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Regulations on Herbal Products in India, United States and European Union: A Review

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Abstract

Herbal products are now being mainstay of about 80% of the world population for primary health care. The belief that herbs are safe is not completely true, as many cases of untoward effects are observed following their imprudent use. Therefore, we need to have regulative measures on herbal products that would keep check on each step of entire process of drug development. Ensuring efficacy and safety of these products is going to increase the global acceptance and would be serving a greater number of populations worldwide in an inculpable manner. Working in this direction almost every country has developed their plan of work for regulation of herbal products that are referred as traditional medicines, alternative medicines, complimentary medicines, natural health product, health supplements etc. Electronic review method was used to compile information for this review on the regulation of herbal product around the world in this study. The data were collected from different databases such as Google scholar, ResearchGate, PubMed, pharma tutor, and etc.

Keywords: Herbal medicine; nutraceutical; herbal cosmetic; phytopharmaceuticals, complementary/alternative medicines (CAM), AYUSH, Complimentary Alternative Medicines (CAM)

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1. Introduction

Allopathic medicines are very well developed and are being widely used all over the world. Although allopathic medicines are effective and have rapid onset of action, but still world wants something safe to consume which not only cure diseases but also prevent diseases. In past few decades world health industry has started to focus on alternative medicines which mainly include herbal plant products like herbal supplement, herbal nutraceutical, herbal cosmetics and some phytopharmaceuticals.

Herbal medicines are defined by the World Health Organization (WHO) as "the aerial or underground plant parts or other plant material that contain an active ingredient as finished labelled medicinal product". (1) It has been reported that around 80% of population use traditional or herbal medicine for their primary health care treatment.

The term nutraceutical was coined from "nutrition" and "pharmaceutical" By Stephen Defelice MD, founder and chairman of the foundation for Innovation in medicine (FIM) Cranford, New Jersy, in 1989. (2) Nutraceuticals are food or part of food that provides medical or health benefits including the prevention and/or treatment of a disease. Herbal nutraceutical products are powerful aid for maintaining general health and to treat nutritionally acute or chronic disease. (3)

Herbal cosmetic is a natural cosmetic which is formulated, using different cosmetic ingredients, to form the base in which one or more herbs or their extracts are added to enhance the effect.

Phytopharmaceutical drug is defined as purified and standardized fraction with defined minimum four bio-active or phytochemical compounds (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation, or prevention of any disease or disorder but does not include administration by parenteral route.

Many of us believe that herbal products have no side effects but this is not true always. In Indian market herbal products does not have to go through pre-clinical or clinical testing and they don't have to produce any data of bioavailability, toxicity, safety of product. As a result, Indian Herbal product fails to compete in global market. Earlier there was no regulation for controlling

the quality and efficacy of herbal product, but now government have formed Regulatory body to control manufacturing, sale, export, important of herbal products in India with an aim to protect public health by controlling the safety and efficacy of products.

Electronic review method was used in this study. The data were collected from different databases such as Google scholar, ResearchGate, PubMed, Pharma tutor, Academia and Researcher.

Herbal Medicines

Use of herbal medicines has been reported worldwide since early ages. During the past few decades, human interest in naturopathy has increased significantly in the industrialized countries, which expand the use of medicinal plants and herbal medicines. An innovative research effort to define the advantages of Traditional systems of medicine with respect to their safety and efficacy could result in a better utilization of these complementary systems of medicine.

Internationally, herbal products are regulated under different classifications, some of which are:

- Complimentary medicines
- Natural health products
- Prescription medicines
- Over the counter medicines
- Health Supplements
- Traditional herbal medicines, etc.

2. Regulations of Herbal medicine

India

Herbal drug products constitute a major share of all the officially recognized systems of health in India. IMCC (Central Council of Indian Medicine) Act, Research Councils (ICMR and CSIR), Department of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy) & Drugs and Cosmetics Act 1940 (Amendment) regulates herbal medicines in India. (4) Herbal remedies and medicinal plants to be incorporated in modern system (Allopathic) must follow Drug Controller General of India (DCGI's) regulations.

Standards of medicines are prescribed in the Drugs and Cosmetic Act 1940 and individual monographs has been prescribed in the respective Pharmacopoeias. A positive step has been taken in this direction by publishing of the Herbal Pharmacopoeias, having standards of 52 drugs. First schedule of the D and C Act has listed authorized texts, which have to be followed for licensing any herbal product under the two categories, ASU drugs and Patent or proprietary medicines. Unfortunately, neither the herbal products nor the herbal Pharmacopoeias have any statutory standing in our country as a result there are a large number of herbal products in the market though it is difficult to categorize these products as per the Drugs and Cosmetics Acts & Rules.

United States

In United States, the term complementary/alternative medicines (CAM) are most commonly used for traditional medicine systems. "Complementary medicine" refers to use of CAM together with conventional medicine. In addition to usual care to help lessen pain FDA in its draft guidance "Guidance for industry on complementary and alternative medicine products and regulation by the food and their regulation by the food and drug administration" clarified different categories of Complimentary Alternative Medicines (CAM) products into cosmetic; device; dietary supplement; drug, as well as "new drug" and "new animal drug;" food; and food additive. These statutory definitions cover some CAM products. It was also clarified neither the FDA Act nor the Public Health Service Act exempts CAM products from regulation. The draft guideline was later withdrawn after recommendations of several agencies including The American Herbal Products Association (AHPA). (5)

European Union

Herbal medicinal products fall within the scope of the European Directive 2001/83/EC that foresees marketing of each medicinal product and requires an adhoc authorisation to be granted on the basis of results of tests and experimentations concerning quality, safety and efficacy. The main features of Directive 2001/EC are traditional herbal medicine definition, simplified registration procedure, provisions for community herbal monographs and community list of herbal substances and preparations and establishment of the Committee for Herbal Medicinal Products (HMPC). European Directive 2004/24/EC on traditional herbal medicinal products has brought forward specifically in recognition of the position that for many herbal medicines it was difficult for companies to meet the full requirements for a marketing authorisation, particularly in relation to efficacy, as are required under Directive 2001/83/EC. The Directive 2004/24/EC has established a HMPC which is part of the EMA, the European Agency responsible for the evaluation of medicinal products and to carry out tasks concerning the simplified registration and authorization of herbal medicinal products. CHMP establish Community herbal monographs and list herbal substances and preparations. (6)

The evidence of traditional use is accepted as evidence of efficacy of the product. However, authorities may still ask for evidence to support safety. Quality control requirement require physicochemical and microbiological test to be included in the product specifications. The bibliographic evidence should support that the product has been in medicinal use for at least 30 years out including at least 15 years within the European community. The application for traditional use registration shall be referred to the committee for Herbal Medicinal Products, if the product has been in the community for less than 15 years, but otherwise qualifies for the simplified registration procedure under the directive.

3. Herbal Nutraceutical

Nutraceuticals are food or part of food that provides medical or health benefits including the prevention and/or treatment of a disease. Nutraceutical has advantage over the medicine because they avoid side

effect, have naturally dietary supplement, etc. Nutraceutical; on the basis of their natural source, chemical grouping, categories into three key terms - nutrients, herbals, dietary supplements, dietary fibre, etc.

Nutraceuticals or functional foods can be classified on the basis of their natural sources, pharmacological conditions, or as per chemical constitution of the products.

- On the basis of natural source, it can be classified as the products obtained from plants, animals, minerals, or microbial sources.
- Nutraceuticals as per the chemical groupings.
- Substances with established nutritional functions, such as vitamins, minerals, amino acids, and fatty acids–Nutrients.
- Herbs or botanical products as concentrates or extracts–Herbals.
- Reagents derived from other sources (e.g., pyruvate, chondroitin sulphate, steroid hormone precursors) serving specific functions, such as sports nutrition, weight-loss supplements, fortified conventional foods, and meal replacements–Dietary supplements.

Most of the nutraceuticals do possess several therapeutic benefits in various disorders. Nutraceuticals have been claimed to have a physiological benefit or offer protection against the different diseases like, cardiovascular agents, antidiabetics, anticancer agents, anti-obese agents, chronic inflammatory, immune boosters, disorders, degenerative diseases. Several examples of nutraceuticals are there that exhibit the therapeutic values like, buckwheat seed proteins have valuable role in obesity and constipation performing similar to natural fibres present in food. 5-hydroxytryptophan and green tea extract may encourage weight loss. Omega-3 fatty acids have been suggested to decrease glucose tolerance in patients inclined to diabetes. Flavonoids found in citrus fruit appear to protect against cancer by acting as antioxidants. Curcumin from curry and soya isoflavones have cancer chemo preventive properties. Phytosterols in diet have the capability to decrease the morbidity and mortality from cardiovascular disorders. (7)

Regulations of nutraceutical products:

India

A food stuff (as a fortified food or a dietary supplement) that provides health benefits, if indeed a claim was made that implied medicinal benefit regarding a nutraceutical product, the product would be required to comply with the regulatory requirements for medicinal products, in respect of safety, efficacy, and quality testing and marketing authorization procedures. For decades, FDA regulated dietary supplements as foods to ensure that they were safe and wholesome and that their labelling was truthful and not misleading. In 2006, the Indian government passed Food Safety and Standard Act of India (FSSAI) to integrate and streamline the many regulations covering nutraceuticals, foods, and dietary supplements.

- These regulations may be called the Food Safety and Standards (Health Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016.
- They shall come into force on the date of their publication in the Official Gazette and Food Business Operator shall comply with all the provisions of these regulations by 1st January, 2018.

United States

Dietary Supplement Health Education Act (DSHEA) 1994 was introduced in the senate by the senator Orrin. G. Hatch, this law gives the definition of the dietary supplement and the legal requirements necessary for the marketing of dietary supplement product in US. The law defines as dietary supplement as follows; a dietary supplement is a product that contains one or more of the following dietary ingredients like vitamin, mineral, herb or other botanical, amino acid, a dietary substance for use by humans to supplement the diet by increasing the total dietary intake of that ingredient; and a concentrate, metabolite, constituent, extract, or combination of any of the above.

DSHEA also states that dietary supplements must be the products that are intended for oral administration. (8)

European Union

Within European Medicines law a nutraceutical can be defined as a medicine for two reasons:

- If it presented for the prevention, treatment or cure of a condition or disease.
- If it can be administered with a view to restoring, correcting or modifying physiological functions in human beings.

Nutraceutical concept in general has been defined. Different pieces of legislation influencing botanical nutraceuticals are described. The regulatory status of botanical nutraceuticals as food supplement, food Ingredient, functional and fortified food, novel foods and foods for particular nutritional use in the diversified, complex and ever Changing European regulatory environment is described. Botanical nutraceuticals present additional problems because of their complex nature and composition particularly with respect to the quality aspects, which in turn affect safety parameters and overall efficacy of the products. Quality issues relating to botanical Sources, growth conditions, end products, their specifications and other technical criteria are highlighted. Guiding principles to be observed for conducting in vitro, in vivo studies in animals and their impact on clinical safety data are discussed. (9)

4. Herbal cosmetics

As per Drugs and Cosmetics Act 1940 and Rules 1945, Cosmetic means any article intended to be rubbed, Poured, sprinkled or sprayed on, or introduced into, or otherwise applied to the human body or any part thereof for Cleansing, beautifying, promoting attractiveness, or altering the appearance, and includes any article intended for use as a Component of cosmetic.

Regulations of herbal cosmetics:

India

Cosmetics products in India are regulated under the Drugs and cosmetics Act 1940 and Rules 1945 and Labelling Declarations by Bureau of Indian Standards (BIS). The Procedure to be followed in order to manufacture cosmetics In India, BIS sets the standards for cosmetics for the Products listed under Schedule 'S' of the D&C Rules 1945. And Schedule M-II classifies cosmetics into 11 Broad product categories.

In India, cosmetics are regulated by Central Drug Standard Control Organization (CDSCO) under Drug and Cosmetic Act 1940& Rules 1945(amended up to Dec. 31st 2016). The Bureau of Indian Standards (BIS) issued standards for ingredient usage in cosmetics.

Before March 2013, there were no requirements to register imported cosmetics, but from April 1st 2013, all cosmetics imported for sale in India require mandatory registration with the Central Drugs General (India) (DCGI).

Domestic cosmetics in India don't require registration, but 11 categories of cosmetics (cosmetics require auditing of factory premises, space, plant, machinery and other requisites) must obtain a loan license before manufacturing. Cosmetics that have been tested on animals are prohibited from import into India.

United States

The FD&C Act does not recognize any such category as "cosmeceuticals" A product can be a drug, a cosmetic, or a combination of both, but the term "cosmeceutical" has no meaning under the law. FDA explain cosmetics in their act as cleansing, beautifying, or altering the appearance of human body by rubbing, sprinkling, pouring or spraying the formulation for intended use [FD&C Act, sec. 201(i)]. Among the products included in this definition are skin moisturizers, perfumes, lipsticks, fingernail polishes, eye and facial makeup preparations, shampoos, permanent waves, hair colours, toothpastes, and deodorants, as well as any material intended for use as a component of a cosmetic product. (10)

European Union

Regulation 1223/2009 states, "for each cosmetic product placed on the market, the responsible person shall ensure compliance with the relevant obligations" set out in the regulation. Certain provisions of the regulation are considered and possible solutions proposed to enable the safe use of personalized cosmetics placed on the market. (11)

5. Phytopharmaceutical

Phytopharmaceutical drug is defined as purified and standardized fraction with defined minimum four bio-active or phytochemical compounds (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation, or prevention of any disease or disorder but does not include administration by parenteral route.

Regulations of Phytopharmaceutical products:

India

In contrast to AYUSH regulation, 2015 regulatory requirements for phytopharmaceuticals are under the purview of the Central Drugs Standards Control Organization (CDSCO). This gazette notification defines regulatory provisions for phytopharmaceuticals and regulatory submission requirements for scientific data on quality, safety, and efficacy to evaluate and permit marketing for an herbal drug on similar lines to synthetic, chemical moieties. When conventional pharmaceuticals suspect everything, AYUSH medicines that trust everything, phytopharmaceutical is a balanced approach which trusts everything but underlines the revalidation of the specification of the plant material.

In Schedule Y, the newly added Appendix I B describes data to be submitted along with the application to conduct clinical trial or import or manufacture of a phytopharmaceutical drug in the country. The regulatory requirements for NDA (new drug application) for the phytopharmaceutical drug include standard requirements for a new drug-safety and pharmacological information, human studies, and confirmatory clinical trials.

United States

Phytopharmaceuticals are in essence the same as a botanical drug in common parlance and it was the US FDA (United States Food and Drug Administration) that first issued "Guidance to Industry on Botanical Drugs" that paved the way for phytopharmaceuticals to get a status of drug and marketing authorization as a drug after review by US FDA. (12)

European Union

In Europe phytopharmaceutical is any medicinal product, exclusively containing as active ingredients one or more herbal substance it is regulated by European medicines agency under Directive 2001/83/EC and Directive 2001/82/EC. (13)

Table 1. Comparative regulation in India, United States, & European Union

Parameters	Authorities	India	United States	European Union
Herbal Medicines	Legislation	• The Drugs and Cosmetics Act 1940 amended 1964. • The Bureau of Indian Standards Act 1986.	• The Dietary Supplement Health and Education Act (DSHEA) of 1994)	• CD 2001/83 ("basic" regulation) • CD 2003/63 of 25 June 2003 (Annex I, criteria) • CD 2004/24 (Traditional herbal medicinal products) • CD 2004/27 of 31 March

				2004 (HMPC)
	Committee	• Department of AYUSH	•Center for Drug Evaluation and Research (CDER). •National Center for Complementary and Alternative Medicine	• Central European Authority with specified tasks. • Herbal Medicinal Products Committee – HMPC
	Responsible Regulatory authorities for Registration of Nutraceuticals	Food Safety and Standards Authority of India (FSSAI)	US Food & Drug Administration (USFDA)	No Uniformity among European Union countries but European food safety authority (EFSA) is there for assessment of health claim of food.
Nutraceuticals	Form & Regulatory Requirements for Registration	Form A, B, & C A. Product evaluation B. Licenses C. Health & label claim	Form 3537 A. Product licensing B. Evidence requirements for safety & efficacy C. Labelling D. Heath claims E. GMP F. Adverse Reaction Reporting G. Clinical Trials	-
	Authority	Central Drug Standard Control Organization (CDSCO)	United States Food and Drug Administration (USFDA)	European medicines agency (EMA)
	Rules & Regulation	D&C Act1940 AND Rules1945	FD&C Act	Regulation 1223/2009
Herbal Cosmetics	Pre-Marketing Approval	Requirement under the state government	Not required	-
	Post Marketing Reporting System	N/A	Yes	Yes
Phytopharma-ceuticals	Authority	Central Drug Standard Control Organization (CDSCO)	United States Food and Drug Administration (USFDA)	European medicines agency (EMA)

6. Discussion

In this review we discussed the regulatory guidelines in some of major countries for herbal medicine, herbal nutraceuticals, herbal cosmetics, and phyto-pharmaceutical products. We find that different countries have different regulation, which need to be strictly followed for safety and efficacy of herbal products. Lack of harmonisation in regulatory guideline can be seen around world while dealing with herbal products.

7. Conclusions

Day by day demand of herbal product is increasing, therefore concern about their safety and usage is main focus of developed and developing countries. Every country has their regulatory body which control and prepare strategy for herbal product, which may be different in other countries. Lack of harmonisation is a major problem which herbal market is facing. For vigilance strict initiatives is required to be taken to harmonise the regulatory requirement around world.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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