REVIEW OF LITERATURE

Research programs in India and China are active in the investigation of their local medicinal plants, but little ethanopharmacological research has been carried out for the ethnic groups who live in areas of maximum biodiversity, where many plants of interest are likely to occur. Medicinal herbs are significant sources of pharmaceutical drugs. Latest trends have shown increasing demand of phytodrugs and some medicinal herbs. The most important classes of herbs for functional liver disease are cholagogues (increase bile flow), choleretics (increasing bile production) and carminatives (expelling gas and antispasmodic). Cholagogue plants usually have a bitter flavor, and all bitter plants are cholagogic to some degree. Some important traditional cholagogues are dandelion (*Taraxacum officinalis*), greater celandine (*Chelidonium majus*), and wormwood (*Artemesia absinthum*). The most commonly used herbs for liver problems include Phyllanthus, Milk Thistle, Sho-saiko-to, Dandelion Root, Licorice Root, and Chicory root. Phyllantus amarus in chronic hepatitis B, glycyrrhizin to treat chronic viral hepatitis, and a number of herbal combinations from China and Japan that deserve testing in appropriate studies.

Liver is often abused by environmental toxins, poor eating habits, alcohol and over-the-counter drug use, that damage and weaken the liver leading to important public health problems like hepatitis, cirrhosis and alcoholic liver diseases (Treadway, 1998). These toxins generally lead to pathologically distinct liver diseases in clinical practice, any or all of the three
conditions can occur together at the same time, in the same patient. These three conditions are fatty liver, hepatitis, and Cirrhosis. Paracetamol and CCl₄-induced hepatic injuries are commonly used models for hepatoprotective drug screening (Plaa Hewitt, 1982).

**Abstinence from Alcohol**

Alcohol consumption has been associated with alcoholic hepatitis, fatty infiltration of the liver, accelerated progression of liver disease, a higher frequency of cirrhosis, a higher incidence of hepatocellular carcinoma, and death. The daily consumption of more than four drinks of alcohol increases the risk of cirrhosis, as well as death from other causes (Thun et al., 1997; Scheig, 1970). Investigators in one study (Corrao and Arico, 1998) found that the effect of alcohol in patients with hepatitis C virus infection is not merely additive but synergistic. The mechanism for the synergistic effect of alcohol and hepatitis C virus is not fully understood, but it has been attributed to the effects of alcohol on viral replication and the immune system, hepatic iron content and hepatic regeneration.

**Influence of Iron**

As many as 30 percent of patients with liver disease have high serum iron levels, and 10 percent have excessive amounts of iron in their liver tissue (Riggio et al., 1997; Di Bisceglie et al., 1992). The most likely mechanisms of liver injury from excess iron are increased generation of free radicals and increased peroxidation of lipids, which, in turn, lead to mitochondrial dysfunction, lysosomal fragility and cell death. Iron has recently been shown
to influence the natural history of hepatitis C virus infection and the response of chronic hepatitis C to treatment (Olynyk et al., 1995; Van Thiel et al., 1994). To date, no evidence suggest that dietary iron is harmful.

**Diet and Exercise**

One controlled study (Ueno et al., 199) demonstrated that a weight reduction program (combined diet and exercise) can improve liver function test results and liver histology in patients with nonalcoholic steatohepatitis. With a weight loss of 4.5 to 6.8 kg (10 to 15 lb), liver transaminase levels often return to normal. Investigators in another study (Deems et al., 199) found a correlation between high fat and oil consumption and elevated liver transaminase levels. The findings of these studies suggest that a low-fat diet and exercise could minimize hepatic steatosis.

**Liver protecting Herbs**

*Ayurveda* remains one of the most ancient and yet living traditions practiced widely in India, Sri Lanka and other countries and has a sound philosophical and traditional basis (Chopra and Doiphode, 2002). *Atharvaveda* (around 1200 BC), *Charak Samhita* and *Sushrut Samhita* (1000–500 BC) are the main classics that give detailed descriptions of over 700 herbs. Polyherbal formulations reputed to have hepatoprotective activity that are available on the Indian market comprise about one hundred Indian medicinal plants (Handa and Sharma, 1986).
Andrographis paniculata

For centuries Andrographis has been an important herb in the Asian healing systems of Ayurveda, Unani and Traditional Chinese Medicine. Traditionally this herb has been used to potentiate immune system response to inflammation and infections, and as an anti-inflammatory, antipyretic (lowers fevers) and a hepatoprotective (liver protector Andrographolide, the active constituent isolated from the plant *Andrographis paniculata* showed a significant dose dependent protective activity against paracetamol-induced toxicity on *ex vivo* preparation of isolated rat hepatocytes (Visen *et al.*, 1993).

Boerhavia diffusa (Punarnava)

An alcoholic extract of whole plant *Boerhavia diffusa* given orally exhibited hepatoprotective activity against experimentally induced carbon tetrachloride hepatotoxicity in rats and mice (Ansari *et al.*, 1991).

Terminalia belerica (Baheda)

Compound I isolated from fraction TB5 of *Terminalia belerica* and finally identified as 3,4,5-trihydroxy benzoic acid (gallic acid) was evaluated for its hepatoprotective activity against carbon tetrachloride (CCL₄) - induced physiological and biochemical alterations in the liver. Administration of compound I led to significant reversal of majority of the altered parameters confirming the presence of hepatoprotective activity in Compound I (Anand *et al.*, 1997).
**Picrorhiza kuroa (Katuki)**

*Picrorrhiza kuroa* is one of the herbs they recommend to support the liver not only in everyday situations, but in cases where severe viral infections attack. Pre-treatment with picroliv prevented the hepatotoxic effects of paracetamol and galactosamine as evidenced by various biochemical and histopathological observations. Maximum hepatoprotective effect was observed with daily oral doses of 6 and 12 mg/kg for 7 or 8 days. The antihepatotoxic action of picroliv seems likely due to an alteration in the biotransformation of the toxic substances resulting in decreased formation of reactive metabolites (Ansari *et al.*, 1991).

**Taraxacum officinale**

Traditionally *Taraxacum officinale* has been used as a remedy for jaundice and other disorders of the liver and gallbladder, and as a remedy for counteracting water retention. Generally, the roots of the plant have the most activity regarding the liver and gallbladder. Oral administration of extracts from the roots of *Taraxacum officinale* has been shown to act as a cholagogue, increasing the flow of bile (Vogel, 1977). Bitter constituents like taraxecerin and taraxcin are active constituents of the medicinal herb (Cordatos, 1992).

**Solanum nigrum**

In Ayurveda, the drug is known as kakamachi. Aromatic water extracted from the drug is widely prescribed by herbal vendors for liver
disorders. Although clinical documentation is scare as far as hepatoprotective activity is concerned, but some traditional practitioners have reported favorable results with powdered extract of the plant.

*Wilkstroemia indica*

*W. indica* is a Chinese herb and has been evaluated in patients suffering from hepatitis B. A dicoumarin, daphnoretin is the active constituent of the herb. The drug has shown to suppress HbsAG in Hep3B cells. It is said to activator of protein kinase C (Chen *et al.*, 1996).

*Curcuma longa*

Like silymarin, turmeric has been found to protect animal livers from a variety of hepatotoxic substances, including carbon tetrachloride (Srinivas and Shalini, 1991), galactosamine, pentobarbitol, 1-chloro-2, 4-dinitrobenzene, 7 4-hydroxy-nonenal (Selvam *et al.*, 1995) and paracetamol. Diarylhepatonoids including Curcumin is the active constituent of the plant.

*Milk Thistle (Silybum marianum)*

The best studied herb for hepatitis and has been shown to help protect and regenerate liver cells. There is no evidence of toxicity related to the pure form of milk thistle, and there is weak evidence of a hepatocyte plasma cell membrane protective effect. For these reasons, it is reasonable not to discourage the use of milk thistle (Flora *et al.*, 1998).
**Piper longum**

The isolated constituents and n-hexane extracts of *Piper longum* were found to show varying degree of antibacterial activity against all the tested bacteria (Lokhande et al., 2007). Administration of alcoholic extract of *Piper longum* (10 mg/dose/animal) as well as piperine (1.14 mg/dose/animal) could inhibit the solid tumor development in mice induced with DLA cells and increase the life span of mice bearing Ehrlich ascites carcinoma tumor to 37.3 and 58.8%, respectively. Administration of *Piper longum* extract and piperine increased the total WBC count to 142.8 and 138.9%, respectively, in Balb/c mice (Sunila and Kuttan, 2004). Ethanol extract of *Piper longum* fruits and five crude fractions, petroleum ether (40-60), solvent ether, ethyl acetate, butanol and butanone were subjected to preliminary qualitative chemical investigations. The ethanolic extract and all other fractions were screened orally for hepatoprotective activity in adult Wistar rats. The ethanolic extract and butanol fraction have shown significant activity, lowering the serum enzymes glutamic oxaloacetic transaminase and glutamic pyruvic transaminase in rats treated with carbon tetrachloride when compared to control and Liv-52-treated rats (Jalalpure et al., 2003)

**Eclipta alba**

The drug is traditionally used against Jaundice (Mehra and Handa, 1968). As a reputed herbal medicine in the Ayurvedic and Unani system of medicine, it is incorporated as a major ingredient in a number of Indian antihepatotoxic phytopharmaceutical formulations. The herb of *E. alba*
contains coumestans, i.e. wedelolactone (W) and demethylwedelolactone (DMW) possessing potent antihepatotoxic activity and is recommended for the treatment of hepatitis and cirrhosis. It cure insomnia (Kulkarni, 1990). The drug also showed antiviral activity in mice experimentally infected with Semliki forest encephalitis virus (Singh, 1983). The drug also has been found to be quite beneficial for treatment of jaundice when tested clinically in children (Dixit and Achar, 1981).