

VALUE ADDITION BY STANDARDIZATION OF HERBAL DRUGS AT GLOBAL LEVEL- A REVIEW

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World Health Organization (WHO) and the European Union (EU) issued several guidelines concerning safe and appropriate use of herbal medicines with consistency in composition and biologic activity as essential requirements. However, herbal drugs frequently fail to meet this standard due to difficulties in identification of plants, genetic variability, variations in growing conditions, diversity in harvesting procedures and processing of extracts, and the lack of information about active pharmacologic principles. This creates a considerable hindrance in the export of even very efficacious good quality but unstandardised products. Therefore standardization of herbal drugs is important parameter for value addition, safety and efficacy of drugs. This communication intends to highlight the role of standardization in of products at global level.

KEYWORDS: Safety and efficacy, Standardization, Value addition.

INTRODUCTION

Traditional medicine (TM) is a comprehensive term used to refer both to systems such as traditional Chinese medicine, Indian Ayurveda and Arabic Unani medicine, and to various forms of indigenous medicine. In countries where the dominant health care system is based on allopathic medicine, or where TM has not been incorporated into the national health care system, TM is often termed "complementary", "alternative" or "non-conventional" medicine [1]. The pharmacopoeia of folk series as well as professional medical systems like Chinese, Ayurvedic, Unani and biomedicine contain thousands of medicines made from leaves, herbs, roots, bark, animal, mineral substances and other materials found in nature [2-3]. Plants and animals have been used as a source of medicines from ancient times [4-6], and even in modern times, animal and plant-based systems continue to play an essential role in health care [7-10]. Wild and domestic animals and their by-products (e.g., hooves, skins, bones, feathers, and tusks) form important ingredients in the preparation of curative, protective and preventive medicine [7]. Additionally, a significant portion of the currently available non-synthetic and/or semi-synthetic pharmaceuticals in clinical use is comprised of drugs derived from

higher plants [8-9], followed by microbial, animal and mineral products, in that order [10]. As a result, the World Health Organization (WHO) and the European Union (EU) issued several guidelines concerning safe and appropriate use of herbal medicines [11-12]. For safe and effective use of herbal drugs, consistency in composition and biologic activity are essential requirements. However, herbal drugs frequently fail to meet this standard due to difficulties in identification of plants, genetic variability, variations in growing conditions, diversity in harvesting procedures and processing of extracts, and the lack of information about active pharmacologic principles [13]. Therefore standardization of herbal drugs is important parameter for safety and efficacy of drugs.

Global market of world

According to American Botanical Council data, total sales of herbal dietary supplements have grown steadily from 2004 to 2005, indicating a 3.4% and 2.1% increase, respectively, compared to 2003 [14]. The Slone Epidemiology Center reported a 20% increase in use of herbals natural supplements from 2004 to 2005, and a noticeable rise in use among the pediatric population (5.3% compared to 2.6% in 2004) was noted [15]. In USA, herbal drugs are currently sold in health food stores with a

turnover of about \$ 4 billion in 1996 which is anticipated to double by the turn of the century [16]. In India, the herbal drug market is about \$ one billion and the export of plant-based crude drugs is around \$ 80 million [17]. Herbal medicines also find market as nutraceuticals (health foods) whose current market is estimated at about \$ 80–250 billion in USA and also in Europe [18]. The basic requirements for gaining entry into developed countries include well documented traditional use, single plant medicines, medicinal plants free from aflatoxins, radioactivity, pesticides, heavy metals, etc., standardization based on chemical and activity profile, and safety and stability. However, mode of action studies in animals and efficacy in human will also be supportive. Such scientifically generated data will project herbal medicine in a proper perspective and help in sustained global market. The herbal medicine market in 1991 in the countries of the European Union was about \$ 6 billion (may be over \$ 20 billion now), with Germany accounting for \$ 3 billion, France \$ 1.6 billion and Italy \$ 0.6 billion [18]. The turnover of herbal medicines in India as over-the-counter products, ethical and classical formulations and home remedies of Ayurveda, Unani and Siddha systems of medicine is about \$ 1 billion with a meager export of about \$ 80 million. Psyllium seeds and husk, castor oil and opium extract alone account for 60% of the exports. 80% of the exports to developed countries are of crude drugs and not finished formulations leading to low revenue for the country. Thus the export of herbal medicines from India is negligible despite the fact that the country has a rich traditional knowledge and heritage of herbal medicine. Considering the huge herbal medicine and nutraceutical market in developed countries, India should reconsider exporting crude herbal drugs. India is the largest grower of Psyllium (*Plantago ovata*) and Senna (*Cassia senna*) plants and one of the largest growers of Castor (*Ricinus communis*) plant. These are also exported in large amounts and yet our market share is dismal because of export of crude extracts/drugs. Twenty other plants are commonly exported as crude drugs worth \$ 8 million. Five of these, namely *Glycyrrhiza*

glabra, *Commiphora mukul*, *Plantago ovata*, *Aloe barbadensis* and *Azadirachta indica* are even used in modern medicine. The plants *Glycyrrhiza glabra*, *Piper longum*, *Adhatoda vasica*, *Withania somnifera*, *Cyperus rotundus*, *Tinospora cordifolia*, *Berberis aristata*, *Tribulus terrestris*, *Holarrhena antidysenterica* and *Boerhavia diffusa* have been used in 52 to 141 herbal formulations and triphala (*Terminalia chebula*, *Terminalia bellerica* and *Embelica officinalis*) alone have been used in 219 formulations (Table 1). India is one of the 12 mega biodiversity centre having over 45,000 plant species. Its diversity is unmatched due to the presence of 16 different agro climatic zones, 10 vegetative zones and 15 biotic provinces. The country has 15,000–18,000 flowering plants, 23,000 fungi, 2500 algae, 1600 lichens, 1800 bryophytes and 30 million micro-organisms [19-20].

Table 1 Frequency of occurrence of medicinal plants in herbal formulations in India

Common name(Botanical name)	No. of herbal formulations
Ashwagandha (<i>Withania somnifera</i>)	109
Cranberry (<i>Vaccinium macrocarpon</i>)	10
Daruharidra (<i>Berberis aristata</i>)	65
Eleuthero (<i>Eleutherococcus senticosus</i>)	9
Gokshura (<i>Tribulus terrestris</i>)	65
Gulacha (<i>Tinospora cordifolia</i>)	88
Kutaja (<i>Holarrhena antidysenterica</i>)	59
Mastak (<i>Cyperus rotundus</i>)	102
Pipali (<i>Piper longum</i>)	135
Punarnava (<i>Boerhavia diffusa</i>)	52
Triphala (<i>Terminalia chebula</i>)	219
Vasaka (<i>Adhatoda vasica</i>)	110
Yashtimadhu (<i>Glycyrrhiza glabra</i>)	141

Regulatory aspects and approval of herbal drugs

The legal process of regulation and legislation of herbal medicines changes from country to country. The reason for this involves mainly cultural aspects and also the fact that herbal medicines are rarely studied scientifically. Thus, few herbal preparations have been tested for safety and efficacy. The WHO has published

guidelines in order to define basic criteria for evaluating the quality, safety, and efficacy of herbal medicines aimed at assisting national regulatory authorities, scientific organizations and manufacturers in this particular area [21]. Furthermore, the WHO has prepared Pharmacopiel monographs on herbal medicines and the basis of guidelines for the assessment of herbal drugs [22-23]. Several regulatory models for herbal medicines currently exist, including prescription drugs, over-the-counter drugs, traditional medicines and dietary supplements. Thus, the need to establish global and/or regional regulatory mechanisms for regulating herbal drugs seems obvious [21].

Indian Herbal Trade in World Scenario

The utilization of herbal drugs is on the flow and the market is growing step by step [24]. The annual turnover of the Indian herbal medicinal industry is about Rs. 2,300 crores as against the pharmaceutical industry's turnover of Rs. 14,500 crores with a growth rate of 15 percent [25]. The export of medicinal plants and herbs from India has been quite substantial in the last few years. India is the second largest producer of castor seeds in the world, producing about 125000 tonnes per annum. The major pharmaceuticals exported from India in the recent years are isabgol, opium alkaloids, senna derivatives, vinca extract, cinchona alkaloids, ipecac root alkaloids, solasodine, Diosgenine/16DPA, Menthol, gudmar herb, mehdi leaves, papian, rauwolfia guar gum, Jasmine oil, agar wood oil, sandal wood oil, etc [26]. The turnover of herbal medicines in India as over-the-counter products, ethical and classical formulations and home remedies of traditional systems of medicine is about \$ one billion and export of herbal crude extract is about \$ 80 million [24]. The herbal drug market in India is about \$1 billion. Some of the important medicinal plants, whose market potential is very high, have been summarized in Table 2.

Need of Standardization

Every Herbal Formulation must be standardized as per WHO guidelines [27]. The objective of WHO guidelines is to define basic criteria for the evaluation of quality, safety and

efficacy of drugs herbal medicines [28]. India is one of the world's twelve leading biodiversity centers with the presence of over 45,000 different plant species, out of this about 15,000- 20,000 plants have good medicinal properties of which only about 7,000-7,500 are being used by traditional practitioners. The Siddha system of medicine uses around 600, Ayurveda 700, Unani 700 and modern medicine about 30 plants species. Projection is being made that after information technology, herbal technology will be India's biggest revenue earner [29].

India has a great role to play, as supplier of herbal products not only to meet the domestic needs, but also to take advantage of the tremendous export potential. To be a global supplier of herbal medicines conforming to international specification the following aspects are still demanding the attention:

1. Proper botanical identification of all medicinal plants in Indian System of Medicine. All herbal ingredients in preparation to be specified by their botanical names besides their popular/common names.
2. Processing of medicinal plants in a scientific, economic and safe way using similar ones used for modern drugs.
3. Isolation and chemical characterization of acute ingredients including inorganic constituents, wherever possible.
4. Pharmacological, toxicological and clinical studies to ascertain their efficacy and safety.
5. Standardization to ensure uniformity. The use of medicinal plants in combination to be limited to facilitate analysis and to apply quality control and standardization parameters to herbal drug preparations.
6. Documentation of research to make it evidence based.

Such scientifically designed aspects will project herbal medicine in a proper perspective and help in sustained global market [30]. An estimate of WHO demonstrates about 80% of world population depends on natural products for their health care, because of side effects and high cost of modern medicine [31]. World Health Organization currently recommends and encourages traditional herbal remedies in natural

health care programs because these drugs are easily available at low cost and are comparatively

Table 2: Medicinal plants with rich market potential in India

<i>S. No</i>	<i>Name of the plant (Family)</i>	<i>Common name</i>	<i>Medicinal uses</i>
1.	Allium sativum (Liliaceae)	Garlic	Anti-hypertensive, Anti hyperlipidemic, Platelet aggregation suppressant
2.	Andrographis paniculata (Acanthaceae)	Kalmegh	Stomachic, Hepatoprotective, Dyspepsia, Anthelmintic, Bitter tonic
3.	Asparagus recemosus (Liliaceae)	Satavatri	Galactogogue, Diurectic, Anti-dysenteric, Nervine disorder
4.	Azadirachta indica (Meliaceae)	Neem	Anthelmintic, Astringent , Anti-septic, Purgative, Emollient, Anti-plaque
5.	Berberis aristata (Berberidaceae)	Daru haridra	Astringent, Febrifuge, Laxative, In menorrhagia, In Liver and spleen Diseases
6.	Commiphora weightii (Burseraceae)	Guggul	Hypocholesteremic, Hypolipidemic, Anti-inflammatory, Anti-rheumatic
7.	Garcinia camboga (Guttiferae)	Kokum	Anti-obesity, Hypolipidemic, Anti-fungal, Anti-ulcer
8.	Gymnema sylvestre (Asclepiadaceae)	Gudmar	Cardiac stimulant, Anti-diabetic, Larvicidal, Stomach ache, Diarrhea
9.	Holarrhena antidysenterica (Apocynaceae)	Kutuja	Amoebicidal, Anti-protozoal, Anti-tuberculous, In facial acne
10.	Nardostachys jatamansi (Valerianaceae)	Jatamansi	Diuretic, Stomachic, In constipation, Anti-spasmodic, In menstruation
11.	Ocimum teniflorum (Labiatae)	Holi basil	Aromatic, Stimulant, Tonic, Anti-oxidant, Anti-inflammatory, Anti-diabetic
12.	Picrorhiza kurroa (Scrophulariaceae)	Kutki	Hepatoprotective, Immunomodulatory, Jaundice, In periodic Fever
13.	Plantago ovata (Plantaginaceae)	Isabgol	Aphrodisiac, Anti-inflammatory, Demulcent, Laxative, Emollient
14.	Saraca indica (Leguminosae)	Ashoka	Gynecologic disorders, Uterine tonic, Sedative, In menorrhagia
15.	Tinospora cordifolia (Menispermaceae)	Guduchi	Anti-cancer, Anti-malarial, Anti-periodic, Anti-allergic, Anti-spasmodic, Anti-inflammatory, Anti-leprotic, Anti-oxidant
16.	Withania somnifera (Solanaceae)	Ashwgandha	Sedative, Anti-rheumatic, Diuretic, Anti-inflammatory, Anti-stress, Anti-tumor, Immunomodulator

safe. People's faith in such remedies is reflected by a whooping turnover of 450 Crores annually in herbal market besides a healthy 11% annual growth rate and the increasing export potential has attracted several large and medium scale pharmaceutical industries and even multinationals to jump on to the band wagon [30]. The importance of medicinal plants in the national economy and their potential for the rapid growth of herbal products, perfumery and allied industry in India has been emphasized from time to time [26]. New trends are emerging in the standardization of herbal raw materials whereby it is carried out to reflect the total content of

phytoconstituents like polyphenols, which can be correlated with biological activity [32]. The major traditional sector pharma, namely

Himalaya, Zandu, Dabur, Hamdard, Maharishi, etc, are Standardizing their herbal Formulations by Chromatography techniques like TLC/HPTLC finger printing, etc [33].

CONCLUSION

The quality of the source materials used in production of herbal products is determined by environmental conditions, cultivation, harvesting time, field conditions and post harvest/ collection and transport and storage .At the same time lack of standard operative procedures and parameters

along with herbal preparations contaminated with pesticides, microbes, heavy metals, chemical toxins and adulterants create a major hurdle for registration of these products in global market. There is lack of evidence based data regarding the quality, safety and efficacy of the products. The most important challenge which prevailing situations pose in front of Indian Herbal product industry is to get registration of the products as per Traditional Herbal Medicinal Products (THMPD) in European Union. Hence Indian herbal industry should be fully aware of all these regulations so that exports can be increased.

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