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Review

Current Regulations For Herbal Products

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Abstract

Officinal plants and their products have great social and economic consequences, and today they are used in four principal sectors: food, cosmetics, health and medicine. The medicinal use of the herbal drugs, Phytotherapy, is differently controlled in different countries, but with only marginal differences because phytotherapeutic products must possess quality, safety and efficacy. The use of herbs as health foods, as well as food supplements, complicates the formulation of regulations by countries throughout the world. The increasing supply of herbal products to international markets makes it necessary for international organizations, such as the World Health Organization (WHO) to develop standards relative to their commercialization throughout the world. The classification of drugs varies from country to country, with active foods, dietary supplements and traditional medicines being included in certain categories. The stability of those products is also unknown and complex to the critical problem in the analysis of herbal products that this is a complex ingredient combination, as well as the elements responsible for the treatment effects. In order to identify the changes to the newly introduced regulations or regulations, detailed literary searches and online searches for herbal medicinal products regulations have been made in South-east Asia and European countries.

Keywords: Harmonization, herbal drugs, herbal products.

INTRODUCTION

Herbal medicine (also herbalism) is the study of pharmacognosy and the use of medicinal plants, which are a basis of traditional medicine.[1] There is limited scientific evidence for the safety and efficacy of plants used in 21st century herbalism, which generally does not provide standards for purity or dosage.[1,2] The scope of herbal medicine commonly includes fungal and bee products, as well as minerals, shells and certain animal parts. Herbal medicine is also called phytomedicine or phytotherapy.[3]

Paraherbalism describes alternative and pseudoscientific practices of using unrefined plant or animal extracts as unproven medicines or health-promoting agents. Paraherbalism relies on the belief that preserving various substances from a given source with less processing is safer or more effective than manufactured products, a concept for which there is no evidence.[4]

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[5]. 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.[6]

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

Traditional Herbal Medicines and Human Health

Herbal medicines which formed the basis of health care throughout the world since the earliest days of mankind are still widely used, and have considerable importance in international trade. Recognition of their clinical, pharmaceutical and economic value is still growing, although this varies widely between countries. Medicinal plants are important for pharmacological research and drug development, not only when plant constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds. Regulation of exploitation and exportation is therefore essential, together with international cooperation and coordination for their conservation so as to ensure their availability for the future.[52]

The United Nations Convention on Biological Diversity states that the conservation and sustainable use of biological diversity is of critical importance for meeting the food, health and other needs of the growing world population, for which purpose access to and sharing of both genetic resources and technologies are essential. Legislative controls in respect of medicinal plants have not evolved around a structured control model. There are different ways in which countries define medicinal plants or herbs or products derived from them, and countries have adopted various approaches to licensing, dispensing, manufacturing and trading to ensure their safety, quality and efficacy. Despite the use of herbal medicines over many centuries, only a relatively small number of plant species has been studied for possible medical applications. Safety and efficacy data are available for an even smaller number of plants, their extracts and active ingredients and preparations containing them.[53]

Regulation and Registration of Herbal Medicines

The legal situation regarding herbal preparations varies from country to country. In some, phytomedicines are well-established, whereas in others they are regarded as food and therapeutic claims are not allowed. Developing countries, however, often have a great number of traditionally used herbal medicines and much folk-knowledge about them, but have hardly any legislative criteria to establish these traditionally used herbal medicines as part of the drug legislation. For the classification of herbal or traditional medicinal products, factors applied in regulatory systems include: Description in a pharmacopoeia monograph, prescription status, claim of a therapeutic effect, scheduled or regulated ingredients or substances, or periods of use. Some countries draw a distinction between "officially approved" products and "officially recognized" products, by which the latter products can be marketed without scientific assessment by the authority.[54]

Categories of Herbal Medicines

The various legislative approaches for herbal medicines fall into one or other of the following categories:

- same regulatory requirements for all products;
- same regulatory requirements for all products, with certaintypes of evidence not required for herbal/traditional medicines;
- exemption from all regulatory requirements for herbal/ traditional medicines;
- exemption from all regulatory requirements for herbal/ traditional medicines concerning registration or marketing authorization;
- herbal/ traditional medicines subject to all regulatory requirements; and
- herbal/ traditional medicines subject to regulatory requirements concerning registration or marketing authorization.

Where herbal medicines and related products are neither registered nor controlled by regulatory bodies, a special licensing system is needed which would enable health authorities to screen the constituents, demand proof of quality before marketing, ensure correct and safe use, and also to oblige[55] license holders to report suspected adverse reactions within a post-marketing surveillance system.[56]

WHO Policy and Activities

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 medicine. Adopting a regulatory mechanism has always helped in ensuring that herbal medicines have acceptable quality, safety and efficacy. The WHO Guidelines for the assessment of herbal medicines may be consulted when assessment processes for herbal medicines are being prepared.[57]

The WHO guidelines on good agricultural and collection practices for medicinal plants are intended for national regulatory bodies and offer advice on cultivation and collection methods, site selection, climate and soil considerations and the correct identification of seeds and plants.[58]

These guidelines also offer guidance on post-harvest operations such as labeling and legal components including national and regional laws on quality standards, patent status and benefits sharing. It is not a binding guideline for any country, but it is a model or a sort of checklist which they can use to make their own national regulations.[59] Protocols on safety, efficacy, standardization and documentation of herbal medicines have also been published by International Union of Pure and Applied Chemistry (IUPAC) subcommittee on bio-molecular chemistry.[60]

EU Regulations

Most individual herbal medicinal products are licensed nationally by member states, the process for licensing and information on herbal substances and, preparations is harmonized across the European Union. In United Kingdom, to get a product registered, companies have to submit a dossier to the Medicines and Healthcare products Regulatory Agency (MHRA) demonstrating that it meets the requirements of quality, safety and patient information as per the Traditional Herbal Registration Scheme (THRS)[61]. 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[62].

US Regulations

In United States, the term complementary/alternative medicines (CAM) are most commonly used for traditional medicine systems.[63] Complementary medicine refers to use of CAM together with conventional medicine, such as using acupuncture, in addition to usual care to help lessen pain.[64] Most use of CAM by Americans is complementary “Alternative medicine” refers to use of CAM in place of conventional medicine. “Integrative medicine" (also called integrated medicine) refers to a practice that combines both conventional and CAM treatments for which there is evidence of safety and effectiveness.[65] CAM practices are often grouped into broad categories, such as natural products, mind-body medicine, and manipulative and body - based practices. Although these categories are not formally defined, they are useful for discussing CAM practices.[66]

Indian Regulations

Herbal drugs today constitute a major share of all the officially recognized systems of health in India viz. Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy excluding Allopathy. Central Council of Indian Medicine (CCIM) is a statutory body under Indian Medicine Central Council Act (IMCC Act), the Research Councils i.e. Indian Council of Medical Research and Council of Scientific and Industrial Research (ICMR and CSIR), the Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) & Drugs and Cosmetics Act 1940(D C Act) regulates the manufacture, distribution and sale of herbal medicines in India. Herbal medicines, remedies and medicinal plants which are to be incorporated in our modern system (Allopathic system) must follow Drug Controller General of India (DCGI’s) regulations. As per the amendment in the Drugs and Cosmetics Act in 1964, Ayurvedic, Siddha or Unani drugs includes all medicines which are intended for internal or external use for treating, diagnosing, mitigation, prevention or curing of any disease or disorder in human beings or animals. These herbal medicines are manufactured strictly in accordance with the formulations described in reference books of Ayurvedic, Siddha and Unani (Tibb) systems of medicine as specified in the First Schedule.[67] It is submitted that the amendment is provided for a limited set of controls, like manufacturing under prescribed hygienic conditions that too under the super vision of a qualified person, use of genuine raw materials and prescribed labeling of all the ingredients used.

Department of AYUSH, ICMR and CSIR work together to achieve safe, effective AYUSH products for the identified diseases and to develop new drugs. AYUSH objectives are to control drug

quality, laying down pharmacopoeial standards, overseeing working of Pharmacopoeial Laboratory of Indian Medicines (PLIM), partnership with the QualityCouncil of India (QCI) and to oversee functioning of Indian Medicine Pharmaceutical Company Limited (IMPCL). AYUSH also controls enforcement of Good Manufacturing Practices (GMP), setting up of common facilities following the Cluster approach and implementing the scheme for Drug Quality Control. With the advent of IPR regime, AYUSH department has also started digitalization of traditional medicinal formulations, knowledge and manuscripts and documentation and promotion of local health traditions.

DISCUSSION

Enforcement of Regulatory Matters

Evolution of Regulatory Issues

It is submitted that traditional medicine/herbal products is generally the knowledge which has been gained via practice which is generally based on skills, theories, experience and beliefs indigenously and it varies from culture to culture, region to the region and also due to availability of the flora and fauna. These traditional medicines/herbal products generally have holistic approach, which is used in improvement of health and to prevent physical and mental illness, by applying various therapies and practices. This maintenance of primary healthcare system has been passed from generation to generation either orally or through scripts or sculptures or inscribes and has been used for thousands of years with main motive i.e. holistic primary health care. The use of traditional medicines/herbal products with the motive of primary healthcare at community level, has now gained popularity worldwide. The floras and faunas are generally being used in traditional medicines/products with a holistic approach i.e. to bring balance/equilibrium of the mind, body and the environment and the main emphasis is on the restoration of health rather than on disease. The flora and fauna also varies according to the environmental conditions and similarly the applicability and its effects, but if we see an overall view the basic idea behind the use of traditional medicine is to improve the overall condition of human being by improving its immunity system. When the patient is suffering from a particular ailment or disease, the traditional medicines rather working on disease by using herbs traditionally as a medicine being core part of it, work on immune system of body and to balance it with the mind and the environment.

We have seen from the previous studies and perhaps even today we see that with the evolution of new species, the basic concept for providing herbal products/medicines for improving the health of mankind has been the main basis of medication and the concept generally remains the same. With the passage of time gradually, the quality concept has come into picture to improve the medication system and to ensure its efficacy and safety. The record of regulations of traditional medicines/ herbal products when it came into light is not available, however in the primitive times physicians or surgeons were not held liable for wrong medication. However in the primitive times physicians or surgeons were not held liable for wrong medication1. In England somewhere in 1540, the Drugs and Stuffs Act was constituted2 under British Statutes to have control on the medicines and also established in the appointment of Inspectors who could inspect the pharmaceuticals i.e. the place where medicines were produced.

Evolution of Acts and Pharmacopeias

History of pharmacopoeias, the official book of drug quality standard dates back to 1240 A.D. and it was issued by Fedrick II of Sicily named as Salerno Medical Addict.3 The first pharmacopeia in Europe was launched in 16th century and the same was Spanish pharmacopeia issued in 1581. The pharmacopeia of England was published in 1618 in the name of the London Pharmacopeia.4 It is submitted that the popularity of regulations of medicines however gained its standards only in 19th century when there was more work on modern medicines i.e. allopathy. During this period various medicines were evolved to cure epidemic diseases and with the progress of life science especially in Chemistry, Pharmacology and Physiology, it laid solid foundations for the modern drug research and development, which flourished more after the Second World War. The development of regulations of medicines came into evolution more vigorously, when in 1957 hundreds of people in the United States died of diethylene glycol poisoning following the use of sulfanilamide elixir, chemical used as solvent without any testing.[5]

In 1938, in United States, the Federal Food Drug and Cosmetic Act was introduced with the premarket notification requirement for new drug. This was introduced to have control on the medicines which were contaminated and was used for curing patients without testing. The act was introduced, as the country was having poor regulatory environment in administering the medicines which were either contaminated or / and had killed various patients in the country. The further development took place in West Germany in 1956 when there was the halidomide disaster which led to regulation of the medicines in Europe.6 Thalidomide was a sedative and hypnotic that first went on sale in Western Germany in 1956. Thereafter between the periods of 1958 to 1960 in various countries worldwide approximately 46 countries, where the said medicines was used, it resulted in more than

10,000 babies born with phocomelia and other deformities which resulted into evolution of the medicines regulatory system.[7]

Thereafter in various countries of European Union and in United States, various acts were enacted to have control on the regulatory issues relating to medicines. In 1963 the Committee on Safety of Drugs was constituted in U.K. to look into the adverse drug reaction followed by another adverse reaction reporting system (Yellow Card System) in 1964. Similarly in United States in the year 1962 the Drugs Amendment Act was passed by the Congress requiring the FDA to approve all new drug applications (NDA) and the said FDA was given authority to that a new drug should be effective and safe. They were also given the authority to have control on Good Manufacturing Practices (GMP) and to maintain the register of such drug and to implement the other requirements in its establishment.8 It is submitted that thereafter various laws and regulations were enacted and laid down along with the administrative actions relating to medicinal products were introduced to stop the disaster of medicine reactions. However it took a very long time in the European Union to bring harmonization in the affairs relating to regulatory issues of proprietary medicines. It took more than 10 years to bring the harmonization and thereafter Council Directives were introduced in respect of matters relating to analytical, pharmacotoxicology & clinical standards and protocols, in respect of testing proprietary medicinal products and the second approximation was on the provisions with regard to regulation, law and administrative actions relating to medicinal products. Further they were able to establish a "common market" authorization as a pre-requirement for sale medicines whether herbal or synthetic medicines and same were published in detail.9

The parallel harmonization at the same time, in relation to medicines also started in other countries like U.S., Japan. World Health Organization (WHO) in 1989, in Paris during the International Conference of the Drug Regulatory Authorities (ICDRA) was held primarily with the need for the harmonization of requirements relating to new innovative drugs. Due to its success, the conference held in the year 1990 led to the establishment of the International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for human use (ICH) which was the collaborative initiative of Japan, Europe and US. This conference was to bring harmonization relating to innovative medicines and also to see the countries with the limited resources and mostly with the generic medicines which may have difficulty in implementing ICH standards. Pharmaceutical regulatory harmonization facilitates the availability of safe, effective and good quality of medicines/products. WHO not only supports harmonization at International level but also supports harmonization of medicines/products on the regional, inter-regional and national level also and primarily works on quality, safety and efficacy standards of generic as well as new medicines/products with fair competition and also on price.[10]

Need for Regulating Drugs/ Herbal Products

It is submitted that the plants are used as medicines either indigenously or the extracts of the same are used for preparing novel medicines but the ultimate end product is the drug which is consumed by the consumer for curing any disease. So, it is necessary to see the drugs which are being consumed by the consumers have potential benefits and is devoid of any risks or to see its safety and quality for which it is being used. The consumer is not in a position to know which drug is safe to him and is beneficial, as no medicine is completely safe. The medicines are provided by the pharmacist or the doctors but regarding the decision of a particular medicine which is safe for human consumption is not possible without special training or necessary information attached to it. The expert opinion and knowledge is required in clinical pharmacology which relates to comprehensive clinical aspects of medicines in relation to its quality, safety and efficacy. There are various scientific issues relating to medicines without which it will not be enough to give fair judgment about the quality, safety and efficacy of the medicines. The use of ineffective, harmful and poor quality medicines can cause further deterioration of health and can also lead to death in certain cases. So, there is need to have an effective control on the production, manufacture and distribution of medicines, so that the money spent in the production of medicine has full worth of it and are safe for human consumption with best of its quality, efficacy and standards. As we have seen that various disasters had occurred in past due to medication without any testing and thus due to this need, the regulation of medicines was required to bring harmonization worldwide. WHO is mainly concerned all over the world to bring and establish strong national regulatory authority to ensure that the manufacture, use and the trade of medicines are regulated effectively so as to protect and promote public health, being its priority issue and that too with the help of the Government. with the evolution of scientific methods and increase in research and development, the regulation of medicines/herbal product is not only limited to a particular technical field but also involves various biological and chemical tests which also operates within the legal frame work. The basic idea behind the regulations of medicines is to bring harmonization in use of medicines which are effective, safe and have a good quality available for human consumption.

How to have Control on Medicine Regulation

It is submitted that the medicine regulation works according to by laws of the country in which it is being produced whether traditional or generic or novel, but the main aim is promoting and protecting the public health. The activity and the scope of regulations regarding its implementation vary from country to country and the main

idea that demands is application of sound medical, scientific and technical knowledge in skills which operates within the legal frame work. The medicine /product regulation starts from the basic concept of the core product which is available in the environment either from flora or fauna which are either used as a whole or in a part or as an extract mixed with some chemical(s) or other ingredient (other flora or fauna) to produce any medicine. The regulations then come into picture includes manufacture, trade both import and export, promotion**,** distribution, advertisement, research, human consumption and the government. Thus it is necessary for the production of any medicine; the laws of the country are to be seen to have effective control on the production, distribution and consumption of medicine.

[11] Principal Medicine's Regulatory Functions

- Licensing of manufacture, import, export, distribution, promotion and advertising of medicines.
- Assessing the safety, efficacy and quality of medicines and issuing marketing authorization for individual products.
- Inspecting and surveillance of manufacturers, importers, wholesalers and dispensers of medicines.
- Controlling and monitoring the quality of medicines on the market including GMP.
- Controlling promotion and advertising of medicines.
- Monitoring safety of marketed medicines including collecting and analyzing adverse reaction reports if any.
- Providing independent information on medicines to professional and the public for analysis.

It is submitted that the regulatory issues relating to medicine is based upon science and the various scientific methods used, to have effective control to meet the criteria of it being safe, effective and of good quality. The regulatory functions that involve in the contribution relating to regulation of medicine not only include researches, manufacturers, traders, consumers, health professionals, government but also deal with socio-economic and political factors which make regulation implementation both technically and politically challenging. Thus it is necessary to have effective control on regulations of these medicines. It is necessary to have effective cooperation between national regulatory authorities of government which include political will and commitment to regulation of the medicines which are easily available and accessible to public at a fair price which are safe, effective and are of good quality. The regulatory issues are not only to be seen in relation to new medicines but are also to be seen in relation to traditional medicines or medicines mentioned in the pharmacopoeia or for the medicines for which no license is required for its production either used individually, indigenously or available for import and export. As we have seen there are various serious problems associated when the drugs are unethical, as it gives misleading information to the consumers, leading to adverse effect. So, it is necessary to have a legal framework to have an effective control on the regulatory issues relating to medicines including herbal products/ traditional medicines. WHO (World Health Organization) has been holding meetings, conferences, seminars etc on such issues and the member signatories to the agreement under WHO (World Health Organization) have to frame the laws accordingly, to bring harmonization of regulatory issues all over the world. India being signatory to WHO and TRIPS, have brought many changes in the laws to bring it in parity with the International standards and has amended the Drugs and Cosmetic Act and Food and Safety Standards Act, time to time. The basic idea behind the guidelines of WHO is to promote the public health and to provide the medicines which are safe, effective and are of good quality either nationally or internationally.

Registration of Drugs (US, EU and India)

It is submitted that broadly speaking in European Union / US there is distinction between the kind of drugs / herbal products available in the market, which can be available either with the prescription or without the prescription. Each country has its own pharmacopeia like India has Indian pharmacopoeia, Europe has the European pharmacopeia etc.

(i) USA

In US the herbal products which are sold in the market without prescription are over-the-counter medicines/ drugs (OTC medicines/drugs) which mean the prescription is not required for these kinds of herbal products and they are obtained on the basis of knowledge and experience being safe for self-medication. The other medicines which are available are only on the basis of prescription. These medicines with or without prescription are distributed and used in the country by the National Competent Regulatory Authority and the manufacturing plants as well as the laboratories are available for inspection to have quality control to ensure the drugs are safe and effective. The drugs can be either vaccine, antibiotics, anti-bodies, life saving drugs, generic drugs, herbal drugs or over-the-counter drugs. The regulatory authorities relating to prescription drugs and non-prescription are different. The nonprescription products are controlled by as per guidelines laid by DESHA (Dietary Supplements Health Education Act) under the FDA (Food Drug Administration) guidelines and the other prescription drugs have to follow the regulatory issues as laid down by FDA (Food Drug Administration) under the guidelines of the

Food, Drug, and Cosmetic Act. WHO has issued guidelines for both over-the-counter and for the prescription drugs. [12]

It is submitted that the herbal plants which are used in production of multivitamins or a support system of the body either as neutraceuticals / anti-oxidants / support system relating to particular system of body or herbal medicines/ products with no claims of definite cure or herbal medicines (ayurveda, siddha or unani or homeopathy) without clinical trials, are sold as dietary supplements. There is no need of clinical tests/trials and are covered under the DSHEA. Whereas the herbal plants which are used in the production of generic medicines or novel medicines or traditional medicines with claims of curing any disease, there is need to follow the procedure mentioned in the Food, Drugs and Cosmetics Act or in the pharmacopeia which clearly specify four stages of clinical tests/trials before any medicine is being available for human consumption which includes the quality, stability, safety and efficacy. The general rules which the pharmaceutical company has to follow also includes good manufacturing practice (GMP) along with the regulatory issues for production of herbal and any other kind of medicines. Under the overall context of quality of herbal medicines, WHO developed the guidelines on GACP for herbal plants for drug preparations. GACP provides general technical guidance on obtaining herbal plant materials (i.e. selection of seed, sowing, collection of herb etc.) to of good quality for the sustainable production of herbal drugs. The main objectives of these guidelines are to guide the formulation of national and/or regional GACP guidelines and GACP monographs for herbal plants and related standard operating procedures and to encourage and support the sustainable cultivation of herbal plants of medicinal value to be of good quality.

(ii) European Union

The Directive in European Union establishes a regulatory approval process of market for all the herbal medicines and homeopathic medicinal products in the European Union (EU) to be safe and of good quality. The herbal medicines sold in the European Union (EU) are required to have prior approval of the market before being actually sold in the market to ensure that these herbal medicines are of acceptable quality and safety. These herbal medicines do not require the clinical trial data before being registered for sale but requires a long history of usage of that herbal medicine in the European Union with monographs. Only those herbal medicines can be sold without market approval in the European Union which has minimum thirty years of history of sale within the European Union and for non-EU herbal medicines with thirty years of history of sale of herbal medicines with minimum period of sale of fifteen years in the European Union. It requires each EU Member State to set up a traditional herbal registration scheme for manufactured traditional herbal medicines that are suitable for use without medical supervision. The scheme of registration is simplified registration procedure for those herbal medicines with a history (above stated) of its traditional use and acceptable for safety and quality.13 Herbal medicine are also known as phytotherapy, botanical medicine, phytomedicine or non-conventional medicines which are system of medicine derived from plants and plant extracts by using various remedies to treat disorders/ disease and maintain good health of body. All manufactured herbal medicines placed on the European market for sale must have either a Traditional Herbal Registration (THR) or a Product Licence (PL). As a result of this EU Directive, the herbal medicines have two key methods for herbal companies to market their herbal remedies i.e. Traditional Herbal Registration or a Product Licence (some herbal medicines sold in UK must demonstrate safety, quality and efficacy as those for pharmaceutical medicine and be accompanied with information on safe usage).[14]

It is submitted that a GRS (Global Regulatory Service) is the product assessment for any product to be sold in EU consists of a high level review on that product including herbal medicine (including literature and comparator product research) and the said preliminary or feasibility report will form part of the full Expert and Safety reports required for submission under the Traditional Herbal Medicines Registration Scheme (THMRS) to judge whether there appears to be sufficient 'Traditional Use' evidence for a herbal sufficient for Product Licence. Good manufacturing practice (GMP) and Good Agricultural and Collection Practice (GACP)guidelines for herbal medicines is also to be followed in all such cases. The pharmacopoeia medicines has also to follow the prescribed regulatory framework with active pharmaceutical ingredient and finished dosage having scientific assessment of safety, efficacy and quality along with GMP and GACP.

(iii) India

It is submitted that in India the manufacture, distribution and sale including import and export of drugs is regulated under the provisions of the Drugs and Cosmetics Act and the Drugs and Cosmetic Rules. The regulation of production herbal medicines (Ayurveda, Siddha, Unani and homeopathy), generic mdicines and allopathic medicines by pharmaceutical companies including their import and export is regulated under the provisions of the said act and its rules. The provisions of Chapter IVA and III, of the Drugs and Cosmetics Act explains the matters relating to manufacture, sale and its distribution of the herbal medicines (Ayurveda, Yoga and Naturopathy, Unani, Siddha) and homeopathy. The allopathic medicines are manufactured, sold and distributed as per the provisions of Chapter IV of the Drugs and Cosmetics Act. The import of medicines is regulated under the Chapter III of the Act. In India all the herbal medicines are sold and distributed as medicines which are manufactured according to the authorized book list mentioned in Schedule A of the Drugs and

Cosmetics Act or the pharmacopeia for Ayurveda, Siddha, Unani and homeopathy medicines and have to follow the same procedure as mentioned therein Schedule B. These medicines are not to follow any four stages of clinical trials / tests as required for synthetic or modern medicines. The herbal medicines (Ayurveda, Siddha, Unani) and homeopathy are manufactured, sold and distributed without any such clinical trials and as per monographs described in detail, mentioned in authorized books of Schedule A (Ayurveda, Siddha, Unani) or Schedule B (homeopathy) or that mentioned in the pharmacopeias. The licence is issued to the pharmaceutical companies and has to follow the guidelines of good manufacturing practices. These pharmaceutical companies also look into the provisions of other Acts i.e. "the Biological Diversity Act", "the Geographical Indications of Goods Act" and "the Protection of Plant Varieties and Farmers Rights Act", when any herb is selected for manufacture of these herbal medicines. Although these are alternate medicines for the outer world but in India these are sold as medicines. The licences are issued to the pharmaceutical companies according to Schedule-T (Ayurveda, Siddha, Unani) as "Classical Medicines" of Schedule Books or mentioned in the pharmacopeia, Schedule-M1 for homeopathic medicines mentioned in the pharmacopeia. However the patent herbal medicines (Ayurveda, Siddha, Unani) and Homeopathy have to follow the same procedure as mentioned in the patent documents, these have to follow the clinical trials/tests as that for modern medicines and the pharmaceutical companies are issued to license under the "proprietary medicines". The allopathic medicines whether having patents or not, have to follow all the stages of clinical trials before being sold in pharmacies. The generic medicines also have to follow the same procedure as that of allopathic medicines. However the herbal medicines which are manufactured or prepared by the doctor for his patients do not require any such license for such manufacturing or preparation.

All the drugs/medicines manufactured have to follow the good manufacturing practice and the pharmaceuticals are required to maintain the records as prescribed under the act. The medicines manufactured should not be adulterated, misbranded or spurious and have to follow all the safety standards as per the Act. The Central Government is authorized under the Drugs and Cosmetics Act to make such rules15after consulting with the board or otherwise, to prohibit the import16/prohibit[17] manufacture, sale and distribution of medicines and prohibit medicines against the public interest[18] or against the provisions of the DC Act, before being notified in the Official Gazette.

Regulatory System in India vis-à-vis in Europe and US

It is submitted that herbal medicines/ products have gained popularity as we see from its consumption since last two few decades. Herbal medicines or traditional medicines or herbal products are the complex mixtures of organic chemicals that may form any raw or processed part of a plant, including root, shoot, stems, leaves, seeds or flowers or fruit which are produced and sold in market as required for pharmaceutical drugs. Although it is generally considered that the herbal products or the herbal medicines which are extracted from it are perceived to be natural and therefore are safe without any side effects. However the commercialization and regulation of herbal medicines has constraints to its access in Indian herbal drug industry with regard to its manufacture and sale abroad. The Indian herbal drug industry is facing at present many challenges with regard to marketing, sale, production and commercialization approval for traditional or herbal medicines in India as well as abroad. The regulatory systems with regard to traditional or herbal medicine/ products in India differs from the regulatory system existing in the foreign countries, due to which various challenges are faced by the Indian drug industry and thus faces major hindrances for exporting it. The major challenge which has emerged for exporting Indian herbal or traditional medicines is the quality, safety and standardization of raw materials and herbal formulations. The major drawbacks being faced by the Indian herbal industry includes insufficient regulatory guidelines for good manufacturing practices, non-implementation of good agriculture and collection practices and weak implementation of the Drug and Cosmetic Act.

As we know that day by day the demand for traditional or herbal medicines/ products is growing and has also gained popularity not only in developing countries but also in developed countries. There is growing demand of ayurveda as well as other traditional medicines worldwide. As we see in India about 80% of the rural population uses traditional medicines or indigenous system of medicines for curing any disease.[21] It is however estimated that around 960 plant species are used by the Indian industry for manufacturing herbal medicines and the turnover is more than Rs.80 billion. And if we see the turn over with regard to the export of herbal medicines of AYUSH products occupy only 3% of total Indian pharmaceutical export. The main export of the herbal sector basically consists of raw materials which is 70% of the total export and is estimated about 10 billion per annum and 30% of the export is of herbal extracts. Thus India's share with regard to export of herbals is less than 1%.[22]

It is submitted that in India as we have seen the use of various traditional medicines have been practiced since ages and are deep rooted in the Indian culture. Even the history of India reveals that there had been invasions of various intruders from the different parts of the world and with them they have brought various indigenous cultures of traditional medicine which are extensively till date being practiced in India.

The Indian herbal manufacturing companies have no facilities for even its research & development and the data has revealed that only 10% of the total herbal drug industry has in-house research & development facilities. The manufacturers of herbs have limited marker-based studies and they generally follow traditional

method for standardizing raw materials and formulations as the data for reference of standards are not available for all the herbal plants used in medicine preparation the manufacturers follow either traditional physical, chemical or physiochemical methods for standardizing the raw materials and formulations required for preparation of herbal medicines. Thus the quality control of herbal medicines is not elaborate and is insufficient due to lack of regulatory guidelines with regard to selection of raw material, sowing, growing, producing or storing and thus the contamination occurs which is one of the main drawback and hindrance of export of herbal medicines from India. The contamination of heavy metals or prohibited metals or pesticides or insecticides etc. can also occur even at stage of production of herbal medicines. Although the guidelines have been issued for preclinical safety evaluation of ASU and other traditional medicines but the guidelines for marker-based identification of active components and standardization of herbal medicines are yet to be achieved. Apart from quality control, safety, efficacy, good agriculture and collection practice (GACP) and goods storage practice are also important for manufacturing of herbal medicines. India in parity with guidelines of world health organization developed the National Medicinal Plants Board to work on guidelines on good agriculture practice and good field collection practice with regard to raw material required for production of good quality, safe and efficacy herbal medicines. The general study has revealed that the manufacturers or the traders are mostly unaware of these guidelines due to lack of awareness and education. Even the laws at present in India are not stringent in this regard so as to have effective control on good agriculture and collection practices. Moreover the companies and the associations associated with post operational period for preparation of herbal medicines like post-harvest of raw material, storage of raw material or transportation of raw material, these companies are not aware of standardized and certified raw materials and does not comply with the Indian pharmacopoeia which is necessary for safe, effective and good quality medicines. However due to this lack of education and guidelines awareness the exporters of Indian Herbal Industry face problem for selling herbal medicines abroad as these regulatory norms including GACP, GSP, common technical dossier(CTD) and Quality Control(QC) are required to be implemented for proper growth of traditional/herbal medicine industry. The goods manufacturing practices also need to include both technical and non-technical aspects to avoid adulteration and contamination in production of herbal medicines, and should run independently and effectively to assure good quality and safe herbal medicine. Therefore apart from Schedule-T other stringent guidelines are also required so that the complete documentation data is available which gives proper quality and efficacy assurance of herbal medicines being produced and are safe in all measures.[29]

Label Claim in India

Labeling

General requirements

1. Every pre-packed food shall carry label in English or Hindi provided any other language in addition to it can be provided as required under the regulations.
2. The label on pre-packed food should not be false or deceptive or misleading or in any manner creating erroneous impression regarding its character.
3. The label should not get separated from the pre-packaged food container.
4. The label contents should be clear, legible, prominent and indelible at the time of purchase and use by the consumer. Where any container is covered by wrapper, the information on the label should be readily legible through outer wrapper and should not be obscured.49

Labeling on pre-packaged food

Other than above mentioned general labeling requirements the label should also contain following information

a. List of ingredients in descending order of their composition used in the product by weight or volume at the time of its manufacture.
b. It should specify the list of ingredients following in the class such as starch, edible vegetable oil/ fat , cheese, milk, milk products, gum base, poultry meat ,cocoa solids, milk solids, crystallized foods etc provided if any pork fat or beef or lard or its extract is present it should be declared by specific names.
c. Where an ingredient is product of two or more ingredients, the list of ingredients should be mentioned in the descending order by weight or volume but if the total quantity of compound ingredient is less than 5% of the food there is no need to declare list of ingredients of compound ingredient.
d. If water is added in the food it should be mentioned in the list of ingredients except in cases where water is part of brine, syrup, or broth used in compound food and be mentioned in the list of ingredients. Provided where any volatile or water ingredient evaporates during the course of manufacture is not to be mentioned. provided where condensed or dehydrated food which is to be re constituted by adding water, the weight or volume is to be declared in descending order in ingredients of the product according to the directions on the label.
e. Where any packaged food is mixture or combination it shall disclose the percentage of the ingredients at the time of manufacture of food and it should be through words or pictures or graphics.
f. Where the ingredient is not within the name of food and is necessary to be characterized, if not mentioned

can mislead or deceive the consumer. Provided where any flavoring agent is used, its ingredients are not to be disclosed. Provided where the drained net weight is indicated on the label or a pictorial representation for serving suggestion is to be made for use and information of consumer, no such ingredients disclosure is required. Provided where any fruit pulp or fruit juice is the bottle containing liquid milk or liquid beverage having milk, soft drink, ready to serve fruit beverages or carbonated water, it is to be mentioned on the bottle body.[50]

WHO Regulations for herbal Medicines

It is submitted that as per WHO global survey on the national policy and for the regulations of these "traditional/ herbal products" various challenges and difficulties are seen monitoring these products to be safe, effective and of good quality for human consumption. As we see that there are various type of herbal products / medicines used worldwide both in developing and developed countries to cure diseases. Broadly we can classify and categorize these arious herbal products / medicines into four types of categories, namely, "indigenous herbal medicine", "herbal medicine in system", "modified herbal medicines" and "imported products with herbal medicine as base". The "indigenous herbal medicines" are generally used by its local community/ indigenous people for the treatment of any kind of disease which is in their folklore. The "herbal medicines in system" are those medicines which are manufactured for classical ayurvedic, siddha, unani and homeopathy medicines or according to the pharmacopoeia. "Modified herbal medicines" similar to modern medicines including specific dose, dosage, mode of administration, ingredients, preparation and medical indications which meets the regulatory standards of quality, safety & efficacy. The "imported products with herbal based medicines" have the complete quality, safety & efficacy data to ensure its authenticity and are submitted to the national authority of the importing country. So we see that the various ingredients either in the "herbal products/medicine/drugs" and in the "dietary supplements" contains vitamins, minerals, proteins, amino acids, enzymes etc. which are sold over- the-counter/ non-prescription as compared to drugs which are only sold in pharmacies on prescriptions. So we see that there is very thin sliver line to distinguish the "herbal products / drugs" as "dietary supplements" or "drugs" to be sold commercially and the categorization of the same highly subjective. There is no specific judicial or statutory yardstick available to measure the categorization that the herbal medicines are either to be treated as "herbal products / drugs" or "dietary supplements" or "drugs". Moreover in India we see the "herbal products / medicines / drugs" which are manufactured by doctor for his patients, too fall in the categories of "drugs" and are not regulated by the D C Act and its rules.

It is submitted that as we see that these dietary supplements being used at global level, with the safe and clean history for treatment of any disease or curing any disease but these products may have contamination of germs, pesticides or toxic heavy metals in the herbs being used for its manufacture. US and WHO has also shown a great concern for the sale of "over-the-counter/ non prescription drugs" as these are being sold in or out of pharmacy' without any clinical data as ensure its quality for the safety of consumers. Even the guidelines have been issued by WHO for the regulations of these "dietary supplements / herbal products or medicines or drugs" to ensure that the herbs used are not toxic, that too without side any side-effect are safe. We have seen as soon as when there is any "claim" in the documentary record that any herb "cures" or "prevent" any disease, it is to be treated as "drugs", whereas the said claim of curing such disease is not be mentioned in the label claim of the drug in which it is sold in the pharmacy on prescription basis. If we see the "herbal products / medicines / dietary supplements" which clearly specifies the list of ingredients in detail on the "label" of the container in which it is sold either "in pharmacy" or "outside pharmacy", which is purchased by the consumer by the seeing contents, for curing any disease, as these "herbal products / medicines / dietary supplements" are readily available on non-prescription basis, though it may or may not be prescribed by the pharmacists/doctors, but no such claim is either mentioned in its documentary records which regulates its manufacturing / production or on the container of the label of the said product in which it is sold.

Herbal Medicine

An herb is usually a plant or plant extract or part of plant used for its scent, flavour, remedy or therapeutic properties. Herbal medicines or products are one type of dietary supplements which is sold in the form of tablets, capsules, extracts, powders, teas, fresh or dried plants. Mostly people use herbal medicines or products to maintain or improve their health by holistic approach. People generally believe that these herbal products / medicines labeled as "natural" are always safe and good for their health which is not necessarily true always. These do not have to go through clinical trials as that for synthetic drugs do. Some herbs like ephedra and comfrey may cause serious harm to the body and some herbs can interact with other drugs or other dietary supplements.

CONCLUSION

The FDA considers herbal supplements foods, not drugs. Therefore, they are not subject to the same testing, manufacturing, and labeling standards and regulations as drugs.

The World Health Organization (WHO), the specialized agency of the United Nations (UN) that is concerned with international public health, published Quality control methods for medicinal plant materials in 1998 to support WHO Member States in establishing quality standards and specifications for herbal materials, within the overall context of quality assurance and control of herbal medicines.

In the European Union (EU), herbal medicines are regulated under the Committee on Herbal Medicinal Products.

In the United States, herbal remedies are regulated dietary supplements by the Food and Drug Administration (FDA) under current good manufacturing practice (cGMP) policy for dietary supplements. Manufacturers of products falling into this category are not required to prove the safety or efficacy of their product so long as they do not make 'medical' claims or imply uses other than as a 'dietary supplement', though the FDA may withdraw a product from sale should it prove harmful.

The growth of the pharmaceutical industry and the unceasing development of new and more effective synthetic and biological medicinal products have not diminished the importance of medicinal plants in many societies. On the contrary, population growth in the developing world and increasing interest in the industrialized nations have greatly expanded the demand for medicinal plants themselves and the products derived from them. Regulations in countries for the assessment of the quality, safety and efficacy of medicinal plants, and the work of WHO in supporting the preparation of model guidelines in this field, have been helpful in strengthening recognition of their role in health care. It is hoped that assessment of these traditional remedies could become the basis for a future classification of herbal medicines, as well as for evaluative studies on their efficacy and safety, and their potential use in national health care systems in different parts of the world.

It is submitted that the legal status and the practice of use of herbal drugs/ medicines/ products vary significantly from one country to another thus making it difficult for its free circulation. European regulations i.e. Directives are the most comprehensive among most of the global regulations for herbal medicinal products. Food and Drug Administration (FDA) guidelines for United States on herbal/ botanical drug products are parallel and closely follow the route as that for a synthetic new chemical entity. Indian regulations are also developing vis-a-vis global regulations for herbal drug products. Indian regulations relating to herbal medicines/ drugs are still at nascent stage as compared to regulations of Europe and US. Harmonization of regulations, like that in European Countries, US and other developed countries could overcome the barrier for efficient trade as well as uniform standards for herbal drugs/ medicinal products.

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