

Herbal medicine

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Herbal medicines are the synthesis of therapeutic experiences of generations of practising physicians of indigenous systems of medicine for over hundreds of years while nutraceuticals are nutritionally or medicinally enhanced foods with health benefits of recent origin and marketed in developed countries. The marketing of the former under the category of the latter is unethical. Herbal medicines are also in great demand in the developed world for primary health care because of their efficacy, safety and lesser side effects. They also offer therapeutics for age-related disorders like memory loss, osteoporosis, immune disorders, etc. for which no modern medicine is available. India despite its rich traditional knowledge, heritage of herbal medicines and large biodiversity has a dismal share of the world market due to export of crude extracts and drugs. WHO too has not systematically evaluated traditional medicines despite the fact that it is used for primary health care by about 80% of the world population. However, in 1991 WHO developed guidelines for the assessment of herbal medicine. Suggestions for herbal medicine standardization are outlined. The scenario and perceptions of herbal medicine are discussed.

HERBAL medicine is still the mainstay of about 75–80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. However, the last few years have seen a major increase in their use in the developed world. In Germany and France, many herbs and herbal extracts are used as prescription drugs and their sales in the countries of European Union were around \$ 6 billion in 1991 and may be over \$ 20 billion now. 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 century¹. In India, the herbal drug market is about \$ one billion and the export of plant-based crude drugs is around \$ 80 million². Herbal medicines also find market as nutraceuticals (health foods) whose current market is estimated at about \$ 80–250 billion in USA and also in Europe³.

India is sitting on a gold mine of well-recorded and well-practiced knowledge of traditional herbal medicine. But, unlike China, India has not been able to capitalize on this herbal wealth by promoting its use in the developed world despite their renewed interest in herbal medicines. This can be achieved by judicious product identification based on diseases found in the developed world for which no medicine or only palliative therapy is available; such herbal medicines will find speedy access into those countries. Backward integration from market demands

will pay rich dividends. Strategically, India should enter through those plant-based medicines which are already well accepted in Europe, USA and Japan. Simultaneously, it should identify those herbs (medicinal plants) which are time-tested and dispensed all over in India.

The basic requirements for gaining entry into developed countries include: (i) well-documented traditional use, (ii) single-plant medicines, (iii) medicinal plants free from pesticides, heavy metals, etc., (iv) standardization based on chemical and activity profile, and (v) 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.

Herbal medicine

The World Health Organization (WHO) has recently defined traditional medicine (including herbal drugs) as comprising therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern medicine and are still in use today⁴. Or say, traditional medicine is the synthesis of therapeutic experience of generations of practising physicians of indigenous systems of medicine. The traditional preparations comprise medicinal plants, minerals, organic matter, etc. Herbal drugs constitute only those traditional medicines which primarily use medicinal plant preparations for therapy. The earliest recorded evidence of their use in Indian, Chinese, Egyptian, Greek, Roman and Syrian texts dates back to about 5000 years. The classical

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Indian texts include *Rigveda*, *Athurveda*, *Charak Samhita* and *Sushruta Samhita*. The herbal medicines/traditional medicaments have, therefore, been derived from rich traditions of ancient civilizations and scientific heritage.

Nutraceuticals

This is a term of recent origin (1979) and comprises nutritionally or medicinally enhanced foods with health benefits³. These include engineered grain, cereals supplemented with vitamins or minerals or genetically manipulated soybean and canola oil without trans fatty acids, etc. Many pharma and biotech companies have moved into this area since it does not involve regulatory clearances and offers large markets. These companies have extended the term nutraceutical to include pure compounds of natural origin like lovastatin (a lipid lowering agent from red rice yeast), docosahexaenoic acid (a cardiovascular stimulant from algae), sterols, curcumin (from plants), etc. Likewise herbal preparations are being marketed as nutraceuticals or health foods and even the minimum standards laid down by WHO are not followed. It is pertinent to mention that herbal medicines are therapeutics of the indigenous/traditional systems of medicine and it is unethical to classify them as health foods. The regulatory agencies should, therefore, step in to prevent such misuse of natural products/herbal medicines as was done by US-FDA by banning the dietary supplement cholestin (i.e. lovastatin).

Nutraceuticals are in great demand in the developed world particularly USA and Japan. Nutraceutical market in USA alone is about \$ 80–250 billion, with a similar market size in Europe and Japanese sales worth \$ 1.5 billion³. Such huge markets have arisen because of the Dietary Supplement Health Education Act passed by USA in 1994 which permits unprecedented claims to be made about food or the dietary supplement's ability about health benefits including prevention and treatment of diseases. This act has motivated pharma to include not only compounds isolated from fauna and flora but also herbal medicines as nutraceuticals, which is unfortunate. The developing countries also see this as a good opportunity and are marketing such products.

Herbal medicine market

As per available records, 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 billion³. Incidentally in Germany and France, herbal extracts are sold as prescription drugs and are covered by national health insurance. In 1996, the US herbal medicine market was about \$ 4 billion and with the current growth rate may be more than double by the turn of

century. Thus a reasonable guesstimate for current herbal medicine market worldwide may be around \$ 30–60 billion. The Indian herbal drug market is about \$ one billion and the export of herbal crude extracts is about \$ 80 million (Table 1).

The 10 best-selling herbal medicines in developed countries¹ are given in Table 2. The sales of these drugs account for almost 50% of the herbal medicine market. These drugs have been well standardized and some of them namely echinacea, garlic, ginkgo, ginseng and saw palmeto are supported with mode of action and clinical studies. Amongst the developed countries Germany holds the lead and has published individual monographs on therapeutic benefits of more than 300 herbs. In developing countries, China has compiled/generated data on over 800 medicinal plants and exports large amounts of herbal drugs. India has prepared only a few monographs and its exports are dismal.

Why herbal medicine?

Herbal medicines are being used by about 80% of the world population primarily in the developing countries for primary health care. They have stood the test of time for their safety, efficacy, cultural acceptability and lesser side effects. The chemical constituents present in them are a part of the physiological functions of living flora and hence they are believed to have better compatibility with the human body. Ancient literature also mentions herbal

Table 1. Market size of herbal medicines

Country	Drug sales in US \$ (billion)
Europe (1991)	
Germany	3.0
France	1.6
Italy	0.6
Others	0.8
Europe (1996)	~ 10.0
USA (1996)	4.0
India (1996)	1.0
Other countries (1996)	5.0
All countries (1998)	~ 30.0–60.0

Table 2. Ten best-selling herbal medicines in USA

Drug	Botanical name	Market rank as per sale
Echinacea	<i>Echinacea species</i>	1
Garlic	<i>Allium sativum</i>	2
Goldenseal	<i>Hydrastis canadensis</i>	3
Ginseng	<i>Panax species</i>	4
Ginko	<i>Ginko biloba</i>	5
Saw palmeto	<i>Serenod repens</i>	6
Aloe gel	<i>Aloe barbadensis</i>	7
Ephedra	<i>Ephedra species</i>	8
Eleuthero	<i>Eleutherococcus senticosus</i>	9
Cranberry	<i>Vaccinium macrocurpon</i>	10

medicines for age-related diseases namely memory loss, osteoporosis, diabetic wounds, immune and liver disorders, etc. for which no modern medicine or only palliative therapy is available. These drugs are made from renewable resources of raw materials by ecofriendly processes and will bring economic prosperity to the masses growing these raw materials.

Herbal medicine scenario in India

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 meagre 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.

Three of the 10 most widely selling herbal medicines in developed countries, namely preparation of *Allium sativum*, *Aloe barbadensis* and *Panax* species are available in India (Table 2). 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 tata*, *Tribulus terrestris*, *Holarrhena antidysenterica*, *Boerhavia diffusa* have been used in 52 to 141 formulations and triphala (*Terminalia chebula*, *Terminalia bellerica* and *Embelica officinalis*) alone have used in 219 formulations (Table 3). In spite of this, we have not been made to preserve their germ-plasm different localities, identification of active plants vis climatic zone and development of agrotechnology their organized farming and use as authentic material for herbal medicines for better economic gains.

India is one of the 12 mega biodiversity centres with over 45,000 plant species. Its diversity is unmatched to the presence of 16 different agroclimatic zone vegetative zones and 15 biotic provinces. The count 15,000–18,000 flowering plants, 23,000 fungi, 2500–1600 lichens, 1800 bryophytes and 30 million microorganisms⁵. India also has equivalent to 3/4 of its exclusive economic zone in the ocean harbouring a

Table 4. Major Indian medicinal plants used in three indigenous systems of medicine

Botanical name	Sanskrit name
<i>Abies webbiana</i>	Taleespatra
<i>Achyranthes aspera</i>	Apamarga
<i>Acorus calamus</i>	Vacha
<i>Aloe</i> sp.	Kumari
<i>Andrographis paniculata</i>	Bhoonimba (Kalmesh)
<i>Asparagus adscendens</i>	Mushali
<i>Asparagus racemosus</i>	Shatavari
<i>Bauhinia variegata</i>	Kachnar
<i>Bergenia ligulata</i>	Pashan bheda
<i>Boerhavia diffusa</i>	Punarnava
<i>Centella asiatica</i>	Mandukaparni
<i>Clerodendrum serratum</i>	Bharangi
<i>Convolvulus pluricaulis</i>	Shankhapushpi
<i>Crataeva nurvala</i>	Varuna
<i>Dioscorea bulbifera</i>	Vidarikand
<i>Embelia ribes</i>	Vidanga
<i>Gymnema sylvestre</i>	Madhunashni
<i>Hedychium spicatum</i>	Shathi
<i>Holarrhena antidysenterica</i>	Kutaja
<i>Mesua ferrea</i>	Nagkesar
<i>Nardostachys jatamansi</i>	Jatamansi
<i>Ocimum</i> sp.	Tulsi
<i>Phyllanthus amarus</i>	Bhumyamalika
<i>Phyllanthus emblica</i>	Amalika (Amla)
<i>Picrorhiza kurrooa</i>	Kutki
<i>Piper longum</i>	Pippali
<i>Pluchea lanceolata</i>	Rasna
<i>Psoralea corylifolia</i>	Bakuchi
<i>Rubia cordifolia</i>	Manjistha
<i>Saraca indica</i>	Ashoka
<i>Saussurea lappa</i>	Kushtha
<i>Sida</i> sp.	Bala
<i>Symplocos racemosa</i>	Lodhra
<i>Terminalia arjuna</i>	Arjuna
<i>Terminalia chebula</i>	Haritaki (Harad)
<i>Tinospora cordifolia</i>	Guduchi
<i>Tribulus terrestris</i>	Gokshura
<i>Valeriana jatamansi</i>	Tagar
<i>Vitex negundo</i>	Nirgundi
<i>Withania somnifera</i>	Ashwagandha

Source: BCIL².

Table 3. Frequency of occurrence of medicinal plants in herbal formulations in India

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

Source: BCIL².

variety of flora and fauna, many of them with therapeutic properties. About 1500 plants with medicinal uses are mentioned in ancient texts and around 800 plants have been used in traditional medicine; the most widely used plants are given in Table 4. Tables 5 and 6 give the names of medicinal plants exported and imported in India, respectively.

The major traditional sector pharma, namely Himalaya, Zandu, Dabur, Hamdard, Maharishi, etc. and modern sector pharma, namely Ranbaxy, Lupin, Allembic, etc. are standardizing their herbal formulations by chromatography techniques like TLC/HPLC finger printing, etc. There are about 7000 firms in the small-scale sector manufacturing traditional medicines with or without standardization. However, none of the pharma has standardized herbal medicines using active compounds as markers linked with confirmation of bioactivity of herbal drugs in experimental animal models.

Role of WHO in herbal medicine

Two decades ago, WHO referred to traditional health systems (including herbal medicine) as 'holistic' – 'that of viewing man in his totality within a wide ecological spectrum, and of emphasizing the view that ill health or disease is brought about by an imbalance or disequilibrium of man in his total ecological system and not only by the causative agent and pathogenic evolution' (WHO⁶), probably implying that the indigenous system drugs (including herbal medicine) restore the imbalance or disequilibrium leading to the cure of ill health or disease. Such an attitude sent signals that WHO as an

organization has failed to provide leadership to establish traditional systems of medicine which provide health care to about 80% of the world population. However, it helped the inclusion of proven traditional remedies in national drug policies and regulatory approvals by developing countries. The World Health Assembly continued the debate and adopted a resolution (WHA 42.43) in 1989 that herbal medicine is of great importance to the health of individuals and communities. The redefined definition of traditional medicine thus issued in the early nineties is given vide supra (see herbal medicine). Consequently, in 1991 WHO developed guidelines for the assessment of herbal medicine⁷, and the same were ratified by the 6th International Conference of Drug Regulatory Authorities held at Ottawa in the same year. The salient features of WHO guidelines are: (i) *Quality assessment*: Crude plant material; Plant preparation; Finished product. (ii) *Stability*: Shelf life. (iii) *Safety assessment*: Documentation of safety based on experience or/and; Toxicology studies. (iv) *Assessment of efficacy*: Documented evidence of traditional use or/and; Activity determination (animals, human).

To the best of my knowledge, WHO has not systematically evaluated any traditional medicine.

Herbal medicine standardization

In indigenous/traditional systems of medicine, the drugs are primarily dispensed as water decoction or ethanolic extract. Fresh plant parts, juice or crude powder are a rarity rather than a rule. Thus medicinal plant parts should be authentic and free from harmful materials like pesticides, heavy metals, microbial or radioactive contamination, etc. The medicinal plant is subjected to a single solvent extraction once or repeatedly, or water decoction or as described in ancient texts. The extract should then be checked for indicated biological activity in an experimental animal model(s). The bioactive extract should be standardized on the basis of active principle or major compound(s) along with fingerprints. The next important step is stabilization of the bioactive extract with a minimum shelf-life of over a year. The stabilized bioactive extract should undergo regulatory or limited safety studies

Table 5. Medicinal plants being exported from India

Botanical name	Part of the plant
<i>Aconitum</i> species (other than heterophyllum)	Root
<i>Acorus calamus</i>	Rhizome
<i>Adhatoda vasica</i>	Whole plant
<i>Berberis aristata</i>	Root
<i>Cassia angustifolia</i>	Leaf and pod
<i>Colchicum luteum</i>	Rhizome and seed
<i>Hedychium spicatum</i>	Rhizome
<i>Heracleum candicans</i>	Rhizome
<i>Inula racemosa</i>	Rhizome
<i>Juglans regia</i>	Bark
<i>Juniperus communis</i>	Fruit
<i>Juniperus macropoda</i>	Fruit
<i>Picrorhiza kurrooa</i>	Root
<i>Plantago ovata</i>	Seed and husk
<i>Podophyllum emodi</i>	Rhizome
<i>Punica granatum</i>	Flower, root and bark
<i>Rauvolfia serpentina</i>	Root
<i>Rheum emodi</i>	Rhizome
<i>Saussurea lappa</i>	Rhizome
<i>Swertia chirayita</i>	Whole plant
<i>Valeriana jatamansi</i>	Rhizome
<i>Zingiber officinale</i>	Rhizome

Source: BCIL².

Table 6. Medicinal plants being imported in India

Botanical name	Native name
<i>Cuscuta epithimum</i>	Aftimum vilaiyti
<i>Glycyrrhiza glabra</i>	Mullathi
<i>Lavendula stoechas</i>	Ustukhudus
<i>Operculina turpethum</i>	Turbud
<i>Pimpinella anisum</i>	Anise fruit
<i>Smilax china</i>	Chobchini
<i>Smilax ornata</i>	Ushba
<i>Thymus vulgaris</i>	Hasha

Source: BCIL².

in animals. Determination of the probable mode of action will explain the therapeutic profile. The safe and stable herbal extract may be marketed if its therapeutic use is well documented in indigenous systems of medicine, as also viewed by WHO. A limited clinical trial to establish its therapeutic potential would promote clinical use. The herbal medicines developed in this mode should be dispensed as prescription drugs or even OTC products depending upon disease consideration and under no circumstances as health foods or nutraceuticals.

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The underground flower

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There are about 250,000 species of flowering plants in the world. Most of these produce flowers above ground. Thirty six species bear flowers on underground shoots. Flowers produced above ground may be of two types – chasmogamous and cleistogamous. The former are the normal flowers which open to receive pollen and/or pollinators. The latter type do not open and pollination is accomplished when they are closed. Flowers borne on underground shoots are invariably cleistogamous. The chasmogamous flowers are larger in size, produce copious amounts of pollen and large number of small seeds. Contrarily, the cleistogamous flowers are generally reduced in size, produce little pollen and few but heavier seeds¹.

FLOWERING involves transformation of a foliar into a floral bud through a series of histological, physiological and biochemical changes^{2–4}. Since flower represents a modified shoot, and shoot is negatively geotropic, flowers almost invariably differentiate above ground. If flowers had been underground, the world would be devoid of the range of colours, variety of scents, and innumerable patterns and forms we see around us. The immense variety and enormous beauty of flowers benefits the plants and appeals the human eye. However, for the plant, underground flower formation could be an asset, as it substantially cuts down resource allocation involved in differentiation of accessory floral parts, biosynthesis of pigments and production of large quantities of pollen and nectar to reward pollinators. Importantly, underground flowers have assured pollination and seed set, with security against predators and vagaries of environment. Nevertheless, the invariable differentiation of flowers above

ground has deprived plants of all the above advantages. However, as compensation the above-ground flowers confer on plants the ability for (i) cross-pollination, which generates variability, assures adaptability and evolutionary plasticity, and (ii) wider dispersal of pollen and seed for greater distribution and reducing intrapopulation competition.

That pollination and seed dispersal are the only major events which aerial flowers help to accomplish is reflected by *Tulipa*, *Sternbergia*, *Ixilioron* and such other bulbous angiosperms in which flower development is completed within the bulb, underground. The hidden flower is thrust above ground for accomplishing pollination, whereafter, seeds and fruits develop above ground.

Geocarpy

Have plants ever tried to combine the advantages of above ground flowering and underground development of fruits? The answer is provided by a few plants of which peanut is the most common example. In this legume, flowers differentiate above ground. Soon after pollination, they shed their petals and bend with the help of a peg to first

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