Chapter-1

INTRODUCTION
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The 21st century has marked the beginning of a new era, receptive to eastern healthcare philosophy through positive attitudes (Cooper, 2008). Plants and animals have intimate biological relationships since remote past and have evolved along parallel lines cooperating and depending upon each other for existence. Medicinal plants have been in the focus as source of life saving drugs right from beginning of human civilization. Herbal plants possessing medicinal properties have been the object of research in both classical and advanced areas of biomedical sciences. In the present scenario, greater emphasis is being laid on the traditional knowledge of ethnic people in bioprospecting of biological resources as a new source of drugs, medicine, food and other industrial and pharmaceutical raw materials (Dixit et al., 2010).

Plants have been the basis of many traditional medicine systems throughout the world for thousands of years and continue to provide mankind with new remedies. Use of plants as a source of medicine has been inherited and is an important component of the health care system in India. In the Indian systems of medicine, most practitioners formulate and dispense their own recipes, hence this requires proper documentation and research. Approximately 80% of the world’s population has employed traditional medicine for health care, which is based predominantly on plant materials (Adewusi, 2010). In western world the use of herbal medicines is steadily growing with approximately 40% of population reporting use of herbs to treat medical illnesses (Bent and Ko, 2004). Public, academic and government interest in traditional medicines is growing exponentially due to the increased incidence of the adverse drug reactions and economic burden of the modern system of medicine (Dubey et al., 2004).

Natural products and particularly medicinal plants remain an important source of new drugs, new drug leads and new chemical entities (NCEs). According to Newman et al., 61% of the 877 small-molecule NCEs introduced as drugs worldwide during 1981–2002 was inspired by natural products. These included natural products (6%), natural products derivatives (27%), synthetic compounds with natural products-
derived pharmacophore (5%) and synthetic compounds designed from natural products (Newman et al., 2003).

Natural products have played a significant role in drug discovery and development especially for agents against cancer and infectious diseases. An analysis of new and approved drugs for cancer by the United States Food and Drug Administration over the period of 1981-2002 showed that 62% of these cancer drugs were of natural origin. The specific mechanisms of action of most phytochemicals in cancer prevention are not yet clear but appear to be varied. Considering the large number and variety of dietary phytochemicals, their interactive effects on cancer risk may be extremely difficult to assess (Heber, 2004). Phytochemicals can inhibit carcinogenesis by inhibiting phase I enzymes, and induction of phase II enzymes, scavenge DNA reactive agents, suppress the abnormal proliferation of early, preneoplastic lesions, and inhibit certain properties of the cancer cell (Waladkhani et al., 1998). Phytochemicals are utilized to a large extent by the pharmaceutical, cosmetics, food, agrochemical, and chemsurgical industries. Ethnomedicinal use of plant-derived natural products has been a major source for discovery of potential medicinal agents. Even in recent times, plants have been an important source of modern drugs like aspirin, ephedrine, digoxin, quinine and tubocurarine, to name only a few (Gilani and Rahman 2005). It has been reported that about 64% of the total global population remains dependent on traditional medicine and medicinal plants for provision of their health-care needs (Cotton, 1996).

In recent years traditional medicine has become of interest to both scientists and the general population for a number of reasons, which include high price of allopathic drugs beyond the reach of the poorer segments of society in almost every country, lack of access to medical clinics and hospitals by the rural population of developing countries, the side-effects and toxicities of modern synthetic drugs, and the realization that phytochemicals present in plants can be effective therapeutic agents by themselves or serve as effective adjunct therapies to modern drugs.

Oxidative stress has been implicated as a cause for many infectious diseases (Cholera, Diphtheria, AIDS/HIV, Leishmaniasis and Malaria) and non infectious diseases (heart disease, diabetes, autoimmune diseases, stroke and cancer) by increasing free radical load. Plants products containing antioxidant activity have shown curative effects.
Antioxidants in herbs may contribute at least part of their reputed therapeutic effects (Balsano and Alisi 2009; Tang and Halliwell 2010).

1.1. Global endorsement of herbal medicine

Ayurveda is one of the oldest extant health systems in the world with fundamental principles and theory-based practices. Ayurveda remains one of the most ancient and yet living traditional system of medicine practiced widely in India, Sri Lanka and other countries and has a sound philosophical and experiential basis (Chopra and Doiphode, 2002). Atharvaveda (around 1200 BC), Charak Samhita and Sushrut Samhita (1000-500 BC) are the main treatises that give detailed descriptions of over 700 herbs (Dahanukar and Thatte, 2000). Indian healthcare consists of medicinal pluralism and Ayurveda still remains dominant compared to modern medicine, particularly for treatment of a variety of chronic diseases (Chopra and Doiphode, 2002). Traditional Chinese medicine (TCM) is an important example of how ancient and accumulated knowledge is applied in a holistic approach in present day health care. TCM has a history of more than 3000 years (Xutian et al., 2009). The book "The Devine Farmer’s Classic of Herbalism" was compiled about 2000 years ago in China and is the oldest known herbal text in the world, though the accumulated and methodically collected information on herbs has been developed into various herbal pharmacopoeias and many monographs on individual herbs exist. TCM is a growing practice around the world and is used for promoting health as well as for preventing and curing diseases. Three of the top-selling botanical products, namely Ginkgo biloba, Allium sativum (garlic), and Panax ginseng, can be traced back to origins in TCM and are today used to treat various diseases (Li et al., 2008; Xutian et al., 2009).

1.2. Indian Medicinal Plant

There are about 45,000 plant species in India, with concentrated hotspots in the region of Eastern Himalayas, Western Ghats and Andaman & Nicobar Island. The officially documented plants with medicinal potential are 3000 but traditional practitioners use more than 6000. India is the largest producer of plant based medicine (Ahmedullah and Nayar, 1999). There are currently about 250000 registered medical practitioners of the Ayurvedic system (total for all traditional systems: approximately 291000), as compared to about 700,000 of the modern medicine system (Seth and Sharma, 2004).
In rural India, 70% of the population is dependent on the traditional system of medicine, the Ayurveda (Bent and Ko, 2004). In India, herbal medicine is a common practice, and about 960 plant species are used by the Indian herbal industry, of which 178 are of a high volume, exceeding 100 metric tons per year (Sahoo et al., 2010). Among active medicinal herbs, *Momordica charantia* L. (Cucurbitaceae), *Pterocarpus marsupium* Roxb. (Leguminosae), and *Trigonella foenumgraecum* L. (Leguminosae) have been reported as beneficial for treatment of type 2 diabetes (Jung et al., 2006). Crude extracts of *Dorema ammoniacum*, *Sphaeranthus indicus*, *Dracaena cinnabari*, *Mallotus philippinensis*, *Jatropha gossypifolia*, *Aristolochia indica*, *Lantana camara*, *Nardostachys jatamansi*, *Randia dumetorum* and *Cassia fistula* exhibited significant antimicrobial activity and properties that support folkloric use in the treatment of some diseases as broad-spectrum antimicrobial agents (Kumar et al., 2006). Ethanolic and petroleum extracts of *Artemisia japonica*, *Artemisia maritimia* and *Artemisia nilegarica* have shown tested for anti-malarial activity, both in vivo and in vitro (Valecha et al., 1994). Various medicinal plants like Neem, Arjuna, Aswagandha, Tulsi, etc. traditionally used for treating fever. The extract prepared from the heart wood of *Acacia catechu*, stem bark and leaves of *Bauhinia racemosa*, *Clome viscosa* spp. etc. reported to have antipyretic activity in rats (Umashanker et al., 2011).

### 1.3 Medicinal Foods

Plants, besides providing nutrition, have always formed an important source of chemical compounds, which can be used for medicinal purposes. Many species of plants synthesize and accumulate extractable organic substances in quantities sufficient to be economically useful as chemical feed stocks or as raw materials for various scientific, technological, and commercial applications. These plants produce economically important organic compounds such as oils, resins, tannins, natural rubber, gums, waxes, dyes, flavors and fragrances, pharmaceuticals, pesticides (e.g., insecticides and rodenticides), saponins and other surfactants, and many specialty products (Gilani and Rahman, 2005). Vegetables, fruits, and whole grains contain a wide variety of phytochemicals that have the potential to modulate cancer development. Antioxidant containing vegetables (e.g. carrot.) and spices when included in the diet can protect liver from oxidative damage caused by toxic chemicals. Carrot juice has been shown to protect mice from CCl₄-induced...
hepatotoxicity (Bishayee, 1995). There are many biologically plausible reasons why consumption of plant foods might slow or prevent the appearance of diseases including cancer. Presence of potentially anticarcinogenic substances such as carotenoids, chlorophyll, flavonoids, indole, isothiocyanate, polyphenolic compounds, protease inhibitors, sulfides, and terpenes in plant foods are responsible for mediating these effects (Waladkhani et al., 1998).

A concept of ‘functional food’ denotes food that not only serves to provide nutrition but also can be a source for prevention and cure of various diseases. In other words, these foods provide health benefits beyond their nutritive values. This is not entirely a novel concept for even in ancient times people added spices to their dietary items not only to impart color, taste or flavoring, but also for their health benefits. Functional foods are often also termed ‘food supplements’ or ‘nutraceuticals’. In recent years, to consider just one country, the functional food market in Taiwan reached US $1.78 billion in 2005 (Sun, 2007). A number of plants or plant products have been demonstrated in scientific studies that they can be classified as functional foods. These include both medicinal plants and commonly consumed plants or plant products. To mention a few examples, carotenoids in green peppers (*Capsicum annuum*, which has been traditionally consumed in Central and South American countries for thousands of years) has been shown to demonstrate antimutagenic activity against some nitroarenes (de Mejia et al., 1998). It may be noted that green peppers are also added to a variety of cooked food items and snacks in various regions of the Indian subcontinent. Chickpea, an edible vegetable (*Cicer arietinum*) is also considered a functional food and intake of chickpeas has been recommended in humans with altered lipid profile such as type IIa hyperlipoproteinemia and diabetes (Zulet, 1999).

Functional foods that have been found to be potentially beneficial in the prevention and treatment of cardiovascular disorders include soybeans, oats, psyllium, flaxseed, garlic, tea, grapes and nuts (Hasler, 2000). Garlic, a commonly used spice contains over 2,000 biologically active substances and is of importance in dietoprophylaxis and dietotherapy (Swiderski et al., 2007). The organosulfur compounds present in garlic appear to be good agents for cancer chemoprevention through multiple mechanisms like carcinogen metabolism modulation, DNA adduct formation inhibition and upregulation of antioxidant defenses and DNA repair systems (Nagini, 2008). The
Zingiberaceae family contains a number of plants whose rhizomes are eaten as vegetable or added to food items as spices. The family contains commonly known spices like ginger and turmeric. Dietary sources of phytochemicals are shown in Table 1.1.

Table 1.1 Dietary sources of phytochemicals (Waladkhani et al., 1998)

<table>
<thead>
<tr>
<th>Phytochemicals</th>
<th>Fruit/Vegitable/other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotenoids</td>
<td>Apricot, peach, nectarine, orange, broccoli, cabbage, spinach, pea, pumpkin, carrots, tomato</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>Green tea, black tea, citrus fruits, onion, broccoli, cherry, wheat, corn, rice, tomato, spinach, cabbage, apple, olives, red wine, soy products</td>
</tr>
<tr>
<td>Polyphenol</td>
<td>Grapes, strawberry, raspberry, pomegranate, paprika, cabbage, walnut</td>
</tr>
<tr>
<td>Protease inhibitors</td>
<td>soy bean, oats, wheat, peanut, potato, rice, mais</td>
</tr>
<tr>
<td>Sulfide</td>
<td>cabbage, chives, allium, onion, garlic</td>
</tr>
<tr>
<td>Terpene</td>
<td>grape fruit, lemon, lime, orange, lavender, mint, celery seeds, cherry</td>
</tr>
</tbody>
</table>

1.4 Oxidative Stress

The term is used to describe the condition of oxidative damage resulting when the critical balance between free radical generation and antioxidant defenses is unfavorable and it is associated with damage to a wide range of molecular species including lipids, proteins, and nucleic acids (Rock et al., 1996; McCord, 2000). Short-term oxidative stress may occur in tissues injured by trauma, infection, heat injury, hypoxia, toxins, and excessive exercise. These injured tissues produce increased radical generating enzymes (e.g., xanthine oxidase, lipoygenase, cyclooxygenase), activation of phagocytes, release of free iron, copper ions, or a disruption of the electron transport chains of oxidative phosphorylation, producing excess reactive oxygen species (ROS). ROS have been implicated in the induction and complications of diabetes mellitus, age-related eye disease, and neurodegenerative diseases such as Parkinson's disease (Rao et al., 2006). Oxidative stress has been associated with over a hundreds of disease states which range from arthritis, connective tissue disorders to
carcinogenesis, aging, physical injury, infection and acquired immunodeficiency syndrome. The initiation, promotion, and progression of cancer, as well as the side-effects of radiation and chemotherapy, have been linked to the imbalance between ROS and the antioxidant defense system.

### 1.5 Free Radicals

A free radical can be defined as any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital. The presence of an unpaired electron results in certain common properties that are shared by most radicals. Many radicals are unstable and highly reactive. They can either donate an electron to or accept an electron from other molecules, therefore behaving as oxidants or reductants (Cheeseman, 1993). The most important oxygen-containing free radicals in many disease states are hydroxyl radical, superoxide anion radical, hydrogen peroxide, oxygen singlet, hypochlorite, nitric oxide radical, and peroxynitrite radical. These are highly reactive species, capable in the nucleus, and in the membranes of cells of damaging biologically relevant molecules such as DNA, proteins, carbohydrates, and lipids (Young et al., 2001). Free radicals attack important macromolecules leading to cell damage and homeostatic disruption (Figure 1.1). Targets of free radicals include all kinds of molecules in the body. Among them, lipids, nucleic acids, and proteins are the major targets.
1.6 Production of free radicals in the human body

Free radicals and other ROS are derived either from normal essential metabolic processes in the human body or from external sources such as exposure to X-rays, ozone, cigarette smoking, air pollutants, and industrial chemicals (Bagchi and Puri, 1998). Free radical formation occurs continuously in the cells as a consequence of both enzymatic and nonenzymatic reactions. Enzymatic reactions, which serve as source of free radicals, include those involved in the respiratory chain, in phagocytosis, in prostaglandin synthesis, and in the cytochrome P-450 system (Liu et al., 1999). Free radicals can also be formed in nonenzymatic reactions of oxygen with organic compounds as well as those initiated by ionizing reactions.
1.7 Antioxidant defense system

An antioxidant is a molecule stable enough to donate an electron to a rampaging free radical and neutralize it by pairing with the unpaired electron and thereby stabilising it and thus reducing its capacity to damage. Antioxidants act as radical scavenger, hydrogen donor, electron donor, peroxide decomposer, singlet oxygen quencher, enzyme inhibitor, synergist, and metal-chelating agents. In aerobic organisms, these antioxidants delay or inhibit cellular damage mainly through their free radical scavenging property (Halliwell, 1995). These low-molecular-weight antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Some of such antioxidants, including glutathione, ubiquinol, and uric acid, are produced during normal metabolism in the body (Shi et al., 1999). Other lighter antioxidants are found in the diet. Anti-oxidant defense involves both enzymatic mechanisms, which utilise specific enzymes such as superoxide dismutase, catalase and glutathione peroxidase, as well as non-enzymatic mechanisms, which utilise nutrients namely vitamin E (α-tocopherol), vitamin C (ascorbic acid), and β-carotene as well as minerals (Lobo et al., 2010; Levine et al., 1999). The body cannot manufacture these micronutrients, so they must be supplied in the diet. Antioxidants reduce the oxidative stress in cells and are therefore useful in the treatment of many human diseases, including cancer, cardiovascular diseases and inflammatory diseases.

1.8 Enzymatic antioxidants

Cells are protected against oxidative stress by an interacting network of antioxidant enzymes (Sies, 1985). Here, the superoxide released by processes such as oxidative phosphorylation is first converted to hydrogen peroxide and then further reduced to give water. This detoxification pathway is the result of multiple enzymes, with superoxide dismutases catalyzing the first step and then catalases and various peroxidases removing hydrogen peroxide (Magnenat et al., 1998).

1.8.1 Superoxide dismutase

Superoxide dismutases (SODs) are a class of closely related enzymes that catalyze the breakdown of the superoxide anion into oxygen and hydrogen peroxide (Zelko et al., 2002). SOD enzymes are present in almost all aerobic cells and in extracellular fluids. There are three major families of superoxide dismutase, depending on the metal
cofactor: Cu/Zn (which binds both copper and zinc), Fe and Mn types (which bind either iron or manganese), and finally the Ni type which binds nickel.

In humans (as in all other mammals and most chordates), three forms of superoxide dismutase are present. SOD1 is located in the cytoplasm, SOD2 in the mitochondria, and SOD3 is extracellular. The first is a dimer (consists of two units), while the others are tetramers (four subunits). SOD1 and SOD3 contain copper and zinc, while SOD2 has manganese in its reactive center (Cao et al., 2008).

1.8.2 Catalase

Catalase is a common enzyme found in nearly all living organisms, which are exposed to oxygen, where it functions to catalyze the decomposition of hydrogen peroxide to water and oxygen (Chelikani et al., 2004). Hydrogen peroxide is a harmful by-product of many normal metabolic processes, to prevent damage it must be quickly converted into other, less dangerous substances. Catalase is frequently used by cells to rapidly catalyze the decomposition of hydrogen peroxide into less reactive gaseous oxygen and water molecules. All known animals use catalase in every organ, with particularly high concentrations occurring in the liver (Chelikani and Loewen, 2004).

1.9 Glutathione systems

The glutathione system includes glutathione, glutathione reductase, glutathione peroxidases, and glutathione S-transferases. This system is found in animals, plants, and microorganisms. Glutathione peroxidase is an enzyme containing four selenium-cofactors that catalyze the breakdown of hydrogen peroxide and organic hydroperoxides. There are at least four different glutathione peroxidase isozymes in animals (Brigelius-Flohe 1999). Glutathione peroxidase 1 is the most abundant and is a very efficient scavenger of hydrogen peroxide, while glutathione peroxidase 4 is most active with lipid hydroperoxides. The glutathione S-transferases show high activity with lipid peroxides. These enzymes are at particularly high levels in the liver and also serve in detoxification metabolism (Hayes et al., 2005).

1.10 Infectious and non-infectious diseases

A disease is a particular abnormal, pathological condition that affects part or all of an organism. It is often construed as a medical condition associated with
specific symptoms and signs. The term disease broadly refers to any condition that impairs the normal functioning of the body. For this reason, diseases are associated with dysfunctions of the body's normal homeostatic process. Commonly, the term disease is used to refer specifically to infectious diseases, which are clinically evident diseases that result from the presence of pathogenic microbial agents, including viruses, bacteria, fungi, protozoa, multicellular organisms, and aberrant proteins known as prions (Glossary US, NIMHR, 2014). An infection that does not and will not produce clinically evident impairment of normal functioning, such as the presence of the normal bacteria and yeasts in the gut, or of a passenger virus, is not considered a disease. By contrast, an infection that is asymptomatic during its incubation period, but expected to produce symptoms later, is usually considered a disease.

A parasitic disease is an infectious disease caused or transmitted by a parasite. Many parasites do not cause diseases. Parasitic diseases can affect practically all living organisms, including plants and mammals. Some parasites like *Toxoplasma gondii* and *Plasmodium* spp. can cause disease directly, but other organisms can cause disease by the toxins that they produce. The three main types of organisms causing these conditions are protozoa (protozoan infection), helminthes (helminthiasis), and ectoparasites. Protozoa and helminthes are usually endoparasites (usually living inside the body of the host), while ectoparasites usually live on the surface of the host. Occasionally the definition of "parasitic disease" is restricted to diseases due to endoparasites (Harms and Feldmeier, 2002). Non-infectious diseases are a medical conditions or diseases that can be defined as non communicable disease (NCD) and non-transmissible among people. These refer to chronic diseases which last for long periods of time and progress slowly such as most forms of cancer, heart disease, diabetes, autoimmune diseases, stroke, genetic disease asthma, chronic kidney disease, osteoporosis, Alzheimer's disease, cataracts, and many more (Singh et al., 2010).

1.11 Cancer

Cancer is the second leading cause of death worldwide in which a group of cells display *uncontrolled growth* (division beyond the normal limits), *invasion* (intrusion on and destruction of adjacent tissues), and sometimes *metastasis* (spread to other
locations in the body via lymph or blood). These three malignant properties of cancers differentiate them from benign tumors, which are self-limited, and do not invade or metastasize. Most cancers form a tumor but some, like leukemia, do not. Recently, a greater emphasis has been given towards the researches on complementary and alternative medicine that deals with cancer management. Several studies have been conducted on herbs under a multitude of ethnobotanical grounds.

Cancer may affect people at all ages, even fetuses, but the risk for most varieties increases with age. Cancer causes about 13% of all human deaths. According to the American Cancer Society, 7.6 million people died from cancer in the world during 2007 (Jang et al., 1997). Nearly all cancers are caused by abnormalities in the genetic material of the transformed cells. These abnormalities may be due to the effects of carcinogens, such as tobacco smoke, radiation, chemicals, or infectious agents. Other cancer-promoting genetic abnormalities may be randomly acquired through errors in DNA replication, or are inherited, and thus present in all cells from birth. The heritability of cancers is usually affected by complex interactions between carcinogens and the host's genome.

A diet which is rich in plant foods contains a variety of secondary metabolites and contributes to protect the body against cancer. Secondary metabolites carry out a number of protective functions in the human body. They can boost the immune system, protect the body from free radicals and relevantly exhibit anti-carcinogenic activity by serving properties as protective agents against various pathogens and as growth regulatory molecules. Due to these physiological functions, secondary metabolites are potential anticancer drugs. They may cause either direct cytotoxicity on cancer cells or may affect processes involved in tumor development (Harvey, 2008). A variety of phytochemicals, such as sulfides, isothiocyanates, glucosinolates, flavonoids, carotenoids, phenols, and diarylhepanoids, are known to mediate chemopreventive responses (Jang et al., 1997).

In 2014, about 585,720 Americans were expected to die of cancer, almost 1,600 people per day. Cancer is the second most common cause of death in the US, exceeded only by heart disease, accounting for nearly 1 of every 4 deaths (Cancer Facts & Figures 2014). Worldwide, over ten million new cases of cancer (all sites excluding non-melanoma skin), with over six million deaths, were estimated in the
year 2000 (Parkin et al., 2001). Since 1990 there has been a 22% increase in cancer incidence and mortality with the four most frequent cancers being lung, breast, colorectal, and stomach and the four most deadly cancers being lung, stomach, liver, and colorectal (Parkin et al., 2001).

Cancers originate within a single cell. Hence, cancers can be classified by the type of cell in which it originates and by the location of the cell. At present more than 100 types of cancer are known. The most common ones are breast cancer, lung cancer, leukemia, liver cancer, colon cancer, prostate cancer, ovarian cancer, and cervical cancer etc.

1.12 Role of Plant Products in Combating Diseases

Plants have been the basis of many traditional medicine systems throughout the world for thousands of years and continue to provide mankind with new remedies. Plant based medicines initially dispensed in the form of crude drugs such as tinctures, teas, poultices, powders, and other herbal formulations, now serve as the basis of novel drug discovery (Samuelsson, 2004). The use of plants as medicines has involved the isolation of active compounds, beginning with the isolation of morphine from opium in the early 19th century (Kingham et al., 2001) and subsequently led to the isolation of early drugs such as cocaine, codeine, digitoxin and quinine, of which some are still in use (Butler, 2004). Search of new compounds of plant origin having pharmacological activity still continues. Their isolation and characterization is need of hour.

Phytochemicals are natural bioactive compounds found in leaves, flowers, seeds, stem, and roots of edible and non-edible plants, which act as a defense system to combat against diseases. The phytochemicals from natural products cover a diverse range of chemical entities such as polyphenols, flavonoids, terpenoids, alkaloids, steroidal saponins, organosulphur compounds and vitamins. A number of bioactive compounds generally obtained from terrestrial plants such as isoflavones, diosgenin, resveratrol, quercetin, catechin, sulforaphane, tocotrienols and carotenoids are proven to reduce the risk of cardiovascular diseases and aid in cardioprotection which is the leading cause of death globally (Vasanthi, 2012). The cardioprotective effects of the various phytochemicals are perhaps due to their antioxidative, antihypercholesterenoic, antiangiogenic, anti-ischemic, inhibition of platelet
aggregation and anti-inflammatory activities that reduce the risk of cardiovascular disorders. The multi-faceted role of the phytochemicals is mediated by its structure-function relationship and can be considered as leads for cardiovascular drug design in future.

1.13 Hepatoprotective

Medicinal herbs are significant source of hepatoprotective drugs. It has been reported that about 170 phytoconstituents isolated from 110 plants belonging to 55 families do possess hepatoprotective activity (Handa, 1991). Hepato protective herbal drugs contain a variety of chemical constituents like phenols, coumarins, curcuminoids, lignans, essentialoils and terpenoids, silymarin, a flavonol lignan mixture extracted from the milk thistle (Silybum marianum) is a popular remedy for hepatic diseases. Andrographolide (Andrographis paniculata), Glycyrrhizin (Glycyrrhiza glabra), Picrorhizin (Picrorrhiza kurroa) and Hypo-phyllanthin (Phyllanthus niruri) are potential candidates with hepatoprotective activity. Approximately 80% of the world’s population has employed traditional medicine for health care, which is based predominantly on plant materials (Adewusi, 2010).

Liv52 is considered to be an Ayurvedic hepatoprotective medicine that contains the Capparis spinosa (Himsara), Cichorium intybus (Kasanî), Mandur bhasma, Solanumnigrum (Kakamachi), Terminalia arjuna (Arjuna), Cassia occidentalis (Kasamarda), Achillea millefolium (Biranjasipha), and Tamarix gallica (Jhavaka). Liv52 has been on the market for over 50 years and has been claimed to be useful in the prevention and treatment a variety of conditions such as viral hepatitis, alcoholic liver disease, protein energy malnutrition, loss of appetite, and radiation and chemotherapy induced liver damage (Sandhir and Gill, 1999). Experimental data suggest that Liv52 inhibits lipid peroxidation, may have a protective effect on alcohol induced fetotoxicity, and inhibits TNF activity. Liv52 has been claimed to be useful as an adjuvant to hepatoprotective drugs (Pandey et al., 1994).

Arteether is a potent anti-malarial drug and is derived from artemisinin, a sesquiterpene lactone isolated from Artemisia annua L. (Asteraceae), a plant used in traditional Chinese medicine (Graul, 2001). Galanthamine is a natural product discovered through an ethnobotanical lead and first isolated from Galanthus woronowii (Amaryllidaceae) in Russia. Galanthamine is approved for the treatment of
Alzheimer’s disease, slowing the process of neurological degeneration by inhibiting acetylcholine esterase as well as binding to and modulating the nicotinic acetylcholine receptor (Heinrich et al., 2004). Tiotropium has been released recently in the US for treatment of chronic obstructive pulmonary disease (Frantz, 2004). Tiotropium is an inhaled anticholinergic bronchodilator, based on ipratropium, a derivative of atropine, isolated from *Atropa belladonna* L. (Solanaceae) and other members of the Solanaceae family (Dewick et al., 2002). Morphine-6-glucuronide is a metabolite of morphine from *Papaver somniferum* L. (Papaveraceae), reported as an alternative pain medication with fewer side effects than morphine (Lotsch et al., 2001). Exatecanis an analogue of camptothecin isolated from *Camptotheca acuminata* (Nyssaceae) and being developed as an anticancer agent (Butler 2004; Cragg et al., 2005). Vinflunine is a modification of vinblastine from *Catharanthus roseus* G. Don (Apocynaceae) for use as an anticancer agent with improved efficacy. (+)-Calanolide A is a dipyranocoumarin compound isolated from *Calophyllum lanigerum* var. *austrocoriaceum* (Whitmore) P.F. Stevens (Clusiaceae), a Malaysian rainforest tree (Yu et al., 2003). (+)-Calanolide A is an anti-HIV drug with specific mechanism of action as a non-nucleoside reverse transcriptase inhibitor of type-1 HIV and is effective against AZT-resistant strains of HIV. It is currently undergoing phase II clinical trials (Yu et al., 2003). Recently, (+)-calanolide A has been reported as an anti-tubercular agent. (+)-Calanolide A was consistently active (MIC 8–16 mg/ml) against drug-susceptible strains of *Mycobacterium tuberculosis*. Efficacy evaluations in macrophages revealed that (+)-calanolide A significantly inhibited intracellular replication of *M. tuberculosis* H37Rv at concentrations below the MIC observed *in vitro*. Preliminary mechanistic studies indicated that (+)-calanolide A rapidly inhibits RNA and DNA synthesis followed by inhibition of protein synthesis. (+)-Calanolide A and related pyranocoumarins represent the first class of compounds identified to possess antimycobacterial and antiretroviral activities and thus, a new pharmacophore for anti-TB activity (Jachak et al., 2006).
Since plants have provided number of effective molecules for treatment of diseases, in present thesis effort has been made to study the biological activities of three plants namely *Piper longum* (Piperaceae), *Bauhinia variegata* Linn. (*Caesalpiniaceae*), *Tinospora cordifolia* (Menispermaceae) complete with the following objectives.

**OBJECTIVES**

1. Extraction of phytoconstituents in various solvents and their partial characterization.

2. To determine the antioxidant potential of extracts using several *in vitro* models.

3. To study the *in vivo* effect of extracts on oxidative stress marker enzymes in aluminium chloride induced hepatotoxicity

4. To assess antibacterial activity of extracts.

5. To evaluate cytotoxic activity of extracts against human cancer cell lines

6. To evaluate anti-malarial and anti-leishmanial activity of extracts