3. Literature Review

3.1 Drug induced liver injury (DILI)

Liver is a major organ that is involved in metabolism food as well as drugs. Because of this, liver is constantly exposed to different drugs as well as their metabolites which may also act as toxic to liver. About one thousand drugs are known to produce idiosyncratic liver injury. Many of the approved drugs have been withdrawn from the market because of their adverse effect on liver. In western country, more than half of the cases of liver failure are because of the drug induced liver injury (DILI) and amongst them, paracetamol is found to be the main offending agent. Because of difficulty in establishing diagnosis and low reporting frequency to the pharmacovigilance authorities, the real incidence of DILI is unknown (Sgro et al., 2002). DILI has now became a clinical challenge because of large number of drugs with known hepatotoxicity are still in use and also because of broad spectrum of injuries that are caused to the liver by these drugs. Cirrhosis and acute liver failure are the outcome associated with the delay in the diagnosis of DILI (Chau, 2008).

Most of the drugs and xenobiotics are able to invade the intestinal cell membranes because of their lipophilic nature. In the liver hepatocytes drugs become more hydrophilic because of biochemical process that results in water soluble products which are excreted out of the body via urine and or bile. In hepatocytes, drugs are subjected to biochemical processes, mostly oxidative processes via cytochrome P-450 enzyme system, yielding hydrophilic products which are excreted in urine or bile. Some of the hydrophilic products are further metabolized via conjugation to glucuronide or sulfate or glutathione. Transport proteins situated on the membrane of hepatocytes transport these products to plasma or bile and further excreted via kidney or gastrointestinal tract (Lee, 2003). Based on alanine aminotransferase (ALT) and alkaline phosphatase (ALP) ratio
DILI is classified as hepatocellular, cholestatic or mixed as shown in table 3.1 while respective examples are shown in table 3.2 (Hussaini and Farrington, 2007).

<table>
<thead>
<tr>
<th>Table 3.1 Classification of drug induced liver injury</th>
</tr>
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<tbody>
<tr>
<td><strong>Type of liver injury</strong></td>
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<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>Hepatocellular</td>
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<tr>
<td>Cholestatic</td>
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<tr>
<td>Mixed</td>
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<table>
<thead>
<tr>
<th>Table 3.2 Different class of drugs causing liver injury</th>
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<tbody>
<tr>
<td><strong>Drug Class</strong></td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td><strong>Antibiotics/antifungal</strong></td>
</tr>
<tr>
<td>Isoniazid</td>
</tr>
<tr>
<td>Pyrazinamide</td>
</tr>
<tr>
<td>Rifampicin</td>
</tr>
<tr>
<td>Tetracycline</td>
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<tr>
<td>Ketokonazole</td>
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<tr>
<td><strong>Cardiovascular</strong></td>
</tr>
<tr>
<td>Amioderone</td>
</tr>
<tr>
<td>Lisinopril</td>
</tr>
<tr>
<td>Losartan</td>
</tr>
<tr>
<td>Statins</td>
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<tr>
<td><strong>NSAIDs</strong></td>
</tr>
<tr>
<td>Diclofenac</td>
</tr>
<tr>
<td>Bromofenac</td>
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<tr>
<td><strong>CNS Drugs</strong></td>
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<tr>
<td>Valproic acid</td>
</tr>
<tr>
<td>Paroxetine</td>
</tr>
<tr>
<td>Bupropion</td>
</tr>
<tr>
<td>Trazodone</td>
</tr>
<tr>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Risparadone</td>
</tr>
<tr>
<td>Nefazodone</td>
</tr>
<tr>
<td><strong>HAART</strong></td>
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</table>
3.2 Epidemiology of DILI

Occurrence of DILI is poorly documented and the reason for this is under reporting and if reported the data comes from retrospective studies. These studies have reported the prevalence of self-medication and use of herbal products amongst the patients. Survey carried out in USA between 1998 and 2008 on 1147 patients revealed different causes of acute liver failure (ALF). Out of those 1147 patients, 46% suffered from ALF because of paracetamol overdose, followed by indeterminate cause (14%), drug-related (11%), hepatitis B virus (7%), other (7%), autoimmune hepatitis (5%) and ischemic hepatitis (4%) (Ichai and Samuel, 2011). In France, study on 4209 in-patients showed 1.4% incidence of DILI (Meier et al., 2005). Whereas, study in an out-patient hepatology clinic in a Swedish University hospital showed that the incidence of around 6.6% (De Valle et al., 2006). Sagro et al. (2002) have reported the annual incidence rate of 13.9 ± 2.4 per 100,000 of hepatic adverse drug reactions between 1997 to 2000. In India, Devarbhavi et al. (2010) demonstrated a prevalence of significant mortality rate of 17.3% which was associated with anti-tubercular, anticonvulsants, sulfonamides and olanzapine drugs.

ALF due to DILI is very common in the western world with strong association with acetaminophen hepatotoxicity. Data collected on 662 patients from 22 tertiary care centers in the United States showed an increase in acetaminophen-related ALF from 28% in 1998 to 51% in 2003 (Larson et al., 2005). Use of antitubercular drug in India has become the commonest cause of DILI especially in adults and children (Kumar et al., 2010; Devarbhavi et al., 2011).

With the newer advancement in phytochemistry and pharmacology, large number of flora and fauna are screened for their claimed traditional uses. Large number of experimental studies suggests that free radicals and reactive oxygen species play a very important role as a main disease producing cause (Govindrajan et al., 2005). Study carried out in Spain
on large cohort of patients with acute hepatitis showed that $7.4 \times 10^6$ patients developed liver diseases which were probably related to drugs (Ibanez et al., 2002). Retrospective study carried out in UK showed that 3.5% amongst 800 of patients had suffered from DILI. The annual prevalence rate of DILI was 1.27 per 100000 patients (Hussaini et al., 2007). A retrospective study carried out in US on 732 patients reported the prevalence of jaundice in 13% of patients, acute viral hepatitis in 9% patients and 4% patients with DILI. Study also reports that most of the reasons of DILI were because of acetaminophen toxicity (Vuppalanchi, 2007). In England, the prevalence of DILI was found to be in about 8.8% in-patients with AST levels $>$400 IU/L (Whitehead et al., 1999).

### 3.3 Drugs involved in DILI

More than 1000 drugs are known that have been associated with hepatotoxicity and amongst them antibiotics and NSAIDs are very common (Chang and Schiano, 2007). Widespread use of statins has a cause of distress amongst the hepatologist. About 3-17% patients treated with antiretroviral therapy are found to be associated with DILI. Few classes of drugs associated with DILI are discussed below.

#### 3.3.1 Antibiotics

Amongst the various studies performed, about 40-75% cases of DILI were found to be associated with antibiotics. Administration of co-amoxiclav (combination of amoxicillin and clavulanic acid) is well known cause of cholestatic liver injury and the incidence of which varies from 1 to 17 per 100000 prescriptions. This liver injury was found to be more in men above the age of 60 years. Younger patients were found to be more prone to hepatocellular liver injury after a short duration of exposure to co-amoxiclav (O’ Donohue et al., 2000). Flucloxacillin is given orally to treat infections caused by *Staphylococcus aureus*. It is penicillínase resistant semisynthetic isoxazolyl penicillin. Reports from UK showed the incidence of flucloxacillin induced liver injury of 3.6 per 100000
prescriptions (Russmann, 2005) while reports from Australia and Sweden this was 6.6 per 100000. Females over the age of 70 years were found to suffer due to flucloxacillin (Devereaux et al., 1995).

3.3.2 Non-steroidal anti-inflammatory drugs (NSAIDs)

About 1-8 cases per 100000 patients are reported for NSAID-induced hepatic injury (Bjornsson et al., 2007). All NSAIDs are known to cause liver injury but diclofenac and sulindac are known to frequently cause liver injury. Liver injury due to NSAIDs usually occurs within 6-12 weeks of initiation of medication. Diclofenac is prescribed in US for the treatment of osteoarthritis, rheumatoid arthritis or ankylosing spondylitis. A retrospective analysis on 180 patients with reported hepatic injury showed involvement of 79% of females amongst them 71% were 60 years or more of age (Banks et al., 1995).

3.3.3 Statins

Statins are found to be associated with a rise less than three times the upper normal limit of the transaminase. Rise above this limit is very rare, about less than 0.3% (ALLHAT 2002; Pfeffer et al., 2002). Acute liver failure due to statins is very rare. Russo et al. (2004) reported only three cases of statin induced acute liver failure.

3.3.4 Antiretroviral therapy

In a randomized controlled trial of highly active antiretroviral therapy (HAART), 1 to 9.5% of HIV patients showed rise of about more than five times the upper limit of normal values of transaminase (Sulkowski, 2004). In a prospective study on 212 HIV patients rise in transaminase level was more than 5 times the upper normal limit. In this study the overall rate of DILI was 10.5%. About 27.5% patients treated with ritonavir were found to develop hepatotoxicity whereas nearly 6% patients showed hepatotoxicity treated with indinavir, nelfinavir or saquinavir (Sulkowski et al., 2000). Drugs like nevirapine, efavirenz and delavirdine which belong to class of non-nucleoside reverse transcriptase
inhibitors (NNRTI) have less viral resistance when compared to non-NNRTIs. But the former are more likely to produce DILI during treatment (Law et al., 2003).

3.4 Pathogenesis of DILI
Liver disorders occurring because of drugs can be classified as predictable (high incidence (e.g. paracetamol) or unpredictable. Predictable incidences are those which occur within a few days of drug administration and are caused by hepatotoxicity because of the drug or its metabolic products. Unpredictable incidences occur as obvious or indicative disease over a time which may vary from 1 to 8 weeks (phenytoin) to 1 year (isoniazid) (Thompson et al., 1995; Shear and Spielberg, 1988). Most of the liver injuries induced by drug are unpredictable and are mediated by immune system hypersensitization or are idiosyncratic in nature. Idiosyncratic type of reactions depends on susceptibility of individual to host factors, which enhances the expression and penetrance of toxic reactions of drug or its metabolite (Boelsterli and Lim, 2007). From pathogenesis point of view, DILI causes the accumulation of drug or its byproduct which causes stimulation of immune system or can disturb the biochemical integrity of the cell. In both the cases ultimate result is the cell death and clinical appearances of hepatitis.

Metabolism of drugs takes place mostly in the liver and that is why liver becomes susceptible to drug induced injury. Whatever the drug metabolites are produced, they are either electrophilic or free radicals which make them highly reactive leading them to undergo various chemical reactions. This may result in reduction in reduced glutathione, covalent binding to the nucleic acid, lipids, and proteins or may result in lipid peroxidation. All these events have a direct effect on cell inclusions like nucleus, mitochondria, endoplasmic reticulum, microtubules etc. This may be collectively called as oxidative stress. Other effects that can occur are initiation and suppression of signaling
kinases, transcription factors and gene expression profiles. This hassle causes cell death caused either by cell shrinkage and apoptosis or necrosis (Kaplowitz, 2004).

In case of immune mediated response, reactive metabolite can bind with liver proteins like cytochrome P450 enzymes. Once binding takes place, this protein-metabolite complex becomes a macromolecule which acts as a heptane and is considered as foreign body by immune system of host causing immune attack on normal hepatocellular cell constituents (Kevin Park and Kitteringham, 1990; Knowles et al., 2000).

3.5 Risk factors associated with DILI

DILI is a rare disorder which is not directly associated with dose of the drug and very slight is known about the individuals who are at the threat. For the study of idiosyncratic DILI, no suitable preclinical model is available and its pathogenesis is also poorly understood. As far as risk factors associated with DILI, it includes majorly non-genetic and genetic factors. Chalasani and Bjornsson (2010) published an excellent review on risk factors associated with DILI.

3.5.1 Age

Medications like valproic acid and aspirin are found to be more toxic in younger age. Whereas risk associated with drugs like erythromycin, halothane, nitrofurantoin, isoniazid and flucloxacillin increases as age increases (Bell and Chalasani 2009; Larrey 2002). Patients of the age group 25-34 years treated with isoniazid showed incidence of hepatotoxicity of 4.4/1000 patients whereas in case of patients of age 50 years and above, the incidence was 20.83/1000 patients (Fountain et al., 2005).

3.5.2 Sex

Based on prevalence of women in published DILI, it can be inferred that women are at high risk than men. However in a study, Lucena et al. (2009) reported that out of 603 patients with DILI 51% were men and 49% were women revealing almost same
susceptibility to DILI by both male and female. But male and female might have susceptibility difference to DILI caused due to different medications. For instance, women are more prone to medications like halothane, flucloxacillin, isoniazid and nitrofurantoin. Whereas azathioprine associated DILI is common in male (Bell and Chalasani 2009; Larrey 2002).

3.5.3 Daily dose
In case of drugs like diclofenac, amoxicillin/clavulanate and flucloxacillin a relationship between dose and liver toxicity has observed. Case report for mianserin, a psychoactive drug of the tetracyclic antidepressant class showed decrease and gradually disappearance of hepatotoxicity with the reduction of dose (Otani et al., 1989). Duloxetine a serotonin-norepinephrine reuptake inhibitor used for depressive disorder has showed incidence of liver toxicity with the gradual increase in dose (Lammert et al., 2008). A study on 600 DILI cases showed that about 9% of patients received less than 10 mg/day of medication, 14% received a dose of between 11 to 49 mg/day and 77% received more than 50 mg/day of medication (Russmann et al., 2009). This clearly shows the relationship between medication dose and liver toxicity.

3.5.4 Metabolism characteristics
In USA, 207 drugs known to be metabolized in liver were studied to find any co-relation between hepatic metabolism and liver toxicity. The drugs which were metabolized to a extent of 50% or more in the liver were found to be associated with high levels of ALT (greater than 3 times the upper limit of normal), liver failure, liver transplantation and fatal DILI. It was also observed that drugs with significant hepatic metabolism when given at a dose greater than 50 mg/day were found to be more hepatotoxic compared with those with non-hepatic metabolism (Lammert et al., 2010).
3.5.5 Drug interactions

Few drugs are known to modify the hepatotoxicity of others by the virtue of enzyme induction leading to the formation of reactive metabolites. Isoniazid and rifampicin (inducer of microsomal enzyme) when given in combination produces more toxicity as compared to when given individually (Steele et al., 1991). Increase in the isoniazid induced liver toxicity by pyrazinamide was also reported (Durand et al., 1995). Other combinations include thioridazine-trzodone (Yasui et al., 1995), simvastatin-amiodarone (Hull et al., 1994) and Raloxifene and fenofibrate (Lucena et al., 2006).

3.5.6 Genetic factors

Oxidation by CYP, followed by conjugation with glutathione transferase and N-acetyltransferase is the general reaction by which drugs are metabolized in the liver. Deficiency in CYP enzyme isotypes due to a variety of genetic polymorphisms may contribute in DILI. About 10% of Europeans are found to be perhexiline hepatotoxicity due to deficiency of CYP2D6 (Morgan et al., 1984). Hepatotoxicity due to sulfonamides is associated with deficiency in two defective genes (NAT2) for N-acetyltransferase which will lead to slow acetylation (Rieder et al., 1991).

3.6 Plants used in liver disorders

In the developed world, herbs as medicine, nutraceuticals and health food etc. are in great demand for prime health care due their efficacy, safety and lesser side effects. Considerable attention has been paid to exploit eco-friendly and bio-friendly plant-based products. With the help of existing high-tech available methods, it is possible to optimize the effectiveness, standardization and clinical testing of these herbs to meet international standards. Large number of medicinal plants and preparations are being used over centuries for various therapeutic activities like antimicrobial, cytotoxic, antidiabetic, antiinflammatory, antiurolithiatic, liver disorder etc. The use of plant based drugs for the
treatment of liver disorder has a long history in various traditional systems of medicine including Ayurveda, Siddha, Unani and Chinese traditional medicines. In recent time a pattern of shift towards therapeutic assessment of plant based medicine in liver diseases by carefully synergizing the strengths of the traditional systems of medicine with that of the current concept of evidence-based medicinal evaluation, standardization of herbal products and randomized placebo controlled clinical trials to support clinical efficacy. Scientists have screened various plants that are either being used by tribal peoples or mentioned in traditional text books for the treatment of liver dysfunctions. The research is mainly focused on confirmation of the therapeutic potential as well as discovery of the mechanism of action of these plants. In order to develop a satisfactory herbal combination for liver disorders, individual plant needs to be systematically evaluated for its antioxidant, antihepatotoxicity, stimulation of hepatocyte regeneration and choleretic activity. Scientific studies have validated such herbal medicines or combinations confirming the biological efficacy and safety which rejuvenate treatment of liver disorders. A number of medicinal plants have already been scientifically documented for their hepatoprotective activity; few of them are listed below.
### Table 3.3 List of medicinal plants used in liver disorders

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Biological Source</th>
<th>Chemical constituents</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk thistle</td>
<td><em>Silybum marianum</em> (Asteraceae)</td>
<td>Silibinin, isosilibinin</td>
<td>Madani et al. 2008</td>
</tr>
<tr>
<td>Malabar nut</td>
<td><em>Adhathoda vasica</em> (Acanthaceae)</td>
<td>Alkaloid- vasicine</td>
<td>Bhattacharyya et al. 2005</td>
</tr>
<tr>
<td>Indian aloe</td>
<td><em>Aloe barbadensis</em></td>
<td>Anthraquinone glycoside barbaloin</td>
<td>Chandan et al. 2007</td>
</tr>
<tr>
<td>Neem</td>
<td><em>Azadirachta indica</em> (Meliaceae)</td>
<td>Nimbin, nimbinitin, and nimbidin</td>
<td>Yanpallewar et al. 2003</td>
</tr>
<tr>
<td>Liquorice</td>
<td><em>Glycyrrhiza glabra</em> (Fabaceae)</td>
<td>Glycyrrhizin</td>
<td>Yoshida et al. 2007</td>
</tr>
<tr>
<td>Tridax daisy</td>
<td><em>Tridax procumbens</em> (Asteraceae)</td>
<td>Flavonoid procubenetin</td>
<td>Ravikumar et al. 2005</td>
</tr>
<tr>
<td>Andrographis</td>
<td><em>Andrographis paniculata</em> (Acanthaceae)</td>
<td>Andrographoloid</td>
<td>Nagalekshmi et al. 2011</td>
</tr>
<tr>
<td>False daisy</td>
<td><em>Eclipta alba</em> (Asteraceae)</td>
<td>Wedelolactone</td>
<td>Thirumalai et al. 2011</td>
</tr>
<tr>
<td></td>
<td><em>Picrorhiza kurroa</em></td>
<td>Kutkosdie, picroside</td>
<td>Saraswat et al. 1999</td>
</tr>
</tbody>
</table>

### 3.7 Title plants

#### 3.7.1 *Clitoria ternatea* L.

**3.7.1.1 Botanical source:** It consists of the dried leaves of the plant *Clitoria ternatea* L. belonging to the family Fabaceae. It is a very well-known Ayurvedic medicine commonly known as butter-fly pea, conch flower, Winged-leaved or shankapushpi and in Indian language is known as Aparajit in Hindi, Aparajita in Bengali, Gokarna in Marathi, Garani in Gujarati and Kakkattan in Tamil language.

![Fig. 3.1 Entire plant of *Clitoria ternatea*](image)
3.7.1.2 Distribution

It may have originated from Latin America or Asia but now grows in all the semi-arid and sub-humid tropics of Asia, Australia and Africa. It grows very commonly in India, especially in southern parts of India. It is found in grassland, open woodland, and near the river. It is also grown as ornamental plant in gardens. After sowing it grows very rapidly with 35-45 days (Heuze et al., 2013).

3.7.1.3 Botanical description

It is a perennial twining herb, stems terete, more or less pubescent. Leaves imparipinnate, petioles 2-2.5 cm long stipules 4 mm long, linear, acute. Leaflets 5-7, subcoriaceous, 2.5-5 by 2-3.2 cm elliptic-oblong, obtuse, glabrous or with a few short appressed hairs, base obtuse or acute; stipels filiform. Flowers axillary, solitary; pedicels 8-13 mm long; bracts small, linear; bracteoles 6-13 mm long, roundish, obtuse. Calyx 1.3-2 cm long; teeth lanceolate, shorter than the tube. Corolla 3.8-5 cm long; standard bright-blue or sometimes white, with an orange centre. Pods 5-10 cm by 8-13 mm, flattened, nearly straing, sharply beaked, sparsely appressedly hairy. Seeds 6-10, yellowish brown, smooth (Kirtikar and Basu, 1991).

3.7.1.4 Parts used

Root, bark, seeds and leaves

3.7.1.5 Chemical constituents

Root bark contains starch, tannin and resins. Seeds contain a fixed oil, a bitter acid resin, tannic acid, glucose. Testa of seeds is brittle and contains a cotyledon which is full of granular starch (Nadkarni, 1976).

3.7.1.6 Medicinal properties and uses

The root is bitter, aphrodisiac, cures dysentery, severe bronchitis, asthma, useful in ascites and abdominal enlargement. In Konkan, the root juice is given in cold milk to remove the
phlegm in chronic bronchitis, it causes nausea and vomiting. The juice of the root of the white flowered variety is blown up the nostrils as a remedy for hemicranias. The root bark is diuretic and laxative, a decoction is given as a demulcent in the irritation of the bladder and urethra. The seeds are purgative and aperient. The infusion of the leaves is used for eruptions. The juice of the leaves, mixed with that of green ginger, is administered in cases of colliquative sweating in hectic fever. The juice of the leaves mixed with common salt is applied warm all around the ear in ear-aches, especially when accompanied with swelling of the neighboring glands. In Madagascar, the Betsimisaraka (ethnic group of Madagascar) use the root as an emetic, and the seeds as a purgative. The seeds are cathartic and the root diuretic. The powdered seeds in combination with ginger powder were found to have laxative action. The root, stem and flower are recommended for the treatment of snake bite and scorpion-sting (Kirtikar and Basu, 1991).

3.7.1.7 Phytochemical review

Extensive phytochemical investigations have been carried out on *C. ternatea* and a number of chemical constituents have been isolated from its different parts. Tiwari and Gupta (1959) reported β-sitosterol and new compound aparajitin (o-lactone of 2-methyl-4-hydroxy- n-pentacosanoic acid) and clitorin from dried leaves. Joshi et al., (1981) reported fatty acid (palmitic, stearic, oleic, linoleic and linolenic acids) in seed oil. Protein constitutes essential amino acid-lysine, histidine, threonine, phenylalanine, tyrosine, valine, methionine, cystine, leucine and isoleucine. Terahara et al., (1990) reported six Ternatins A1, A2, B1, B2, D1 and D2 from CT flowers; their structures were partly characterized as highly acylated delphinidin derivatives. Pentacyclic triterpenoids, taraxerol and taraxerone have been isolated and identified by Banerjee and Chakravarti (1963, 1964) from the roots of *C. ternatea*. Isolation and antimicrobial activity of flavonol glycoside 3,5,4’-trihydroxy-7-methoxyflavonol-3-O-β-D-xylopyranosyl-(1,3)-O-β-D-
galactopyranosyl (1,6) -O- β-glucopyranoside from the seeds of *C. ternatea* have been reported by Yadava and Verma (2003). Ranaganayaki and Singh (1979) isolated kaempferol from the flowers while Saito et al., (1985) detected kaempferol and its glycosides and quercetin along with its glycosidal derivatives from the flowers.

### 3.7.1.8 Pharmacological review

#### 3.7.1.8.1 Antiasthmatic activity

Taur and Patil (2011) investigated the antiasthmatic activity of ethanol extract of roots based on its traditional claim using milk induced leucocytosis and eosinophilia in mice, egg albumin induced mast cell degranulation in rats and passive cutaneous anaphylaxis in rats. Plant extract significantly decreased milk induced leucocytosis and eosinophilia. It also protected egg albumin induced degranulation of mast cells in mice and inhibited area of blue dye leakage in passive cutaneous anaphylaxis in rats. Authors conclude that flavonoids or saponins present in the plant may be responsible for the activity.

#### 3.7.1.8.2 Antidiabetic activity

Daisy et al., (2009) investigated the beneficial effects of leaves and flowers on diabetes induced by alloxan in rats. Oral administration of aqueous extract of leaves and flowers (400 mg/kg body weight) for 84 days significantly reduced serum glucose, glycosylated haemoglobin, total cholesterol triglycerides, urea, creatinine and the activity of gluconeogenic enzyme glucose-6-phosphatase, but increased serum insulin, HDL-cholesterol, protein, liver and skeletal muscle glycogen content and the activity of glycolytic enzyme glucokinase. *C. ternatea* leaves treated rat showed a slight better activity than *C. ternatea* flowers treated diabetic rats for above mentioned parameters. Study result confirms the antihyperglycemic and antihyperlipidemic effect of *C. ternatea* leaves and flowers. Further, *C. ternatea* shows improvement in liver and renal damage due to alloxan-induced diabetes mellitus in rats. In another study ethanolic extract of
seeds of *C. ternatea* has been evaluated for its antidiabetic activity in streptozotocin induced diabetic rats. The study results has showed significant decrease in increased blood glucose, cholesterol, alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase compared to diabetic control (Kalyan et al., 2011).

### 3.7.1.8.3 Anti-inflammatory, analgesic and antipyretic activity

Devi et al., (2003) reported the anti-inflammatory, analgesic and antipyretic activity of methanolic extract of roots of *C. ternatea*. Extract was tested for its anti-inflammatory activity by carrageenan-induced rat paw oedema and acetic acid-induced vascular permeability in rats. The extract showed a significant inhibition of the oedema induced by carrageenan by 21.6% and 31.8%, respectively, at 200 and 400 mg/kg. Furthermore, the extract reduced the intensity of peritoneal inflammation by 35.9 and 55.1% as observed in the reduction of Evan blue dye leakage induced by acetic acid in rats compared with that of diclofenac as the standard drug. The extract showed a reduction in yeast-induced fever confirming its antipyretic activity. The extract showed distinct reduction in the number of writhings at both tested doses by 50.1 and 63.8% compared to the reduction of 70.9% induced by standard drug aspirin (150 mg/kg) suggesting its analgesic activity.

### 3.7.1.8.4 Antimicrobial activity

Small protein molecule named as finotin was purified from the seeds of *C. ternatea*. It has showed promising antifungal activity against various fungal higher plant pathogens. It also inhibited the growth of bean bacterial blight pathogen *Xanthomonas axonopodis* pv. phaseoli (Kelemu et al., 2004). These activities point towards the potential of *C. ternatea* as possible antifungal agent in humans (Mukherjee et al., 2008). Antimicrobial activity against different bacteria and fungi by roots of *C. ternatea* has been reported by Yadava and Verma (2003).
3.7.1.8.5 Effect on general behavior

Boominathan et al., (2003) showed that the root ethanol extract possesses improvement in different neuropharmacological actions in rats and mice. Animals were tested for exploratory behavioral pattern by the head dip and Y-maze test and muscle relaxant activity by rotarod. Along with this extract significantly improved the sleeping time induced by phenobarbitone. Effect of alcoholic extract of aerial part on special discrimination in rats has been studied by Kulkarni et al., (1988). Oral treatment (460 mg/kg) with alcoholic extract significantly extended the time taken to traverse the maze, which was same to that produced, by chlorpromazine.

3.7.1.8.6 Effect on learning and memory

Taranalli et al. (2000) examined the efficacy of alcoholic extracts of aerial and root parts of *C. ternatea* on learning and memory. Significant memory retention was found at a dose of 300 mg/kg by the roots extract. They also studied the effect of extracts on central cholinergic activity. For this, they estimated the acetylcholine content of the complete brain and measured the acetylcholinesterase activity at various parts of the rat brain. Results suggest that *C. ternatea* extracts increase rat brain acetylcholine content and acetyl cholinesterase activity. Rai et al. (2002) observed a rise in acetylcholine level in hippocampus of rats (neonatal and young adult age groups) when treated with aqueous extract of *C. ternatea* (100 mg/kg) for 30 days. Improvement in learning and memory may be attributed due to escalation in acetylcholine content of the hippocampus. Memory enhancing effect of aqueous extract of roots of *C. ternatea* has been demonstrated by Rai et al. (2005) which may be attributed due to increase in the functional growth of amygdala neurons. After 30 days of oral treatment rats were subjected to passive avoidance tests followed by sacrifice and processing of amygdala. Study results exhibited a substantial proliferation in dendritic intersections, branching points and
dendritic processes arising from the soma of amygdaloid neurons in treated groups compared to non-treated.

3.7.1.8.7 Effect on nootropic and anxiolytic activity

Jain et al. (2003) has showed the nootropic, anxiolytic, antidepressant, anticonvulsant and antistress activity of methanolic extract of aerial parts of *C. ternatea*. The plant was explored for its influence on cognitive behaviour, depression, anxiety, convulsions and stress. The extract demonstrated the anxiolytic activity as it improved the tenure in the open arm of elevated plus maize by 160% and in the lit box of the light/dark exploration test by 157%. The plant also showed antidepressant activity as evident by decrease in the duration of immobility in tail suspension test and reduction in stress induced ulcers. In conclusion, the extract was found to possess nootropic, anxiolytic, antidepressant, anticonvulsant and antistress activity.

3.7.1.8.8 Hepatoprotective activity

Hepatoprotective activity of ethanolic extract of leaf against CCl₄ intoxicated rats have been studied by Shanmugasundaram et al. (2010). Daily treatment of the rats with ethanol extract (100 mg/kg) for 21 days to the CCl₄ intoxicated rats resulted in decrease in the elevated serum marker enzymes and increased total protein. Solanki and Jain (2011) investigated the hepatoprotective activity of defatted seed extract (50% v/v alcohol) in paracetamol and CCl₄ intoxicated rats. Extract has showed significant hepatoprotective activity as evident by reduction in elevated levels of serum marker enzymes.
3.7.2 *Tephrosia purpurea* Pers.

3.7.2.1 **Botanical source:** It consists of the dried leaves of *Tephrosia purpurea* Pers. belonging to the family Fabaceae. In English it is known as Fish poison, Sarphenka in Hindi, Pulechashtree in Sanskrit, Bennlgaoh in Bengali and Kolluk-kay-welai in Tamil language.

3.7.2.2 **Distribution:** *Tephrosia purpurea* is native to Australia, China, Sri Lanka and India. It is distributed throughout India, on waste lands and along road-sides (Warrier et al., 2004). It also grows abundantly in upper Gangetic plains, Western Himalayas and commonly grown as a green manure in paddy fields in India (Khare, 2004).

3.7.2.3 **Botanical description:** It is a copiously branched herbaceous perennial 30-60 cm high, branches spreading, glabrous or sparsely pilose. Leaves 5-10 cm long; petioles 6-12 mm long; stipules linear-subulate, nerved, erect or sometimes reflexed. Leaflets 11-21, ob lanceolate, obtuse or retuse, mucronate, 2-2.8 by 0.8-1.2 cm, glabrous above, clothed with fine appressed silky hairs beneath, base cuneate; nerves close, ascending, slender, conspicuous on both surfaces; petiolules of lateral leaflets 1.5-2.5 mm, those of the terminal 3-4.5 mm long. Flowers in leaf opposed lax racemes 7.5-12.5 cm long, the lower flowers of the racemes fascicled; pedicels slender; bracts subulate. Calyx 4 mm long, thinly silky; teeth triangular-subulate, as long as the tube. Corolla twice as long as the calyx; standard pubescent on the back. Style flattened, glabrescent; stigma penicillate. Pods 3-4.5 cm long, linear, slightly curved, mucronate, at first thinly hairy, finally glabrescent. Seed 5-6 in number (Kirtikar and Basu, 1991).
3.7.2.4 Parts used: leaves

3.7.2.5 Chemical constituents: Plant contains gum, albumin, quercetin, querritrin, glycoside, pongamol, β- sitosterol, ursolic acid, spinosterol, rotenone, tephrosin, betulinic acid, dimethyl glabranin, exopyo flavones, roots contain lanceolatin B, purpuren, maackain (Jarald and Jarald, 2006).

3.7.2.6 Medicinal properties and uses: The root is used as antidote in snake bite; good for ulcers and wounds; useful in splenomegaly. The seeds are useful in poisoning due to rat bite. The whole plant is bitter and acrid; anthelmintic, digestible, antidote, alternative, antipyretic; cures diseases of the liver, spleen, heart, blood; cures tumours, ulcers, leprosy, asthma, bronchitis, piles and dental caries. Root has a bitter bad taste; diuretic; reduces thirst; enriches the blood; cures diarrhoea; useful in bronchitis, asthma, liver and spleen diseases, inflammation, boils, pimples. The leaves are a tonic to the intestines; improve the appetite; useful in diseases of lungs and of the chest; good in piles, syphilis, gonorrhea. Fresh root-bark, ground and made into a pill, with a little black pepper, is frequently given in cases of obstinate colic. An infusion of the seeds is given as a cooling medicine. In Ceylon, it is employed as an anthelmintic for children (Kirtikar and Basu, 1991).

3.7.2.7 Phytochemical review

It shows the presence of rotenoids and flavonoids. Laevorotatory flavanone isolonchocarpin was isolated from chloroform root extract of T. purpurea (Rao and Raju N, 1979). Purpurenone, a new β- hydroxychalcone, (+)-purpurin, a diastereoisomer (-)-purpurin, dehydroisoderricin, and (-)-maackiain have been isolated from the roots (Rao and Raju, 1984).

Gupta et al. (1980) isolated new flavanone purpurin from the benzene extract of seeds. The petroleum ether extract gave β-hydroxybenzofuranchalcone (enol form of the
compound pongamol), isolonchocarpin, karanjin, lanceolatin-B, kanjone and β-sitosterol. Two new prenylated flavonoids, purpuritenin and purpureamethide, have been isolated and characterized from the defatted methanolic seed extract together with the known compounds pongamol, karanjin and lanceolatin B (Sinha et al., 1982). The aerial parts have reported to contain tephrosin, pongaglabol and semiglabrin. An aromatic ester, a sesquiterpene and prenylated flavonoid were also reported in methylenechloride/methanol (1:1) extract (Khalafalah et al., 2010). NMR (1D, 2D) spectroscopy, HR-MS analysis as well as X-ray analysis confirmed the presence of rare prenylated flavonoids, tephropurpulin A, isoglabratephrin and glabratephrin (Hegazy et al., 2009). Prenylated flavone, named terpurinflavone, along with the known compounds lanceolatin A, semiglabrin and lanceolatin B have been isolated stem (Juma et al., 2011). The presence of β-hydroxybenzofuranchalcone (enol form of pongamol), β- sitosterol, ursolic acid and spinasterol-α have been reported in the whole plant (Parmar et al., 1989). Chang et al. (1997) reported the presence of isoflavone, 7,4’-dihydroxy-3’,5’-dimethoxyisoflavone, and a chalcone, (+)-tephropurpurin, as well as six known compounds viz. (+)-purpurin, pongamol, lanceolatin B, (−)-maackiain, (−)-3-hydroxy-4-methoxy-8,9-methylenedioxypterocarpan, and (−)-medicarpin.

3.7.2.8 Pharmacological review

3.7.2.8.1 Anti-allergic activity

The ethanolic extract of *T. purpurea* was studied for its *In vitro* effect on rat mast cell degranulation and erythrocyte membrane integrity. Dose-dependent inhibition of rat mast cell degranulation induced by compound 48/80 and egg albumin was observed at concentration of 25-200 µg/ml. Plant was found to inhibit erythrocyte haemolysis induced by hypotonic solution whereas heat induced haemolysis was accelerated at a concentration of 100 µg/ml. The studies reveal that the ethanolic extract may inhibit
degranulation of mast cells by a mechanism other than membrane stabilization (Gokhale et al., 2000). The ethanolic extract of the aerial parts significantly reduced an elevated WBC count in response to antigen challenge in sensitized mice at doses of 50, 100 and 200 mg/kg orally and inhibited eosinophil infiltration without any significant change in the mononuclear cell population. The extract failed to alter neutrophil adhesion to nylon fibres. In In-vitro assay, a significant inhibitory activity on enzyme lipoxygenase at concentrations of 100 and 200µg/ml has been observed. The inhibitory effect of T. purpurea on late-phase allergy could be attributed to the inhibition of leukotriene synthesis (Gokhale and Saraf, 2000). The flavonoid fraction of the plant was studied for its effect on cellular (delayed type of hypersensitivity reaction) and humoral antibody response and on macrophage phagocytosis in mice. Sheep red blood cells induced delayed types of hypersensitive reactions were significantly inhibited after the administration of flavonoid fraction at a dose of 10-40 mg/kg orally. Decrease in sheep erythrocyte-specific haemagglutination antibody titre was also observed in a dose dependent manner (Damre et al., 2003).

3.7.2.8.2 Anticancer activity

The modulatory effect of T. purpurea on benzoyl peroxide-induced cutaneous oxidative stress has been studied. Benzoyl peroxide increased the microsomal lipid peroxidation, hydrogen peroxide generation and decreased the activity of various cutaneous antioxidant enzymes along with the depletion in cutaneous glutathione levels. Prophylactic treatment of mice with T. purpurea 12 h before benzoyl peroxide treatment resulted in the reduction of benzoyl peroxide-mediated damage as evident by the significant decrease in the lipid peroxidation and hydrogen peroxide generation along with increase in the glutathione level and increase in the activity of antioxidant enzymes (Saleem et al., 1999).
**T. purpurea** was investigated for its anticancer activity on 12-O-tetradecanoyl phorbol-13-acetate induced cutaneous oxidative stress and toxicity in murine skin. In study 7, 12-dimethyl benz(a)anthracene was used as tumor initiator followed by twice weekly topical application of croton oil as tumor promoter. Significant protection against cutaneous carcinogenesis induced by croton oil was observed due to topical application of **T. purpurea**. The activity was found to be dose dependent. Treatment caused a decrease in tumor incidence and tumor yield compared to the control group (croton oil treated). It also resulted in the significant recovery of depletion in the levels of glutathione, glutathione S-transferase, glutathione reductase and catalase in skin (Saleem et al., 2011). Kavitha et al (2006) showed the chemoprotective potential and antilipidperoxidative effects of ethanolic root extract of **T. purpurea** in hamster. Different fractions of **T. purpurea** were investigated for anticancer activity by using human MCF 7 cell line by trypan blue exclusion method. Among the different fractions, only the benzene fractions from acetone soluble and insoluble extracts were shown the potential activity (Gulecha and Sivakumar, 2011).

### 3.7.2.8.3 Antihyperglycemic and antihyperlipidemic activity

Aqueous extract of **T. purpurea** leaves was evaluated for its antihyperglycemic and antihyperlipidemic effects in streptozotocin induced diabetic rats. Oral administration of **T. purpurea** to diabetic rats at a dose of 600 mg/kg body weight intensely altered the concentrations of blood glucose, lipids and lipoproteins levels. It also reduced the level of blood glucose and increased the level of plasma insulin as well as normalized the lipids and lipoproteins profile (Pavna et al., 2007). Pavna et al. (2009) showed significant improvement in hyperglycemia, liver glucose-6-phosphatase activites, raised lipid peroxidation in liver and kidney and disturbed
enzymatic and non-enzymatic antioxidant status after oral administration of aqueous seed extract of T. purpurea (600 mg/kg).

The beneficial effect of ethanolic extract of seed of *T. purpurea* on glycoprotein components in streptozotocin induced diabetic rats was investigated. The plasma glucose and insulin levels were significantly improved in groups treated with *T. purpurea*. The plasma erythrocyte glycoprotein components levels were brought back to near normal range in diabetic animals treated with *T. purpurea* and glibenclamide. Protein bound hexose, hexosamine and fucose contents were significantly increased whereas the sialic acid content was significantly decreased in liver and kidney of diabetic animals as compared to control the glycoprotein components levels were brought back to near normal range in diabetic animals treated with *T. purpurea*. The results indicate the potent role of *T. purpurea* in modifying altered glycoprotein components in streptozotocin induced diabetic rats (Pavna et al., 2008).

### 3.7.2.8.4 Antiinflammatory activity

Antiinflammatory activity of orally administered ethanolic extract of *T. purpurea* was studied in carrageenan induced paw edema as acute model and cotton pellet granuloma as subacute inflammatory models in rats. In the acute model, *T. purpurea* did not exhibit any significant decrease in paw volume and serum ceruloplasmin levels as compared to the control and aspirin treated groups; while in subacute model there was significant decrease in the weight of granuloma in *T. purpurea* and aspirin treated groups as compared to control (Shenoy et al., 2010).

Different fractions of *T. purpurea* were studied for their anti-inflammatory and analgesic activity. Anti-inflammatory activity was evaluated using carrageenan-induced rat paw edema and cotton pellet-granuloma formation in rats. Analgesic activity was evaluated by using acetic acid induced writhing in mice and tail flick test in rats. Among five
different fractions tested fraction TPI, and TPIII (20 and 40 mg/kg b.w) were found to be more effective in carrageenan induced rat paw edema model. Oral treatment of these fractions reduced inflammation by 63.75% and 50% respectively. Oral treatment with TPI and TPIII (40 mg/kg) to rats showed significant ($p<0.01$) inhibition in the weight of cotton pellet. In case of analgesic activity TPI and TPIII significantly inhibited nociception in rats by 17.60% and 22.02% respectively. Also they have showed significant inhibition of pain perception. In acetic acid induced writhing in mice TPI and TPIII showed significant ($p<0.01$) activity at 40 mg/kg dose level compared to control group (Gulecha et al., 2011).

3.7.2.8.5 Antioxidant activity

Alcoholic extract of the *T. purpurea* was investigated for its free radical scavenging activity, antilipid peroxidation potential and hydroxyl radical scavenging activity. It was found that the *T. purpurea* extract showed significant free radical scavenging activity and it interacted significantly with free radical DPPH at concentration of 10 to 200 µg/ml. *T. purpurea* inhibited the *In vitro* lipid peroxidation significantly in a dose dependent manner (10 to 140 µg/ml). However, it failed to show any significant scavenging effect on hydroxyl radicals (Soni et al., 2003). Ethanol extract of *T. purpurea* and its ethyl acetate fraction were studied for their antioxidant activity in carbon tetrachloride induced lipid peroxidation and superoxide generation *in vivo* as well as *in vitro* lipid peroxidation and DPPH model. In both the *in vitro* assay models the IC$_{50}$ value was found to be significantly lowered by ethyl acetate fraction as compared to the ethanolic extract. Same results were also found in *in vivo* test models. the study thus confirms the antioxidant potential of ethanolic extract of *T. purpurea* and its ethyl acetate soluble fraction (Soni et al., 2006).
Root extracts of *T. purpurea* were screened for *In vitro* antioxidant by using ABTS, DPPH, FRAP and oxygen radical absorption capacity assay methods. In the same study xanthine oxidase inhibitory activity was also evaluated on purified milk xanthine oxidase. Along with significant free radical scavenging activity, the root extracts has also showed concentration-dependent and noncompetitive mode of inhibition of bovine milk xanthine oxidase (Nile and Khobragade, 2011).

Successive petroleum ether, chloroform and methanol extracts of leaves of *T. purpurea* were evaluated for their antioxidant potential using FRAP and DPPH radical scavenging assay methods. The extracts were also evaluated for their total phenolic, total flavonoid, tannins and total alkaloid content estimation. The results showed higher content of phytochemicals in methanolic extract compared to chloroform and petroleum ether extract. At the same time methanolic extract has also showed better antioxidant activity compared to other two extracts (Rao et al., 2011).

### 3.7.2.8.6 Antiulcer activity

Antiulcer activity of aqueous extract of roots of *T. purpurea* was investigated in gastric and duodenal ulceration model in rats. Graded doses of *T. purpurea* were administered orally 30 min before the induction of ulcer. For the assessment of antiulcer activity, ulcer index was calculated for the groups treated with test drug and compared with ulcer index of vehicle control group. Aqueous extract of *T. purpurea* significantly reduced the ulcer index in all the tested models compared to control group. Antiulcer property was more noticeable in gastric ulcer induced model. Omeprazole used as reference drug exhibited a significant activity when compared to control group (Deshpande et al., 2003).

### 3.7.2.8.7 Hepatoprotective activity

*T. purpurea* is a well-known remedy for hepatobiliary dysfunction mentioned in Ayurveda. The hepatoprotective potential of *T. purpurea* was evaluated in D-
galactosamine HCI (acute) and carbon tetrachloride (chronic) induced hepatotoxicity model in rats. *T. purpurea* aerial part powder was administered orally at a dose of 500 mg/kg. Biochemical and histopathological results of the study indicated that the administration of *T. purpurea* offered a protective action in both acute (D-galactosamine) and chronic (CCl₄) models (Murthy and Srinivasan, 1993).

Livex, a compound herbal formulation, containing *T. purpurea* as one of its ingredients was tested in wistar albino rats for its hepatoprotective activity. Erythromycin estolate was used as hepatotoxin which resulted in significant increase in liver enzyme parameters. Oral administration of Livex caused a significant protection against toxic insult as evident by the reduction in the elevated serum enzyme levels and other parameters. The results were further supported by histopathological examination of liver sections (Venkateswaran et al., 1997).

HD-03, another polyherbal formulation containing *T. purpurea* as one of the ingredient was tested for hepatoprotective activity by Mitra et al. (1998) against several different hepatotoxins (paracetamol, thioacetamide and isoniazid). In all the tested models, the tested formulation showed significant protection against toxicant induced liver enzyme elevation and other parameters.

Ethanol extract of leaves and flavonoid (isolated from leaves extract) from *T. purpurea* were evaluated against CCl₄ induced hepatotoxicity. The ethanol extract and fraction were administered orally at a dose of 100 mg/kg/day. Serum level of transminases, alkaline phosphate, and total bilirubin were used as biochemical markers of hepatotoxicity. Histopathological changes in the liver were also studied. A significant reduction (*p*<0.05) in the level of SGOT (390.42 ± 6.24), SGPT (235.31 ± 5.05), ALP (588.39 ± 10.23) and total bilirubin (1.47 ± 0.92) was observed in group treated with ethanol extract of *T. purpurea* when compared with group treated with CCl₄ alone.
Ethanol extract was found to be more potent compared to isolated fraction. The presence of flavonoid may be responsible for the higher activity of leaves extract due to their synergistic effect (Jain et al., 2006).

In thioacetamide induced hepatotoxicity rat model aqueous-ethanolic extract of aerial parts of *T. purpurea* was evaluated. Oral administration of *T. purpurea* at 500 mg/kg caused a significant decrease in the levels of different enzyme parameters compared to toxic control. The extract also showed increase in liver glutathione. The results were further supported by histopathological examination of liver sections (Khatri et al., 2009).

A randomized, single blind, placebo controlled study was conducted to compare the safety and efficacy of Livina (a polyherbal preparation containing *T. purpurea* as one of the ingredient) and placebo. Patients were treated for two months with four antitubercular drugs (rifampicin, isoniazid, pyrazinamide and ethambutol) followed by a four month treatment with two drugs (rifampicin and isoniazid). Liver enzyme parameters were estimated at different time intervals, before and after antitubercular treatment. Analysis of the compliance data of two groups indicated better tolerance of antitubercular treatment in Livina treated group, resulting in completion of course of chemotherapy. Treatment with Livina also showed more increase in body weight as compared to placebo group indicating possible better efficacy of test drug. Decrease in the level of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase was observed in Livina treated group compared to placebo at both time intervals (4 and 8 weeks) of assessment, suggesting protective effect against antitubercular drug induced liver dysfunction in the patients suffering from pulmonary tuberculosis (Gulati et al., 2010).
3.7.3 *Malvastrum coromandelianum* (L.) Garcke

3.7.3.1 **Botanical source:** It consists of the dried leaves of *Malvastrum coromandelianum* (L.) Garcke belonging to the family Malvaceae. In Hindi it is known as ‘Kharenti’ and ‘Sannabindige gida’ in Kannada language.

3.7.3.2 **Distribution:** Widely occurring in Peninsular India. It is a successful colonizer of degraded and disturbed area right from the sea-coast to the foot hills of Western Ghats and also as a weed in agricultural lands (Pradeep and Sivarajan, 1996).

3.7.3.3 **Botanical description:** *M. coromandelianum* is a strong-stemmed, woody-rooted herb, grows upto 1 m in height. Leaves are ovate or ovate-elliptic, 4.5 cm long, 3.5 cm wide, with sharp or blunt apex, prominent midrib, margins serrated, 3-nerved from base. Leaf stalks are 1.5-4 cm long.

3.7.3.4 **Parts used:** Aerial parts, Leaves, Roots

3.7.3.5 **Medicinal properties and uses:** Various parts of this plant are used by numerous tribal populations throughout the world. Mexican Kickapoo Indians use the crushed leaves of this herb along with salt or alcohol to cure ringworm infection (Dolores and Felipe, 1977). Bhil tribes of Rajasthan use this plant in the form of decoction to cure jaundice (Sebastian and Bhandari 1984). In Mexico leaf infusion of this plant is used to cure diabetes (Andrade-Cetto A and Michael H. 2005). In traditional Indian system of medicine the plant is reported as an antiinflammatory, analgesic and antidyseretic (Kirtikar and Basu 1995; Anonymous 1992; Fyson 1974).
3.7.3.6 Phytochemical review

Alam et al. (1996) reported the presence of malvastrone in the leaves. The aerial parts are also known to contain β-phenylethylamine, dotriacontane, dotriacontanol, β-sitosterol, stigmasterol, campesterol, lutein, N-methyl- β-phenylethylamine and unidentified indole alkaloid.

Reddy et al. (2001) reported that successive petroleum ether, chloroform, acetone, and methanol extracts gave positive tests for steroids, glycosides, steroids, triterpenoids, tannins and phenolics, saponins.

3.7.3.7 Pharmacological review

3.7.3.7.1 Anti-inflammatory and antinociceptive activity

Reddy et al. (2001) reported that the antinociceptive activity of aerial parts of *M. coromandelianum* in the 0.6% acetic acid-induced writhing test in mice, the effects of acetone extract (200 mg/kg) was found to be comparable with standard drug acetylsalicylic acid (100 mg/kg). Khonsung et al. (2006) investigated the anti-inflammatory activity in carrageenan induced hind-paw edema in rats, analgesic effects on the formalin test, and the antipyretic effects on yeast-induced hyperthermia models of the aqueous extract of *M. coromandelianum*. The results demonstrated that the aqueous extract inhibited the carrageenan induced hind-paw oedema. The extract also reduced the licking time of rats and showed an analgesic activity in the formalin test. However, the extract failed to show antipyretic effect on yeast-induced hyperthermia in rats.

3.7.3.7.2 Antimicrobial activity

Sittiwet et al (2008) studied the antibacterial activity of aerial parts of aqueous extract of *M. coromandelianum* against methicillin resistant and methicillin sensitive strains of *Staphylococcus aureus*. Study results showed moderate antibacterial activity for *M.*
*M. coromandelianum* against methicillin sensitive as well as methicillin resistant strains of *S. aureus*.

Jain et al. (2010) studied the antimicrobial effect of hexane and methanolic extract of leaves of *M. coromandelianum* against *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis* by agar well diffusion method. Both the hexane and methanolic extract have shown antibacterial activity against *E. coli* and *B. subtilis* but no activity against *S. aureus*. In the same study phytochemical screening of both the extracts showed the presence of steroid, glycosides, tannins and flavonoids. Contradictory to these results Suresh et al. (2010) in their effort to establish the antibacterial activity of 28 different plants from Palar river basin failed to show antibacterial activity of methanolic and chloroform extract of *M. coromandelianum*. They tested the extracts for their antibacterial activity against six human pathogenic bacterial strains *S. aureus*, *B. cereus*, *Enterococcus faecalis*, *E. coli*, *Salmonella typhi* and *Proteus mirabilis*.

### 3.7.3.7.3 Wound healing activity

Gangrade et al. (2012) evaluated the ethanolic extract for its wound healing activity in rats by using the incision and the dead space wound model. The ointment of the ethanolic extract produced significant response in both of the wound types tested. In the incision model, wounds treated with the extract were found to get covered with epithelial cells faster along with higher wound contraction, when compared to control group. In the incision model, tensile strength was found to increase, suggesting the facilitation of healing process.
3.8 References


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Literature Review


