Original Article

A review on the status of quality control and standardization of herbal drugs in India

Abstract

Background: Most of the herbal medicines in the world originate from the developing countries. There are ample opportunities for these countries to expand their global export. The world market for botanical medicines including drug products and raw materials has been estimated to have an annual growth rate between 5% and 15%. Total global botanical drug market is estimated at US$62 billion and is expected to grow to the tune of US$5 trillion by the year 2050. In the USA alone, the usage of botanicals has been increased by 380% between the years 1990 and 1997. **Materials and Methods:** Ayurveda, the Indian system of medicine, is one of the ancient, yet living traditions that face a typical Western bias. Widespread and growing use of botanicals has created public health challenges globally in terms of quality, safety, and efficacy. **Results and Discussion:** The development of parameters for standardization and quality control of botanicals is a challenging task. Various regulatory authorities, research organizations, and botanical drug manufacturers have contributed in developing guiding principles and addressing issues related to the quality, safety, and efficacy. **Conclusions:** The present review describes the regulatory aspects of herbal drugs in India and various other countries.

Key words:
Herbals, India, quality control, regulatory, standardization

Introduction

Herbal medicines have been in use since the dawn of civilization to maintain health and to treat diseases. The WHO estimates that about three-quarters of the world's population currently use herbs and other forms of traditional medicines to treat their diseases. The herbal formulations, which are sold as over-the-counter (OTC) products, have a different protocol regarding preparation, acquiring license, and marketing. The active principles of herbal preparations are not often well defined. In addition, the regulations regarding safety and efficacy are not known to scientists or consumers.[1]

A drug is defined as being safe, if it causes no known or potential harm to users. There are three categories of safety that need to be considered, as these would dictate the nature of the safety requirements that need to be ensured. The three categories are as follows:

- Category 1: Safety established by use over long time
- Category 2: Safe under specific conditions of use (such herbal medicines should preferably be covered by well-established documentation) and
- Category 3: Herbal medicines of uncertain safety (the safety data required for this class of drugs will be identical to that of any new substance).[2]

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According to the WHO (1996 a and b, 1992), standardization and quality control of herbals is the process involved in the physicochemical evaluation of crude drug-covering aspects, such as selection and handling of crude material, safety, efficacy, and stability assessment of finished product, documentation of safety and risk based on experience, provision of product information to consumer, and product promotion.[3] Scientifically validated and technologically standardized herbal medicines may be derived using a safe path of reverse pharmacology approach based on traditional knowledge database. This may play a vital role in drug discovery, development, and therapeutics, in addition to dealing with a typical Western bias against Ayurveda.[4] The WHO has set certain standards for herbal drugs, which involve the various parameters [Figure 1].[5]

Standardization of herbal formulation requires execution of good manufacturing practices. In addition, study of various parameters such as pharmacodynamics, pharmacokinetics, dosage, stability, shelf-life, toxicity evaluation, and chemical profiling of the herbal formulations is considered vital. Other factors such as pesticide's residue, aflatoxin content, heavy metals contamination, and good agricultural practices in herbal drug standardization are equally important. DNA analysis has been proved as an important tool in herbal drug standardization. This technique is useful for the identification of phytochemically indistinguishable genuine drug from substituted or adulterated drug.[6] Fingerprinting of herbal medicines is utilized on the authenticity and quality control of herbal medicines and the total producing process of herbal preparation. The combination of qualitative fingerprinting and quantitative multicomponent analysis is a novel and rational method to address the key issues of quality control of herbal medicine.[7]

All medicinal products including herbal medicinal products may only be marketed in Europe when they have obtained a marketing authorization (MA) or a registration application by the competent authorities. The MA procedure requires the documentation of pharmaceutical quality, safety, and efficacy, in addition to all other data concerning the medicinal product including name, pharmaceutical form, indication fields, dosage, and risk information.[8]

Inclusions of herbal drugs in pharmacopoeias

The Chinese Pharmacopoeia 1997 edition has 647 traditional drugs,[9] European Pharmacopoeia 2000 edition contains monographs on 152 crude drugs,[10] and Indian Pharmacopoeia 1996 edition number shrinks to 57 including only 12 crude drugs.[11]

The Pharmacopoeial Laboratory for Indian Medicines, Ghaziabad, is the only laboratory to develop pharmacopoeial standards at present. The Government of India has published standards on 540 single drugs and 101 compound formulations. However, about 2000 single drugs and about equal number of compounded formulations still require standards to be developed.[12]

Organizational setup in India for the regulation of herbal drugs

It is the cardinal responsibility of the regulatory authorities to ensure that consumers get the medication, which assures purity, safety, potency, and efficacy. The quality control of crude drugs and herbal formulations is of paramount importance in justifying their acceptability in modern system of medicine. However, one of the major problems faced by the herbal drug industry is the nonavailability of rigid quality control profile for herbal materials and their formulations.[13] The organizational setup in India for regulations of herbal drugs at central and state level is given in Figure 2.[14]

Regulatory laws in India for herbal drugs

There are various regulatory laws in India for the regulation of herbal drugs. Some of these are Drugs and Cosmetics Act,

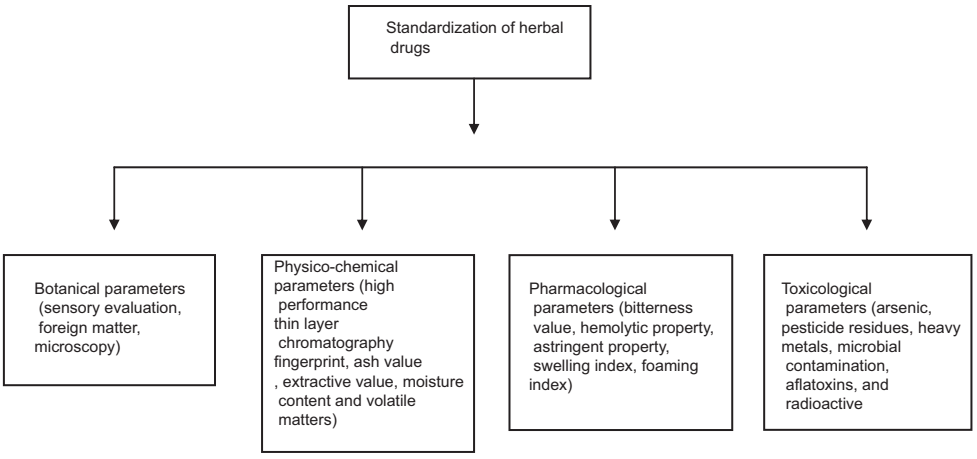

Figure 1: Parameters for standardization of herbal drugs

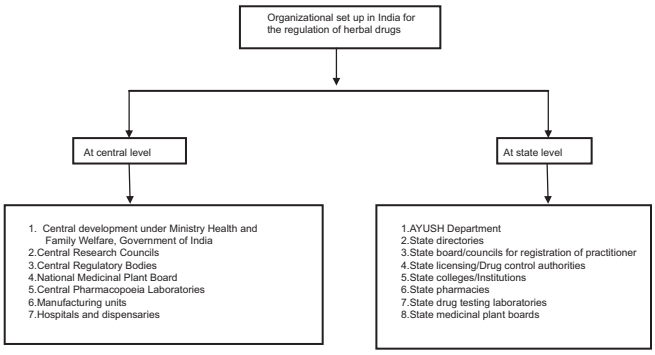

Figure 2: Organizational setup in India for the regulation of herbal drugs

1940, Indian Medicine Central Council Act, 1970, Drugs and Magic Remedies Act (Objectionable Act), 1954, Biological Diversity Act, 2002, Wild Life Protection Act, 1972, and Indian Forests Act, 1865.[14]

Indian Drugs and Cosmetics Act, 1940 (for herbal drugs regulation)

All traditional medicines such as Ayurveda, Unani, and Siddha products containing primarily one or more medicinal plant ingredients are governed under Chapter IVA of Drugs and Cosmetics Act, which was introduced in 1969. Before this amendment, definition of products containing herbs or herbal ingredients was nonexistent in the Indian Drug Laws.[15] A recent amendment of the Drugs and Cosmetics Act, 1940, has made some of its provisions applicable to the ayurvedic drugs, which are defined to include medicines for internal or external use in human beings for diagnosis, prevention, mitigation, or treatment of diseases and which are mentioned in and manufactured exclusively in accordance with the formulae described in literature listed in Schedule I of the act.[16]

Indian Medicinal Central Council Act, 1970

Central government is vested with power to grant permission for opening of new colleges, increase of admission capacity, and starting of new or higher courses of study. Central government grants permission on the basis of recommendations of state government, affiliating University and Regulatory Council, and availability of infrastructure as per the prescribed norms. Qualifications awarded by universities are included in the act with the approval of central government. Central Council shall be a body corporate by the name of Central Council of Indian Medicine having perpetual succession and a common seal, with power to acquire, hold, and dispose of property, both movable and immovable and to contract, and shall by the said name sue and be said.[17] The act also includes that the Central Council shall appoint such number of medical inspectors as it may deem requisite to inspect any medical college, hospital, or other institution, where education in Indian medicine is given.[18]

Wild Life Protection Act, 1972

The Government of India enacted Wild Life (Protection) Act, 1972, with the objective of effectively protecting the wildlife of this country and to control poaching, smuggling, and illegal trade in wildlife and its derivatives. The Ministry has proposed further amendments in the law by introducing more rigid measures to strengthen the act. The objective is to provide protection to the listed endangered flora and fauna and ecologically important protected areas.[19] The act provides the establishment of Wildlife Advisory Board and appointment of wildlife wardens and other staff to implement the act. In the year 1991, the wildlife act was further modified. This amendment was based on the recommendations of Indian Wildlife Board and Ministry of Environment and Forests.[20] The Chief Wildlife Warden may, on application, grant to any person a permit to enter or reside in a sanctuary for all or any of the following purposes, namely: (a) Investigation or study of wildlife and purposes, ancillary or incidental thereof; (b) photography; (c) scientific research; (d) tourism; and (e) transaction of lawful business with any person residing in the sanctuary.[21]

Standing Committee of the National Board

The National Board may in its discretion, constitute a Standing Committee for the purpose of excising such powers and performing such duties as may be delegated to the committee by the National Board. The Standing Committee shall consist of the Vice-Chairperson, the Member-Secretary, and not more than ten members to be nominated by the Vice-Chairperson from among the members of the National Board. The National Board may constitute committees, sub-committees, or study groups, as per the requirement, from time to time, for proper discharge of its functions.[22]

Biodiversity Act, 2002

The act aims at the conservation of biological resources and associated knowledge as well as facilitating access to them in a sustainable manner and through a process. For the purposes of implementing the objectives of the act, it establishes the National Biodiversity Authority in Chennai.[23] The National Biodiversity Authority may appoint such officers and other employees as it considers necessary for the efficient discharge of its functions under this act.[24]

Import of herbal drugs

There is no provision for import of ayurvedic, Siddha, and Unani drugs. The drugs being indigenous to the country are not manufactured outside India and as such no provisions for their import have been made.[16]

Manufacture of ayurvedic drugs

Ayurvedic, Siddha, and Unani drugs are required to be manufactured according to the formulae prescribed in the first schedule of the act. A license is necessary for

the manufacture of these drugs and is required to be manufactured from genuine and properly identified raw materials.[25] The manufacture of drugs should be carried out under the directions and supervision of competent technical staff and one of whom should have at least one of the following qualifications:

- A degree or diploma in Ayurveda or Ayurvedic Pharmacy or Unani system of medicines recognized by the central or the state government
- A degree or diploma in pharmaceutical chemistry with at least 1 year experience or a degree in chemistry or botany with at least 2 years of experience in the manufacture of the ayurvedic drugs
- A Vaid or Hakim registered in a State Register of Practitioners of indigenous systems of medicines having experience of at least 4 years in the manufacture of ayurvedic or Siddha or Unani drugs[16,25]
- Qualified pharmacist in Ayurveda, Siddha, or Unani system of medicine with at least 8-year experience in the manufacture of ayurvedic drugs.

Conditions for the manufacture of herbal drugs

In case of the manufacturing of herbal drugs, proper details of the manufacturing procedure should be kept in records and the tests for raw materials must be validated, recorded, and properly maintained. Duly authorized inspectors should inspect the premises and send the samples of raw materials and finished products to the quality control department. The inspectors may also inspect the conditions of the manufacturing premises and manufacturing must comply with the proper hygienic conditions specified under Schedule T of the Drugs and Cosmetics Act, 1940.

Manufacture on more than one set of premises

If ayurvedic (including Siddha) or Unani drugs are required to be manufactured on more than one set of premises, a separate application shall be made and a separate license shall be obtained with regard to each such set of premises.[25]

Indian Drugs and Cosmetics Act-spurious drugs

Person who manufactures any spurious drugs shall be liable to imprisonment for 1–3 years and a fine of not < Rs. 5000 on first conviction and an imprisonment for 2–6 years and a minimum fine of Rs. 10,000 on subsequent convictions.

For the manufacture of adulterated drugs or manufacture without a valid license, imprisonment up to 2 years and a fine of at least Rs. 2000 for any subsequent conviction are prescribed.

Sale of Ayurvedic, Siddha, and Unani drugs

No license is necessary for effective sale of Ayurveda, Siddha, and Unani drugs, but dealers in such drugs can sell only products manufactured by a person licensed to manufacture drugs under the act. Some of the largest OTC brands in India are registered as "Ayurvedic Medicines" because of their plant-based natural active ingredients (e.g. Vicks VapoRub, Amrutanjan Pain Balm, Zandu Pain Balm, Iodex Pain Balm, Moov Pain ointment, Itch Guard Cream, Eno Fruit Salt antacid, Vicks Cough Drops, Halls Lozenges, Dabur's Pudina Hara, and Calcium Sandoz, etc.).[26]

Administrative agencies regarding the regulation of herbal drugs

The central government and state government appoint some administrative bodies for efficient running of the act. These bodies are divided into three parts: Advisory, analytical, and executive. Advisory body includes Drug Consultative Committee and Drug Technical Advisory Board, the analytical body involves Central Drugs Laboratory, Drug Control Laboratories in States and Government Analyst, and the executive body comprises Licensing Authorities, Drug Inspectors, and Custom Collectors. The Board is required to be constituted of the Director General of Health Services, Drug Controller of India, Director of Central Drugs Laboratory, a Principal officer dealing with indigenous system of medicines in the Ministry of Health, a government analyst for ayurvedic and Unani drugs, a pharmacognosist, a phytochemist and in addition, four persons, two from among the members of the Ayurveda Pharmacopoeia Committee and each from the members of the Siddha/Unani Pharmacopoeia Committee, one person, who is a teacher in Dravyaguna and Bhaishajya, Kalpana, one teacher in Pharmacology and pharmacy, and one person each to represent Ayurvedic and Unani systems of medicine.

Labeling provisions (Rule-161) of herbal drugs

Label must have the following: (1) Name of the formulation; (2) true list of ingredients used in the formulation together with the quantity of each ingredient; (3) if the list is long, a separate list has to be enclosed with the packing and references to be made on the label; (4) if ingredients are from Schedule E (I) the word "Caution: To be taken under medical supervision" should be printed both in English and Hindi languages; (4) correct statements of weights and measures; (5) name and address of the manufacturers; (6) manufacturing license number; (7) batch number; (8) date of manufacturing and expiry date; (9) the words, "for external use only," if the medicine is meant for external application; (10) testing for heavy metals limits for export is mandatory with effect from January 1, 2006.

Initiatives taken by the government of India regarding the regulations of herbal drugs

The Department of Indian Systems of Medicine (at present AYUSH) has been a nodal agency for the documentation

and digitalization of indigenous knowledge under the Traditional Knowledge Digital Library programme. Furthermore, in 2003, the Golden Triangle Partnership scheme between AYUSH, Council of Scientific and Industrial Research (CSIR), and Indian Council of Medical Research for the validation of traditional ayurvedic drugs and development of new drugs has emerged to achieve safe, effective, and standardized classical ayurvedic products for the identified diseased conditions and to develop novel ayurvedic and herbal products effective in diseased conditions of national/global importance. Pharmacopoeial laboratories of Indian medicines have been set for laying down standard operating procedures and pharmacopoeial standards. In addition, New Millennium Indian Technology Leadership Initiative has been launched by CSIR to attain a global leadership position in a team India spirit for Indian industry by synergizing the best competencies of publicly funded R & D institutions, academia, and private industry.[14,27]

Regulatory aspects of herbal drugs in other countries

The regulatory situation for botanical preparation varies from country to country. The WHO has tried to establish internationally recognizable regulatory guidelines to define the basic criteria for the evaluation of quality, safety, and efficacy of botanical medicines. The first stage in assuring the quality, safety, and efficacy of botanical medicines is identification and selection of correct plant species.

Conclusion

Plant materials are used throughout the world, in developed as well as developing countries, as home remedies, in OTC drug products, and as raw material for the pharmaceutical industry, and they represent a substantial proportion of the global drug market. Assurance of safety, quality, and efficacy of medicinal plants and herbal products is a key issue, which needs to be addressed. It is clear that the herbal industry can make great strides in India, with the co-operation among drug regulatory authorities, scientists, and industries. However, standardization of methods and quality control data on safety and efficacy are required for proper understanding of the use of herbal medicines. Therefore, it is essential to establish internationally recognized guidelines for assessing their quality. It has now become evident that there is a need for a holistic approach to health care, and the untapped potential of traditional medicines should be utilized. However, this will not be easy as it requires a thorough search for medicinal plants, proper guidelines for their identification, validation of the scientific methods of isolation of active ingredients, preclinical evaluation of their pharmacological and toxicological profiles, and clinical evidence of their usefulness. Clinical trials should be conducted to establish facts such as the average effective dose for any drug, as well as potential side effects a compound may cause. In short, these herbal drugs need to be analyzed in the same way as any modern drug that is with randomized controlled clinical trials. This will improve the quality of the drug and also motivates the practitioners to get more involved in the standardization process.

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Conflicts of interest

There are no conflicts of interest.

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