A recent update in research on the antihapatotoxic potential of medicinal plants

Anju Dhiman\textsuperscript{1,}, Arun Nanda\textsuperscript{1}, Sayeed Ahmad\textsuperscript{2,3}
\textsuperscript{1} Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak 124001, Haryana, India
\textsuperscript{2} Bioactive Natural Product Laboratory, Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Jamia Hamdard, New Delhi 110062, India
\textsuperscript{3} Division of Kidney Diseases and Hypertension, Feinstein Institute for Medical Research, New York 11021, USA

ABSTRACT: Hepatic damage is a global metabolic and epidemic disease, affecting essential biochemical activities in almost every age group. Conventional drugs used in the treatment of liver disorders are often inadequate. Also, the spectrum of liver abnormalities caused by allopathic drugs is found to be broad. In view of severely undesirable side effects of synthetic agents, it is necessary to search for alternative drugs for the treatment of liver diseases to replace the currently used drugs, which are of doubtful efficacy and safety. Therefore, there is growing focus to follow systematic research methodology and to evaluate scientific basis for the traditional herbal medicines that are claimed to possess hepatoprotective activities. Use of herbal drugs in the treatment of liver diseases has a long tradition, especially in Eastern medicine and can be traced back as far as 2100 B.C. in ancient China (Xia Dynasty) and India (Vedic period), but evidence for efficacy is sparse. The current study is aimed at providing an overview of clinical and experimental studies carried out on the most effective and commonly used hepatoprotective plants and their beneficial aspects.

KEYWORDS: plants, medicinal; plant extracts; hepatoprotective agents; review

Over recent decades, herbal medicine has become an item of global magnitude, having both medicinal and economic implications. Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents for the prevention of diseases and ailments\textsuperscript{41}. Liver diseases remain one of the most serious health problems\textsuperscript{21}. In view of severely undesirable side effects of synthetic agents and the absence of reliable liver-protective drugs in modern medicine, there are a number of medicinal preparations in the Ayurvedic system of Indian medicine recommended for the treatment of liver disorders. Their usage has been popular for centuries.
and are quite often claimed to offer significant relief\(^5\). Also, there is a growing trend to follow systematic research methodology and to evaluate the scientific basis for traditional herbal medicines that are claimed to possess hepatoprotective potential\(^6\). As the efficacy of herbal medicinal products in preclinical liver diseases is not well documented, accurate scientific assessment has become a prerequisite for acceptance of herbal health claims. In the present study, an attempt has been made to review the most prospective medicinal plants having pharmacologically reputable antihepatotoxic activities.

1 Some potential medicinal plants with reported hepatoprotective activities

1.1 *Ailanthus excelsa*  *Ailanthus excelsa* Roxb. (Simaroubaceae) is commonly known as “Mahanimba” due to its resemblance with neem tree (*Azadirachta indica*). It is a fast growing tree extensively cultivated in many parts of India\(^5\), found in Bihar, Chota Nagpur, Madhya Pradesh, forests of Ganjam, Vizagapatam and Deccan\(^6\). The ethanol extract of *A. excelsa* leaves showed protective effect against carbon tetrachloride (CCL\(_4\))-induced liver injury as evidenced by a significant reduction in the CCL\(_4\)-induced elevated enzyme levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP). The presence of phenolics might be the responsible factor for the above activities\(^5\).

1.2 *Andrographis paniculata*  *Andrographis paniculata* (Burm. f.) Nees (Acanthaceae), native to China and India, is a medicinal herb with an extremely bitter taste used to treat liver disorders, bowel complaints of children, colic pain, common cold and upper respiratory tract infection\(^7\). The hepatoprotective activity of aqueous extract of *A. paniculata* (12 mg/kg body weight, orally) on hexachlorocyclohexane-induced severe liver damage in Swiss male mice has been reported. It was found to act by decreasing activity of liver enzymes such as AST, ALT and lipid peroxidase\(^8\).

1.3 *Alstonia scholaris*  *Alstonia scholaris* Linn. R.Br. belongs to the family Apocynaceae and grows throughout India, in deciduous and evergreen forests, also in plains. The plant is widely found in India in sub-Himalayan region from the Yamuna eastward ascending to 900 m above the sea level, and abundantly found in West Bengal and South India. The hepatoprotective effect of *A. scholaris* on liver injuries induced by CCl\(_4\), \(\beta\)-D-galactosamine, acetaminophen and ethanol was investigated by serum biochemical and histopathological examinations. All serological and histopathological effects were comparative with those of *Bupleurum chinense* DC., which has been reported previously as treatment criteria of hepatitis. A tendency was shown to inhibit cell necrosis and inflammatory cell infiltration caused by \(\beta\)-D-galactosamine in histopathological examination\(^9\).

1.4 *Bacopa monnieri*  *Bacopa monnieri* Linn. (Scrophulariaceae) is a creeping, glabrous, succulent herb, rooting at nodes, distributed throughout India in all plain districts, ascending to an altitude of 1320 m. The ethanolic extract of *B. monnieri* aerial parts was found to protect against ethanol-induced liver injury in rats. The crude extract was investigated for hepatoprotective activity in albino rats (300 mg/kg, orally) and compared with standard drug silymarin (25 mg/kg, orally). The hepatoprotective potential of the ethanolic extract of *B. monnieri* aerial parts was found to be related to the free radical-scavenging properties of saponins present in high concentration of the extract\(^10\).

1.5 *Berberis tinctoria*  The plant *Berberis tinctoria* Lesch (Berberidaceae) is a shrub, very variable in size and form, in the open often 60 to 90 cm high, but in the forest sometimes reaching a height of 4.5 m with thick stem and long slender branches bearing numerous slender leafy twigs. It is locally called as “Oosikala” and medicinally used by the Kurumbas, the Nilgiri tribe in India, for stomachache (root paste). Hepatoprotective activity of the methanolic extract in paracetamol-induced liver toxicity has been studied, which showed significant reduction in the elevated levels of enzymes. Results suggested that the plant may have potential therapeutic value in the treatment of some liver disorders, probably by its

---

**Related Articles**


antioxidative effect on hepatocytes\textsuperscript{[11]}.

1.6 Boerhaavia diffusa  Boerhaavia diffusa var. hirsuta Kuntze (Nyctaginaceae) is commonly known as "Punarnava". The roots are used to treat various disorders, and especially tribes use this plant to treat liver disorders. The plant is a weed found throughout India\textsuperscript{[9]}. The hepatoprotective activity of aqueous extract of roots was examined in thioacetamide-intoxicated rats and was found to be better than powder form probably owing to the better absorption of the liquid form through the intestinal tract. It was found to act by stabilizing lysosomal membranes and maintaining parenchymatous cells. An alcoholic extract of the whole plant given orally exhibited hepatoprotective activity against experimentally induced CCl\textsubscript{4} hepatotoxicity in rats and mice. The action may be owing to its antioxidant effects\textsuperscript{[15,18]}.

1.7 Capparis moonii  Capparis moonii Hook. f. Thoms. (Capparidaceae), commonly known as “Rudanti” is a rambling shrub growing to a height of 3 to 5 m. Its natural habitat is the deep forests of Konkan and Sri Lanka at 1 000 m above the sea level. The effects of C. moonii fruits were studied in CCl\textsubscript{4}-induced hepatotoxicity in rats. The extract of C. moonii produced significant lowering of the elevated serum ALT, AST and ALP levels, and a rise of depleted total protein when compared with the toxic control. It appeared that the plant extract had interfered with cytochrome P450 and hinder the formation of hepatotoxic CCl\textsubscript{4} free radical to exert its hepatoprotective action\textsuperscript{[14]}.

1.8 Chamomile recutita  The effects of aqueous ethanolic extract of Chamomile recutita (400 mg/kg, per oral) on blood and liver glutathione, Na\textsuperscript{+}-K\textsuperscript{+}-ATPase activity, serum marker enzymes, serum bilirubin, glycogen and thiobarbituric acid-reactive substances (TBARS) against paracetamol-induced liver damage in rats have been studied to find out the possible mechanism of hepatoprotection. It was observed that the extract of C. recutita has reversal effects on the serum parameters and possesses significant hepatoprotective activity, which may be due to normalization of impaired function\textsuperscript{[17]}.

1.9 Cichorium intybus  Cichorium intybus, also known as chicory, common chicory, suncyry and wild succory, is a wild plant of the family Compositae. It is found wildly in India, such as Punjab, N. W. Frontier province and Hyderabad and is cultivated in Nadiad, Broach and Amalsad in Mumbai\textsuperscript{[9]}. In a study, the protective activity of polyphenolic extracts of Silybum marianum and C. intybus were investigated on thioacetamide-induced hepatotoxicity in rat. Significant decreases in the activities of AST, ALT, ALP and bilirubin were observed in the groups treated with the extracts and thioacetamide compared with the group that was treated with thioacetamide alone. The levels of Na\textsuperscript{+} and K\textsuperscript{+} and liver weight between different groups were not significantly altered. The protective effects of these extracts on liver cells can be due to the presence of flavonoid compounds and their antioxidant effects\textsuperscript{[86]}.

The effects of different concentrations of the hydro-alcoholic extract of dried powdered leaves of C. intybus on CCl\textsubscript{4}-induced hepatotoxicity in vivo in rats and CCl\textsubscript{4}-induced cytotoxicity in isolated rat hepatocytes were investigated. The extract with concentrations of 60 to 600 µg/mL protected the cells against CCl\textsubscript{4}-induced cytotoxicity, but concentrations of 1.5 mg/mL and higher increased the CCl\textsubscript{4}-induced cytotoxicity. C. intybus extract itself was toxic towards isolated hepatocytes in concentrations above 3.6 mg/mL. The results of the study supported the traditional beliefs on hepatoprotective effect of the C. intybus extract; however, high concentrations were hepatotoxic\textsuperscript{[37]}.

The presence of plant extracts of Solanum nigrum and C. 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 effect was dependent on the concentration of the plant extracts. However, the effect of C. intybus was much pronounced as compared to the effect of S. nigrum. These studies suggested that the observed hepatoprotective effect of these crude plant extracts may be due to their ability to suppress oxidative degradation of DNA in the tissue debris\textsuperscript{[39]}.

1.10 Citrus limon  Citrus limon (L.) Burm. f. (Rutaceae), commonly known as lemon, is used in tribal medicine for the treatment of liver ailments and jaundice\textsuperscript{[15]}. The plant is cultivated all over India, particularly in home gardens and small-sized orchards in Uttar Pradesh, Mumbai, Madras and Mysore\textsuperscript{[9]}. The ethanol extract of C. limon fruits was investigated for its effects on experimental liver damage in rats induced by CCl\textsubscript{4}, and the ethyl acetate-soluble fraction of the extract was evaluated on HepG2 cell line. The ethanol extract normalized the levels of AST, ALT and ALP, and total and direct bilirubin, reduced the levels of malondialdehyde (MDA), hence the lipid peroxidation, and raised the levels of antioxidant enzymes superoxide dismutase (SOD) and catalase. Three doses of ethanol extract (150, 300, and 500 mg/kg) were evaluated. The effect was dose-dependent, and the effect of the highest dose was almost equal to the standard drug silymarin. The probable mechanism of action could be the inhibition of intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and tumor necrosis factor-α released by naringin and naringenin\textsuperscript{[15]}.

1.11 Citrus reticulate  Citrus reticulate (Rutaceae) is cultivated in most parts of India. The areas of concentrated cultivation lie in Assam, Sikkim, Madhya Pradesh, Punjab and Coorg\textsuperscript{[91]}. C. reticulata essential oil was studied for hepatoprotective potential
in isoniazid-induced liver damage (50 mg/kg, per oral for 30 d) in Wistar rats. The essential oil (200 mg/kg, per oral) was administered every 24 h for 30 d, and the standard group received Liv52. The animals treated with essential oil of C. reticulata and Liv52 showed significant reduction in all the biochemical parameters such as AST, ALT and bilirubin while total protein content was significantly reduced\[20\].

1.12 Cleome viscosa Cleome viscosa is a common weed used extensively in the traditional Indian medical system. It is an annual, sticky herb belonging to the family Capparaceae. The plant is distributed throughout the plains in India. The aqueous seed extract of C. viscosa was evaluated against CCl4-induced liver damage in Wistar rats. The aqueous seed extract of C. viscosa (200 mg/kg) was administered orally to the animals with CCl4-induced hepatotoxicity and silymarin (200 mg/kg) was given as a reference standard. Significant reductions in serum enzymes AST, ALT, ALP and \( \gamma \)-glutamyl transpeptidase (\( \gamma \)-GT) and lipid peroxidase and increases in reduced glutathione suggested that the aqueous extract may have membrane-stabilizing activity and could protect the liver against CCl4-induced hepatotoxicity\[21\].

1.13 Coriandrum sativum Coriandrum sativum L. (Apiaceae) is a glabrous annual herb, native to eastern Mediterranean region, now widespread as both a cultivated and a naturalized weedy species throughout warmer regions of the world\[22\]. The ethanolic extract of dried powdered leaves of C. sativum (300 mg/kg) was screened for hepatoprotective potential against CCl4, with estimation of serum AST, ALT, ALP and bilirubin levels, along with liver histopathology. The ethanolic extract, rich in alkaloids, phenolic compounds and flavonoids was found to possess significant hepatoprotective potential as was evident from reduced liver weight, activities of AST, ALT and ALP and direct bilirubin content of CCl4-intoxicated animals\[23\].

1.14 Curcuma longa Curcuma longa or turmeric is a member of family Zingiberaceae, which is a perennial herb with short and thick rhizomes. It is known as kunyit in Malaysia and Indonesia. Tumeric has been used extensively in traditional Chinese medicine and Ayurvedic medical system\[24\]. The plant is cultivated in India, West Pakistan, China and Malaysia\[25\]. The rhizome has long been employed both as a spice and as a colouring agent (Crocus indicus). The principal component, curcumin, is now attracting considerable interest because of its anti-inflammatory, antihyperlipidemic, antitumor and cancer-preventive properties\[26\].

The hepatoprotective activity of the ethanolic extract of C. longa was investigated against paracetamol-induced liver damage in rats. Pretreatment of rats with the ethanolic extract of C. longa (100 mg/kg) prior to paracetamol at 600 mg/kg statistically lowered the activities of serum liver enzymes AST, ALT and ALP. Moreover, treatment of rats with only the ethanolic extract of C. longa (100 mg/kg) had no effects on liver enzymes. These results suggested that the ethanolic extract of C. longa has potent hepatoprotective effect against paracetamol-induced liver damage in rats\[27\].

The hepatoprotective effect of the standard extracts from C. longa and Andrographis paniculata were evaluated. An oral administration of the extract was given to adult male mice 24 h prior to hepatotoxicins and the leakage of hepatic enzymes in plasma was evaluated 24 h later. The turmeric extract exhibited hepatoprotective activities against CCl4, but not acetaminophen whereas the A. paniculata extract showed hepatoprotective activities against both CCl4 and acetaminophen-induced toxicities\[28\].

1.15 Cyperus rotundus Cyperus rotundus L. (Cyperaceae) is a cosmopolitan weed, commonly known as mustaka, found in all tropical, subtropical and temperate regions of the world. In India, it is common in open, disturbed habitats to an elevation of about 1 800 m\[29\]. It is widely distributed in the Mediterranean basin areas\[30\]. Ethyl acetate extract and two crude fractions, solvent ether and ethyl acetate, of the rhizomes of C. rotundus were evaluated for hepatoprotective activity in rats by inducing liver damage by CCl4. The ethyl acetate extract at an oral dose of 100 mg/kg exhibited a significant protective effect by lowering serum levels of AST, ALT, ALP and total bilirubin\[30\].

1.16 Enicostemma littorale Enicostemma littorale Blume (Gentianaceae) is found through India up to 15 000 feet, from Punjab and Gangetic plain to Ceylon\[4\]. The alcohol extract of the whole plant of E. littorale was evaluated for its antihypertensive activity against CCl4-induced hepatic damage in rats. A significant reduction was observed in AST, ALT, ALP and total bilirubin and increased protein levels in the groups treated with silymarin as standard and the alcohol extract of E. littorale. The enzyme levels were nearly restored to the normal level and the extract showed remarkable hepatoprotective effect due to its flavonoids content\[31\].

1.17 Ficus glomerata Ficus glomerata (Moraceae) is cultivated throughout India. The methanolic extract of F. glomerata extract was evaluated for antioxidant and hepatoprotective properties. The methanol extract of the bark when given orally along with CCl4, at doses of 250 and 500 mg/kg body weight showed a significant reversal of the biochemical changes towards the normal when compared to CCl4-treated control rats in serum, liver and kidney. The observed effect may be due to its potent antioxidant activity\[32\].

1.18 Glycyrrhiza glabra Glycyrrhiza glabra L. (Leguminosae) is found in Baluchistan and sub-Himalayan tracts. Glycyrrhizin is an important phytoconstituent present in the plant. Experimental
hepatitis and cirrhosis studies on rats have found that it can promote the regeneration of liver cells and at the same time inhibit fibrosis. Glycyrrhizin can alleviate histological disorder due to inflammation and restore the liver structure and function from the damage owing to CCl₄. The effects include lowering of ALT, reducing the degeneration and necrosis, and recovering the glycogen and RNA of liver cells. Effects of glycyrrhizin have been studied on free radical generation and lipid peroxidation in primary cultured rat hepatocytes[33]. The potential efficacy of G. glabra in protecting tissues from peroxidative damage in CCl₄-intoxicated rats has been reported[34].

1.19 Grifola frondosa The whole extract and isolated compounds from Grifola frondosa, a popular mushroom in Asia, have shown biological effects such as modulation of the immune system. The pre-administration of water extract of G. frondosa for 14 d significantly prevented the changes in AST and ALT activities. In addition, water extract of G. frondosa blocked the local infiltration of inflammatory cells in the liver[35].

1.20 Ichnocarpus frutescens Ichnocarpus frutescens (Linn.) R. Br. (Apocynaceae), locally called “Botilai”, is occasionally found in village surroundings and hedges throughout India. The plant is used by the local people of Mohuda, Berhampur and Orissa in India for simple fevers and to treat liver disorders. The entire plant including the flowers of I. frutescens was evaluated for hepatoprotective effect of chloroform and methanol extracts (both at 250 and 500 mg/kg doses) on paracetamol-induced liver damage in rats. Both the extracts at a dose level of 250 and 500 mg/kg produced significant hepatoprotection by decreasing the activities of serum enzymes, bilirubin and lipid peroxidation, while they significantly increased the levels of glutathione, SOD and catalase in a dose-dependent manner. It was concluded that the chloroform and methanol extracts of I. frutescens are not only effective hepatoprotective agents, but also possess significant antioxidant activity because of their free radical-scavenging effect[36].

1.21 Justicia simplex Justicia simplex D. Don (Acanthaceae) is a well-known traditional medicinal plant, native to the Western Himalayas and used as an antifatigue and stimulating agent[37]. The lignan-rich petroleum ether extract and the isolated lignans, simpelixolin and sesamolin of J. simplex were tested for the protective effect on CCl₄-induced hepatotoxicity in rats. Pretreatment with the extract and the isolated lignans at the dose of 100 mg/kg, per oral, respectively, normalised these toxic levels. The lignans present in the plant extract contain methylenedioxy group, which could be responsible for the protective effect exerted by these lignans. The in vivo metabolites of lignans used in the study might also be respon-sible for their hepatoprotection through their antioxidant potential[38].

1.22 Lawsonia alba Lawsonia alba Lam. (Lythraceae) is cultivated and naturalized all over India[6]. The hepatoprotective potential of the leaves, bark and whole plant of L. alba has been investigated on CCl₄-induced liver toxicity, and was found to act by protecting against biochemical and histological changes induced by CCl₄ in rats[39] and also caused reduction in total serum protein, liver glutathione, glutathione peroxidase, AST, glycogen, SOD and catalase activities and possesses antioxidant activity[40] and inhibited the production of free radicals and peroxidation of microsomal lipids in a dose-dependent manner[40].

1.23 Leucas ciliata Leucas ciliata (Lamiaceae) commonly known as “Burumbi” is a shrub having ovate or lanceolate leaves with serrate margins. It is frequently distributed along the Ghats and in plains along forest edges in Ahmednagar, Dhule, Kolhapur, Mumbai, Satara, Sindhudurg and Thane regions of Maharashtra in India. The ethanolic extract of L. ciliata leaves was evaluated for possible antioxidant and hepatoprotective potential. Hepatoprotective activity of the extract was evaluated by CCl₄-induced liver damage in rats. Pretreatment with ethanolic extract of L. ciliata (100, 200 and 400 mg/kg, per oral) inhibited the increase in serum levels of AST, ALT, ALP and total bilirubin and the inhibition was comparable with silymarin (100 mg/kg, per oral). It was revealed that L. ciliata leaves may have significant radical-scavenging and hepatoprotective activity[41].

1.24 Oenothera gratissimum Oenothera gratissimum (L.) is an erect multi-branched perennial shrub that grows up to a height of 2 m, cultivated and found throughout India[42]. The methanolic extract of O. gratissimum leaves (40 mg/kg) was screened for hepatoprotective potential in CCl₄-induced (0.5 mL/kg) liver damage in albino rats. The extract significantly reduced liver enzyme levels. Histopathological studies also supported the results and the extract was found to be a potent antihepatotoxic agent[42].

1.25 Pergularia daemia Pergularia daemia Forsk. (Asclepiadaceae), found throughout India in hotter parts[41], was studied for its hepatoprotective effect of acetone and ethanol sub fraction obtained from total ethanol extract, using CCl₄-induced toxicity in primary cultured rat hepatocytes. In vitro activity was assessed by determining the change in hepatocyte viability and other biochemical parameters such as AST, ALT and total protein. Acetone and ethanol sub fractions showed significant protective effect by restoring altered parameters in the selected in vitro model. The flavonoids present in acetone and ethanol sub fractions of total alcohol extract from P. daemia may be responsible for its significant hepatoprotective properties[43].
1. 26 *Phyllanthus niruri*  
*Phyllanthus niruri* (Phyllanthaceae) is found throughout the hotter parts of India from Punjab to Assam and southwards to Travancore, ascending the hills up to 900 m\(^4\). The protective role of the aqueous extract of *P. niruri* was evaluated against nimesulide-induced hepatic disorder in mice by determining levels of AST, ALT and ALP in serum and by measuring the hepatic content of antioxidant enzymes SOD and catalase, free radical-scavenger, reduced glutathione and TBARS. Intrapерitoneal pretreatment of the extract (100 mg/kg body weight for 7 d) reduced nimesulide-induced (750 mg/kg body weight for 3 d) increased levels of serum marker enzymes\(^4\).

1. 27 *Physalis peruviana*  
*Physalis peruviana* L. (Solanaceae) is a medicinal herb used by Muthuivan tribes and Tamilian native who reside in the Shola forest regions of Kerala, India against jaundice\(^6\). It is grown in Indian gardens and tropical America\(^4\). It was evaluated for its antihepatotoxic activity and acute toxicity in rats. Water, ethanol and hexane extracts of *P. peruviana* (500 mg/kg body weight) showed antiahepatotoxic activities against CCl\(_4\)-induced hepatotoxicity. The ethanol and hexane extracts showed moderate activity compared to water extract, which showed activity at a low dose of 125 mg/kg. Histopathological changes induced by CCl\(_4\) were also significantly reduced by the extract. Further, the extract administration to rats resulted in an increase in hepatic glutathione and a decrease in MDA. The extract was found to be devoid of any conspicuous acute toxicity in rats. The antioxidant activity of the herbal extract would have cured the excessive peroxidation\(^4\).

The antioxidant activities of *P. peruviana* aqueous extract and its protective effect against acetaminophen-induced hepatotoxicity in rats were examined. The extract showed a dose-dependent increase in antioxidant activities, with total antioxidant activity (IC\(_{50}\) 0.81 \(\mu\)g/mL) close to that of vitamin C (IC\(_{50}\) 0.89 \(\mu\)g/mL). Acetaminophen at 850 mg/kg significantly increased the levels of serum AST, ALT and ALP. However, pretreatment with aqueous drug extract at doses of 150, 300 and 600 mg/kg body weight significantly prevented the increase in these enzymes, which are the major indicators of liver hepatitis. Biochemical assays of liver homogenate showed that aqueous extract at 150 to 600 mg/kg significantly enhanced SOD, catalase and glutathione peroxidase concentrations, and decreased the level of TBARS. High-performance liquid chromatographic analysis showed that ellagic acid could be the major component contributing to the antioxidant and hepatoprotective activities of *P. peruviana* aqueous extract\(^4\).

1. 28 *Prosthechea michuacana*  
*Prosthechea michuacana* W.E. Higgins (Orchidaceae), is a member of the family Orchid, commonly found available in traditional markets of the Mexican state Oaxaca. This orchid has a great reputation in folk medicine for the treatment of liver disorders and diabetes. The flavonoids, scutellarein 6-methyl ether, dihydroquercetin, apigenin 7-O-glucoside, apigenin-7-neohesperidoside and apigenin-6-O-\(\beta\)-D-glucopyranosil-3-O-\(\alpha\)-L-rhamnopyranoside, isolated from methanol extract of *P. michuacana* were investigated on CCl\(_4\)-induced liver damage in mice. The hepatoprotective effects were evaluated by measuring AST, ALT, ALP, glutamate and total bilirubin levels, lactate dehydrogenase (LDH), total serum protein and lipid peroxidation (TBARS) assay in mice. Treatment with flavonoids significantly prevented the biochemical changes and showed good hepatoprotective effect\(^4\).

1. 29 *Psidium guajava*  
*Psidium guajava* L. (Myrtaceae), commonly known as guava, is cultivated and naturalized throughout India, up to 1500 m\(^1\) and reported to have antidiarrheal, hepatoprotective, hypoglycemic, lipid-lowering, antibacterial and antioxidant activities. Guava trees spread widely throughout the tropics because they thrive in a variety of soils, propagate easily and bear fruits quickly\(^4\).

The hepatoprotective effect of aqueous leaf extract (500 mg/kg) of *P. guajava* was studied on CCl\(_4\)-induced rat liver damage. The aqueous leaf extract at the dose of 500 mg/kg produced significant hepatoprotection. In another study, pretreatment with asiacic acid (a triterpenoid extracted from *P. guajava* leaves and fruit) at doses of 25, 50 and 100 mg/kg significantly blocked the lipopolysaccharide and D-galactosamine-induced increases in serum AST and ALT levels, and showed improved nuclear condensation, ameliorated proliferation and less lipid deposition. Several studies have indicated the ability of guava to reduce several parameters associated with liver injury\(^4\).

1. 30 *Pterocarpus species*  
*Pterocarpus marsupium* Roxb. (Papilionaceae) is found in Western Peninsula and South India. The gum obtained from the stems, leaves and flowers of the plant is used in the treatment of several ailments. The effect of methanol and aqueous extract of the stem bark was examined in CCl\(_4\)-treated male Wistar albino rats\(^5\).

*P. santalinus* is an endangered plant species, and its wood is used by local tribes for several ailments including diabetes, fever, snakebite and jaundice. Hepatoprotective activities of crude aqueous and ethanol stem bark extracts and suspensions of methanolic extract of heartwood using respectively CCl\(_4\) and galactosamine-induced hepatic damage in male Wistar albino rats have been reported and the possible mechanism of action may be by causing a decrease in serum levels of the markers and a significant increase in total protein, indicating the recovery of hepatic cells without any cellular necrosis and fatty infiltration\(^6,7\).

1. 31 *Punica granatum*  
*Punica granatum* L. (Punicaceae) is found wildly in salt range and in
the Himalayas from 900 to 1800 m, and cultivated in many parts of India. The effect of 70% acetone extract of *P. granatum* fruits on hepatic marker enzymes, antioxidants and tissue peroxidative damage was investigated during isoniazid- and rifampicin-induced hepatotoxicity. Isoniazid and rifampicin (each at dose of 50 mg/kg body weight) for 15 d caused liver injury in rats, manifested by significant elevation in marker enzymes (AST, ALT, LDH and ALP), and by significant decreases in enzyme antioxidants (SOD, catalase and glutathione peroxidase) and nonenzymic antioxidants (reduced glutathione, vitamin C and vitamin E). Co-treatment with 70% acetone extract of *P. granatum* fruits significantly prevented these alterations and restored the enzyme activities and lipid peroxides to near normalcy. The fruits of *P. granatum* offered protection to the liver and significantly counteracted the oxidative stress by reducing lipid peroxidation, inactivating free radicals and increasing antioxidant levels.

1.32 *Silybum marianum*  *Silybum marianum* (Asteraceae) is found in India such as Punjab, N.W. Himalayas, Peshawar, Hazara, Kashmir and Jammu from 1800 to 2400 m. The putative hepatoprotective and antioxidant activities of silymarin which is the main constituent of *S. marianum* (milk thistle plant) were investigated on diethylnitrosamine (DEN)-induced liver damage in male Wistar rats. In rats with DEN-induced hepatotoxicity, when treated with silymarin (50 mg/kg, orally) for 30 d, the levels of AST, ALT, ALP, LDH, γ-GT and bilirubin reverted to near normalcy, whereas the hepatic concentrations of catalase, SOD, vitamin C and vitamin E were significantly increased, and that of lactoperoxidase significantly lowered. The results suggested that silymarin is able to significantly alleviate the hepatotoxicity and oxidative stress induced by DEN in rats. Silymarin treatment was found to offer a high degree of protection to the liver from peroxidative damage as noticed by a highly significant fall in lactoperoxidase. This might be due to the effective quenching of free radicals by silymarin, thereby protecting the liver from further oxidative damage.

1.33 *Solanum nigrum*  *Solanum nigrum* L. (Solanaceae) is a herbal plant found throughout India, up to 2800 m, in the Western Himalayas, used as hepatoprotective and anti-inflammatory agent in Chinese medicine. The protective effects of water extract of *S. nigrum* against liver damage were evaluated in CCl₄-induced chronic hepatotoxicity in rats. The extract of *S. nigrum* significantly lowered the CCl₄-induced serum levels of hepatic enzyme markers (AST, ALT, ALP, and total bilirubin), SOD and hydroxyl radical. The hepatic content of glutathione, and activities and expressions of SOD, glutathione transferase, ALT, and GST that were reduced by CCl₄ were brought back to control levels by the supplement of *S. nigrum* aqueous extract. Liver histopathology showed that *S. nigrum* extract reduced the incidence of liver lesions including hepatic cells cloudy swelling, lymphocytes infiltration, hepatic necrosis, and fibrous connective tissue proliferation induced by CCl₄ in rats. This hepatoprotective effect might be contributed to modulation of *S. nigrum* water extract on detoxification enzymes and its antioxidant and free radical-scavenging effects. Ethanol extract of *S. nigrum* was investigated for its hepatoprotective activity against CCl₄-induced hepatic damage in rats. The ethanol extract showed remarkable hepatoprotective activity. The activity was evaluated using biochemical parameters such as AST, ALT, ALP and total bilirubin. The histopathological changes of liver sample in treated animals were compared with respect to control.

1.34 *Spirulina laxissima*  *Spirulina laxissima* West (Pseudanabaenaceae), an important source of phycocyanin, was investigated for protecting liver against CCl₄-induced hepatotoxicity in male albino rats. The ethanol extract of *S. laxissima* (50 and 100 mg/kg) exhibited maximum antioxidant property in vitro. Also, there were statistically significant decreases in antioxidant enzyme activities and increases in TBARS and liver marker enzymes in the serum of the CCl₄-treated group compared with the control group. The significant increase in the level of antioxidant enzymes in *S. laxissima* Ethanolic extract-treated animals was a clear manifestation of its hepatoprotective potential that might be correlated with its antioxidant and radical-scavenging effects.

1.35 *Taxacum officinale*  *Taraxacum officinale* (Asteraceae or Compositae), also known as dandelion, is a common plant in the northern hemisphere and known to have hepatoprotective activity in traditional Korean medicine. The hepatoprotective activity of dandelion water extract was investigated against D-galactosamine-induced hepatitis in rats. Dandelion was found to have a potential therapeutic material for treating chemically induced or viral hepatitis. Dandelion hot water extract was also found to have protective effect on acute liver inflammation induced by CCl₄ in rats.

1.36 *Tephrosia purpurea*  *Tephrosia purpurea* (Fabaceae), known as “Sarapunkha” in Ayurveda for its hepatoprotective action, is found all over India and ascending the Himalayas up to 1800 m. The plant was evaluated for its efficacy in rats by inducing hepatotoxicity with D-galactosamine (acute) and CCl₄ (chronic). *T. purpurea* (aerial parts) powder was administered orally at a dose of 500 mg/kg. Serum levels of AST, ALT and bilirubin and histopathological changes in the liver indicated that the administration of *T. purpurea* along with the hepatotoxins offered a protective
action in both acute (D-galactosamine) and chronic (CCI₄) models [46].

The aerial parts of *T. purpurea* and stem bark of *Teckomella undulata* (Bignoniaceae) were evaluated against thioacetamide-induced hepatotoxicity. Oral administration of *T. purpurea* (500 mg/kg) and *T. undulata* (1000 mg/kg) resulted in a significant reduction in serum AST (35% and 31%, respectively), ALT (50% and 42%, respectively), γ-GT (56% and 49%, respectively), ALP (46% and 37%, respectively), total bilirubin (61% and 48%, respectively) and liver MDA levels (65% and 50%, respectively), and significant improvement in liver glutathione (73% and 68%, respectively). Histology of the liver sections of the animals treated with the extracts also showed a dose-dependent reduction of necrosis[31].

1.37 *Teucrium polium*  *Teucrium polium* L. (Lamiaceae) is found in Mediterranean region[34]. Hepatoprotective activity of ethyl acetate extract of *T. polium* was investigated using rats with CCl₄-induced liver damage. Specific biochemical parameters like glutathione peroxidase, SOD, reduced glutathione and total antioxidative status were estimated in blood and in liver homogenate. The liver biopsy of all experimental groups treated with *T. polium* ethyl acetate extract showed significant restoration of the normal histomorphological pattern of liver cells. The possible mechanism underlying the potential hepatoprotective activity of *T. polium* extract includes the prevention of glutathione depletion and destruction of free radicals[32].

1.38 *Trianthema portulacastrum* *Trianthema portulacastrum* L. (Lamiaceae) is cultivated throughout India[36]. The ethanolic leaf extract of *T. portulacastrum* was investigated for aflatoxin-induced hepatic damage in rats. Ethanolic leaf extract of *T. portulacastrum* showed a dose-dependent decrease in the levels of ALT, AST, ALP and total bilirubin. Minimum effective dose of the extract was found to be 100 mg/kg body weight. Results obtained from histopathological studies also supported its hepatoprotective activity against aflatoxin-induced hepatotoxicity[35].

1.39 *Tylophora indica* *Tylophora indica* (Burm. f.) Merill. (Asclepiadaceae) leaves, commonly known as “Antamool” in Ayurveda, is found in India such as north and east Bengal, Assam, Orissa, Konkan and all plain districts in the Madras state and up to 900 m in the hilly country[37]. The methanolic extract was screened for hepatoprotective activity in CCl₄-induced hepatotoxicity in albino rats. *T. indica* leaves (200 and 300 mg/kg) exhibited significant reduction in serum hepatic enzymes when compared to rats treated with CCl₄ alone[41].

The alcoholic and aqueous extracts of leaves of *T. indica* were investigated against ethanol-induced hepatotoxicity. Ethanol produced significant changes in physical (increased liver weight and volume), biochemical (increase in serum ALT, AST, ALP, direct bilirubin, total bilirubin, cholesterol and triglycerides levels and decrease in total protein and albumin levels), histological (damage to hepatocytes) and functional (thiopentone-induced sleeping time) liver parameters. Pretreatment with alcoholic or aqueous extract significantly prevented the physical, biochemical, histological and functional changes induced by ethanol in the rat liver. The alcoholic extract was found to exhibit greater hepatoprotective activity than the aqueous extract. Antioxidants may exhibit hepatoprotective activity by blocking the conversion of ethanol to acetaldehyde[46].

1.40 *Vernonia amygdalina*  *Vernonia amygdalina* Del. (Compositae) is used in Nigerian folk medicine as a tonic and remedy against constipation, fever, high blood pressure, and many infectious diseases. The aqueous extract of *V. amygdalina* leaves was evaluated for hepatoprotective and antioxidant effects against acetaminophen-induced hepatotoxicity and oxidative stress in mice in vivo. Pre-administration of *V. amygdalina* resulted in a dose-dependent (50 and 100 mg/kg) reversal of acetaminophen-induced alterations of all the liver function parameters by 51.9% to 84.9%, respectively. Suppression of acetaminophen-induced lipid peroxidation and oxidative stress by the extract was also dose-dependent (50 and 100 mg/kg)[38].

2 Conclusion

The above mentioned scientific reports reviewed in detail the therapeutic potentials of medicinal plants in alleviating liver diseases. Despite the availability of extensive pharmacological information, the toxicological data on herbs and herbal preparations seem to be scanty[47]. That’s why herbal remedies form one of the effective strategies for management of hepatic disorders. Also, the traditional system of medicine recommends various hepatoprotective agents and preparations to treat hepatic disorders. Therefore, many polyherbal formulations have been developed for the treatment of liver disorders by exploiting the knowledge of traditional system of medicine.

Plants used in traditional systems of medicine require detailed investigation from an ethnopharmacological approach for the treatment of liver disorders because hepatic ailments remain a serious health problem caused by drugs, chemicals and alcohol. Various medicinal plants and their formulations are used in the Indian traditional system of medicine for their hepatoprotective potential. Also, the potential of plant-based hepatoprotective agents or drugs contains the diversity of major active constituents such as phenols, coumarins, lignans, terpenoids, carotenoids, glycosides, flavonoids, organic acids, alkaloids and xanthines. Several phytomolecules have been
reported as having potent hepatoprotective principles. So, investigations into the lead molecules, that may produce better therapeutic effects, is required to overcome the pharmaceutical imbalance between remedies that protect the liver and drugs that induce hepatotoxicity.

3 Competing interests

The authors declare that they have no competing interests.

REFERENCES


59 Park CM, Cha YS, Youn HJ, Cho CW, Song YS. Amelioration of oxidative stress by dandelion extract through CYP2E1 suppression against acute liver injury induced by carbon tetrachloride in Sprague-Dawley rats. Phytother Res. 2010; 24(9): 1347-1353.


药用植物抗肝毒性的最新研究进展

Anju Dhiman¹, Arun Nanda¹, Sayeed Ahmad²-³

1. Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak 124001, Haryana, India
2. Bioactive Natural Product Laboratory, Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Jamia Hamdard, New Delhi 110062, India
3. Division of Kidney Diseases and Hypertension, Feinsteins Institute for Medical Research, New York 11021, USA

摘要：肝脏损害是由于微循环障碍、肝细胞变性坏死而引起的肝功能异常。它影响到几乎每个人年龄段人群肝脏细胞的重要生物活性，而常规用药物来抑制肝脏损害是远远不够的。因此，由于对抗疗法所用药物往往具有肝毒性，反而加剧了肝脏功能的紊乱。为了寻找安全有效的替代药物，人们逐渐把目光转向了具有保肝作用的药用植物，并对其进行系统性的方法学研究和药用原理评估。药用植物治疗肝病具有悠久的历史，最早可追溯到公元前 2100 年的中国夏朝和古印度吠陀时期，但是能证明那个时期药用植物有效治疗肝病的证据却很难寻觅。本文旨在系统性地概述现今在临床治疗和实验研究中最常用以及最有效的保肝类药用植物。

关键词：植物，药用，植物提取物，护肝药，综述