2.1 Hepatoprotection

Till date there is no effective medicine for hepatic diseases which is primarily caused by xenobiotics and hepatitis viruses. Consequently, control of liver diseases has become a major goal of modern medicine. The drugs offered by modern medicine for the treatment of liver diseases are corticosteroids and immunosuppressants which provide only symptomatic relief mostly without influencing the disease process and their use is associated with the risk of relapse and danger of side effects (Ram and Goel, 1999).

In traditional systems of medicine, like Ayurveda, medicinal plants and their formulations are used to cure liver diseases. Some of these plants and herbal preparations have been evaluated for their protective actions against hepatotoxins. Some of the polyherbal preparations were proved to be antihepatotoxic in action as evidenced by clinical trials.

2.2 Antihepatotoxic medicinal plants

Bhanwra et al. (2000) studied the effect of aqueous leaf extract of *Azadirachta indica* in paracetamol-induced hepatotoxicity in rats. The liver
damage due to paracetamol administration resulted in elevation in the activities of serum transaminases and gamma glutamyl transpeptidase (GGT). The extract of A. indica (500mg/kg) significantly reduced the elevated activities of these enzymes in serum. A. indica was also found to be effective in reducing paracetamol-induced liver necrosis as evidenced by histopathological studies.

Aqueous extract of Artemisia campestris exhibited hepatoprotective and antioxidant activities (in vivo and in vitro). The extract showed scavenging action of 1,1-diphenyl picrylhydrazyl, hydroxyl and superoxide anion radicals. Pre-treatment (intraperitoneal / oral) with the extract significantly reduced the CCl₄-evoked elevation of serum transaminases in mice. The authors suggested that the protective action of A. campestris extract may be due to the scavenging action of the plant for free radicals formed by CCl₄ treatment (Aniya et al., 2000).

Pre-treatment of rats with the 50% ethanol extract of the bark of Lawsonia alba showed hepatoprotective activity against CCl₄-induced oxidative stress (Ahmed et al., 2000). The protective activity of the extract was shown by the reduction in the activities of serum transaminases and lactate dehydrogenase (LDH) in rats against the rise in the activities of the enzymes when challenged with CCl₄. Moreover, the plant extract prevented CCl₄ induced oxidative stress by maintaining the levels of reduced glutathione, its metabolizing enzymes and simultaneously inhibiting the production of free radicals.

The in vitro antioxidant and free radical scavenging properties of the bark extracts of Anadenanthera macrocarpa, Astronium urundeuva, Mimosa verrucosa and Sideroxylon obtusifolium were studied using different bioassays by Desmarchelier et al. (1999). All the extracts (aqueous and methanolic extracts) were active.
Bhakta et al. (1999) evaluated the antihepatotoxic effect of the n-heptane extract of *Cassia fistula* leaves in CCl₄ : liquid paraffin (1:1) treated rats. Biochemical and histopathological investigations indicated that the extract of *C. fistula* (400 mg/kg body weight) has hepatoprotective effect.

Biochemical and histopathological studies on the effect of the leaves of *Cassia occidentalis* (aqueous-ethanolic extract) on paracetamol and ethanol intoxication in rats revealed its hepatoprotective activity (Jafri et al., 1999).

Turmeric antioxidant protein isolated from the aqueous extract of turmeric (*Curcuma longa*) has been found to exhibit hepatoprotection in CCl₄- treated rats. Decrease in the activities of antioxidant enzymes in liver due to CCl₄ intoxication was nearly normalized on treatment with the protein. The authors suggest that the protection exhibited by the protein may be due to the stabilization of the oxidative stress induced changes (Lalitha and Selvam, 1999).

Germano et al. (1999) studied the effect of *Mitracarpus scaber* (decoction of aerial parts) on CCl₄-induced acute liver damage (*in vivo* and *in vitro*) in rats. *In vivo* results showed that pre-treatment with *M. scaber* reduced the elevated activities of serum GOT and GPT due to CCl₄ treatment. *In vitro* results indicated that addition of *M. scaber* extracts to the culture medium reduced the CCl₄-evoked elevation in the activities of GOT and GPT. *In vitro* study also revealed the free radical scavenging properties of *M. scaber*.

Picroliv, the active constituent isolated from *Picrorhiza kurroa*, exhibited protection against ethanol-induced hepatic injury in rats. *Ex vivo* and *in vivo* studies showed that picroliv treatment (3-12mg / kg p.o x 45 days) restored the altered parameters in a dose-dependent manner (Saraswat et al., 1999).
The ethanolic extract of *P. kurroa* was also shown to protect against D-galactosamine-induced hepatitis in rats (Anandan *et al.*, 1999).

Seed extract of *Schisandra chinensis* showed protective effect on Phase I oxidative metabolism against CCl₄-induced hepatic dysfunction in rats. Pretreatment with the herbal extract 30 min before liver intoxication exhibited prominent protection (Zhu *et al.*, 1999).

The 50% aqueous methanolic extract of the bark of *Betula platyphylla* var. *japonica* was found to show potent inhibitory activity on CCl₄ or D-galactosamine / lipopolysaccharide induced liver injury in mice (Matsuda *et al.*, 1998).

The water extracts of *Boehmeria var. nivea* and *B. nivea* var. *tenasissima* exhibited antihepatotoxic activity against CCl₄-induced liver injury in rats. These medicinal herbs also showed anti-oxidant effects in FeCl₂-ascorbate induced lipid peroxidation in rat liver homogenate. Moreover, *B. nivea* var. *tenasissima* displayed superoxide scavenging activity as evidenced by electron spin resonance spin-trapping technique (Lin *et al.*, 1998).

The natural root and root callus extracts of *Cichorium intybus* were compared for their anti-hepatotoxic effects in albino rats against CCl₄-induced hepatic damage (Zafar and Ali, 1998). Biochemical studies and histopathological examination of liver sections revealed that *C. intybus* root callus extract could afford a better protection against CCl₄ induced hepatocellular damage compared to the natural extract. The methanol soluble fraction and water soluble fraction of the aqueous extract of the seeds of *C. intybus* also exhibited protection against CCl₄ and paracetamol induced biochemical changes (Gadgoli and Mishra, 1997). Incubation of rat hepatocytes with the herb and thioacetamide resulted in significant hepatoprotection.
Monomethyl fumarate isolated from the methanolic extract of the whole plant of *Fumaria indica* was screened for its antihepatotoxic activity in albino rats (Rao and Mishra, 1998). Biochemical and histopathological evidences showed that methyl fumarate showed antihepatotoxic activity against thioacetamide *in vitro*, and against CCl₄, paracetamol and rifampicin *in vivo* to a significant extent.

Anthocyanins obtained from the petals of *Hibiscus rosasinensis* protect against CCl₄-induced acute liver damage in rats (Obi et al., 1998). Increase in the activities of serum AST and ALT due to CCl₄-intoxication was normalized by anthocyanin treatment.

*Phyllanthus kozhikodianus*, *P.maderaspatensis*, and *Solanum indicum* were screened for their ability to protect against paracetamol and CCl₄-induced liver damage in rats (Asha and Pushpangadan, 1998). *P. kozhikodianus* (whole plant) and *P.maderaspatensis* (leaf) were found to be protective against paracetamol induced liver damage in rats as evidenced by biochemical evaluation (serum marker enzymes) and liver histopathology. They also showed protection against CCl₄-toxicity evidenced by the reduction in CCl₄-induced prolongation of hexabarbitone induced necrosis. *S.indicum* did not show hepatoprotection. *P.maderaspatensis* showed marked choleretic activity in anaesthetised normal rats whereas *S.indicum* (fruit) and *P.kozhikodianus* showed only marginal activity.

Rao and Mishra (1998) studied the effect of the powder and different extracts of the whole plant of *Sida cordifolia* against CCl₄, paracetamol and rifampicin-induced hepatotoxicities in rats. The methanolic extract against CCl₄ and total aqueous extract against rifampicin showed maximum antihepatotoxic activity. The hepatoprotective activity of the plant may be attributed to the more polar phytoconstituents as explained by the investigators.
The protective activity of verbenalin from *Verbena officinalis* (whole plant) against CCl₄-induced liver injury in rodents was reported (Singh *et al.*, 1998). The protective activity of verbenalin is evident from shortened hexabarbitone sleeping time and zoxazolamine-induced paralysis time which were increased by CCl₄ treatment. Pre and post-treatment with verbenalin reduced plasma bromsulphthalein (BSP) in mice, serum transaminases and bilirubin in rats.

Lipopolysaccharide and peptidoglycan induced stress (lipid peroxidation) in rabbits and mice was found to be inhibited by aqueous extract of the root of *Withania somnifera* (Dhuley, 1998).

Lin *et al.* (1997) studied the hepatoprotective effect of various fractions of *Scutellaria rivularis* against CCl₄, D-galactosamine and acetaminophen induced toxicity in rats. CHCl₃ fraction and EtOAc fractions exhibited the greatest hepatoprotective effects on CCl₄-induced liver injuries, the CHCl₃ fraction and n-hexane fraction were most effective against D-galactosamine intoxication, and the CHCl₃ fraction represented the most liver protective effect on acetaminophen-induced hepatotoxicity.

Emodin isolated from the stem of *Ventilago leiocarpa* exhibited hepatoprotective effects on CCl₄ and D-galactosamine-induced liver damage. Emodin significantly reduced the activities of SGOT and SGPT. Histopathological examination of the liver also showed the protective efficacy of emodin (Lin *et al.*, 1996).

Gadgoli and Mishra (1995) evaluated the protective effects of the aerial parts of *Achillea millefolium*, seeds of *Cichorium intybus* and aerial parts of *Capparis spinosa* in CCl₄ and paracetamol-induced hepatic dysfunction in rats.
The aqueous extract of *C.spinosa* was found to be most effective against CCl₄-toxicity model while the chloroform extract of the plant was found to be most effective against paracetamol-induced toxicity model. All the extracts (aqueous, methanol, and chloroform) of these three herbs showed varying degrees of hepatoprotection against the toxicities induced by the two different hepatotoxins.

Methanolic extracts of the seeds of *Apium graveolens* and *Hygrophila auriculata* were proved to be protective against paracetamol and thioacetamide intoxication in rats (Singh and Handa, 1995). Both these herbs reversed the hepatotoxin-induced alterations of various biochemical parameters (activities of transaminases, alkaline phosphatase, sorbitol dehydrogenase, and glutamate dehydrogenase in serum; level of serum bilirubin and hepatic triglycerides). The histopathological pattern of the hepatotoxin-induced liver toxicity of the rats treated with the seed extracts (of *A.graveolens* / *H.auriculata*) showed a normal pattern.

The protective effect of aqueous-methanolic extract of *Artemisia absinthium* was evaluated on acetaminophen and CCl₄-induced hepatic injury (Gilani and Janbaz, 1995). Pre-treatment of rats with the plant extract (500 mg/kg) prevented the acetaminophen as well as CCl₄-induced rise in serum transaminases. Post-treatment with three successive doses of the extract (500 mg/kg) restricted the hepatic damage induced by acetaminophen, but CCl₄-induced hepatotoxicity was not altered.

*Artemisia maritima* is used in the treatment of jaundice (Baquar, 1989). Biochemical studies by Janbaz *et al.* (1995) on the hepatoprotective activity of the aqueous-methanolic extract of *A.maritima* against acetaminophen and CCl₄-
induced liver damage in mice justifies the traditional use of this plant against liver
diseases. In their investigation pre-treatment of rats with the plant extract (500
mg/kg) prevented the hepatotoxin-induced rise in serum transaminases.

Lin et al. (1995) evaluated the protective efficacy of *Curcuma xanthorrhiza*
on acetaminophen and CCl₄-induced hepatic dysfunction in mice. Their study
revealed that the medicinal herb reduced the acute elevation of serum
transaminases induced by the two hepatotoxins. *C.xanthorrhiza* also alleviated the
degree of liver damage after the intraperitoneal administration of the hepatotoxins.

The protective activity of aqueous-methanolic extract of *Cyperus scariosus*
was investigated against acetaminophen and CCl₄-induced hepatic damage in mice
(Gilani and Janbaz, 1995). Pre-treatment of rats with plant extract (500 mg/kg)
significantly lowered the elevated activities of serum transaminases and ALP
induced by acetaminophen and CCl₄. The plant extract also prevented CCl₄-
induced prolongation in pentobarbital sleeping time.

Pre-treatment with the extract of *Daucus carota* (carrot) reversed the CCl₄-
evoked serum and biochemical responses of mice (Bishayee et al., 1995).

Treatment with the water extract of *Ganoderma lucidum*, *G.formosanum*
and *G.neo-japonicum* caused significant decrease in CCl₄-induced toxicity in rat
liver and showed free radical scavenging activity. *G.formosanum* showed greatest
antihepatotoxic and free radical scavenging activity (Lin et al., 1995).

The traditional medical practitioners in Sri Lanka use the mature leaves of
the plant *Osbeckia octandra* for its antihepatotoxic properties (Jayaweera, 1982).
Thabrew et al., (1995) studied the effect of the aqueous extract of *O.octandra*
against injury induced by D-galactosamine and t-butyl hydroperoxide (TBH) in
freshly isolated rat hepatocytes. The extract (500 µg/ml) significantly reduced the inhibition of protein synthesis in hepatocytes incubated for 1hr with galactosamine and decreased the release of cellular lactate dehydrogenase and aspartate aminotransferase into the medium. With TBH, the plant extract decreased lipid peroxidation also.

Sanc et al. (1995) compared the hepatoprotective activity of Phyllanthus amarus and P.debilis (whole plants) in the treatment of liver damage in rats exposed to CCl₄. All the biochemical alterations in plasma and liver of rats due to CCl₄-intoxication was restored by treatment with the medicinal herbs (0.66 g/kg). However, P.debilis has been found to be a better hepatoprotectant than P.amarus.

Sultana et al. (1995) showed that the presence of the extracts of Solanum nigrum and Cichorium intybus in the reaction mixture containing calf thymus DNA and free radical generating system protected DNA against oxidative damage to its deoxyribose sugar moiety. The hepatoprotective effect of these crude extracts may be due to their ability to suppress the oxidative degeneration of DNA in the tissue debris as suggested by the investigators.

Oshima et al. (1995) studied the protective effect of e-viniferin, active principle of the medicinal herb, Vitis coignetiae against CCl₄-induced hepatic injury in mice. Pre-treatment with e-viniferin significantly reduced the CCl₄-induced elevation in serum ALT level in mice. Histopathology of the liver pre-treated with e-viniferin also revealed hepatoprotection.

The active component of Andrographis paniculata, andrographolide, showed a significant protective activity against paracetamol-induced toxicity on ex vivo preparation of isolated rat hepatocytes. It significantly increased the per cent
viability of the hepatocytes and reversed the toxic effects of paracetamol on certain enzymes in serum as well as in isolated hepatic cells (Visen et al., 1993). Pre-and post-treatment with the aqueous extract of the leaves of *A. paniculata* revealed protection against alcohol-induced alteration of serum and liver transaminase activities (Choudhury and Poddar, 1983).

The ethanol/water extract of *Eclipta alba* counteracted the CCl₄-induced inhibition of the hepatic microsomal drug metabolizing enzyme amidopyrine N-demethylase and membrane bound glucose-6-phosphatase. Pre-treatment of *E. alba* normalized the CCl₄-induced decrease of acid phosphatase and alkaline phosphatase activities. Saxena et al. (1993), suggest that the hepatoprotective activity of *E. alba* may be by regulating the levels of hepatic microsomal drug metabolising enzymes.

### 2.2.1 Human clinical trials using *Silybium marianum*

Products of the medicinal herb, Milk thistle (*Silybium marianum*) have been used as remedies for diseases of the liver and biliary tract for almost 2000 years in countries like the United States. *S. marianum* belongs to the family Asteraceae.

The active extract of Milk thistle is silymarin, a mixture of the flavonolignans, silydianin, silychristine and silybin. Fruit is the medicinal part. Silybin is hypothesized to have antioxidant properties (Mira et al., 1994). It is also thought to enhance hepatocyte protein synthesis by stimulating the activity of ribosomal RNA polymerase (Takahara et al., 1986).
Human clinical trials using silymarin to assess the effect of it on acute viral hepatitis (Magliulo et al., 1978), toxin and drug-induced hepatitis (Hruby, 1984), alcoholic liver disease (Salmi and Sarna, 1982) etc. are encouraging. Biochemical and histopathological data substantiate the use of Milk thistle as a remedy for liver ailments.

2.3 Present scenario of the selected medicinal plants

2.3.1 Elephantopus scaber Linn.

*Elephantopus scaber* Linn. of the family Asteraceae, is a perennial herb. It is distributed throughout India, especially in dry localities (Sivarajan and Indira, 1994).

Leaf, bark, root and the whole plant of *E. scaber* is used medicinally (Hammer and Johns, 1993). The entire plant of *E. scaber* is used in chapped lips, gonorrhea, rheumatism, tetanus, galactogogue, hepatitis and to speed up child birth and expulsion of placenta. Its bark is used to heal wounds. Leaf of *E. scaber* is used in arthritis, dysentery, to prevent inflammations after birth and to stop vomiting. Its root is used in filariasis, heart troubles, liver troubles, gonorrhoea, colic pain, fever, cough medicine, diarrhoea and to speed up child birth.

*E. scaber* has antibacterial (Chen et al., 1989), anti-inflammatory (Tsai and Lin, 1999) and uterine stimulant (Hammer and Johns, 1993) activities.

The active principles isolated from *E. scaber* are dotriacontan-1-ol, triacontan-1-ol (alkanes); Elephantopin, 11, 13-dihydrodeoxy; Elephantopin 11, 13-dihydro; Elephantopin, deoxy; Elephantopin, isodeoxy (Sesquiterpenes); Friedelanol, epi, Lupeol (triterpenes) (Hammer and Johns, 1993).
2.3.2 *Glycyrrhiza glabra* Linn.

*Glycyrrhiza glabra* of the family Fabaceae is a tall perennial undershrub cultivated in Punjab and the sub Himalayan tracts (Warrier *et al.*, 1995).

The dried, peeled or unpeeled underground stems and roots constitute the drug known in the trade as liquorice or licorice.

The principal constituent of liquorice which gives it a characteristic sweet taste is glycyrrhizin, which is present in different varieties in a concentration of 2-14%. Other constituents present in liquorice are: glucose (upto 3.8%), sucrose (2.4-6.5%), mannite, starch (30%), asparagine, bitter principles, resins (2-4%), a volatile oil (0.03-0.0355), and colouring matter. The yellow colour is due to the anthoxanthin glycoside, iso liquiritin which undergoes partial conversion to liquiritin during drying and storage of roots. On hydrolysis isoliquiritin gives isoliquiritigenin while liquiritin gives liquiritigenin as a glucone. Both isoliquiritin and liquiritin are bitter with a sweet after taste and stimulate the salivary glands (the herbal database of Himalaya Drug Company).

*G. glabra* is used in the treatment of liver diseases (Luper, 1999). An interferon stimulator (Stronger Neo Minophagen-C) derived from *G. glabra* was found to be useful in viral hepatitis (Acharya *et al.*, 1993). The anti-arthritic and anti-inflammatory effect of Glycyrrhizin on formaldehyde induced rat paw edema in adrenalectomised rats has been reported (Gujral *et al.*, 1961). Isoflavones from *G. glabra* were shown to be effective in protecting mitochondrial function against oxidative stress (Haraguchi *et al.*, 2000). Studies on the effect of *G. glabra* on the metabolism of acetaminophen in rats revealed that it might enhance the
glucuronidation pathway of acetaminophen (Moon and Kim, 1997). Licorice has been reported to possess hypoglycemic action and counteract the abnormal biochemical status of the liver and kidney of hypercholesterolaemic rats (Sitohy et al., 1991). However, excessive amounts of the root, herbal teas or candy derived from G. glabra may be harmful as it increases salt retention and depletes the potassium in the body, causing lack of energy, weakness and even death (the database of Himalaya Drug Company).

2.3.3 *Leucas aspera* (Wild) Spr.

*Leucas aspera* of the family Lamiaceae is an erect herb. In India, it is found as a weed in cultivated fields, waste lands and road sides.

The whole plant is used medicinally. It is a reputed home remedy for worms, fever and intestinal catarrh in children. It is used in anorexia, cough, dyspepsia, fever, helminthic manifestation, jaundice and skin diseases (Sivarajan and Indira, 1994). Its anti-inflammatory and anti-fungal activities have been reported (Kannappareddy et al., 1986; Thakur et al., 1982, Damayanti et al., 1996).

2.3.4 *Woodfordia fruticosa* (L.) Kurz.

*Woodfordia fruticosa* is a bushy shrub found throughout India.

Flowers are used medicinally. Dried flowers are used in dysentery, haemorrhoids, impaired hepatic function, leucorrhoea, menorrhaga and considered as a safe stimulant in pregnancy (Chatterjee and Pakrashi, 1994).
2.4 Antihepatotoxic herbal formulations

HD-03 is a multi-herbal formulation containing Solanum nigrum L. (whole plant), Cichorium intybus L (seeds), Picrorrhiza kurroa Benth (roots), Tephrosia purpurea L. (whole plant) and Andrographis paniculata Nees (leaves). Pretreatment of rats with HD-03 (750 mg/kg body weight) prevented the elevation of SGPT, SGOT and serum bilirubin and also depletion in liver glycogen due to galactosamine intoxication (Mitra et al., 2000). Report of the protective efficacy of HD-03 against paracetamol, thioacetamide and isoniazid is also available (Mitra et al., 1998).

HPN-12 is an ayurvedic preparation containing the following medicinal herbs: Glycyrrhiza glabra, Picrorrhiza kurroa, Berberis aristata, Piper longum, Phyllanthus niruri, Solanum dulcamara, Zingiber officianale, Curculigo orchioides, Elettaria cardamomum, Tinospora cordifolia, Desmodium triflorum and Saccharum officinarum. The effect of this herbal drug on CCl₄-induced hepatic dysfunction in rats was evaluated (Latha et al., 1999). The CCl₄-induced biochemical alterations were ameliorated more or less to the normal state by this herbal preparation.

Liv. 100 is an ayurvedic formulation which contains extracts of Cichorium intybus, Solanum nigrum, Phyllanthus amarus, Picrorrhiza kurroa, and Emblica officinalis. Saraswathy and Shyamala devi (1999) studied the antihepatotoxic potential of Liv. 100 on anti-tubercular drugs (isoniazid, rifampicin, and pyrezinamide)-induced mitochondrial damage in rat liver. Activities of TCA cycle enzymes (succinate dehydrogenase, isocitrate dehydrogenase, malate dehydrogenase, α-ketoglutarate dehydrogenase) and respiratory marker enzymes
(cytochrome c oxidase, NADH dehydrogenase) decreased and mitochondrial lipid peroxidation increased upon anti-TB drug treatment. Co-administration of Liv. 100 significantly reduced the anti-TB drug-induced biochemical changes. The authors suggest that the mechanism of action of Liv. 100 may be due to its antioxidant nature against drug-induced lipid peroxidation.

Farooq et al. (1997) evaluated the protective role of Koflet, an ayurvedic preparation against cellular toxicity caused by CCl₄ and flyash in albino rats. The ingredients of Koflet are: Vitis vinifera L. (Vitaceae), Ocimum sanctum L. (Labiatae), Embelia ribes Burm. f. (Myrsinaceae), Adhatoda vasica Nees (Acanthaceae), Balsamodendron makal Hook.ex Slock (Burseraceae), Cinnamomum zeylanicum Blume (Lauraceae), Solanum xanthocarpum Schrad. et Wendl. (Solanaceae), Zingiber officinale Rose (Zingiberaceae), Emblica officinalis L. (Euphorbiaceae), Codia dichotoma Forst. (Boraginaceae), Malva sylvestris L. (Malvaceae), Glycyrrhiza glabra Linn. (Leguminosae), Piper longum L. (Piperaceae) Sausurea lappa Clarke (Compositae) and Myristica fragrans Hout. (Myristicaceae). Most of the biochemical alterations observed in lung, trachea and serum due to the administration of CCl₄ and flyash were counteracted by Koflet.

Livex is a crude drug formulation consisting of Trephrosia purpurea (Leguminosae), Aconitum heterophyllum (Ranunculaceae), Solanum nigrum (Solanaceae), Cichorium intybus (Asteraceae), Cassia occidentalis (Caesalpiniaceae), Tamarix gallica (Tamaricaceae), Embelia ribes (Myrsinaceae), Andrographis paniculata (Acanthaceae) and Piper longum (Piperaceae). Venkateswaran et al. (1997) studied the effect of Livex in rats against erythromycin estolate-induced toxicity. The increased level of serum enzymes (AST, ALT and ALP) bilirubin, serum and tissue cholesterol, triglycerides,
phospholipids and free fatty acids observed in toxicity induced rats were very much reduced when treated with livex.

A new indigenous drug, Livzon has been reported to possess hepatoprotective action in a model of obstructive jaundice in rats (Ratan et al., 1997).

The herbal formulation, “Rhinax”, consists of a mixture of water extracts of medicinal plants: *Withania somnifera* L. (Solanaceae; root), *Asparagus racemosus* Wild. (Liliaceae; root), *Mucuna pruriens* Baker non DC (Papilionaceae; root) *Phyllanthus emblica* Gasertn. (Euphorbiaceae; fruit), *Glycyrrhiza glabra* L. (Papilionaceae; root), *Terminalia chebula* Retz.(Combretaceae; fruit) and *Myristica fragrans* Houtt. (Myristicaceae; seed). Oral administration of Rhinax at a dose of 80 mg/kg significantly reduced the hepatotoxic effects of CCl₄ (Dhuley and Naik, 1997).

In Nigeria, a herbal preparation, “Blood wort” is used by the traditional healers to treat jaundice. It contains equal amounts of dried barks of *Rumex acetosa* L. (Polygonacease) and *Cinchona succirubra* Pav. (Rubiaceae). Biochemical studies of the aqueous extract of Blood wort on CCl₄-induced liver dysfunction in rats revealed its hepatoprotective action (Okonkwo and Msonthi, 1995). CCl₄ treatment resulted in the elevation of serum transaminase activities and post-treatment with the aqueous extract prevented this change.

Phyllanthus niruri Linn. and Hook, Plantago major Linn., Rosa damascena Linn., and Solanum xanthocarpum (Schrad and Wemdl). Kapur et al. (1994) studied the effect of oral pre-treatment with Jigrine on hepatic damage induced by alcohol-CCl₄ and paracetamol in rats. Alcohol-CCl₄ and paracetamol treatment produced increase in serum transaminases, bilirubin, plasma prothrombin time and lipid peroxides in liver. The activities of the parameters were reduced by pre-treatment with Jigrine. Histopathological examination of liver sections confirmed the hepatoprotective effect of the preparation.

One of the ayurvedic preparations with well documented hepatoprotective effect against several hepatotoxins is Liv. 52 (Pandey et al., 1994). For this reason, it is widely used in experimental approaches to compare the hepatoprotective effect of other herbal preparations as well as single herbs.

Administration of ayurvedic drugs, kumari asav, kumari kalp, arogyavardhini and tamra bhasma concomitant with CCl₄ counteracted the alterations in the activities of lipolytic enzymes during hepatic necrosis induced by CCl₄ in liver, kidney and adipose tissue of albino rats (Patil et al., 1993).

BR - 16A (Mentat) is a herbal preparation containing Bacopa monnieri, Asparagus racemosus, Acorus calamus, Withania somnifera, Tinospora cordifolia, Emblica officinalis, Evolvulus alsinoides, Saurssurea lappa, Terminalia chebula, and T. bellirica. Chronic administration of ethanol and its withdrawal after 6 days produced anxiogenic reaction in mice and rats. Administration of BR - 16A prior to ethanol intoxication for 6 days prevented withdrawal induced anxiety in rats and mice. Ethanol withdrawal also sensitized the convulsogenic reaction to pentylenetetrazole. A non-convulsive dose of pentylenetetrazole produced full
blown convulsions and increased mortality in ethanol withdrawal rats and mice. Both acute and chronic administration of the drug exhibited significant protection against ethanol withdrawal induced reduction in pentylenetetrazole threshold in rats and mice (Kulkarni and Verma, 1993).

Mandur bhasma is an ayurvedic preparation of iron which is used in traditional medicine against hepatitis. Devarshi et al. (1986) studied the hepatoprotective property of this drug in albino rats with CCl₄-induced hepatic injury. The activities of acid lipase, alkaline lipase and lipoprotein lipase in liver, kidney and adipose tissue and hormone sensitive lipase in adipose tissue exhibited significant alterations in CCl₄-induced hepatic injury. Simultaneous treatment with Mandur bhasma prevented the CCl₄ mediated changes in the enzyme activities.

2.4.1 Human clinical trials

There are reports of clinical trials as to the efficacy of certain herbal formulations on liver diseases:

Ghoda et al. (1998) reported the hepatoprotective efficacy of Hepafyt on ten patients manifesting symptoms of alcohol-induced hepatotoxicity. Hepafyt tablet contains aqueous extracts of the medicinal plants, Picrorrhiza kurroa Royle, ex Benth, Andrographis paniculata Nees, Eclipta alba, Tecoma undulata, G. Don., and Tinospora cordifolia Miers. They carried out biochemical and haematological investigations in addition to ultrasonography and monitored symptoms like nausea, sleep disturbances, right upper abdominal pain, fatigue / weakness and anorexia. After treatment with Hepafyt, there was a decrease in the activities of
serum enzymes like AST, ALT, ALP, GGT and in the levels of cholesterol and bilirubin. There was significant improvement in anorexia, fatigue, vomiting, sleep disturbances and right upper abdominal pain.

Liv. 52 has been reported to improve the biochemical parameters in patients of alcoholic cirrhosis (Dubey et al., 1994). It exhibited significant increase in total protein, serum albumin, blood volume and improvement in liver function tests, after six weeks of treatment.

2.5 Kamilari as a hepatoprotective drug

Kamilari has been clinically evaluated to determine its effect on alcoholic liver cirrhosis (Rajesh et al., 2000). Before treatment, the activities of serum transaminases, alkaline phosphatase, cholesterol and bilirubin showed significant elevation compared to normal control. However, the concentration of serum proteins decreased. All these alcohol-induced biochemical changes improved significantly after treatment with Kamilari for a period of four months.

Kamilari has also been clinically evaluated for its efficacy in viral hepatitis (Shirwaikar, 1996). Treatment of the patients with the herbal formulation (for 7 days) led to the disappearance of the clinical symptoms like anorexia, abdominal discomfort, lethargy, nausea and jaundice. Biochemical investigation showed that treatment with the herbal drug for 7 days significantly reduced the activities of serum transaminases (AST and ALT) and also the level of serum bilirubin.