

Chapter 1

General Introduction

India is unique country and has one of the oldest, richest and most diverse cultural traditions associated with the use of medicinal plants from the prehistoric times. This knowledge, accessible from hundreds of medical texts and manuscripts in the form of Vedic literature as a channel through which this continuous medical tradition reached down to the earliest systematisers. Ancient Indian literatures incorporate a remarkably broad definition of medicinal plants and considers 'all' plants as potential sources of medicinal substances ("Jagatyevananaoushadham na kincit vidyate dravyam vasannanartha yogayoh" (Ashtanga hridaya. SU.9-10). Vedic Samhitas, Nighantus (lexicons) and regional commentaries, has developed a unique system for using plants. The wonderful reference and treatises on herbal cure that have been available in India talk about the work of Dhanwantari, Nagarjun and Charak. In India, there is systematized use of herbal drugs and has been practiced from almost the very beginning of civilization. There are at least 5 different systems of medicine practised in India such as **Ayurveda, Unani, Siddha, Homeopathy, Naturopathy and Sowa-Rigpa**. These systems contain a large number of plants with proven or highly reliable medicinal properties. India alone boasts of more than 2000 medicinal plants, while the total number of medicinal herbs in the world used in varying systems is about 70,000.

Ayurveda

Ayurveda, one of the most Ancient systems of medicine practised in India, traces its origin to Brahma, the creator of the Universe who taught the science to Prajapati, he to Ashwini Devtas and they in their turn to Atreya etc. It dates back to Vedic age, (1500-800B.C). The term comes from the Sanskrit root, Ayu (life) and veda (Knowledge). As the name indicates, it is a system which covers the entire gamut of happy human life, involving the physical, metaphysical and the spiritual aspects. Sasruta considered the major aim of Ayurveda is to help people maintain

health. The treating of the disease is considered secondary. The concept of Ayurveda is as old as the "Vedas". The Rigveda, which is written between 4500-1600BC is one of the oldest repositories of human knowledge, mentions the use of 67 plants for therapeutic use. The Yajurveda enlists 81 plants whereas the Atharvaveda is written during 1200 BC describes 290 plants of medicinal value. The next landmark was when Sasruta samhita (600 BC) recorded 395 medicinal plants.

According to Ayurveda, all the objects in the universe including the human body, are composed of five basic elements ("panchamahabhutas") namely, earth, water, fire, air, and vacuum (ether). These elements in different proportions are in a balanced state to suit the needs requirements of different structures and function of the body matrix and its parts. These five elements combine to form the three basic forces, "tridoshas", which exist in everything in the Universe and influence all mental and physical processes. From earth and air, the air principle Vata is created. Fire and water yield the fire principle pitta ; and earth and water produce the water principle kapha. All of us are born with a particular balance of these doshas. The proportions are largely determined by the balance of doshas in our parents at the time of conception. Our body type and temperament and susceptibility to illness are largely governed by the predominant doshas.

Ayurveda, by and large, is an experience with nature. Unlike in Western Medicine many of the concepts elude scientific explanation in the modern sense of term. Western Medicine relies heavily on principles of basic sciences to explain various aspects of health science (Majumdar, 1989). The concept of science is an anathema to men of Ayurveda.

The concept of science cannot be limited to physical science alone; instead it should explore physical, living and conscious phenomena. There were attempts to equate the three doshas with biochemical neurohumours liberated by brain and its nerve endings (Udupa, 1983). Thus vata is equated with acetylcholine liberated by cerebral cortex and peripheral and parasympathetic nerve endings; pitta with catecholamines liberated by the nerve endings, hypothalamus, sympathetic nerve endings and adrenal medulla and kapha with histamine secreted by brain stem.

The drugs, when administered, act by promoting or destroying the respective neurohumours or their precursors. It is also observed that a person of vata-prakriti is lean and thin with an excess of acetylcholine, that of pitta-prakriti is muscular with a predominance of catecholamines and kapha-prakriti has a heavy body with an excess

of histamine.

Udupa, unlike many others who equate agni and pitta, also holds that they are different and agni refers to hormones and equates jatharagni with hormones with intestinal secretions, bhutagni with hormones regulating liver activities and dhatragini with hormones produced by endocrine gland that regulate cellular metabolism. Such experimental studies in Ayurveda, however lead us to the trodden path of Western medicine, leaving the much acclaimed “holistic approach” to total neglect (Laping 1984; Singh and Singh, 1990).

The concept of drug in ayurveda is somewhat different from those of the western systems of medicine. The term drug derived from the French word ‘drogue’ (a dry herb) and is defined as “any substance or product used to modify or explore physiological systems or pathological states for the benefit of recipient”. Bhesaja or ausadha is the ayurvedic equivalent of the drug. It overcomes bhesam or osa, diseases or even fear of diseases, and includes anything, material or means, used for this purpose. Therefore even food, fasting, penance, incantations, sleep, sunlight, shade and faith in physicians are prescribed in ayurvedic therapeutic for recuperation from illness.

Siddha

The Siddha system is one of the oldest systems of medicine in India. The term “Siddha” means achievement and “siddhars” were saintly figures who achieved results in medicine through the practice of yoga. In Siddha systems, the literature is in Tamil and they are practised in the Tamil speaking parts of India. The system is also called the Agasthya system after its famous exponent, sage Agasthya.

The Siddha system is largely therapeutic in nature. The principles and doctrines of this system, both fundamental and applied, have a close similarity to Ayurveda; with specialisation in iatro-chemistry. According to this system, the human body is the replica of the universe and so are the foods and drugs, irrespective of their origin. Like Ayurveda, this system believes that all object in the Universe, including the human body, are composed of five basic elements such as earth, water, fire, air and sky. The food that the human body takes and the drugs it uses are all made of these five elements. The proportion of the elements present in drugs vary and their preponderance is responsible for certain action and therapeutic results.

According to tradition, it was Shiva who unfolded the knowledge of siddha system of medicine to his consort, Parvati, who handed it down to Nandideva and he then to siddhars. Thus it is called “Saiva sampradayam” (tradition of Shiv) or “Siddha sampradayam”.

Unani

The Unani system of medicine owes its origin to Greece and has a long and impressive record in India. It was introduced in India by the Arabs and Persians sometime around the eleventh century. The theoretical framework of Unani medicine is based on the teachings of Hippocrates. It aims at restoring the equilibrium of various elements and faculties of the human body. The Unani system lays great emphasis on the maintenance of proper ecological balance on one hand, and on keeping water, food and air free from pollution on the other. In this process they made extensive use of the science of Physics, Chemistry, Botany, Anatomy, Physiology, Pathology, Therapeutics and Surgery. Treatment in the Unani system of medicine is done mainly through diet control for a simple disease in the initial stages followed by the administration of a single drug, failing which a compound preparation may be administered.

Yoga and Naturopathy

Yoga, which is rooted in Hindu religious principles, had been in practice for the last 500 yrs. Derived from the Sanskrit word, *yoga* meaning “union” encompasses a variety of disciplines designed to ultimately bring its practitioners close to God. According to Maharishi Patanjali, Yoga is the suppression of modifications of the mind. It offers a significant variety of proven health benefits though it is not a cure for any medical ailment. A yoga exercise increases the efficiency of heart and slows the respiratory rate, improves fitness, lowers blood pressure, promotes relaxation and reduces stress and anxiety. It also serves to improve coordination, posture, flexibility, and range of motion, concentration, sleep and digestion. It is a supplementary therapy for conditions such as cancer, diabetes, asthma, migraine and AIDS. It also helps to combat addictions like smoking.

Naturopathy is a system of man building in harmony with the constructive principles of Nature on physical, mental, moral and spiritual planes of living. It has

great health promotive, disease preventive and curative as well as restorative potential. According to the manifesto of British Naturopathic Association, "Naturopathy is a system of treatment which recognises the existence of the vital curative force within the body." It therefore, advocates aiding human system to remove the cause of disease i.e. toxins by expelling the unwanted and unused matters from human body for curing diseases (<http://indianmedicine.nic.in>).

Homeopathy

This practice originated in Germany. The word "homeopathy" is derived from the Greek words, *homios* means "similar" and *pathos* means "suffering". Homeopathy means treating diseases with remedies prescribed in minute doses, which are capable of producing symptoms similar to the disease, when taken by healthy people. It is based on the natural law of healing- "Similia Similibus Curantur" which means "likes are cured by likes". It was given a scientific basis by Dr. Samuel Hahnemann (1755-1843) in the early 19th century. Homeopathy today is a rapidly growing system and is being practiced almost all over the world. In India it has become a household name due to the safety of its pills and gentleness of its cure. This is practiced by about 10% of Indian population. This system is different from other systems of medicine in that very dilute solutions of alcoholic extracts of plants have been used and the potency is increased by dilution. The scientific principle behind this is not well known.

Sowa-Rigpa

"*Sowa-Rigpa*" commonly known as Amchi system of medicine is one of the oldest, Living and well documented medical tradition of the world. It has been popularly practiced in Tibet, Mongolia, Bhutan, some parts of China, Nepal, Himalayan regions of India and few parts of former Soviet Union etc. There are various schools of thought about the origin of this medical tradition, some scholars believe that it is originated from India, some say China and others consider it to be originated from Tibet itself. The majority of theory and practice of *Sowa-Rigpa* is similar to "*Ayurveda*". The first *Ayurvedic* influence came to Tibet during 3rd century AD but it became popular only after 7th centuries with the approach of Buddhism to Tibet. Thereafter this trend of exportation of Indian medical literature, along with Buddhism and other Indian art and sciences were continued till early 19th century.

India being the birth place of Buddha and Buddhism has always been favorite place for learning Buddhist art and culture for Tibetan students; lots of Indian scholars were also invited to Tibet for propagation of Buddhism and other Indian art and sciences. This long association with India had resulted in translation and preservation of thousands of Indian literature on various subjects like religion, sciences, arts, culture and language etc. in Tibetan language. Out of these around twenty-five text related to medicine are also preserved in both canonical and non-canonical forms of Tibetan literatures. Many of these knowledge were further enriched in Tibet with the knowledge and skills of neighboring countries and their own ethnic knowledge. “*Sowa-Rigpa*” (Science of healing) is one of the classic examples of it. *Gyud-Zi* (four tantra) the fundamental text book of this medicine was first translated from India and enriched in Tibet with its own folklore and other medical tradition like Chinese and Persian etc. The impact of *Sowa-Rigpa* along with Buddhism and other Tibetan art and sciences were spread in neighboring Himalayan regions. In India this system has been practiced in Sikkim, Arunachal Pardesh, Dargeling (West Bangal), Lahoul & Spiti (Himanchal Pardesh) and Ladakh region of Jammu& Kashmir etc. (<http://indianmedicine.nic.in>).

All these traditional systems suffered a severe setback during the British rule in India and faced almost complete neglect for about two centuries. The allopathic system was introduced and gained ground. The withdrawal of State Patronage could not harm much as the masses reposed faith in traditional systems and it continued to be practiced. After independence the Indian systems of medicine received a fresh boost under the patronage of the National Government and its people.

Government of India took several steps for the all round development of these systems. It passed laws to regulate and promote its education and training. It established research institutions, testing laboratories and standardized regulations for the production of drugs and for its practice. Department of Indian Systems of Medicine and Homoeopathy (ISM&H) was created in March,1995 and re-named as Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) in November, 2003 with a view to providing focused attention to development of Education & Research in Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy systems. The Department continued to lay emphasis on upgradation of AYUSH educational standards, quality control and standardization of drugs, improving the availability of medicinal plant material, research and

development and awareness generation about the efficacy of the systems domestically and internationally (<http://indianmedicine.nic.in>).

Protection of India's Traditional Knowledge

To protect India's Traditional Knowledge and intellectual property, Council of Scientific and Industrial Research (CSIR) and Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Ministry of Health and Family Welfare, Govt. Of India is developing a collaborative database (Digital Library) known as '**Traditional Knowledge Digital Library**' (TKDL).TKDL involves documentation of the knowledge available in public domain on traditional knowledge from the existing literature related to Ayurveda, Unani and Siddha indigitized format, in five international languages which are English, French, German, Spanish and Japanese. So far, the TKDL includes about 2.12 lakh medicinal formulations (Ayurveda: 82,900; Unani: 1,15,300; Siddha: 12,950), from 148 books available in public domain. Creation of TKDL – Yoga is under process and till date about 900 no. of Yoga postures from 14 old yoga books in public domain have been transcribed, which will also be video graphed and added to TKDL database.

The genesis of the maiden Indian effort dates back to the year 2000, when an interdisciplinary Task Force of experts was set up by Department of AYUSH and CSIR, to devise a mechanism on protection of India's Traditional Knowledge, after the wrong patents granted on the wound healing properties of turmeric (US patent No. 5,401,504) by USPTO and on the bio-pesticidal property of Neem (EPO patent No. 436257) by EPO, came to notice which were later fought and got revoked. Pursuant to this, studies were carried out to find out the extent of misappropriation of India's traditional knowledge which show that there is a continuous rise in misappropriation of traditional medicinal knowledge of India at the International Patent Offices. The reason for this misappropriation at International Patent Offices, as identified, is that the traditional medicinal knowledge exists in local languages, such as Sanskrit, Urdu, Arabic, Persian and Tamil which is neither available nor can be understood by patent examiners even in case of availability, at international patent offices since the information exists in local languages. In other words, there exists a language and format barrier due to which patents are being taken on the existing traditional knowledge of India. To break this language and format barrier Traditional Knowledge

Digital Library (TKDL) was created by India, which with the help of Information Technology tools and a novel classification system i.e., Traditional Knowledge Resource Classification (TKRC), makes the knowledge available to patent examiners in patent application format and in a language that can be understood by them. TKDL has enabled inclusion of approx. 200 subgroups instead of few subgroups available earlier in the International Patent Classification (IPC). The decision was taken in 35th IPC Union Meeting of World Intellectual Property Organization (WIPO) on the initiative of India. This is likely to have significant impact on the system of search and examination while granting patents in the area of traditional knowledge whereby the possibilities of grant of wrong TK patents shall get significantly reduced (<http://indianmedicine.nic.in>).

Herbal Medicines

In addition to the above systems wherein a large number of plants are used for alleviating the suffering of people, a large number of plants also are being used in remote areas of India and other countries. These plants are being “rediscovered” by the ethnobotanical surveys and are being used as medicines as such. The studies on bioprospecting and chemoprospecting also unearth a good number of plants having pharmacological activity. These “new” plants discovered recently add to the “herbal medicines” practised all over the world.

Active Principles

There is an ever-growing demand of medicinal plants in the global market. To approach the Western Market, at times, we have to equate our knowledge in terms of the Western Medicine. Anybody in the west, who is interested in plant medicines, would wish to satisfy himself with the data on active principles, shelf life, the pharmacological activities and side effects if any. Therefore we have to provide such data to all the customers for a better marketing of herbs.

Every medicine owes its activity to a single or a group of pharmacological active compounds (pharmacophores). In many cases, the active principle is the major compound that occurs in appreciable quantities, but in some other cases, the major compound need not be the best pharmacophore. The famous *Vinca* (*Catharanthus*) alkaloids never exhibited any antineoplastic property. It was only when the alkaloid

extract was fractionated, and each individual alkaloid was subjected to chemical studies, the anticancerous properties of vincristine and vinblastine (which occur in very low concentrations in roots) were discovered. The major alkaloids in *Catharanthus* are ajmalicine and serpentine and the antineoplastic alkaloids from a very minor fraction of the total alkaloids. The existing data on a number of medicinal plants only indicate that the aqueous/lipid extracts exhibit various pharmacological actions. But in many cases, the different components of a plant drug are found to exert widely different properties. In the case of Punarnava (*Boerhaavia diffusa*), the roots are found to contain punarnavoside, rotenoids such as the boeravinones A, B, C, D & E, Lignans such as liriodendrin and syringaresinol, flavones, sterols, boeravine (an isofuroxanthone) and hypoxanthine-9-L arabinofuranoside. Pharmacological studies proved that punarnavoside is the antifibrinolytic agent. Liriodendrin and hypoxanthine-9-L arabinofuranoside are found to be antihypertensive and the former is a Ca^{++} channel antagonist but the whole plant extract exhibits anti-inflammatory, diuretic and hepatoprotective activities probably due to the other compounds present in the plant. This clearly proves that the compounds other than the so-called active principle also are active in the healing processes attributed to the drug. Similarly in *Withania somnifera*, the total alkaloidal fraction exhibits hypotensive, bradycardic and respiratory stimulant activities, while the major group of components withanolides possess antiarthritic, immunosuppressive, antitumour and antibacterial properties.

The minor components, which are normally phenolics, are never attributed with any activity. It is in this context, Duke's (1997) observations are interesting and informative. Duke (1997) describes ferulic acid, gentisic acid, kaempferol glycosides and salicylic acid as pain relievers while ascorbic acid, cinnamic acid, coumarin, myricetin, quercetin and resveratrol are explained to be anti-inflammatory. Even the variety of chemicals and their richness (concentration) in a medicinal herb is of great value in assessing its property. Duke's database states that both coriander and liquorice contain 20 chemicals with antibacterial action; oregano and rosemary have 19; ginger 17; nutmeg 15; cinnamon and cumin 11; Black pepper 19; Bay 10 and garlic 13. Quantity wise, liquorice contains up to 33%; bactericidal compounds (dry weight basis), thyme 21%, oregano 88%, rosemary 4-8%, coriander 22% and fennel 1.5%.

It is the alkaloids, steroids, tannins which were considered the conventional active principle of a plant drug, but this concept is changing these days. The major compounds need not be the active compounds. A number of new compounds having

pharmacological action are reported recently as also new properties are discovered for some of the known compounds. e.g. polysaccharides and lectins are found to exhibit distinct pharmacological properties.

Antioxidants

In addition to the active principles, a plant extract, prepared either in water or alcohol contains a large number of antioxidants. According to the present knowledge, in addition to the traditional role of protecting the fats, proteins and carbohydrate, the biological antioxidants manage repair system such as iron transport protein (transferrin, ferritin, caeruloplasmin etc), antioxidant enzymes and factors affecting signal transduction, vascular homeostasis and gene expression (Frankel and Mayer, 2000). But environmental pollutants such as air/water contaminants, radiation, pesticides etc, produce a large influx of free radicals in the body and tip the balance between prooxidant (free radicals) and anti free radicals (antioxidants) in favour of the former, resulting in a cumulative damage of protein, lipid, DNA, carbohydrates and membranes leading to oxidative stress. The oxidative stress, in which the free radicals outweigh antioxidants in number, is suggested to be the cause of ageing and other diseases like atherosclerosis, stroke, diabetes, cancer and neurodegenerative diseases such as Alzheimer's disease and Parkinsonism. We normally receive a good amount of antioxidants through our diet consisting of spices, vegetables, pulses and cereals, which contain a large variety of these compounds, and their role in preventing human diseases includes cancer, atherosclerosis, stroke, rheumatoid arthritis, neurodegeneration and diabetes (Fang *et al.* 2002). At the time of oxidative stress, a good amount of external antioxidants are to be pumped into and this is the basis of various antioxidant-based therapeutics.

Nutraceuticals

Most of the herbal drugs are not marketed as drugs in western countries, but are used as food supplements having pharmacological activities. They are known as nutraceuticals. Nutraceuticals are food supplemented with compounds having pharmaceutical properties. They contain a sizable amount of nutrients in the form of carbohydrates or proteins (the major compounds) and a good dose of compounds having varied pharmacological properties. In developed countries the food, especially

those which are canned are fortified, are with a good dose of minerals, vitamins etc and are prepared to take good care of health. Calcium enriched beverages, food bars, cereals, yoghurt and fermented foods dominate the nutraceutical market in Japan; while in Europe it is omega 3 fatty acids along with calcium. A number of nutritional factors are added to nutraceuticals. They are L-lipoid factor (an antioxidant to scavenge free radicals), creatinine monohydrate (to increase muscle strength), inulin (to increase calcium absorption), L- carnitine (as a fat burner) and phytosterols (to reduce cholesterol). Recently herbal medicines in the form of plant powder or extracts (containing active components) are added to prepare nutraceuticals. For example fenugreek is added to prevent and treat diabetes or it is the isoflavones (to prevent breast cancer and to reduce the incidence of osteoporosis) added.

India can produce a wide variety of nutraceuticals. They can be prepared with all the “rasayana” drugs. The plants like Ashwagandha, Amrut, Punarnava, Shataveri, Amla etc are general tonics which can be mixed with food materials. They will take care of all body functions and regulate all body systems. These provide principles active in normalizing the metabolism and contain, in addition, a number of vitamins, minerals, co-factors and anti-oxidants. The well-known preparations like “Chavanprash, Dhanvantari, rasayana, Ashwagandhadi” etc. contain plant drugs with energy rich ghee, sugar etc. These preparations can be recommended as nutraceuticals. Global market for nutraceuticals is 40-50 billion US Dollars and this market is estimated to grow at the rate of 6% per annum. Nutraceuticals also are subjected to the regulatory systems applied to pharmaceuticals or foods. “Prevention is better than cure” is the principle of nutraceuticals.

Synergism

A plant metabolome (all the compounds present within a plant) contains about 20000 compounds. A plant extract (water or alcohol) would contain at least 200 - 2000 compounds which include all types of compounds like carbohydrates, amino acids, phenolics, vitamins etc. These compounds, if possessing any pharmacological action, will also contribute to the action of active principle within the drug. The phenolic antioxidants when present, may give a free-radical free environment or protect the active principle from deterioration. The medicinal properties of simple common phenols like ferulic acid, caffeic acid, kaempferol etc. are already explained.

The beneficial activities of the compounds other than the “active principles” will be an added benefit to the patient. In certain cases the different compounds present within are found to support various systems, which are complimentary to each other. For example in *Hypericum perforatum* (St. John’s Wort) where in a number of different molecules are found to have the same activity is interesting. The plant is used for treating anxiety, depression and sleep disorders. The compounds present in plant are lipid soluble hypericins (up to 0.75%), flavonoids (2-4%), xanthonces (0.0004%), procyanidins (8%), hyperforin (2-8%) and volatile oil (0.1-1%) of which hypericins, xanthonces and hyperforin are characteristic to St. John’s Wort. It was shown earlier that hypericin inhibits mono amine oxidase (MAO) and this increases the amount of neurotransmitters in the synapse between neurons and leads to enhanced mood (Suzuki *et al.*, 1984). Recent studies have shown that flavonoids and xanthonces in *Hypericum* extracts inhibit catechol-O- methyl transferase, another enzyme that catabolises neurotransmitters (Thiede *et al.*, 1994). Perovic and Muller, (1995) have shown that *Hypericum* extract decreases the uptake of the neurotransmitter, serotonin, in all rat synaptosomes. Thus it appears that a number of mechanisms act synergistically to increase the neurotransmitter signal.

Adulteration/substitution in herbal drugs

In the historic times the question of procuring drugs and controlling their quality did not arise as the physician himself used to take care of these aspects. He were well acquainted with the herbs used by them as medicine for treatment of an ailment. They were not only used to collect medicinal plants from the nearby forests, but also preparing various drug formulations themselves as per needs of the patients. Therefore, there was a least chance of using material other than the genuine one as medicine. But present day scenario is entirely different and has gone dramatic change during the last century on account of the shift of manufacturing process from home scale produce to industrial production and most of the herbal practitioners and plant based Pharmaceutical Companies largely depend upon the crude drug dealers and traders to meet their requirement of raw materials. Thus the supply of drugs became a booming business.

Adulteration is the substitution of the original crude drug partially or fully with other substances which is either free from or inferior in therapeutic and chemical

properties. The term adulteration covers a number of conditions which may be intentional or accidental. It often occurs when a drug is difficult to obtain or when its price is comparatively high. The adulterator chooses a exhausted drugs or apparently similar material that is cheap and readily available. Other methods of use for adulteration are addition of synthetic principles to fortify inferior products, large amounts of parts of plant other than that which constitutes the drug and worthless heavy material such as sand, stone. Since flowers form the key tool for identification of a plant, in their absence, the vegetative parts are considered for identification purpose. Similar looking leaves can mislead a person and thus cause wrong identification of the plant. Collection of the wrong plant erroneously by unskilled collectors also is a major reason contributing to the adulteration of the plant of interest. The adulteration may be unintentional due to confusion in vernacular names between indigenous systems of medicine and local dialects, lack of knowledge about the authentic plant, similarity in morphology and or aroma.

The usage of such adulterated or spurious raw materials for manufacturing medicine in place of genuine one is responsible for lowering quality and efficacy of the drug because the adulterated material may not have the active compound. Moreover, it may have toxic compound that may cause deleterious effect on human health. Consequently, reliability of the finished products at national and international level is affected and betraying the faith of people on Indian Systems of Medicine.

Quality control

Herbal medicines or herbal market suffers greatly because of the poor quality of the medicine or the inconsistency of the medicinal preparations available to the society so it's a big challenges of meeting global requirements of Quality efficacy, safety and standardization. Many factors contribute to this factor and they are the following.

- a) Wrong identification of the source material.
- b) Plant material collected at wrong times i.e. collected at times when the active components are not at maximum like very young plant parts, old plant parts etc.
- c) Poor storage conditions which will lead to microbial contamination and aflatoxins.
- d) Improper extraction methods and
- e) Poor knowledge on the shelf life of the extracts etc.

All these factors lead to the poor acceptance of the herbal preparations. Therefore, practices of GAP (good agricultural practice), GLP (good laboratory practices etc.) are brought in by regulatory authorities. However the quality of medicinal preparation can be judged by finding out the amount of biomarkers or active principle in a preparation. So this makes the knowledge of Biomarkers mandatory. But Biomarkers of a large number of plants are poorly known and this contribute greatly to the poor quality of medicines available in the market.

Biomarkers

Biomarkers are the compound/s or the cells/tissue/cellular contents specific to a particular plant. They indicate the presence and availability of the plant drug in a medicinal preparation. Knowledge of the quality and quantity of biomarkers in a sample, raw material, extract or formulation is a prerequisite for marketing the products. It is also useful in judging the amount of active components in a sample and also on the genuineness of the drug. The absence of a biomarker indicates that the drug is completely adulterated. Lesser quantities of biomarkers indicate poor quality of the raw material or the sample is adulterated. Compounds other than the biomarkers indicate that the drug contains some other plant/drug.

There are basically two types of biomarkers.

1. Chemical Biomarkers.
2. Pharmacognostic Biomarkers.

Chemical biomarkers

A chemical marker is a compound, whether it is a primary or secondary metabolite, or an assortment of compounds, which are seen in plant in detectable concentrations. An ideal Biomarker should be stable, easy to isolate, characteristic and should be immune to ecological changes. Any compound occurring in appreciable concentration can be a reliable biomarker. In cases where two or more plants/samples possess the same compound, a second compound present in any one of the two in combination with the first form the Biomarker. In such cases the two biomarkers in a plant need not be of the same chemical class. They can be widely different in their properties.

Pharmacognostic biomarkers

These are the tissues, cells or cell inclusions characteristic to a particular drug plant. They are of immense use in finding out the purity and genuineness of raw material in the whole form or powder form.

Pharmacognostic markers can point on the identity of the plant. For example:

- (a) The presence of aerenchyma indicates that the sample is an aquatic species.
- (b) Large number of starch grains is an indication that the drug is a storage organ like the root, seed, bark etc.
- (c) Bark cells denote that the source is a stem or root.
- (d) The presence of palisade and stomata in large number indicates that the drug is a leaf. The location of bark cells, more vessels and tracheids, indicate that this drug is adulterated.

Export potential of herbal and medicinal plants of India

In India nearly two thousand species are reported to be of medicinal value and at present about fifteen hundred drug yielding plants are well identified and are used as medicaments. Over six thousand pharmacies are reported to be functioning in the country and there are 4,246 registered herbal medicines, and the total annual demand is of thousands of quintals of herbal drugs and the acceptance and recognition of herbal medicine is increasing day by day. The international demand for herbal drugs also has increased rapidly because Ayurvedic/herbal healthcare products are considered safe under the impression that they are derived from natural products.

Worldwide, alternative medicine is becoming popular and herbal medicine has become one of the most common forms of alternative therapy. The international herbal market is approximately \$61 billion. Annual sales of herbal medicinal products (HMPs) are approximately \$3 billion in Germany and \$1.5 billion in the US (Smet 2002). Annual turnover of Indian Ayurvedic industry is \$ 0.8 billion (Rs 35,000 million) (Anon.2001). The Indian market is growing at 15-20% per annum (Rs 7,000 million or \$150 million). With world demand growing at 1% annually (\$ 610 million), the size of export market for medicinal plants appears bigger than the Indian domestic market. As compared to China, which boasts of herbal exports of \$ 3 billion, Indian exports are dismal - \$ 100 million (Bhatt).

China has been successful in acquiring the single largest share in this export

market because of its well-designed national policy on the traditional Chinese medicine. Despite contradictory claims regarding India's share in the world market of medicinal plants, one thing is very clear that ideally it should have the second largest share, but the country lags far behind China owing to its unorganised trade system and inadequate policy. The Government of India has however been quite active since 2000 to overcome this problem, and has adopted many measures to give a boost to the export of medicinal plants. A National Medicinal Plant Board has been constituted to facilitate the conservation, propagation and marketing of important medicinal plants, and its state level counter parts are also operating to implement this mandate at the level of individual states. So far the value of export is concerned, both India and China have the same problem that most of their export is in the form of low-value added products which lowers the price (Rath,2005). ISM is also facing a problems of adulteration and other malpractices and obtaining authentic drug material as a result faith in herbal drugs has declined and this remains the greatest drawback in promotion of herbal products locally or internationally. Fail in meeting global requirements of Quality, Efficacy, Safety and Standardization is also one of the major concern for India to lesser acceptance of its herbal products internationally.

Present study

From the above discussion it becomes mandatory that all our plants/ drugs are to be subjected to a detailed and thorough study on their pharmacognostic characters, biomarkers, synergistic compounds, chemical spectrum, ash and extractive values, HPTLC fingerprinting etc. essential to maintain high quality of final products so that they are accepted to the international as well as local market, so an attempt is made here to conduct a systematic study on substitutes/adulterants of five drugs commonly used in Indian system of medicine which would help in distinguishing substitutes/adulterants from genuine drugs.

Drugs selected

(I) *Fumaria parviflora* Lam. (Fumariaceae). In local market the plant is sold under the name of 'Parpata' or 'Pitpapra'. The whole plant is medicinal and used in all types of fevers. The plant is bitter , cooling, expectorant; constipating; increases 'vata', removes indigestion, biliousness, fever, burning of the body, tired feeling, wandering

of the mind, intoxication, urinary discharges, vomiting, enriches the blood; good in leprosy.

Substitutes/Adulterants of *Fumaria parviflora*:

- *Justicia procumbens* L. (**Acanthaceae**). Part used : Whole Plant.
- *Oldenlandia corymbosa* L. (**Rubiaceae**). Part used : Whole Plant.
- *Peristrophe bicalyculata* Nees. (**Acanthaceae**). Part used : Whole Plant.
- *Polycarpea corymbosa* (L.) Lam.(**Caryophyllaceae**).Part used : Whole Plant.
- *Rungia repens* (L.) Nees.(**Acanthaceae**). Part used : Whole Plant.

(II) *Glycyrrhiza glabra* L. (**Fabaceae**) popularly known as 'Liquorice'(English) and 'Mullethi' (Hindi) or 'Yastimadhu' or 'Jethirnadha' (Gujarati). The dried rhizomes and roots of this plant is used as expectorants, anti-inflammatory, demulcents and for bronchitis. It is cooling, heavy of digestion, sweet, good for the eye, improves bodily strength and complexion, is very demulcent, improves or stimulates production of semen beneficial for the hair, improves voice, overcomes vitiation of pitta (certain enzymes or enzymatic secretions which increase metabolic and other changes) of vata (corresponding to nervous and allied factors) and of blood, inflammation, cases of poisoning, vomiting, thirst, weakuess, and wasting diseases. According to Nighanturatnakara it is also beneficial in ulcer, oedema, (s'otham) combined pathological conditions of nervous and allied factors and of blood (vataraktam), haemorrhage resulting from mutual vitiation of pitta and of blood, and fresh wound (sadyovranam).

Substitutes/Adulterants of *Glycyrrhiza glabra*:

- *Abrus precatorius* L. (**Fabaceae**). Part used : Root.
- *Alysicarpus longifolius* W. & A. (**Fabaceae**). Part used : Root.
- *Taverniera cuneifolia* (Roth) Am. (**Fabaceae**). Part used : Root.
- *Maerua arenaria* (DC.) Hook. f. &Thorns.(**Capparaceae**).Part used : Root.

(III) *Bergenia ligulata* (Wall) Engl. (**Saxifragaceae**). The rhizome of this plant is the main part or source of drug and commonly called as 'Pashanabhed'. It has been in use in indigenous system of medicine since the historic period of Charaka. As the name implies, it is considered a specific remedy against kidney and bladder stones. It has been known to have various pharmacological activities and thus has several traditional uses. This is one of the twenty one drugs that constitute the *Virataradi* or

Vellantaradi gana of Vagbhata which eradicates diseases due to *vata*, vesical calculus, gravels, dysuria, and anuria (Mooss, 1980). It is light, cool, bitter, have useful effect in cough and cold (Harsoliya *at.el.*,2011). The drug enters into the composition of preparations like *Pashanabhedadi kavatha*, *Pashanbhedadaya ghruta*, *Pushayanug churna*, *Putikaranjasavam*, *Traikantada ghrtam*, *Valiya Marmagulika*, etc.

Substitutes/Adulterants of *Bergenia ligulata*:

- *Aerua lanata* (L.) Juss. (**Amaranthaceae**). Part used : Root.
- *Ammannia baccifera* L. (**Lythraceae**). Part used : Root.
- *Celosia argentea* L. (**Amaranthaceae**). Part used : Root.
- *Coleus amboinicus* Lour. (**Amaranthaceae**). Part used : Root.
- *Glossocardia linearifolia* (L.f.) DC. (**Asteraceae**).Part used : Root.

(IV) *Polygala senega* L.(**Polygalaceae**).The root of this plant is popularly known as snakeroot and has sustained a reputation in the past, as an antidote to the poison of venomous reptiles. In the treatment of chronic asthma this is an efficient remedy. The drug has a high reputation in international market and sold at high cost.

Substitutes/Adulterants of *Polygala senega*:

- *Acalypha indica* L. (**Euphorbiaceae**). Part used : Root.
- *Adhatoda vasica* Nees. (**Acanthaceae**). Part used : Root.
- *Polygala chinensis* L. (**Polygalaceae**). Part used : Root.
- *Xeromphis spinosa* (Thunb.) Keay. (**Rubiaceae**). Part used : Root.

(V) *Saraca asoca* (Roxb.)deWilld.(**Caesalpiniaceae**).This is one of the sacred trees of Hindus and Buddhists, commonly known as ‘Ashoka’. The bark of this plant has been very widely used in Ayurvedic medicine. The bark is bitter, cool astringent and used in dysentery, fever, leucorrhoea, inflammations, syphilis etc. and is help in the cure of various female diseases unfortunately this drug is subjected to a bad type of adulteration which surely stakes its merit as a therapeutic agent. Truly speaking, it is not a case of adulteration but a case of total substitution with a completely different source material. The genuine Ashoka, which they the identify as *S.asoca* is an ornamental tree mostly found only in gardens. The demand of this drug is huge due to its extensive uses in Ayurvedic preparation like

‘Ashokarishta’ and extracts and tinctures, manufactured as galenicals, by the Indian Pharmaceutical concerns. Such collection is only possible if trees grow wild in abundance. But the case is not so, as stated above so obviously, it has created an easy means of substitution with quite a trash material. This fact prompted to undertake a thorough investigation of the stem bark of *S.asoca* and its Substitutes/Adulterants.

Substitutes/Adulterants of *Saraca asoca*:

- *Bauhinia variegata* Linn. (Caesalpiniaceae). Part used : Stem bark.
- *Bombax ceiba* L. (Bombacaceae). Part used : Stem bark.
- *Polyalthia longifolia* (Sonia.) Thus. (Annonaceae). Part used : Stem bark.
- *Shorea robusta* Gaertn. (Dipterocarpaceae). Part used : Stem bark.
- *Trema orientalis* (L) Bl. (Ulmaceae). Part used : Stem bark.

The chemistry and pharmacognosy of these plants, which are highly essential for finding out the active principles and biomarkers, are known only for a few plants or genuine drugs such as *Glycyrrhiza glabra*, *Bergenia ligulata* and *Saraca asoca*. While very little data on phytochemistry and pharmacognosy are available for their substitutes/adulterants. Therefore the present study is undertaken to find out the active constituents and biomarkers within the main part or source of drug of all the plants where such data are not procured. In cases where the chemistry has been worked out, data are available only on their alkaloids which are considered as the active principles and in some cases, of steroids. No data on other constituents such as polyphenols and mucilages, which also may be responsible for the curative or a synergistic action are given any consideration anytime. Therefore the present project is undertaken to subject these plants to a detailed chemical, pharmacognostic, physico-chemical study and variation in the HPTLC fingerprints to detect the biomarkers which distinguishes the genuine drug from their substitutes/adulterants.

The objectives of the present Ph.D programme are the following:

1. To find out pharmacognostic biomarkers of all the substitutes/adulterants.
2. To find out active principles and chemical biomarkers of all the substitutes/adulterants.
3. To study features of purity & strength in form of ash value & extractive values of all the substitutes/adulterants.
4. To produce TLC fingerprinting of all individual substitutes/adulterants.

5. To check whether substitute/adulterant drugs are as potent as the genuine drug in terms of chemical constituents.