

## Phcog Rev.: Short Review

### Care with Nature's Cure: Herbal Drugs

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#### ABSTRACT

The acceptance and recognition of herbal medicine is increasing day by day. One of the important reason in increasing this interest is the perception of natural remedies being somehow more efficacious and less harmful than synthetic chemicals. This perception is not exactly true. In this review article, we have discussed several popular herbs and tried to provide a comprehensive review that summarizes adverse effects of herbal remedies. For being vigilant about the adverse effects one must have sufficient data and information about safety parameters. The hurdles in evaluating the safety of herbal drugs are lack of standardization, insufficient quality control and overall under reporting. The challenges posed in evaluating and improving safety of herbal drugs are need of standardization and quality control, availability of official compendia, dissemination of information, additional research, pharmacovigilance and need of regulation. With concentric efforts to surmount these challenges, the wealth of traditional knowledge will be put to judicious use in the form of herbal remedies and will be awarded with their rightful place in the health care system.

**KEYWORDS:** Adverse Effects, Standardization, Quality Control, Regulations.

#### INTRODUCTION

Three decades ago only a few had any appreciation of the number of remedies that had their origin in herbal medicine and most had a vague impression of what herbal medicine, traditional medicine, or other forms of complementary and alternate medicine practices implied (1). For a variety of reasons more individuals nowadays prefer to take personal control over their health with use of herbal medicines, not only in the prevention of diseases but also to treat them. This is particularly true for a wide variety of illness readily treated at home (common cold etc.)(2). Herbal products are also commonly used by patients with certain chronic medical conditions, including breast cancer (12%)(3), liver disease (21%)(4), human immunodeficiency virus (22%)(5), asthma (24%)(6), and rheumatological disorders (26%)(7). The WHO estimates that about three-quarters of the world's population currently use herbs and other forms of traditional medicines to treat their diseases. Even as we commence the new century with its exciting prospect of gene therapy, herbal medicines remain one of the common forms of therapy available to the world population.

The acceptance and recognition of herbal medicine in part is due to the acknowledgement of the value of traditional and indigenous pharmacopoeias, incorporation of some medicines derived from these sources into pharmaceuticals(8,9,10), the need to make health care affordable for all, and the perception that pharmaceutical drugs are increasingly overprescribed, expensive, even dangerous. Another important perception fomenting this interest is that natural remedies are somehow safer and more efficacious than remedies that are pharmaceutically derived(11,12).

#### HERBAL MEDICINE

The increasing awareness of herbal medicines is acknowledged by World Health Organization (WHO). 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 today. 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.

#### HERBAL MEDICINE- CURRENT STATUS

The art of herbal medicine is extremely ancient, probably predates modern Homo sapiens(13). In ancient cultures, people methodically and scientifically collected information on herbs and developed well-defined herbal pharmacopoeias. The earliest recorded evidence of such efforts in Indian, Chinese, Egyptian, Greek, Roman and Syrian texts dates back to about 5000 years. The classical Indian texts include *Charak Samhita* and *Sushruta Samhita*.

Irrespective of the decline in use of herbal medicines, the importance of botanicals in the evolution of medicine remains unchallenged. Many drugs are developed with phytochemicals or taking phytochemicals as lead molecules. The valuable mainline drugs include digitalis, cinchona, taxol, ergotamine, morphine, cocaine, reserpine and numerous others. Despite the importance of plant led discoveries in the evolution of medicine some regulatory bodies such as the U.S. Food and Drug Administration (FDA) consider herbal remedies to be insignificant or potentially dangerous(14). Indeed, today in the United States, herbal products can be marketed only as food supplements under Dietary Supplement Health and Education Act of 1994 (DSHEA) and manufacturer or distributor cannot make a specific claim on the label regarding the ailments for which the product might be used without FDA approval.

With or without the interference from the regulatory authorities the use of herbal medicines is on the surge and the market is increasing day by day(15). The global market for herbal medicines currently stands at over \$60 billion annually.

Sales are projected to increase at an average annual growth rate at 6.4% through 2007. In India, the herbal drug market is about \$ 1 billion.

#### ADVERSE EFFECTS OF HERBAL REMEDIES

Because herbal products are thought to be "natural", many people believe that they are inherently safe(16). The perception that herbal remedies are inherently safe is based on traditional use rather than on systematic studies designed to detect adverse effects. However, herbal products can be as toxic as or even more toxic than prescription medicine. The evidence of the toxicity of such products has accumulated(17). This is not surprising since botanicals are complex mixtures of chemicals, described by Robbers and Tyler as 'Crude drugs of vegetable origin'. They can produce adverse effects, cause drug interactions and possibly create surgical problems. These physiologic and pharmacological effects of herbal products are of growing scientific interest.

Adverse drug reaction is an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product. The reports of such reactions caused by herbal products surface intermittently. Almost forgotten is the striking outbreak of eosinophiliamyalgia syndrome associated with a dietary supplement containing L-tryptophan that occurred in 1989. There were more than 1500 cases and at least 37 deaths(18). More recently, hepatotoxicity associated with kava has resulted in warnings to consumers or the removal of kava containing products from the market of several European countries and the advice by FDA (Food and Drug Administration)(19). Other herbs found to be hepatotoxic are pyrrolizidine alkaloid containing Senecio, Crotalaria, Symphytum, Heliotropium. Also, the association between comfrey and veno-occlusive disease, as well as between aristolochic acid and renal failure, urothelial carcinoma has resulted in actions of varying severity from different national regulatory agencies, including the FDA, which advised dietary supplement manufacturers to remove comfrey products from the market (US Food and Drug Administration) and sent a letter to health care professionals expressing concern about the safety of aristolochic acid (US Food and Drug Administration). Care should also be taken with use of herbal medications to treat cardiovascular problems (CVS)(20). While some herbal medicines to treat CVS problems may be worthwhile, many contain natural cardiac glycosides, blood thinners, or affect blood pressure and are not only bioreactive on their own but can work with prescribed medications to potentiate or diminish their action(21). For example, ginger contains a potent inhibitor of thromboxane synthetase(22) that prolongs bleeding time. According to Miller(23) its use could result in adverse implications for pregnant patients or those on concomitant warfarin therapy. It is noteworthy nonetheless, that ginger is still a favored remedy to treat nausea from morning or motion sickness. Feverfew has the potential of enhancing platelet inhibitors and its use as a headache remedy should be avoided during therapy with blood thinning agents(24). It is also

recommended that heparin-like herbs not be taken during pregnancy or lactation, since cranial bleeding or other associated effects could be induced in the fetus or nursing infant, respectively(25,26).

Allergic reactions can occur with herbal use and are manifested in a variety of forms(27). Both Type I immediate hypersensitivity reactions leading to rhinitis, headache, dermatitis (hives), and/or anaphylactic shock are commonly induced by cross-reactions among Asteraceous (daisy family) plants taken internally, whereas delayed Type IV, contact dermatitis is more prevalent when topical applications are used. Other adverse effects are listed in Table 1.

#### DIFFICULTIES IN EVALUATING SAFETY

##### A) Lack of standardization

Consistency in composition and biologic activity are essential requirements for the safe and effective use of therapeutic agents. However, botanical preparations rarely meet this standard because of problems in identifying plants, genetic variability, variable growing conditions, differences in harvesting procedures, storing and processing, nature of formulation and above all, the lack of information about active pharmacologic principles(28).

Botanical identity can be difficult to establish since two different drugs can be called by the same name by two different collectors. For eg Sarothami scoparii flos can be of two different species as Sarothammus scoparius and Spartium junceum. Such kind of misunderstanding may lead to serious adverse conditions. Example, replacement of *Stephania tetrandra* (fangji) with the root of *Aristolochia Fangchi* (guangfangji) in a slimming treatment that included conventional medicines resulted in numerous cases of progressive renal interstitial fibrosis, complicated in some persons by urothelial carcinoma(29). Similar problems may arise when the Chinese herbal ingredient 'mutong' is taken from *A. manshuriensis* (guanmutong) instead of akebia or clematis(30,31).

Product identification can be a next obstacle. Many commercially available products contain multiple ingredients. For instance, Sinupret (Bionorica), the best selling herbal medicinal product in Germany, contains five different medicinal plants. Asian herbal mixtures typically contain about twice that amount. In such cases, it is often impossible to discover which ingredient caused a reported health problem.

Brand names suffer from confusion(32). One herbal extract can be contained in dozens of different brands, and not infrequently identical brand names contain different mixtures of plants. Labeling of commercial products is often less than sufficient. Associations between one herbal ingredient and a reported adverse effect can therefore be difficult, sometimes impossible to establish.

Accidental adulterations in herbal remedies are particularly disconcerting since they occur so unexpectedly. Usually they remain undetected unless they can be linked to an outbreak or epidemic. An example in this respect is veno-occlusive disease due to over hundred pyrrolizidine alkaloids found within species of the Asteraceae, Borginaceae, and Fabaceae which can be life-threatening or fatal(33).

Table 1: Adverse effects of different herbs.

| Herb  | Use<br>[Phytochemicals]   | Adverse effect  | Ref.   |
|---|---|---|--------|
| Ashwagandha<br>( <i>Withania somnifera</i> )          | In arthritis, energizer<br>[Alkaloids]  | Decrease in body temperature, upset stomach, breathing problems, chest pain, skin hives, rash, itchy or swollen skin.   | 44, 45 |
| Astragalus root<br>( <i>Astragalus membranaceus</i> ) | Immunostimulant<br>[Cycloartane triterpene glycosides]  | Low blood pressure, low blood sugar and increased urine production. May result in dizziness and fatigue.  | 46, 47 |
| Attractylodes<br>( <i>Bai-zhu, Pai-chu</i> )          | Supplements spleen and dries dampness<br>[Volatile oil]   | Liver toxicity, sedation, dehydration (diuretic), lowers blood sugar.   | 46, 47 |
| Artemisa,<br>[ <i>Artemisia annua</i> ]               | Antimalarial<br>[Aromatic oils]   | Allergic reactions, skin rashes and altered mental status.  | 47     |
| Betel nut<br>( <i>Areca catechu</i> )                 | Stimulant<br>[Alkaloids]  | Deterioration of psychosis in patients with preexisting psychiatric disorders.  | 48     |
| Bitter almond seeds<br>( <i>P. amygdalus</i> )        | Mild laxative<br>[Fixed oil]  | May cause cyanide poisoning if consumed in very large quantities.   | 49     |
| Black cohosh<br>( <i>Cimicifuga racemosa</i> )        | Gynecologic disorders,<br>Rheumatism<br>[Isoferulic acid]   | Nausea, vomiting and gastroenteritis.   | 50     |
| Buckthorn Bark<br>( <i>Rhamnus frangula</i> )         | Cancer treatment<br>[Anthraquinones]  | Increased bowel movements and diarrhea.   | 49     |
| Cassava beans<br>( <i>Manihot esculenta</i> )         | Treat <u>hypertension</u> ,<br>headache and pain<br>[Carbohydrate]  | Cyanide poisoning and death if consumed in large quantities.  | 49     |
| Chamomile<br>( <i>Chamaemelum nobile</i> )            | Stomach upsets, Nausea,<br>Insomnia.<br>[Sesquiterpene lactones]  | Allergy belongs to ragweed family.  | 51     |
| Chaparrel<br>( <i>Larrea divaricata</i> )             | Slimming<br>[Lignans<br>Nordihydroguaiaretic acid]  | Nausea, vomiting, diarrhea, cramps, skin irritation, mouth sores and may promote tumor growth. Severe hepatitis.  | 52, 53 |
| Choke cherry pits<br>( <i>Prunus virginiana</i> )     | Diarrhea and pulmonary complaints<br>[Prussic acid]   | May cause cyanide poisoning and death if consumed in large quantities.  | 49     |
| Comfrey ( <i>Symphytum officinale</i> )               | Wound healing<br>[Pyrrolizidine<br>Alkaloids]   | Genotoxic, carcinogenic, hepatotoxic. Liver toxicity: Veno-occlusive disease, fatal liver intoxication.   | 54     |
| Dong Quai Root,<br>( <i>Angelica sinensis</i> )       | Menstrual disorders.<br>[Aromatic oil]  | Hypersensitivity to the herb which may lead to bleeding and fever. Photosensitization. Slight laxative effect.  | 55, 56 |
| Echinacea<br>( <i>Echinacea purpurea</i> )            | Treatment of viral, bacterial and fungal infections, chronic wounds, ulcers and arthritis. [Polysaccharide] | Anaphylaxis, Skin rash and insomnia. Allergic reaction. Aggravate autoimmune disorders (like lupus). Trigger immunosuppression, poor wound healing and infection. | 57, 58 |
| Evening Primrose Oil,<br>( <i>Oenothera biennis</i> ) | Conditions related to deficiency of essential fatty acids and alcoholism.<br>[Linolenic acid]               | Mild gastrointestinal effects and headache.   | 59     |
| Feverfew ( <i>Tanacetum parthenium</i> )              | Treatment of migraines, fever, menstrual disorders.<br>[Sesquiterpene<br>Lactones]                          | Mouth ulceration or gastric disturbance. Contact dermatitis.  | 60     |

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| Ginsegn Asian, ( <i>Panax ginseng</i> )              | Tonic for invigoration, physical or mental exhaustion, stress, inadequate resistance to infections<br>[Ginsenosides]  | Hypertensive and chronotropic activities, Ginseng Abuse Syndrome (GAS) on long-term use. Produce morning diarrhea, insomnia, nervousness, depression, confusion, skin rashes and high blood pressure. Breast swelling or tenderness and changes in menstrual cycle (amenorrhea). | 61 |
| Ginsegn Russia ( <i>Eleutherococcus senticosus</i> ) |   |  |    |
| Ginger Root, ( <i>Zingiber officinale</i> )          | Prevent nausea and vomiting, dyspepsia, stomachic.<br>[Gingerol]  | Heartburn  | 62 |
| Goldenseal ( <i>Hydrastis Canadensis</i> )           | Anti-infective<br>[Hydrastine, berberine]   | Uterotonic, induces neonatal jaundice. May oppose anticoagulants. In large doses causes GI upset, hypertension, seizures, respiratory failure, and cardiac spasms. Anorexia, dermatomyositis, elevated serum iron, psychosis, swollen liver, damaged stomach lining, death.      | 63 |
| Germander ( <i>Teucrium poliumm</i> )                | Weight loss<br>[Furano Diterpenoids]  | Acute liver failure. Inflammation of the liver (hepatitis), liver injury and death.  | 64 |
| Guar gum ( <i>Cyamopsis psoroliodes</i> )            | Obesity<br>[Galactose]  | Obstructions of the bowel and esophagus, particularly among those with esophageal abnormalities.   | 65 |
| Guggul ( <i>Commiphora mukul</i> )                   | Hypocholesterolemic<br>[Resin, volatile oils, gum]  | Headache, mild nausea, eructation, and hiccup.   | 66 |
| Guarana ( <i>Paullinia cupana</i> )                  | Stimulant<br>[Caffeine]   | Agitation and insomnia.  | 67 |
| Horse chestnut ( <i>Aesculus Hippocastanum</i> )     | Varicose veins<br>[Saponin]   | Pruritus, nausea.  | 68 |
| Hawthorn ( <i>Crataegus spp.</i> )                   | Heart failure.<br>[Vitamin C, flavonoids, glycosides]   | Nausea, dizziness and fatigue.   | 69 |
| St. John's Wort ( <i>Hypericum perforatum</i> )      | Mild to moderate depressive states.<br>[Hypericin and pseudohypericin]  | Gastrointestinal disturbances, allergic reactions, fatigue, dizziness, confusion, dry mouth, and photosensitivity.   | 70 |
| Kelp ( <i>Fucus vesiculosus</i> )                    | Weight loss<br>[Iodine]   | Hyperthyroidism  | 71 |
| Kava ( <i>Piper methysticum</i> )                    | Conditions of nervous anxiety, stress, and restlessness, Sedative.<br>[Kavalactones]  | Sedation, oral and lingual dyskinesia, torticollis, oculogyric crisis, exacerbation of Parkinson's disease, hepatotoxicity, mild gastrointestinal disturbances.  | 72 |
| Khat ( <i>Catha edulis</i> )                         | Stimulant<br>[Cathinone]  | Chronic liver dysfunction.   | 71 |
| Lobelia ( <i>Lobelia inflata</i> )                   | Respiratory stimulant.<br>[Lobelic acid, chelidonic acid]   | Lobeline can cause autonomic nervous system stimulation or depression. At low doses: bronchial dilation and increased respiratory rate. Higher doses: respiratory depression, sweating, rapid heart rate, hypotension, coma and death.   | 73 |
| Licorice ( <i>Glycyrrhiza glabra</i> )               | For catarrhal conditions of the upper respiratory tract and gastric/duodenal ulcers. Bronchitis. Adrenocorticoid insufficiency<br>[Glycosides, flavonoids, asparagine, isoflavonoids] | On prolonged use and higher doses: mineralocorticoid effects, sodium and water retention and potassium loss, hypertension, edema, and hypokalemia, in rare cases, globinuria. High blood pressure, water retention and even serious heart problems.                              | 74 |
| May apple ( <i>Podophyllum peltatum</i> )            | Liver tonic<br>[Resin]  | Nausea, vomiting, inflammation and edema of the bowel, diarrhea, elevated liver enzymes and hematologic abnormalities.   | 75 |

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|---|---|--|--------|
| Milk Thistle, ( <i>Silybum arianum</i> )  | Liver damage, hepatic cirrhosis<br>[Silybin, silydianin]                                | A mild laxative effect.  | 63     |
| Rauwolfia ( <i>Rauwolfia serpentina</i> ) | Antihypertensive, sedative action<br>[Reserpine]  | Sedation, inability to complete tasks, mental depression, nasal congestion, increased gastric secretion and mild diarrhea  | 76, 77 |
| Senna ( <i>Cassia senna</i> )             | Laxative, skin diseases<br>acne, ringworm<br>[Hydroxyanthracene glycosides, sennosides] | Dependency for normal bowel movements. Loss of fluids, low potassium levels and diarrhea, dehydration and potentially negative effects on the heart and muscles. Acute liver toxicity. | 78     |

### B) Insufficient Quality control

In most countries, herbal medicines are not regulated as medicines but marketed as dietary supplements hence mandatory quality controls of medicines can be easily surpassed. The quality of some products has repeatedly been shown to be suboptimal(34). Some of the most extreme examples include Asian herbal mixtures that can be contaminated (for example with botanicals, micro-organisms, microbial toxins, heavy metals, pesticides or adulterated with powerful prescription drugs). The drugs and metals reported to be found were ephedrine, chlorpheniramine, ethyltestosterone, phenacetin, glyburide, sildenafil, colchicine, adrenal steroids, alprazolam, phenylbutazone, and fenfluramine; lead, mercury(35-39). In 1991 WHO developed guidelines for the assessment of herbal medicine. 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).

### C) Lack of systematic data

Herbal medicines are usually not patentable. Therefore, keen commercial impetus for systematic research rarely exists. Consequently there is a lack of hard data on herbal safety. Much of the available evidence is either built on nonclinical investigations or on incomplete and thus inconclusive clinical data(32). Depending on the circumstances, both under-reporting and over-reporting of herbal adverse effects have been suspected, and the unduly strong influence of the press in this area is a well recognized aggravating factor(40,41). Users of herbal medicines often do not inform their doctor, and conventional healthcare professionals sometimes lack sufficient knowledge of herbal medicine to advise their patients responsibly. As a consequence, the evidence regarding the nature and incidence of adverse effects caused by herbal medicines is woefully incomplete.

It is more difficult, however, to recognize adverse effects that develop over time e.g., hypokalemia from anthranoid laxatives. Embryotoxic, fetotoxic, and carcinogenic effects of herbal remedies are also likely to remain unrecognized in traditional settings. Although aristolochia plants have been used for centuries, their capacity to induce urothelial carcinoma by DNA-adduct formation has only recently become clear(42). The traditional experience is not always a reliable tool for the detection of rare reactions; it has limited value in

predicting risks associated with nontraditional preparations or with use under nontraditional circumstances (e.g., in combination with conventional drugs).

### CHALLENGES IN IMPROVING SAFETY OF HERBAL REMEDY

#### A) Need of Standardization and quality control of herbal drugs

Consistency in the quality of the herbal drugs can be maintained by practicing the Good Agricultural Practices and Good Field Collection Practices for cultivation and collection of herbal drugs. Standard practices for preservation and presentation has to be developed and practiced similarly. For quality control and quality assurance of the herbal drugs, the standardization techniques with respect to authentication, purity profile and assay has to be developed and bring into practice. The use of chromatographic techniques and marker compounds to standardize herbal preparations promotes batch to batch consistency. This, but, does not ensure consistent pharmacologic activity or stability. Moreover, analyses of purportedly standardized herbal preparations reveal that botanical products often do not contain the amount of the compound stated on the label(28).

#### B) Need of Official compendia

Several pharmacopoeias have provided parameters to maintain quality and standardize procedures in identification/ authentication of herbal inputs and there products. Most countries have evolved their pharmacopoeial standards, however, it is apparent that no country has a complete list of plants included in it and there is a lot desired to format different pharmacopoeias as per recommendations of WHO. The European Pharmacopoeia 2002 has 174 monographs on herbal drugs and preparations. British Herbal Pharmacopoeia has 233 monographs, British Herbal Compendium has 84 monographs, United States Pharmacopoeia and the National Formulary has 28 official monographs of the most commonly used plants in the country. The countries with strong background of traditional medicine as China and India are leading. Chinese Pharmacopoeia 2000 has 992 monographs and Ayurvedic pharmacopoeia of India [API] has about 1000 single drugs and 8000 compound formulations of recognized merit used in India. The United States Pharmacopoeia (USP) is also compiling standard monographs for herbal dietary supplements and dispensatory information (DI). They have already published 11 monographs and an additional 12 are under preparation.

As a complement to these efforts a number of organizations are preparing monographs to delineate details of herbs that are popularly used as phytomedicines and medicinal plant preparations so that their recognition as official medicines may culminate. The well recognized monographs are from German Commission E (380 monographs) and European Scientific Cooperative On Phytotherapy (ESCOP) (60 monographs). In order to set standards to document the quality of herbal products and outline the therapeutic parameters for safe and effective use, publication of the WHO Monographs on Selected Medicinal Plants is on-going with Volume 1 (1999) of 28 monographs on 31 plant species and Volume 2 (2000) of an additional 30 monographs and Volume 3 of an additional 31 plants. Also, the herb trade, in recognizing its responsibility to provide appropriate guidelines, has recently published through the American Products Herbal Association (AHPA) The Botanical Safety Handbook, 2nd edition (1998). The most ambitious attempt in this respect is that of the American Herbal Pharmacopoeia and Therapeutic Compendium which plans to publish at least 2000 monographs of this nature.

#### **C) Need of Dissemination of information**

Dissemination of the information is positively important in helping the patient or consumer to make educated choice, this can be expedited by making use of internet sources like the National Center for Complementary and Alternative Medicine (<http://nccam.nih.gov>), American Botanical Council ([www.herbalgram.org](http://www.herbalgram.org)), US Food and Drug Administration ([www.fda.gov](http://www.fda.gov)), and the US Pharmacopoeia ([www.U.S.P.org](http://www.U.S.P.org)), International Bibliographic Information on Dietary Supplements (IBIDS) (<http://odp.od.nih.gov/ods>). Currently, IBIDS contains 400, 000 citations and abstracts of published international, scientific literature on dietary supplements, including vitamins, minerals, and botanicals and is updated quarterly.

The dissemination of information to the leity should be complemented by sensitizing allopathic practitioners to the aspect of herbal products. It is recognized that allopathic practitioners have little training in understanding various forms of complementary and alternate medicine practices even if it has impact on the health of their patients, who are often, also under prescriptive medication. The sensitized practitioner will be eager to acquire information from the patients about concurrent uses of herbal products and alternative medicines without being judgmental.

To increase the sensitivity of future practitioners, a number of US medical schools are developing courses in Complementary and Alternative Medicine, including some exposure to herbal medicinal practices. The practice of sagacious use of the herbal remedies should be inculcated among the users abiding to rational use of drugs and herbs.

#### **D) Need of Additional Research and Surveillance of Adverse Effects**

The pressing need in the additional research related to traditionally used herbal remedies is identification of active principles. Without the knowledge of active principle it is difficult to standardize the product and its dose. For example Valerian is the oldest sleep aid yet after 2000 years of use we

still do not know its active principles. There is an urgent need to establish suitable procedures for identifying, analyzing and determining the concentration of active components in herbs. Another area of research need is of clinical trials to establish efficacy, safety and other parameters of herbal medicines in scientific and systematic manner.

Adverse effects from herbal remedies are not rare, but their frequency and severity are unknown, because, other than spontaneous reporting of events and case reports, there is no mechanism for collecting and assessing them. DeSmet (1995b)<sup>43</sup> proposed that post marketing surveillances (pharmacovigilance) of herbal remedies be conducted to 'detect serious adverse reactions, quantify their incidence and identify contributive and modifying factors'. Obviously, the success of such endeavors depend on those willing to voluntarily and spontaneously report such events to appropriate health care officials, pharmacologists (<http://www.faseb.org:aspet:HETMIG3.htmctop>), regulatory bodies (FDA 'MEDWATCH' ([http://www.vmcfsan.fda.gov:\\_dms:aems.html](http://www.vmcfsan.fda.gov:_dms:aems.html))), and responsible parties in the herb trade industry itself, like the American Botanical Council (<http://www.herbs.org>), who are collating these data for public dissemination.

#### **E) The need for regulations**

1) Some herbs such as St. John warts are classified as phytomedicines as well as food supplements. Ironically the pharmacological activity will be the same you call by whatever name. Hence the line of demarcation should be made clear by regulatory authorities.

2) The regulatory requirements mandatory for conventional drug manufacturing should be made applicable to herbal product manufacturer. The extension of good manufacturing practices to manufacturers of herbal products would help towards preventing adulteration and improving the standardization of marketed botanical products.

3) The manufacturers of herbal products should obtain premarketing approval from the regulatory authorities demonstrating that their products present no substantial or unreasonable risk of injury under conditions of recommended use, as suggested on the label

4) The labels of herbal products should contain a list of constituents that unambiguously identifies herbs by their botanical and common names. Information about possible adverse effects, including the potential for herb-drug interactions, should be included.

5) Measures are needed to ensure that nonmedical practitioners who prescribe herbal treatments receive adequate training and continuous education to reach and maintain a high standard of practice. The United Kingdom Department of Health is already making progress in this domain, having proposed statutory self-regulation of herbal practitioners.

6) The manufacturers of herbal products should be required to report all adverse effects promptly to the regulatory authorities analogous to essential element of postmarketing surveillance required for all prescription drugs and some over-the-counter drugs and expert panels should review the safety of all.

## CONCLUSION

The practice of use of herbal remedies is as old as civilization. However it should be remembered that argument about use of herbal remedies by ancestors since time immemorial cannot be a substitute for compiled data on either efficacy or safety. The time has come to apply a scientific approach to this practice as the popularity of herbal remedies is escalating. The scientific studies of herbal remedies with respect to their efficacy, safety profile, adverse interactions, standardization etc should be taken up with utmost priority by not only the manufacturers but by the fraternity of pharmacy and medicine also. The fundings should be made available for such endeavors. The patients as well as conventional practitioners should be made aware of the adverse effects of herbal remedies as well as their potential to cause interactions on concomitant use with conventional medicines. The government should take initiatives with respect to laying down regulations for safe use of herbal remedies and implementing them. With these concentric efforts, the wealth of traditional knowledge will be put to judicious use in the form of herbal remedies and will be awarded with their rightful place in health care system.

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