Chapter II

Review of Literature
2. REVIEW OF LITERATURE:

The importance of medicinal plants in traditional health care practices, providing clues to new areas of research and in biodiversity conservation is now well recognized. In the 18th century, the medicinal plants were ignored and thought that synthetic drugs can replace them. But the synthetic drugs can not hide the glaring inconsistencies that characterize it. Toxic medications, out of hand rejection of new research and time proven traditional medical techniques and especially the prevalence of side effects from its own treatments have made these drugs one of the major cause of death and suffering.

Today herbal medicaments are replacing the synthetic drugs and antibiotics. The plants stand in first position in the development of modern drugs because they are the store houses of complex chemical substances having biodynamic compounds with unrealized potential for the use in modern medicine.

Right from the beginning documentation of medicinal uses of plants provided important drugs of modern day. Even today there is much scope in this field of research because almost 80 % of human population in the developing countries is dependent on plant for the health care.
2.1. Plants investigated:

2.1.a. Name of the plant: *Adhatoda vasica* L.

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Lamiales
Family: Acanthaceae
Genus: *Adhatoda*
Species: *vasica*
Common name: Vasaca (S), Banna (H), Adulsa (M), Aduso (G), Addasaramu (Te), Adadorai (T).
Habit: Shrub.

Geographical distribution:

It is indigenous to India, and found from the Himalayan track up to an altitude of 1000 m in the Konkan region including Maharastra. It is also found in Myanmar, Sri Lanka and Malaya. In Karnataka it is found in Bangalore, Belgaum, Chikmaglur, Coorg, Dharwar, Kolar, Mysore, North Kanara, Shimoga, South Canara.

Key characters: A bunch of leaves on woody stem. Evergreen branched shrub.
Flowers large, white with red or yellow at throat.
The leaves have quinazolin derivatives such as vasicine, vasicinone and 6-hydroxy vasicine. Biologically vasicine is oxidized to its ketonic derivative vasicinone and which acts as a bronchodilator. It also contains volatile oil and vasakin. It also contains adhatodic acid (Kokate et al., 2002). The leaves also contain betaine, fats, resins, sugar, mucilage, vitamin C, essential oil containing limonene. The inflorescence contains vasicinone, vascinine and β-sitosterol. Flowers contain vascinine. Colouring matter in the flower includes luteolin, quercetin, kaempferol and β-amyrin, tritriacontane and β-sitosterol. Seeds contain fatty oil and resin. Aerial parts contain aliphatic hydroxyl ketones, aliphatic alcohol.

The juice samples of the leaf of Adhatoda vasica were evaluated for the total alkaloid content by spectro photometric method and vasicine content by thin layer chromatography densitometric method using high performance thin layer chromatography, which was validated for precision, repeatability and accuracy. The total alkaloid content varied from 0.3 mg/ml to 5.93 mg/ml and that of vasicine content varied from 0.2 mg/ml to 5.64 mg/ml in juice samples obtained using different methods. The steaming of fresh leaves under 15 lb pressure yielded same quantity of juice as the traditional bolus method (25 ml/100g leaf) and its alkaloid content and vasicine content (4.05 ± 0.12 and 3.46 ± 0.06 mg/ml) respectively were very high when compared to the other methods (Soni et al., 2008).
Bromohexine and abroxol, semisynthetic derivatives of vasicine from the Indian shrub *Adhatoda vasica* shows growth inhibitory effect on *Mycobacterium tuberculosis* (John *et al.*, 1996).

High performance liquid chromatographic method for the determination of the quinazoline alkaloids vasicine and vascinone in *Adhatoda vasica* Nees. and studies on the stability of vasicine in solution and in plant extracts are reported and vasicinone appears to be an artifact of extraction and storage (Keith *et al.*, 1983).

A study of absorption of vasicine from methanol and ethanol extract of vasaka in the small intestine of rats using Dolusisio technique showed that maximum absorption of vasicine was observed in the duodenal region (673± 5.256%) and minimum absorption was observed in the colon (42.6 ± 7.314%) and moderate absorption was observed in the jejunum and ileum (77.2± 3.415% and 46.9± 3.217%) (Ram *et al.*, 2007).

The previous assigned 3R configuration of (-) –vascinone as been reversed and this pyrrolo (2-1-b) quinazoline -9-one has been shown to have the 3,5 configuration (3) on the basis of an X-ray diffraction study of (+) vasicinone hydrobromide. The 3R stereochemistry assigned earlier to (-) vasicine has been reversed by reinvestigation of the x-ray diffraction analysis of the hydrobromide. The absolute stereochemistry of the alkaloids (+) vasicinol and vasicinolone have been interrelated and should also have the 3S configuration (Balawant *et al.*, 1996). *Adhatoda vasica* has a good antitussive activity. Intra venously it was 1/20
- 1/40 as active as codein on mechanically and electrically induced coughing in rabbits and guinea pigs (Dhuley, et al., 1999). A new quinazoline alkaloid isolated from the leaves of *Adhatoda vasica* has been identified as 1, 2, 3, 9- tetrahydro-5-methoxypyrrolo (2,1-b) quinazoline – 3- ol (Chowdhury et al., 1985).

The methanolic extract of leaves of *Adhatoda vasica* showed the highest sucrase inhibitory activity with sucrose as substrate. Vasicine and vasicinol showed a high sucrase inhibitory activity and the IC$_{50}$ values were 12 µm and 250 µm respectively. Both the compounds were reversible inhibitors of sucrase. Kinetic data revealed that the compounds inhibited sucrase hydrolyzing activity of rat intestinal $\alpha$ – glucosidase competitively with Ki values of 82 µm and 183 µm respectively (Hong Gao et al., 2008).

The leaf extracts of *Adhatoda vasica* showed significant hepatoprotective effect at doses of 50 – 100 mg/kg P.O. on liver damage induced by d-galactoamine in rats (Dipankar et al., 2005).

Two new pyrroloquinazoline alkaloids viz. 1, 2, 3, 9- tetrahydropyrrolo (2, 1-b) quinazolin -9 - one - 3R- hydroxyl - 3 (2’ - dimethylamino phenyl (desmethoxyaniflorine) and 7- methoxy 3 -R - hydroxy- 1,2, 3, 9 - tetrahydropyrrolo (2,1-b) – quinazolin – 9-one (7-methoxyvasicinone) together with several known compounds were isolated from the leaves of *Adhatoda vasica*. Their structures were established by spectroscopic and X-ray diffraction analysis (Rajinder et al., 1996).
2.1.b. **Name of the plant:** *Tabernaemontana coronariae*

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Gentianales

Family: Apocynaceae

Genus: *Tabournaemontana*

Species: *coronariae*.

**Common name:** Nandyavartha (S), Dudh mogra (H), Chandini (M), Chandini (G), Nandyavarthamu (Te), nandiyarvattam (T), Nandivattam (Mal), Nandibatta (Canarese).

Habit: Small shrub.

**Geographical distribution:**

*Tabernamontana coronariae* is a cultivated plant and is distributed in the Western Ghats, Bellary and Vishakapatnam districts of Madras presidency.

Key characters: Woody stem with milky latex and white flowers. Leaves opposite, elliptic – oblong. Flowers white, solitary or in few flowered cymes.

Pillay (1938) found that the roots of the plant contain fatty acids, phytosterols, and some easily oxidisable amorphous bases. Tabernaemontananine, 

\[(C_{20}H_{26}N_2O_3)\] a colourless crystalline alkaloid (m.pt. 208° – 209°C) coronarine a
yellow crystalline alkaloid (C_{44}H_{56} N_{4}O_{6}) (m.pt. 196° – 198° C) have been isolated from the alkaloids soluble in light petroleum (b.pt. 40° to 60° C) fractions.

The other constituents identified in alcolholic extract of the bark are fatty matter cerotic and loliec acids, resin acids, a colourless crystalline substance which appeared to be a resin alcohol (C_{17}H_{32}O_{4}) and (m.pt. 180° C) caoutchouc, resins, sugars and potassium salts.

The ethanol and aqueous extracts of *Tabernaemontana coronariae* flowers showed *in vitro* superoxide, hydroxyl radicals, nitric oxide scavenging and lipid peroxidation inhibiting activities. Antiinflammatory activity of the ethanol extract has been evaluated (Priya *et al.*, 2006). A preliminary qualitative analysis of the latex of the two varieties of *Tabernaemontana* shows that it contains proteolytic enzymes, carbohydrates, dehyllrogenases, lysozyme, and organic particles (Rao & Manju, 1965).

*Tabernaemontana sanonna* Ruiz and Pav. (Apocynaceae) together with bark of *Vismia tomentosa* Ruiz and Pav. (Clusiaceae), fruits of *Solanum straminifolium* Var *Straminofolium* Jacq. (Solanaceae) and stems of *Zamia lindenii* Regel ex. Anndre. (Cycadaceae) showed low activity against amastigote stage of *Leishmania* (IC_{50} around 50 μg/ml). *Tabernaemontana sanonho* displayed good activity on promastigotes (IC_{50}<10μg/ml) (Estevez *et al.*, 2007).

The bark of *Tabernaemontana markgrafiana* yielded five acetylated pentacyclic triterpenes and 24 monoterpene indole alkaloids (Helene *et al.*, 1994).
Hexane extract from old leaves, roots, flowers, and stems of *Tabernaemontana divaricata* was rich in hydrocarbons (Behra and Colleagues, 1995). Cell culture studies were made to investigate the biosynthesis and metabolism of secondary metabolites (Schripsema *et al.*, 1991). The cell culture of the plant has non-alkaloids like anthranilate synthase (Poulsen *et al.*, 1991), isopentenyl diphosphate isomerase, prenyl transferase, squalene synthetase, qualene 2, 3-oxide, cycloartenol cyclase, squalene 2, 3-oxide cyclase (Fluton *et al.*, 1994). A-amyrin acetate (Rastogi *et al.*, 1980), lupeol acetate (Dagnino *et al.*, 1991), a-amyrene, lupeol, cycloartenol, β-sitosterol, campesterol (Van der Heijden *et al.*, 1989) are present in the root bark.

The leaves, flowers, and roots contain alkaloids like Methoxy-N-methuldihydropericyclivine, isovoacangine and isovoacristine (Arambewela *et al.*, 1991), the leaves contain 5-Hydroxyvoaphylline (Atta-Ur-Rahaman *et al.*, 1986), 5-oxo-11-hydroxyl voafillin (Atta-Ur-Rahaman *et al.*, 1985) and lahoricine (Atta-Ur-Rahaman, 1984). Conodusarine in the stems and barks (Kam *et al.*, 2004), conophylline (Kam *et al.*, 1992) conophillidine (Kam *et al.*, 1993), conofoline and pachysiphine (Kam *et al.*, 1995) are present in the leaves. Conilidine, conolobine A and conolobine B are present in the stems and barks of *Tabernaemontana coronariae* (Kam *et al.*, 2004), conophysillinine from the leaves (Kam *et al.*, 2003), cononaridine found in the leaves (Raj *et al.*, 1974), 19-hydroxycoronaridine and 3-oxocoronaridine (Rastogi *et al.*, 1980), 20-dihydroervahanine A is present in the stem of *Tabernaemontana coronariae*.
Cell suspension culture has Voaphylline hydroxyindolenine (Van der Heijden et al., 1988), tubotaiwine (Pawelka and Stoeckight, 1983), pericyclivine and perivine (Van der Heijden et al., 1988). The leaves of *Tabernaemontana coronariae* contain voafiridine (Kam et al., 1996). Vocraangine hydroxyindolenine, voacristine and voacristine hydroxyindolenine present in the whole plant (Sharma et al., 1988). The root bark contains α-amyrin lupeol, cycloartenol, β-sitosterol, campesterol, benzoic acid and aurantiamide acetate (Van der Heijden et al., 1989).

Coronaridine shows analgesic effect (Kupchan et al., 1963), hypotension and bradycardia (Taesotikul et al., 1998) and antiinflammation (Taesotikul et al., 2003) *in vivo*. An *in vitro* study demonstrated that apparicine (18) at the concentration of 250 μg/ml can inhibit the activity of Polio III virus (Andrade et al., 2005). The alkaloids of *Tabernaemontana divaricata* enhance cholinergic activity (Taesotikul et al., 1998). Hippocratic or behaviour screening in an *in vivo* study of ethanol extract from *Tabernaemontana divaricata* was made by Taesotikul and Colleagues (1989). *Tabernaemontana divaricata* may be a new therapeutic target for Alzheimer's disease. Moreover, *Tabernaemontana australis* has also shown acetyl cholinesterase inhibiting activity *in vitro* (Andrede et al., 2005). The antioxidative effects of *Tabernaemontana divaricata* have been studied by various investigators using carbon tetra chloride induce hepatotoxicity mode (Gupta et al., 2004). Voacangine potentiated the hypnotic effects of barbiturates and had an analgesic as well as a local anesthetic activity in a mouse model (Okuyama et al., 1992).
Tabernaemontana pandacaqui extracts include hypotensive and negative chronotropic and inotropic effects observed in a rat model (Taesotikul et al., 1989).

The indole alkaloids were extracted from Tabernaemontana catharinensis using super critical carbon dioxide as solvent and ethanol as co-solvent. The high global yields were obtained at 350 bar (1.30 x 10⁻² and 1.54 x 10⁻² kg/kg) at temperature of 35⁰ to 45⁰C respectively. The cost of manufacturing the extracts obtained at 350 bar, 45⁰C using 5% (v/v) of ethanol was US$ 79.35 Kg⁻¹ of extract.

Indole alkaloid enriched fraction obtained from the leaf extracts of Tabernaemontana catharinensis in a mixture of carbon dioxide and ethanol exhibited a potent effect against intracellular amastigotes of Leishmania amazonensis, a causative agent of new World cutaneous leishmaniasis. The indole alkaloid enriched fraction also inhibited TGF –β production, which could have facilitated AF3 mediated parasitic killing (Deivie Costa Soares et al., 2007).

A new bisindole alkaloid, 19, 20-dihydroeravahanine A was isolated from the stems of Ervatamia coronaria grown in Brazil, together with five known alkaloids, coronaridine, heyneanine, voacristine, voacamine, decarbomethoxy voacamine and five phenolic acids: vanillic, gentisic, syringic, 4- hydroxybenzoic and salicylic acid. The aqueous and alcoholic extracts when administered P.O. or i.p. to rats in before sub plantar injection of carrageenin had a significant anti-
inflammatory effect. The alcoholic extract also had an analgesic effect and increased to pentobarbital induced sleeping time (Henriques et al., 1996).

Anthranilate asynthase is an enzyme detected from the *Tabenaemontana diverticata* cell cultures by HPLC assay (Poulsen et al., 1991).

Five known enzymes that were detected for the first time in *Tabernaemontana diversicata* cell suspension culture isopentenyl diphosphate isomerase, pronyl transferase, squalene synthetase, qualene 2, 3, oxide cycloartenol cyclase and squalene 2,3 – oxide cyclase (Fluton et al., 1994).

Reinvestigation of leaves and twigs from *Tabernaemontana glandulosa* yielded 11 indole alkaloids besides six ubiquitous phenyl propanoid (Hans Achenback et al., 1994).

2.1.c. **Name of the plant: Asparagus racemosus**

Kingdom: Plantae

Division: Magnoliophyta

Class: Liliopsida

Order: Asperagales

Family: Liliaceae

Genus: *Asparagus*

Species: *racemosus*
Common name: Shatavari (S), Sharavar (H), Asaith (M), Shathavari (G), Chellagadda (Te), Shadvari (T).

Habit: A woody climbing shrub.

**Geographical distribution:**

It is distributed throughout the tropical Asia, Africa and Australia. In India it is found in the tropical parts and from Himalaya to the altitude of 1,300 to 1,400 m. It is also found in the dry deciduous forests of Maharashtra. In Karnataka it is found in Bangalore, Belgaum, Chikmaglur, Coorg, Dharwar, Hasan, Kolar, Mysore, North Kanara, Shimoga, South Canara and Tumkur.

**Key characters:**

Perennial tuberous scandant shrubs with triquetrous cladodes and stem with spines. Flowers white, in simple or branched racemes. Berry globose. The stem is thorny with feathery leaves.

**Chemicals:**

Shatavari roots contain four steroid saponins shatavarin I – IV (0.2%). Shatavarin I is the major glycoside with three glucose and rhamnose moieties attached to sarsapogenin, where as the in shatavarin IV two glucose and one rhamnose moieties are attached.

Flowers and fruits contain querceitin, rutin and hyperoside, while leaves contain diosgenin and quercetin.
Shatavari roots are used as galactogogue tonic and diuretic. Shatavarin I is reported to possess antioxidic property. Roots are largely used for medicinal oil recommended in the treatment of rheumatism and nerve disorders. It is used in Ayurvedic for abortion and safe delivery justified by uterine blocking activity.

Two major steroidal saponins Shatavarin I and IV were isolated by RD-HPLC and the structures were determined by NMR studies. The structures 3-0 \{[\beta-d-glucopyranosyl (1-2)] [\alpha-1-rhamnopyranosyl (1-4)] -\beta-d-glucopyranosyl\} -26-O- (\beta-d-glucopyranosyl) -(25S) – 5 \beta – flurostan – 3 \beta, 22 \alpha, 26 – triol and 3-O- \{[\beta-d- glucopyranosyl (1-2)] [\alpha- 1- rhamnopyranosyl (1-4)] – \beta - d-glucopyranosyl\} - (25S)- 5\beta – spirostan – 3 \beta – ol did not match with the structures reported previously (Patricia et al., 2006).

A new steroidal saponin, shatavarin V, (3-0- { [\alpha-L-rhamnopyranosyl (1-2)] [\beta-d- glucopyranosyl (1-4)] - \beta – d – glucopyranosyl} - (25S) – 5 \beta- spirostan – 3 \beta – ol) was isolated from the roots of *Asparagus racemosus* by RP – HPLC and its structure was determined by 1D and 2 D NMR studies (Patricia et al., 2006).

The roots of *Asparagus racemosus* were used as a source of inulin for the production of inulinase from *Kluyveromyces marxianus* YS-1 (Singh et al., 2006.)

Five steroidal saponins shatavarins V – X, together with five known saponins, shatavarin I (or asparoside B), Shatavarin IV (or asparinin B), shatavarin
V, immunoside and schidigerasaponin D5 (or asparanin A) have been isolated from the roots by RP HPLC and characterized by spectroscopic experiments (Patricia et al., 2006).

Phytoecdysteroids, plant steroids which are analogue of invertebrate steroid hormones have been identified in the four species (Asparagus falcatus, Asparagus larscinus, Asparagus ramosissimus and Asparagus scandens) have been identified (Laurence Dinan et al., 2001).

Three steroidal saponins racemoside A(1), B (2) and C (3) were isolated from the methanolic extract of fruit of Asparagus racemosus and characterized as (25 S) – 5 β –spirostan 3 β –ol-3-O- {β –D-glucopyranosyl (1-6) – [α – rhamnopyranosyo (1-6) β –d -glucopyranoside}, (25S) – 5 β – spirostan – 3β- ol-3-O- α -1 – rhamnopyranosyl (1-6) – β-d- glucopyranosyl (1-6) –β –d -glucopyranoside and (25S) - 5β – spirostan – 3 β – ol – 3-O- {α- 1-rhamnopyranosyl (1-6) – [α 1 rhamnopyronosyl (1-4) ] - β –d- glucopyranoside} respectively using chemical and spectrometric analysis (Debayan Mandel et al., 2006).

A new 9, 10 – dihydrophenanthrenen derivative named racemosol was isolated form the roots of Asparagus racemosus and its structure was elucidated by spectraoscopic analysis as 9, 10 – dihydro – 1’-5- dimethoxy – 8 – methyl – 2, 7 – phenanthreneoil (Toshi Kozu Sekine et al., 1997).
The ulcer protective effect of methanolic extracts of fresh roots showed significant protection against acute gastric ulcers induced by cold restrain stress, pyloric ligation, aspirin plus pyloric ligation and duodenal ulcers induced by cysteamine. It also healed chronic gastric ulcers induced by acetic acid after 10 days treatment (Sairam et al., 2003).

*Asparagus racemosus* significantly inhibited OTA – induced suppression of chemotactic activity and production of IL – 1 and TNF –α by macrophages. It induced excess production of TNF –α in macrophages obtained from mice treated with the carcinogen ochratoxin A (Dhuley, 1997).

The plant has potent antioxidant properties in vitro in mitochondrial membranes of rat liver (Jayashree et al., 2000).

The methanolic extract of the root showed significant antitussive activity on sulfur dioxide induced cough in mice (Subhash et al., 2000). Aqueous and ethanolic extracts of *Asparagus racemosus* exhibited high mortality rate against *Biomphalaria pfeifferi* and *Lymnaea natalensis*. The activities are attributed to the presence of terpenoids, steroids and saponins in the plant extracts (Chifundera et al., 1993).

*Asparagus racemosus* exhibited various immunopharmacological activities in cyclophosphamide (CP) treated mouse ascetic sarcoma (Sham Diwanay et al., 2004).
The methanolic extracts have significant antidepressant activity and this effect is probably mediated through the serotonergic and noradrenergic system and augmentation of antioxidant defenses (Girish et al., 2004).

2.1.d. **Name of the plant:** *Leucas aspera*

**Kingdom:** Plantae  
**Division:** Magnoliophyta  
**Class:** Magnoliopsida  
**Order:** Lamiales  
**Family:** Lamiaceae (Labiatae)  
**Genus:** *Leucas*  
**Species:** *aspera*  

**Common name:**  
Drona pushpi, chitrapatrika, phalepushpa, karabhapriya (S), tumbe (K), chottahalkusha (H), tumba, thumba, thumpa (Mal) (Eby. Abraham)

**Habit:**  
A small erect much branched annual herb grows up to 60 cm in height. It is erect herb with diffuse quadrangular branches.

**Geographical distribution:**  
It grows as a weed on wastelands and road sides all over India. In Karnataka it is found in Bangalore, Bellary, Kolar and Mysore.
Uses:

Juice of leaves applied externally in psoriasis, chronic skin eruptions and painful swellings. Flowers given with honey in coughs and colds. Herb used as an antipyretic.

The plant is used as an insecticide and indicated in traditional medicine for coughs, colds, painful swellings and chronic skin eruptions. The plant contains long chain aliphatic compounds, a triterpene leucolactone, sterols – sitosterol, campesterol, stigmasterol and novel phenotic compound (Mangathyaru et al., 2005). Flavonoids, reducing sugars, sterols, alkaloids, saponins and volatile terpenes have been analyzed using preliminary phyto-chemical analysis (Mangathayaru et al., 2005). Methanol extract of Leucas aspera has shown hepatotoxicity in rats (Mangathayaru et al., 2005). The crude alkaloid and non alkaloid fractions of Leucas aspera has shown anti-inflammatory activity. A liquid alkaloid has been isolated from the aerial parts of Leucas aspera (Willd). Link and identified as nicotine, based on phyto chemical, TLC, HPTLC and R-P HPLC analysis (Mangathyaru et al., 2005).

Four different crude extracts petroleum ether, chloroform, ethanol and water of Leucas aspera Spreng. were investigated for anti-inflammatory and analgesic activities in albino rats and mice. Ethanol and distilled water also exhibited significant anti-inflammatory activity and significant analgesic effect was shown by petroleum ether and ethanol extract (Saundane et al., 2000).
Inhibitory fraction of *Leucas aspera* on Prostaglandin induced contraction in Guinea pig ileum provided four new diterpenes, leucasperones A (1) and B (2) and leucasperols A (3) and B (4) and three new isopimarane glycosides, lucasperosides A, B, and C (5-7) with asperphenamate, maslinic acid (-) – isololiolide, and linifolioside. Leucasperone A(1), leucasperoside A (5) and B (6) and linifolioside showed inhibition of prostaglandin induced contractions (Samir Kumar Sadhu *et al.*, 2005).

Two new long chain compounds 1- hydroxytetratriacontan -4- one and 32 – methyltetratriacontan – 8-al, along with dotriacontanol have been isolated from the shoots of *Leucas aspera* and characterized by spectral data and chemical studies (Triguna Misra *et al.*, 1992).

The ethanolic extract of *Leucas aspera* root produced significant writhing inhibition in acetic acid induced writhing in mice at the doses of 250 and 500 mg/kg. The extract showed a significant free radical scavenging activity with an IC$_{50}$ of 8 µg/ml. The extract also showed significant lethality to brine shrimp with an LC$_{50}$ value (Rahman *et al.*, 2007).

Leucolactone, isolated from the root of *Leucas aspera* has been characterized as 3 β, 16 α – dihydroxyoleanan – 28 – 13 β –olide on the basis of $^1$H, $^{13}$C NMR, 2D NMR and mass spectral studies (Bhim Prasad Pradhan *et al.*, 1990).
Methanolic extract of leaf of *Leucas hirta* was found to possess significant wound healing activity and the aqueous extract decreased the period of epithelialization and increased the rate of wound contraction, skin breaking strength, granulation tissue dry weight, hydroxyproline content and breaking strength of granulation tissue histopathological study of the granulation tissue evidenced increased collagenation (Manjunatha et al., 2007).

The analgesic activity of the methanol and acetone extracts of *Leucas inflata* has CNS depressant properties, manifested as antinociception and sedation. The extract also has anti inflammatory and antipyretic actions (Alyousuf et al., 2002).

2.1.e. Name of the plant: *Mimosa pudica*

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Fabales

Family: Fabaceae

Sub-Family: Mimosoidae.

Genus: *Mimosa*

Species: *pudica*

Common name:

Sensitive plant, sleeping grass (E), sensitive plant (F), Lajvanti (H), Tottavadi (H), Tottal vadi (H).
Key characters: Prickly woody herbs with diffuse branches. Leaves bipinnate. Flowers in clustered heads, pinkish.

Geographical distribution:

The species is native to South America, Central America, Tanzania, South Asia, Pacific Islands, Australia. It has been introduced in Nigeria, Seychelles, Mauritius and East Asia.

Chemicals:

The seeds and other plant parts of sensitive plant contain mimosin, an amino acid that is known to cause hair loss and depressed growth in mammals (Arora, 1983). Extracts of the plant have been shown to be diuretic, depress duodenal contractions similar to atropine sulphone, promote regeneration of nerves and reduce menorrhagia (Modern natural, 2001).

Antidepressant activity has been demonstrated in rats (Martinez et al., 2002). The root extracts are strong emetic (Guzman, 1975). Ethanolic extract of Mimosa pudica leaves given by oral route to mice at a dose of 250 mg/kg showed a significant hyperglycemic effect (Amalraj et al., 2002).

Two new C-glycosyl flavones were isolated from the whole plant of Mimosa pudica and their structures were determined as 6, 7, 3’, 4’-tetrahydroxy – 8-C- (D-L rhmnopyranosyl- (1-2) – β-D-glucopyranosyl flavone (1), 5,7,3’,4’ – tetra hydroxyl – 8-C (β-D- apiose – (1-4) –β-D- glycopyranosyl flavone (2). Their
structures elucidated by chemical and spectroscopic analysis including IR, MS, 1D and 2D NMR spectra (Ke Yuan et al., 2007).

4’’ – Hydroxymaysin and cassiaoccidentalin B, two unusual – C-glycosylflavones from *Mimosa pudica* (Mimosaceae) (Annelise Lobstein et al., 2002). Flavonoid glycosides were isolated from the leaves of *Mimosa pudica* (Umi Kalsom Yusuf et al., 2003).

The dried methanol extract of the root at a dose of 300 mg/kg body weight/day prolonged the length of the estrous cycle with significant increase in the duration of the diestrous phase and reduced the number of litters in albino mice. The root extract altered gonadotropin release and estradiol secretion (Mausumi Ganguly et al., 2007).

Aqueous extracts of dried roots of the plant showed a significant inhibitory effect on the lethality, myotoxicity and tested enzyme activities of venom compared with a alcoholic extracts. The aqueous extracts of root possess compound which inhibit the activity of cobra venom (Monimal Mahanta & Ashish Kumar, 2001).

The aqueous root extract of *Mimosa pudica* dose dependently inhibited the hyaluronidase and protease activities of Indian snakes (*Naja naja, Vipera russelii* and *Echis carinatus*) venom (Girish et al., 2004).
The decoctions of *Mimosa pudica* leaves given intraperitonially at dose of 1,000 – 4,000 mg/kg protected mice against pentylenetetrazol and strichnine induced seizures. It also antagonized N-methyl D-aspartate induced turning behaviour (Ngo Bum *et al.*, 2004).

Comparative antioxidant, antibacterial activities and general toxicity studies on the n-hexane, dichloromethane and methanol extracts of *Mimosa pudica* and *Mimosa rubicaulis* using the 2, 2-diphenyl -1- picryl -hydrazyl assay, the resazur in microtre plate based assay and brine shrimp lethality assay. The dichloromethane and methanol extracts showed prominent antioxidant property, with RC$_{50}$ values ranging from 4.70 x 10-1 to 2.10 x 10 - 2 mg/ml. The dichloromethane and methanolic extracts of *Mimosa pudica* displayed bacteriostatic activity against *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Amphicillin resistant Escherichia coli*, *Stapylococcus aureus* and *Pseudomonas aeruginosa* (Samuel Genest *et al.*, 2008).

2.1. f. **Name of the plant:** *Alstonia scholaris*

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order; Gentianales.

Family: Apocynaceae.

Genus: *Alstonia*

Species: *scholaris*
Common name: White cheek wood, milky pine, pulai.

Habit: It is a tall, green tree with grayish rough bark.

Geographical distribution:

It occurs in Asia pacific region from India, Srilanka, main land, south east Asia and Southern China, Malaysia, Northern Australia and Soloman Islands. Most common in low land coastal areas with annual rainfall of 1,000 to 3,800 mm but is found up to 1,000 m in altitude. In Karnataka it is found in Bangalore, Coorg, Hassan, North Kanara, Shimoga and South canara.

Uses:

The bark is bitter tonic, febrifube, anthelmintic and galactogogue. Used in the liquid extract form for chronic diarrhea, asthma, cardiac troubles. Leaves used in beri-beri, dropsy and congested liver. Latex applied to sores, ulcers, tumours and rheumatic swellings.

Chemicals:

The bark is used in traditional medicines to treat dysentery and malaria. The leaves of Alstonea scholaris collected in India, Pakistan, Thailand contain picrinine alkaloids, while those from Indonesia and Phillipines contain alkaloids based on the angustilobine skeleton. The leaves also contain cholaricine and tubotaiwine.

The major alkaloids obtained from the bark is echitamine, which has antitumour effect on fibrosarcoma in rats and cytotoxic effects on ehrilich ascites carcinoma cell cultures. The extracts of bark have shown the immunostimulating and hepatoprotective effects in mice and antifertility effects in male rats.
The bark is bitter, astringent, acrid, thermogenic, digestive, laxative, antihelminthic, febrifuge, antipyretic, depurative, galactogogue, stomachic, cardiotonic and tonic. It is useful in fevers, malarial fevers, abdominal disorders, dyspepsia, leprosy, skin diseases. Pruritus, tumours, chronic and foul ulcers, asthma, bronchitis, cardiopathy, helminthiasis, agalactia and debility. Juice of the leaves and tincture of the bark are used as galactogogue. It is also used to treat snake bite. It has anti mutagenic activity. The methalonic extract shows antiplasmodial activity.

The aqueous extract shows cellular immune response at low dose and inhibits delayed type of hypersensitivity reaction in high dose. Echitamine shows anticancer effect against sarcoma 180. The plant shows hepatoprotective activity on liver injury induced by CCl₄, β - D - galactosamine, acetaminophen and ethanol. The juice of the plant heals ear ache (Arul Mozhi et al., 2007).

Ursolic acid (3 - β - hydroxyuro - 12 enolic acid) isolated from the flowers is a triterpenoid compound has hepatoprotective activity, anti-inflammatory activity, hypoglycemic activity anti - tumour and antihyperlipidemia activity (Prabha Shetty et al., 2007).

The petroleum ether extract and methanol extract of the bark of *Alstonia schloarisis* were found to be devoid of antimalarial activity in mice infected with *Plasmodium berghei* (Manoj and Virender, 1990).
The major alkaloid echitamine displayed little antiplasmodial activity, but quinoline alkaloids from *Alstonia coriaceae* (corialstonine and corialstonidine) have some activity against *Plasmodium falciparum* (Colin Wright *et al*., 1993).

The petrol, dichloromethane, ethyl acetate and butanol fractions exhibit improved and broader spectrum of antibacterial activity (Khan *et al*., 2003).

19-epischolaricine, N6-Methyl scholaricine, N8-Methyl bunamine and vallesamine Nb-oxide were isolated and their structures determined by spectral and chemical methods. The leaves of the plants from Taiwan and Thailand have alkaloids like Picrinine, nareline and alschomine. The leaves of plants from Indonesia and Philippines have angustilobine B (Tatsuo Yamauchi *et al*., 1990).

12-Methoxyechitamidine was isolated from the leaves of *Alstonia scholaris* (Avijit & Arup, 1981). A new alkaloid, scholaricine has been isolated to which structure (demethyl scholarine) has been assigned (Atta-Ur-Rahman *et al*., 1985). A new indole alkaloid, alstonamine and sitsirikine type indole alkaloid, rhazimanine isolated from the leaves of *Alstonia scholaris* (Atta-Ur-Rahman *et al*., 1987).

Quercetin 3-o-β-D-Xylopyranosyl, β-D galactopyranoside and lyoniresinol-3-o-β-D glucopyranoside are the active principles present in the
aqueous methanol extract of dried Devil tree, which is used to insulin dependent diabetes mellitus (Nilubon Jong Anurakkun et al., 2007).

Nareline ethyl ether, 5-epinareline ethyl ether and scholarine –N(4) –oxide were isolated form *Alstonia scholaris* (Toh-Seok Kam et al., 1997).

The acute toxicity test of hydroalcoholic extract on mice depends on the season of collection. The Swiss Albino mice were found to be most sensitive followed by the DBA and C57BL. The rats are more sensitive than mice as the LD₅₀ dose of *Alstonia scholaris* was lesser for rats than mice (Manjeshwar Shrinath Baliga et al., 2004). Akuammicine -N₆-oxide; Ψ Akuammigine: N₆ -demethylechitamine: tubotaiwine have been isolated from the roots (Warank Boonchuay et al., 1976).

The chemopreventive effect of various doses of hydroalcoholic extract of *Alstonia scholaris* was studied on the benzo(a) pyrene induced fore stomach carcinoma in female mice. The treatment of mice with different doses in drinking water before and after treatment with carcinogen, exhibited chemopreventive activity (Ganesh Chandra et al., 2003).

Three new indole alkaloids 17-o-adetyl –Nb-demethylechitamine, echitamidine N – oxide and echitaminic acid have been isolated form the stem bark of *Alstonia glaucescence* along with one iridoid compound sweroside and five known indole alkaloids, echitamidine, Nb-demethylechitamine, 20-epi-19 –
2.2. Antibacterial activity:

Finding healing powers in plants is an ancient idea. People on all continents have long applied poultices and imbibed infusions of hundreds of indigenous plants dating back to prehistoric period. Clinical microbiologists have two reasons to be interested in the topic of antimicrobial plant extracts. **First**, it is very likely that these phytochemicals will find their way into the arsenal of antimicrobial drugs prescribed by physicians; several are already being tested in humans. The people are aware of over prescription and unsure of traditional antibiotics.

Plants have an almost limitless ability to synthesize aromatic substances, most of which are phenols or their oxygen substituted derivatives. Most are secondary metabolites, of which at least 12,000 have been isolated. The antimicrobial phytochemicals can be divided into several categories as phenolics, polyphenols, quinones, flavones, flavonoids, flavonols, tannins, terpenoids, coumarines, essential oils, alkaloids, lectin and polypeptides.

Antibacterial activity of medicinal plants have been worked by many scientists and some of them are *Adenocalymma alliaceum* (Ganapaty and Beknal, 2004), *Wendlandia tinctoria* (Dinda et al., 2004), *Lantana camara* (Dabur et al., 2004), *Bolusanthus* species (Erasto et al., 2004), *Curcuma longa* (Singh et al., 2004), *Ocimum canum* (Shimpi and Bendri, 2004), *Machaerium multiflorum*
((Muhammad et al., 2003), *Holarrhena antidysenterica* Wall. (Kavita et al., 2004), *Swertia corymbosa* (Ramesh et al., 2002), *Terminalia brownii* (Zakaria Mbwambo et al., 2007). Some of the workers have isolated active constituents from the plants and have studied their antibacterial activity.

2.3. **Wound healing activity:**

Wound may be caused by:

Trauma either accidental or surgical.

Physical, chemical and microbial agents.

Ischaemia, which leads to infarction.

Repair and inflammation are intimately associated. Inflammation, is the immediate response to injury, repair replaces the damaged tissues. Our ability to repair damaged tissue is limited. In the animals of lower kingdom, repair is more complete and extensive. In humans this ability is to a limited degree. Usually, our injuries are repaired by fibrous collagenous tissue, in the process called wound healing leading to scarring, however the lost tissue is not regenerated as in case of animals of lower kingdom. Wound healing is always much the same, although the effect varies widely, depending on factors like kind of injury, its size and the part of body affected.

Medicinal plants are found to be the best alternative for the subsidence of bleeding during formation of wounds.
Due to presence of plant products like active terpenes, alkaloids, flavonoids, vitamins especially high content of folic acids and amino acids, plants possess good therapeutic potential anti-inflammatory agents and promoter of wound healing. The abundant natural resources of India have spurred scientist interest into this field. Few such examples are as follows, Chidambara Murthy et al., (2004) showed that the phenolic compounds present in the methanolic extracts of dried pomegranate (*Punica granatum*) showed wound healing activity, Ghosh et al., (2004) showed the wound healing activity of ethanolic extract of *Tagetes erecta*. The aqueous and methanol extracts of the roots of *Berberis lyceum* (Asif et al., 2007), oleanolic acid obtained from the *Anredera diffusa* (Gustavo Moura Letts et al., 2006), aqueous methanolic extracts of *Leucas hirta* (Manjunath et al., 2006), ethanolic extracts of flowers of *Catheranthus roseus* (Nayak et al., 2006), ethanol extracts of leaf of *Lycopodium serratum* (Manjunath et al., 2007), aqueous extracts of *Allamanda cathartica* and *Lausus nobilis* (Shivananda et al., 2006), deoxyelephantopin isolated from the leaves of *Elephantopus scaber* Linn. (Singh et al., 2005), ethanol extracts of *Morinda citrifolia* L. (Shivananda et al., 2007) also showed wound healing activity.

The chloroform extract of leaves of *Alternanthera sessilis* (Sunil et al., 2008), hydro alcoholic extracts of the leaves of *Ficus religiosa* (Naira Nayeem et al., 2009), the extracts of the flowers of *Matricaria recutita* (Shivananda et al., 2007), the ethanolic extract of *Abutilon indicum* (Roshan et al., 2008), the leaf extracts of *Lantana camara* (Nayak et al., 2008), the alcohol and petroleum ether extracts of rhizomes of *Gentiana lutea* (Matheus et al., 2003), the ethanolic and aqueous
extracts of *Achyranthes aspera* (Jain *et al.*, 2008), *Vanda roxburghii* (Nayak *et al.*, 2006) also showed the wound healing activity.

### 2.4. Analgesic activity:

Analgesics are used to relieve pain. Use of analgesics is causing addiction but herbal drugs show analgesic property with out side effects. Several types of receptors have been identified in the brain allowing *in vitro* binding tests. But *in vitro* test can partially substitute for animal experiments involving pain. Although *in vivo* methods have been used more extensively in part they are still necessary in present research on analgesic tests in animals before herbal extract be administered to the human body. Earlier physicians used portions concocted from herbal extracts for relieving pain. Hippocrates used alcohol and methanolic extract of Opium for the production of the insensibility to pain. It was only when the first alkaloid morphine isolated in 1803 by Sertumer, the scientific era of analgesia was realized. Analgesia can be defined as a reduction of pain perception without the loss of consciousness. The diminution of pain may be a consequence of febrifuge effect of the drug. After the discovery of morphine as an analgesic, lot of research work has been carried out to increase the efficacy of morphine and reduce it’s undesired side effects.

Formukong *et al.*, (1988) showed that cannabinoid (ethanol extract) and the cannabinoids (petroleum extracts) present in the *Cannabinus sativa* showed analgesic activity. The arjunolic acid and dichloromethane and butanol extracts of
the leaves and branches of *Marlierea tomentosa* showed analgesic activity (Karina Louise, 2008).

Other works include *Caesalpinia ferrea* (Carvalho et al., 1996), *Ochna obstusa* (Sivaprakasam et al., 1996), *Psidium guajava* (Kulkarni et al., 1999), *Melia dubia* (Cinu and Rama Sarma, 1999), *Tragia involucrata* (Dhara et al., 2000), *Parkia biglobosa* (Kouadio et al., 2000), *Sida cordifolia* (Franzotti et al., 2000), *Neorautanenia mitis* (Vongtau et al., 2000), *Landolphia owariensis* (Owayele et al., 2001), *Enhydra fluctuans* (Rahaman et al., 2002), *Polygonum hydropiper* (Rahaman et al., 2002), *Pergularia extensa* (Jalalpure et al., 2002), *Chloroxylon swieteni*a (Sentil Raja and Ramakumar, 2003), *Cissus quadrangularis* Linn. (Chatpalliwar et al., 2003), *Carthamus lanatus* (Bocheva et al., 2003), *Coccina grandis* (Thangathirupathi et al., 2003), *Barringtonia racemosa* (Deraniyagala et al., 2003), *Capparis zeylanica* (Chaudhary et al., 2004), *Melastoma malabaricum* (Sulaiman et al., 2004), *Sapindus rarak* (Roujjanawate et al., 2004), *Cussonia paniculata* (Adeolu et al., 2008), extracts of *Piper nigrum* (Pooja et al., 2007) also showed analgesic activity.

The isolates of few plants have shown analgesic activity, which include 6 – methoxy -5, 7, 4 – trihydroxy flavone from *Helichrysum bracteatum* (Kavimani et al., 2000), sesquerterpene dilactone from *Mikania cordata* (Ahmed et al., 2001), diterpene from *Egletes viscosa* (Guedes et al., 2002).
2.5. Hepatoprotective activity:

Interferon is a natural protein in the cell that is formed when the cells are exposed to viruses. It protects the cells from viruses. Interferons form a protective layer on the cells. Interferon also protects the cell from hepatitis virus. Normally the interferon is injected for four months. The success of treatment depends on the duration of infection.

Hepatitis continues to be a major cause of illness and death among all communicable diseases. In country like India many people rely upon the plant based traditional medicines to cure jaundice. The allopathic treatment is too costly and interferon treatment is highly sophisticated and beyond the reach of people living below the poverty line. Many indigenous drugs and herbs are clinically screened to evaluate the hepatoprotective activity against toxic hepatitis or cirrhosis.

Jayasekharan et ai. (1997) showed that the ethyl acetate extract of Acacia catechu gives hepatoprotection against carbon tetra chloride induced liver damage.

Other works include Sarcostemma brevistigma (Sethuraman et al., 2003), Pterocarpus marsupium (Mankani et al., 2005), Porchezhian and Ansari (2005) showed that the aqueous extracts of Abutilon indicum has hepatoprotective activity against paracetamol and carbon tetra chloride induced hepatotoxicity in rats.
Moringa oleifera (Pari et al., 2002), Diospyros malabarica (Susanta Kumar Mondal et al., 2005), meadowsweet plant (Shilova et al., 2006), leaves of Nyctanthes arbor-tristis Linn. (Hukkeri et al., 2006), aqueous and alcoholic extracts of fruit pulp of Litchi chinensis (Marina Gladys et al., 2007), aqueous and alcoholic extracts of Cleome viscose (Sengottuvelu et al., 2007) on carbon tetrachloride induced hepatotoxicity, methanolic extracts of Ficus carica Linn. (Krishna Mohan et al., 2007), Annona squamosa (Mohamed Saleem et al., 2008) also showed the hepatoprotective activity against carbon tetrachloride induced hepatotoxicity.

The hepatoprotective activity of the aqueous and ethanolic extracts of Chamomile recutita capitula on paracetomol induced hepatotoxicity was shown by Ajay Kumar Gupta and Neelam Mishra, 2006.