417.

Source of Support: Nil; Conflict of Interest: None declared

Received: 19.02.14; Revised: 28.02.14; Accepted:01.03.14