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PharmTech

International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.1, No.4, pp 1330-1334, Oct-Dec 2009

Hepatoprotective activity of some indigenous plants

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Abstract: Herbal plants or botanical medicines have been used traditionally by herbalist worldwide for the prevention and treatment of liver disease. The plant kingdom plays a major role in the life of human beings and animals. The plant, as one of the important sources, still maintains its original place in the treatment of various diseases, including liver disorders, with no ill effects. Considerable studies have been carried out on ethno medicinal plants; however, only few medicinal plants have attracted the interest of scientists, to investigate them for a remedy for hepatoprotective. Clinical research in this century has confirmed the efficacy of several plants in the treatment of liver disease. Hence, this review article contributes to the knowledge of reported indigenous plants, which are prevalent for prevention and treatment of liver disorders.
Key words: Hepatoprotective plants, liver, Pharmacognosy, Pharmacological activities, Natural products, Medicinal herbs,

Introduction

The liver is the largest glandular organ in the body, and has more functions than any other human organ. A person's entire blood supply passes through the liver several times a day; The Liver has a pivotal role in human metabolism. Liver produces and secretes bile, it also produces prothrombin and fibrinogen, both blood-clotting factors, and heparin, a mucopolysaccharide sulfuric acid ester that helps keep blood from clotting within the circulatory system. The liver converts sugar into glycogen,

Liver diseases have become one of the major causes of morbidity and mortality in man and animals all over globe and hepatotoxicity due to drugs appears to be the most common contributing factor[1]. Among the many diseases that can affect the liver the most common is 'viral hepatitis' (Inflammation of liver caused by viral infection). Hepatitis can be caused by drugs, viruses, bacteria, mushrooms, parasites like amoebas or giardiasis. About 20,000 deaths found every year due to liver disorders. The use of natural remedies for the treatment of liver diseases has a long history and medicinal plants and their derivatives are still used all over the world in one form or the other for this purpose. Scientific evaluation of plants has often shown that active principles in these are responsible for therapeutic success. A large number of medicinal plants have been tested and found to contain active principles with curative properties against a variety of diseases[2]. Liver protective plants contain a variety of chemical constituents like phenols, coumarins, lignans, essential oil, monoterpenes, carotinoids, glycosides, flavanoids, organic acids, lipids, alkaloids and xanthenes[3]. Recent experience has shown that plant drugs are relatively non-toxic, safe and even free from serious side effects[4]. This review article has been presented to enumerate some indigenous plants that have hepatoprotective properties.

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Hepatoprotective plants-

Andrographis lineata *nees* Hepatoprotective effect of *Andrographis lineata* (Acanthaceae) extracts in CCl(4)-induced liver injury in rats. Male Wistar rats with chronic liver damage, induced by subcutaneous injection of 50% v/v CCl(4) in liquid paraffin at a dose of 3 mL/kg on alternate days for a period of 4 weeks, were treated with methanol and aqueous extracts of A. lineata orally at a dose of 845 mg/kg/day. The biochemical parameters such as serum glutamate oxaloacetate transaminase, serum

glutamate pyruvate transaminase, serum bilirubin and alkaline phosphatase were estimated to assess the liver function. Histopathological examinations of liver tissue corroborated well with the biochemical changes. The activities of extracts were comparable to a standard drug[5].

Andrographis paniculata (kalmegh) Antihepatotoxic activity of the *Andrographis paniculata* (acanthaceae) methanolic extract (equivalent to 100 mg/kg of andrographolide) and 761.33 mg/kg ip, of the andrographolide-free methanolic extract (equivalent to 861.33 mg/kg of the methanolic extract) of the plant, using CCl4-intoxicated rats. Biochemical parameters like serum transaminases--GOT and GPT, serum alkaline phosphatase, serum bilirubin and hepatic triglycerides were estimated to assess the liver function. The results suggest that andrographolide is the major active antihepatotoxic principle present in *A. paniculata*[6].

Azadirachta indica (Neem) Effect of *A. indica* leaf *(meliaceae)* extract on serum enzyme levels (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase) elevated by paracetamol in rats was studied with a view to observe any possible hepatoprotective effect of this plant. It is stipulated that the extract treated group was protected from hepatic cell damage caused by paracetamol induction. The findings were further confirmed by histopathological study of liver.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[7].

Careya arborea The methanol extract of *Careya arborea bark*, (myrtaceae) was tested for antioxidant and hepatoprotective activity in Ehrlich ascites carcinoma (EAC) tumor-bearing mice. Tumor control animals inoculated with EAC showed a significant alteration in the levels of antioxidant and hepatoprotective parameters[8]. The extract treatment at 50, 100 and 200 mg/kg body weight doses given orally caused a significant reversal of these biochemical changes towards the normal in serum. Liver and kidney when compared to tumor control animals indicating the potent antioxidant and hepatoprotective nature of the standardized extract.

Cassia fistula (Amaltas) Hepatoprotective activity of the n-heptane extract of *Cassia fistula* (Fabaceae) leaves was investigated by inducing hepatotoxicity with paracetamol in rats. The extract at a dose of 400 mg/kg body wt. exhibited orally, significant protective effect by lowering the serum levels of transaminases (SGOT and SGPT), bilirubin and alkaline phosphatase (ALP). The effects produced were comparable to that of a standard hepatoprotective agent[9].

Cleome viscosa Linn (Tickweed) The hepatoprotective activity of the *Cleome viscosa* Linn (Capparidaceae) extract was assessed in CCI $_4$ induced hepatotoxic rats. The test material was found effective as hepatoprotective, through in vivo and histopathological studies. The extract was found to be effective in shortening the thiopental induced sleep in mice poisoned with CCl $_4$. The hepatoprotective effect of ethanolic extract was comparable to that of silymarin, a standard hepatoprotective agent[10].

Eclipta Alba (Bhringaraj) The hepatoprotective effect of the ethanol/water (1:1) extract of *Eclipta Alba* (Asteraceae) was studied at subcellular levels in rats against (CCl_4) -induced hepatotoxicity. The loss of hepatic lysomal acid phosphatase and alkaline phosphatase by (CCl_4) was significantly restored by *Eclipta Alba*. The study shows that hepatoprotective activity of *Eclipta Alba* is by regulating the levels of hepatic microsomal drug metabolising enzymes[11].

Fumaria indica (hauskn) *Fumaria indica* (Fumariceae) were studied for their hepatoprotective activity against carbontetrachloride, paracetamol and rifampicin-induced heptatotoxicites in albino rats. The petroleum ether extract against carbonetrachloride, total aqueous extract against paracetamol and methanolic extract against rifampicin-induced hepatotoxicities showed similar reductions in the elevated levels of some of the serum biochemical parameters in a manner similar that of silymarin indicating its potential as a hepatoprotective agent[12].

Morinda citrifolia *L. (noni)* The hepatoprotective effects of Noni juice (TNJ) (Rubiaceae) against CCl(4)-induced chronic liver damage in female Sprague Dawley (SD) rats. Histopathological examination revealed that liver sections from the TNJ + CCl(4) appeared similar to controls, whereas typical hepatic steatosis was observed in the placebo + CCl(4) group. Serum alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transaminase (ALT), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels were increased in the placebo group compared with the TNJ group. In contrast, high-density lipoprotein (HDL) was increased in the TNJ group and decreased in the placebo group. Thus, TNJ juice appears to protect the liver from chronic exogenous CCl(4) exposures[13].

Phyllanthus amarus (Bhuiamala) Ethanolic extract of *Phyllanthus amarus* (euphorbiaceae), at (0.3g kg (-1) BW 0.2 ml (-1) day (-1) was given to all groups except control groups (gp. I and gp. V), after 30 min of aflatoxin administration. The entire study was carried out for 3 months and animals were sacrificed after an interval of 30 days till the completion of study. *Phyllanthus amarus* extract was found to show hepatoprotective effect by lowering down the content of thiobarbituric acid reactive substances (TBARS) and enhancing the reduced glutathione level and the activities of antioxidant enzymes, glutathione peroxidase (GPx), glutathione-S-

transferase (GST), superoxide dismutase (SOD) and catalase (CAT) [14].

Phyllanthus emblica (amla) Ethanol extract of *Phyllanthus emblica* Linn. (Euphorbiaceous) (PE) induced rat hepatic injury. PE (0.5 and 1 mg/ml) increased cell viability of rat primary cultured hepatocytes being treated with ethanol (96 µl/m) by increasing % MTT and decreasing the release of transaminase. Pretreatment of rats with PE at oral dose of 25, 50 and 75 mg/kg or SL (silymarin, a reference hepatoprotective agent) at 5 mg/kg, 4 h before ethanol lowered the ethanol induced levels of AST, ALT and IL-1beta. The 75 mg/kg PE dose gave the best result similar to SL. Treatment of rats with PE (75 mg/kg/day) or SL (5 mg/kg/day) for 7 days after 21 days with ethanol (4 g/kg/day, p.o.) enhanced liver cell recovery by bringing the levels of AST, ALT, IL-1beta back to normal[15].

Phyllanthus polyphyllus Methanolic extract of *Phyllanthus-polyphyllus* (euphorbiaceae) was evaluated for hepatoprotective and antioxidant activities in rats. The plant extract (200 and 300 mg/kg, p.o.) showed a remarkable hepatoprotective and antioxidant activity against acetaminophen induced hepatotoxicity as judged from the serum marker enzymes and antioxidant levels in liver tissues[16]. The activity of the extract at dose of 300 mg/kg was comparable to the standard drug, silymarin (50 mg/kg, p.o.). Histopathological changes of liver sample were compared with respective control.

Phyllanthus reticulates (Potato bush) Two partially purified organic fractions designated by PR1 and PR2 of the fat free ethanol (95%) extract of aerial parts of *Phyllanthus reticula*tus (Euphorbiaceae), were tested for the hepatoprotective activity in rats against CCl(4)-induced liver damage. The rats receiving the fractions showed promising hepatoprotective activity as evident from significant changes of pentobarbital-induced sleeping time, changes in serum levels of sGPT, sGOT, sALP and bilirubin and also from histopathological changes as compared to CCl(4)-intoxicated rats[17].

Picrorhiza kurroa (Kutki) Administration of picroliv, a standardized fraction of alcoholic extent of *Picrorhiza kurroa* (Scrophulariaceae) (3-12 mg/kg/day for two weeks) simultaneously with P. berghei infection showed significant protection against hepatic damage in Mastomys natalensis. The increased levels of serum glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase, lipoprotein-X (LP-X) and bilirubin in the infected animals were marked reduced by different doses of picroliv. In the liver, picroliv decreased the levels of lipid peroxides and hydroperoxides and facilitated the recovery of superoxide dismutase and glycogen[18, 19].

Polygala arvensis Chloroform extract of leaves of *Polygala arvensis* (polygalaceae), in 0.3% carboxy methyl cellulose (CMC) was evaluated for hepatoprotective activity in Wistar albino rats by inducing hepatic injury with d-galactosamine (400 mg/kg). The chloroform extract of *Polygala arvensis* at an oral dose of 200 mg/kg and 400 mg/kg exhibited a significant ($P<0.001$, $P<0.01$ and $P<0.05$) protection effect by normalizing the levels of aspartate amino transferase. (ASAT, GOT), alanine amino transferase (ALAT, GPT), alkaline phosphatase (ALP), total bilirubin (TB), lactate dehydrogenase (LDH), total cholesterol (TC), triglycerides (TGL), albumin, total protein (TP) which were significantly ($P<0.001$) increased in rats by treatment with 400 mg/kg i.p. of d-galactosamine. Silymarin (25 mg/kg), a known hepatoprotective drug used for comparison exhibited significant activity ($P<0.001$)[20].

Pterocarpus santalinus (Kanak champa) the aqueous (45 mg/ml) and ethanol (30 mg/ml) extracts of *Pterocarpus santalinus* (Fabaceae) stem bark in 1% gum tragacanth was administered orally for 14 days and the hepatoprotective activity studied in CCl4 induced hepatic damage model. There was a significant increase in serum levels of bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase with a decrease in total protein level, in the CCl4 treated animals, reflecting liver injury. In the extracts treated animals there was a decrease in serum levels of the markers and significant increase in total protein, indicating the recovery of hepatic cells. Ethanol extract treated animal's revealed normal hepatic cords without any cellular necrosis and fatty infiltration[21].

Ptrospermum acerifolium (Kanak champa) the hepatoprotective activity of the ethanol extract of the leaf of *Ptrospermum acerifolium* (Sterculiaceae) was investigated in rats. Hepatotoxicity was induced in male Wistar rats by intraperitoneal injection of carbon tetrachloride (0.1 ml/kg/d p.o. for 14 d). Ethanol extract of *P. acerifolium* leaves were administered to the experimental rats (25 mg/kg/d p.o. for 14d). The Hepatoprotective effect of these extracts was evaluated by liver function biochemical parameters (total bilirubin, serum protein, alanine aminotransaminase, asparatate aminotransaminase and alkaline phosphates activites) and histopathological studies of liver. In ethanol extract-treated animals, the toxicity effect of carbon tetrachloride was controlled significantly by restoration of the levels of serum bilirubin and enzymes as compared to the normal and standard drug silymarin-treated groups[22].

Solanum nigrum (Makoi) and ***Cichorium intybus*** (Kasni) The presence of plant extracts of *Solanum nigrum* (solanaceae) and *Cichorium intybus* (Asteraceae) in the reaction mixture containing calf thymus DNA and free radical generating system protect DNA against oxidative damage to its deoxyribose sugar moiety. The

effect was dependent on the concentration of plant extracts. However, the effect of Cichorium intybus was much pronounced as compared to the effect of *Solanum nigrum*. These studies suggest that the observed hepatoprotective effect of these crude plant extracts may be due to their ability to suppress the oxidative degradation of DNA in the tissue debris[23].

Swertia Chirata (Chirayata) Simultaneous treatments with *S. Chirata* (Gentianaceae). (in different doses, viz, 20, 50, and 100 mg/kg body wt daily) and (CCl_4) caused improvement at both biochemical and histopathological parameters compared to that of (CCl_4) treatment alone but it was most effective when S. chirata was administered in a moderate dose (50 mg/kg body wt)[24, 25].

Wedelia calendulacea L (Bhanra) Hepatoprotective activity of the ethanolic-leaf extract of *W.calendulacea* (Asteraceae) (EEWC) was studied by estimating serum enzyme activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), protein and bilirubin. 4 The treatment with EEWC showed a dose-dependent reduction of CCl induced elevated serum levels of enzyme activities with parallel increase in total protein and bilirubin, indicating the extract could preserve the normal functional status of the liver[26]. .

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