CHAPTER 2

REVIEW OF LITERATURE
Throughout the ages, humans have relied on nature for their basic needs, for the production of food, shelter, clothing, transportation, fertilizers, flavours and fragrances, and medicines (Cragg and Newman, 2005). Plants have formed the basis of sophisticated traditional medicine systems that have been in existence for thousands of years and continue to provide mankind with new remedies. Although some of the therapeutic properties attributed to plants have proven to be erroneous, medicinal plant therapy is based on the empirical findings of hundreds and probably thousands of years of use. The first records, written on clay tablets in cuneiform, are from Mesopotamia and date from about 2600BC (Heinrich et al., 2004).

The interest in nature as a source of potential chemotherapeutic agent continues. Natural products and their derivatives represent more than 50% of all the drugs in clinical use in the world today. Higher plants contribute not less than 25% of the total. (Farnsworth et al., 1985; Cragg and Newman, 2005). Approximately half (125000) of the world’s flowering plant species are found in the tropical forests. Tropical rain forests continue to support a vast reservoir of potential drug species. They continue to provide natural product chemicals with invaluable compounds as starting points for the development of new drugs. The potential for finding more compounds is enormous as to date only about 1% of tropical species have been studied for their pharmaceutical potential (Cragg and Newman, 2005).
In some countries, the use of medicinal plants is often associated with witchcraft and superstition, because people do not have the scientific insight to explain and predict the curative action of plants. One example of such an irrational concept is the Doctrine of Signatures, elements of which are found in many of the healing cultures of the world. (Boehme, 1982). It is based on the assumption that the appearance of plants may give clue to their medicinal properties – it is interpreted as God’s signature on the plant. Red juice and sap, for example is associated with blood and menstrual ailments; yellow flowers with bile and jaundice; the human shape of certain roots with the female form of fertility and so on.

In India, knowledge and wisdom have been passed on from one generation to the next through songs and poems, which scholars and physicians had to learn and recite by heart. The Veda is an ancient text in four parts (Rig Veda, Sama Veda, Yajur Veda and Atharva Veda), the earliest of which date back to 2000 years BC. The principles of Ayurvedic medicine and the medicinal uses of plants are contained in thousands of poetic hymns in the Rig Veda. The first school to teach Ayurvedic medicine was at the University of Banaras in 500 BC where the great Samhita (or encyclopedia of medicine) was written. Another great encyclopedia was written 700 years later, and these two together forms the basis of the Ayurveda (Chopra, 2000).

Drug discovery from medicinal plants has traditionally been lengthier and more complicated than other drug discovery methods. Therefore, many
pharmaceutical companies have eliminated or scaled down their natural product research (Butler 2004; Koehn and Carter, 2005). Recently there has been a rekindling of interest in 'rediscovering natural products'. As stated by one authority “we would not have the top-selling drug class today, the statins; the whole field of angiotensin antagonists and angiotensin-converting enzyme inhibitors; the whole area of immunosuppressives, nor most of the anticancer and antibacterial drugs. Imagine all of these drugs not being available too physicians or patients today”. It is clear that nature has played and will continue to play, a vital role in the drug discovery process (Cragg and Newmann, 2005).

Terminalia chebula

The second largest genus of Combretaceae, Terminalia, consists of 200 species, distributed in the tropics and subtropics (Wickens, 1973). About 30 species of Terminalia are found in Africa (Wickens, 1973). Species of Terminalia vary greatly in morphology, anatomy and karyotype evidence (Excell, 1954; Stace, 1965; Ohri, 1996). The species of Terminalia are small to large trees depending on the growth habitat. In rainforest they can reach heights of up to 50 m, and often grow as emergents, reaching above the upper tree stratum.

Terminalia chebula is a tree whose trunk towers from 40 to 70 feet, its verticillate branches giving the tree a symmetrical head. The leaves are short-petioled, alternate, entire, or slightly denate, arrange on the ends of the branches, coriaceous and spotted. The 10-stamened flowers are white or yellowish, and borne in racemes or spikes. The fruit is a drupe about the size of a large plum.
*Terminalia chebula* exhibited antibacterial activity against a number of bacterial species (Ahmad, Mehmood and Mohammad, 1998). One group of researchers found that it is effective in inhibiting the urease activity of *Helicobacter pylori* (*H. pylori*), an ubiquitous bacterium implicated in the development of gastritis, ulcers and stomach cancers (Malczadeh *et al.*, 2001). Antibacterial activity of *Terminalia chebula* against both Gram positive and Gram negative human pathogenic bacteria has also been reported (Sato *et al.*, 1997).

An aqueous extract of *Terminalia chebula* exhibits antifungal activity against a number of dermatophytes and yeasts (Dutta *et al.*, 1998; Ray and Majumdar, 1976). It is effective against the pathogenic yeast *Candida albicans* and dermatophytes *Epidermophyton floccosum*, *Microsporum gypseum* and *Trichophyton rubrum*. (Vonshak *et al.*, 2003) *Terminalia chebula* fruits afforded four immunodeficiency virus type 1 (HIV-1) integrase inhibitors, gallic acid (Kirtikar, and Basu 1935) and three galloy glucoses. *Terminalia chebula* has also retroviral reverse transcriptase activity (Suthienkul *et al.*, 1993). It protects epithelial cells against influenza A virus, supporting its traditional use for aiding in recovery from acute respiratory infections. (Badmaev and Nowakowski, 2000). It also showed a significant inhibitory activity on the effects of immunodeficiency virus-1-transcriptase (Mekkawy 1995).

A group of researchers have reported the inhibition action on cancer cell growth by the phenolics of *Terminalia chebula* Retz fruit and found that chebulinic acid, tannic acid and ellagic acid were the most growth inhibitory phenolics of
*Terminalia chebula* (Saleem *et al.*, 2002). Besides, acetone extract of bark and fruit powder of *Terminalia chebula* harbors constituents with promising antimutagenic/anticarcinogenic activity (Arora *et al.*, 2003).

Six extracts and four compounds of *Terminalia chebula* fruit exhibited antioxidant activity at different magnitudes of potency (Cheng *et al.*, 2003). Its fruit exerts antioxidant and radioprotective activity in rats (Naik *et al.*, 2004). It has stronger antioxidant activity than alpha-tocopherol; HPLC analysis with diode array detection indicated the presence of hydroxybenzoic acid derivatives, hydroxycinnamic acid derivatives, flavonol aglycones and their glycosides, as main phenolics compounds (Saleem *et al.*, 2001).

Topical administration of an alcoholic extract of *Terminalia chebula* leaves on the healing of rat dermal wounds showed that *Terminalia chebula* treated wounds healed faster as indicated by improved rates of contraction and decreased period of epithelialization. (Sugana *et al.*, 2002). Aqueous extract of *Terminalia chebula* produced an increase in humoral antibody (HA) titer and delayed type hypersensitivity (DTH) in mice (Shivaprasad *et al.*, 2006).

*Terminalia chebula* Retz. (black myrobalan) is an important plant in both Indian as well as Korean and Chinese traditional medicine, where fruits of *T. chebula* are used for treatment of diarrhea, as an astringent, as an ingredient in Triphala, a mixture containing *T. chebula, T. bellerica* and *Emblica officinalis*, (Reddy *et al.*, 1990), as well as for their diuretic and cardiotonic properties (Singh, 1990). Gallic acid, chebulinic acid, chebulagic acid and 1,2,3,4,5,6-penta-O-
galloyl-β-D-glucopyranose, isolated from a methanolic fruit extract of *T. chebula* were found to show moderate cytotoxic effects against melanoma and ovarian cancer cell lines. Saleem *et al.*, (2002) found that a 70% methanol extract of the fruits of *T. chebula* decreased cell viability, inhibited cell proliferation and induced cell death in a dose dependent manner against human breast carcinoma (MCF 7), mouse breast carcinoma (S155), human osteosarcoma (HOS-1) and a prostate cancer cell line (PC-3). Chebulinic acid, tannic acid and ellagic acid were the most cancer cell growth inhibitory phenolics isolated from the fruits of *T. chebula* (Saleem *et al.*, 2002). Ellagic acid may arise from the hydrolysis of ellagitannins in the human gut and it has been found to be ten times more antioxidative than tannic acid (Puech *et al.*, 1999). Thus, the good *in vitro* anticancer effects. Saleem *et al.*, (2002) observed for this compound might be due to its antioxidative properties. Ellagic acid has also been found to induce cell cycle arrest and apoptosis (Narayanan *et al.*, 1999), as well as inhibit tumor formation and growth in animals (Stoner & Morse, 1997; Khanduja *et al.*, 1999). Triphala has been found to possess antimutagenic properties, and especially extracts made in acetone and chloroform were effective, whereas a water extract gave no activity(Kaur *et al.*, 2002b).

**Semecarpus anacardium**

*Semecarpus anacardium* Linn. (Family: Anacardiaceae) is distributed in sub-Himalayan region, tropical and central parts of India. The nut is commonly known as 'marking nut' and in the vernacular as 'Ballataka' or 'Bhilwa'. It has high priority and applicability in indigenous system of medicine(Chopra 1982 and Khare 1982).
*Semecarpus anacardium* Linn. (Family: Anacardiaceae) is a plant well-known for its medicinal value in Ayurvedic and Siddha system of medicine. Chemical and phytochemical analyses of its nut reveal the presence of biflavonoids, phenolic compounds, bhilawanols, minerals, vitamins and amino acids. A variety of nut extract preparations from this source are effective against many diseases, viz., arthritis, tumors, infections and so on. However, the mechanism of the pharmacological action of its nut can be greatly aided by the isolation of its active principle and determination of structure-function relationship.

### Antioxidant activity

*Semecarpus anacardium* has been reported in various studies to possess potent antioxidant activity. Verma *et al.*, (2008) investigated antioxidant activity of the aqueous extract of nuts of medicinal plant SA in AKR mouse liver during development of lymphoma. Administration of the aqueous extract of SA to lymphoma-transplanted mouse leads to increase in the activities of antioxidant enzymes, whereas LDH activity is brought down significantly indicating a decrease in carcinogenesis.

Sahoo *et al.*, (2008) investigated the antioxidant activity of ethyl acetate extract of stem bark of SA. Ethyl acetate extract showed the stronger antioxidant activity (due to presence of highest total phenolic content of 68.67% measured as pyrocatechol equivalent) compared to the other (hexane, chloroform and methanol) extracts. The isolation of the ethyl acetate extract of SA stem bark yielded a bright-yellow solid crystal, which was identified as butein. This compound exhibited antioxidant activity (IC50 values of 43.28 ±4.34 μg/ml), which was comparable to rutin taken as a standard.
**Antimicrobial activity**

Mohanta *et al.*, (2007) prepared the aqueous and organic solvent extracts of the plant and screened for antimicrobial (disc diffusion method) and phytochemical properties. The petroleum ether (PEE) and aqueous extract fractions (AQE) showed inhibitory activity against *Staphylococcus aureus* (10 mm) and *Shigella flexneri* (16 mm) at 100 mg/ml, respectively. While chloroform extract showed inhibition against *Bacillus licheniformis*, *Vibrio cholerae* and *Pseudomonas aeruginosa*, the ethanol extract showed inhibition to *Pseudomonas aeruginosa* and *S. aureus*.

Nair *et al.*, (1996) found that the alcoholic extract of dry nuts of SA (Bhallatak) showed bactericidal activity *in vitro* against three gram negative strains (*Escherichia coli*, *Salmonella typhi* and *Proteus vulgaris*) and two gram positive strains (*Staphylococcus aureus* and *Corynebacterium diphtheriae*). Subsequent studies have shown that the alcoholic extracts of different parts of the plant (leaves, twigs and green fruit) also possess anti-bacterial properties, especially the leaf extract. No dermatoxic effect (irritant property) was observed in the mouse skin irritant assay.

**Anti-carcinogenic activity**

Mathivadhani *et al.*, (2007) studied SA nut extract for inhibitory effect on human breast cancer cells (T47D). Cytotoxicity analyses suggested that these cells had become apoptotic. *Semecarpus anacardium* was discovered to induce rapid Ca (2+) mobilization from intracellular stores of T47D cell line, and its cytotoxicity against T47D was well correlated with altered mitochondrial transmembrane...
potential. At the molecular level, these changes are accompanied by decrease in Bcl(2) and increase in Bax, cytochrome C, caspases and PARP cleavage, and ultimately by internucleosomal DNA fragmentation. Taken together, our results provide unprecedented evidence that SA triggers apoptotic signals in T47D cells (Veena et al., 2006).

Arulkumaran et al., (2007) investigated the protective efficacy of preparation named as Kalpaamruthaa (KA) (includes SA nut milk extract, dried powder of Phyllanthus emblica fruit and honey) on the peroxidative damage and abnormal antioxidant levels in the hepatic mitochondrial fraction of 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary carcinoma rats. DMBA-treated rats also showed decline in the activities of mitochondrial enzymes. In contrast, rats treated with SA and KA showed normal lipid peroxidation antioxidant defenses in mitochondrial enzymes, and indicate the anticarcinogenic activity of KA during DMBA-initiated mammary carcinogenesis. On the basis of the observed results, KA can be considered as a readily accessible, promising and novel cancer chemopreventive agent.

Sugapriya et al., (2008) showed restoration of energy metabolism in leukemic mice treated by SA nut milk extract. Leukemia-bearing mice showed a significant increase in LPOs, glycolytic enzymes, a decrease in gluconeogenic enzymes and significant decrease in the activities of TCA cycle and respiratory chain enzymes as compared to control animals. Semecarpus anacardium treatment was compared with standard drug imatinib mesylate. Semecarpus anacardium
administration to leukemic animals resulted in clearance of the leukemic cells from the bone marrow and internal organs.

**Immunomodulatory activity of medicinal plants**

Fruits of *Emblica officinalis* (Family: Euphorbiaceae) and whole plant of *Evolvulus alsinoides* (family: Convolvulaceae) has been extensively used in Indian Ayurvedic medicine for varieties of medical disorders. The immunomodulatory properties of *Emblica officinalis* and *Evolvulus alsinoides* were evaluated in adjuvant induced arthritic rat model. The crude aqueous extracts of both the herbs were administered intraperitonially following a repeated treatment profile. There was a significant reduction in swelling and redness of inflamed areas in treated animals than in untreated controls. The anti-inflammatory response of both extracts was determined by lymphocyte proliferation activity and histopathological severity of synovial hyperplasia. Both extracts showed a marked reduction in inflammation and edema. At cellular level immune-suppression occurred during the early phase of the disease. There was mild synovial hyperplasia and infiltration of few mononuclear cells in treated animals. The induction of nitric oxide synthase was significantly decreased in treated animals as compared to controls. These observations suggest that both the herbal extracts caused immune-suppression. Both are as potent as dexamethasone, traditionally used immunosuppressant for arthritis (Ganju et al., 2003).

Mehrota described *in vitro* immunosuppressive potential of ethanolic extract of *Acorus calamus* rhizome. Ethanolic extract of *A. calamus* inhibited proliferation
of mitogen (phytohaemagglutinin) and antigen (purified protein230 Mahiuddin Alamgir and Shaikh Jamal Uddinderivative) stimulated human peripheral blood mononuclear cells (PBMCs). In addition, *A. calamus* extract inhibited growth of several cell lines of mouse and human origin. It also inhibited production of nitric oxide (NO), interleukin-2 (IL-2) and tumor necrosis factor-α (TNF-α). Intracytoplasmic interferon-γ (IFN-γ) and expression of cell surface markers, CD16 and HLA-DR on human PBMC, were not affected on treatment with *A. calamus* extract but CD25 expression was down regulated (Mehrotra et al., 2003).

Crude extract of *Tinospora cordifolia* contained a polyclonal B cell mitogen which enhanced immune response in mice. An arabinogalactanpolysaccharide, G1-4A from the stem of *Tinospora cordifolia* examined to modulate induced immunosuppression. Mice pre-treated with G1-4A exhibited protection against lipopolysaccharide (LPS) induced mortality [Desai et al., 2007]. Partially purified immunomodulator, G1-4A prevented lipid peroxidation and restored the activities of superoxide dismutase and catalase enzymes. Likewise, oxidative damage, induced by peroxynitrite, was also inhibited by partially purified immunomodulator similar to selective inhibitors of reactive oxygen species (ROS) like mannitol, superoxide dismutase, sodium azide and antioxidants, GSH and vitamin C [Desai et al., 2002]. In further studies, intraperitoneal administration of alcoholic extract of *Tinospora cordifolia* in Dalton's lymphoma bearing mice not only augmented the basic function of macrophages such as phagocytosis, but also their antigen presenting ability and secretion of IL-1 and TNF. It was also indicated that the extract slow down the tumor growth and increases the life span of tumor bearing
host, thus showing its anti-tumor effect through destabilizing the membrane integrity of Dalton's lymphoma cells directly or indirectly. Thus, the study demonstrated alcoholic extract of *Tinospora cordifolia* activated tumor-associated macrophages and showed antitumor effect on the spontaneous T-cell lymphoma and may have some clinical implications (Singh *et al.*, 2004).

Ethanolic extract of *Boerhaavia diffusa*, a plant used in Indian traditional system of medicine, significantly inhibited the cell proliferation [Mungantiwar *et al.*, 1999]. Extracts of *B. diffusa* roots inhibited human NK cell cytotoxicity *in vitro*, production of nitric oxide in mouse macrophage cells, interleukin-2 and tumor necrosis factor-α (TNF-α), in human PBMCs. Whereas, intracytoplasmic interferon-γ (IFN-γ) and cell surface markers such as CD16, CD25, and HLA-DR did not get affected on treatment with *B. diffusa* extract and demonstrates immunosuppressive potential of *B. diffusa* (Mehrotra *et al.*, 2002).

Aqueous leaves extract of biopesticidal plant *Nyctanthes arbor-tristis* has been found as a potent immunomodulatory (Puri *et al.*, 1994). The extract has been evaluated as immunorestorative or anti-immunosuppressive agent in the malathion-exposed immunosuppressed mice by studying various immunological parameters (humoral, cell mediated immune, numerical values of immunocytes and functions of phagocytes) in treated or untreated malathion-exposed mice. The results revealed that the immunological parameters which were suppressed with malathion either reverted back to normal or showed a trend towards normalcy, when treated with aqueous leaves extract of *Nyctanthes arbor-tristis* [Bhatia *et al.*, 2001].
Methanol extract of *Eclipta alba* and *Centella asiatica* whole plant showed phagocytic index and antibody titer has been increased significantly. The F ratios of the phagocytic index and WBC count were also significant with linearity in the dose-response relationship (Jayathirtha and Mishra 2004). The ethanol extract of the root of the plant *Cryptolepis buchanani* caused significant stimulation of the delayed type hypersensitivity reaction and humoral antibody production in mice [Kaul 2003].

An aqueous extract of *Rhodiola imbricata* rhizome stimulated production of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) in human PBMCs as well as RAW 264.7 cell line. It also increased production of nitric oxide synergistically in combination with lipopolysaccharide in RAW 264.7. Furthermore, it increased the phosphorylated-IkB expression and activated the nuclear translocation of NF-κB in human PBMCs. Thus, *Rhodiola* most likely activated proinflammatory mediators via phosphorylated inhibitory κBand transcription factor NF-κB (Mishra *et al.*, 2006).

The immune system is affected by the environmental and dietary habits and it is believed that diet rich in antioxidants and micronutrients can boost the immune system. An earlier study carried out in Africa revealed that Moringa powder supplementation might act as an immune stimulant for patients suffering from HIV infection. (Burger *et al.*, 2002). Sonkar Rinki and Mishra (2011) reported that megaExtract of Triphala has good immunomodulatory property and could be attributed to the presence of flavanoids, alkaloids, tannins, saponin glycosides and phenolic compounds.
It is revealed that the alcoholic extracts of *T.cordifolia* obtained from the dried ripe fruits possess good immunomodulatory activity. (Aher and Arunkumar Wahi 2010). According to Shendige Esv.ara Rao Bharani, (2010) the extract of *Morus alba* has a significant effect on the humoral and cell mediated immunity in experimental animals.

Haridradi Ghrita (HG) is a panchgavya based polyherbal formulation claimed to have hepatoprotective and immunostimulant activity in traditional practices. The ingredients of the Haridradi Ghrita are *Emblica officinalis*(4g), *Terminalia chebula* (4g), *Azadirachta indica* (4 g), *Sida cordifolia* (4g), *Glycyrrhiza glabra*(4 gm) and cow ghee ( 76 gm). (Fulzele et al., 2003).

Tannins obtained from the stem bark of *Bauhinia variegate* Linn found to possess immunomodulatory property. Thus, Patil, (2010) results support the immunomodulatory activity of *Bauhinia variegate* claimed as an enhancer of general immunity against various physical and mental disorders in the indigenous system of medicine. On the other hand, *Acacia catechu* extract produced a significant increase in the serum immunoglobulin levels, increase in the haemagglutination titre values and decreased the mortality ratio in mice, suggesting its effect on the humoral arm of the immune system.

The extract of *Achyranthes aspera* Linn (Amaranthaceae) was found to enhance the induction of ovalbumin (OVA) specific humoral antibody response in mice, on intraperitoneal injection of extract along with OVA. The antibody response was evaluated by passive cutaneous anaphylaxis (PCA) and ELISA for
IgE and other classes or subclasses of antibodies, respectively. Furthermore, the plant extract was found to increase the induction of OVA-specific antibody response in a dose-dependent manner. (Rao. Vasudeva et al., 2002)

The leaves of *Morus alba* Linn. Commonly known as mulberry are mainly used as food for the silkworms and they are sometimes eaten as vegetable or used as cattle fodder in different parts of the world. The effect of *Morus alba* on the immune system was evaluated by using different experimental models such as carbon clearance test, cyclophosphamide induced neutropenia, neutrophil adhesion test, effect of serum immunoglobulins, mice lethality test and indirect hemagglutination test. The extract of *Morus alba* has a significant effect on the humoral and cell mediated immunity in experimental animals. (Shendige Eswara Rao Bharani et al., 2010)

**Antitumor activity of medicinal plants**

Traditional medicine has a long history of serving peoples all over the world. India is without doubt a herbal hub. Medicinal plants that are native to India and their use in various traditional systems of medicine are indeed awe-inspiring. The ethnobotany and ubiquitous plants provide a rich resource for Natural drug research and development. In recent years, the use of traditional medicine information on plant research received considerable interest. The medicinal plants contain several phytochemicals such as vitamins, carotenoids, terpenoids, flavonoids, polyphenols, alkaloids, tannins, saponins, enzymes, minerals etc. These phytochemicals possess antioxidant activities, which, prevent or can be used in the
treatment of many diseases, including cancer. There are the several medicinal plants all over the world, including India, which are being used traditionally for the prevention and treatment of cancer (Dixit and Ali, 2010).

Cancer is one of the dreadful diseases of 20th century and moving vastly towards 21st century. According to the studies, worldwide about 6 million new incidences are reported every year. It is the second major cause of death after cardiovascular diseases (Sunyana Jain et al., 2009). Cancer, characterized by uncontrolled growth and spread of abnormal cells, is caused by both external and internal factors (Uma Devi et al., 2009). Many of the chemotherapeutic agents sold for the treatment of cancer are highly expensive, mutagenic, carcinogenic and teratogenic and marrow inhibition limits their applications (Kumarappan et al., 2007).

Nature is and will still serve as the man’s primary source for the cure of his ailments. However, the potential of higher plants as sources for new drugs is still largely unexplored (Oke et al., 2002). Herbal medicines have recently attracted much attention as alternative medicines useful for treating or preventing lifestyle related disorders and relatively very little knowledge is available about their mode of action. There has been a growing interest in the analysis of plant products which has stimulated intense research on their potential health benefits (Kangralkar et al., 2010). Herbal decoctions consisting of multiple herbs each possessing tremendous potential for a cancer cure are commonly used in Ayurveda. The benefit of a herbal decoction is that it can nourish the body as a whole by supporting various organ systems (Sunyana Jain et al., 2009).
The demand for herbal medicines continuously increased due to their lesser side effects when compared with synthetic drugs (Varahalarao Vadlapudi et al., 2010). Antioxidants have been found to play a major role in protecting the human body against damage induced by reactive free radicals (Halliwell and Gutteridge, 1990; Mates et al., 1999) by reacting with free radicals, chelating and also by acting as oxygen scavenger (Shahidi and Wanasundara, 1992; Buyukokuroglu et al., 2001).

The plant *Casuarina equisetifolia* Forst belongs to the family Casuarinaceae extracts of leaves exhibit anticancer properties (PJS 1967). Leaf juice of *Cajanus cajan* belonging to the family Papilionaceae, is useful in jaundice and disease of the mouth. Aqueous and alcoholic extracts of leaves exhibit anti-hepatotoxic activity in rats (Maity et al., 1996). Infusion of leaves of *Glycosmis pentaphylla* Corr is used in fever, liver complaints, cough and jaundice (Chakravaty et al., 1996). The plant *Bixa orellana* Linn of which local name is lotkan, shidhur, belongs to the family Bixaceae. Seeds are used in fever, appetising agent and stimulant. Extracts of the plant *Argemone Mexicana* Linn., locally named as prickly poppy belonging to the family Papaveraceae possesses tonic, anthelmintic, diuretic and hypnotic properties. Latex and extract of plants are used in jaundice, tumors, cancers and eye diseases (Lloydia, 1970). Alkaloid of the plant *Physalis minima* belonging to the family Solanaceae may have potential use for leukemia chemotherapy (Ma, 1991).

Chemically induced carcinogenesis models are widely used for studying the biology of cancer and for developing and evaluating cancer prevention strategies.
The most used chemical carcinogen models, 1-methyl-1-nitrosourea (MNU), 7,12-dimethylbenzanthracene (DMBA), diethylnitrosoamine (DEN) or azoxymethane (AOM) have been used predominantly used in the investigation of a variety of novel cancer chemopreventive agents (Macejova and Brtko 2001).

N-Nitrosodiethylamine (DENA) is the most important environmental carcinogen among the nitrosamines described as an effective hepatotoxin and hepatotoxic in experimental animals. Foodstuffs such as cheese, soybeans, smoked, salted and dried fish, cured meat, alcoholic beverages and a few varieties of vegetables are the principal sources of DENA (Tricker et al., 1991; Liao et al., 2001; Bansal et al., 2005). Metabolism of certain therapeutic drugs is also reported to produce N-nitrosodiethylamine (Akintonwa, 1985). Oxidative stress is considered as critical mechanism contributing to DENA-induced hepatotoxicity, and the use of antioxidant agents reduced liver damage (Vitagilone et al., 2004). Lipid peroxidation and associated membrane damage are key features of DENA-induced carcinogenesis (Anis et al., 2001).

It is heartening that a traditional Indian plant has now led to several therapeutically and useful preparation and compounds, which generates enough encouragements among the scientists in exploring more information about these medicinal plants. As the global scenario is now changing towards the use of non-toxic plant products having traditional medicinal use, development of modern drug from medicinal plants should be emphasized for the control of various diseases including cancer.
The present study was undertaken with the following objectives.

1. (a) To screen the bioactive components of *Terminalia chebula* and *Semecarpus anacardium*)
(b) To elucidate the structure of the bioactive components of *Terminalia chebula* and *Semecarpus anacardium*.

2. To screen the antimicrobial activity of *Terminalia chebula* and *Semecarpus anacardium*.
   (a) Antibacterial activity.
   (b) Antifungal activity.
   (c) Antiviral activity.

3. To screen the antioxidant property of *Terminalia chebula* and *Semecarpus anacardium*
   (a) Screening for the antioxidant activity.
   (b) Quantitative assay of antioxidant activity.

4. To screen the wound healing activity of methanolic extracts of *Terminalia chebula* using animal models.
   (a) Excision wound healing activity of the methanolic extract of *Terminalia chebula* using animal models.
5. To screen the immunomodulatory activity of *Terminalia chebula* using animal models
   
   (a) Cell mediated immunity:
   
   • Neutrophil adhesion test.
   
   • Cyclophosphamide induced neutropenia.
   
   (b) Humoral immunity:
   
   • Serum immunoglobulin estimation.
   
   • Indirect haemagglutination assay.

6. To screen the antitumor property of *Semecarpus anacardium* using animal models.

   (a) Estimation of enzymatic antioxidants
   
   • Assay of superoxide dismutase.
   
   • Assay of catalase.

   (b) Estimation of liver marker enzymes:
   
   • Assay of Aspartate aminotransferase
   
   • Assay of Alkaline Phosphatase
   
   • Assay of Alanine amino transferase
   
   • Assay of Lactate dehydrogenase

7. Histopathological analysis of the animals induced by chemical carcinogen.

   • Histology of control animals.
   
   • Histology of synthetic antioxidant treated animals.
   
   • Histology of methanolic extract treated animals.