

# Globalisation of Herbal Drugs: A Bliss and Concern

Jyoti Ahlawat<sup>1</sup>, Nidhi Verma<sup>2</sup>, Anita R. Sehrawat<sup>3</sup>

<sup>1, 2, 3</sup>Department of Botany, M. D. University, Rohtak, India

**Abstract:** A “man earth relationship” has been well canvassed to encourage the usage of botanicals. The use of plants for healing purposes predates to the Neanderthal period in human history and forms the origin of much modern medicine. 25% of drugs prescribed worldwide come from plants. India has about 45000 plant species out of which 15,000-20,000 have active principles of proven medicinal values. India ranks second in the world in herbal medicine and there is enormous scope to emerge as a major player. Natural plant products are perceived to be healthier than manufactured medicine Herbal medicines are now in great demand in the developing world for primary health care not because they are inexpensive but also for better cultural acceptability, better compatibility with the human body and minimal side effects. However recent findings indicate that traditional herbal products are heterogeneous in nature and may not be safe and impose a number of challenges to qualify control, quality assurance, effectiveness and the regulatory process. Some products contain mercury, lead, arsenic and corticosteroids and poisonous organic substances in harmful amount. Hepatic failure and even death following ingestion of herbal medicine have been reported. Medicinal plant materials and possibly herbal tea, if stored improperly allow the growth of *Aspergillus flavus* a known producer of aflatoxin mycotoxin. Herbal preparation should be used with extreme caution on the advice of a herbalist familiar with the relevant conventional pharmacology. The manufacturers, the researchers and the regulatory agencies of the herbal products must adhere to rigorous scientific methodologies, good manufacturing practices (GMPs) and preclinical testing to gain public trust and to bring quality herbal product into mainstream of today health care system worldwide. Herbal medicines should be purchased from authentic and reputable provider, company or internet site to avoid any disguise. Despite herbal medicines offers bright opportunities for Indian Farmers and Entrepreneurs, a hard fact is that most of the overseas markets are very difficult to penetrate, their stringent rules and regulations allows the entry of most deserving and quality products. Hence an eye on the negative list of exporters must be kept. Alarmingly herbal medicines in some cases are found to be admixed with allopathic medicine which implies the synergistic effect of component. Hence, in the absence of pharmacopoeia data on the various plant extracts, it is not possible to isolate or standardize the active contents having the desired effects. Ayurvedic pharmacopoeia compiled on modern lines and updated periodically is an urgent requirement. A combination therapy integrating Ayurveda and allopathy whereby the side effects and undesirable reactions could be controlled can be thought of. Modern science and technology have an essential role to play in the process. An integrated approach for the cultivation, conservation and preservation of important plant species through plant molecular biology, plant tissue culture; research on the rationale and methodology of Ayurvedic medical practice; isolation of active constituents and their development into new therapeutics; standardization and validation of known herbal medicines and other related aspects need to be focussed upon.

**Keywords:** Herbal drugs, Nutraceuticals, Cosmeceuticals, Nanopharmaceuticals, Pharmacopoeia

## 1. Introduction

A “man earth relationship” has been well canvassed to encourage the usage of botanicals. The use of plants for healing purposes predates to the Neanderthal period in human history and forms the origin of much modern medicine. 25% of drugs prescribed worldwide come from plants. India has about 45000 plant species out of which 15,000-20,000 have active principles of proven medicinal values. India ranks second in the world in herbal medicine and there is enormous scope to emerge as a major player. Natural plant products are perceived to be healthier than manufactured medicine Herbal medicines are now in great demand in the developing world for primary health care not because they are inexpensive but also for better cultural acceptability, better compatibility with the human body and minimal side effects. However recent findings indicate that traditional herbal products are heterogeneous in nature and may not be safe and impose a number of challenges to qualify control, quality assurance, effectiveness and the regulatory process. Some products contain mercury, lead, arsenic and corticosteroids and poisonous organic substances in harmful amount. Hepatic failure and even death following ingestion of herbal medicine have been reported. Medicinal plant materials and possibly herbal tea, if stored improperly allow the growth of *Aspergillus flavus* a known producer of aflatoxin mycotoxin. Herbal preparation should be used with extreme caution on the advice of a herbalist familiar with the relevant conventional pharmacology. The

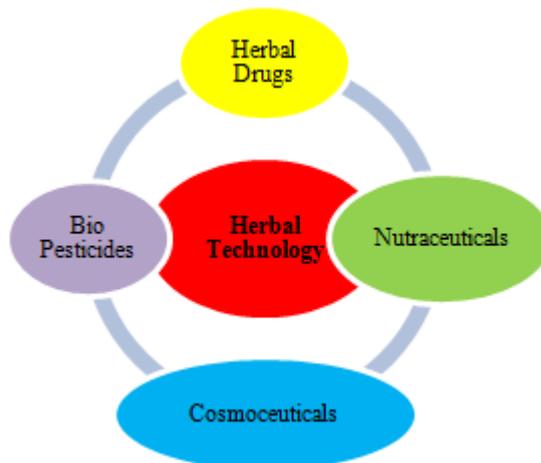
manufacturers, the researchers and the regulatory agencies of the herbal products must adhere to rigorous scientific methodologies, good manufacturing practices (GMPs) and preclinical testing to gain public trust and to bring quality herbal product into mainstream of today health care system worldwide. Herbal medicines should be purchased from authentic and reputable provider, company or internet site to avoid any disguise. Despite herbal medicines offers bright opportunities for Indian Farmers and Entrepreneurs, a hard fact is that most of the overseas markets are very difficult to penetrate, their stringent rules and regulations allows the entry of most deserving and quality products. Hence an eye on the negative list of exporters must be kept. Alarmingly herbal medicines in some cases are found to be admixed with allopathic medicine which implies the synergistic effect of component. Hence, in the absence of pharmacopoeia data on the various plant extracts, it is not possible to isolate or standardise the active contents having the desired effects. Ayurvedic pharmacopoeia compiled on modern lines and updated periodically is an urgent requirement. A combination therapy integrating Ayurveda and allopathy whereby the side effects and undesirable reactions could be controlled can be thought of. Modern science and technology have an essential role to play in the process. An integrated approach for the cultivation, conservation and preservation of important plant species through plant molecular biology, plant tissue culture; research on the rationale and methodology of Ayurvedic medical practice; isolation of active constituents and their development into

new therapeutics; standardisation and validation of known herbal medicines and other related aspects need to be focussed upon.

## 2. Scope of Herbal Drugs

Medicinal herbs as potential source of therapeutics aids has attained a significant role in health system all over the world for both humans and animals not only in the diseased

condition but also as potential material for maintaining proper health. Determining the biological (activity) properties of plants used in traditional medicine is helpful to the rural communities and informal settlements. Several scientific investigations are currently being undertaken to isolate the active compounds by bioassay-guided fractionation from the species that showed high biological activity during screening.



Several drugs have entered the international market through study of ethnopharmacology and traditional medicine. Cosmeceuticals are the products that forms interconnect between the drug and cosmetics. Nutraceuticals i.e. nutrition and pharmaceuticals, have established health benefits and their utilization will keep diseases away and allow humans to sustain an overall good health. There is rich biodiversity of medicinal plants worldwide where many species of both medicinal and biopesticides plants are utilized. There is a

necessity to educate and sensitize the younger age group on the potential and importance of conserving the local biodiversity, native knowledge and practices. In India almost all generations use herbal drugs for their health benefits. These herbal drugs and Indian medicinal plants are also rich sources of beneficial compounds including antioxidant, anti-inflammatory, antiseptic and antimicrobial properties and other components that can be used in functional foods.

**Table 1:** Common Herbs As Nutraceuticals

Herbal drugs	Biological name/ Family	Chemical constituents	Uses
<b>Garlic</b>	<i>Allium sativum</i> / Liliaceae	It contains S-allylcysteine, S-allylmercaptocysteine, saponins, Nalpha-fructosylarginine etc .	It has a characteristic pungent, spicy flavor that mellows and sweetens considerably with cooking .
<b>Ginger</b>	<i>Zingiberofficinale</i> / Zingiberaceae	It contains zingerone, shogaols, gingerols, $\beta$ -sesquiphellandrene, bisabolene, farnesene, $\beta$ -phelladrene, cineol, citraletc23.	It used as spice, in recipes such as gingerbread, cookies, crackers, cakes, ginger ale, ginger beer, ginger tea 24.
<b>Turmeric</b>	<i>Curcuma longa</i> / Zingiberaceae	It contains curcumin, demethoxycurcumin, bisdemethoxycurcumin, turmerone, turmerone, Curcuminoidsetc25.	It is used to color, and enhance the flavors of certain dishes, dairy products, orange juice, biscuits, popcorn color, sweets, cake etc26.
<b>Aloes</b>	<i>Aloe vera</i> / Liliaceae	It contain Aloe-emodin, aloetic-acid, anthranol, barbaloin, isobarbaloin, emodin, Arachidonic acid, campesterol, etc27.	It has been used as a food products, for the production of gel-containing health drinks and beverages 28.
<b>Onion</b>	<i>Allium cepa</i> / Liliaceae	It contains thioallyl compound, alliins, quercetin, disulfides trisulfides, cepaene, and vinyl dithiins29.	It is used as an ingredient in various hearty warm dishes, or onion chutney, they can be baked, boiled, eaten raw in salads 30.
<b>Liquorice</b>	<i>Glycyrrhizaglabra</i> / Leguminosae	It contain Glycyrrhizin, starch, glucose, asparagines, fat, resins, mannitol, gum 31	It is used worldwide as a natural sweetener, as well as a flavoring32
<b>Ginkgo</b>	<i>Ginkgo biloba</i> / Ginkgoaceae	It contain myricetin, quercetin, terpenoids, ginkgolides, bilobalides, biflavones, alkylphenols, 6-hydroxykynurenic acid, and polyphenols33.	It is used in congee, and is often served at special occasions such as weddings, cooked seeds are often eaten along with other dishes 34.
<b>Asafoetida</b>	<i>Ferula asafoetida</i> / Umbelliferae	It contains resin, endogeneous gum, volatile oil, ash, asaresinotannols 'A' and 'B', ferulic acid, umbelliferone35.	It is used as a digestive aid, in food as a condiment, and in pickles. It is used in Indian cuisine, in lentil curries, such as dal etc36.
<b>Goldenseal</b>	<i>Hydrastis Canadensis</i> /	It contains hydrastine, berberine, berberastine, hydrastinine canadine, tetrahydroberberastine, and canalidine 37.	It is used as a multi-purpose remedy, digestion aid, and may remove canker sores

	Ranunculaceae		when gargled 38.
<b>Valeriana</b>	<i>Valeriana officinalis</i> / Valerianaceae	It contains valerenic acid, beta-sitosterol, ursolic acid, caryophyllene acid, valerane, naphthalene, linoleic acid, myrtenyl acetate 39.	It is used to distill into oils and ointments, or dried and used in teas or capsules, in the home medicine cabinet 40.

**Table 2:** Common Herbs as Cosmeceuticals

Herbal drugs	Biological source/ Family	Chemical constituents	Uses
<b>Areca palm</b>	<i>Areca chatechu</i> / Piperaceae	It contains Arecaidine, arecoline, arecatannins, querceti, liquiritigenin, resveratrol, ferulic acid, vanillic acid, beta-sitosterol, cycloartenol .	It is used for treatment of a mental disorder called schizophrenia, an eye disorder called glaucoma; as a mild stimulant, and as a digestive aid .
<b>Green tea</b>	<i>Camellia senensis</i> / Theaceae	It contains epicatechin, epigallocatechin, epicatechingallate, epigallocatechingallate, kaempferol, quercetin, and myricetin .	It is a powerful antioxidant and provides effective protection from the sun. The health benefits come into the body by drinking hot tea or cold.
<b>Buckweed</b>	<i>Fagopyrum esculentum</i> / Polygonaceae	It contains potassium, phosphorous, calcium, iron, zinc, vitamins B, E and rutin.	It is used for high quality edible oil, natural cosmetics, food additive, and health-care food.
<b>Centella</b>	<i>Centella asiatica</i> / Apiaceae	It contain centellin, asiaticin, centellicin, brahminoside, centelloside, madasiatic acid, centic acid, cenellic acid <sup>41</sup>	It is used in skin care, collagen production, reduce fine lines and wrinkles, sun damage repair, scar care, , anti-oxidant <sup>42</sup> .
<b>Psorolia seed</b>	<i>Psoraliacorylifolia</i> / Fabaceae	It containcorylinin, isopsoralen, psoralen, sophoracoumestan A, daidzin and uracil.	It is used to Improve Skin Tone, Vegetarian Liquid Formula, to use for Dull Skin, and Aging <sup>44</sup> .
<b>Chamomile</b>	<i>Matricariachamomilla</i> / Asteraceae	It contains $\alpha$ -bisabolol, bisabolol oxides, chamazulene, and enyn-dicycloethers etc <sup>45</sup> .	It is used in skin cosmetics to serve as an emollient, and enhance the color of blonde hair <sup>46</sup> .
<b>Garlic</b>	<i>Allium sativum</i> / Alliaceae	It contain trisulfide, di-2-propenyl; disulfide, di-2-propenyl; trisulfide, methyl 2di-2-propenyl and diallyldisulfide <sup>47</sup> .	It is used in cosmetic compositions for topical application for the beauty or the skin care, for the prevention of topical cellulite <sup>48</sup> .
<b>Grape Vine</b>	<i>Vitisvinifera</i> / Vitaceae	It contain Resveratrol, vinferrin, balanocarpol, B-glucopyranosyl 8-balanocarpol <sup>49</sup>	It is used as an anti-caries agent, anti-dandruff agent, anti-fungal agent, antioxidant <sup>50</sup> .
<b>Carrots</b>	<i>Daucuscarota</i> / Apiaceae	It contain Petroselinic, linoleic, palmitic, carotol, daucene, germacrene D, trans-a-bergamotene, selinene, daucol and copaenol <sup>51</sup>	It is used tosmoothes wrinkles, gives skin more intensive color and freshness, protects it from harmful UV rays <sup>52</sup> .
<b>Tomato</b>	<i>Lycopersicon esculentum</i> / Solanaceae	It contain germacrene A, gualaia-6,9-diene, germacrene B, beta-caryophyllene, alpha-humulene <sup>53</sup> .	It is used as neoplastic disorder, metastatic cancer, an angiogenesis-dependent cancer or tumor <sup>54</sup> .

**Table 3:** Common Herbs as Biopesticides:

Herbal drug	Biological source/family	Chemical constituents	Uses
Tobacco	<i>Nicotianarustical</i> / Solanaceae	It contains Anabasine, l-nornicotine, l-anabasine, l-nicotine and etc.	It is effective against aphids, bollworms, thrips, green leafhopper, grups .
ginger	<i>Zingiberofficinale</i> / Zingiberaceae	It contains beta-sitosterolpalmitate, isovanillin, p-hydroxybenzaldehyde, adenine, 6-gingerol.	It is effective against Root knot, burrowing, and lesion.
Castor oil	<i>Ricinuscommunis</i> / Euphorbiaceae	It containpalmitic acid, linoleic acid, ricinoleic acid.	It is effective against acaricidal, insecticidal activities, hematophagous, <i>Hippobosca maculate</i> .
Neem	<i>Azadirachtaindica</i> / Meliaceae.	Melianol, Desfurano-6 $\alpha$ – hydroxyazadiradione, Zeeshanol, Meliacinol, Meliatetraone, Odoratone, Nimocinol.	It is effective against nematodes, white ants, bird repellent, especially for sparrow.
Lonchocarpus	<i>Lonchocarpusutilis</i> / Fabaceae.	It contain rotenone and deguelin.	It is effective against Lonchocarpusurucu, commercial insecticide and piscicide (fish poison).
Lonchocarpus root	<i>Lonchocarpusurucul</i> / Fabaceae.	It contains rotenone, deguelin, rotenolone, and tephrosin.	It is effective against as a commercial insecticide and piscicide (fish poison).
Derris	<i>Derris elliptical</i> / Fabaceae.	It contains pipecolic acid, tubaic, $\beta$ -tubaic acids, imino alcohol, deguelin, tubaic and $\beta$ -tubaic acids.	It is poisonous to fish, larvicidal and insecticide, poisonous to cattle, Ipoh arrow-poison.
Common Mullein	<i>Verbascum Thapsus</i> / Scrophulariaceae	It contains Verbascose, verbascoside, verbasterol, thiamin, ribpflavin.	It is used for hair dye, insecticides and etc.
Turraea	<i>Turraeawakefieldii</i> / meliaceae	It contains Rohitukin, prierurianin and etc.	It is effective against mosquito larvicidal activity, third-instar larvae of Anopheles.

Table 4: Common Herbs as Herbal Drugs:

Herbal drugs	Biological source/ Family	Chemical constituents	Uses
Horse chestnut	<i>Aesculus hippocastanum</i> / Hippocastanaceae.	It contains Aescin, prosapogenin. alpha- and beta-aescin, cryptoaescin, hippoaesculin .	it is used as anti-oedema, antioxidant, anti-inflammatory, cancer, obesity.
Kava-kava	<i>Piper methysticum</i> / Piperaceae	It contains ethylethylene, pyrones, chalcones, yangonin, methysticin, dihydromethysticin, kavain, dihydrokavain.	It is used as anxiolytic, psychosis, depression, migraines, chronic fatigue syndrome, tuberculosis and cancer prevention.
St. John's wort	<i>Hypericum perforatum</i> / Hypericaceae	It contains epigallocatechin, rutin, hyperoside, amentoflavone, astilbin, miquelianin .	It is used in wounds, abrasions, burns, muscle pain, inflammatory skin diseases.
Myrtle	<i>Myrtus communis</i> / Myrtaceae	It contains $\alpha$ -pinene, 1, 8-cineole, myrtenyl acetate, 1, 8-cineol.	It is used as anti-cancer, anti-inflammatory, diabetics, Alzheimer disease.
Stinging nettle	<i>Urtica dioica</i> / Urticaceae	It contains Histamine, acetylcholine, choline, serotonin, oleanol acid, sterols.	It is used as arthritis, benign prostatic hyperplasia, rubefacient, galactagogue.
Saw palmetto	<i>Serenoa repens</i> / Arecaceae	It contains caproic, caprylic, linolenic; anthranilic acid, sterols including $\beta$ -sitosterol, $\beta$ -sitosterol, campesterol, lupeol.	It is used in prostate gland, benign prostatic hyperplasia, bladder disorders, hair loss, hormone imbalances, and cancer.
Milk thistle	<i>Silybum marianum</i> / Compositae	It contains silybin (silibinin), silychristin (silichristin), silichristin B, silidianin, neosilyhermin.	It is used in jaundice, chronic inflammatory liver disease, chronic hepatitis, heartburn complaints.
Soya beans	<i>Glycine max</i> / Fabaceae	It contains phytic acid, alpha-linolenic acid, isoflavones, cellulose, hemicellulose, and pectin.	It is used in sedative, anti-spasmodic, diaphoretic, anti-pyretic properties, fever, and restlessness.
Mistletoe	<i>Viscum Album</i> / Loranthaceae	It contains quercetin, chalcone, oleanic acid, beta-sitosterol, ursolic acid, lupeol.	It is used in cancer, lower blood pressure, arthritic pain, Sleep/Insomnia, headache, hepatitis.
Chamomile	<i>Matricaria chamomilla</i> / Asteraceae	It contains apigenin, apigenin-7-O-glucoside, apigenin-7-O-glucuronide, rutin, luteolin, patuletin, and quercimeritrin.	It is used in anti-inflammatory, antihyperglycemic, antigenotoxic .
Comfrey	<i>Symphytum officinale</i> / Boraginaceae	It contains allantoin, caffeic acid, chlorogenic acid, lithospermic acid, and silicic acid.	It is used in cuts, bruises, pulled muscles and ligaments, fractures, sprains, and osteoarthritis.
Eucalyptol	<i>Eucalyptus globulus</i> / Myrtaceae	It contains 1,8-Cineole, Sabinene and alpha-Terpinyl acetate, $\alpha$ -Pinene, alpha-Phellandrene and trans-/beta-osimen.	It is used in mouthwash, cough suppressant, as well as an inactive ingredient in body powder, insecticide and insect repellent.
Black cohosh	<i>Cimicifuga racemosa</i> / Ranunculaceae	It contains 26-deoxyactein, cimigloside, cimifugoside M, cimicifugosides.	It is used in anxiety, and cough, menopause, premenstrual syndrome, and painful menstruation.
Bromelain	<i>Ananas comosus</i> / Bromeliaceae	It contains bromelain, ananain, and comosain, glycoproteins, carbohydrates, peroxidases, phosphatases.	It is used in inflammation, hay fever, swelling, ulcers, pulmonary edema, muscle contractions, preventing cancer.

- Herbs are staging a comeback and herbal 'renaissance' is happening all over the globe and the blind dependence on synthetics is over and people are returning to the naturals with hope of safety and security.
- Developed countries such as United States, plant drugs constitute as much as 25% of the total drugs, while in fast developing countries such as China and India, the contribution is as much as 80%. Thus the economic importance of medicinal plants is much more to countries such as India than to rest of the world.
- Cultivation of medicinal plants is urgently needed to ensure their availability to the industry as well as to people associated with traditional system of medicine. *In situ* conservation of these resources alone cannot meet the ever increasing demand of pharmaceutical industry. It is, therefore, inevitable to develop cultural practices and propagate these plants in suitable agroclimatic regions. Commercial cultivation will put a check on the continued exploitation from wild sources and serve as an effective means to conserve the rare floristic wealth and genetic diversity.
- Medicinal plants play a vital role for the development of new drugs. The bioactive extract should be standardized on the basis of active compound. The bioactive extract should undergo safety studies.
- Medicinal plants play a central role not only as traditional medicines but also as trade commodities, meeting the demand of distant markets. India has a very small share of this ever-growing global market.
- To compete with the growing market, there is urgency to expeditiously utilize and scientifically validate more medicinally useful plants. Medicinal plants are being used for trade purpose and been a source of export and import to benefit the people at global end.

**Table 5:** Parts of Medicinal Plant Exported and imported From India

Exporting Of Herbs		Importing Of Herbs	
<i>Acoruscalamus</i>	Rhizome	<i>Aloe vera</i>	Dried
<i>Argemonemexicana</i>	Fruit	<i>Adhatodavastica</i>	Whole
<i>Curcuma amada</i>	Rhizome	<i>Cinnamomum</i>	Bark
<i>Curcuma longa</i>	Rhizome	<i>Garciniaindica</i>	Fruit
<i>Curcuma</i>	Wild	<i>Juniperuscommunis</i>	Fruit
<i>Cassia lanceolata</i>	Leaves	<i>Ricinuscommunis</i>	Seed
<i>Glycyrrhizaglabra</i>	Root	<i>Rauwolfiaserpentina</i>	Root
<i>Withaniasomnifera</i>	Vegetable	<i>Ocimum sanctum</i>	Leaf
<i>Myricanagi</i>	Leaf	<i>Tylophorapurpuria</i>	Root
<i>Zingiberofficinale</i>	Rhizome	<i>Vincarosea</i>	Leaf

### 3. Challenges Encountered In Globalization of Herbal Products:

#### a) Potential negative outcomes:

While many benefits can be derived from the use of herbs, potential negative outcomes cannot be ignored. Saper et al. (2008) reported that 20% of Ayurvedic medicines purchased via the Internet contained detectable levels of lead, mercury, and arsenic. Many herbal product adulterations have been detected primarily containing drugs like sildenafil (Viagra®), lovastatin (Mevacor®, and others), estrogen, alprazolam (Xanax®, and others), indomethacin (Indocin®, and others), and warfarin (Coumadin®, and others). There is an apparent trend of adding drugs or analogues to herbs to make them more effective, especially for weight loss and enhanced sexual function (Cohen et al., 2009). Herbs that have caused major adverse events include creosote bush (hepatotoxicity), ephedra or Mau Huang (cardiovascular complications and hepatotoxicity), and kava (hepatotoxicity). Using the proper parts of the plant and the appropriate processes for obtaining the ingredients could prevent toxicity, as seen in kava-induced toxicity (Teschke et al., 2010). Herbs that may alter bleeding are also of importance especially in patient populations with coagulopathies, on antiplatelet or anticoagulant drugs, or in surgical patients. We reported a case of a surgical patient with a prolonged unexplained bleeding after taking large quantities of an herbal tea that contained Mexican arnica (Rivera et al., 2009). Keep in mind that many medications used today may cause similar adverse events if not monitored or used correctly.

#### b) Role of Internet and the Global Economy:

With the advances of the internet and increased emphasis on a global economy, consumers have much greater access to herbal products from anywhere in the world. Furthermore, industries are using internet sites as a vehicle to increase sales with most companies being less concerned with protecting the public as with making a profit. While many of these sites may claim that their products are safe, effective, standardized, pure, etc., such claims cannot be verified. The burden of investigation

lies on the consumer, who should first research the company and its reputation in addition to looking into the product of interest before making a purchase. The international community needs a system for monitoring the legitimacy of internet sites that sell herbs similar to those of internet pharmacies verified by the National Association of Boards of Pharmacy.

#### c) Selected herb/drug interactions:

The potential for interactions between medications and herbs is one of the significant consequences resulting from the use of several medications, herbal products and supplements. Unfortunately, many consumers of herbal products assume that because these products are "natural" they are also safe. The mechanisms for these herb/drug interactions are not fully understood, but both pharmacokinetic and pharmacodynamic processes have been identified as playing a role. In general, herbal products may mimic, increase, or decrease the effects of medications. Examples of herbs that enhance the therapeutic effect of a medication include Ephedra used with amphetamines, valerian or Kava with benzodiazepines. This may lead to supratherapeutic effects or toxicities, complicating the management of medical conditions and the corresponding medications. Herbs that induce metabolism of medications can lead to decreased medication levels, which may result in decreased efficacy of the medication or therapeutic failure.

#### d) Toxicity of herbs:

Less than 10% of herbal products in the world market are truly standardized to known active components and strict quality control measures are not always diligently adhered to. For majority of these products in use, very little is known about their active and/or toxic constituents. In many countries including the U.S, herbal medicines are not subjected to the same regulatory standards as orthodox drugs in terms of efficacy and safety. This raises concern on their safety and implications for their use as medicines. Many plants produce toxic secondary metabolites as natural defence from adverse conditions. In some toxicologically and medicinally relevant plant species like *Digitalis purpurea*, *Hyoscyamus niger*, *Atropa belladonna*, *Physostigmavenenosum*, *Podophyllumpeltatum* and *Solanumnigrum*, these toxic substances are not distinguished from therapeutically active ingredients. Plants have evolved different means of adaptation to challenging environments and co-existence with herbivores and pathogenic microorganisms. Thus, they synthesize an array of metabolites characterized as 'phytoanticipins' or as general 'phytoprotectants' that are stored in specialized cellular compartments and released in response to specific environmental stimuli like damage due to herbivores, pathogens or nutrient depletion (Kawashimae et al., 2007).

**Table:** Potential toxic effects associated with some common herbal medicines marketed for different indications

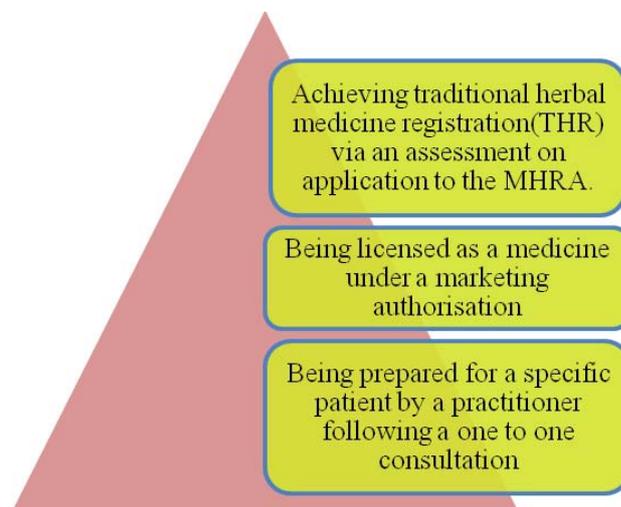
Common name	Plant source/parts used	Intended indications	Potential toxicity
Ginseng	<i>Panax ginseng</i> roots	Relieves stress, promotes mental and physical activity	Central nervous system stimulation, hypertension, skin eruptions
St. John's wort	<i>Hypericum perforatum</i> aerial parts	Antidepressant, mood stabilizer	Highly potent cytochrome P450 enzyme inducer which affects drug metabolism. Also causes hepatotoxicity and nephrotoxicity in pregnancy and lactation
Kava kava	<i>Piper methysticum</i> roots	Sedative, anxiolytic	Hepatotoxic, cytochrome P450 enzyme inhibitor
Ginkgo	<i>Ginkgo biloba</i> leaves	Impotence, vertigo, circulatory disorders, improves mental Alertness	Gastric irritability, spontaneous bleeding
Danshen	<i>Salvia miltiorrhiza</i> exterior taproot	Angina pectoris, antihyperlipidemic, ischemic stroke	Bleeding, anticoagulant effects
Hawthorn	<i>Crataegus oxycantha</i> Flowers, roots, berries	Mild to moderate congestive heart Failure	Cardiac arrhythmias, lowered blood pressure
Comfrey	<i>Symphytum officinale</i> Leaves	Anti inflammatory, antidiarrhoeal and treatment of thrombophlebitis	Hepatotoxicity, Carcinogenicity
Licorice	<i>Glycyrrhiza glabra</i> roots	Antiulcer, anti inflammatory, Antihypertensive	Hypokalemic myopathy, pseudoaldosteronism, thrombocytopenia
Chaparral, creosote bush	<i>Larrea tridentata</i> leaves and twigs	Blood thinner, weight loss, antioxidant, anticancer, anti arthritis	Carcinogenic, nephrotoxic, Hepatotoxic

#### 4. Addressing Opportunities in Globalization of Herbal Drugs

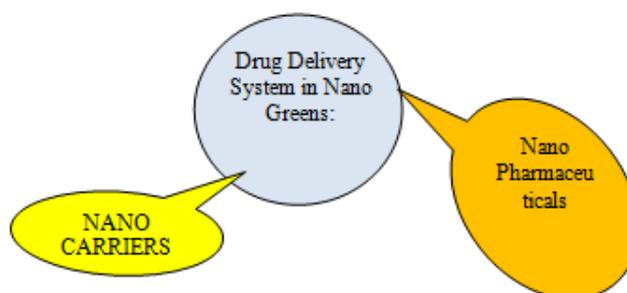
During the past decades, public interest in natural therapies has increased greatly in industrialized countries, with expanding use of medicinal plants and herbal medicines. The many and various forms of traditional medicinal products have evolved against widely different ethnological, cultural, climatic, geographical, and even philosophical backgrounds. The evaluation of these products and ensuring their safety and efficacy through registration and regulation present important challenges. The contributions from governments, institutions, and others would be greatly appreciated in formulating policies on traditional medicinal products and in introducing measures for their registration and regulation, and to facilitate information exchange on these subjects among Member States.

##### 4.1 Regulations of Herbal Medicines

The EU Directive on Traditional Herbal Medicinal Products replaces most existing member state regulations and creates a unified licensing system for traditional herbal medicine products (in use for at least 30 years, of which 15 must usually have been in the EU). The Directive came into full effect on 30 April 2011. The Directive has the potential to have a significant impact on some herbal medicinal products; there are three ways in which herbal medicinal products can continue to be sold in the UK:



##### 4.2 Credits of Nanotechnology



Nanotechnology plays a great role and the use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Nano herbal drug delivery systems have a potential future for enhancing the activity and overcoming the problems associated by medicinal plants. So the nanocarriers help to treat the dangerous diseases like cancer, Diabetes etc.

### 4.3 Nano Carriers

A nanocarrier is nanomaterial being used as a transport module for another substance, such as a drug. Commonly used nanocarriers include micelles, polymers, carbon-based materials, liposomes and other substances (Cajota et al., 2012). Nanocarriers are currently used in drug delivery and their unique characteristics demonstrate potential use in chemotherapy. Nanocarriers include polymer conjugates, polymeric nanoparticles, lipid-based carriers, dendrimers, carbon nanotubes, and gold nanoparticles. Lipid-based carriers include both liposomes and micelles. Examples of gold nanoparticles are gold nanoshells and nanocages. Different types of nanomaterial being used in nanocarriers allows for hydrophobic and hydrophilic drugs to be delivered throughout the body. Since the human body contains mostly water, the ability to deliver hydrophobic drugs effectively in humans is a major therapeutic benefit of nanocarriers (Yu et al., 2012). Micelles are able to contain either hydrophilic or hydrophobic drugs depending on the orientation of the phospholipids molecules. Some nanocarriers contain nanotube arrays allowing them to contain both hydrophobic and hydrophilic drugs.

### 4.4 Nano Pharmaceuticals

Nanopharmaceuticals offer the ability to detect diseases at much earlier stages and the diagnostic applications could build upon conventional procedures using nanoparticles. Nanopharmaceuticals represent an emerging field where the sizes of the drug particle or a therapeutic delivery system work at the nanoscale. In the pharmaceutical industry a long standing issue is the difficulty of delivering the appropriate dose of a particular active agent to specific disease site. Nanopharmaceuticals have enormous potential in addressing this failure of traditional therapeutics which offers site-specific targeting of active agents. Such precision targeting

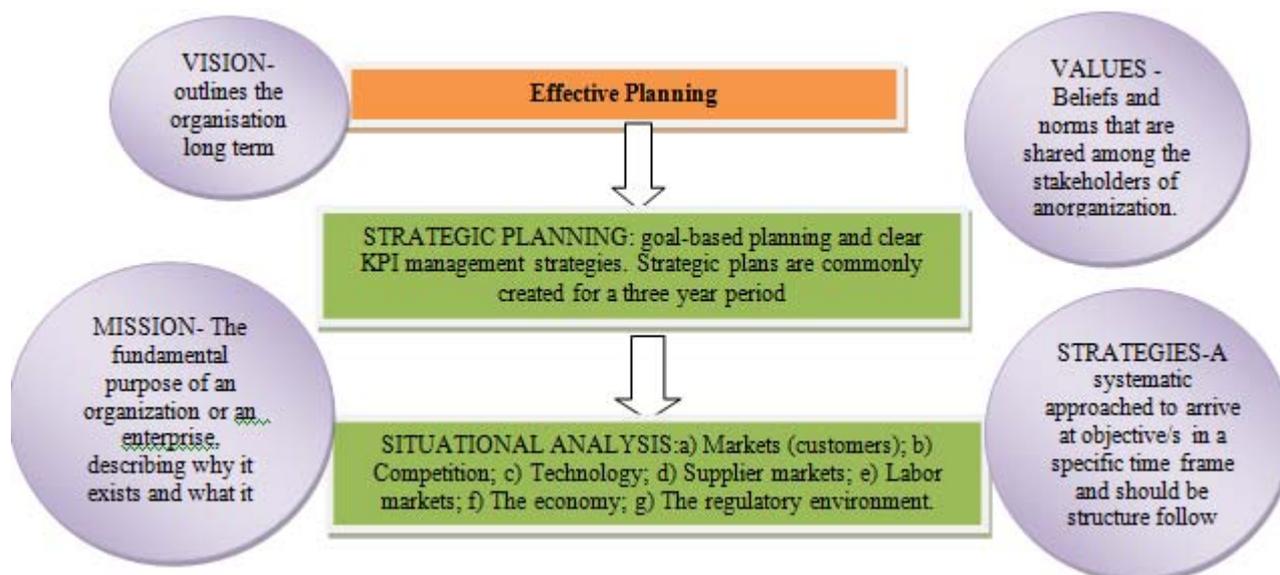
via nanopharmaceuticals reduces toxic systemic side effects, resulting in better patient compliance

### 4.5 Future Prospects of Nanomedicines

Herbal remedies and natural products research is more familiar throughout the world. The development of herbal remedies in the drug delivery system in a number of institutes is being carried out at basic and clinical trial levels. To improve the proper delivery systems at the sites or locations in the whole body in a particular dose will not compromise with the existing treatment. This would not only give relieve from side effects like toxicity and hypersensitive reactions but also will increase the patient's strength from inside is very much desirable. In the future, the concept of herbal nanoparticles for cancer drug delivery may also fascinate some potential research groups and potentially create attention grabbing results.

## 5. Pioneering Developmental Strategies

The importance of Strategic planning to business organizations either big or small has been emphasized in strategic management literature. Not many researches were conducted to study the applicability of strategic planning in the herbal industry. This chapter attempts to provide insight to the strategic planning in the herbal industry as well as identifying issues, prospect and future of the herbal industry. Herbal industry was classified in two major streams that are culinary herbs, medicinal herbs. The issues identified are such as regulatory issues, consumption of herbal products, product quality, research and development, side effect, imported herbal medicine, pricing, current market status, technology and human resources. An effective plan should include the vision, mission, objective, strategy and policy.



Standardization of drugs means confirmation of its identity and determination of its quality and purity. At present due to advancement in the chemical knowledge of crude drugs various methods like botanical, chemical, spectroscopic and biological methods are used for estimating active

constituents present in the crude drugs in addition to its physical constants. Plants have been known to relieve various diseases in Ayurveda. Therefore, the researchers today are emphasizing on evaluation and characterization of various plants and plant constituents against a number of

diseases based on their traditional claims of the plants given in Ayurveda and the authenticity, quality and purity of herbal drugs are established by reference given in pharmacopoeia. The pharmacopoeia prescribes (numerical value) like structural, analytical, physical standards for the drugs. The pharmacopoeial standards are mandatory to be adhered for all herbal drug organisation to avoid any side effect due to deviation in the authenticate information.

### 5.1 Standardization Parameter for Plant Drugs

The pharmacopoeial standards in Ayurvedic Pharmacopoeia of India are not adequate enough to ensure the quality of plant materials since the materials received in the manufacturing premises are not in a condition that effective microscopic examination can be done. Therefore chemical, methods, instrumental methods and then layer chromatographic analysis would determine the proper quality of plant material. Non standardized procedures of extraction may lead to the degradation of the phytochemical present in the plants and may lead to the variations thus leading to the lack of reproducibility. Efforts should be made to produce batches with quality as consistent as possible (within the narrowest possible range) and to develop and follow the best extraction processes.

### 6. Conclusion

The growth of the pharmaceutical industry and the unceasing development of new and more effective synthetic and biological medicinal products has 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.

### References

- [1] Verma H, Prasad S.B, Yashwant, Singh H, Herbal Drug Delivery System: A Modern Era Prospective, *International Journal of Current Pharmaceutical Review and Research*, 2013; 4(3); 88-101.
- [2] Pathak K, Das R.J, Herbal Medicine- A Rational Approach in Health Care System, *International Journal of Herbal Medicine* 2013; 1 (3): 86-89.
- [3] Kaur R, Kushwah A.S, Kaur P, Status of Herbal Drugs in Cardiovascular Research: A Review, *Indian Journal of Pharmaceutical & Biological Research (IJPBR)*, 2013;1(1).
- [4] REPORT OF THE IBC (International Bioethics Committee) ON TRADITIONAL MEDICINE SYSTEMS AND THEIR ETHICAL IMPLICATIONS, SHS/EGC/IBC 19/12/3 Rev.Paris, 8 Feb 2013.
- [5] Agarwal P, Shashi Alok, Fatima A and Verma A: Current scenario of Herbal Technology worldwide: An overview. *Int J Pharm Sci Res* 2013; 4(11): 4105-17. doi: 10.13040/IJPSR.0975-8232.4(11).4105-1
- [6] Regulatory Situation of Herbal Medicines: A worldwide Review, Dr Xiaorui ZHANG Traditional Medicine Programme, WHO/TRM/98.1.
- [7] Sundaresan S and Senthilkumar B A survey of traditional medicinal plants from the Vellore District, Tamilnadu, India., *International journal of ayurvedic & herbal medicine* 2013;3(5) (1347-1355).
- [8] IARC MONOGRAPHS VOLUME 82, History of Use of Traditional Herbal Medicines.
- [9] Ifeoma O and Oluwakanyinsola S. Screening of Herbal Medicines for Potential Toxicities. (<http://creativecommons.org/licenses/by/3.0>), 2013.
- [10] Eddouks M and Ghanimi D. The Use of Medicinal Plants in Human Healthcare: A Scoop on Safety. *PharmaceutReg Affairs* 2013; 3:1.
- [11] Verma H, Prasad S B, Yashwant, Singh H. Herbal Drug Delivery System: A Modern Era Prospective. *International Journal of Current Pharmaceutical Review and Research* 2013. 4(3), 88-101.
- [12] Ahmad Sand Othman N. Strategic Planning, Issues, Prospects and the Future of the Malaysian Herbal Industry. *International Journal of Academic Research in Accounting, Finance and Management Sciences*. 2013; Vol. 3, 91-102.
- [13] Pandey A, Tripathi S. Concept of standardization, extraction and pre phytochemical Screening strategies for herbal drug. *Journal of Pharmacognosy and Phytochemistry*. 2014; (5): 115-119.
- [14] Dixit P K, Mittal S. A Comprehensive Review on Herbal Remedies of Diuretic Potential. *International Journal of Research in Pharmacy and Science*. 2013, 3(1), 41-51.
- [15] Rajagopala P.L, Dhilna K.K, Kumar P.N.S, John J. Herbs in Inflammation A Review. *International Journal of Ayurvedic and Herbal Medicine*. 2013; 3(4), 1289 - 1307.
- [16] M. Padmavathi. Drug Delivery System in Nano Greens. *International Journal of Herbal Medicine* 2013; 1 (3): 56-60.
- [17] Regulation of herbal medicines. Directive 2004/24/EC. House of commons; 2014.
- [18] Qusaj Y 1, 2, Leng A2, Alshihabi F 1, Krasniqi B 2 and Vandamme T 1. Development strategies for herbal products reducing the influence of natural variance in dry mass on tableting properties and tablet characteristics.
- [19] Supplementary guidelines on good manufacturing practices for the manufacture of herbal Medicines. World Health Organization, WHO Technical Report Series, No. 937, 2006
- [20] Sanjoy Kumar Pal, Yogeshwer Shukla. Herbal Medicine: Current Status and the Future. *Asian Pacific J Cancer Prev* 2003;4, 281-288.
- [21] Rivera JO1-3, Loya AM1-3 and Ceballos R3. Use of Herbal Medicines and Implications for Conventional Drug Therapy Medical Sciences. *Altern Integ Med* 2013, 2(6).

- [22] RajeswaraRao B.R., Rajput D.K., Nagaraju G. and Adinarayana G. Scope and potential of medicinal and aromatic plants products for small and medium enterprises. *Journal of Pharmacognosy*. 2012; 3(2) 112-114.
- [23] Kim JS, Park SI, Yang HW, Shin JH and Kim TY: Cytotoxic components from the dried rhizomes of *Zingiber officinale* Roscoe. *Archives of Pharmacal Research* 2008; 31(4) 415-418.
- [24] Nievergelt A, Huonker P, Schoop R, Altmann KH and Gertsch J: Identification of serotonin 5-HT<sub>1A</sub> receptor partial agonists in ginger. *Bioorganic & Medicinal Chemistry* 2010; 18(9): 3345-3351.
- [25] Li S, Yuan W, Deng G, Wang P, Yang P and Aggarwal B: Chemical Composition and Product Quality Control of Turmeric (*Curcuma longa* L.). *Pharmaceutical Crops* 2011; 2: 28-54.
- [26] Mahady GB, Pendland SL, Yun G and Lu ZZ: Turmeric (*Curcuma longa*) and curcumin inhibit the growth of *Helicobacter pylori*, a group 1 carcinogen. *Anticancer Res* 2002; 22 (6C): 4179-4181.
- [27] Ni Y, Turner D, Yates KM and Tizard I: Isolation and characterisation of structural components of Aloe vera L. leaf pulp. *Int. Immunopharmacol* 2004; 4: 1745-1755.
- [28] Eshun K and He Q: Aloe vera: A valuable ingredient for the food, pharmaceutical and cosmetic industries – A review. *Crit. Rev. Food Sci Nutr* 2004; 44: 91-96.
- [29] Bajaj KL, Kaur G, Singh J and Gill SPS: Chemical evaluation of some important varieties of onion (*Allium cepa* L.). *Plant Foods for Human Nutrition* 1980; 30(2): 117-122.
- [30] Patricia C: Onion-Culinary Foundation and Medicine. The Epicurean Table. Retrieved, 2013.
- [31] Kuwajima H, Taneda Y, Chen WZ, Kawanishi T and Hori K: Variation of chemical constituents in processed licorice roots: quantitative determination of saponin and flavonoid constituents in bark removed and roasted licorice roots. *Yakugaku Zasshi* 1999; 119(12): 945-955.
- [32] Kitagawa I: Licorice root. A natural sweetener and an important ingredient in Chinese medicine. *Pure Appl. Chem* 2002; 74(7): 1189-1198.
- [33] Teris A and Beek V: Chemical analysis of *Ginkgo biloba* leaves and extracts. *Journal of Chromatography* 2002; 967(1): 21-55.
- [34] Ginkgo Seed Poisoning. *Pediatrics* 2002; 109(2): 325-327.
- [35] Rekha S, Singhal P and Kulkarni R: Handbook of Indices of Food Quality and Authenticity. Food industry and trade. Woodhead Publishing 1997; 395.
- [36] Srinivasan K: Role of Spices Beyond Food Flavoring: Nutraceuticals with Multiple Health Effects. *Food Reviews International* 2005; 21(2): 167-188.
- [37] Weber HA, Zart MK and Hodges AE: Chemical comparison of goldenseal (*Hydrastis canadensis* L.) root powder from three commercial suppliers. *Journal of Agricultural and Food Chemistry* 2003; 51(25): 7352-7358.
- [38] Foster S and Duke J: 2000. A Field guide to Medicinal Plants and Herbs of Eastern and Central North America. New York.
- [39] Jiang X, Zhang JC, Liu YW and Fang Y: Studies on chemical constituents of *Valeriana officinalis*. *Zhong Yao Cai* 2007; 30(11): 1391-1393.
- [40] Questions and Answers About Valerian for Insomnia and Other Sleep Disorders. Office of Dietary Supplements. National Institutes of Health. 2006. Retrieved 2007.
- [41] Zheng CJ and Qin LP: Chemical components of *Centella asiatica* and their bioactivities. *Journal of Chinese Integrative Medicine* 2007; 5(3): 187-189.
- [42] www.bulkactives.com.
- [43] Ruan B, Kong LY, Takaya Y and Niwa M: Studies on the chemical constituents of *Psoralea corylifolia* L. *J Asian Nat Prod Res* 2007; 9(1): 41-44.
- [44] www.seacoast.com.
- [45] Orav A, Kailas T and Ivask K: Volatile constituents of *Matricaria recutita* L. from Estonia. *Proc. Estonian Acad. Sci. Chem* 2001; 50(1): 39-45.
- [46] Baumann LS: Less-known botanical cosmeceuticals. *Dermatologic therapy* 2007; 20(5): 330-342.
- [47] Douiri LF, Boughdad A, Assobhei O and Mounni M: Chemical composition and biological activity of *Allium sativum* essential oils against *Callosobruchus maculatus*. *IOSR Journal of environmental science, toxicology and food technology* 2013; 3(1): 30-36.
- [48] www.google.com.
- [49] elicio JD, Santos RS and Gonçalez E: Chemical constituents from *Vitis vinifera* (Vitaceae). *Arq. Inst. Biol* 2001; 68(1): 47-50.
- [50] Gottschalck TE and Breslawec HP: 2012. International Cosmetic Ingredient Dictionary and Handbook. 14th ed. Washington: Personal Care Products Council.
- [51] Musa OM and Claude CJ: Chemical composition of carrot seeds (*Daucus carota* L.) cultivated in Turkey: characterization of the seed oil and essential oil. *Academic Journal* 2007; 58(4): 359.
- [52] www.biocosmetics.com.
- [53] Colby SM, Crock J, Rizzo BD and Lemaux PG: Germacrene C synthase from *Lycopersicon esculentum* var. 'cherry tomato': cDNA isolation, characterization, and bacterial expression of the multiple product sesquiterpene cyclase. *Proc. Natl. Acad. Sci* 1998; 95(6): 198-200.
- [54] www.faqs.org.
- [55] Agarwal R, Agarwal C, Ichikawa H, Singh RP and Aggarwal BB: Anticancer potential of silymarin: from bench to bedside. *Anticancer Res* 2006; 26(6B): 4457-4498.
- [56] Singh O, Khanam Z, Misra N and Srivastava MK: Chamomile (*Matricaria chamomilla* L.): An overview. *Pharmacogn Rev* 2011; 5(9): 82-95.
- [57] Ramawat KG and Goyal S: The Indian Herbal Drugs Scenario in Global Perspectives. *Bioactive Molecules and Medicinal Plants* 2008; 9(3): 325-347.