Since medieval times, plants have been the source of medicine for the treatment of various diseases. In spite of the availability of wealth of synthetic drugs, plants remain an integral part of health care in different countries, especially the developing ones. By the end of 20th century, plant based products, nutraceuticals and food supplements have gained a big share in drug market in the developed countries. This swell in the use of plant based products is perhaps, associated with the belief that herbs can provide benefits over and above allopathic medicines (Izevbigie, 2003). Plant based drugs possess low toxic potential, high effectiveness with broad spectrum of activity and emphasize mostly on preventive action, whereas allopathic medicines bear high costs, side effects and other therapeutic limitations (Park and Pezzuto, 2002).

Internationally, the scientific community is concentrating on developing plant related drugs for the treatment of many major diseases such as cancer, diabetes, hepatitis etc., Traditional medicine is the amalgamation of therapeutic experience of generations of practicing physicians of indigenous systems of medicine and these preparations comprise medicinal plants, minerals, organic matters etc. The plant based medicines initially dispensed in the form of crude drugs such as tincture, tea, poultice, powder and other herbal formulations, these now serve as the basis of novel drug discovery (Samuelsson, 2004). The use of herbal drugs is documented by Indian, Chinese, Egyptian, Greek, Roman and Syrian and dates back to about 5000 years. The world’s most ancient traditional system of medicine i.e., Ayurveda, is well recognized in India, where it is practiced along with other indigenous systems of medicine viz., Siddha, Unani, Homeopathy, Yoga and Naturopathy (Sanjappa, 2005). More than 70% of India's population is still draw on these non-allopathic systems of medicine for the treatment of various ailments (Vaidya and Devasagayam, 2007). It is estimated that about 80,000 species of plants are collectively utilized by all these different systems of Indian medicine, the codified traditions has about 25,000 plant drug formulations and over 50,000 formulations are believed to exist in the folk and tribal traditions (Prajapati et al, 2005; Kumar et al, 2006). Unfortunately, the use of medicinal plants in the country is based primarily on empirical knowledge and many of the plants have not been scientifically evaluated for their safety and efficacy.
2.1. INDIAN SCENARIO AND BIODIVERSITY

Indian subcontinent is a vast repository of medicinal plants and it is estimated that worldwide there are approximately 5,00,000 plant species, out of which only 1% have been phytochemically investigated (Neogi et al., 2007). The United Nations Environment Programme and World Conservation Monitoring Centre showed that with the current extinction rate of plants and animals, the world is losing one major drug in every 2 years (Groombridge and Jenkins, 2002), that increases our responsibility to use our heritage judicially. India inherit 2 (the Eastern Himalayas and the Western Ghats) of the 18 hotspots of plant biodiversity in the world. Interestingly, India ranks seventh among the 16 megadiverse countries, where 70% of the world’s species occur collectively and has its own rich collection of flora, i.e., endemic plant species (5725 angiosperms, 10 gymnosperms, 193 pteridophytes, 678 bryophytes, 260 liverworts, 466 lichens, 3500 fungi and 1924 algae). Unfortunately, due to various reasons including inaccessibility of some tough terrains, only 65% flora of the country had been surveyed so far (Goutam et al., 2007). This also enhances the probability of getting novel molecules from the plants.

2.2. WORLD TRADE FOR MEDICINAL PLANTS

The world market for plant-derived chemicals / pharmaceuticals, fragrances, flavors, and color ingredients, alone exceeds several billion dollars per year. Classic examples of phytochemicals in biology and medicine include taxol, vincristine, vinblastine, colchicine as well as the Chinese antimalarial - artemisinin and the Indian ayurvedic drug forskolin. Trade in medicinal plants is growing in volume and in exports. According to the WHO estimates, the present demand for medicinal plants is about 14 billion US dollars per year (Dubey et al., 2004). Projected demand by the year 2050 is estimated to be around 5 trillion US dollars (Samthirakani et al., 2006). The results of national survey indicated a marked increase in number of individuals using alternative therapies (Gohil and Patel, 2007). The botanical market inclusive of herbs and medicinal plant in the USA is estimated approximately 1.6 billion US dollar per annum and India with 32,000 tonnes per annum dominates the international market. To satisfy growing market demands,
surveys are being conducted to unearth new plant sources of herbal remedies and medicines (Hoareau and DaSilva, 1999).

2.3. MEDICINAL PLANTS IN DRUG DISCOVERY

Current research in drug discovery from medicinal plants involves a multifaceted approach which includes botanical, phytochemical, biological and molecular techniques. Medicinal plant drug discovery continues to provide new and important leads against various pharmacological targets including cancer, AIDS, Alzheimer’s, malaria etc. Despite the recent interest in molecular modeling, combinatorial chemistry, other techniques of synthetic chemistry, pharmaceutical companies and funding organizations are giving emphasis on natural products (particularly medicinal plants) that remain an important source of new drugs and new chemical entities (NCEs). 61% of the 877 small-molecule NCEs introduced as drugs worldwide during 1981–2002 were inspired by natural product (Newmann et al, 2003). These include natural products (6%), natural product derivatives (27%), synthetic compounds with natural products-derived pharmacophore (5%) and synthetic compounds designed from natural products (natural products mimic 23%) (Jachak and Jain, 2006).

FDA approved anticancer and anti-infectious drug preparations from natural origin have a share of 60% and 75% respectively (Balunas and Kinghorn, 2005) and for this purpose large number of plant species are screened and bio-assayed worldwide (Abu-Dahab and Afifi, 2007). Of the 121 prescription drugs in use today for cancer treatment, 90 are derived from plants and almost 74% of these, including taxol, were discovered by investigating a folklore claim. Between 1981 and 2002, 48 out of 65 drugs approved for cancer treatment were natural products, based on natural products, or mimicked natural products in one form or another (Aggarwal et al, 2006). Furthermore, many phytochemicals with different pharmacological properties have shown responses for the prevention or treatment of different tumors e.g., flavones, flavanols, isoflavones, catechins, and taxanes (Demeule et al, 2002; Surh, 2003; Dorai and Aggarwal, 2004; Ghersi et al, 2005).
The success of anti-cancer drug development can be illustrated from the efforts of the National Cancer Institute (NCI), USA. In this effort, field explorations are largely guided by the so-called biodiversity or ‘random’ collection approach, with ethnobotanical or ethnopharmacological information playing a minimal or no role. NCI launched its effort in 1955 and from 1960–82 about 114,000 extracts from an estimated 35,000 plant samples (representing 12,000–13,000 species) collected mostly from temperate regions of the world were screened against a number of tumor systems (Cragg and Boyd, 1996).

### 2.4. PLANT BASED ANTICANCER AGENTS IN CLINICAL USE

Commercially nine plant-derived compounds have been approved since 1961 for use as anticancer drugs in the US viz., vinblastine (Velban), vincristine (Oncovin), etoposide, teniposide, taxol (paclitaxel), navelbine (Vinorelbine), taxotere (Docetaxel), topotecan (Hycamtin) and irinotecan (Camptosar). The last three drugs were approved by the Food and Drug Administration in 1996 (Dholwani et al., 2008). Increased efforts are being made to isolate bioactive products from medicinal plants for their possible utility in cancer treatment (Kinghorn et al., 2004). Anticancer agents from plants currently in clinical use can be categorized into four main classes of compounds: vinca alkaloids, epipodophyllotoxins, taxanes and camptothecins.

#### 2.4.1. Vinca Alkaloids

The properties of the Madagascar periwinkle plant *i.e.*, *Catharanthus roseus* has been described in folklore in various parts of the world (Johnson, 1968). The plant yielded four active dimeric alkaloids viz., vinblastine, vincristine, vinueurosidine and vinorelbine. Vinblastine and vincristine are important clinical agents for the treatment of leukemias, lymphomas and testicular cancer. Vinorelbine has important activity against lung cancer and breast cancer (Budman, 1997).
The vinca alkaloids are asymmetric dimeric compounds that are cell cycle specific agents. The mechanism of action of these alkaloids and several of their semi-synthetic derivatives are in common with other drugs like colchicine, taxane etc that block cells in mitosis phase by disrupting microtubules, causing dissolution of mitotic spindles, leading to metaphase arrest in dividing cells and finally disruption of the cell cycle that induces programmed cell death (Ter-Minassian-Saraga and Madelmont, 1983; Binet et al, 1990; Hartwell and Kastan, 1994).

Vinblastine and vincristine are used clinically from 40 years and are approved as a component of combination therapy for use in Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, rhabdomyosarcoma of childhood, neuroblastoma and Wilms’ tumor (Sarna et al, 1985). Four semisynthetic analogs of Vinca alkaloids have been introduced into the clinical treatment of cancer viz., vindesine, vinzolidine, vinepedine, vinorelbine.

### 2.4.2. Epipodophyllotoxins

The two clinically-active agents viz., etoposide (VM 26), teniposide (VP 16-213) are semi-synthetic derivatives of plant product. Epipodophyllotoxin (an isomer of podophyllotoxin) is linked to a plant originally used for the treatment of “cancer”. The *Podophyllum* species (Podophyllaceae), *P. peltatum* Linnaeus (commonly known as the American mandrake or Mayapple) and *P. emodii* Wallich from the Indian subcontinent have a long history of medicinal use including the treatment of skin cancers and warts (Cragg et al, 1993).
Fig 2.2:  A. Structure of Podophyllotoxin             B. Structure of Etoposide

Etoposide and its thiophene analog, teniposide are used clinically to treat small cell lung cancer, testicular cancer, leukemia, lymphoma, small cell lung carcinoma and other cancers (Harvey et al, 1999; Dholwani et al, 2008). However, myelosuppression, drug resistance and poor bioavailability, limit their use and necessitate further structural modifications (Van Maanen et al, 1988). Etoposide and teniposide are similar in their actions as both block the cell cycle specific places, block the phase between the last division and the start of DNA replication (the G1 phase) and also block the replication of DNA (the S phase) in the spectrum of human tumors affected. They inhibit the enzyme DNA topoisomerase II (topo II) and increase DNA cleavage (Cragg and Suffness, 1988).

2.4.3. Paclitaxel

Paclitaxel, isolated in 1971 (Wani et al, 1971) from the bark of the Western yew tree i.e., Taxus brevifolia Nut (Taxaceae), possesses antitumor and antileukemic activity. It became an effective drug for the treatment of breast and ovarian cancers (McGuire et al, 1996). It has subsequently been found in the roots, leaves, stems of the tree and in related members of the yew family (Fuchs and Johnson, 1978). Paclitaxel is a diterpinoid compound that contains a complex taxane ring as its nucleus. The side chain linked to the taxane ring at carbon 13 is essential for its antitumor activity.
Paclitaxel treated cells arrest cell cycle in the G2 and M phases and contain disorganized arrays of microtubules, often aligned in parallel bundles and formation of abnormal spindle asters (Schiff and Horwitz, 1980). Paclitaxel is also used in combination with various drugs for the treatment of cancer like cisplatin (for non-small cell lung cancers), carboplatin (for lungs and the ovaries). The importance of this class of anti-cancer agents may be judged from the fact that 12 and 23 taxane analogs were in clinical and preclinical development respectively (Cragg and Newmann, 2004) in recent past.

2.4.4. Camptothecin

Camptothecin, a natural alkaloid isolated from the Chinese ornamental tree *Camptotheca acuminata* Decne (Nyssaceae). Camptothecin (as its sodium salt) was advanced to clinical trials by the NCI in the 1970s, but was dropped because of severe bladder toxicity and myelosuppression. Its interest was revived when it was found to act by selective inhibition of topoisomerase I (Cragg and Newman, 2004). However, extensive research was performed by several pharmaceutical companies in a search for more effective
Camptothecin derivatives like Topotecan (Hycamtin®) and Irinotecan (CPT-11; Camptosar®). These are now in clinical use, but the extensive structural modification still continues because of the limited natural availability and poor water solubility of the parent compound. These drugs are used for the treatment of several cancers as Topotecan for ovarian and small-cell lung cancers, while Irinotecan for colorectal cancers. Moreover, these drugs are used either as a single agent or in combination with other anti-cancer agents.

Fig 2.4: Structure of Camptothecin

2.5. OTHER PLANT-DERIVED AGENTS IN CLINICAL USE

Homoharringtonine, an alkaloid isolated from the Chinese tree Cephalotaxus harringtonia (Cephalotaxacea), has shown efficacy against various leukemias. 4-Ipomeanol is a pneumotoxic furan derivative, isolated from the sweet potato Ipomoeca batatas (Convolvulaceae) and has been under clinical evaluation as a lung cancer specific antineoplastic agent. Elliptinium, a semi-synthetic derivative from ellipticine, which can be derived from Apocynaceae such as Bleekeria vitensis and is presently used in Europe in the treatment of advanced breast cancer. Flavopiridol is a first anti-cancer agent that
targets cell cycle progression. It is a synthetic flavone derived from the plant alkaloid rohitukine, which was isolated from the leaves and stems of *Amoora rohituka* and later from *Dysoxylum binectariferum* (Maliaceae). Several other promising plant derived compounds are in clinical trials through the auspices of the U.S. National Cancer Institute as potential cancer chemopreventive agents including curcumin (Phase I colon), genistein (Phase I breast and endometrial), soy isoflavones (Phase II prostate), indole-3-carbinol (Phase I breast recurrence), perillyl alcohol (Phase I breast), various forms of retinoic acid (over 100 clinical trials in progress), phenethyl isothiocyanate (Phase I lung), green tea/epigallocate F gallate (Phase II breast, Phase I unspecified cancer, Phase II bladder recurrence) and resveratrol (Phase I unspecified cancer) (Greenwald, 2002; Kelloff *et al.*, 2000). These and other promising phytochemical chemopreventive agents work by various mechanisms of action targeting initiation, promotion and progression of carcinogenesis. Some cytotoxic drugs developed from source are given in Table 2.1.

We have observed copious examples of active principle(s) discovered from medicinal plants (and their analogues thereof) that provided numerous clinically useful drugs. In this connection, the medicinal plants documented in Indian System of Medicine are of immense value and should be explored for drug discovery. Based upon the background of diversified therapeutic values, available scientific literature and use in folklore/traditional system for cancer treatment, five medicinal plants were selected in this study to determine their anticancer potential.
Table 2.1: Anticancer drugs developed from plant source

<table>
<thead>
<tr>
<th>Drug</th>
<th>Origin</th>
<th>Therapeutic use</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camptothecin</td>
<td>Camptotheca acuminate</td>
<td>Used clinically in China against gastrointestinal tumors</td>
<td>Enhances binding of topoisomerase I to DNA</td>
</tr>
<tr>
<td>Topotecan</td>
<td>Analogue of Camptothecin</td>
<td>Antineoplastic agent against ovarian cancer</td>
<td>DNA topoisomerase I inhibitor</td>
</tr>
<tr>
<td>Hycamtin®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Taxus baccata</td>
<td>Antineoplastic agent for treatment of ovarian, breast and bronchial carcinomas</td>
<td>Binding to tubulin subunits and stabilization of microtubulii</td>
</tr>
<tr>
<td>Taxotere®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Taxus brevifolia and T. cuspidate</td>
<td>Antineoplastic agent against breast carcinoma and metastasing</td>
<td>Binding to tubulin subunits and stabilization of microtubulii</td>
</tr>
<tr>
<td>Taxol®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td>Podophyllum species</td>
<td>Antineoplastic agent against SCLC, leukaemia, non-Hodgkin lymphoma, Hodgkin’s disease and testicular cancer</td>
<td>DNA topoisomerase II inhibitor,</td>
</tr>
<tr>
<td>Eposin®, Exitop ® Etopofos® Vepesid®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teniposide</td>
<td>Closely related to Etoposide</td>
<td>Antineoplastic agent used in combinational therapies</td>
<td>DNA topoisomerase II inhibitor</td>
</tr>
<tr>
<td>Vumon®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinblastine</td>
<td>Vinca rosea</td>
<td>Antineoplastic agent used for treatment of Hodgkin’s disease and choreocarcinoma</td>
<td>Antimitotic</td>
</tr>
<tr>
<td>Velbe®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vincristine</td>
<td>Vinca rosea</td>
<td>Antineoplastic agent used in therapies against SCLC, leukaemia and malign lymphoma</td>
<td>Antimitotic</td>
</tr>
<tr>
<td>Oncovin®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vincristine®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>Semi-synthetic, synthesized from Vinblastine</td>
<td>Antineoplastic agent used for treatment of NSCLC and breast cancer</td>
<td>Antimitotic</td>
</tr>
<tr>
<td>Navelbine®</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
2.6.  *Calotropis procera*

2.6.1.  Description and distribution

*Calotropis procera*, known as Akanda/Ak/Sodom Apple, is a small and compact shrub of 5.4 m high with milky latex. The bark of the plant is soft and leaves are sub-sessile, elliptic or obovate. Flowers are white, purple-spotted or pink, in umbellate cymes. Seeds are numerous and ovoid. The plant grows in dry, sandy-alkaline soils and warm climate. It grows well on roadsides and sand dunes upto an altitude of 1050 m. In India, it is found from Punjab, Rajasthan to Assam and Kanyakumari.

2.6.2.  Chemical constituents

Mudarine is isolated from leaves of the plant as a principal active constituent. A yellow bitter acid, resin and 3 toxic glycosides *viz.*, calotropin, uscharin and calotoxin were also isolated from the plant. Few compounds like α- and β- Amyrins, cyanindin-3-rhamnoglucoside, cyclosadol, multiflorenol, procestrol, quercetin-3-rutinoside has been isolated from leaves, stem, latex and root; β-sitosterol, calactin, calotoxin, caltropagein, calotropin, syriogenin, procreroside, uscharin, voruscharin have been isolated from latex; β-sitost-4-en-3-one, stigmasterol have been isolated from flowers; polysaccharide containing D-arabinose, D-glucose, D-glucosamine 3-proteinase have isolated from leaves and benzoliselineolone, was isolated from root-bark of the plant (Chatterjee and Prakashi, 1991). A new norditerpenyl ester namely Calotropterpenyl ester and two unknown pentacyclic triterpenoids namely calotropurenynl acetate and calotrofriedelenyl acetate have been isolated from the root bark. A powerful bacteriolytic agent has been found to be present in the latex.

2.6.3.  Traditional value

The plant enjoys high reputation in Indian system of medicine. Plant is used in spleen complaints, rheumatism, epilepsy, hemiplegia, sores, anthelmintic, smallpox, protracted labor, leprosy, ulcers, piles and tumors (Kumar and Arya, 2006). The whole dried plant is bitter and used as expectorant, thermogenic, anthelmintic and anticarcinogenic. The leaves are used in the treatment of paralysis, arthritis, swellings, leprosy, skin diseases, wounds, ear disease and cancer. The flower is bitter, astringent, digestive, appetizer,
Taxonomical classification

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Gentianales
Family : Asclepiadaceae
Genus : Calotropis
Species : procera

A. AERIAL PART

B. FLOWERS

C. ROOTS AND LEAVES

Fig 2.5: Calotropis procera
tonic, antisialagogue and used against stomachache, piles, asthma, tumors, cholera, asthma (Larhsini et al., 2001). The root bark is bitter, febrifuge, anthelmintic and used against intestinal worms, cough, ascites, anasarca, chronic cases of dyspepsia, flatulence, constipation, loss of appetite, indigestion and mucus in stool.

2.6.4. Pharmacological properties

Root extract has been found to produce cytotoxic effect on COLO-320 tumor cells (Smit et al., 1995). A semi synthetic derivative of a cardenolide isolated from the root- bark showed cytotoxic effect on several human cancer lines and high in vivo tolerance to tumor growth and prolonged survival in the human xenograft models of nude mice (Van Quaquebeke et al., 2005). The chloroform-soluble fraction of roots, ethanolic extract of flowers, aqueous and organic extract of dried latex of the plant also exhibit strong anti-inflammatory activity in animal models of acute and chronic inflammation (Mascolo et al., 1988; Basu and Chaudhuri, 1991). Calotropin, isolated from latex and roots of C. procera inhibits spermatogenesis in male and induce abortion in female rats and rabbits (Arya and Kumar, 2005). Latex of this plant possesses anti-diarrhoeal (Kumar et al., 2008), antihelmintic (Shivkar and Kumar, 2003), anti-inflammatory (Arya and Kumar, 2004), anti-malarial, anti-oxidant (Ahmed et al., 2005) and anticancer (Choedon et al., 2006) activities.

2.7. Cassia occidentalis

2.7.1. Description and distribution

*Cassia occidentalis*, known as Kasondi / Negro coffee, is a small plant that grows 5–8 m high. The leaves of the plant are in 3-5 pairs, flowers yellow, fruits cylindrical and seeds ovoid (Chatterjee and Prakashi, 1991). The species varies from a semi-woody annual herb in warm temperate areas to a woody annual shrub or sometimes a short-lived perennial shrub in frost free areas. The plant is scattered from Himalayas to South in India.

2.7.2. Chemical constituents

The *Cassia* plants are well known for a group of chemicals with strong laxative actions called anthraquinones and bianthraquinones (Ginde et al., 1970; Niranjan and Gupta, 1973; Tiwari and Singh, 1977). The ethanolic extract of the leaves yields flavonoids, glycosides, emodin and roots produce chrysophenol, emodin, physcion and β- sitosterol, which is also found in the flowers and seeds. Anthraquinone contents are higher in the
seeds than roots and leaves (Rai and Shok, 1983). Two new bis (tetrahydro) anthracene derivatives, occidentalol-I and occidentalol-II were isolated from the roots. 1, 8-Dihydroxy-and oxymethyl-anthraquinones, emodol, luteolin, dimethylether-rhamnoside, quercetin and polysaccharides have been reported from the plant (Chatterjee and Prakash, 1997).

2.7.3. Traditional value

The roots, leaves, flowers and seeds of the plant are used extensively in indigenous and folklore medicine systems in India and around the world (Chopra et al, 1992). In the Indian system of medicine, the plant has been documented as bitter, sweet, depurative, thermogenic, purgative, diuretic, expectorant and recorded as useful in vitiated condition of “vata” and “kapha”. The roots are anti-inflammatory, digestive and used in diabetes, strangury, elephantiasis, ring worm, colic, flatulence and scorpion sting. The leaves are used in leprosy, erysipelas, pruritus, wounds, asthma, pharyngodynia and hydrophobia. The seeds are used in leprosy, erysipelas, strangury, flatulence, menstrual problems, tuberculosis, diuretic anemic and liver complaints (Krithikar and Basu, 1933). In Unani medicine, it is used as an antidote of poisons, blood purifier, expectorant, anti-inflammatory agent and a remedy for the treatment of liver diseases. In Mali, the leaves considered to be diuretic, used against oedema, pregnant women yellow fever, headache, conjunctivitis and the seeds brewed into a coffee-like beverage for asthma, malaria, fevers and stomach complaints (Adjanohoun et al, 1985).

2.7.4. Pharmacological Properties

Various researchers have reported its immunostimulant (Bin-Hafeez et al, 2001), antimutagenic (Sharma et al, 2000; 1999), laxative (Grote and Woods, 1951), anti-inflammatory (Sadique et al, 1987), anti-dermatophyte (Caceres et al, 1993), antibacterial (Evans et al, 2002), antiplasmodial (Tona et al, 2004), antifertility (Badami et al, 2003), antimalarial (Tona et al, 2001), antiplasmodial (Gasquet et al, 1993) and antidiabetic (Swanston-Flatt et al, 1989) activity. The leaf extracts had shown ability to protect the liver from various chemical toxins and are also beneficial to normalize enzyme processes and repair damage of the liver (Sharma, et al, 2000).
Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Falbales
Family : Leguminosae
Genus : Cassia
Species : occidentalis

A. WHOLE PLANT

B. SEEDLING

C. MATURE PLANT

Fig 2.6: Cassia occidentalis
2.8. *Cuscuta reflexa*

2.8.1. Description and distribution

The *Cuscuta reflexa* is commonly known as Amarvel or Dodder. It is a slender, leafless, yellowish-green stem parasite on shrub/tree, which almost covers them without contact with the soil. The flowers are subracemose, sometime solitary or in clusters of 2-4. The fruits/capsules are with black marks containing 2-4 black seeds. The plant is found throughout India at high altitudes, grows as parasite on various plants like *Duranta repens*, *Zizyphus mauritiana*, *Acacia nilotica* and sometimes also infest nursery crops, landscaped sites and agricultural crops *viz.*, alfalfa, clovers and tomatoes with broad host range. The parasitic plant used for the study was collected from the host plant *Euphorbia royleana* Boiss.

2.8.2. Chemical constituents

Chemical constituents reported from the plant are D-Mannitol, kaempferol, myricetin, β-sitosterol (berries of the parasitic on *Melia azadirachta*), amarbelin (pigment), cuscutin, cerothic, linolenic, linolic, oleic, stearic and palmitic acid. Isorhamnetin-3-O-neohesperidoside, apigenin-7-O-rutinoside and lycopene from fresh plant (parasitic on *Wrightia tinctoria*), mangiferin (parasitic on *Mangifera indica*), D-mannitol (parasitic on *Santalum album*), luteolin (parasitic on *Glycosmis pentaphylla*), scoparone, melanettin, quercetin and hyeroside (parasitic on *Bougainvillea spectabilis*) are also reported from the plant (Chatterjee and Prakash, 1991; Rastogi and Mehrotra, 1993; Rai *et al.*, 2000; Tripathi *et al.*, 2005).

2.8.3. Traditional value

As reported in the Indian system of medicine, the plant is arcid, bitter, astringent to bowels, aphrodisiac, expectorant, carminative, anthelmintic, act as tonic, purifies the blood and used against muscle pain, headache, cough, vomiting, lumbago, heat of the brain, paralysis and diseases of the spleen. The plant is also used by different tribes for ailments like fits, melancholy and insanity (Agarwal and Dutt, 1935; Sastri, 1950;
Kirtikar and Basu, 2001; Chopra et al, 1992). The decoction of the stem is useful in bilious affections, skin disease and juice of the stem and branches is used to kill lice (Rastogi and Mehrotra, 1993; Yadav et al, 2004). The seed gives a bitter bad taste, used as sedative, diuretic, demulcent, diaphoretic, quartan and against chronic fever, griping, hiccough (Chatterjee and Prakashi, 1991).

2.8.4. Pharmacological action

The plant had reported for anti-fertility (Chauhan, 1999) and α- glucosidase inhibitory activity (Anis et al, 2002). The two novel tetrahydrofuran derivatives namely swarnalin and cis-swarnalin from the aerial parts show significant free radical scavenging activity (Uddin et al, 2007). Methanolic extract of C. reflexa stem inhibits steroidogenesis and possess anticonvulsive properties and shows a broad spectrum of antibacterial properties (Pal et al, 2006). Petroleum ether extract of C. reflexa stem causes psychopharmacological effects in Swiss albino mice (Pal et al, 2003) and reported for hair growth promoting activity (Rathi et al, 2008). The ethanolic extract of C. reflexa possesses antioxidant activity (Yadav and Tripathi, 2004).

2.8.5. Host plant Euphorbia royleana Boiss.

Euphorbia royleana Boiss. belongs to the family Euphorbiaceae, is a shrub of 15 feet with alternate, spathulate, thick and deciduous fleshy leaves. It is commonly found on the outer dry slopes of the western Himalayas at an altitude of 900- 1500 m above sea level. Its fresh latex is claimed to possess anthelminthic, antiseptic, germicidal properties and in traditional system of medicine it is used as a remedy for joint pains and to fill the cavities of decayed teeth (Kirtikar and Basu, 1935; Kaushik, 1988). The latex has demonstrated anti-inflammatory activity and its ethyl acetate fraction has demonstrated immunosuppressive properties in mice (Bani et al, 2000; Bani et al, 2005).
Taxonomical classification

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Solanales
Family : Convolvulaceae
Genus : Cuscuta
Species : reflexa

A. *Cuscuta reflexa* (Whole plant)

B. *Euphorbia royleana* (Host plant)

Fig 2.7: Holoparasitic plant *Cuscuta reflexa* and its host plant *Euphorbia royleana*
2.9. *Eucalyptus citridora*

2.9.1. Description and distribution

*Eucalyptus citridora* Hook. (Myrtaceae) is also known as Blue grass/yukeliptus / Nilgiri. Eucalyptus is a tall, evergreen tree, although native to Australia and Tasmania, it is successfully introduced worldwide and now extensively cultivated in many other countries including India (Nadkarni, 1976). The genus name Eucalyptus comes from Greek word eucalyptus, meaning “well-covered”, and refers to its flowers that in bud are covered with a cup-like membrane (Grieve, 1979). The plant has smooth, uniform or slightly mottled bark, color is white to coppery in summer, narrow-leaved crown which smells strongly of lemons. Flowers are in pear-shaped bud and covered with a cup-like membrane (Grieve, 1979).

2.9.2. Chemical constituents

Chemical constituents isolated are borneol, camphene, cineole, citronellal, citronellyl acetate, p-cymene, limonene, linalool, phellandrene, α- and β-pinenes, piperitone, γ-terpinene, terpin-1-en-4-ol and α-terpineol (Rastogi and Mehrotra, 1991). Leaves are reported to contain essential oil, eucalyptin, β-sitosterol, p-menthane –cis/trans-3, 8-diols, ferulic acid, triterpenoids, quertin and citriodorin (Asolkar et al., 1992). Phytochemical analysis showed that the plant contains monoterpenoid, citronellal, citronellol and eucalyptol (1, 8-cineole), known to be as the active component of the oil (Juergens et al, 1998a; Dagne et al, 2000).

2.9.3. Traditional value

Though native to Australia, it is used therapeutically in traditional medicine systems, including Chinese, Brazilian folk, Indian Ayurvedic and Greco-European (Silva et al, 2003; Trivedi and Hotchandani, 2004). Leaves used traditionally as aboriginal herbal remedy and hot water extract of dried leaves is used as analgesic. The plant is antipyretic, anti-inflammatory and used for the symptoms of respiratory infections such as cold, flu, sinus congestion (Buchman, 1979). Oil of eucalyptus had been traditionally used in
Ayurveda as an antiseptic, for respiratory tract infections, muscle antispasmodic and showed antibacterial activity (Nadkarni, 1976).

2.9.4. Pharmacological properties

_Eucalyptus citriodora_ plant extract possesses antifungal properties (Ramezani _et al_, 2002; Musyimi and Ogur, 2008). Essential oils from _Eucalyptus_ species reported to possess analgesic and anti-inflammatory effects (Silva _et al_, 2003). Oil is used in pharmaceuticals such as cough syrup, lozenges, nasal drops mouthwash (Adeniyi and Ayepola, 2008) and widely used in modern cosmetics, perfumery, food/pharmaceutical industry. It is also used as herbicide, disinfectant, insect repellent (Cribb, 1981; Chevallier, 1996; Gomes-Carneiro _et al_, 1998; Ahmad _et al_, 2002; Setia _et al_, 2007). Monoterpenoid components of the aromatic constituents of the oil are commercially available for the treatment of the common cold and other symptoms of respiratory infection. Citronellal is effective against bacterial and fungal infections. Eucalyptol has been reported to inhibit the production/synthesis of tumor necrosis factor, interleukin-1, leukotriene B4, and thromboxane B2 in inflammatory cells (Nair _et al_, 2008; Cockcroft _et al_, 1998; Juergens _et al_, 1998a; Juergens _et al_, 1998b; Pattnaik _et al_, 1996; Trigg, 1996). Resin contains tannin, known as powerful astringent and used internally in the treatment of diarrhoea and bladder inflammation (Grieve, 1984; Bown, 1995). Some studies have indicated that citronellal and phellandrene, (found in some _Eucalyptus species_) are weak mutagenics and carcinogenics respectively (Takasaki _et al_, 1995).
A. TREE

B. LEAVES

Fig 2.8: *Eucalyptus citriodora*
2.10. *Ficus hispida*

2.10.1. Description and distribution

*Ficus hispida* Linn. belong to Moraceae family and commonly known as Gobla / Peyatti. It is a moderate size tree that grows up to 5 meters in height. Leaves of the plant are opposite, long and with scrubby surfaces. The plant grows well in damp locality, shady places, evergreen forests, waste lands and found throughout India.

2.10.2. Chemical constituents

Chemical and pharmacological studies showed that the plant possesses phenanthroindolizidine alkaloids (Venkatachalam and Mulchandani, 1982), n-alkanes (Bhar and Thakur, 1981), coumarins (Acharya and Kumar, 1984) and triterpenoids (El-Khrisy *et al*., 1980). Leaves of the plant are known to contain hispidin, oleanolic acid, bergapten, β-amyrin and β-sitosterol (Khan *et al*., 1991; Huong and Trang, 2006). Bark comprises of lupeol acetate, β-sitosterol and β-amyrin acetate (Wang and Coviello, 1975; Acharya and Kumar, 1984). Ficustriol and phenanthroindolizidine alkaloid O-methylthylophorindine (Peraza-Sancheza *et al*., 2002) have been isolated from this plant.

2.10.3. Traditional value

The parts of *Ficus hispida* are used in Indian traditional medicine for the treatment of various ailments. All parts are reported to be bitter, cooling, acrid, astringent to the bowels, antidysenteric and useful in “Kapha”, ulcers, billiousness, anemia, piles, jaundice, leukoderma, psoriasis, inflammations, fever, alopecia and diseases of the blood (Kiritikar and Basu, 1987). The fruit act as a coolant, aphrodisiac, tonic, lactagogue and emetic (Condit, 1969; Corner, 1981). A mixture of honey and the juice of the fruits is antihemorrhagic (Nadkarni, 1996). Bark act as emetic and hypoglycemic (Condit, 1969; Corner, 1981). Plant recorded as antitussive, antipyretic, anti-inflammatory, depurative, hemostatic and used in the treatment of anemia and ulcer (Kiritikar and Basu, 1956; Nadkarni, 1976; Rastogi and Mehrotra, 1993).
2.10.4. Pharmacological properties

Leaves of the *F. hispida* are documented for various activities. The methanolic extract of leaves had showed anti-diarrhoeal (Mandal *et al.*, 2002) anti-inflammatory (Vishnoi and Jha, 2004) activity and found to be hepatoprotective in rats (Mandal *et al.*, 2000). Leaves of the plant protect the cardiac tissue by scavenging the free radicals and has cardioprotective effect on cyclophosphamide provoked oxidative myocardial injury in a rat model (Shanmugarajan *et al.*, 2008). The plant is also known for anti-oxidant and antiperoxide activities against the prooxidant-antioxidant imbalance elicited by azothiprine (Shanmugarajan and Devki, 2008). Bark of *F. hispida* has been reported for hypoglycemic activity in normal and diabetic albino rats (Ghosh *et al.*, 2004).
A. PLANT

B. LEAVES

C. FIG

Fig 2.9: Ficus hispida

Taxonomical classification

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Urticales
Family: Moraceae
Genus: Ficus
Species: hispida