Available online at www.elixirpublishers.com (Elixir International Journal)

Pharmacy

Elixir Pharmacy 112 (2017) 48954-48957

ISSN: 2229-712X

Regulatory compliance: The key for global expansion of Indian system of medicine

Nagendra S.R., M.P. Venkatesh, Balamuralidhara.V and T.M.Pramod Kumar

Pharmaceutical Regulatory Affairs Group, Dept. of Pharmaceutics, JSS College of Pharmacy, Jagadguru Sri Shivarathreeshwara Nagar, Mysuru-570015

ARTICLE INFO

Article history:

Received: 12 July 2017;

Received in revised form:

1 November 2017;

Accepted: 10 November 2017;

Keywords

GMP,

AYUSH,

Indian Medicine,

Traditional Medicines.

ABSTRACT

Today Medical science gives us quick relief but not the guarantee of health. For health guarantee, we need to approach holistic health care. The Indian traditional medicine has rich scientific heritage of healing humans. The system of medicines which are considered to be Indian in origin; or the systems of medicine which are practised abroad and got assimilated in to Indian culture are known as Indian Systems of Medicine. Nowadays, there is a drastic change in the use of medicine from modern medicine to Traditional system of medicine due to their adverse drug events. It is observed that the regulator is focused more on modern medicine than on AYUSH products. While international standards for good manufacturing practices (GMP) have been prescribed by the WHO for herbal medicines, AYUSH regulations was still short of international standards such as the GMP. Although, over the years the Department of AYUSH has taken several initiatives to streamline regulations regarding labelling, packaging, improving quality of formulations through maintenance of GMP requirements, setting up testing facilities, inspections, etc. We need to travel far ahead to ensure the availability of quality-assured drugs for consumption or trial. However, in the absence of proper standards, guidelines and regulatory mechanism, the industry has failed to gain credibility and make a mark in global markets.

Introduction

Today, Medical science gives us quick relief but not the guarantee of health. For health benefits, we need to approach holistic health care. The Indian traditional medicine has a rich heritage of science healing humans. India is a land of different group of people who have their own religion, beliefs, culture, language and dialects.

Thus, diverse medicinal systems have developed in this region.

A number of medicinal systems introduced here from other regions have enriched in India. Since ancient time, Indian society depends on traditional medicinal systems practiced here. Introduction of allopathic drug during British era and neglecting Indian traditional medicine by British ruler are responsible for significant erosion of Indian traditional medicine.

High scientific progress in allopathic medicine and modern facilities also resists the growth of traditional medicine.

In the last decade, there has been a global upsurge in the use of Herbal medicine in both developed and developing countries. Today, certain forms of Herbal medicine play an increasingly important role in health care and health sector reform globally. Hence, the safety and efficacy, as well as the quality control of Herbal medicine have become important concern for both health authorities and the public.

Herbal Medicines

According to European Union definitions, herbal medicinal products (medicines) are "medicinal products containing as active ingredients exclusively plant material and/or vegetable drug preparations.''

Herbal drug technology involves converting botanical materials into medicines, where standardization and quality control with proper utilization of modern scientific techniques. Herbal medicines are widely used for treatment of human ailments in various systems of medicines like Ayurvedic, Homeopathic, Sidha, Unani and other regional systems of medicines.

Herbal drug products classification vary from country to country, some categories include functional foods, dietary supplements and traditional medicines.

Traditional medicine is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness .

Herbal medicines generates handsome revenue worldwide which has driven counterfeit, poor quality, or adulterated herbal products entry in international markets leading to serious patient safety issues. Safety, effectiveness and quality tests to herbal medicines are limited due to their complex nature, authentication issues and lack of appropriate standardization.

The safety, effectiveness and quality of finished herbal medicine products depend on the quality of their source materials, which can include hundreds of natural constituents, and how elements are processed while manufacturing them.

Tele: 9886506306

E-mail address: venkateshmpv@jssuni.edu.in

Countries have their own set of laws and regulations for herbal medicines and traditional medicines. WHO recommends that each country or area should adopt a regulatory system to manage the appropriate use of herbal medicines. Adopting a regulatory mechanism has always helped in ensuring that herbal medicines have acceptable quality, safety and efficacy.

Requirement for assessment of safety of herbal medicines

Safety

There are three categories of safety that need to be considered,

Category 1: Safety established by use over long time

Category 2: Safe under specific conditions of use (such herbal medicine should preferably be covered by well established documentation)

Category 3: Herbal medicines of uncertain safety.

Discussion

1. Europe

The European Community has developed a comprehensive legislative network to facilitate the free movement of goods, capital, services and persons in the Community.

According to Directives 65/65/EEC and 75/318/EEC, pharmaceutical products require pre-marketing approval before gaining access to the market. Requirements for the documentation of quality, safety, and efficacy, the dossier and expert reports are laid down in Directive 91/507/EEC. Article 39 para 2 of Directive 75/319/EEC obliged Member States to check all products on the market at that time, with a deadline of 12 years, to determine whether they met the requirements of these directives. (1)

Monographs in European Pharmacopoeia provide the quality requirements for herbal substances and preparations. Committee for Herbal Medicinal Products (HMPC) has also addressed general quality matters in several guidance documents concerning to non-clinical, quality, clinical efficacy and safety issues. The HMPC is responsible for identifying the priority herbal substances/preparations/combinations to be covered by a monograph or a list entry. Herbal substances proposed for assessment can be found in an inventory and herbal substances under assessment can be found in apriority list.

Most individual herbal medicinal products are licensed nationally by member states, the process for licensing and information on herbal substances and, preparations is harmonised across the European Union.

Community herbal monographs prepared by the Committee on Herbal Medicinal Products (HMPC) at the Agency are relevant for the traditional use, registration as well as the well established use.

A Community herbal monograph comprises the scientific opinion of the HMPC on safety and efficacy data concerning a herbal substance and its preparations intended for medicinal use.

The HMPC evaluates scientifically all available information including non-clinical and clinical data but also documented long-standing use and experience in the Community. Community monographs are divided into two columns: well-established use (marketing authorisation) and traditional use (simplified registration). Well-established use section describes the safety and efficacy data while traditional use section is accepted on the basis of sufficient safety data and plausible efficacy. A final Community monograph can be used in application reference material by a marketing authorisation applicant (well-established use part) and by a traditional use registration applicant (traditional use part).

In contrast to the Community herbal monographs, the Community list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products is legally binding to applicants and competent authorities in the Member States in so far as:

- An applicant will not be required to provide evidence of the safe and traditional use of a medicinal product for which he seeks a traditional use registration if he demonstrates that the proposed product and related claims in the application comply with the information contained in the Community list.
- Competent authorities will not have the opportunity to require additional data to assess the safety and the traditional use of the product.

A list entry document contains

- The scientific and botanical name, and the common name in all EU languages;
- Used for (the indication);
- The specified strength and the posology;
- The route of administration and;
- any other information necessary for the safe use of the herbal substance or preparation used as an ingredient of a traditional herbal medicinal product, including warnings, precautions and contraindications.

Table 1: Summary of requirements – Marketing Authorization or Registration as Traditional herbal medicinal products directive (2)

Modules	Type of Data	MA	Traditional Use
Module 1	Administrative Information	✓	✓
Module 2	Expert Summaries	✓	✓
Module 3	Quality Data	✓	✓
Module 4	Safety Data	Results of Tests	Bibliographic review of safety
Module 5	Efficacy Data	Results of Trials	Evidence of traditional use

Traditional herbal medicinal products Directive (THMPD)

The European Directive on Traditional Herbal Medicinal Products, formally the Directive 2004/24/EC amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use, was established by the European Parliament and Council on 31 March 2004 to provide a simplified regulatory approval process for traditional herbal medicines in the European Union (EU).

Under this regulation, all herbal medicinal products are required to obtain an authorisation to market within the EU. Those products marketed before this legislation came into force can continue to market their product until 30 April 2011, under the transitional measures defined in the Traditional Herbal Medicinal Products Directive. Once this time limit has expired, all herbal medicinal products must have prior authorisation before they can be marketed in the EU.

Directive 2001/83/EC requires that applications for authorisation to place a medicinal product on the market have to be accompanied by a dossier containing particulars and documents relating in particular to the results of physico-chemical, biological or microbiological tests as well as pharmacological and toxicological tests and clinical trials carried out on the product and thus proving its quality, safety and efficacy.(3)

The Objective of this directive is

- Protection of consumer health, providing access to medicines of their choice provided safeguards are met.

- To facilitate a single market in the EU for herbal via harmonized rules.

2. India

Herbal preparations are defined as natural products in which the predominant active constituents are of plant origin. In India, traditional medicines are governed by the Drugs and Cosmetics Act of 1940 and the Drugs and Cosmetics Rules of 1945. They regulate the import, manufacture, distribution and sale of drugs and cosmetics. In 1959, the Government of India recognized the traditional Indian systems of medicine and amended the Drugs and Cosmetics Act to include drugs which are derived from traditional Indian medicine.

No products derived from traditional systems may be manufactured without a licence from the State Drug Control Authorities. Patent and proprietary medicines derived from the traditional systems must contain ingredients which are mentioned in the recognized books of the above systems, as specified in the Drugs and Cosmetics Act.

The government is advised by a special committee and an advisory board for Ayurvedic, Siddha and Unani drugs. Pharmacopoeia committees have been constituted to prepare pharmacopoeias for all these systems.

In 1993, an expert committee appointed by the Indian government developed guidelines for the safety and efficacy of herbal medicines which were intended to be incorporated into the Drugs and Cosmetics Act and rules. It was proposed that no new herbal medicines other than those authorized by the licensing authorities be allowed to be manufactured or marketed, except for those mentioned in and manufactured in compliance with the formulae given in the "authoritative" books for Ayurveda, Siddha and Unani herbal medicines. A manufacturer of a new herbal medicine must include safety data and appropriate efficacy data in the marketing authorization application. (4)

Ayush

The Ministry of AYUSH was formed on 9th November 2014 to ensure the optimal development and propagation of AYUSH systems of health care. Earlier it was known as the Department of Indian System of Medicine and Homeopathy (ISM&H) which was created in March 1995 and renamed as Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) in November 2003,with focused attention for development of Education and Research in Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy.(5)

The objectives of AYUSH were

- To upgrade the educational standards of Indian System of Medicines and Homoeopathy colleges in the country.
- To strengthen existing research institutions and to ensure a time-bound research programme on identified diseases for which these systems have an effective treatment.
- To draw up schemes for promotion, cultivation and regeneration of medicinal plants used in these systems.
- To evolve Pharmacopoeial standards for Indian System of Medicine and Homoeopathy drugs.(6)

This new independent regulatory body started functioning to regulate and standardize AYUSH products and related degree courses on the lines of the Central Drug Controller for modern scientific medicines and also want the Centre to curb production and sale of fake AYUSH products, including those claiming to help reduce fat and increase sexual power.

There are promising formulations available, but they need to be subjected to the same rigorous manufacturing norms for use in clinical trials to provide evidence for global acceptance and at the same time protect the research participants as is insisted upon for clinical trials using new drugs. More attention is paid to recast the regulatory provisions according to the need of the hour and implement the existing guidelines or regulations related to traditional formulations or natural products, it would add to the Government's endeavour to improve public health.

The AYUSH industry regulations gets neglected, since many States not even having qualified manpower for regulating and hence, on the ground the consumer does not get access to quality products as intended under the regulation. The manufacturer should have an in-house drug testing laboratory which should be approved by the AYUSH Ministry and have the National Accreditation Board for Testing and Calibration Laboratories (NABL) accreditation.

Many of the significant Indian plants do not find place in the list of importable herbs in many countries. For example TGA (Therapeutic Goods Administration) of Australia does not recognize any of the Indian pharmacopoeias while it recognizes Pharmacopoeia of the PRC (People's Republic of china) of China.

US FDA (Food and Drug Administration) or MHRA (Medicines and Healthcare products Regulatory Agency) of UK, MCC (Medicines Control Council) of South Africa, TGA of Australia etc., have their own list of positive drugs which are safe and effective for permitting imports. We do not have such an official list that clearly states the important Indian medicinal plants that are safe and effective with reliable documentation.

Department of AYUSH concentrates on the overall governance, education, regulation, development and growth of Indian System of Medicine in the India.The department has few subordinate offices, several autonomous bodies in the form of research councils, professional council, pharmacopoeia laboratories, national institutes, academy and hospitals. In the year 2002, National Policy on Indian Systems of Medicine & Homoeopathy was introduced.

The objectives of National Policy on Indian Systems of Medicine & Homoeopathy are,

- Utilize the AYUSH to endorse good health and spread out the outreach of healthcare to our people (mainly who cannot afford or reach to the modern healthcare facilities) through preventive, promotive, mitigative and curative approaches.
- To provide affordable AYUSH services & drugs which are safe and efficacy
- To ensure the availability and genuine of raw drugs as required by pharmacopoeial standards to help improve quality of AYUSH drugs, for domestic and/or export purpose.
- Incorporate AYUSH in healthcare delivery system and national programmes and to ensure the best possible utilization of huge infrastructure of hospitals, dispensaries and physicians.
- To offer full opportunity for the expansion and development of Indian System of Medicine and utilization of the potentiality, strength and revival of their glory.

Although, over the years the Department of AYUSH has taken several initiatives to streamline regulations regarding labelling, packaging, improving quality of formulations through maintenance of GMP requirements, setting up testing facilities, inspections, etc. We need to travel a long way to ensure the availability of quality-assured drugs for consumption or conducting trial. Therefore, it is essential to establish internationally recognized guidelines for assessing their quality. Stringent quality control should be enforced.

Quality control of traditional medicines is a critical and essential issue to be considered in assuring the therapeutic efficacy, safety and to rationalize their use in the health care. Quality assurance is an integral part of traditional medicine, which ensures that it delivers the required quantity of quality medicament.

Global requirements

- Good Agricultural and Collection Practices(GACP)
- Good Manufacturing Practices(GMP)
- Quality
- Safety
- Pharmacovigilance

Good Agricultural and Collection Practices (GACP)

In order to ensure appropriate and consistent quality of medicinal plant/herbal substances it is necessary to establish good agricultural and collection practice for herbal starting materials(GACP). The concept of Good Manufacturing Practice for the manufacture, processing, packaging and storage of Active Pharmaceutical Ingredients (APIs) also applies to medicinal plants/herbal substances. (7)

The objectives of GACP are:

- Contribute to the quality assurance of medicinal plant materials used as the source for herbal medicines, which aims to improve the quality, safety and efficacy of finished herbal products;
- Guide the formulation of national and/or regional GACP guidelines and GACP monographs for medicinal plants and related standard operating procedures; and
- Encourage and support the sustainable cultivation and collection of medicinal plants of good quality in ways that respect and support the conservation of medicinal plants and the environment in general.(8)

Good Manufacturing Practices (GMP)

Good manufacturing practice is that part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization. GMP are aimed primarily at diminishing the risks inherent in any pharmaceutical production. Such risks are two types: Cross contamination (in particular of unexpected contaminants) and mix-ups (confusion) caused by, for example, false labels being put on containers.(9)

Pharmacovigilance

The nationwide programme, sponsored and coordinated by the National Pharmacovigilance Resource Centre (NPRC) for Ayurveda, Siddha and Unani drugs to establish and manage a data of Adverse Drug Reactions (ADR) for making uniformed regulatory decisions regarding marketing authorization of drugs in India for ensuring safety of drugs.

There is a need to frame separate standards and guidelines for AYUSH products, which are very different from the allopathic ones. Also, it is important that regulatory officials are trained specifically in these streams and have knowledge about these. However, in the absence of proper standards, guidelines and regulatory mechanism, the industry has failed to gain credibility and make a mark in global markets, even as other nations like China have excelled and there is a brighter future for these systems.

Conclusion

Although, over the years the Department of AYUSH has taken several initiatives to streamline regulations regarding labelling, packaging, improving quality of formulations through maintenance of GMP requirements, setting up testing facilities, inspections, etc. Still, there is a lacuna exist with the quality testing of herbal formulations. Therefore, it is essential to establish internationally recognized guidelines for assessing their quality. To be accepted internationally, stringent quality control should be enforced to gain credibility and make a mark in global markets.

References

1.27.1.pdf [Internet]. [cited 2017 Jun 14]. Available from: http://www.florajournal.com/archives/2013/vol1issue4/PartA/27.1.pdf

2.Dr Deepika Gunawant.pdf [Internet]. [cited 2017 Jun 14]. Available from: http://cii.in/WebCMS/Upload/Dr%20Deepika%20Gunawant.pdf

3.PDF.pdf [Internet]. [cited 2017 Jul 7]. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32004L0024&from=EN

4.whozip57e.pdf [Internet]. [cited 2017 Jun 14]. Available from: http://apps.who.int/medicinedocs/pdf/whozip57e/whozip57e.pdf

5.About the Ministry | Ministry of AYUSH | GOI [Internet]. [cited 2017 Jun 14]. Available from: http://ayush.gov.in/about-us/about-the-ministry

6.Background | Ministry of AYUSH | GOI [Internet]. [cited 2017 Jul 10]. Available from: http://ayush.gov.in/about-us/background

7.WC500003362.pdf [Internet]. [cited 2017 Jul 7]. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003362.pdf

8. 9241546271.pdf [Internet]. [cited 2017 Jun 21]. Available from: http://apps.who.int/iris/bitstream/10665/42783/1/9241546271.pdf

9.s14215e.pdf [Internet]. [cited 2017 Jul 7]. Available from: http://apps.who.int/medicinedocs/documents/s14215e/s14215e.pdf