CHAPTER 1

INTRODUCTION

1.1 GENERAL INTRODUCTION

Medicinal herbs are moving from fringe to mainstream use with a greater number of people seeking remedies and health approaches free from side effects caused by synthetic chemicals [1]. Undoubtedly, the plant kingdom still holds many species of plants containing substances of medicinal value which have yet to be discovered. India is a land of immense biodiversity in which two out of eighteen hot spots of the world are located. India is also one of the twelve mega biodiversity countries in the world [2]. India enjoys the benefit of varied climate, from alpine in the Himalaya to tropical wet in the south and arid in Rajasthan. Such climatic conditions have given rise to rich and varied flora in the Indian subcontinent.

Recently, considerable attention has been paid to utilize eco-friendly and biofriendly plant-based products for the prevention and cure of different human diseases. Considering the adverse effects of synthetic drugs, the western population is looking for natural remedies which are safe and effective. It is documented that, about 80% of the world's population has faith in traditional medicine, particularly plant drugs for their primary healthcare [3]. India is sitting on a gold mine of well-recorded and traditionally well-practiced knowledge of herbal medicine. This country is perhaps the largest producer of medicinal herbs and is rightly called the Botanical Garden of the World. There are very few medicinal herbs of commercial importance which

are not found in this country. India officially recognizes over 3,000 plants for their medicinal value. It is generally estimated that over 6,000 plants in India are in use in traditional, folk and herbal medicine, representing about 75% of the medicinal needs of the Third World countries [4].

There has been a shift in universal trend from synthetic to herbal medicine, which we can say 'Return to Nature'. Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents for the prevention of diseases and ailments. Nature has bestowed our country with an enormous wealth of medicinal plants. Countries with ancient civilizations such as China, India, South America, Egypt, etc. are still using several plant remedies for various conditions. In this regard India has a unique position in the world, where a number of recognized indigenous systems of medicine viz., Ayurveda, Siddha, Unani, Homeopathy, Yoga and Naturopathy are being utilized for the health care of people. No doubts that the herbal drugs are popular among rural and urban community of India. The one reason for the popularity and acceptability is belief that, all natural products are safe. The demand for plant based medicines, health products, pharmaceuticals, food supplement, cosmetics etc are increasing in both developing and developed countries, due to the growing recognition that the natural products are non-toxic, have less side effects and easily available at affordable prices [5]. Nowadays, there is a revival of interest with herbal-based medicine due to the increasing realization of the health hazards associated with the indiscriminate use of modern medicine.

Since time immemorial man has used various parts of plants in the treatment and prevention of many ailments [6]. Historically all medicinal preparations were derived from plants, whether in the simple form of plant parts or in the more complex form of crude extracts, mixtures, etc. Today a

substantial number of drugs are developed from plants [7] which are active against a number of diseases. The majority of these involve the isolation of the active constituents found in a particular medicinal plant and its subsequent semisynthetic modification. In the developed countries 25 percent of the allopathic drugs are based on plants and their derivatives [8] and the use of medicinal plants is well known among the indigenous people in rural areas of many developing countries. In the past, our ancestors made new discoveries of the healing power of plants through trial and error method. Although some of the therapeutic properties attributed to plants have proven to be erroneous, Medicinal plant therapy is based on the empirical findings of hundreds and thousands of years [9].

Moreover, towards the end of the 20th century plant based over the counter (OTC) products, nutraceuticals and food supplements comprising the complementary and alternative therapies have gained a big share in the drug market in the developed countries [10]. Medicinal plants –either through systematic screening programs or by serendipity - possess an important position in the drug discovery and many modern drugs have their origin in traditional medicine of different cultures. Hence, despite the advantages of the synthetic and combinatorial chemistry as well as molecular modeling, medicinal plants remains an important source of new drugs, new drug leads and new chemical entities. The latter study reported that of the 877 new chemical entities (NCEs) introduced between 1981 and 2002, nearly the half (49%) were natural products, semi-synthetic natural products, semi-synthetic natural products analogues or synthetic compounds based on natural products [11].

1.2 NATURAL PRODUCTS AND MODERN THERAPY

Health and well-being has been a subject of man’s primary concern since time immemorial. From man’s early experiments with herbs and plants

growing in his environment and treatment of disease, man was eventually able to establish empirical systems of medicine. The use of plants, plant extracts or pure compounds isolated from natural products to treat disease is a therapeutic modality, which has stood the test of time even if much of the science behind such therapy is still in its infancy. Phytochemical examination of plants and animal cure available to earlier civilizations has often shown that these contained active principles, responsible for therapeutic success. Presently synthetic drugs outnumber those of natural origin in modern medicine and research into the isolation and pharmacology of natural products now lags behind than that of synthetic drugs. Nevertheless, there are still many drugs which have their origin in natural products derived from animals or vegetable sources. Indeed today many, if not most, pharmacological classes of drugs include a natural product prototypes are morphine, digoxin, quinine, atropine, reserpine, physostigmine, pilocarpine, vinblastine, vincristine, artemisinin and taxol are few examples of what medicinal plants have given us in the past[12].

There has been a resurgence of scientific interest in medicinal plants during the past 20 years, being rekindled by the world-wide importance of medicinal plants and crude drugs in traditional medicine. Moreover, empirical studies on medicinal plants revealed the fact that for a plant extracts to be active clinically, it is not necessary for the active component to be isolated and the structure to be established. A large number of crude plant extracts are now being utilized in naturopathic remedies in addition to the purified natural substances [13].

A large proportion of the human population is on herbal remedies, however, only a limited number of plants have been investigated pharmacologically. The inherent biological complexity in plants makes it

imperative to evaluate the safety, efficacy and quality during development of plant-based drugs.

The World Health Organization (WHO) estimates that 4 billion people, nearly 80 percent of the world population, presently use herbal medicine for some aspect of primary health care. Herbal medicine is a major component in all indigenous people traditional medicine and a common element in Ayurvedic, homeopathic, naturopathic, traditional oriental, and Native American Indian medicine. WHO notes that of 119 plant-derived pharmaceutical medicines, about 74 percent are used in modern medicine in ways that correlated directly with their traditional uses as plant medicines by native cultures [14]. Major pharmaceutical companies are currently conducting extensive research on plant materials gathered from the rain forests and other places for their potential medicinal value.

Substances derived from the plants remain the basis for a large proportion of the commercial medications used today for the treatment of heart disease, high blood pressure, pain, asthma and other problems. For example, ephedra is a herb used in Traditional Chinese Medicine for more than two thousand years to treat asthma and other respiratory problems. Ephedrine, the active ingredient in ephedra, is used in the commercial pharmaceutical preparations for the relief of asthma symptoms and other respiratory problems.

Another example of the use of an herbal preparation in modern medicine is the foxglove plant. This herb had been in use since 1775. At present, the powdered leaf of this plant is known as the cardiac stimulant digitalis to the millions of heart patients it keeps alive worldwide. Recent estimates suggest that over 9,000 plants have known medicinal applications in various cultures and countries and this is without having conducted comprehensive research amongst several indigenous and other communities [15].

The use of plants as medicines dates as far back as the origin of mankind and perhaps even earlier as even animals are known to seek out and consume certain plants when ill. Since the beginning of mankind people have relied primarily on plants for nourishment. Through trial and error, they have discovered that, some plants are good for food, that some are poisonous, and some produce bodily changes such as increased perspiration, bowel movement, urination, relief of pain, hallucination and healing. Over the millennia these observations were passed orally from generation to generation, with each generation adding to and refining the body of knowledge. Every country in the world over has developed a body of herbal knowledge as a part of its tradition. Traditional medicine or folk medicine practice based on the use of plants and plant extracts is called *herbalism* [16].

1.3 MEDICINAL BENEFITS OF HERBALS

Herbal medicine is the oldest form of healthcare known to mankind. Herbs had been used by all cultures throughout history. It was an integral part of the development of modern civilization. Primitive man observed and appreciated the great diversity of plants available to him. The plants provided food, clothing, shelter and medicine. Much of the medicinal use of plants seems to have been developed through observations of wild animals and by trial and error. As time went on, each tribe added the medicinal power of herbs in their area to its knowledge base. They methodically collected information on herbs and developed well-defined herbal pharmacopoeias. Indeed, well into the 20^{th} century much of the pharmacopoeia of scientific medicine was derived from the herbal lore of native people. Many drugs commonly used today are of herbal origin. Some are made from plant extracts, others are synthesized to mimic a natural plant compound.

The medicinal benefits of herbs have been known for centuries. A record of Indian medical practices shows that herbs were used extensively to cure practically every known illness. The practice has existed since prehistoric times and is used today by up to 80% of the world's population as a primary form of medicine.

Herbs may be used directly as extracts or they may be used in the production of drugs. Many herbs contain powerful ingredients that, if used correctly, can help to heal the body. The pharmaceutical industry was originally based upon the ability to isolate these ingredients and make them available in a pure form. Herbalists, however, believe that nature provides other ingredients in the same herbs to balance the more powerful ingredients. These other components, though they may be less potent, may help to act as buffers, synergists or counter-balance to work in harmony with the more powerful ingredients. Therefore, by using herbs in their complete form, the body's healing process utilizes a balance of ingredients provided by nature.

Many people believe that herbs are just as effective as drugs, but without the side effects. Herbs do perform many healing functions in the body, but they must be used appropriately, not indiscriminately. Although herbal remedies are less likely than most conventional medicines to cause side effects, herbs nevertheless can be very potent. Moreover, not all plant life is beneficial. There are poisonous plants, and some of them are deadly, especially if used for long period of time. In fact, it is important to point out that qualified herbalists use herbs with great care. Also, since herbs contain active ingredients, one should be aware that some of these elements may interact negatively with prescribed medications. Certain herbs should be used only for healing purposes and not for extended periods of time.

Herbal therapy has been criticized because medicinal plants have not been tested for efficacy according to rigid pharmaceutical standards.

However, there's a continuing debate over whether such testing should be performed on the entire herb or only on its active ingredients. Some remedies depend on the actions of several components (or several herbs) working together. Another problem is that sometimes, herb's active ingredients are not known. Proponents of herbal therapy point out that the pharmaceutical industry grew out of herbal treatment and that plant extracts are still used to make drugs. For example, digitalis, used to treat heart disease, comes from foxglove and morphine comes from the opium poppy. About 25 percent of today's prescription drugs are at least partially derived from plants.

Some herbs are safe in modest amounts but they may become toxic at higher doses. For example, whereas liquorice root can be used safely for treating duodenal and gastric ulcers, deaths from its excessive use have been reported. Large amounts of liquorice can cause serious side effects such as hypokalaemia, high blood pressure and heart failure [17]. Germander, an herb used in weight-loss programs, has been reported to cause fatal hepatitis [18].The Chinese herbs caowu and chuanwu are used to treat rheumatism, arthritis, bruises and fractures. They may contain highly toxic alkaloids such as aconitine, which produces neurologic, cardiovascular and gastrointestinal disturbances. Use of these herbs can even results in death [19].

1.3.1 Herbs for Antioxidant Activity

Oxidative stress can cause oxidative damage to large bio molecules such as proteins, DNA and lipids, resulting in an increased risk for cancer and cardiovascular disease [20]. Fruit and vegetables contain a wide variety of antioxidant compounds such as carotenoids and phenolics that may help to protect cellular systems from oxidative damage and lower the risk of chronic diseases. Anthocyanins are the water-soluble pigments responsible for the red, pink, blue, purple, and violet colours for many types of flowers and fruit. Hawthorn, red wine, grapes, juniper berries and rose hips are some examples

of herbs that contain anthocyanin. Because anthocyanins are effective in inhibiting LDL-cholesterol oxidation and platelet aggregation, these herbs may provide some protection against heart disease. Anthocyanins may also be useful for the treatment of vascular disorders and capillary fragility [21].Liquorice extract [free of glycyrrhizinic acid] and the isoflavone glabridin, a major polyphenolic compound found in liquorice and tea flavonoids, specifically the catechins from green tea leaves or the aflavins [catechin dimers] from black tea leaves were shown to markedly inhibit LDL oxidation via a mechanism involving scavenging of free radicals [22,23].

Turmeric has been shown to suppress the development of stomach, breast, lung and skin tumors. Its activity is largely due to the antioxidant curcumin[diferuloylmethane], which has been shown to be an effective anti-inflammatory agent in humans [24]. Carotenoids are the pigments found in green, leafy herbs, rose hips and the herbs used as colouring agents, such as paprika, saffron and annatto. The carotenoid pigments are effective antioxidants that quench free radicals, provide protection against oxidative damage to cells and also stimulate immune function.

Indian medicinal plants provide a rich sources of antioxidants. A review of literature revealed that there are over 40 Indian medicinal plants showing antioxidant abilities at various levels of protection.The medicinal plants that show significant antioxidant activity include *Acacia catechu*, *Achyranthes aspera*, *Aegle marmelos* (Bengal quince, Bel), *Aglaia roxburghiana* (Priyangu), *Allium cepa* (Onion), *Allium sativum*, *Aloe vera*, *Amomum subulatum*, *Andrographis paniculata*, *Asparagus racemosus*, *Azadirachta indica*, *Bacopa monneira*, *Bauhinia purpurea*, *Brassica campastris*, *Butea monosperma*, *Camellia sinensis*, *Capparis decidua*, *Capsicum annum*, *Centella asiatica*, *Cinnamomum verum*, *Commiphora mukul*, *Crataeva nurvala*, *Crocus sativus*, *Curcuma longa*, *Cymbopogan*

citrates, *Emblica officinalis*, *Emilia sonchifolia*, *Garcinia atroviridis*, *Garcinia kola*, *Glycyrrhiza glabra*, *Hemidesmus indicus*, *Hypericum perforatum*, *Indigofera tinctoria*, *Melissa officinalis*, *Momordica charantia*, *Morus alba*, *Murraya koenigii*, *Nigella sativa*, *Ocimum sanctum*, *Picrorrhiza kurroa*, *Piper beetle*, *Plumbago zeylanica*, *Premna tomentosa*, *Punica granatum*, *Rubia cordifolia*, *Sesamum indicum*, *Sida cordifolia*, *Swertia decursata*, *Syzigium cumini*, *Terminalia arjuna*, *Terminalia bellarica*, *Tinospora cordifolia*, *Trigonella foenum-graecum*, *Withania somnifera* and *Zingiber officinalis*. There are also a number of ayurvedic formulations containing ingredients from medicinal plants that exhibit antioxidant activity. These are Abana, Amrita bindu, C-phycocyanin, Centalaplus, Chapparal, Geriforte, Jigrine, Liv-52, Maharishi formulations, Muthumarunthu, Ophtacare, P55A, Sandhika, Student rasayana and Tamrabhasma [25].

1.3.2 Herbs for Anticancer Activity

Several commonly used herbs have been identified by the National Cancer Institute as possessing cancer-preventive properties. Those include members of the *Allium* sp. [garlic, onions and chives]; members of the Labiatae family [basil, mints, oregano, rosemary, sage, and thyme]; members of the Zingiberaceae family [turmeric and ginger]; members of the *Umbelliferae* family (anise, caraway, celery, chervil, cilantro, coriander, cumin, dill, fennel, and parsley) [26].

In addition, many herbs contain a variety of phytosterols, triterpenes, flavonoids, saponins, and carotenoids, which have been shown from studies of legumes, fruit, and vegetables to be cancer chemoprotective [27]. Garlic is known to have antitumor properties, owing to its content of a wide variety of organic sulphides and polysulphides. Case-control studies in Greece have shown that high consumption of onions, garlic, and other *Allium* species is protective against stomach cancer. Korean studies suggest that

ginseng [*Panax ginseng*] may lower the risk of cancer in humans. Ginseng extract and powder have been found to be more effective than fresh sliced ginseng, ginseng juice, or ginseng tea for reducing the risk of cancer [28].Ginseng seemed to be most protective against cancer of the ovaries, larynx, pancreas, oesophagus and stomach and less effective against breast, cervical, bladder and thyroid cancers. The main active ingredients in ginseng root are thought to be a family of 6 triterpene saponins called ginsenosides.

Paclitaxel [TAXOL, Bristol-Myers Squibb, Princeton, NJ], a new chemotherapy agent discovered by the National Cancer Institute screening program, is obtained from the bark of the Pacific yew [*Taxus brevifolia*] as well as the needles of some other new species. Patients with metastatic breast cancer, advanced lung cancer, cancers of the head and neck, melanoma, ovarian cancer and lymphomas have responded positively to Taxol [29]. Vinblastine, vinleurosine, vincristine and vinrosidine are alkaloidal substances can be obtained from *Vinca rosea.* Vinblastine has proved to control chorioepithelioma, Hodgkin's disease and other lymphomas, and a number of beneficial results have been obtained in carcinoma of the breast and bronchus [30].

Flax seed (*Linum usitatissimum*) contains a rich supply of lignans. Mammalian lignans appear to be anticarcinogenic; lignan metabolites bear a structural similarity to oestrogens and can bind to oestrogenic receptors and inhibit the growth of oestrogen-stimulated breast cancer. Turmeric [*Curcuma longa*] has been shown to suppress the development of stomach, breast, lung, and skin tumours.Persons with high serum concentrations of carotenoids have reduced risk of both heart disease and cancer [31–33].

Polyphenols in green tea (*Camellia sinensis*) are known to possess antimutagenic and anticancer activity. Some evidence suggests that tea has a protective effect against stomach and colon cancers [34]. Lentinan, β-glycan

found in shiitake mushrooms (*Lentinus edode*), has been shown to have antitumor activity; it was active against lung carcinoma and 2 human melanomas [35]. It is thought that Lentinan has its effects by activating the host immune system. Lentinan stimulates increased production and activity of natural killer cells and macrophages, which destroy tumour cells [36].

Table 1.1 List of herbs used for various medicinal purposes

Botanical source	Active constituents	Type	Therapeutic use
Alkaloids			
Solanaceous spp.	Atropine, hyoscyamine	Tropane alkaloid	Anticholinergic
Camptotheca acuminata	Camptothein	Indole alkaloid	Antineoplastic
Capsicum spp.	Capsaicin	Phenylalkyl-amine alkaloid	Topical analgesic
Papaver somniferum	Codeine , morphine	Opium alkaloid	Analgesicand antitussive
Erythroxylum coca	Cocaine	Cocaine alkaloid	Local anesthetic
Colchicum autumnale	Colchicine	Isoquinoline alkaloid	Anti-gout
Leucojumae sativum	Galanthamine	Isoquinoline alkaloid	Cholinesterase inhibitor
Nicotiana spp.	Nicotine	Pyrrolidine alkaloid	Smoking cessation therapy
Physostigma venenosum	Physostigmine	Indole alkaloid	Cholinergic
Pilocarpus jaborandi	Pilocarpine	Imidazole alkaloid	Cholinergic
Cinchona spp.	Quinine, Quinidine	Quinoline alkaloid	Antimalarial, Cardiac depressant
Chondodendron tomentosum	Reserpine	Indole alkaloid	Psychotropic
Steroids			
Dioscorea spp.	Diosgenin, hecogenin, stigmasterol	Steroids	Oral contraceptives and hormonal drugs.

Table 1.1 (Continued)

Terpenoids			
Artemisia annua	Artemisinin	Sesquiterpene lactone	Antimalarial
Taxus brevifolia	Taxol and other taxoides	Diterpenes	Antineoplastic
Glycosides			
Digitalis spp.	Digoxin, digitoxin	Steroidal glycosides	Cardiotonic
Cassia angustifolia	Sennosides A and B	Hydroxy-anthracene glycosides	Laxative
Tribulus terrestris	Furostanols and Spirostanols	Steroidal saponins	Anti-bacterial and anti-viral (herpes) effects.
Flavonoids			
Allium cepa	Quercetin	Flavonols	Antiinflammatory, Antioxidant, Diarrrhoea.
Citrus fruits	Hesperidin	Flavanones	Benefits in capillary permeability
Camellia sinensis	Catechin, epicatechin, epicatechingallate,	Flavan-3-ols	Used in cancer and heart disease
Others			
Cephaelis ipecacuanha	Ipecac	Mixture of alkaloids and other omponents	Emetic
Podophyllum peltatum	Podophyllotoxin	Lignan	Antineoplastic

Herbal medicines have good values in treating many diseases including non-infectious diseases like cancer and diabetes. Interest in traditional medicines in India has continuously been increasing. Herbal drugs obtained from plants are believed to be much safer. This has been proved in the treatment of various ailments like cancer and diabetes. But herbal medicines are potent and at the same time they are nontoxic in nature.

1.4 MODERN MEDICINE FROM HIGHER PLANTS

Medicinal plants play a vital role for the development of new drugs. During 1950-1970 approximately 100 plants based new drugs were introduced in the USA drug markets which are derived from higher plants. From 1971 to 1990 new drugs such as ectoposide, E-guggulsterone, teniposide, nabilone, plaunotol, Z-guggulsterone, lectinan, artemisinin and ginkgolides appeared all over the world. 2% of drugs were introduced from 1991 to 1995 including paciltaxel, toptecan, gomishin, irinotecan etc.

Plant based drugs provide outstanding contribution to modern therapeutics; for example: serpentine isolated from the root of Indian plant *Rauwolfia serpentine* in 1953, was a revolutionary event in the treatment of hypertension and lowering of blood pressure. Vinblastine isolated from the *Catharanthus roseus* [37] is used for the treatment of Hodgkin's, choriocarcinoma, non-Hodgkin's lymphomas, leukaemia in children, testicular and neck cancer. Vincristine is recommended for acute lymphocytic leukaemia in childhood advanced stages of Hodgkin's, lymophosarcoma, small cell lung, cervical and breast cancer [38]. Podophyllotoxin is a constituent of *Podophyllum emodi* currently used against testicular, small cell lung cancer and lymphomas. Indian indigenous tree of *Nothapodytesnim moniana* (*Mappiafoetida)* are mostly used in Japan for the treatment of cervical cancer. Plant derived drugs are used to cure mental illness, skin diseases, tuberculosis, diabetes, jaundice, hypertension and cancer.

Medicinal plants play an important role in the development of potent therapeutic agents. Plant derived drugs came into use in the modern medicine through the uses of plant material as indigenous cure in folklore or traditional systems of medicine. More than 64 plants have been found to possess significant antibacterial properties; and more than 24 plants have been found to possess antidiabetic properties, antimicrobial studies of plants [39],

plant for antidotes activity – *Daboia russellii* and *Naja kaouthia* venom neutralization by lupeol acetate isolated from the root extract of Indian sarsaparilla *Hemidesmus indicus*R.Br [40]. Which effectively neutralized *Daboia russellii* venom induced pathophysiological changes [41].

The extensive research work performed by the natural chemists during 1950-1960 on plants have given the valuable information about the isolation and characterization of several natural components viz., steroids, triterpenoids, alkaloids, Flavanoids, Saponins, tannins, etc. having antitumor, antidiabetic, hepatoprotective and anti-inflammatory activity [42].

Today the pharmacologically active ingredients of many Ayurvedic medicines are being identified and their usefulness in drug therapy being determined. As mentioned in the introduction only a certain percentage of plants are used in traditional medicines. The Indian subcontinent is a vast repository of medicinal plants that are used in traditional medical treatments [43]. In India, around 15000 medicinal plants have been recorded however traditional communities are using only 7,000 - 7,500 plants for curing different diseases.

The valuable medicinal properties of different plants are due to presence of several constituents i.e. Saponins, tannins, alkaloids, alkenyl phenols, glycol-alkaloids, flavonoids, sesquiterpenes lactones, terpenoids and phorbol esters. Among them some are act as synergistic and enhance the bioactivity of other compounds. Artemisinin produced by *Artemisia annua* plant is very effective against *Plasmodium falciparum*, *P. vivax*and also drug resistant parasite. The main active constituents of *Artemisia annua* are sesquiterpenoid lactones, endoperonides named artemisinin and artemisinic acid. For more than century quinine, an alkaloid obtained from the bark of various species of cinchona trees has been used in the treatment of Malaria and interestingly was one of the first agents used for the treatment of amoebic

dysentery. Reserpine isolated from raw plant extract of *Rauwolfia serpentina* is used as tranquilizer and in control of high blood pressure. From 2000 years, the powdered root of *Rauwolfia serpentina* has been used in treatment of mental illness in India. Although synthetic drugs are often used in treatment of certain disease but a remarkable interest and confidence on plant medicine was found [44].

1.5 MEDICINAL PLANT BASED INDUSTRIES IN INDIGENOUS SYSTEM OF MEDICINE

In India, it is estimated that there are about 25,000 licensed pharmacy of Indian system of medicine. Presently about 1000 single drugs and about 3000 compound formulations are registered. Herbal industry in India uses about 8000 medicinal plants. From about 8000 drug manufactures in India, there are however not more than 25 manufactures that can be classified as large scale manufactures which includes Ansar Drug Laboratories, Surat, Acis Laboratories, Kanpur, Amil Pharmaceutical, New Delhi, Alrasin Marketing, Mumbai, Allen Laboratories, Kolkatta, Bhartirasanagar, Kolkatta, Dabur India Ltd., Ghaziabad,Dattatraya Krishan Sandu Bros., Mumbai, Herbals Pvt. Ltd., Patna, Herbo-med (P) Ltd., Kolkatta, The Himalaya Drug Co., Bangalore, Indian Herb and Research Supply co., Saharanpur, J and J Dechane Laboratories pvt. Ltd., Hyderabad, Madona Pharmaceutical ReaearchPvt. Ltd., Kolkatta,Kruzer Herbals, New Delhi,Shilpachem, Indore, Hamdard (Wakf) Laboratories, Delhi,Zandu Pharmaceutical Works Ltd., Bombay, Baidyanath Ayurveda Bhavan, Jhansi Charak Pharmaceuticals, Bombay [45].

1.6 NEW SOURCES OF TRIBAL MEDICINE FOR FUTURE INVESTIGATION

Tribal healers in most of the countries, where ethno medical treatment is frequently used to treat cuts, wounds, skin infection, swelling,

aging, mental illness, cancer, asthma, diabetes, jaundice, scabies, eczema, venereal diseases, snakebite and gastric ulcer, provide instructions to local people as how to prepare medicine from herbal[46]. They keep no records and the information is mainly passed on verbally from generation to generation [47]. World Health Organization (WHO) has shown great interest in documenting the use of medicinal plants by tribal from different parts of the world [48]. Many developing countries have intensified their efforts in documenting the ethno medical data on medicinal plants. Research to find out scientific evidence for claims by tribal healers on Indian herbs has been intensified. Once these local ethno medical preparations are scientifically evaluated and disseminated properly, people will be better informed regarding efficacious drug treatment and improved health status [49].

Consumption of fruit and vegetables, as well as grains, has been strongly associated with reduced risk of cardiovascular disease, cancer, diabetes, Alzheimer disease, cataracts, and age-related functional decline. Keeping this view as a main source and after thorough literature survey, one such fruit was selected for the present thesis and it was planned to prove the traditional medicinal claims for the well-known fruit of the tree *Limonia acidissima* Linn, which is popularly known as Elephant apple or Wood apple which was extensively used in the local areas of South India in the form of sherbet for liver disorders, ulcers, cut wounds, snakebite etc.,