



Comparative study of regulatory requirements for herbal products in India and Europe

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Abstract

Nowadays, Herbal products are rapidly spreading throughout the world. These herbal products are used for various diseases in humans. The herbal medicines are available in various systems like Homoeopathic, Ayurvedic, Siddha, and Unani. Herbal medicines are derived from plant sources or plant parts. Herbal products are used to improve health, cure diseases, and increase immunity without having any side effects. Some herbal medicines are included in dietary supplements and in traditional medicine. It contains detailed information about the regulatory requirements and approval process of herbals in India and Europe. In India, the department of AYUSH under the Drugs and Cosmetics Act provides guidelines on quality, safety, and efficacy of herbal products. In India and Europe, the herbal guidelines were introduced to regulate the quality, nonclinical studies and clinical safety studies. India published a herbal pharmacopoeia to maintain quality herbal medicine. This comparison study helps to find the differences in regulatory requirements and approval process of herbal medicines in between different countries.

Keywords: herbal products, ayurvedic, siddha, unani, homeopathy, regulatory requirements

Introduction

Now-a-days the herbal medicines are used in world wide. The herbals medicines are derived from plants and its parts like leaves, roots, stem, flowers, and seeds also known as botanical medicine or phytomedicines. Herbal remedies have been utilized in India since the Vedic period, according to the Rigveda. In the Charak Samhita, it is stated. Herbs were first utilized by individuals in traditional ways based on their knowledge, and then a group of specialists known as apothecaries emerged. Herbal remedies have been utilized in various nations for a long time, such as China. Herbal remedies are utilized in India's Ayurveda, Siddha, Unani, and Homoeopathic medical systems. Ayurvedic medicine has been practiced since 6000 B.C., Chinese herbal medicine since 5000 B.C., and Western medicine has been practiced since 1800 A.D ^[1]. The preparation and use of Herbals is based medical treatment since hundreds of years and are still widely used in the 21st century. Herbal medicines are divided into three categories by the WHO: raw plant materials, processed plant materials, and therapeutic herbal products. Herbal medicine has been used in India, China, Egypt, Greece, Rome, and Syria for about 5000 years, according to their literature. Due to its well-established and generally accepted use, herbal medicines are utilized by practitioners of traditional systems of medicine all over the world. Herbal remedies are becoming increasingly popular as a result of the widely acknowledged and accumulated expertise of many practitioners and patients over a long period of time. In addition, herbal medication is typically and currently recognized as safe. Under Indian circumstances, we have about 45,000 plant species, of which 15,000-20,000 have been shown to have therapeutic potential. In their compositions, traditional

systems utilize around 7,000-7,500 species. In modern medicine, Ayurveda utilizes 2000, Unani 1000, Siddha 1300, Tibetan 500, and 200 variations. Herbal medicines have grown in popularity in recent decades, not just in emerging and poor nations, but also in wealthy countries. A large number of pharmaceutical companies have begun to reorient their business strategies by investing money in the field of research and to manufacture of herbals. Some government agencies also focus more on research on herbal medicines ^[2]. In present situation the usage of herbals products has increased rapidly and they play important role in increasing the immunity to fight against the various viral and bacterial diseases.

Herbal medications can be used to treat a wide range of ailments, including acute and chronic illnesses. Herbal treatments are commonly regarded as complementary or alternative medicine since they are not strictly based on scientific evidence. Herbal medicine is mostly used as a supplement to other treatments. However, the herbal medicine can show some side effects when interact with other medicines.

For example, Echinacea purpurea may show some side effects when administered along with other medication (including some antibiotics) might increase or decrease the mechanism of action and side effects. For these each country they developed their own regulations and guidelines by these they can increase safety and effective usage of herbal medicines by eliminating side effects.

Herbal Materials

Crude products of herbals are derived from whole plants or parts of medicinal plants. They may be resins, fixed oils, gums, herbs, and dry powders of herbs.

Herbal Preparations

Herbal preparations serve as the foundation to complete the herbal products preparation and can comprise comminuted or powdered herbal materials as well as extracts, tinctures, and fatty oils, expressed juices, and processed exudates of herbal materials. Extraction, distillation, expression, fractionation, purification, concentration, fermentation, and other physical or biological processes are used to create them^[3]. Herbal Preparations can be prepared by various methods like Maceration, Decoction, extraction procedures by using alcohols (methanol or ethanol) as solvents or in other materials, are also included.

Homoeopathy

Dr. Christian Friedrich Samuel Hahnemann, founder of homeopathy, was a great pharmacist, linguist, and a respected German physician. Homeopathy is one of the most popular medical systems and is sought after by suffering patients. It plays an important role in the integrated public health system of India due to its wide acceptance among the population. This acceptance is due in large part to its simplicity, affordability, security, and holistic approach^[4].

The Central Council for Homeopathy Research is an autonomous organization of the Ministry of Ayurveda, Yoga, Unani, Siddha and Homeopathy of India (AYUSH). Homeopathy is currently used in more than 80 countries. It is legally recognized as an individual medical system in 42 countries and recognized as part of complementary and alternative medicine in 28 countries^[5]. The WHO considers homeopathy as one of the most used forms of Traditional and Complementary Medicine (T&CM).

Siddha

One of the oldest traditional medicinal systems in India is Siddha which treats not only the body but also mind and soul. The name "Siddhi" means "achievement, or an object to be attained" and the "Siddhars" were holy figures who used yoga to attain success in medicine^[6]. After its most renowned exponent, the sage Agasthya, the Siddha system is also known as the Agasthar system. In India, the siddha system is mostly used for medicinal purposes.

Unani

The Unani scientific device gives the remedy of sicknesses that have an effect on all of the structures and organs of the human body. The basic, diagnostic and remedy modalities of the device are primarily based totally on medical standards and holistic ideas of fitness and healing. In diagnosing and treating sicknesses, first rate significance is connected to the temperament (mizaj) of a patient^[7]. It takes under consideration the character when it comes to her surroundings and emphasizes the fitness of the body, thoughts and soul. Therapies for continual situations and sicknesses of the skin, liver, musculoskeletal device, and reproductive organs, in addition to immune and way of life problems have demonstrated to be surprisingly powerful and acceptable.

Ayurveda System

The term ayurveda is derived from AYU and VEDA. AYU means life VEDA means science or knowledge and it defines the science of life. Charaka defines ayurveda is a science that are dealing with advantages and disadvantages,

as well as happy and unhappy states of life, as well as good and bad for life, its measure and life itself". It is divided into three main branches, namely Nara Ayurveda; which deals with human life, Satva Ayurveda; the science that deals with animal life and its diseases, Vriksha Ayurveda; the science that deals with plant life, Your growth and diseases takes care of your diseases^[8]. It is perfectly clear that Ayurveda is not only a medical system, but also a way of life to achieve completely positive health and spiritual achievement.

Registration Requirements of Herbals in India

In India the herbals are regulated by Department of AYUSH, IMCC (Central Council of Indian Medicine) Act, Research Councils (ICMR and CSIR), & and & Drugs and Cosmetics Act 1940 and rules in 1945. The AYUSH Department regulates the Ayurveda, Yoga & Naturopathy, Unani and siddha. In 2009, the AYUSH department established a certification programme for AYUSH medicinal items in conjunction with QCI. Concerns improve the role of AYUSH products in terms of safety, effectiveness, and quality^[9]. A new optional certification method for AYUSH products has been launched by collaborating with QCI in order to meet standard requirements. There are two levels of AYUSH Certification. AYUSH Standard Mark, which is based on domestic regulatory compliance; and AYUSH Premium Mark, which is based on one or both of the following options: Option A: Conformity to GMP Requirements based on WHO Guidelines and Contaminant Levels as specified in the Certification Criteria document. Option B: Adherence to any importing country's regulatory standards, as long as they are more rigorous than Option A.

Schedule T was introduced by the AYUSH Department to specify the requirements of factory premises and hygienic conditions. The main objective for introducing Schedule-T is to maintain a standard for herbals and to maintain Good Manufacturing Practices for the manufacturers. GMP regulations are mandatory for all the manufacturers of ASU drugs. The Indian government issued 'Schedule T' on June 23, 2000, under Rule 157 of the Drugs and Cosmetic Rules, and later revised Good Manufacturing Practices (GMP) on March 7, 2003. From June 23, 2000, all ayurveda, siddha, and unani medicine manufacturing plants were required to follow the guidelines^[10]. Schedule TA is a form used to keep track of how much raw material ayurveda, siddha, or unani licensed manufacturing units used throughout the fiscal year.

GMP for Ayurvedic, Siddha and Unani medicines are described in 2 parts

Part I-Good manufacturing practices

1. Factory premises

- a. Receiving and storing raw material
- b. Manufacturing process areas
- c. Quality control section
- d. Finished goods store
- e. Rejected goods/ drugs store^[10]

2. General requirement

- a. Location and surroundings
- b. Buildings
- c. Water supply
- d. Disposal of waste
- e. Containers

- f. Stores
- g. Raw Materials
- h. Health, Clothing, Sanitation and Hygiene of Workers

Part II

- A. A List of machinery, equipment and minimum manufacturing premises necessary for the manufacture of different Categories of Ayurvedic, and Siddha system medications ^[11].
- B. A List of machinery, equipment and minimum manufacturing facilities necessary for the manufacture of various categories of unani medicines.
- C. In-house quality control Section equipment.

Registration Process for Herbals in India

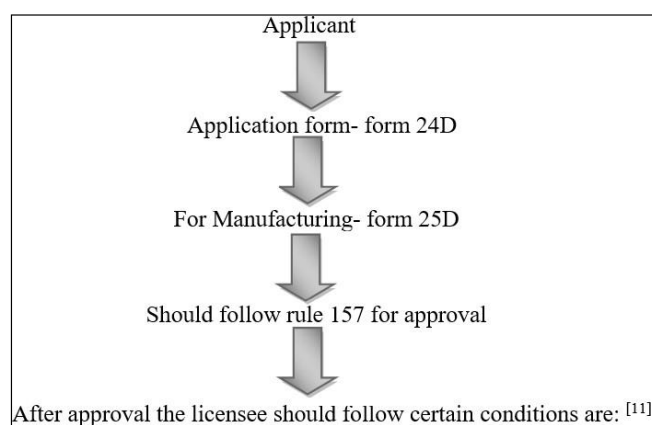


Fig 1

- Licensee should maintain proper records
- Licensee should allow inspector to inspect the premises
- Inspection book-Form 35
- Fees:Rs.1000/-
- Renewal: 1200+600= 1800/-
- Duplicate copy: 150/-

Marketing Authorization

To manufacture the herbal products in India the manufacturer should require a product license for that product before introducing them into market ^[13]. The product approval is granted in Form 25D with the same validity as the manufacturing license.

Registration requirements of Herbals in Europe

Under the European Medicines Agency, the Committee on Herbal Medicinal Products (HMPC) offers scientific reviews on herbal medicines and preparations, as well as

information on suggested uses and safe conditions. This provides a clear reference point for enterprises and national competent authorities when drafting or evaluating an application for marketing authorization or registration of herbal medical products in EU Member States.

The main functions HMPC

- The HMPC provides the EU monographs that containing therapeutic uses and safe conditions of well-established and traditional use for herbal substances and preparations.
- Providing a list of Herbal products, preparations and their combinations for use in traditional herbal medicinal products ^[14].

The Medicines and Healthcare Products Regulatory Agency in the European Union recently established the Traditional Herbal Medicines Registration Scheme (THMRS). They introduced Directive 2004/24/EC, which was amended by Directive 2001/83/EC, to make the registration process for traditional herbal medicinal items easier. The major goal of these guidelines is to safeguard public health while also increasing the commercialization of herbal medicines ^[15]. A traditional herbal medicinal product includes herbal substances, herbal preparations or a combination as a active agent. The herbal substances must have been in continuous medical use for at least 30 years before to the date of application, including atleast 15years in the European Union.

There are three regulatory pathways to market the herbal products in EU member states

- Traditional use registration (Directive 2001/83/EC in article 16a) ^[14].
- Well-established use marketing authorization (Directive 2001/83/EC in article 10a).
- Stand- alone or mixed application (Directive 2001/83/EC in Article 8(3)).

Marketing Authorization

The herbal products must have marketing authorisation approval before introducing it into the market ^[16]. Based on application there are 4 pathways for applying a marketing authorisation within EU. They are:

1. Centralised procedure
2. Decentralized procedure
3. Mutual recognition procedure(MRP)
4. National procedure

Regulatory Requirements Fo Herbal Products in India and Europe

Table 1

Content	Europe	India
Definition	Any medical product containing exclusively one or more herbal substances or one or more herbal preparations as active ingredients, or one or more such herbal substances in conjunction with one or more such herbal preparations, is referred to as a traditional herbal medicinal product." ^[11]	All medications intended for internal or exterior use for or in the diagnosis, treatment, mitigation, or prevention of sickness or disorder in humans or animals exclusively in accordance with the formulas given in authorized publications are considered ASU pharmaceuticals."
Application forms	24E For manufacturing- form 25E Certificate of renewal-form 26E	Application form-24D For manufacturing-form 25D Certificate of renewal-Form 26D
Regulation	European Union Directive 2004/24/EC Directive 2001/83/ EC	Drugs and Cosmetics Act, 1940 Drugs and Cosmetics Rules, 1945
Country of filling	EU	INDIA
Regulating agency	European Medicines Agency	Ministry of AYUSH and CDSCO

Regulating ministry	Science medicines of health	Ministry of Health and Family Welfare
Pharmacopoeia	European Pharmacopoeia	Ayurvedic Pharmacopoeia of India
Market	Regulated market	Emerging market
Submission format	Country specific	ICH e-CTD format
Mode of submission	Electronic submission	Paper submission
Manufacturing	EudralexvoL-4 (annexure7) GMP	Good Manufacturing Practices followed schedule T Require license for Manufacturing
Application requirement	<ul style="list-style-type: none"> ▪ The application for traditional medicinal are: <ol style="list-style-type: none"> a. Name and permanent address of the manufacturer b. Name of the medicinal product c. Qualitative and quantitative particulars of all the Constituents of the medicinal product d. Evaluation of the potential environmental risks posed by the medicinal product e. Description of the manufacturing method f. Therapeutic indications, contraindications and adverse reactions g. Posology, pharmaceutical form, method, and route of administration and expected shelf life. h. Reasons for any precautionary and safety measures to be taken for the storage of the medicinal product. i. Description of the control methods employed by the manufacturer. j. Summary of product characteristics k. A document showing that the manufacturer is authorized in his own country to produce medicinal products 	<ul style="list-style-type: none"> Drug information <ol style="list-style-type: none"> a. Name of the product b. Formula shall contain Shastric/ Tibbi name, part c. used and quantity d. Detailed method of preparation e. Purification of drugs wherever required f. Indications g. Dosage schedule in detail h. Side effects i. Anti-doses j. Diet restrictions, if any” ▪ Plan and layout of the premises showing the installation of machinery and equipment. ▪ Attested copies of documents relating to the ownership/ rent/ lease^[1] <ul style="list-style-type: none"> ▪ Appointment letter to full-time technical supervisor ▪ Declaration of the partnership deed/memorandum. ▪ Detailed list of manufacturing and analytical equipment as required for formulations applied. ▪ Attested copies of certificates of academic qualification, experience certificate from Ayurveda/Unani, and declarations of technical. ▪ Staff in the prescribed pro forma with photo duly attested <ul style="list-style-type: none"> ▪ Draft labels of the product ▪ Self-addressed envelope with sufficient postal ▪ Stamps for registered post
Schedule t required		<ul style="list-style-type: none"> ▪ General requirements <ul style="list-style-type: none"> ▪ Location and surrounding <ul style="list-style-type: none"> ▪ Buildings ▪ Water supply ▪ Stores ▪ Raw materials ▪ Packaging materials ▪ Health, clothing, sanitation, and hygiene of workers <ul style="list-style-type: none"> ▪ Machineries and equipment ▪ Distribution records ▪ Record of market complaints
Approval timeline	210 days	3 months
Period of marketing	7 years	1-5 years

Conclusion

The Herbal products played a significant role in human life which are derived from natural source. The current review provides sufficient knowledge on registration requirements for herbal in respective countries, particularly India and Europe. In India the herbal medicines are regulated by Department of AYUSH, under Drugs and Cosmetics Act to evaluate the safety and effectiveness for identifiable diseases and to develop new drugs in pharmaceutical company. In Europe the herbal medicines are regulated by committee for Herbal Medicinal products (HPMC) under European Medicines Agency and recently it was amended by Traditional Herbal Medicines Registration Scheme through herbal directives to provide guidelines for quality, safety clinical and non-clinical studies.

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