



# INTERNATIONAL JOURNAL OF ADVANCE RESEARCH, IDEAS AND INNOVATIONS IN TECHNOLOGY

ISSN: 2454-132X

Impact factor: 4.295

(Volume3, Issue3)

Available online at [www.ijariit.com](http://www.ijariit.com)

## Current Regulations for Herbal Products

**Chaduvu Ramkrishna**

Pharmaceutics & Drug Regulatory Affairs  
[ramsmt73@gmail.com](mailto:ramsmt73@gmail.com)

**Jayachandra Reddy .P**

Krishna Teja Pharmacy College  
[pmanreddy@gmail.com](mailto:pmanreddy@gmail.com)

**Alagusundaram .M**

Pharmaceutics  
[alagusundaram77@gmail.com](mailto:alagusundaram77@gmail.com)

**Abstract:** Herbal medicines make up an important component of the modern toward alternative medicine. Herbal medicine is becoming ever more popular in now a day's world as people seek out natural remedies. 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. A detailed literature survey for regulations of herbal drug products in Europe, US and India, Russia, Africa, south Korea was performed to identify recently introduced changes in regulations or newly introduced regulations compliance with the regulatory bodies. Committee for Herbal Medicinal Products (HMPC), Committee of European Medicines Agency (EMA) is developing guidelines for quality, nonclinical studies, clinical efficacy and safety. Traditional herbal medicines registration scheme (THMRS) has been recently introduced by Medicines and Healthcare Products Regulatory Agency (MHRA, UK). US FDA has issued draft guidance for Industry on "Complementary and Alternative Medicine Products and Their Regulation". Drugs and Cosmetics Rules have been amended recently to control the quality, safety and efficacy of herbal drug products in India. This article provides an overview of herbal medicines and aimed to explain the regulations of various herbal medicines, standardization of herbal medicines, pharmacovigilance and marketing surveillance regulatory status of herbal medicines.

**Keywords:** Herbal Drug, Efficacy, Regulations, Practices, Quality, Safety, Traditional Uses.

### INTRODUCTION

Herbal medicines are the natural plants and their parts which are being used for medicinal purpose. This is one of the oldest types of medicine in human history. Herbal medicine is still widely practiced all over the world. This practice also is known as Herbalism<sup>1</sup>. Herbalism is one of the forms of Alternative Medicine. A number of old books available about the plants and their medicinal use called Herbals. The ancient Chinese, Indians, Egyptians, Babylonians, and Native Americans were all herbalists a Chinese herbal that is probably a compilation of an even older oral tradition the ancient Greeks and Romans were also renowned herbalists. Surgeons traveling with the Roman army spread their herbal expertise throughout the Roman Empire, in Spain, Germany, France, and England. Dioscorides (c. 40-c. 90) and Galen (131-200 A.D.), both Greek surgeons in the Roman army, compiled herbals that remained the definitive materia medica texts for 1500 years.<sup>2</sup>

The 16<sup>th</sup> and 17<sup>th</sup> centuries were the golden eras of Herbal Medicine. The more and more plants incorporated during 18<sup>th</sup> and 19<sup>th</sup> centuries in Americas. In the 19<sup>th</sup> century, analysis of chemical came in practice. Researchers and scientists began to extract and analyze active ingredients from plants.

### Classification of herbal medicines

(Based on their origin, evolution and the forms of current usage)

#### Category 1: Indigenous herbal medicines

- Historically used in a local community or region and is very well known through long usage by the local population in terms of its composition, treatment, and dosage. Detailed information on this category of TM, which also includes folk medicines, may or may not be available.

#### Category 2: Herbal medicines in systems

- Medicines in this category have been used for a long time and are documented with their special theories and concepts, and

accepted by the countries. Ayurveda, Unani, and Siddha.



### **Category 3: Modified herbal medicines**

- These are herbal medicines as described above in categories 1 and 2, except that they have been modified in some way—either shape or form including dose, dosage form, mode of administration, herbal medicinal ingredients, methods of preparation and medical indications. They have to meet the national regulatory requirements of safety and efficacy of herbal medicines.

### **Category 4: Imported products with a herbal medicine base**

- This category covers all imported herbal medicines including raw materials and products. Imported herbal medicines must be registered and marketed in the countries of origin. The safety and efficacy data have to be submitted to the national authority of the importing country and need to meet the requirements of safety and efficacy of regulation of herbal medicines in the recipient country.

### **The role of herbal medicines in traditional healing**

- The pharmacological treatment of disease began long ago with the use of herbs (Schulz et al., 2001). Methods of folk healing throughout the world commonly used herbs as part of their tradition. Some of these traditions are briefly described below, providing some examples of the array of important healing practices around the world that used herbs for this purpose.

#### **1. Traditional Chinese medicine**

Traditional Chinese medicine has been used by Chinese people from ancient times. Although animal and mineral materials have been used, the primary source of remedies is botanical. Of the more than 12 000 items used by traditional healers, about 500 are in common use (Li, 2000). Botanical products are used only after some kind of processing. Which may include, for example, stir-frying or soaking in vinegar or wine. In clinical practice, traditional diagnosis may be followed by the prescription of a complex and often individualized remedy. Traditional Chinese medicine is still in common use in China. More than half the population regularly uses traditional remedies, with the highest prevalence of use in rural areas. About 5000 traditional remedies are available in China; they account for approximately one fifth of the entire Chinese pharmaceutical market.

#### **2. Japanese traditional medicine**

Many herbal remedies found their way from China into the Japanese systems of traditional healing. Herbs native to Japan were classified in the first pharmacopeia of Japanese traditional medicine in the ninth century.

#### **3. Indian traditional medicine**

Ayurveda is a medical system primarily practiced in India that has been known for nearly 5000 years. It includes diet and herbal remedies while emphasizing the body, mind, and spirit in disease prevention and treatment.

### **DISCUSSION**

Among the survey respondents, 74 companies were found to export formulations to various countries. Of these, 46 companies export to the United States, 26 companies export to European countries, and 17 companies export to Southeast Asian countries. Some companies also export to Australia and Middle Eastern and African countries. The survey revealed that achieving regulatory compliance is one of the major hurdles for exporters. Differences in the country-specific GMP standards and drug registration requirements are considered the major impediments for Indian manufacturers.

#### **Differing regulatory requirements**

Differing regulatory by requirements and subsequent delays in application submission and review process emerged as a major concern for the herbal medicine manufacturers from the survey results. Therefore, a comparative analysis of drug registration requirement was performed for countries such as India, the United States, and European nations to understand the differences in approval procedures and submission requirements. In India, the traditional herbal medicines, such as Ayurveda, Siddha, and Unani (ASU), are considered safe because of their long history of use. As such, no safety and efficacy studies are required for marketing approval, as per the Drugs and Cosmetics Act of 1940 (DCA)<sup>(37)</sup>.

In the European Union (EU), however, the application for marketing authorization for traditional medicinal products requires bibliographic evidence and preclinical safety data (such as the toxicologic and pharmacologic test data). As per the Traditional Herbal Medicinal Product Directive (2004/24/EC), to obtain traditional use registration, the applicant has to submit the quantitative and qualitative particulars of constituents of the medicinal product, a description of manufacturing methods, therapeutic indications, contraindications, adverse reaction, posology, and form and route of administration [Article 8(3)(a) to (h), (j) and (k)]. The application also requires the summary of product characteristics without the clinical particulars as specified in Article 11(4) of Directive 2001/83/EC. In case of combinations, information relating to the combination, pharmacologic effects or efficacy of the medicinal product, evidence for longstanding use, and experience is required. As per Directive 2004/24/EC, many products from non-EU countries that are yet to be used in the EU would be excluded because a minimum of 15 years of marketing history in EU is required.

### **Lack of regulatory guidelines**

The survey revealed that insufficient regulatory guidelines for different aspects of production are an important reason for quality issues with herbal medicinal products. More than 60% of the respondents in the survey suggested that guidelines on quality control of herbal medicines be developed or elaborated. Establishment of government-certified raw-material supply centers in every state was suggested; this would help the manufacturers procure authentic raw materials. The respondents also suggested more elaborate regulatory guidelines in terms of raw material standardization and quality control during production<sup>(53,54)</sup>.

### **Regulatory status of herbal medicines**

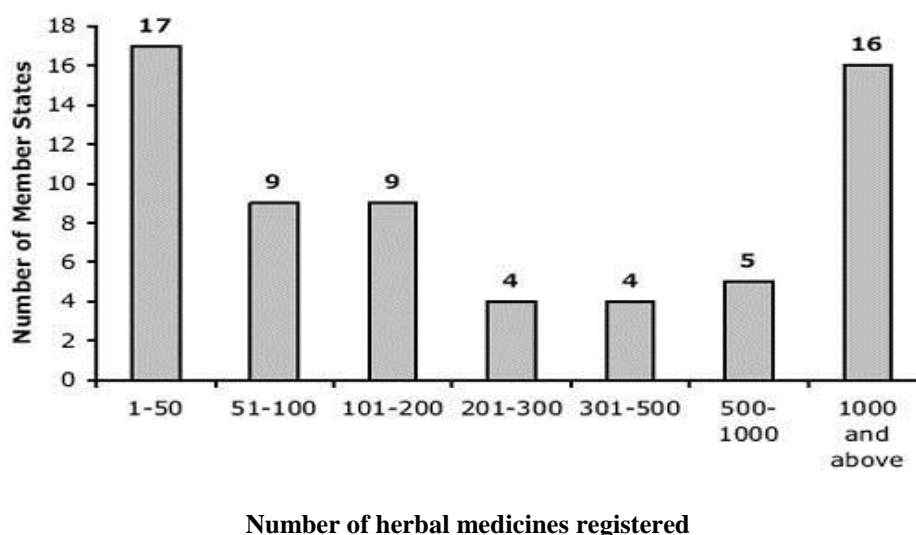
Member States were asked about the regulatory status or statuses that are used for herbal medicines in their regulatory frameworks. Detailed descriptions of seven possible regulatory categories for herbal medicines were given on the survey form. The options were the following: prescription medicines, over the counter medicines, self-medication only, herbal medicines as a separate regulatory category, dietary supplements, health foods, functional foods and another status.

Responses were provided by 131 Member States; as each was able to choose more than one category, the total number of responses exceeds the number of respondents. The regulatory category most often chosen was that of over the counter medicine, accounting for 97 responses. The next most popular responses accounted for 23-38% of the total and included the following categories: prescription medicines, dietary supplements, and self-medication only. A total of 23 countries indicated that there was no regulatory status established for herbal medicines.

Countries also had the option of describing other regulatory categories defined by their legislation; 13 countries provided this information. The other regulatory categories applied to herbal medicine include the following: health products, cosmetics, traditional medicines, herbal remedies, supportive medicines, homeopathic, bioactive and probiotic substances, and complementary products.

### **Registration system for herbal medicines**

Countries were asked whether a registration system exists for herbal medicines; 139 countries answered the question. Eighty-five countries (61%) reported that they have registration systems for herbal medicines. If countries reported having a registration system for herbal medicines, they were asked to provide the number of herbal medicines registered. Sixty-four countries provided a number for registered herbal medicines. The reported number of registered herbal medicines ranged from 0 to 10 000. Several countries could not provide a number of registered medicines or indicated that no medicines were yet registered, as the systems had recently been implemented.<sup>(57)</sup>



## **DIFFERENT REGULATIONS ON VARIOUS COUNTRIES**

### **1. European Regulations & Practices and Guidelines**

Herbal medicinal products fall within the scope of the European Directive 2001/83/EC that foresees marketing of each medicinal product and requires an ad hoc authorization 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 authorization, particularly in relation to efficacy, as are required under Directive 2001/83/EC. The Directive 2004/24/EC has established an 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. <sup>(58)</sup>

As per Directive the definitions of the herbal medicinal product, herbal drug substances, and herbal preparations are as follows:

#### **A. Herbal substances:**

All mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried, form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety, and author).

#### **B. Herbal preparations:**

Obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates. Medicinal products containing herbal substances/preparations must fall within one of the following three categories to reach the market.

- ❖ A product can be classified under traditional medicinal use provisions (traditional use) accepted on the basis of sufficient safety data and plausible efficacy: the product is granted a traditional use registration (simplified registration procedure) by a Member State.
- ❖ A product can be classified under well-established medicinal use provisions (well-established use). This is demonstrated with sufficient safety and efficacy data. As a result, the product is granted a marketing authorization usually by a Member State or by the European Medicines Agency under certain conditions. (While both classifications has specific requirements, both regulatory paths involve the assessment of mostly bibliographic safety and efficacy data, which are usually combined, for well-established use products, with product specific data.)
- ❖ A product can be authorized after evaluation of a marketing authorization application consisting of only “product-specific safety and efficacy data” (full dossier). As a result, the product is granted a marketing authorization by a Member State or by the Agency via the centralized procedure if all requirements are met.

Minor claims are permitted on the basis of evidence of traditional usage. Irrespective of the regulatory pathway to access the market, the quality of the herbal medicinal product must always be demonstrated. 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 marketing authorization.

### **2. Africa Regulations**

A recent WHO report (WHO Regional Report dated July 5th, 2011 ref AFR/RC61/PR/2) on the status of traditional medicine in Africa indicates the following:

- ❖ In 2000 only 10 African countries had laws on the use of herbal medicines. By 2010 the figure was 20 countries.
- ❖ In 2000 only 4 African countries had a registration system of traditional healers. By 2010 the figure was 15 countries.
- ❖ In 2000 only 1 African country had issued a market authorization for traditional herbals. By 2010 the figure was 12 countries.
- ❖ Egypt where all herbal medicines are regulated and manufactured with licenses similar to Europe.

The protection of the intellectual properties of traditional healers has become an increasingly important aspect of the regulatory scenario. 8 countries, including South Africa, Ghana, and Nigeria, have national laws relating to IPR and traditional medicine. There is, however, a wide gap between the existence of the legislation and the application of the law in practice

### **3. South Korea Regulations**

Although the medical system in Korea is divided into two systems: a modern medical system and a Korean traditional medical system, medicines are controlled by a single regulatory system established by the Pharmaceutical Affairs Act. The Korea Food and Drug Administration (KFDA) is in charge of establishing standards and pre-market approval, post-market inspection, and management of the product quality system for herbal. Medicines.



#### **Regulations :<sup>(78)</sup>**

The Pharmaceutical Affairs Act, passed in 1954, deals with pharmaceutical affairs including herbal medicines. Other regulations concerning the control of herbal medicines are 'Regulations on the demand/supply, distribution, and product management of herbal medicines' (Ministry of Health and Welfare Notification) and 'Regulations for Imported Medicines' (KFDA Notification).

#### **Standardization of herbal medicines in Korea**

Standards for commonly used herbal materials and preparations are included in the 'Korean Pharmacopoeia', 'Korean Herbal Pharmacopoeia', and 'Korean Pharmaceutical Codex'. In terms of the safety of herbal medicines, a number of hazardous substances such as heavy metals, pesticides, and aflatoxins are restricted by the 'Regulations on Limits and Test Methods for Residues and Contaminants in Herbal Medicines'. Since 2005, a collaborative study has been conducted to establish a method for the standardization of herbal medicines through the support of the Korea Food & Drug Administration (KFDA). Nevertheless, the ambiguity of the origins of the herbs makes them more difficult to be utilized for both clinical and industrial purpose, and thus, both standardization and modernization of TMs is essential.

### **4. PHILIPINES**

#### **Regulatory System:**

The Philippines defines Traditional Medicine (TM) as the totality of knowledge, skills, and practice of health care that cannot be explicitly explained in a scientific framework but its impact in maintaining health and wellness has been recognized by the society to be reflective of their culture, history and social consciousness. It uses various terms such as herbal and/or traditional drug, herbal medicine (HM), traditionally used herbal products (TUHP) and herbal supplements (HS) which include food supplements (FS). The regulatory policies in the Philippines are categorized according to the type of product. Summary of the traditional and health supplement regulatory requirements in the Philippines.

#### **Criteria for safety, traditional use, scientific validity and quality:**

To ensure the safety of TM and HS, the Philippine FDA requires the submission of technical data for safety and a Good Manufacturing Practice (GMP) certificate of the manufacturer for product registration. Pre-marketing Evaluation requires references to support safety. These may include monographs, pharmacopeias and websites for TM; and websites for HS. Toxicity studies are also compulsory for their premarketing evaluation. On the other hand, registration of TUHP requires also the submission of technical data for safety, including toxicity studies, and a list of references supporting it. However, there should be a documented traditional experience of the use of at least 5 decades. For all these products, submission of technical data for efficacy or claimed application is required for product registration. Pre-marketing Evaluation of TM and HS in the Philippines involves verification of claims of raw material and finished product efficacy. Additionally, TM should undergo clinical trials. For TUHP, only a verification of claims of the raw material efficacy is needed. In ensuring the product quality of TM and HS, technical data for quality and a GMP certificate should be submitted for product registration. Evaluation of formula, raw material, manufacturing processes, and finished product specification are conducted prior to product marketing. Results of the following quality control parameters are required: stability study, determination of water content, disintegration time and microbial count. The requirement for submission of technical data for quality is also applicable for TUHP.

#### **Post-marketing surveillance of herbal medicines**

Countries were first asked whether they had a post marketing surveillance system for herbal medicines. If countries responded "yes", the next question asked whether there is a national system to monitor adverse effects of herbal medicines. If such a system exists, the date of establishment was requested. If the Member State reported that a post marketing surveillance system for herbal medicines did not exist, the next question asked if there are plans to establish such a system.

#### **The sale of herbal medicines**

In this question, countries were asked about the methods of sale of herbal medicine. Countries were requested to select all methods of sale employed on their territory from the following options: in pharmacies as prescription drugs; in pharmacies as over the counter drugs; in special outlets; by licensed practitioners; no restrictions on selling herbal medicines; and other ways. If "other ways" was selected, a description was requested.

A total of 137 countries reported on the location and methods of sale of herbal medicines. Figure 41 provides details of how countries responded. By far the most commonly selected category is that of sale in pharmacies as over the counter drugs, with 101 countries reporting this method of sale. Interestingly, the next most popular selection is that which states that there are no restrictions on the sale of herbal medicines, selected by 70 countries. The next most popular method of sale is in special outlets, chosen by 59 countries, followed by a sale in pharmacies as prescription medicines (48 countries) and finally by licensed practitioners (30 countries). Twenty-two countries selected the option "other ways", including the following: peddling in markets and in ambulatory sales (e.g. selling door to door); by unlicensed practitioners; in indigenous communities; in herbal clinics and traditional healers; in health shops, supermarkets and food markets; and through mail order and multi-level marketing systems.

#### **Main difficulties faced by countries**

In this section, countries were asked about their specific needs and given the opportunity to provide feedback on the types of support they most needed from WHO. main difficulties faced by each Member State regarding regulatory issues for herbal

medicines. The options, from which the countries could select all that applied, included the following: lack of research data; lack of expertise within the national health authorities and drug control agency; lack of appropriate mechanisms for control of herbal medicines; lack of education and training; other. A total of 129 countries answered this question; The category chosen by the most countries was that of a lack of research data (109 countries), followed by lack of appropriate mechanisms for the control of herbal medicines (93 countries), lack of education and training (86 countries), lack of expertise within the national health authorities and control agency (70 countries) and other (33 countries).

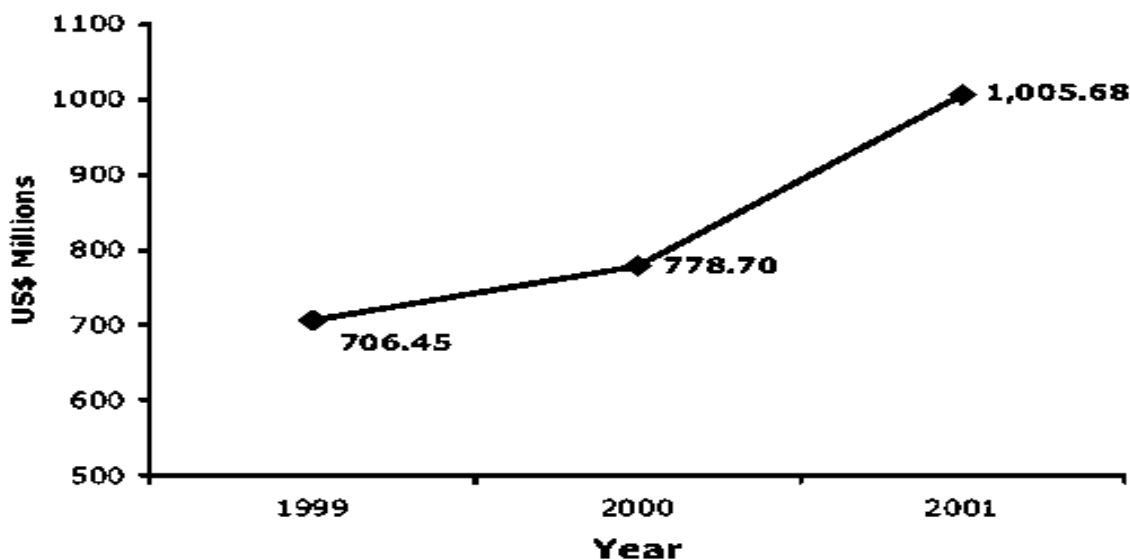
#### **Main difficulties regarding regulatory issues for herbal medicines**

Those countries selecting “other”, the following were the responses which were included as major difficulties regarding regulatory issues on herbal medicines: lack of funding for research, lack or inadequacy of literature, lack of support, insufficient personnel, no national quality control laboratory, herbal medicines placed on the market as food, lack of awareness of the importance of the topic, adulteration of herbal medicines and lack of support for an accreditation system for practitioners.

#### **Annual market sales of herbal medicines**

In the final question in this section related to the regulation of herbal medicines, countries were asked to provide data about annual market sales for herbal medicine for the most recent three years. The question also asked for clarification of the source of the figures provided.

The nine States included in the results below are Bhutan, Canada, Czech Republic, Islamic Republic of Iran, Madagascar, Malaysia, Pakistan, Sudan and Sweden. When figures were given in local currency, they were converted to United States dollars, using the exchange rates published by the United Nations on 1 November 2003. The data excluded from the compilation above provide further evidence of the rise in annual market sales of herbal medicine globally.



**Annual market sales of herbal medicines in nine countries, 1999-2001**

#### **Market Importance of Herbal Medicines**

The percentage of herbal medicines prescribed in medical treatment is still increasing. Several places have already succeeded in using 100% plant-based drugs which reduce the burden of the State's subsidy on medicines. Thousands of communes have achieved a certain percentage of herbal drugs to be used in treatment, as set by the Ministry of Health. The successful combination of modern and traditional medicine has given impetus to the gradual modernization of herbal medicine to facilitate handling and promote exports. Medicines are produced from plant extracts and purified products, and they are exported as finished or semi- WHO/TRM/98.1 page 38 finished products. All medicines prepared from medicinal plants can be used in Viet Nam as substitutes for Western drugs and Chinese herbs which, in former times, have been more important.

#### **CONCLUSION**

Regulatory authorities of different countries have contributed in developing guiding principles addressing issues related to this aspect of herbal medicines. The legal status and the practice of use of herbal drug products vary significantly from one country to another thus making it difficult for the free circulation of such products. European regulations are most comprehensive among most of the global regulations for herbal medicinal products. Indian regulations are also developing to global regulations for herbal drug products. Indian regulations are still at the nascent stage when compared to regulations of Europe and US. The Russian healthcare market is expanding rapidly, drawing more interest by offering massive opportunities for Herbal Pharmaceutical companies. A thorough study of regulatory requirements of herbal medicinal products in Russia is essential for gaining quicker marketing approval. As evidence-based submissions are becoming increasingly essential for establishing the safety and efficacy of herbal

products both in the domestic and the export market, more focus should be given to scientific and technological advancement in the field of herbal medicine.

## REFERENCES

1. Current Prospects of Herbal Medicines in the World.
2. Brief history of herbalism <http://exhibits.hsl.virginia.edu/herbs/briefhistory/>
3. Review on quality safety and legislation for herbal products Patel Vishal, Patel N.M., Patel
4. <https://monographs.iarc.fr/ENG/Monographs/vol82/mono82-6A.pdf>
5. Current Scientific Status and Regulatory Control of Herbal Medicine. [http://www.ijrap.net/admin/php/uploads/639\\_pdf.pdf](http://www.ijrap.net/admin/php/uploads/639_pdf.pdf)
6. Regulatory issues of herbal medicine. Available at [www.clininvent.com](http://www.clininvent.com)
7. Regulatory situation of herbal medicine worldwide
8. WHO guideline on safety monitoring.
9. Guidelines for the appropriate use of Herbal Medicines.
10. Framework for overcoming barriers of complementary and alternative medicine acceptance into conventional Healthcare system.
11. Pharmacovigilance of Herbal Products. Available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3159283/>
12. Pharmacovigilance of Herbal Products in India.
13. Report on the regulation of herbal medicines and practitioners.
14. Eguchi, K., Hyodo, I. & Saeki, H. (2000) Current status of cancer patients' perception of alternative medicine in Japan. A preliminary cross-sectional survey. *Sup. Care Cancer*, 8, 28–32 EMEA (Europea Agency for the Evaluation of the Evaluation of Medicinal Products) (2000) Working Party on Herbal Medicinal Products: Position paper on the risks associated with the use of herbal.
15. Products containing Aristolochia species (EMEA/HMPWP/23/00), London
16. ESCOP (European Scientific Cooperative on Phytotherapy) (1999) ESCOP Monographs on the Medicinal Uses of Plant Drugs, Exeter, UK
17. European Commission (1965) Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by Law, Regulation or Administrative Action relation to proprietary medicinal products. *Off. J.*, P22,
18. European Commission (1975) Second Council Directive 75/319/EEC of 20 May 1975 on the approximation of Provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products. *Off. J.*, L147, 12
19. European Commission (1992a) Council Directive 92/28/EEC of 31 March 1992 on the advertising of medicinal Products for human use. *Off. J.*, L113, 13–18
20. Review of the regulations for clinical research in herbal medicines in the USA
21. Current status of herbal product: Regulatory Overview
22. Review of the regulations for clinical research in herbal medicines in the USA
23. Review article: herbal and dietary supplement hepatotoxicity.
24. Traditional use and safety of herbal medicines
25. Use of Herbal Medicines and Implications for Conventional Drug Therapy Medical Sciences
26. Current prospects of herbal medicines in the world Arpita Pithava
27. Herbal medicine: women's views, knowledge, and interaction with doctors: a qualitative study
28. Current regulatory challenges and approaches in the registration of herbal drugs in Europe
29. Pharmacovigilance of herbal medicines: Current state and future directions.
30. Attitudes and Beliefs of Consumers of Herbal Medicines in Riyadh, Saudi Arabia
31. Berger, E. (2001) the Canada Health Monitor Surveys of Health Issues in Canada, Survey 22, Ottawa, and Health Canada
32. Bhat, K.K.P. (1995) Medicinal plant information databases. In: *Non-Wood Forest Products*.
33. Medicinal Plants for Conservation and Health Care, Rome, Food, and Agriculture Organization
34. The Complete German Commission E Monographs: Therapeutic Guide to Herbal
35. Medicines, Austin, TX/Boston, MA, American Botanical Council/Integrative Medicine Communications
36. Calixto, J.B. (2000) Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). *Braz. J. med. biol. Res.*,
37. Directive 2004/24/EC of the European Parliament and of the Council [homepage on the Internet] Online Document
38. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the community code relating to medicinal products for human use [homepage on the Internet] Online document
39. Centre for Research in Indian Systems of Medicine (CRISM) [homepage on the Internet] Online document at: [www.crism.net](http://www.crism.net) Accessed June 20, 2012
40. Sahoo N, Manchikanti P, Dey SH. Herbal drugs standards and regulation. *Fitoterapia* 2010; 81:462–471[PubMed]
41. Mitra SK, Kannan R. A note on unintentional adulterations in ayurvedic herbs. *Ethnobotanical Leaflets* 2007; 11:11–15

42. Dargan PI, Gawarammana IB, Archer JRH, House IM, Shaw D, Wood D. Heavy metal poisoning from Ayurvedic traditional medicines: an emerging problem? *Int J Env Health* 2008; 2:463–474
43. Saper RB, Kales SN, Paquin J, et al. Heavy metal content of ayurvedic herbal medicine products. *JAMA* 2004; 292:2867–
44. Saper RB, Phillips RS, Sehgal A, et al. Lead, mercury, and arsenic in the US- and Indian-manufactured Ayurvedic medicines sold via the Internet. *JAMA* 2008; 300:9 45. Ernst E. Toxic heavy metals and undeclared drugs in Asian herbal
46. National Center for Complementary and Alternative Medicine (NCCAM) Ayurvedic medicine: an introduction [Homepage on the Internet].
47. Bandaranayake WM. Quality control, screening, toxicity, and regulation of herbal drugs. In: Ahmad I, editor; Aqil F, editor; Owais M, editor. , eds. *Modern Phytomedicine—Turning Medicinal Plants into Drugs*. Weinheim, Germany: Wiley-VCH Verlag; 2003: 25–57
48. Li S, Han Q, Qiao C, et al. Chemical markers for the quality control of herbal medicines: an overview. *Chin Med* 2008;3:7. [PMC free article] [PubMed]
49. Saxena PK, Cole IB, Murch SJ. Approaches to quality plant based medicine: significance of chemical profiling. In: *Applications of Plant Metabolic Engineering*, Verpoorte R, editor; Alfermann AW, editor; Johnson TS, editor, eds. Dordrecht, the Netherlands: Springer; 2007:311–330
50. Fan X, Cheng Y, Ye Z, et al. Multiple chromatographic fingerprinting and its application to the quality control of herbal medicines. *Anal Chim*
51. Zeng Z, Liang Y, Chau F, et al. Mass spectral profiling: an effective tool for quality control of herbal medicines. *Anal Chim Acta* 2007;604:89–98 [PubMed]
52. <http://www.florajournal.com/archives/2013/vol1issue4/PartA/27.1.pdf>