CHAPTER 1

INTRODUCTION

1.0 Introduction

1.1 Sikkim: The geography and population

Sikkim is a beautiful tiny Himalayan state situated on the flanks of Eastern Himalayas at the latitude of 27°00'46" to 28° 07' 48" and 88°00'58" to 89°55'20' longitude north. The state is bounded by Tibet in the North and North-East, Bhutan in the South- East, Nepal in the West and West Bengal in the South. The Pangolakha Range of mountains separates Bhutan, Singalila range separates Nepal and Chola range separates Tibet from Sikkim. The state has a very rugged topography defined with towering mountains and deep valleys. Even though the total geographical area is only 7096 sq. kms, its altitude varies from 244 mt. at Melli to 8,598 mt. at Mt. Kanchandzonga forming the mountaineering climate. The other important peaks in the state such as Kumbhakana (7,711 mt.), Penden (6706 mt.), Narsing (5,825 mt.), Kabru Dome (6,545) are also found in the Kanchandzonga range. Glaciers descend from these mountaineering peaks to form the source for important rivers like Teesta and Rangit in Sikkim (Anonymous 1, 2007; Pant, 2003).

Due to its rugged topography, land locked condition and altitudinal variations the state is facing backwardness compared to the other states in India but the richness of flora, fauna, water falls, hot springs, Orchids, Rhododendron, snow capped mountains, adventure trekking, world renowned Monasteries, river rafting, customs and culture offer a great potential for tourism development (Rai *et.al.,* 2000). The total population of Sikkim as per the Census of Sikkim is 540,851 in the year 2001. The overall density of population in the state is 76 persons per sq km, which is one of the lowest in India. The total number of literates (7 years and above) in the state is 234,135 of whom 137,745 are male and 96,390 are female. The Schedule Caste population according to census 2001 was 5.03 % and the Schedule Tribe population 20.62%. The main language of Sikkim is Nepali. Besides Nepali Bhutia, Limbu, Hindi, English are also the running languages.

1.2 Tribal Communities

India is one of the twelve mega diversity countries in the world and has 17,000 flowering plants. Among the 25 hotspots in the world, the Eastern Himalayas and the Western Ghats are the two hotspots of India. The country possesses a total of 427 tribal communities. The largest proportion of tribes is found in Mizoram (95%), followed by Lakshadweep (93%), Nagaland (88%), Meghalaya (86%) and Arunachal Pradesh (64%) (Kala, 2005).

Tribal peoples throughout the world including India, have developed their own cultures, customs, religious rites, taboos, legends and myths, folk tales, medicine and food habits. They are the repository of accumulated experience and of the knowledge of indigenous vegetation which can be utilized in tribal development. These days greater emphasis is being laid on this traditional knowledge and on the 'bioprospecting' of natural products as a new source of food and medicine (Ganesan *et al.*, 2007).

In early times mankind developed, through observation and experience; knowledge of the properties of plants as a source of food and medicines. Although food and medical facilities are more readily available to most of the people in our times, still in several underdeveloped and less accessible areas of the country, food deficiency and lack of medical facilities are prevalent. Plant parts like fruits, tubers, flowers, leaves, etc., are consumed as principal or supplementary food and employed as medicines (Singh, 2001).

1.2.1 Tribal medicine

Tribal medicinal practices first came to be of interest mainly to the anthropologists and ethnographers from the western countries. The subject still continues to draw their interests' world over. Their interests in the matter have mainly to project the indigenous knowledge base of the tribal people regarding their health and survival. But more often than not the tribal practices have also been highly publicized as exotic cultural elements mixed with voodoo and witchcraft. The role of the shaman, magic, divination and cure has thus been overhyped. Of late, of course the social and psychological support value of tribal etiology is being widely projected (Roy Burman, 2003).

The interest in the tribal medicinal practices as evident in Sikkim has also followed more or less the same course as in other tribal areas. Initially the western colonial administrator/ ethnographers documented in details about the medicinal practices of the Lepcha and Bhutias, the two main autochthonous tribes of the states, in their monographs that covered almost all the facets of tribal life. While Waddell dealt more with the Tibetan-Mahayana Buddhist influence on the Sikkimese people, Gorer stressed more on the influence of the earlier Bon religion and the ancient pre-Bon animistic religion on the lives of the Lepchas. Similar descriptive accounts are also available in the later studies by some of the local people, like Foning or even in the western stints-as dealt by Barbara Aziz (Aziz, 1996). Taking this into consideration the present study does not aim at repeating such descriptive accounts of the ritualistic dimension of medicinal practices of the local tribal. The anthropologists summarize the physical reasons attributed to diseases by the tribals are: 1. weather 2. Food 3. Accidents

and natural calamities. However they suggest that treatment of diseases among the tribes may not resemble the modern scientific method as prevalent in western medicine, but it would be wrong to assure that it has no science. It rather moves in a way which covers not only a scientific principle, but also involves the society at large to over come the catastrophe. In the recent years tribal medicine is being supported by many so as to able to combine it with modern medicine. Many are also stressing that Tribal medicine should be incorporated with the primary health scheme.

1.3 Flora and Fauna

The state is listed among the world's ten most critical centers for biodiversity and endemism. Even though the state has only 0.2% of the countries geographical area it houses over 4500 species of flowering plants, 550 species of Orchids, 362 species of Ferns and its allies, 11 species of oaks, 9 species of Tree Ferns, 30 species of Primulas and 20 species of Bamboos. The faunal wealth of Sikkim comprises of 144 species of mammals, 600 species of birds, 400 species of butterflies and moths and 33 species of reptiles. Several species of medicinal plants and herbs are found throughout the state (Poudyal, 2006).

1.4 The medicinal plants

In the tropical zone the followings are some of the important medicinal plants: *Terminalia chebula* (Harra), *Terminalia bellerica* (Barra), *Emblica officinalis* (Amla) are less frequently available. *Costus speciosus* (Bet Lauri), *Dioscorea bulbifera* (Githa tarul), *Piper retrofaction* (Chaba), *Piper longum* (Pipla), *Calotropis gigantia* (Ank), *Gloriosa superba* (Langare tarul). The natural habitats of *Gloriosa* are over exploited. *Ocimum Sanctum* (Tulasi), *Adathoda vasica* (Asuru), *Melia azadirachta* (Bakaina), *Azadirachta indica* (Neem), *Aegle marmelos* (Belpata) very rare in occurrence, *Vitex nigundo* (Sewali), *Woodfordia fruticosa* (Dhunyeri), *Bacopa monnieri* (Brahmi), *Alstonia scholaris* (Chatiwan), *Bassia butyraceae* (Chiwri), *Garuga pinnata* (Dabdabe), *Oroxylum indicum* (Totala), *Tinospora cordifolia* (Gurjo), *Aloe barbadensis* (Ghew kumari), *Holarrhena* (Kiramar), *Smilax* sp (Kukurdaine), *Lawsonia inermis* (Mehendi), *Boerhavia diffusa* (Punarnava), *Moringa oleifera* (Sajana).

Orchids: Orchids mostly epiphytic are dominant in the area, the following are some of the important ones - *Vanda cristata, Dendrobium aphyllum, D. nobile, D. eriaeflorum, D.cumulatum, Cymbidium pendulum, Eria pania, E. paniculata, E. bambusifolia, E. stricta, E. graminifolia,, Cryptochilus sanguines, Parpax elwesii, Bulbophylum hirtus, B. bisectum, B. affine, B. scabratum, B. thomsonii, B. cauliflorum, C. fimbriata, C. cristata, Liparis cordifolia, Malaxis acuminata, M. latifolia, Pholidota recurva.*

Oil bearing seed plants: *Pyrularia edulis* (Amphi), *Gynocardia odorata* (Gantee), *Viburnum mullah* (Ghora Khari), *Bassia butyraceae* (Chiwri), *Juglans regia* (Okhar) are important ones. *Thysanolaena maxima* (Amliso) is recently recognized as economically important grass having multipurpose uses such as broom grass for its inflorescence, fodder grass, soil conserving plant and also as firewood.

1.5 Herbal medicine

Medicinal herbs have been used for thousands of years. Through lore, documentation, and experimentation herbal medicine has withstood the scientific trends of the 20th century. There has been a re-emergence of interest in herbal alternatives for medical treatment. There are, however, challenges to effective treatment using herbs. We lack standardization criteria, knowledge, and understanding of herbal applications and trust and knowledge from the traditional medicine sector. These challenges can be overcome with realization of respect, understanding, and acceptance from the traditional medical sector and the alternative herbal medicine sector (Maggie, 2004).

Herbal medicine and herbal use dates back 60,000 years. In addition, ritualistic and mythological use combined with medicinal use has resulted in misinformation and countless misinterpretations of the use of herbs. The challenge before us is to separate knowledge from lore and misinformation from factual data to create herbal alternatives in our technologically oriented world.

The challenge is for traditional Western medicine and herbal medicine to work collaboratively to improve the individual's health care quality. Traditional Western practitioners utilize technology and research findings to assist diagnosis, treatment, and prevention. Herbal medicine uses a gentle, less intrusive approach to health care. The emphasis on prevention is a predominate factor in herbal health care. Perhaps most important, herbal medicine supports and strengthens the body's complex physical, emotional, and spiritual system to heal the body as a whole.

1.5.1 A brief history of herbology

Although evidence has been found that dates the use of herbs to the Neanderthal era, written descriptions of curative herbs, minerals, and animals date back only to the 1st century A.D. with Dioscorides's De Materia Medica (Hobbs, 1995). With over 950 entries, complete with description, illustration, medical properties, application, and contraindications, this work is, perhaps, one of the most important pieces of herbal information even today. The Greek physician Hippocrates, considered the father of modern medicine, utilized natural remedies

such as vinegar, honey, and herbs for preventative medicine. Many of his concepts are still used in herbal practices as an integral part of health care regime.

The Chinese played an important role in the development of herbal medicine. Even today, many herbalists use or specialize in Chinese herbs for treatment of physical and emotional ailments. Text dated to the 3rd century B.C. and written on silk discusses exercise and diet. One manuscript included in this text, Prescriptions for Fifty-Two Ailments describes more than 250 substances derived from herbs, wood, grains, legumes, fruits, vegetables, and animal parts. By the 1st century A.D. the Chinese Classic of the Materia Medica was compiled as a descriptive interpretation of herbs and their medicinal effects (Balick et al., 2002).

Ayurvedic herbal medicine originated in India probably about 2000 years ago and emphasizes herbal uses, breathing exercises, yoga, and dietary considerations. Ayurveda focuses on a person's overall health imbalance as a means of diagnosis and treatment, rather than on a single symptom. Treatment begins with an evaluation of the patient's doshas (attributes, heredity makeup) that consist of vata (air), pitta (fire), or kapha (water) and herbal and diet recommendations are prescribed.

During the 15th and 16th centuries, European influence on the medicinal use of herbs is well documented. Herbs gained mystical superstitious importance with accounts of their use in magical powers and ritualistic use by witches. During this time thousands of women and men were executed in an effort to rid the world of impending evil. However, also during this era, the rise of the neighborhood apothecary became a familiar sight. Herb gardens were located near the apothecary, where the proprietor could easily harvest herbs to make tinctures and ointments. Physicians regularly patronized these establishments to obtain what they needed to effectively treat their patients.

Nicholas Culpeper wrote The Complete Herbal in 1651 and linked the use of herbs, medicine and astrology together. Connecting these three areas of study as one science was a popular focus during 16th and 17th century Europe. Culpeper's work was highly regarded for its thoroughness in cataloging plants and herbal usages. He also was known for his translation of London Pharmacopoeia from Latin to English, which was considered, for a time, to be the physicians' Bible. The translated work became even more popular and useful because it was made available to commoners and was instrumental in sharing herbal and home remedies to the people.

Herbal usage and study began to take a more scientific approach during the 17th and 18th centuries. Carl von Linne introduced the world to the concepts of genus and species as

descriptive accounts of plants, thereby establishing a universal system for describing and categorizing plants. His work Species Plantarum is evidence of the new descriptive system that is still so important in herbal usage today. As explorers discovered the Americas, they also discovered Native American Indian medicine. Although at first thought of as uncivilized people, after a disastrous winter, American Indians became an important information resource to the settlers. Goods were traded for knowledge, and early immigrants were taught which herbs to use to build endurance and treat injuries and simple physical ailments. This knowledge was passed from generation to generation, and until the 1940s herbal treatment was still an important element of health care.

Along with Native American Indian herbal knowledge, Shakers also became a resource, not only for knowledge but for commercial herbal medicinal products. Between 1787 and 1892, Shaker medicine grew from wild crafted herbs to cultivated herbs; from intercommunity healing to pharmaceutical suppliers (Miller, 1998).

As medicine and technology progressed in the 20th century, our culture began to treat herbal medicine with disdain. Reliance on synthetic application and symptomatic treatment has become the focus of health care today. The medical community has, in general, lost touch with our herbal heritage. There is too little knowledge and lack of documented research in the United States for traditional Western medicine to effectively integrate herbal medicine into their treatment.

Today, the U.S. Food and Drug Administration (FDA) prohibit the marketing of herbal products as anything but food supplements. Manufacturers are prohibited from making suggested herbal treatments for specific ailments on labels. It is important to note that many prescribed and over the-counter medications still contain herbal components. Compounds such as glycosides, found in the leaves of wild cherry trees are used in cough remedies and medical tonics. Digitalis, a cardiac stimulant, contains powdered foxglove (*Digitalis purpurea*) and is another example of a glycoside component used in traditional medicine. Yet another example of a glycoside, salicin, found in the bark of the white willow (*Salix* sp.) is one of the components in aspirin. Alkaloids are another compound used in traditional medicine. Used in small doses, plant alkaloids can be found in quinine, codeine, morphine, and nicotine. Plant tannins are valued for their astringent qualities and used to make skin and blood vessels constrict. Sulfur from garlic (*Allium sativum*), glycosides from mustard (*Sinapis* sp.), and alkaloids in water lilies (*Nymphaea* sp.) are used in the production of antibiotics.

In 1998, Time magazine reported that 60 million Americans use herbal supplements, spending over $12 billion dollars on natural herbal products. The World Health Organization estimates that healing herbs are the primary medical treatment for two thirds of today's population.

1.5.2 Herbs for prevention and treatment

Research of herbal applications to health care has been done primarily abroad in Europe, India, and Asia. Some of the best and most extensive studies have taken place in Europe where the effectiveness of herbal supplements (termed Phytomedicines in Europe) is well documented. Phytomedicines are produced as tablets or capsules under stringent guidelines and incorporated into conventional medical practice. These products are sold as health care herbal supplements and have been successfully integrated into traditional Western medical applications. These same products can be found in the United States in the food supplement section of many grocery store, pharmacy, and health stores.

Herbs and herbal medicine have been an integral part of our health care for centuries and will continue to develop and expand in our future health care system. Individuals are seeking alternatives to traditional Western medicine at a surprising rate, and all of us in health care related fields must begin to expand our views to encompass all modalities. Wellness, as a whole, is physical, emotional, and spiritual, and it is the responsibility of all of us to ensure that each individual receives complete health care. To successfully integrate herbology with traditional Western medicine, a call for thorough clinical research of herbal applications is necessary to provide educated answers and quality care to patients. Traditional Western and alternative/ herbal medicine can complement each other with understanding and appreciation for the science and art of health.

By definition, the word natural is an adjective referring to something that is present in or produced by nature and not artificial or man-made. When the word natural is used in verbiage or written, many times it is assumed that the definition is something good or pure. However, many effective poisons are natural products (Schoental, 1965). The term natural products today is quite commonly understood to refer to herbs, herbal concoctions, dietary supplements, traditional Chinese medicine, or alternative medicine. Nature has provided many things for humankind over the years, including the tools for the first attempts at therapeutic intervention. Natural products are generally either of prebiotic origin or originate from microbes, plants, or animal sources (Nakanishi 1, 1999; Nakanishi 2, 1999). As chemicals, natural products include such classes of compounds as terpenoids, polypeptides, amino acids, peptides, proteins, carbohydrates, lipids, nucleic acid bases, ribonucleic acid (RNA), deoxyribonucleic acid (DNA), and so forth. Natural products are not just accidents or products of convenience of nature.

More than likely they are a natural expression of the increase in complexity of organisms (Jarvis, 2000). Interest in natural sources to provide treatments for pain, palliatives, or curatives for a variety of maladies or recreational use reaches back to the earliest points of history. Drug development over the years has relied only on a small number of molecular prototypes to produce new medicines (Harvey, 2001). Indeed, only approximately 250 discrete chemical structure prototypes have been used up to 1995, but most of these chemical platforms have been derived from natural sources. While recombinant proteins and peptides are gaining market share, low molecular-weight compounds still remain the predominant pharmacologic choice for therapeutic intervention.

1.5.3 Herbal Medicine in therapeutics

An herb is a plant or plant part used for its scent, flavor or therapeutic properties. Herbal medicine products are dietary supplements that people take to improve their health. Many herbs have been used for a long time for claimed health benefits. They are sold as tablets, capsules, powders, teas, extracts and fresh or dried plants. However, some can cause health problems, some are not effective and some may interact with other drugs we are taking. Research into the use of plant-derived natural products alone in just the field of medicine covers a broad spectrum of activities (Dahanukar *et al.*, 2000, Havsteen, 1983, Wrigley *et al.*, 1997, Yao *et al.*, 1998, Yu *et al.*, 2000). Examples of such biological activity profiles would include, but are not limited to nootropics, psychoactive agents, dependence attenuators, anticonvulsants, sedatives, analgesics, anti-inflammatory agents, antipyretics, neurotransmission modulators, autonomic activity modulators, autacoid activity modulators, anticoagulants, hyoplipidemics, antihypertensive agents, cardioprotectants, positive ionotropes, antitussives, There are many medicinal plants on which significant research leads have been obtained with respect to their pharmaceutical potential for which processing and agrotechnology need to be established (**Table 1.1**) and drugs for which no synthetic one is currently available are given in **Table 1.2** (Kumar *et al*, 1997).

Table 1.1 Medicinal plants on which significant research leads with their pharmaceutical potential have been obtained (Kumar *et al*, 1997).

Andrographis paniculata	*Coleus forskohlii*	*Picrorhiza kurroa*
Artemisia annum	*Commiphora wightii*	*Sida rhombifolia*
Boswellia serrata	*Curcuma longa*	*Taxus baccata*
Centella asiatica	*Phyllanthus amarus*	*Withania somnifera*

Table 1.2 Medicinal plant drugs for which no synthetic one is currently available (Kumar *et al.*, 1997).

Drug	Plant Source	Use
Vinblastine	*Catharanthus roseus*	Anticancer
Vinblastine	*Catharanthus roseus*	Anticancer
Ajmalacine	*Catharanthus roseus*	Anticancer, hypotensive
Rescinnamine	*Rauvolfia serpentina*	Tranquilizer
Reserpine	*Rauvolfia serpentina*	Tranquilizer
Quinine	*Cinchona sp.*	Antimalarial, dysentery
Pilocarpine	*Pilocarpus jaborandi*	Antiglucoma
Cocaine	*Erythroxylum coca*	Topical anaesthetic
Morphine	*Papaver somniferum*	Analgesic
Codeine	*Papaver somniferum*	Anticough
Atropine	*Atropa belladonna*	Spasmolytic, cold
Atropine	*Hyoscyamus niger*	Spasmolytic, cold
Cardiac glycosides	*Digitalis sp.*	Congestive heart failure
Artemisinin	*Artemesia annua*	Antimalarial
Taxol	*Taxus baccata*	Cancer, antitumour
Taxol	*Taxus brevifolia*	Cancer
Berberine	*Berberis*	Leishmaniasis
Pristimerin	*Celastrus paniculata*	Antimalarial
Quassinoids	*Ailanthus*	Antiprotozoal
Plumbagin	*Plumbago indica*	Antibacterial, antifungal
Diospyrin	*Diospyros Montana*	Antifungal
Gossypol	*Gossypium sp.*	Antispermatogenic
Allicin	*Allium sativum*	Antifungal, amoebiasis
Ricin	*Ricinus communis*	Amoebiasis
Emetine	*Cephaelis ipecacuanha*	Amoebiasis
Glycyrrhizin	*Glycyrrhizia glabra*	Antiulcer
Nimbidin	*Azadirachta indica*	Antiulcer
Catechin	*Acacia catechu*	Antiulcer
Sophoradin	*Sophora subprostrata*	Antiulcer
Magnolol	*Magnolia bark*	Peptic ulcer
Forskolin	*Coleus forskohlii*	Hypotensive, cardiotonic
Digitoxin, Digoxin	*Digitalis, Thevetia*	Cardio tonic
Thevenerin	*Thevetia*	Cardio tonic
Nerrifolin	*Thevetia*	Cardio tonic
Podophyllin	*Podophyllum emodi*	Anticancer
Indicine N-oxide	*Heliotropium indicum*	Anticancer
Elipticine	*Ochrosia*	Anticancer
Homoharringtonine	*Cephalotaxus*	Anticancer
Camptothecine	*Camptotheca acuminata*	Anticancer

1.6 Natural product research and development

The World Health Organization estimates that approximately 80 percent of the world's population relies primarily on traditional medicines as sources for their primary health care (Farnsworth *et al.*, 1985). Over 100 chemical substances that are considered to be important drugs, which are either currently in use or have been widely used in one or more countries in the world, have been derived from 100 different plants as described in Table 1.3. Approximately 75 percent of these substances were discovered as a direct result of chemical studies focused on the isolation of active substances from plants used in traditional medicine (Cragg 1 *et al.*, 2001; Cragg 2 *et al.*, 2001).The number of medicinal herbs used in China in 1979 has been estimated to be numbered at 5267 (Nakanishi 1,1999; Nakanishi 2, 1999). More current statistics based on prescription data from 1993 in the United States show that over 50 percent of the most prescribed drugs had a natural product either as the drug or as the starting point in the synthesis or design of the actual end chemical substance (Newman, 2000). Thirty-nine percent of the 520 new drugs approved during the period 1983 through 1994 were either natural products or derivatives of natural products (Harvey, 2001). Indeed, if one looks at new drugs from an indication perspective over the same period of time, over 60 percent of antibacterial and antineoplastic were again either natural products themselves or based on structures of natural products. Of the 20 top-selling drugs on the market in the year 2000, 7 of these were either derived from natural products or developed from leads generated from natural products. This select group of drugs generates over 20 billion U.S. dollars of revenue on an annual basis (Grabley, *et al.*, 2003; Harvey, 2001).

Drug development over the years has relied only on a small number of molecular prototypes to produce new medicines (Harvey, 2001). Indeed, only approximately 250 discrete chemical structure prototypes have been used up to 1995, but most of these chemical platforms have been derived from natural sources. While recombinant proteins and peptides are gaining market share, low molecular-weight compounds still remain the predominant pharmacologic choice for therapeutic intervention (Grabley *et al.*, 2003).Just a small sampling of the many available examples of the commercialization of modern drugs from natural products along with their year of introduction, indication, and company are: Orlistat, 1999, obesity, Roche; Miglitol, 1996, antidiabetic (Type II), Bayer; Topotecan, 1996, antineoplastic, SmithKline Beecham; Docetaxel, 1995, antineoplastic, Rhône-Poulenc Rorer; Tacrolimus, 1993, immunosuppressant, Fujisawa; Paclitaxel, 1993, antineoplastic, Bristol-Myers Squibb. The overwhelming concern today in the pharmaceutical industry is to improve the ability to find new drugs and to accelerate the speed with which new drugs are discovered and developed. This will only be successfully accomplished if the procedures for drug target elucidation and lead compound identification and optimization are themselves optimized. Analysis of the human genome will

provide access to a myriad number of potential targets that will need to be evaluated (Grabley *et al.*, 2003; Harvey, 2001). The process of high-throughput screening enables the testing of increased numbers of targets and samples to the extent that approximately 100,000 assay points per day are able to be generated. However, the ability to accelerate the identification of pertinent lead compounds will only be achieved with the implementation of new ideas to generate varieties of structurally diverse test samples (Grabley *et al.*, 2003; Harvey, 2001; Harvey, 1999). Experience has persistently and repeatedly demonstrated that nature has evolved over thousands of years a diverse chemical library of compounds that are not accessible by commonly recognized and frequently used synthetic approaches.

Natural products have revealed the ways to new therapeutic approaches, contributed to the understanding of numerous biochemical pathways and have established their worth as valuable tools in biological chemistry and molecular and cellular biology. Just a few examples of some natural products that are currently being evaluated as potential drugs are given in **Table 1.3**.

Table 1.3 Natural drugs having high pharmaceutical potential (Grabley *et al.*, 2003).

Natural Product	Source	Target	Indication	Status
Manoalide	Marine sponge	Phospholipage-A2 Ca^{2+} release	Anti-inflammatory	Clincial trials
Dolastatin 10	Sea hare	Microtubules	Antineoplastic	Nonclinical
Staurosporine	Streptomyces	Protein kinase C	Antineoplastic	Clinical trials
Epothilone	Myxobacterium	Microtubules	Antineoplastic	Research
Calanolide A, B	Tree	DNA polymerase action on reverse transcriptase	AIDS	Clinical trials
Huperzine A	Moss	Cholinesterase	Alzheimer's disease	Clinical trials

The costs of drug discovery and drug development continue to increase at astronomical rates, yet despite these expenditures, there is a decrease in the number of new medicines introduced into the world market. Despite the successes that have been achieved over the years with natural products, the interest in natural products as a platform for drug discovery has waxed and waned in popularity with various pharmaceutical companies. Natural drugs having numerous biological activity profiles are in use such as nootropics, psychoactive agents, dependence attenuators, anticonvulsants, sedatives, analgesics, anti-inflammatory agents, antipyretics, neurotransmission modulators, autonomic activity modulators, lavones activity

modulators, anticoagulants, hyoplipidemics, antihypertensive agents, cardioprotectants, positive ionotropes, antitussives, antiasthmatics, pulmonary function enhancers, antiallergens, hypoglycemic agents, antifertility agents, fertility-enhancing agents, wound healing agents, dermal healing agents, bone healing agents, compounds useful in the prevention of urinary calculi as well as their dissolution, gastrointestinal motility modulators, gastric ulcer protectants, immunomodulators, hepato-protective agents, myelo-protective agents, pancreato-protective agents, oculo-protective agents, membrane stabilizers, hemato-protective agents, antioxidants, agents protective against oxidative stress, antineoplastics, antimicrobials, antifungal agents, antiprotozoal agents, antihelminthics, and nutraceuticals (Dahanukar *et al.*, 2000).

Many frontiers remain within the field of natural products that can provide opportunities to improve our quality of life. Fungal disease has historically been a difficult clinical entity with which to effectively deal. Fungal diseases can include more than just a mycosis and can also include allergic reactions to fungal proteins and toxic reactions to fungal toxins. Mycoses as a group include diseases that are significantly more serious and life-threatening than nail infestations, athlete's foot, or "jock-itch." Indeed, increasing numbers of overly healthy individuals are becoming victims of the complications of fungal infestation. The reasons for this are that increasing numbers of people are receiving immunomodulatory treatment for an organ transplant or some underlying chronic systemic pathology, antineoplastic chemotherapy for cancer, or have been the recipients of proper or improper use of powerful antibiotics. Additionally there are a number of individuals within society that are infected with the human immunodeficiency virus (HIV). The available drugs to treat mycoses have been limited (Barrett, 2002). Furthermore, in this armamentarium, there are problems with dose-limiting nephrotoxicity, the rapid development of resistance, drug–drug interactions of concern, and a fungistatic mechanism of action. Thus there is an urgent need for the development of more efficacious antifungal agents with fewer limitations and less side effects. Ideally such compounds should possess good distribution characteristics, a novel mechanism of action, and a broad-spectrum fungicidal activity. The discovery and isolation of an echinocandin-type lipopeptide (FR901379) and lipopeptidolactone (FR901469) from microbes has been a significant achievement. These compounds are water soluble and inhibit the synthesis of 1, 3-b-glycan, a key component of the fungal cell wall. Furthermore, since the cell wall is a feature particular to fungi and is not present in eukaryotic cells, such inhibitors certainly have the potential to demonstrate selective toxicity against the fungi and not against the animal or human host. The ultimate modifications of the lipopeptide and lipopeptidolactone referenced above led to the discovery of micafungin (FK463), which is currently in phase III clinical trials. This work along with the relatively recent approval of caspofungin (Merck) as a therapeutic

agent for the treatment of disseminated aspergillosis are significant achievements in that they demonstrate that a melding of the proper research to identify and develop appropriate targets with the chemical and biological diversity found in natural products can be very rewarding. Much ado has been made over recent years about endocrine disruptors and their effects on humans (Crews *et al.*, 2000). It needs to be recognized that endocrine disruptors are not just synthetic chemicals but can also be natural products. The use of natural product endocrine disruptors may provide significant insight into our understanding of the mechanisms by which the evolution of the genome can protect transactivation of the sex hormone receptors and aid in the development of drugs, which can protect the embryo during its development from hormone disruptive effects. Diabetes is a multi-systemic affliction, having impact on nearly every body organ. As a disease, it kills more individuals on a per annum basis than AIDS and breast cancer combined (Shapiro *et al.*, 2002). The impact on the quality of life of an individual suffering with diabetes is profound. A number of natural products currently exist that demonstrate hypoglycemic activity. Indeed, depending upon the source that one might use, there are approximately 800 to 1200 plants that exhibit hypoglycemic activity. While research and development efforts in this particular area thus far are largely restricted to traditional medicine uses, future research may well identify a potent antidiabetic agent. The incidences of neuropsychiatric disorders are steadily increasing as our population increases in size and age. Such disorders include, but are not limited to, seizure disorders, schizophrenia, dementia, mania, aggression, memory loss, psychoses, age-related cognitive decline, depression, anxiety states, mood disorders, substance abuse, and substance dependence. There is a large body of data available that suggests the use of many natural products as potential treatments for these conditions and other neuropsychiatric disorders (Chung *et al.*, 1995; Lake, 2000; Bindseil *et al.*, 2001). Indeed, a number of plant extracts have been associated with the treatment of various categories of mental symptoms and various types of receptor selectivity (Chung *et al.*, 1995). A very controversial potential psychotherapeutic agent is *Gingko biloba* (Fugh-Berman *et al.*, 1999). A lack of understanding of mechanism of action, misidentification of materials, contamination of materials, intrinsic toxicity, and absence of standardization all contribute to this controversy. Further fractionation, isolation, and characterization of active components of these and other plants will undoubtedly lead to the discovery of novel neuropsychiatric agents as well as the debunking of other alleged therapies. There are numerous blood-based diseases that afflict humans. These would include, but are not limited to, anemia, blood group incompatibility, blood protein disorders, bone marrow diseases, hemoglobinopathies, hemorrhagic diatheses, leukemia, disorders of leukocyte dysfunction, platelet disorders, and erythrocyte aggregation disorders.

A number of natural products have been reported in the literature to be of value in the treatment of Epstein-Barr virus infection, leukemia, thrombosis and coagulopathies, malaria, anemia, and bone marrow diseases (Miles *et al.*,1998). Extracts from the fungus *Trichothecium roseum*, the sea cucumber *Cucumaria japonica*, the legume *Amorpha fruitcosa*, the tree *Magnolia officinalis*, and others may be useful in the therapeutic management of Epstein-Barr virus infection. Extracts from the basidiomycetes *Mycena pura* and *Nidula candida* may be useful in the treatment of leukemia. Compounds isolated from *Streptomyces platensis* may be useful in the treatment of thrombocytopenia. Compounds obtained from the marine sponge *Aplysina archeri* have been reported to inhibit the growth of the feline leukemia virus. Scalarane-type bishomo-sesterterpenes isolated from the marine sponge *Phyllospongia foliascens* have been reported to exhibit cytotoxic, antithrombocytic, and vasodilation activities. It should be noted that a number of natural products are based on the coumarin nucleus and as such may exhibit antithrombotic and antipatelet activities. A number of blood-sucking animals have small, low-molecular-weight proteins in their saliva that interfere with the clotting of blood and therefore might be of value as potential anticoagulants. Streptomyces, hygroscopicus and ascomyceticus manufactures a macrolide that has been reported to have immunosuppressant activity and may prove to be beneficial in preventing transplant rejection in humans. It is entirely possible that these compounds and others offer sufficient structural diversity, range of biological activities and differing mechanisms of action that new, safer, and more efficacious drugs to treat blood-based disorders could well burgeon from this library. A wide variety of natural products are claimed to possess immunosuppressant activity, but it is often difficult to dissect this activity away from associated cytotoxicity (Mann, 2001).

Since the first heart transplant in the late 1960s, medicine has progressed to the point where most organ transplants have become relatively routine procedures. The survival of individuals with transplants is owed in large part to the discovery of the fungal metabolite cyclosporine A in 1970 and its widespread use starting in 1978. Indeed, cyclosporine A has achieved such success that it is currently being evaluated for value in the treatment of Crohn's disease, systemic lupus erythematosus, and rheumatoid arthritis. Research efforts abound in the area of natural products and immunosuppression. A methyl analog of oligomycin F isolated from *Streptomyces ostreogriseus* has been reported to quite effectively suppress B cell activation and T-cell activation in the presence of mitogens at concentrations comparable to that of cyclosporine A. Concanamycin F first isolated from *Streptomyces diastatochromogenes* in 1992 has been found to possess a wide array of biological activities including immunosuppressive and antiviral activities. The experimental immunosuppressant (+)-discodermolide isolated from the marine sponge *Discodermia lavones* exhibits relatively nonspecific immunosuppression, causing the cell cycle to arrest during G_2 and M phases. This compound's current primary

interest is as a potential antineoplastic agent since it stabilizes microtubules and prevents depolymerization, effectively causing cell cyclic arrest during the metaphase to anaphase transition. This same mode of activity is shared with Taxol (Paclitaxel), the epothilones, eleutherobin, and the sarcodictyins. The didemnins, cyclic peptides, were first isolated from the marine tunicate *Trididemnum solidum* and exhibit immunosuppressive activity through a generalized cytotoxicity mediated by inhibition of progression through the G_1 phase of the cell cycle by an unknown mechanism. The trichopolyns I to V from the fungus *Trichoderma polysporum* are lipopeptides that suppress the proliferation of lymphocytes in the murine allogeneic mixed lymphocyte response assay. Triptolide from the plant *Tripterygium winfordii* demonstrates immunosuppressant activity through the inhibition of IL-2 receptor expression and signal transduction.

The novel heteroaromatic compound lymphostin, obtained from Streptomyces KY11783 has demonstrated immunosuppressant activity through its potent inhibition of the lymphocyte kinase. Over the last decade, research activities on immunosuppressants of natural product origin have focused on the mechanisms of inhibition of T-cell activation and proliferation. This approach has been fruitful, leading to the generation of significant information about signaling pathways between T cells, greater detail about the roles of T cells in immune function, and the discovery of Tacrolimus (Prograf) from the soil fungus *Streptomyces tsukubaensis*. As immunological research progresses, increasingly more potential targets will be elucidated for immunomodulatory therapeutic intervention. Natural products will undoubtedly provide a sound platform for the delivery of natural-product-based therapeutic agent candidates. Natural-products-based anticancer drug discovery continues to be an active area of research throughout the world (Da Rocha *et al.*, 2001; Mann, 2002; Mehta *et al.*, 2002; Schwartsmann *et al.*, 2002). While cancer incidences and the frequencies of types of cancer may vary from country to country, the most common sites for the development of neoplasia are generally considered to be the breast, colon, rectum, prostate, cervix, uterus, esophagus, stomach, pancreas, liver, lung, urinary bladder, kidney, ovary, oral cavity, and blood (leukemia and non-Hodgkin lymphoma) (Schwartsmann *et al.*,2002).

Currently, the chemotherapeutic management of these tumors involves a variety of different plant-based chemicals that are either currently in use or in clinical trials and include such drug classes as the *Vinca* alkaloids, lignans, taxanes, stilbenes, flavones, cephalotaxanes, camptothecins, and taxanes. Despite the wide range of organ structure, type, and function, great similarities exist between the organs with regard to the pathogenesis of cancer. As more and more details of the molecular biology of cancer are revealed, more targets will present themselves for possible therapeutic chemical intervention in the growth and development of neoplasms. A final note with regard to this approach is that it is important to appreciate that

the distinction between chemopreventive agent and chemotherapeutic agent can become quite blurred. A recurrent theme in neoplasia is the alteration of cell cycle control. One therapeutic approach to the treatment of neoplasia is the development of a treatment that would return to normal the altered cell cycle (Sausville *et al.*, 2000). The introduction of active agents derived from natural sources into the anticancer weaponry has already significantly changed the futures of many individuals afflicted with cancer of many different types. Continued research into natural sources will continue to deliver newer and more promising chemicals and chemical classes of anticancer agents with novel mechanisms of action that will improve survival rates to even higher degrees. For the period 1983 to 1994, seven out of 10 synthetic agents approved by the Food and Drug Administration (FDA) for use as antivirals were based on a natural product. These drugs are famciclovir, stavudine, zidovudine, zalcitabine, ganciclovir, sorivudine, and didanosine. The viral genome can be composed of either RNA or DNA and HIV.

The general potential targets of antiviral chemotherapy are:

(1) Attachment of virus to host cell,

(2) Penetration of the host cell by the virus,

(3) Viral particle uncoating, release, and transport of viral nucleic acid and transport proteins,

(4) Nucleic acid polymerase release/activation,

(5) Translation of mRNA (messenger RNA) to polypeptides (early proteins),

(6) Transcription of mRNA,

(7) Replication of nucleic acids,

(8) Protein synthesis (late proteins),

(9) Viral polypeptide cleavage into polypeptides necessary for maturation,

(10) Assembly of viral capsids and precursors,

(11) Encapsidation of nucleic acid,

(12) Envelopment, and

(13) Release.

Early antiviral research focused on compounds that inhibited viral DNA synthesis, purine, and pyrimidine nucleoside analogs. Today most current antiviral agents target RNA-based viruses and the inhibition of reverse transcriptase in order to block the transcription of the RNA genome to DNA. Such inhibition would prevent the synthesis of viral mRNA and proteins.

Protease inhibitors affect the synthesis of late viral proteins and viral packaging activity. There are no currently available drugs that target early viral protein synthesis. Antiviral compound research has included alkaloids, carbohydrates, chromones, coumarins, flavonoids, lignans, phenolics, quinines, xanthones, phenylpropanoids, tannins, terpenes, steroids, iridoids, thiopenes, polyacetylenes, lactones, butenolides, phospholipids, proteins, peptides, and lectins. While plants have been a common hunting ground, many other sources are now starting to be explored, especially the marine environment. The use of natural products in the field of antiviral research appears to be limited only by the imagination of the researcher. Natural products are indeed viable sources and resources for drug discovery and development (Artuso, 1997). Indeed, without natural products, medicine would be lacking in therapeutic tools in several important clinical areas such as neurodegenerative disease, cardiovascular disease, solid tumors treatment, and immunoinflammatory disease (Banerji, 2000; Harvey, 2000; Nisbet *et al.*, 1997). Furthermore, the continual emergence of new natural product chemical structure skeletons, with interesting biological activities along with the potential for chemical modification and synthesis bode well for the utility of natural products. Finally, the uses of natural products need to be by no means restricted to pharmaceuticals but can also be expanded to agrochemicals. For example, the use of pyrethrins obtained from *Chrysanthemum* sp. As insecticides has been very popular over the years and persists today. Research continues into the use of natural products as pesticides. The new medicinal uses of plants like *Achyranthes* (hypoglycaemic and estrogenic), *Aegle* (hypoglycaemic), *Phyllanthus* (contraceptive) and *Sida* (antiplaque activities) and new active components of *Sida*, *Aloe*, *Boerhavia*, *Eclipta* and *Phyllanthus* were taken as models and the role of minor components like phenolics has been emphasized.

Sikkim and Darjeeling Himalayan region is characterized by a rich floral diversity and an equally rich Ethnomedicinal tradition. Herbal medicine is the dominant system of medicine practiced by the local tribes of this region for the treatment of diabetes (Chhetri *et al.*, 2005).

Today there are at least 120 distinct chemical substances derived from plants that are considered as important drugs currently in use in one or more countries in the world. Where several of the drugs sold today are simple synthetic modifications or copies of the naturally obtained substances. The original plant substance/chemical name is shown under the "Drug" column rather than the finished patented drug name. For example, many years ago a plant chemical was discovered in a tropical plant, *Cephaelis ipecacuanha*, and the chemical was named emetine (see **Table 1.3**). A drug was developed from this plant chemical called Ipecac which was used for many years to induce vomiting mostly if someone accidently swallowed a poisonous or harmful substance. Ipecac can still be found in pharmacies in many third world countries but has been mostly replaced by other drugs in the United States. Another example

of this is the plant chemical named taxol shown in the drug column below. The name taxol is the name of the plant chemical originally discovered in the plant. A pharmaceutical company copied this chemical and patented a drug named Paclitaxel which is used in various types of tumors today in the U.S. and many other countries.

There are 120 substances which are sold as drugs worldwide but not in all countries. Some European countries regulate herbal substances and products differently than in the United States. Many European countries, including Germany, regulate herbal products as drugs and pharmaceutical companies prepare plant based drugs simply by extracting out the active chemicals from the plants. A good example is the plant substance, cynarin (**Table 1.3**). Cynarin is a plant chemical found in the common artichoke (*Cynara scolymus*). In Germany, a cynarin drug is sold for liver problems and hypertension which is simply this one chemical extracted from the artichoke plant or a plant extract which has been standardized to contain a specific milligram amount of this one chemical. These products are manufactured by pharmaceutical companies, sold in pharmacies in Germany and a doctor's prescription is required to purchase them. In the United States artichoke extracts are available as natural products and sold in health food stores. Some products are even standardized to contain a specific amount of the cynarin chemical. One can purchase these natural and standardized extracts over the counter without a prescription and one could not go to a pharmacy in the U.S. and obtain a cynarin drug with a prescription. Another similar example is the plant chemical, Silymarin, shown in **Table 1.1**. Silymarin is a chemical found in the milk thistle plant and natural milk thistle extracts standardized to contain specific amounts of Silymarin are found in just about every health food store in the United States. However in Germany, Silymarin drugs and milk thistle standardized extracts are sold only in pharmacies and require a doctor's prescription for liver problems.

Some of the drug/chemicals shown in **Table 1.3** are still sold as plant based drugs requiring the processing of the actual plant material. Others have been chemically copied or synthesized by laboratories and no plant materials are used in the manufacture of the drug. A good example of this is the plant chemical quinine, which was discovered in a rainforest tree (*Cinchona ledgeriana*) over 100 years ago. For many years the quinine chemical was extracted from the bark of this tree and processed into pills to treat malaria. Then a scientist was able to synthesize or copy this plant alkaloid into a chemical drug without using the original tree bark for manufacturing the drug. Today, all quinine drugs sold are manufactured chemically without the use of any tree bark. However, another chemical in the tree called quinidine which was found to be useful for various heart conditions couldn't be completely copied in the laboratory and the tree bark is still harvested and used to extract this plant chemical from it. Quinidine extracted from the bark is still used today to produce quinidine-based drugs. In the U.S. there

are four patented brand-name heart drugs sold in pharmacies containing bark-extracted quinidine: Cardioquin™, Quinaglute Dura-tabs™, Quinidex Extentabs™ and Quin-Release™. The National Cancer Institute (NCI) has several ongoing lavones tive programs which screen plants for the possiblility of new drugs and active plant chemicals for cancer and AIDS/HIV.

Because well over 50 percent of the estimated 250,000 plant species found on earth come from tropical forests, NCI concentrates on these regions. Plants have been collected from the African countries of Cameroon, the Central African Republic, Gabon, Ghana, Madagascar, and Tanzania. Collections are now concentrated in Madagascar (one of the most rapidly disappearing rainforest regions in the world), and collaborative programs have been established in South Africa and Zimbabwe.

In Central and South America, samples have been collected from Belize, Bolivia, Colombia, the Dominican Republic, Ecuador, Guatemala, Guyana, Honduras, Martinique, Paraguay, Peru, and Puerto Rico. The NCI has established collaborative programs in Brazil, Costa Rica, Mexico, and Panama. Southeast Asian collections have been performed in Bangladesh, Indonesia, Laos, Malaysia, Nepal, Pakistan, Papua New Guinea, the Philippines, Taiwan, Thailand, and Vietnam. Collaborative programs have been established in Bangladesh, China, Korea, and Pakistan. In each country, NCI contractors work in close collaboration with local botanical institutions.

Since 1986, over 40,000 plant samples have been screened, but thus far only five chemicals showing significant activity against AIDS have been isolated. Three are currently in preclinical development. Before being considered for clinical trials in humans, these agents must show tolerable levels of toxicity in several animal models. For AIDS, three agents are presently in preclinical or early clinical development. The following are plants and chemicals which are still under research for cancer and AIDS/HIV:

(+)-Calanolide A and (-)-Calanolide B (Costatolide) are isolated from *Calophyllum lanigerum* and *Calophyllum teysmanii*, respectively, trees found in Sarawak, Malaysia. Both these agents are licensed to Medichem, Inc., Chicago, which is developing them in collaboration with the Sarawak State Government through a joint company, Sarawak Medichem Pharmaceuticals, Inc. (+)-Calanolide A is currently in early clinical trials in the United States.

Conocurovone, isolated from the shrub species, *Conospermum incurvum* (Saltbush), found in Western Australia, has been licensed for development to AMRAD, a company based in Victoria, Australia.

Michellamine B, from the leaves of *Ancistrocladus korupensis*, a vine found in the Korup rainforest region of southwest Cameroon, has undergone extensive preclinical study, but is considered too toxic for advancement to clinical trials.

Prostratin, isolated from the wood of *Homolanthus nutans*, a tree found in Western Samoa, has been placed on low priority, largely due to its association with a class of compounds shown to be tumor promoters.

A tree native to China *Camptotheca acuminate* is the source of four promising anticancer drugs, two of which have been approved by the FDA and are described above. The other two chemicals still under research include:

(i) (9-aminocamptothecin): Currently in clinical trials for several types of cancer, including ovarian and stomach cancers and T-cell lymphoma.

(ii) Tothecin: While no clinical trials are being performed in the United States, trials are ongoing in China. Homoharringtonine from the Chinese tree, *Cephalotaxus harringtonia* are in early clinical trials. Perillyl alcohol, and flavopiridol, a totally synthetic compound based on a flavones isolated from are in early clinical trials.

Table 1.4 Currently used important drugs derived from plant sources as per WHO. (Muhammad *et al.,* 2005)

Drug/Chemical	Action/Clinical Use	Plant Source
Acetyldigoxin	Cardiotonic	*Digitalis lanata*
Adoniside	Cardiotonic	*Adonis vernalis*
Aescin	Anti-inflammatory	*Aesculus hippocastanum*
Aesculetin	Anti-dysentery	*Frazinus rhychophylla*
Agrimophol	Anthelmintic	*Agrimonia supatoria*
Ajmalicine	Circulatory Disorders	*Rauvolfia sepentina*
Allantoin	Vulnerary	*Several plants*
Allyl isothiocyanate	Rubefacient	*Brassica nigra*
Anabesine	Skeletal muscle relaxant	*Anabasis sphylla*
Andrographolide	Baccillary dysentery	*Andrographis paniculata*
Anisodamine	Anticholinergic	*Anisodus tanguticus*
Anisodine	Anticholinergic	*Anisodus tanguticus*
Arecoline	Anthelmintic	*Areca catechu*
Asiaticoside	Vulnerary	*Centella asiatica*
Atropine	Anticholinergic	*Atropa belladonna*
Benzyl benzoate	Scabicide	*Several plants*
Berberine	Bacillary dysentery	*Berberis vulgaris*

Table 1.4 continued

Drug/Chemical	Action/Clinical Use	Plant Source
Bergenin	Antitussive	*Ardisia japonica*
Betulinic acid	Anticancerous	*Betula alba*
Borneol	Antipyretic, analgesic, antiinflammatory	*Several plants*
Bromelain	Anti-inflammatory, proteolytic	*Ananas comosus*
Caffeine	CNS stimulant	*Camellia sinensis*
Camphor	Rubefacient	*Cinnamomum camphora*
Camptothecin	Anticancerous	*Camptotheca acuminata*
(+)-Catechin	Haemostatic	*Potentilla fragarioides*
Chymopapain	Proteolytic, mucolytic	*Carica papaya*
Cissampeline	Skeletal muscle relaxant	*Cissampelos pareira*
Cocaine	Local anaesthetic	*Erythroxylum coca*
Codeine	Analgesic, antitussive	*Papaver somniferum*
Colchiceine amide	Antitumor agent	*Colchicum autumnale*
Colchicine	Antitumor agent, anti-gout	*Colchicum autumnale*
Convallatoxin	Cardiotonic	*Convallaria majalis*
Curcumin	Choleretic	*Curcuma longa*
Cynarin	Choleretic	*Cynara scolymus*
Danthron	Laxative	*Cassia species*
Demecolcine	Antitumor agent	*Colchicum autumnale*
Deserpidine	Antihypertensive, tranquillizer	*Rauvolfia canescens*
Deslanoside	Cardiotonic	*Digitalis lanata*
L-Dopa	Anti-parkinsonism	*Mucuna sp*
Digitalin	Cardiotonic	*Digitalis purpurea*
Digitoxin	Cardiotonic	*Digitalis purpurea*
Digoxin	Cardiotonic	*Digitalis purpurea*
Emetine	Amoebicide, emetic	*Cephaelis ipecacuanha*
Ephedrine	Sympathomimetic, antihistamine	*Ephedra sinica*
Etoposide	Antitumor agent	*Podophyllum peltatum*
Galanthamine	Cholinesterase inhibitor	*Lycoris squamigera*
Gitalin	Cardiotonic	*Digitalis purpurea*
Glaucarubin	Amoebicide	*Simarouba glauca*
Glaucine	Antitussive	*Glaucium flavum*
Glasiovine	Antidepressant	*Octea glaziovii*
Glycyrrhizin	Sweetener, Addison's disease	*Glycyrrhiza glabra*

Table 1.4 continued

Drug/Chemical	Action/Clinical Use	Plant Source
Gossypol	Male contraceptive	*Gossypium species*
Hemsleyadin	Bacillary dysentery	*Hemsleya amabilis*
Hesperidin	Capillary fragility	*Citrus species*
Hydrastine	Hemostatic, astringent	*Hydrastis canadensis*
Hyoscyamine	Anticholinergic	*Hyoscyamus niger*
Irinotecan	Anticancer, antitumor agent	*Camptotheca acuminata*
Kaibic acud	Ascaricide	*Digenea simplex*
Kawain	Tranquillizer	*Piper methysticum*
Kheltin	Bronchodilator	*Ammi visaga*
Lanatosides A, B, C	Cardiotonic	*Digitalis lanata*
Lapachol	Anticancer, antitumor	*Tabebuia sp.*
a-Lobeline	Smoking deterrant, respiratory stimulant	*Lobelia inflata*
Menthol	Rubefacient	*Mentha species*
Methyl salicylate	Rubefacient	*Gaultheria procumbens*
Monocrotaline	Antitumor agent (topical)	*Crotalaria sessiliflora*
Morphine	Analgesic	*Papaver somniferum*
Neoandrographolide	Dysentery	*Andrographis paniculata*
Nicotine	Insecticide	*Nicotiana tabacum*
Nordihydroguaiaretic acid	Antioxidant	*Larrea divaricata*
Noscapine	Antitussive	*Papaver somniferum*
Ouabain	Cardiotonic	*Strophanthus gratus*
Pachycarpine	Oxytocic	*Sophora pschycarpa*
Palmatine	Antipyretic, detoxicant	*Coptis japonica*
Papain	Proteolytic, mucolytic	*Carica papaya*
Papavarine	Smooth muscle relaxant	*Papaver somniferum*
Phyllodulcin	Sweetner	*Hydrangea macrophylla*
Physostigmine	Cholinesterase Inhibitor	*Physostigma venenosum*
Picrotoxin	Analeptic	*Anamirta cocculus*
Pilocarpine	Parasympathomimetic	*Pilocarpus jaborandi*
Pinitol	Expectorant	*Several plants*
Podophyllotoxin	Antitumor anticancer agent	*Podophyllum peltatum*
Protoveratrines A, B	Antihypertensives	*Veratrum album*
Pseudoephredrine*	Sympathomimetic	*Ephedra sinica*

Table 1.4 Continued

Drug/Chemical	Action/Clinical Use	Plant Source
Quinidine	Antiarrhythmic	*Cinchona ledgeriana*
Quisqualic acid	Anthelmintic	*Quisqualis indica*
Rescinnamine	Antihypertensive, tranquillizer	*Rauvolfia serpentina*
Reserpine	Antihypertensive, tranquillizer	*Rauvolfia serpentina*
Rhomitoxin	Antihypertensive, tranquillizer	*Rhododendron molle*
Rorifone	Antitussive	*Rorippa indica*
Rotenone	Piscicide, Insecticide	*Lonchocarpus nicou*
Rotundine	Analagesic, sedative, traquillizer	*Stephania sinica*
Rutin	Capillary fragility	*Citrus species*
Salicin	Analgesic	*Salix alba*
Sanguinarine	Dental plaque inhibitor	*Sanguinaria canadensis*
Santonin	Ascaricide	*Artemisia maritma*
Scillarin A	Cardiotonic	*Urginea maritima*
Scopolamine	Sedative	*Datura species*
Sennosides A, B	Laxative	*Cassia species*
Silymarin	Antihepatotoxic	*Silybum marianum*
Sparteine	Oxytocic	*Cytisus scoparius*
Stevioside	Sweetner	*Stevia rebaudiana*
Strychnine	CNS stimulant	*Strychnos nux-vomica*
Taxol	Antitumor agent	*Taxus brevifolia*
Teniposide	Antitumor agent	*Podophyllum peltatum*
a-Tetrahydrocannabinol	Antiemetic, decrease occular tension	*Cannabis sativa*
Tetrahydropalmatine	Analgesic, sedative, traquillizer	*Corydalis ambigua*
Tetrandrine	Antihypertensive	*Stephania tetrandra*
Theobromine	Diuretic, vasodilator	*Theobroma cacao*
Theophylline	Diuretic, brochodilator	*Theobroma cacao and others*
Thymol	Antifungal (topical)	*Thymus vulgaris*
Topotecan	Antitumor, anticancer agent	*Camptotheca acuminata*
Trichosanthin	Abortifacient	*Trichosanthes kirilowii*
Tubocurarine	Skeletal muscle relaxant	*Chondodendron tomentosum*
Valapotriates	Sedative	*Valeriana officinalis*
Vasicine	Cerebral stimulant	*Vinca minor*

Table 1.4 Continued

Drug/Chemical	Action/Clinical Use	Plant Source
Vinblastine	Antitumor, Antileukemic agent	*Catharanthus roseus*
Vincristine	Antitumor, Antileukemic agent	*Catharanthus roseus*
Yohimbine	Aphrodisiac	*Pausinystalia yohimbe*
Yuanhuacine	Abortifacient	*Daphne genkwa*
Yuanhuadine	Abortifacient	*Daphne genkwa*

1.6.1 Natural products and High Throughput Screening

Natural products are the most important anticancer and anti-infective agents. More than 60% of approved and pre-new drug application (NDA) candidates are either natural products or related to them, not including biologicals such as vaccines and monoclonal antibodies (Cragg *et al.*, 1997). Secondary metabolism has evolved in nature in response to needs and challenges of the natural environment which enables the nature continually carrying out its own version of combinatorial chemistry (Verdine, 1996) for the over 3 billion years during which bacteria have inhabited the earth (Holland,1998). During that time, there has been an evolutionary process going on in which producers of secondary metabolites evolved according to their local environments. If the metabolites were useful to the organism, the biosynthetic genes were retained, and genetic modifications further improved the process. Combinatorial chemistry practiced by nature is much more sophisticated than that in the laboratory, yielding exotic structures rich in stereochemistry, concatenated rings, and reactive functional groups (Verdine, 1996). As a result, an amazing variety and number of products have been found in nature. The total number of natural products produced by plants has been estimated to be over 500,000 (Mendelson *et al.*, 1995). One-hundred sixty thousand natural products have been identified (Chapman, 2001), a value growing by 10,000 per year (Henkel *et al.*, 1999). About 100,000 secondary metabolites of molecular weight less than 2500 have been characterized, half from microbes and the other half from plants (Fenical *et al.*, 1993; Berdy, 1995; Roessner *et al.*, 1996)

It is not generally appreciated that a number of synthetic products of wide medical use have a natural origin from microbial, plant, and even animal systems. The predecessor of aspirin has been known since the fifth century BC, at which time it was extracted from willow tree bark by Hippocrates. It probably was used even earlier in Egypt and Babylonia for fever, pain, and childbirth (Kiefer, 1997). Salicylic acid derivatives have been found in plants such as white willow, wintergreen, and meadowsweet. Synthetic salicylates were produced on a large scale in 1874 by the Bayer Company in Germany. In 1897, Arthur Eichengrun at Bayer discovered that

its acetyl derivative was able to reduce its acidity, bad taste, and stomach irritation (Shapiro, 2003); thus was born aspirin, of which 50 billion tablets are consumed each year. The drugs Acyclovir (Zovirax) used against herpes virus and Cytarabine (Cytostar) for non-Hodgkin's lymphoma were originally isolated from a sponge (Rayl, 1999). Drugs inhibiting human immunodeficiency virus (HIV) reverse-transcriptase and protease were derived from natural product leads screened at the National Cancer Institute (Yang *et al.*, 2001). Angiotensin-converting enzyme (ACE) inhibitors, widely used for hypertension and congestive heart failure, are chemicals based on peptides isolated from snake venom (Ondetti *et al.*, 1971; Patchett, 2002). In the last decade, some large pharmaceutical companies, emphasizing combinatorial chemistry, left natural products and attempted to fill the void with large numbers of synthetic molecules. Unfortunately, the chemistry employed did not create sufficiently diverse or pharmacologically active molecules. Fortunately, some small biotechnology companies have revitalized the interest in natural products. Approaches such as diversity-oriented synthesis, which mimics the structures of natural products, are emerging for drug discovery (Schreiber, 2000).

A few years ago, it was thought that combinatorial chemistry and high-throughput screening (HTS) would yield many new hits and leads, but the result has been disappointing, despite the extraordinary amount of money spent (Ausman, 2001; Horrobin, 2001). After it was developed in the early 1990s, HTS methods achieved speed and miniaturization but discovery of new leads did not accelerate. HTS methods allowed 100,000 chemicals to be assayed per day, and combinatorial and other chemical libraries of 1 million compounds were available commercially. Despite this, no drugs had been approved that resulted from HTS by 1999 (Fox, 1999). The advent of combinatorial chemistry, HTS, genomics, and proteomics has "not yet delivered the promised benefits" (Ernst, 2000). Investment in genomics and HTS has had no effect on the number of products in preclinical development or phase I clinical trials. The problems are that HTS has not been applied to natural product libraries, and combinatorial chemistry has not been applied to natural product scaffolds (Demain, 2002; Kingston *et al.*, 2002; Waldmann *et al.*, 2002). Natural product collections have a much higher hit rate in high-throughput screens than do combinational libraries (Breinbauer1 *et al.*, 2002; Breinbauer 2 et al. 2002) pointed out that the numbers of compounds in a chemical library are not the important point; it is the biological relevance, design, and diversity of the library, and that a scaffold from nature provides viable, biologically validated starting points for the design of chemical libraries. In the past few years, some companies have dropped the screening of their natural product libraries because they considered that such extracts were not amenable to HTS (Fox, 1999). Even worse, we hear that combinatorial chemistry is replacing natural product efforts for discovery of new drugs, and that most companies have even dropped their natural product programs to

support combinatorial chemistry efforts. This makes no sense, since the role of combinatorial chemistry, like those of structure–function drug design and recombinant DNA technology two and three decades ago, is that of complementing and assisting natural product discovery and development, not replacing them (Paululat *et al.*, 1999). Instead of downgrading natural product screening, there is real opportunity in combining it with HTS, combinatorial chemistry, genomics, proteomics, and new discoveries being made in biodiversity.

Although the performance of the pharmaceutical industry has been dismal recently because of poor decisions, the biotechnology industry is doing very well. Between 1997 and 2002, 40% of the drugs introduced came from biotechnology companies. The five largest pharmaceutical companies have in-licensed from 6 to 10 products from biotechnology or specialty pharmaceutical companies, yielding 28–80% of their revenue. The biotechnology industry had two drug/vaccine approvals in 1982, none in 1983–1984, one in 1985, rising to 32 in 2000! The number of patents granted to biotechnology companies rose from 1500 in 1985 to 9000 in 1999. Some biotechnology companies are entering the area of natural product screening and, in the end, may save this valuable resource from falling into obscurity (Arnold *et al.*, 2005).

1.7 Ethnomedicinals from the Eastern Himalayan region of India

In the North East India, each state contains a number of tribal groups. Sikkim is a state of N.E. India, which is the highest number of orchid species known from any single state of India. Such a rich biodiversity in the state has provided an initial advantage to its inhabitants for observing, and scrutinizing the rich flora and fauna for developing their own traditional knowledge. Most of the tribe economies have been historically engaged in subsistence agriculture or hunting and gathering. Over the years, they have developed a great deal of knowledge on the use of plants and plant products in curing various ailments. A review of the literature reveals that many tribal areas and tribal communities in the eastern Himalayan region of India are either under explored or unexplored with regard to their floral wealth used in curing diseases (Bhanumathi *et al*, 2000). Therefore, a need was felt to gather in-depth information on the plant species used by this tribal group and suggest that similar studies need to be carried out across the various groups of tribes for comparison as well as for documenting the knowledge which may be under threat due to the influence of modernization (Kala, 2005). The present study thus aims to highlight and record in detail the traditional knowledge of the local tribes on the use of medicinal plant species growing in and around their settlements.

1.7.1 Medicinal plants survey

A literature survey was carried out for compilation of existing information on the medicinal plants used by Majhitar villagers were undertaken during May and June 2005 to gather data on the indigenous uses of medicinal plant species. During the survey period, information was also gathered using semi-structured questionnaires on types of ailments cured by the traditional use of medicinal plants and plant parts used in curing different ailments. Cross-checking of data was made with the help of group discussions among different age classes. The data obtained is almost same as the earlier worker of this region (Kala, 2005) (**Table 1.6**).

1.8 Alternative medicine

Some of the alternative methods provide help by strengthening the body and controlling the side effects of conventional treatments. Other approaches, because of their gentle noninvasive nature, may in some cases be preferred over more orthodox treatments offered by modern medicine.

Alternative medicine is usually holistic in approach. Holistic means that the goal is to treat the whole body, rather than just the affected area. Many also aim to treat the individual on a number of different levels, including physical, mental, spiritual and emotional. Some scientist's reject the above classification and to varying degrees reject the term "alternative medicine" itself.

The following three commentators argue for classifying treatments based on the objectively verifiable criteria of the scientific method, not based on the changing curricula of various medical schools or social sphere of usage. They advocate a classification based on Evidence-based medicine, i.e., scientifically proven evidence of efficacy (or lack thereof). According to them it is possible for a method to change categories (proven vs. nonproven) in either direction, based on increased knowledge of its effectiveness or lack thereof:

George D. Lundberg, former editor of the Journal of the American Medical Association (JAMA), and Phil B. Fontanarosa, Senior Editor of JAMA, state: 'There is no alternative medicine. There is only scientifically proven, evidence-based medicine supported by solid data or unproven medicine, for which scientific evidence is lacking'.

Whether a therapeutic practice is 'Eastern' or 'Western,' is unconventional or mainstream, or involves mind-body techniques or molecular genetics is largely irrelevant except for historical purposes and cultural interest. As believers in science and evidence, we must focus on

fundamental issues-namely, the patient, the target disease or condition, the proposed or practiced treatment, and the need for convincing data on safety and therapeutic efficacy".

Richard Dawkins, Professor of the Public Understanding of Science at Oxford, defines alternative medicine as a"...set of practices which cannot be tested, refuse to be tested, or consistently fail tests. If a healing technique is demonstrated to have curative properties in properly controlled double-blind trials, it ceases to be alternative. It simply becomes medicine." He also states that "There is no alternative medicine. There is only medicine that works and medicine that doesn't work."

Other well-known proponents of evidence-based medicine, such as the Cochrane Collaboration and Edzard Ernst, Professor of Complementary Medicine at the University of Exeter, use the term "alternative medicine" but agree with the above commentators that all treatments, whether "mainstream" or "alternative", ought to be held to standards of the scientific method. Oxford University Press publishes a peer-reviewed journal entitled Evidence-based Complementary and Alternative Medicine (eCAM).

1.8.1 Alternative Medicine vs conventional Medicine

Alternative therapies provide some services not available from conventional medicine. Examples are patient empowerment and treatment methods that follow the biopsychosocial model of health.

Advocates of alternative medicine hold that the various alternative treatment methods are effective in treating a wide range of major and minor medical conditions, and contend that recently published research proves the effectiveness of specific alternative treatments. They assert that a PubMed search revealed over 370,000 research papers classified as alternative medicine published in Medline-recognized journals since 1966 in the National Library of Medicine database. Advocates of alternative medicine hold that alternative medicine may provide health benefits through patient empowerment, by offering more choices to the public, including treatments that are simply not available in conventional medicine: "Most Americans who consult alternative providers would probably jump at the chance to consult a physician who is well trained in scientifically based medicine and who is also open-minded and knowledgeable about the body's innate mechanisms of healing, the role of lifestyle factors in influencing health, and the appropriate uses of dietary supplements, herbs, and other forms of treatment, from osteopathic manipulation to Chinese and Ayurvedic medicine. In other words, they want competent help in navigating the confusing maze of therapeutic options that are

available today, especially in those cases in which conventional approaches are relatively ineffective or harmful."

Evidence-based medicine (EBM) applies the scientific method to medical practice, and aims for the ideal that healthcare professionals should make "conscientious, explicit, and judicious use of current best evidence" in their everyday practice. Prof. Edzard Ernst is a notable proponent of applying EBM to CAM.

Although advocates of alternative medicine acknowledge that the placebo effect may play a role in the benefits that some receive from alternative therapies, they point out that this does not diminish their validity. Researchers who judge treatments using the scientific method are concerned by this viewpoint, since it fails to address the possible inefficacy of alternative treatments.

Complementary and alternative medicine (CAM), as defined by the National Center for Complementary and Alternative Medicine (NCCAM), is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine. Complementary medicine is used together with conventional medicine. Alternative medicine is used in place of conventional medicine.

The results of studies of CAM use have been inconsistent. One large-scale study published in the November 11, 1998, issue of the Journal of the American Medical Association found that CAM use among the general public increased from 33.8 percent in 1990 to 42.1 percent in 1997. However, an analysis of data from the 1999 National Health Interview Survey indicated that only 28.9 percent of U.S. adults (age 18 and over) had used at least one CAM therapy in the past year. These results were published in the journal Medical Care in 2002.

Several surveys of CAM use by cancer patients have been conducted with small numbers of patients. One study published in the February 2000 issue of the journal Cancer reported that 37 percent of 46 patients with prostate cancer used one or more CAM therapies as part of their cancer treatment. These therapies included herbal remedies, vitamins, and special diets.

A larger study of CAM use in patients with different types of cancer was published in the July 2000 issue of the Journal of Clinical Oncology. This study found that 69 percent of 453 cancer patients had used at least one CAM therapy as part of their cancer treatment. Additional information about CAM use among cancer patients can be found in a review article published in Seminars in Oncology in December 2002.

It is important that the same rigorous scientific evaluation used to assess conventional approaches be used to evaluate CAM therapies. The National Cancer Institute (NCI) and NCCAM are funding a number of clinical trials (research studies) at medical centers to evaluate CAM therapies for cancer.

Conventional approaches to cancer treatment have generally been studied for safety and effectiveness through a rigorous scientific process that includes clinical trials with large numbers of patients. Less is known about the safety and effectiveness of complementary and alternative methods. Some CAM therapies have undergone rigorous evaluation. A small number of CAM therapies originally considered to be purely alternative approaches are finding a place in cancer treatment—not as cures, but as complementary therapies that may help patients feel better and recover faster. One example is acupuncture. According to a panel of experts at a National Institutes of Health (NIH) Consensus Conference in November 1997, acupuncture has been found to be effective in the management of chemotherapy-associated nausea and vomiting and in controlling pain associated with surgery. In contrast, some approaches, such as the use of laetrile, have been studied and found ineffective or potentially harmful.

1.8.2 Use of Complimentary and Alternative Medicine worldwide

The Canadian Complementary Medical Association is a network of Canadian physicians, osteopaths, residents and medical students with a special interest or expertise in complementary medicine. It was founded at a meeting in Banff, AB in 1996 to promote the best in both unconventional and orthodox therapeutics in medical practice. Membership in the association is limited to those holding a recognized medical degree (M.D., D.O., or equivalent), or to retirees and students in these fields. CAMline is an evidence-based website on complementary and alternative medicine (CAM) for healthcare professionals and the public, with a Canadian perspective. It is funded by the Change Foundation of the OHA (Ontario Hospital Association) and the Richard Ivey Foundation, both of which are based in Toronto. It offers access to evidence-based information on natural health products, CAM therapies and practitioners and health conditions; at the moment (May 2002), there is not a lot of information available under some of the headings. It is to be hoped that the development of this site occurs rapidly because there is a great need for the kind of information promised by this site. The founders (5 partner institutions) and expert advisors are all listed; their credentials indicate that they are drawn mainly from the various disciplines of allopathic, traditional medicine and medical practice

In 1999, a document outlining the situation with respect to complementary and alternative health practices in Canada and their relationship to Canadian health system policies and

practices was prepared for Health Canada by the York University Centre for Health Studies in Toronto. The panel of distinguished authors/consultants includes faculty from universities in several provinces. Although the specific details may no longer be absolutely current, the document contains a wealth of information about CAM in Canada and is made available here for that reason.

The Complementary Medical Association is a British organization whose primary aim is to promote ethical, responsible, professional complementary medicine to the public and the medical profession. The public will find useful the five windows offering access to information about: Therapies, Remedies, Supplements, Conditions, and Drug-Herb Interactions.

1.8.3 Alternative Medicine Practice and Internet

The Internet Health Library offers a large collection of information about a great variety of alternative therapies and health problems; there is information about diet and lifestyle, environmental health, women's health, and so on, from the point of view of the complementary and alternative health practitioner. There is a collection of health news, updated regularly, and access to information also about professional organizations of practitioners and training in the various disciplines of CAM.

The Alternative Medicine Foundation is a U.S. charitable organization which is formed to provide evidence-based resources for health care professionals and reliable information on alternatives to conventional western biomedicine for patients and consumers. The programmes it has set up to deliver this information seem a bit thin at the moment. There is: Herb-Med, described as an "interactive, evidence-based herbal formulary", and **TibetMed,** a website devoted to Tibetan medicine. The herbal formulary has potential, but no text; under standard headings for each herb, the information seeker is directed to lists of references which are not summarized; they are merely cited. In some cases, an abstract of the article cited may be available from **PubMed,** but this is not always so. The foundation is the home of the Journal of Alternative and Complementary Medicine, but none of this material appears to be available via the website. The curious are directed to online subscription information at the site of the publisher Mary Ann Liebert, Inc. Alternative Health News Online is prepared by journalists for the public and aims at helping us to separate the hogwash from the promising therapies in alternative medicine. It is updated daily and covers topics such as diet and nutrition, mind/body control, alternative medical systems, manual healing and longevity. It offers a free, weekly e-mail newsletter, bulletins and alerts on health news and a column of reviewed and recommended books on alternative health care. It also offers links to other sources of health

information on the Internet. This is a great place to begin -- and to come back to -- when searching for alternative health information on the Internet.

The Alchemical Medicine Research and Teaching Association (AMRTA) maintained a complex and very helpful web site on alternative health care which used to be called: Natural Medicine, Complementary Health Care and Alternative Therapies, but has now become: healthwwweb: The Science of Nature. Their stated goal is to reunite the art of healing with the science of medicine. This site offers access to information regarding organizations in the field of alternative health care, training for practice, Internet resources of many kinds, mailing lists, professional journals and computer support for practice of alternative therapies.

The Health World Online Village, although not entirely composed of references to alternative and complementary therapies, has such a wide range and so many good explanations of unconventional therapies presented cheek-by-jowl with standard allopathic treatments and topics that it has to be presented here so that you won't miss it. Resources for consumers and health care professionals in the whole panorama of health care interests are available here: from acupuncture, through aromatherapy and flower medicine, to spas and retreats where you can rest and relax in a health-enhancing way. This is a site not-to-be-missed!

The Health Action Network Society, also known as HANS, of Burnaby, BC, is a non-profit society accepting individual memberships. Their website offers lots of information regarding alternative therapies and practitioners in Canada.

The Holistic Healing Web Page offers a great variety of web resources in alternative health care in a number of classes. The site can be used to present ideas about therapy that can be discussed with an individual's health care provider and is a great collection of diverse ideas and sources.

The Healing Spectrum offers access to resources that support healing from many different points of view. Both Alternative and Allopathic Medicine are profiled on this site, as well as other disciplines that can be used to promote healing. Creator Dianne Marcotte has pulled together a large range of Internet information sources to explain disease and to promote interest in a variety of routes to wellness.

The National Center for Complementary and Alternative Medicine, part of the U.S. National Institutes of Health, identifies and evaluates unconventional health care practices. The NCCAM supports and conducts research and research training on these practices and disseminates information. Their web site offers an overview of the six broad categories of alternative medicine: diet-nutrition-lifestyle changes, mind-body interventions, bioelectromagnetic

applications, alternative systems of medical practice, manual healing, pharmacological and biological treatments, and herbal medicine. There is a FAQ which explains Complementary and Alternative Medicine and the involvement of the National Center with alternative therapy.

The Research Council for Complementary Medicine (RCCM) is a British charity which carries out, promotes and evaluates rigorous research in complementary medicine to encourage safe, effective practice and improved patient care. The RCCM exists not just to educate, to inform or to research but primarily to ensure that the patients are offered treatments that have been show to be effective, treatment that is safe. It is the well-being of patients that is ultimately at stake. The RCCM believes that: research of the highest scientific rigour, supported by reliable information, is essential if complementary options of healthcare are to be made more widely available. The RCCM maintains a database -- the Centralised Information Service for Complementary Medicine (CISCOM) -- of over 60,000 references to the literature of complementary medicine which can be searched for you by contacting them; there is a charge for the service. A small collection of citations to randomised trials in various areas of complementary medicine is available on the website. The RCCM is also involved in creating and maintaining a registry and archive of randomised trials in complementary medicine for the Cochrane Collaboration Field in Complementary Medicine. This work is supported by the U.S. NCCAM, through the University of Maryland. The RCCM is active in medical education in the U.K., as well.

The famous Dr. Andrew Weil, author of the currently popular: 8 Weeks to Optimum Health and many other books and articles now answers your questions at his own web site, called: Ask Dr. Weil. Dr. Andrew Weil is a leader in the integration of Western medicine and the exploding field of alternative medicine.

Wellways.com is a large new collection of links to alternative healthcare resources on the web and to articles of topical interest. The Center for Alternative Medicine Research at Beth Israel Deaconess Medical Center (Harvard Medical School) has a website which offers some access to research and some information for the general public The Milbank Memorial Fund, an endowed national foundation that supports nonpartisan analysis, study, research and communication on significant issues in health policy, has recently published: Enhancing the Accountability of Alternative Medicine on the WWW. This study deals with the use of CAM (Complementary and Alternative Medicine) in the U.S. today, cost and reimbursement issues, and evaluation of the various therapies offered

NOAH: New York Online Access to Health offers a large collection of information on many topics in health and healthcare. One of these collections focuses on alternative medicine. Called

Complementary and Alternative Medicine, this collection offers access to a wide range of topics in the alternative healthcare arena. The collection draws heavily on other sources, but organizes its material in a useful fashion.

The Holistic Channel advertises itself as a source of alternative healthcare news from around the world, but it is also much more than a news source. In addition to news, it offers live radio on natural healthcare, "healing" music and live (but not free) consultations with various sorts of healthcare practitioners. I am not able to find any evidence of the availability of information in non-English languages, nor of the large database of scientifically-validated information, both of which are advertised. There is a lot of marketing of a whole variety of health-related (and not-so-closely-related) stuff going on at this site from a selection of links to online health stores. There is even a section for "deals", but, as always, it is up to you to decide whether the "deal" is real!

AlternativeDr.com offers information about a wide array of alternative medicine resources on the Internet. One can find information about alternative therapies (acupuncture, energy medicine, naturopathy, among others) that are commonly included on sites that deal with complementary and alternative medicine (CAM), and on others (beauty and spa, midwifery, pet therapy) that are not so commonly encountered on CAM sites. There is a discussion board, information about how the drugs are taken and possible interactions with the dietary supplements (herbs, minerals, and vitamins), special reports on CAM topics, and a directory of practitioners (mainly U.S.) One may want to consult. Consumers can access suppliers of alternative therapy supplies in the 'storefront', and exploring the site will uncover many features not mentioned here.

International Health News is a service based in Victoria, BC, which scans 50 respected medical and scientific journals every month and summarizes important medical, health and nutrition news. Our focus is on complementary and preventive medicine, specifically in regard to diet, supplements, vitamins, exercise and lifestyle. We also report on the latest in the fight against arthritis, cancer, heart disease and other degenerative conditions and keep a sharp eye out for warnings about medical procedures and side effects of pharmaceutical drugs. The full database and monthly updates are available only to subscribers, but a collection of essays on various topics, with extensive references to the latest published research, is available free of charge. Some of the essay topics are: Parkinson's disease, breast cancer prevention, prostate cancer prevention, vitamin B_{12}, and fish oils. There are also free excerpts from the database on various topics and sample issues of the monthly newsletter. This site is a real find for those interested in the progress of research into CAM topics.

The Consumer Health Organization of Canada is committed to making people aware of the "holistic" or "alternative" approach to health. They emphasize the prevention of disease through nutrition, whole foods, dietary supplements, herbs and other healing modalities. The organization believes in the philosophy that society benefits from healthy individuals. They work to prevent disease by sharing knowledge and aim to reduce health care costs by avoiding illness. Their website offers access to articles on topics of interest and directs readers to other websites in related areas

The PULSE of Oriental Medicine deals with alternative and traditional oriental medicine resource for the public. It aims to offer information about oriental medicine in easily understood language. EnerChihealth.com is the name of a web site which offers a wealth of information about complementary and alternative medicine in the Canadian context. Holly Gerrish, B. N. (from BC, now living in Alberta) is the founder of Enerchi Health Inc., a company dedicated to presenting objective, research based information on complementary and alternative health practices. On this site, one can find information about medical conditions, and complementary and alternative therapies. There are links to books, articles, related web sites, professional associations and training centers for each therapy. Drug/herb interactions, vitamins, nutritional information and recipes for special diets are available in the site. There is a FAQ which explains many of the terms involved and lots of information about questions to ask a practitioner before engaging her services. There is also a Calendar of Events which is currently blank, but offers to list complementary and alternative medicine events across the country. It is to be hoped that these features are developed soon because they look to be very helpful. The Continuum Center for Health and Healing, an initiative of Beth Israel Medical Center in New York city offers an expanded, integrative practice of health care, and a wonderful web site for anyone seeking information on alternative therapies. One don't have to travel to NYC to use their extensive collection of information; no attempt to be exhaustive is made. Instead, in the Health conditions in A-Z section, research and review articles were selected with a view to providing reliable information from scientific studies showing the complementary/alternative therapeutic approaches that have been studied for each health condition and the significant results to date. There are also collections of information available (and others are being developed) on Complementary/Alternative Therapies, and Traditional and Indigenous Healing Systems. Each entry in these sections follows a pattern which offers information such as history and philosophy of the practice, treatment approaches, and training and licensing of practitioners, among other things. There is an extensive section on professional education for the various alternative disciplines, with links to web sites and recommended resources. This is a thoroughly useful web site; it bears a lot of exploring to plumb its depths.

The Integrative Medicine Institute is a clinic in Calgary, AB, providing a combination of approaches to health care. Practitioners at the clinic bring the best of conventional western medicine and alternative therapies to the partnerships they form with their patients. The site offers information about the beliefs the practitioners have about healing and the services they offer. In addition to a family physician and a psychiatrist, the clinic staff includes naturopathic doctors, a dentist, a nurse, a physiotherapist, a registered holistic nutritionist, and others qualified in Chinese medicine and acupuncture, flower essence therapy, massage and a host of other alternative therapies. There is a list of courses offered at the clinic and information about the therapies used in the care of patients.

The Integrative Health Institute, also located in Calgary, integrates conventional, complementary and alternative health care practices to educate people and corporations interested in improving their personal health. They offer education and research services to support their goal. A site called: Herbal Healing, seems badly titled at first glance. While the site has a lot of information about ayurvedic herbs and herbal healing, it also has extensive space devoted to many other alternative modalities: reiki, yoga, religious healing (from a variety of faiths), tai chi, acupuncture, and more. There is no information about the compilers of this information or about who is responsible for it on the site, which always tends to make one cautious about any advice offered, but there is a lot of variety here not found elsewhere. Explore this site with the awareness that whoever has put this interesting site together does not, apparently, stand behind the information they offer.

Herbal medicines are the oldest remedies known to mankind. Herbs had been used by all cultures throughout history but India has one of the oldest, richest and most diverse cultural living traditions associated with the use of medicinal plants. In the present scenario, the demand for herbal products is growing exponentially throughout the world and major pharmaceutical companies are currently conducting extensive research on plant materials for their potential medicinal value. In many journals, national and international, we find an increasing number of research publications based on herbal drugs. Many analysis-based studies regarding pharmacological research in India have been conducted in the past. Out of these, one study has shown an upward trend in indigenous drug research but there are only few studies on the exclusive analysis of herbal drug research in India. Therefore, the present study was undertaken to analyze the recent trends of herbal drug research in India keeping the Indian Journal of Pharmacology as a marker. The issues of the Indian Journal of Pharmacology from 1995 to August 2003 were reviewed manually in the central library of Govt. Medical College, Jammu, and the Herbal Drug Research Trend Index (HDRTI) was worked out for presentations at IPS conferences as well as for paper publications in the Indian Journal of Pharmacology. Abstracts of the annual IPS conferences and articles (full communications/short

communications/letters/correspondence) published in the Indian Journal of Pharmacology were reviewed in the present study. HDRTI was worked out as a three-year average percentile of herbal drug research for both the parameters respectively. or this, yearly data were collected first and then a three-year average percentage of herbal drug research for the parameters was calculated for the years (1995-1997), (1998-2000) and (2001 to August 2003) by dividing the total percentage for three-year herbal drug research by number of years. Herbal medicines form a major part of remedies in traditional medical systems such as Ayurveda, Rasa Sidha, Unani, and Naturopathy. Hence, all animal and clinical studies on herbal medicines were reviewed. The data for the years 1981-1983 were taken as baseline for the comparison of recent herbal drug research trends.

1.9 Herbal drug research in India

The present study showed that interest has increased in herbal drug research in India, which supported the findings of Adithan (1996), its maximum utilization of the phytotherapeutic approach wherein crude plant preparations were used. The maximum work was observed with polyherbal preparations. To use herbal products, adequate precautions should be exercised. Herbal medicines are the oldest remedies known to mankind. Herbs had been used by all cultures throughout history but India has one of the oldest, richest and most diverse cultural living traditions associated with the use of medicinal plants (Bhatt, 1999).

Ashwagandha (*Withania somnifera*) is often described as the Indian equivalent of ginseng — the Chinese medicinal plant that has captured a huge chunk of the global market. Yet the Indian herb is not a commercial success. One of the reasons for this is the lack of standards, which has led to a wide variation in the chemical composition of ashwagandha-based drugs. The discrepancy, detected during a recent study, occurs in herbal products of even reputable companies.

These drugs are portrayed as potent healers with a wide range of benefits like improving memory, cognition, stamina, vigour and resistance to diseases, as well as relieving tension and depression. But experts feel that in view of the latest findings, a huge question mark hangs on the efficacy of these medicines.

The study was published in the February 2004 issue of Current Science, a journal brought out by the Indian Institute of Science, Bangalore. Entitled 'Phytochemical variability in commercial herbal products and preparations of *Withania somnifera*, it was conducted by three institutes of the Council of Scientific and Industrial Research (CSIR), the Central Institute of Medicinal and

Aromatic Plants (CIMAP) and National Botanical Research Institute, both in Lucknow, and the Regional Research Laboratory in Jammu.

During the study, the amount of withaferin A — one of the withanolides of ashwagandha was analysed in 10 products being sold in the market (**Table 1.5**). Withanolides are secondary chemicals produced by the plant. The scientists assumed withaferin a to be an indicator of the presence of ashwagandha. They found that the amount of the chemical per gramme of ashwagandha varied from 100 per cent to merely 0.9 per cent. In nine of the products, the quantity was less than 50 per cent.

The research highlights these inconsistencies to underscore the importance of standardizing herbal products. It also points out that the anomaly can only be corrected through stringent legislation, which doesn't exist in the country at present. Several factors like sources of raw materials, harvest and post-harvest conditions, and processing and manufacturing techniques have to be regulated for controlling the quality of herbal products. But the Drugs and Cosmetics Act, 1940, which governs the herbal medicine industry, only lays emphasis on making drugs in clean factories and testing raw materials for genuineness. G S Lavekar, director, Central Council for Research in Ayurveda and Siddha, under the Union ministry of Health and Family Welfare, says: "Parameters such as chemical and biological markers should be set so that an acceptable range can be established for chemical constituents."

R S Sangwan of CIMAP, a member of the study team, suggests that ashwagandha should be marketed as a single plant product and not a traditional medicine where a combination of plants is used. While modern scientists are in favour of identifying active ingredients in herbal products and using them as medicines, conventional practitioners believe that such isolates cease to be traditional medicines.

The report has evoked a mixed response from the industry. Some companies are of the opinion that the laws should be strengthened. At the same time, there are others who claim their products are up to the mark. Paranjay Sharma, president of Shree Baidyanath Ayurved Bhawan Private Limited, says a manufacturer can only be penalized if are not exist. He feels quality control should be introduced in the production process at the raw material stage itself. Significantly, the good manufacturing practices that are stipulated currently do not deal with this aspect.

S K Mitra of Himalaya Drug Company says his company uses chemical indicators to ensure that even products in different batches conform to a uniform standard. Further, it conducts trials on humans to ensure the efficacy of the drugs. A senior representative of another manufacturer

implicated in the study asserts: "The researchers did not find the withanolide because it could have been masked by other chemicals present in the product." Sharad Goel, spokesperson for Dabur, says: "We believe that the researchers should have estimated total withanolides, which is a widely accepted biological benchmark, for the purpose of comparing different products available in the market" (Anonymous, 2004).

Table 1.5 Ten herbal products that were subjected to scan test

(Anonymous, 2004)

Brand name	Manufacturer
Ashwagandharista	Baidyanath Ayurved Bhawan
Himalaya Ashwagandha	Himalaya Drug Company
Stresswin	Baidyanath Ayurved Bhawan
Stresscom	Dabur India Ltd
Himalaya massage oil	Himalaya Drug Company
Lovemax	BACFO Pharma Ltd
Vigomax	Charak Pharma Ltd
Vital Plus	Mukthi Pharma
Amrutha Kasthuri	Pankajakasthuri Herbals India Ltd
Brento	Zandu Pharmaceutical Works Ltd

1.10 Herbal technology – Concepts and scope

Herbal technology circumscribes all the advancing technical frontiers (except genes) meant to tap myriads of modes of manipulating plants around us. A large number of technologies have been developed to harvest the bountiful products that the plants manufacture, including natural dyes, biofertilizers, biopesticides and biofuel. Emphasis to be given on new medicinal plants (from ethnobotanical surveys), new uses of known medicinal plants, active components and biomarkers, viable substitutes and methods of cultivation, storage, extraction, formulations, efficacy and quality control. In India, it is reported that, more than 150 plants used as biopesticides (bacteria, fungi, virus and protozoa), sources of liquid resins (*Copaifera longdorfii*, *Hardwickia pinnata* and *Dipterocarpus turbinatus*) which can be used as biodiesel, petrocrops, sources of ethanol and a large number of plants yielding non-edible oils as well as production of biodiesel by methylating the oils and medicinal natural dyes.

In the last few decades there has been an exponential growth in the field of herbal medicine (Adhithan, 1996). It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. In olden times, **vaidyas** used to treat patients on individual basis, and prepare drug according to the requirement of the patient. But the scene has changed now; herbal medicines are being manufactured on a large scale in mechanical

units, where manufacturers come across many problems such as availability of good quality raw material, authentication of raw material, availability of standards, proper standardization methodology of single drugs and formulations, quality control parameters, etc. Ambiguity of our own system of medicine – the Ayurveda, is reflected in the interpretation of names and description of drugs given in the books like Charaka Samhita and Sushruta Samhita, etc. Due to lack of scientific names in the original texts, under one name, different plants are known in different parts of the country as per the description, which makes the drug controversial, e.g. Jivanti, Brahmi (Harish, 2001). These controversies should be eliminated (Tandon *et al.*, 2006).

In the present scenario, the demand for herbal products is growing exponentially throughout the world and major pharmaceutical companies are currently conducting extensive research on plant materials for their potential medicinal value in India and many research articles regarding analysis based studies are published (Dandiya, 1974; Adhithan, 1996 and Singh, 2000).

There is an increased interest on herbal drug research in India (Adithan, 1996) with maximum utilization of the phytotherapeutic approach wherein crude plant preparations were used, mostly with polyherbal preparations. This inclination may be due to: Firstly, people all over the world is looking to various alternative systems of medicine, especially herbal drugs which are claimed to be safe, equally effective in comparison to allopathic drugs and which provide some answer to chronic diseases. Secondly, either these herbal drugs are marketed with exaggerated claims or in some cases are credited with innumerable pharmacological activities which are not mentioned in the text of various traditional systems of medicine. And lastly, as compared to the modern medicines, herbal medicines have a strong traditional or conceptual base and the potential to be useful as drugs in terms of safety and effectiveness but they lack an experimental base. In conclusion, it can be said that there is upward trend of herbal drug research in India recently.

Table 1.6 Medicinal plant species, parts used to treat ailments by tribal people (Kala, 2005) .

Sl No.	Species	Family	Part used	Uses
1	*Acorus calamus* L.	Araceae	Root	Cut, wounds, skin diseases, bone fracture
2	*Ageratum conyzoides* L.	Asteraceae	Leaf	Cut, wounds
3	*Allium cepa* L.	Liliaceae	Bulb	Eye pain
4	*Allium hookeri Thwait.*	Liliaceae	Bulb	Eruption of skin, cough, cold, wounds
5	*Alocasia forniculata (Roxb.) Schott.*	Araceae	Root	Crack of heels
6	*Alstonia scholaris* (L.) Br.	Apocynaceae	Leaf, bark	Headache, stomach disorder, menstrual disorder
7	*Amomum aromaticum* Roxb.	Zingiberaceae	Leaf, seed	Fever, abortion
8	*Amorphophallus paeoniifolius* (Dennst.) Nicolson	Araceae	Corn	Piles
9	*Andrographis paniculata* (Burm. f.) *Wall. ex Nees*	Acanthaceae	Leaf	Dysentery
10	*Anisomeles indica* (L.)	Lamiaceae	Shoot	Bodyache
11	*Angiopteris evecta* (Forst.) Hoffm.	Angiopteridaceae	Stem	Health tonic
12	*Antidesma acidum* Retz.	Euphorbiaceae	Leaf	Wounds
13	*Argemone mexicana* L.	Papaveraceae	Shoot	Skin diseases
14	*Artemisia indica* Willd.	Asteraceae	Leaf	Bodyache, asthma, skin diseases
15	*Artemisia maritima* L.	Asteraceae	Shoot	Blood purification
16	*Artemisia nilagirica* (Cl.) Pamp.	Asteraceae	Leaf	Cough, headache, sores
17	*Asplenium nidus* L.	Aspleniaceae	Leaf	Ulcer
18	*Barleria prionitis* L.	Acanthaceae	Leaf	Cough
19	*Begonia roxburghii* (Miq.) DC.	Begoniaceae	Leaf	Indigestion
20	*Berberis wallichiana* (Wall.) Brongn.	Berberidaceae	Fruit, root	Indigestion, bodyache
21	*Bergenia ciliata* (Haw.) Sternb.	Saxifragaceae	Root, leaf	Cut, wounds
22	*Brassiopsis glomarulata* (Bl.) Regel.	Araliaceae	Fruit	Cough
23	*Buddleja asiatica* Lour.	Buddlejaceae	Leaf	Inflammation
24	*Callicarpa macrophylla* Vahl	Verbenaceae	Leaf	Headache
25	*Callicarpa vastita* Roxb.	Verbenaceae	Leaf	Indigestion
26	*Calotropis gigantea* (L.) Br.	Asclepiadaceae	Root	Dog bite
27	*Canarium resiniferum* Brace ex King	Burseraceae	Fruit	Urinary complaints
28	*Capparis spinosa* Lam.	Capparaceae	Root	Rheumatic pain
29	*Cardamine hirsuta* L.	Brassicaceae	Leaf	Indigestion

Contnued Table 1.6.

S No.	Species	Family	Part used	Uses
30	*Castanopsis tribuloides* DC.	Fagaceae	Stem	Cough, goiter, indigestion
31	*Centella asiatica* L.	Apiaceae	Shoot	Constipation, gastritis, blood purification
32	*Chenopodium ambrosioides* L.	Chenopodiaceae	Leaf	Toothache
33	*Christella parasitica* (L.) Lev.	Thelypteridaceae	Fronds	Cut, Wounds
34	*Chromolaena odorata* (L.) King & Robinson	Asteraceae	Leaf	Cut, wounds, headache, fever
35	*Cirsium lapskyle* Petral.	Asteraceae	Shoot	Indigestion
36	*Cissampelos pareira* L.	Menispermaceae	Tuber	Health tonic
37	*Clerodendrum glandulosum* Coleb. ex Wall.	Verbenaceae	Leaf	Blood pressure, fever, cough
38	*Clerodendrum serratum* (L.) Moonb	Verbenaceae	Leaf	Eye disorders
39	*Coelogyne pectata* Lindl.	Orchidaceae	Pseudobulb	Burns
40	*Colocasia affinis* Schott	Araceae	Leaf	Fever, respiratory disorder
41	*Crassocephalum crepidioides* (Benth.) Moore	Asteraceae	Leaf	Indigestion, headache, stomachache, cut, wounds
42	*Crotolaria pallida* Ait.	Fabaceae	Root	Bodyache
43	*Croton roxburghii* Balak	Euphorbiaceae	Fruit	Indigestion
44	*Curcuma caesia* Roxb.	Zingiberaceae	Rhizome	Cough, asthma
45	*Curcuma aromatica* Salisb.	Zingiberaceae	Whole plant	Blood purification
46	*Curcuma zedoaria* Rosc.	Zingiberaceae	Rhizome	Cold, cough
47	*Cuscuta reflexa* Roxb.	Cuscutaceae	Whole plant	Purgative
48	*Cyathea gigantea* (Wall. ex Hk. f.)	Cyatheaceae	Leaf	Bodyache
49	*Cyathula prostrata* (L.) Bl.	Amaranthaceae	Shoot	Appetizer, dysentery, skin diseases
50	*Cymbidium aloifolium* (L.) Sw.	Orchidaceae	Tuber	Wounds
51	*Dendrocnide sinuta* (Bl.) Chew.	Urticaceae	Leaf	Urogenital disorder, toothache, dysentery
52	*Dicranopteris linearis* (Burm. f.) Und.	Gleicheniaceae	Whole plant	Indigestion
53	*Dicrocephala bicolor* (Roth) Sch.	Asteraceae	Shoot	Digestive problems

Contnued Table 1.6.

S No.	Species	Family	Part used	Uses
54	*Dillenia indica* L.	Dilleniaceae	Furit	Stomachache
55	*Dioscorea alata* L.	Dioscoraceae	Tuber	Indigestion
56	*Dioscorea bulbifera* L.	Dioscoraceae	Tuber	Indigestion
57	*Dioscorea hamiltonii* (Hk. f.)	Dioscoraceae	Tuber	Dysentery
58	*Diplazium esculentum* (Retz.) Sw.	Athyriaceae	Fronds	Constipation
59	*Ecbolium viride* (Forsk) Alston	Meliaceae	Root	Rheumatism
60	*Eclipta prostrata* (L.) L.	Asteraceae	Shoot	Cut, wounds
61	*Elaeagnus caudata* Sch. ex Momiyama	Elaeagnaceae	Fruit	Health tonic
62	*Elaeagnus pyriformis* Hk. f.	Elaeagnaceae	Fruit	Constipation
63	*Elatostema platyphyllum* Wedd.	Urticaceae	Root	Vomiting
64	*Elsholzia blanda* (Benth.)	Lamiaceae	Leaf	Itching
65	*Eluesine coracana* (L.) Gaertn.	Poaceae	Grains	Stomach disorder, tonic, cold
66	*Eupatorium odoratum* L.	Asteraceae	Leaf	Wounds, cut
67	*Erigeron bonariensis* L.	Asteraceae	Leaf	Nose block
68	*Eryngium foetidum* L.	Apiaceae	Seed	Madness, headache
69	*Ficus benjamina* L.	Moraceae	Stem	Stomach disorder
70	*Ficus hirta* Vahl	Moraceae	Fruit	Wounds, cut
71	*Gerbera pilosellioides* (L.) Cass.	Asteraceae	Leaf	Rheumatic pain
72	*Gloriosa superba* L.	Liliaceae	Tuber	Killing lice in hairs
73	*Gmelina arborea* Roxb.	Verbenaceae	Leaf	Stomach disorders
74	*Gynostemma pedata* Bl.	Cucurbitaceae	Leaf	Throatache
75	*Gynura biscolor* (Roxb. ex Willd.) DC.	Asteraceae	Leaf	Intestinal worms
76	*Gynura nepalensis* DC.	Asteraceae	Leaf	Indigestion
77	*Hedychium coronarium* Koen.	Zingiberaceae	Rhizome	Bodyache
78	*Hedychium dekianum*	Zingiberaceae	Rhizome	Cut, wounds
79	*Hedychium spicatum* Buch.-Ham. ex Sm.	Zingiberaceae	Rhizome	Stomach disorder
80	*Hibiscus rosa-sinensis* L.	Malvaceae	Flower	Reproductive disorders

Contnued Table 1.6.

S No.	Species	Family	Part used	Uses
81	*Houttuynia cordata* Thunb.	Saururaceae	Shoot	Freshness, good sleep, heart disorders
82	*Hyptis suaveolens* (L.) Poit.	Lamiaceae	Leaf	Itching, cough, cold
83	*Hypericum japonicum* Thunb. ex Murr.	Hypericaceae	Stem	Cut, wounds
84	*Impatiens latifolia* L.	Balsaminaceae	Leaf	Headache, digestive disorder
85	*Impatiens racemosa* DC.	Balsaminaceae	Leaf	Digestive disorder
86	*Indigofera tinctoria* L.	Fabaceae	Root	Wound
87	*Jasminum humile* L.	Oleaceae	Root	Ringworm
88	*Laginaria siceraria* (Molina) Standl.	Cucurbitaceae	Fruit	Burns
89	*Leonotis nepetifolia* R. Br.	Lamiaceae	Seed	Burns
90	*Lithocarpus dealbatus* (Miq.) Rehder	Fagaceae	Fruit	Indigestion
100	*Mucuna pruriens* (L.) DC.	Lauraceae	Fruit	Cough, cold, hair tonic, indigestion, good sleep
101	*Murraya koenigii* (L.) Spr.	Lauraceae	Fruit	Bone fracture, stomach disorder
102	*Musa paradissica* L.	Musaceae	Fruit	Indigestion
103	*Myrica esculenta* Ham. ex D. Don.	Myricaceae	Fruit, bark	Indigestion, skin eruption
104	*Myrsine semiserrata* Wall.	Myrsinaceae	Seed	Skin diseases
105	*Oenanthe javanica* (Bl.) DC.	Apiaceae	Shoot	Indigestion
106	*Oroxylum indicum* (L.) Vent.	Bignoniaceae	Seed	Purgative, headache
107	*Osbeckia stellata* Buch.-Ham. ex D. Don	Melastomatac eae	Leaf	Toothache
108	*Oxalis corniculata* L.	Oxalidaceae	Shoot	Appetizer, headache
109	*Paedaria foetida* L	Rubiaceae	Stem	Gastritis, diarrhea, stomach disorder
110	*Passiflora foetida* L.	Passifloraceae	Fruit	Respiratory disorder
111	*Photinia integrifolia* Lindl.	Rosaceae	Fruit	Indigestion
112	*Perilla frutescens* (L.) Britt.	Lamiaceae	Seed	Fever, headache
113	*Physalis angulata* L.	Solanaceae	Fruit	Gastric trouble

Contnued Table 1.6.

Sl No.	Species	Family	Part used	Uses
114	*Physalis minima* L.	Solanaceae	Fruit	Gastric trouble
115	*Physalis peruviana* L.	Solanaceae	Leaf	Pain in pregnancy
116	*Picrorhiza kurrooa* Benth.	Scrophulariaceae	Root	Cold, fever
117	*Pinus roxburghii* Sarg.	Pinaceae	Seed	Indigestion
118	*Piper brachystachyum* Wall.	Piperaceae	Seed	Cough
119	*Piper trioicum* Roxb.	Piperaceae	Root	Cough
120	*Plantago major* L.	Plantaginaceae	Leaf	Constipation
121	*Plectranthus japonicus* (Burm. f.) Koidz.	Acanthaceae	Leaf	Fever
122	*Polygonum nepalense* Meissn.	Polygonaceae	Leaf	Indigestion
123	*Polygonum perfoliatum* L.	Polygonaceae	Leaf	Indigestion
124	*Portulaca oleracea* L.	Portulacaceae	Stem, Leaf	Appetizer
125	*Pouzolzia hirta* (Bl.) Hassk.	Urticaceae	Root	Constipation
126	*Pterospermum acerifolium* Willd.	Sterculiaceae	Flower	Earache
127	*Rhus chinensis* Miller	Anacardiaceae	Fruit	Blood dysentery
128	*Rubia cordifolia* L.	Rubiaceae	Shoot	Stomachache
129	*Rubus calycinus* Wall.	Rosaceae	Fruit	Stomach disorder
130	*Rubus ellipticus* Sm.	Rosaceae	Fruit	Indigestion
131	*Rubus paniculatus* Sm.	Rosaceae	Fruit	Stomach disorder
132	*Rubus roseafolius* Sm.	Rosaceae	Fruit	Indigestion
133	*Rumex nepalensis* Spr.	Polygonaceae	Leaf	Indigestion
134	*Saurauria roxburghii* Wall.	Saurauriaceae	Leaf	Constipation
135	*Schefflera glomerata* L.	Araliaceae	Fruit	Indigestion
136	*Schizostachium capitatum* (Munro) *Majumdar*	Poaceae	Shoot	Diarrhea, dysentery, stomach disorder
137	*Senna alata* (L.) Roxb.	Caesalpiniaceae	Leaf	Skin diseases

Contnued Table 1.6.

Sl No.	Species	Family	Part used	Uses
138	*Senna tora* (L.) Roxb.	Caesalpiniaceae	Leaf	Low blood pressure
139	*Sphenomeris chinensis* (L.) Maxon	Lindsaeceae	Fronds	Sprains
140	*Solanum kurzii* Brace ex Prain	Solanaceae	Fruit	Cough, worms infestation
141	*Solanum myriacanthum* Dunal	Solanaceae	Seeds	Toothache
142	*Solanum nigrum* L.	Solanaceae	Leaf	Liver tonic, indigestion
143	*Solanum torvum* Sm.	Solanaceae	Fruit	Cough, skin diseases
144	*Sonchus asper* (L.) Hill	Asteraceae	Shoot	Indigestion
145	*Sonchus arvensis* L.	Asteraceae	Shoot	Stomachache, gastritis
146	*Spilanthus clava* L.	Asteraceae	Leaf	Throat pain
147	*Spilanthes paniculata* DC.	Asteraceae	Leaf	Constipation
148	*Stellaria media* (L.) Vill.	Caryophyllaceae	Leaf	Itching
149	*Stereospermum chelonoides* (L. f.) DC.	Bignoniaceae	Leaf	Sprain
150	*Strobilanthus helictus* T. Anders	Acanthaceae	Shoot	Indigestion
151	*Terminalia chebula* Retz.	Combretaceae	Fruit	Cough
152	*Toddalia aculeata* Pers.	Rutaceae	Fruit	Throat pain
153	*Urtica dioica* L.	Urticaceae	Leaf	Bone fracture
154	*Vernonia cinerea* (L.) Less	Asteraceae	Leaf	Indigestion
155	*Zanthoxylum acanthopodium* DC.	Rutaceae	Fruit	Dysentery
156	*Zanthoxylum armatum* DC.	Rutaceae	Fruit	Cold, cough, fever, appetizer
157	*Zanthoxylum oxyphyllum* Edgew.	Rutaceae	Fruit	Stomach disorder
158	*Zingiber officinale* Rosc.	Zingiberaceae	Rhizome	Cough

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