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REVIEW ON THE CHALLENGES OF HERBAL MEDICINES

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ABSTRACT

The major healthcare systems in India include Ayurved, Naturopathy, Unani, Siddha as well as folk medicine which entirely depend upon natural medicinal plants and have an enormous economic importance. This country is perhaps the largest producer of medicinal herbs and due to the prevalence of a variety of climatic conditions is truly called the botanical garden of the world. The efficacy of any herb is directly proportional to its identity, purity and quality. The quantitative data as well as qualitative data about safety and efficacy of traditional medicine are distant from adequate to meet the criteria obligatory to support its use globally. Careless processing of medicinal drugs is a major reason for ineffectiveness of some of our traditional medicines. Such deteriorated drugs will definitely not be accepted in the global market. This article enlightens these limitations and challenges regarding standardization of medicinal plants including several factors like diversity of herbal medicine, difficulties in plant identification, diversity in harvesting procedure, variation in its growing condition etc. Moreover the present review is an effort to highlight the various challenges of herbal medicine regarding drug production sector, quality and safety in addition to efficacy.

KEYWORDS: challenges, herbal medicines, quality, efficacy.

INTRODUCTION

Herbs are highly honoured for millennia as a rich source of therapeutic agents for prevention and treatment of diseases. Those plants which have shown positive biological activity on any one ailment or any curative property for any human or animal disorder are called as

medicinal plant. The role of natural products as remedies has been identified since ancient times. Plant-based drugs used in the traditional medicine have paid immense attention since it is easily available, less expensive and also have no side effects.[1] India is well-known as the Emporium of Medicinal plants owing to availability of several thousands of medicinal plants in the different bioclimatic zones.[2] Moreover India has a treasure of well-recorded and well-practiced knowledge of traditional herbal medicine. In Ayurveda, Siddha and Unani, utilizing a large number of medicinal plants were used for the management of human diseases.[3] Ayurved i.e. an ancient system of medicine has used various remedies for several thousand years. Ethno-medicines are the plants known to be used by traditional system or known from folklores. Herbal drugs constitute mainly those traditional medicines which primarily use medicinal plant preparations for therapy and according to W.H.O, about 80% of the world population rely mainly on herbal remedies because of its cultural acceptability, affordability and accessibility. The awareness about the side effects and complications of chemicals & synthetic drugs and inclination towards the use of herbal medicines and products has been growing tremendously in the eastern and western countries. World Health Organization has made an endeavour to identify all medicinal plants used worldwide and listed more than 20,000 species.

Most of the medicinal plant parts are used as raw drugs and they have diverse medicinal properties.[4] The preparations are either as single herbs or as collections of herbs in composite formulae. This may be the chief cause of more difficult quality control of oriental herbal drugs than that of western drug. The efficacy of any drug is directly proportional to its identity, purity and quality. Careless processing of medicinal drugs is a major reason for ineffectiveness of some of our traditional medicines. Such deteriorated drugs will certainly not be accepted in the global market. This review article explains these limitations and challenges regarding standardization, drug production sector, safety and efficacy.

Standardization challenges[5,6,7]

For safe and effective use of herbal drugs, consistency in composition and biological activity are important requirements. However, herbal drugs frequently fall short to meet these standards, owing to a range of problems like difficulties in identification of plants, genetic variability, variations in growing conditions, diversity in harvesting procedures and processing of extracts and the lack of information about active pharmacologic principles.

Difficulties in identification of plants

Most of the plants used traditionally are known by their local names. In Ayurvedic classics, Samhitakaras and Nighantukaras have mentioned their synonyms which are based on historical, botanical & pharmacological characters of plants. The plants are known by more than one synonym while some synonyms are found common to many plants. In Ayurved identification of herbs is mainly based on Panchendriya Parikshan (Organoleptic evaluation). But these has been subjective & an element of personal experience.

India officially recognizes over 3000 plants for their medicinal value. It is generally estimated that over 6000 plants in India are in use in traditional, folk and herbal medicine. Out of known 48000 plants flowering plants are about 17000 in India. Out of these 7500 species have medicinal value. At present only about 120 species are used in day to day medicine. Besides these, numbers of plants are used as a traditional medicine by rural & tribal population. More than 2000 plants are mentioned in Ayurved, but out of these so many plants are not yet identified.

According to modern science combination of organoleptic, physico-chemical and pharmacognostic methods give broad based objective information on sound scientific footing. A crude material have species/ variety/ organ specific quantitative & qualitative- external morphological characters, anatomical characters, histological & histo-chemical characters and cellular cytological/cyto-chemical characters. These characters help to know age, developmental stage, season of collection & geographical sources of crude drug which are important also from Ayurvedic point of view. The plant parts have characteristic tissues & cell layers which have typical chemicals accumulated. These are diagnostic & can be detected by histo-chemical/ micro-chemical methods. There is need to evolve some methods to identify single drug powder which will serve as a model for future research work.

The burning issues regarding herbs are variability in crude drugs, controversial or ambiguous medicinal plants, unidentified herbs and they can be resolved by proper Ayurvedic study of medicinal plants, ethno-botanical survey along with careful botanical examination of these herbs. On 1st May, 1753 Carl Linnaeus proposed a binomial system of nomenclature for plants. This system is now followed everywhere and incorporated in International code of Botanical Nomenclature.

Diversity of herbal medicine

The diversity of herbal medicine enhances the challenges of herbal medicines including basic questions such as defining the most appropriate naming system (botanical, common, pharmaceutical name) for herbs and validation of the botanical identity of the herbal ingredients.

In recent times, one of the speedily expanding areas of pharmacognosy has involved the application of tissue culture of plant cells, tissues and organs in the study of medicinal herbs. This includes development of commercial production of expensive bio-medicaments, discovery of new metabolites, selection of superior strains of medicinal plants and improvement of medicinal plant species by genetic engineering. Medicinal plants growing in diverse geographical regions of India may exhibit geographic chemotypes. The chemical races of our indigenous medicinal plants, whether they be of natural origin or produced by plant breeding, can offer significant scope for the improvement of therapeutic value of the drug, either by adjustment of individual constituents or by increase in overall yield. Such biotechnological approaches would be advantageous in providing standardized drugs of Indian pharma in bulk for commercial availability in the global market.

Variation in growing condition

The levels of components in any given batch of an herb may be influenced by the environmental factors including soil, altitude, seasonal variation in temperature, atmospheric humidity, length of daylight, rainfall pattern, shade, dew and frost conditions.

During collection of herb, age and developmental stage of the plant (guna of medicinal herbs depends on these factors), geographical sources (desh) and season of collection (rutu) should be taken into consideration. The season at which each drug is collected is a matter of considerable significance as the amount and nature of active constituents is not constant throughout the year. The age of the plant also decide its medicinal potency and governs the total quantity of the active constituents produced as well as the relative proportions of the active principles. Hence, the authentic part of medicinal plants of a particular age should be harvested in a particular season before processing for drug manufacture, to prevent any alteration in its medicinal potency. The medicinal potency of an angiospermic taxon also differs among its populations occurring in different geographical localities. Moreover, the period of storage in sun or shade conditions also affects medicinal properties of the plants. According to Aacharya Vagbhata the herbs eaten by termites, grown in barrel land, marshy

places, burial grounds, sand dunes, foot paths, moth eaten, affected by forest fires, shrunken in severe cold are unsuitable for medicinal purpose.

Diversity in harvesting procedure

Precautions during harvesting of medicinal plants are not observed by most of the firms and it ultimately results in deterioration in efficacy of the herbal drugs. Duration of the drying conditions of the harvested medicinal herb also varies from a few hours to many weeks. If enzyme action is to be encouraged, slow drying at moderate temperatures is essential. Storage of the harvested plant parts under hygienic conditions is another main issue to be considered during processing of the drug. Herbal drugs having mycotoxins above the tolerance limit fixed by WHO for human consumption, will be definitely rejected in the global market. This is due to improper storage and processing of herbal drugs by Indian firms. The situation is alarming and suitable quality control measures have to be taken immediately. The efficacy reduces particularly during storage resulting in the loss of the active ingredients, formation of metabolites with no activity and, in extreme cases, the production of toxic metabolites. Physical factors such as air (oxygen), humidity, light, and temperature can bring about deterioration directly or indirectly. Other factors like infections, insects, planting density, competition with other plant species, seeding time, and genetic factors play a vital role. The cultivation of some medicinal plants in demand under appropriate environmental conditions will provide better development of plants owing to improved conditions of the soil, pruning, and control of insect pests and better facilities for treatment after collection. It is necessary to monitor compliance of the product with a suitable quality specification throughout the shelf life. Records of all shelf life studies need to be recorded. Therefore current methods of standardization which are mentioned in pharmacopoeias as well as Charak's guidelines mentioned in Charak Samhita Vimansthan 8/87[8] should be followed to obtain thoroughly authentified, qualified, pure and efficacious drug. The drug-manufacturing firms in India should take care during processing of medicinal herbs like some firms in other Asian countries which are our real competitors in the global market. A number of research institutes have carried out studies on the cultivation practices of medicinal plants, which were found appropriate and remunerative for commercial cultivation.

Lack of information of active principle

According to Ayurved entire herbal drug is regarded as a medicinal plant. In Ayurvedic literature there is no clarity about active ingredients of medicinal plants. For ensuring

maximum efficacy of a drug, Charak has taken– nature of the drug [plant genetics], soil quality, weather, time of collection, temperature, age of plant, plant part, storage condition[microbial contamination]; these points into consideration. Plants have a huge potential for producing new drugs and used in traditional medicine to treat chronic and even infectious diseases.[9] Studies by various researchers have provided evidence that plants are one of the main sources for drug discovery and development.[10,11,12]

To design a new herbal drug, information about Ayurvedic pharmacology is also necessary. It is obvious that different constituents of plant species have different mode of action on same disease. Therefore it is very essential not only to know active components of the plant but also to know the mode of action of the therapeutic compounds on the basis of modern medicine parameter. Due to lack of proper evidence regarding the proven reliability of various medicinal plants for their curative properties & effects in modern terms of understanding, they have remained unacceptable to large section of people.

Even today in western medicine and despite in synthetic chemistry 25% of prescription medicines are still derived either directly or indirectly from plants.[13] A plant possesses a massive amount of several molecules that synergistically act on targeted elements of the cellular complex pathway.[14] In our research reports many of the plants mentioned in our ancient literature, have been found not to be true to their described properties although they have been constantly used in Ayurved and other traditional system of medicine very successfully. Therefore it can be stated that our approach in investigating medicinal plant is faulty. Potential of medicinal plants is remained properly untapped. Most of the Ayurvedic and herbal medicines are prescribed to be used in the form of water extracts, but at many research centres all the extracts used for testing were in various solvents except in water as water poses problem for evaporation and extracts do not dry properly. Therefore many of our traditional and folk-lore medicines and information available regarding their specific use remains without properly investigated till today due to improper choice of solvent system for extraction and use of unsuitable methods for isolation of active compound and incorrect selection of models for testing of active principles. Very often we do not know what particular effect a solvent system (water extract-natural medium, cow's urine- mild acidic medium, wines- alcohol medium) will have on active principle. Otherwise we will end up in destroying active molecules in the plant material and isolating unwanted inactive artefact. In

addition, the processing of herbs, such as heating or boiling, may alter the dissolution rate, or even the pharmacological activity of the organic constituents.

Quality challenges[15,16]

If herbal remedy is effective, quality assurance is required to ensure that the product has the expected effects. Even in the deficiency of data on efficacy, quality assurance is imperative, as adulteration of plants is grave problem. The botanicals, toxic metals, microorganisms, microbial toxins, pesticides, and fumigation agents are some of the common adulterants. For this reason, quality is a crucial determinant of safety.

Quality issues of herbal medicines can be divided into two groups: external and internal. The external issues include contamination (e.g. toxic metals, pesticides residues and microbes), adulteration and misidentification whereas complexity and non-uniformity of the ingredients in herbal medicines are the internal issues which affect the quality of herbal medicines. The meticulous implementation of Good Agricultural and Collection Practices (GACP) and Good Manufacturing Practices (GMP) would certainly reduce the risk of external issues. By application of modern analytical methods and pharmaceutical techniques, formerly unsolved internal problems have converted into solvable.

Herbal drugs from traditional plants which are now fetching global market require standardization. Now-a-days, compliance of Good Laboratory Practice [G.L.P.], Standard Operating Procedure [S.O.P.] has become important legislative requirement by regulatory authorities for accepting data of drug report. The protocol for standardization is scientifically described in Charka Samhita Vimansthan, Chapter 8, and Shloka 87[8] which is very important in current era for ensuring identity, purity & quality of a herbal drug.

In ancient era, identification, collection, formulation of drug as well as management of diseases was done by the same physician. In due course of time, due to urbanization, commercialization and globalization, the mode of this practice is changed. There is a long chain between collectors & users of drugs from plant origin. Many a times false, inferior, defective, spoiled, useless other parts of same or different plant or a part of other plant species or harmful substances or drug which do not confirm with the official standards or artificially manufactured commodities is adulterated with the original one. Plants collected in the wild may include non-targeted species, particularly either by accidental substitution or intentional adulteration. Hence physician is not sure about the drug which he receives. The

efficacy of any drug is directly proportional to its identity, purity & quality. Therefore standardization is a need of time. Sarcastically, many Indian products are not available in standardized form, which is the least requirement for introducing a product in the Western market.

The short-cuts in acquiring the materials for the use have resulted in over-exploitation of the material. This has caused adulteration in required material. The result is that only some of the exported products have come back with rejection but some of them have produced fatal results discrediting the whole system of Ayurvedic medicine. The adulterants can be evaluated by pharmacognostic & physico-chemical standardization.

The revival of traditional medicine system in India & abroad has put extra pressure on our forest for milking medicinal plants for trade. This is causing extinction of number of important medicinal plant species. Due to biopiracy and over exploitation, some of the ethnomedicinal plants are becoming rare. Reserves of medicinal plants are diminishing and are in danger of extinction due to unfriendly harvesting techniques, loss of growth habitat and their unmonitored trades. By 2050, it is estimated that 30% of present angiosperms will become extinct. Between 4000 and 10000 medicinal species might now be endangered.[17] The more attention should be focussed on conservation & cultivation of endangered, vulnerable, rare and threatened species like *Aconitum heterophyllum*, *Hedychium spicatum*, *Nardostachys jatamansi*, *Picrorrhiza kurroa*, *Swertia chirata*, *Valeriana wallichii* etc. keeping in view the demand of their drugs in the global market. The study of substitute plants should be encouraged.

Clinical Trials (Drug efficacy) challenges[10]

The most important challenge for clinical trials is a complex structure of herbal medicines. In order to overcome this problem, it is required to gain public trust and to bring herbal product into mainstream of today's health care system. The researchers, the producers and the regulatory agencies must apply accurate scientific methodologies and clinical trials to make sure the quality and lot-to-lot consistency of the heterogeneous traditional herbal products which rely mostly on the quality control of source materials and their manufacturing into the final products. The quality and consistency of the herbal products can be monitored by using modern technologies. A well-designed clinical trial is the method of choice to prove the safety and effectiveness of a therapeutic product which will play a significant role in global health.

While randomized control trials (RTCs) are regarded as the 'gold standard' of allopathic research, RTCs are not the appropriate methodology for herbal research. The *Dove Press Journal* review article of 2010 explains why and describes some possible research designs to overcome these challenges. There are more than 1.5 million practitioners of traditional medicinal system using medicinal plants in preventive, promotional and curative applications.[9] All research should hold the potential to achieve social value. This can be accomplished by judicious product identification based on diseases prevalent in the developed world for which no medicine or palliative therapy is available. Such herbal medicines will find speedy access into those countries.

Safety challenges[18,19]

Scientific evidence from tests done to evaluate safety & effectiveness (clinical trials) of traditional medicine products & practices is limited.

India with its prime storehouse of medicinal herbs in the world may maintain a remarkable position in the production of raw materials either directly for crude drugs or as the bioactive components in the formulation of pharmaceuticals and cosmetics etc.[20]

Safety is a basic principle in the provision of herbal medicines and herbal products for health care, and a critical component of quality control. It has been observed that most of the problems related with the use of traditional and herbal medicines arise mainly from the classification of many of these products as foods or dietary supplements in some countries. For itself, evidence of quality, efficacy, and safety of these herbal medicines is not needed before marketing. In the same vein, quality tests and production standards tend to be less rigorous or controlled and in some cases, traditional health practitioners may not be certified or licensed.

The most profitable form of conventional medicine is generating billions of dollars in revenue in the global market. The safety of traditional and herbal medicines has therefore become a major concern to both national health authorities and the general public. But scientific evidence from tests done to evaluate safety & effectiveness (clinical trials) of traditional medicine products and practices is limited. Hepatotoxicity, nephrotoxicity and most critically, drug interactions with synthetic medicines are common in some of the herbal practices. The toxic effects of herbal drugs may also be because of adulteration, contamination by pesticides and the diseased state of herbs. WHO has laid down guidelines

for determination of adverse reactions as essential requirements for human applications. Keeping these facts in view, the safety limit profile of the herbal drugs should be recorded in order to popularize Indian pharma in the global market. The government and drug industry must come forward in funding and undertaking this task, so that good quality and safe herbal preparations are a reality. Safety assurance system encompassing rational clinical practice and risk monitoring should be set up to improve the safety of herbal medicine and to play more imperative role in maintaining human health.[21,22,23]

There are no systemic side-effects of the herbs reported for humans in the literature. Reports that some herbal medicines are contaminated, toxic or interfere with the metabolism of drugs used to treat cancer or AIDS has decreased the enthusiasm of United Sates consumers for herbal medicines. Consequently, the sale of herbal products in United States has reduced in the last two years. There is rising awareness at several levels to develop pharmacovigilance practises for herbal medicine. The numerous problems relate to the ways in which medicinal plants are named, recognized, sourced and used. ADR monitoring is the most important method of monitoring safety of herbal medicines.

Pharmacovigilance challenges[24,25]

The herbal medicines are completely safe, and hence can be consumed safely by the patient on his/her own, without a physician's prescription is the commonest myth regarding these drugs. This belief has resulted in large-scale self-medication by people all over the world, often resulting in side-effects or unwanted after-effects and disappointing end-results. Large scale awareness of people is required to develop pharmacovigilance practices for herbal medicines. Furthermore there should be consideration of pharmaco-genetics & pharmaco-genomics, patients' reporting and modification of existing methodology for safety monitoring of herbal medicines in optimising their safety.

Herbal medicines afford clinical and research opportunities that must not be neglected, when greater regulation of the product is considered. W.H.O. should prop up traditional medicines into National health system in combination with National policy and regulation for production, practices and providers to ensure safety & quality. Global synchronization of legislation is necessary to guide the responsible production and marketing of herbal medicines.

India should adopt organized cultivation of medicinal plants that have export potential and import substitutions. Efforts should be made to cultivate potential medicinal plants as field crops. Their conservation should be done in proper ecological conditions. With the intention of pushing India as an important player in the global herbal product market, herbal products should be standardized as per WHO guidelines.

Conservation of data and medicinal plants

We are lacking in having data regarding list of commonly used medicinal plants according to state, annual availability of different species from various regions, list of medicinal plants with proven specific pharmacological action etc. Even today our knowledge regarding quantitative distribution & availability of many medicinal plants is inadequate. The scientific publication on medicinal plants from all journals, details of Ayurvedic information from Veda, Samhita, Rasagrantha, Nighantus, report of ethno-botanical survey, research work done by scholars from all universities & institutes, conference proceedings, advance search & full text search on database on medicinal plants from all over the world should be available online on website to give a holistic picture of a plant. Training the youth of the country in taxonomy of ethnomedicinal plants would help in developing such databases. This will be helpful for future planning of research work on medicinal plants. Patenting & National resource of medicinal plants will play an important role in bringing honour to our motherland. For conservation of material and data, herbarium should be maintained as they serve as a reference centre, documentation facility and data storehouse. Now, the time has arrived to compile and document available knowledge on our precious plant resources and to prove their utility scientifically through detailed phytochemical, biological and pharmacological investigations at selected centres in different regions of the country.

Bioprospecting would be one of the challenging areas for future research in the 21st Century. It would enable us to make use of our rich biological heritage. Bioprospecting can enhance the conservation value of Indian medicinal plants. In addition, this would check illegal exploitation of such indigenous plants through biopiracy or gene robbing by biotechnologically developed countries and would be helpful in many fold enhancement of Indian herbal medicine in the global market. If quick and urgent steps are not taken in bioprospecting our ethnomedicinal plants, the fate of some of the valuable Indian plants will be like that of Neem and Turmeric. There is a scope for herbal medicine in the field of Plant monographs.

India should focus on agro-technology, process technology, standardization, quality control, research and development of herbal drugs. Without doubt, the therapeutic potential of many herbs is yet to be completely discovered. The quality of the data and the quality of the herbal products themselves as well as regulatory control of herbal medicines should improve to a great extent. While herbal medicine can potentially contribute to the advancement of healthcare, many major challenges must be overcome prior to the successful integration of herbal remedies into mainstream medicine. Once we know our plant correctly and their biological & pharmacological properties, we can utilise them much better way & explore the potential of their depleting wealth. This will certainly give us confidence to face this current era!

REFERENCES

1. Cathrine L, Prabavathi N. Preliminary Phytochemical Analysis and Antibacterial Activity of leaf extracts of *Vitex leucoxlon* L.F. Int J Curr Pharm Res., 2011; l3: 71-73.
2. Prabhu TP, Panneerselvam P, kumar RV, Atlee WC, Subramanian SB. Anti-inflammatory, anti arthritis and analgesic effect of ethanolic extract of whole plant of Merremia emarginata Burm.F. Central European Journal of Experimental Biology, 2012; 1(3): 94-99.
3. Valsaraj R, Pushpangadan P, Smitt UW, Adersen A, Nyman U. Antimicrobial screening of selected medicinal plants from India. J Ethnopharmacol, 1997; 58: 75-83.
4. Mahesh B,Sathish S. Antimicrobial Activity of some important medicinal plant against plant and Human Pathogens. World J Agri Sci., 2008; 4: 839-843.
5. Current Scientific Status and Regulatory Control of Herbal medicine. Available at http://www.ijrap.net/admin/php/uploads/639_pdf.pdf
6. Regulatory issues of herbal medicine. Available at www.clininvent.com/.../Regulatory%20issues%20for%20tradintionl%2
7. Regulatory situation of herbal medicine worldwide. Available at http://apps.who.int/medicinedocs/pdf/whozip57e/whozip57e.pdf
8. Acharya Charak, *Charak Samhita*, Vol.II, (1000 B.C.), ed. Pandit Kashinath Shastri, Dr. Gorakhnath Chaturvedi, Choukhamba Bharati Academy, Varanasi, Charak Samhita Vimansthan, 1996; 8/87: 594-595.
9. Panda SK, Thatoi HN, Dutta SK. Antibacterial activity and phytochemical screening of leaf and bark extracts of *Vitex negundo* from Similipal biosphere reserve Orissa. J Med Plant Res., 2009; 3(4): 294-300.

10. Rates SMK, Plants as source of drugs, Toxicon, 2001; 39: 603-613.
11. De Pasquale A, Pharmacognosy: the oldest modern science, Journal of Ethnopharmacology, 1984; 11: 1-16.
12. Gordon MC, David JN, Biodiversity: A continuing source of novel drug leads, Pure Appl Chem., 2005; 77: 7-24.
13. Farnsworth N R and Soejarto D D. Global importance of medicinal plants, Akereleo, Heywood V and synge H (eds.). Cambridge U.press, Cambridge, UK. Conservation of medicinal plants, 1991; 2: 25-51.
14. Durmowicz A G and Stenmak K R. Mechanisms of structural remodeling in chronic pulmonary, Hypertension, Pediator Review, 1999; 20: 91-101.
15. WHO guideline on safety monitoring. Available at *Avdhesh Kumar1*, International journal of ayurvedic & herbal medicine, Jan. Feb. 2016; 6(1)(2149-2161): 2161. apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf
16. Guidelines for the Appropriate use of Herbal Medicines. Available at apps.who.int/medicinedocs/en/d/Jh2945e/11.html
17. Edwards, R. No remedy in sight for herbal ransack. New Sci., 2004; 181: 10–11.
18. WHO guideline on safety monitoring. Available at apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf
19. Guidelines for the Appropriate use of Herbal Medicines. Available at apps.who.int/medicinedocs/en/d/Jh2945e/11.html
20. Tiwari S. "Plants: Arich source of herbal medicine", Journal of natural products, 2008; 1: 27-35.
21. Standardization of herbal medicines. Available at http://www.academicjournals.org/article/article1380017716_Kunle%20et%20al.pdf
22. Regulatory situation of herbal medicines. Available at http://www.dcscience.net/Report_on_Regulation_of_Herbal_Medicines_and_Practitioners.pdf
23. Report on the regulation of herbal medicines and practitioners.
24. Pharmacovigilance of Herbal Products. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3159283/
25. Pharmacovigilance of Herbal Products in India. Available at https://www.researchgate.net/publication/51620397_Pharmacovigilance_of_Herbal_Products_in_India