

A REVIEW ON TRADITIONAL PLANTS WITH HEPATOPROTECTIVE ACTIVITY

Ravi Kiran Y*, Manjunath C, Rupesh kumar M, Brahmaiah Y, Ashok kumar U, Tamizhmani T

Dept. of Pharmacology, Bharathi College of pharmacy, Bharathinagara, Mandya, Karnataka, India – 571422

Summary

Liver is one of the largest organs in human body and the chief site for intense metabolism and excretion of xenobiotics from the body. Maintaining a healthy liver is a crucial factor for overall health and well being. But continuous exposure to environmental toxins, viral infections, bacterial invasion, and chemical or physical changes within the body, poor drug habits, alcohol consumption, prescribed & over-the-counter drug which can eventually lead to various liver ailment like hepatitis, cirrhosis, necrosis, fatty liver and alcoholic liver disease. Modern medicines have little to offer for alleviation of hepatic diseases, therefore many folk remedies from plant origin are tested for its potential antioxidant and hepatoprotective liver damage in experimental animal model. The present review is aimed at compiling data on promising phytochemicals from traditional plants *Apium graeolens (L)*, *Spermacoe hispida*, *Flacourtia indica*, *Centella asiatica (L)*, *Portulaca oleracea (L)*, *Polycarpea corymbosa*, *Feronia elephantum*, *Careya arborea*, *Wedelia calendulacea*, *Symplocos racemosa* that have been tested in hepatotoxicity models.

Keywords: Cirrhosis, fatty liver, antioxidant, Hepatoprotective and hepatotoxicity.

Corresponding author

Ravi kiran. Yatagiri*, M.Pharm,

Department of Pharmacology,

Bharathi College of Pharmacy,

Bharathinagara,

Mandya Dist

Karnataka, India- 571 422.

Tel no: +917676946879.

E-mail: ravi.kiran.cips@gmail.com

Introduction

The liver performs many vital functions, including metabolic and detoxification activities. Liver is important because a person's nutritional level is not only determined by what he or she eats, but by what the liver processes. Unfortunately it is extremely difficult to detect early warning symptoms specific to liver metabolic imbalances. People can suffer for a long time from a liver ailment without knowing of it. Beyond the treatment of liver disorders, everyday care of the liver lays a cornerstone for total body health. Modern medicines have little to offer for alleviation of hepatic diseases. The incredible complexity of liver chemistry and its fundamental role in human physiology is so daunting to researchers thought that simple plant remedies might have something to offer is astonishing and incredible. Therefore, many folk remedies from plant origin are tested for its potential antioxidant and hepatoprotective liver damage in experimental animal model. The Indian Traditional Medicine like Ayurveda, Siddha and Unani are predominantly based on the use of plant materials. Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness.

Herbal-based therapeutics for liver disorders has been in use in India for a long time and has been popularized world over by leading pharmaceuticals. A large number of plants and formulations have been claimed to have hepatoprotective activity. Nearly 160 phytoconstituents from 101 plants have been claimed to possess liver protecting activity. In India, more than 87 plants are used in 33 patented and proprietary multi ingredient plant formulations². After extensive search of the modern and traditional literature on this subject we are proud to present a range of safe herbal alternatives from India that can serve as an excellent hepatoprotectives if consumed as per directions.

Apium graeolens (L)³

The hepatoprotective activity of the *Apium graeolens* Linn (Apiaceae) against CCl₄ induced hepatotoxicity in albino rats. The degree of protection was measured by using biochemical parameters like serum transaminases (SGOT and SGPT), alkaline phosphatase, total protein and albumin. The methanolic extracts showed the most significant hepatoprotective activity comparable with standard drug silymarin. Other extracts namely petroleum ether and acetone also exhibited a potent activity.

Spermacoce hispida⁴

Ethanollic extract of the *Spermacoce hispida*.Linn (SHE) against carbon tetra chloride (CCl₄) induced hepatotoxicity in rats. Liver functions were assessed by the determination of SGOT, SGPT, ALP and bilirubin. Histopathological studies were carried out. The serum biochemical analysis results suggest that the use of Ethanollic extract of *Spermacoce hispida*.Linn exhibited significant protective effect from hepatic damage in CCl₄ induced hepatotoxicity model. Histopathological studies revealed that concurrent administration of the extract with CCl₄ exhibited protective effect on the liver, which further evidenced its hepatoprotective activity.

Flacourtia indica⁵

The extract of the aerial parts of *Flacourtia indica* (Burm.f.) Merr., were evaluated for hepatoprotective properties. In paracetamol-induced hepatic necrosis in rat models, all extracts were found to reduce serum aspartate transaminase (AST), serum alanine transaminase (ALT) and serum alkaline phosphatase (ALP). The most significant reduction of the serum level of AST and ALT were exhibited by petroleum ether and ethyl acetate extracts at a single oral dose of 1.5g/kg of body weight with a reduction of 29.0% AST & 24.0% ALT level by petroleum ether extract, and 10.57% AST & 6.7% ALT level by ethyl acetate extract compared to paracetamol (3 g/kg of body weight) treated animals. Histopathological examination also showed good recovery of paracetamol-induced necrosis by petroleum ether and ethyl acetate extracts. On the other hand, the methanol extract did not show any remarkable effect on paracetamol-induced hepatic necrosis. The hepatoprotective effects exhibited by petroleum ether and ethyl acetate extract might be mediated through the inhibition of microsomal drug metabolizing enzymes²⁵. But, in this study the dose they have used is too high and it is not successful or rationale for human dose.

Centella asiatica (L)⁶

Alcohol extract of *Centella asiatica* is evaluated for its hepatoprotective effect in carbon tetrachloride-induced liver injury in rats. Rats were treated with extract orally in two doses (20 and 40 mg/kg/day) for 3 months along with intraperitoneal injection of carbon tetrachloride (1 ml/kg). Biochemical parameters such as serum total protein, albumin and marker enzymes (SGPT, SGOT, ALP) were estimated both before and after the experiment. Histopathological studies of liver were also carried out to confirm the biochemical changes. Carbon tetrachloride-induced hepatotoxic effects were evident by a significant increase in the serum marker enzymes and a decrease in the total serum protein and albumin. Administration of extract effectively inhibited changes in a dose-dependent manner; maximum effect was with 40 mg/kg. Histopathological examination of liver tissue corroborated well with the biochemical changes. Hepatic steatosis, hydropic degeneration and necrosis were observed in carbon tetrachloride-treated group, while these were completely absent in the treatment group. *Centella asiatica* extract exhibited hepatoprotective action against carbon tetrachloride-induced liver injury. This effect is attributed to the presence of asiaticoside (14.5%) in the extract.

Portulaca oleracea (L)⁷

The suspensions of methanol and petroleum ether extracts of entire plant of *Portulaca oleracea* in carboxy methyl cellulose (CMC) were evaluated for hepatoprotective activity in Wistar albino rats by inducing hepatic injury with D-galactosamine (400 mg/kg). D-galactosamine induced hepatic damage was manifested by a significant increase in the activities of marker enzymes. Biochemical data exhibited significant hepatoprotective activity of Methanol extract of *Portulaca oleracea* at oral dose of 200 and 400 mg/kg against D-galactosamine. Silymarin was used as reference standard also exhibited significant hepatoprotective activity against D-galactosamine. The study showed Pre treatment with methanol extract of *P. oleracea* and Silymarin for 14 days protected the rat livers from D-galactosamine induced histopathological changes. The results suggest that extracts from *P. oleracea* possess significant protection against galactosamine induced hepatotoxicity in rats.

Polycarpea corymbosa⁸

Polycarpea corymbosa whole plant extract was studied for the evaluation of the hepatoprotective activity of against carbon tetra chloride (CCl₄) induced hepatotoxicity. Hepatotoxicity was induced in male wistar rats by administration of CCl₄(1.25ml/kg/day for 7days). Methanolic extract of whole plant of Polycarpea corymbosa were administered to the experimental animals (20 mg/kg/day,p.o.for 7 days). The hepatoprotective effect of these extract was evaluated by the assay of liver function biochemical parameters (alanine aminotransferase, aspartate aminotransferase and alkaline aminotransferase) and histopathological studies of the liver. In methanol extract-treated animals, the toxic effect of CCl₄ as controlled significantly by restoration of the levels of enzymes levels as compared to the normal and the standard drug silymarin-treated groups. Histology of the liver section of the animals treated with the extract showed the presence of normal hepatic cords, absence of necrosis and fatty infiltration, further support the hepatoprotective activity.

Feronia elephantum⁹

Methanolic Fruit extract of Feronia elephantum is taken for the elucidation of the hepatoprotective activity against paracetamol induced liver damage in Wistar rats. Liver damage was produced by paracetamol (2gm/kg,p.o.) in 1% CMC. The Plant extract (200mg/kg, p.o.) was administered every 24 hrs for seven days, while standard group received N-acetyl l-cystine. At the end of the study the marker enzymes in serum were analysed. The methanolic extract showed significant hepatoprotective activity and efficacy of extract was almost comparable to that of N-acetyl l-cystine. Feronia elephantum fruit have been reported to contain flavanoids, sterol and glycosides in addition to alkaloids, tannins, saponins etc. Hepatoprotection offered by Feronia elephantum extract could be attributed to these constituents.

Careya arborea¹⁰

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. 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.

Wedelia calendulacea¹¹

The hepatoprotective activity of ethanolic extract of Wedelia calendulacea L. (Family: Asteraceae) was studied against CCl₄-induced acute hepatotoxicity in rats. The treatment with ethanolic extract of Wedelia calendulacea showed a dose-dependent reduction in CCl₄ induced elevated serum enzyme activities with parallel increase in total proteins and bilirubin, indicating the extract could enhance the return of normal functional status of the liver comparable to normal rats. The weight of the organs such as liver, heart, lung, spleen and kidney in CCl₄-induced hepatic damaged animals that received ethanolic extract of Wedelia calendulacea showed an increase over CCl₄-treated control group.

Symplocos racemosa¹²

Ethanol extract of *Symplocos racemosa* bark was evaluated for the hepatoprotective activity in carbon tetrachloride (CCl₄) induced hepatic damage in rats. CCl₄ with olive oil (1 : 1) (0.2 ml/kg, i.p.) was administered for ten days to induce hepatotoxicity. Extract (200 and 400 mg/kg, p.o.) and silymarin (100 mg/kg p.o.) were administered concomitantly for fourteen days. The degree of hepatoprotection was measured using serum transaminases (AST and ALT), alkaline phosphatase, bilirubin, albumin, and total protein levels. Metabolic function of the liver was evaluated by thiopentone-induced sleeping time. Antioxidant activity was assessed by measuring liver malondialdehyde, glutathione, catalase, and superoxide dismutase levels. Histopathological changes of liver sample were also observed. Significant hepatotoxicity was induced by CCl₄ in experimental animals. Treatment showed significant dose-dependent restoration of serum enzymes, bilirubin, albumin, total proteins, and antioxidant levels. Improvements in hepatoprotection and morphological and histopathological changes were also observed in the treated rats. It was therefore concluded that extract of the bark is an effective hepatoprotective agent in CCl₄-induced hepatic damage, and has potential clinical applications for treatment of liver diseases.

Aegle marmelos¹³

Aegle marmelos leaves (Bael, family of Rutaceae) which is also called as Bilva in ancient Sanskrit, was used as herbal drug in the Indian System of medicine. The hepatoprotective effect of *Aegle marmelos* in alcohol-induced liver injury was evaluated in rats using essential marker biochemical parameters. The results indicated that, the Bael leaves have excellent hepatoprotective effect. Similar findings were also reported by other workers.

Discussion

The present study reveals plant extracts with hepatoprotective properties against toxic chemicals that cause liver injury, seeming to validate their use in folk medicine. This approach will help exploring the real therapeutic value of these natural pharmacotherapeutic agents and standardize the dosage regimen on evidence based findings to become more than a fashionable trend. Due to lack of scientific-based pharmacological data, most of the herbal formulations cannot be recommended for the treatment of liver diseases¹⁴.

Conclusion

In this review article, effort has been taken to collect and compile the details regarding a few hepatoprotective natural products, which will be useful to the society to venture in to a field of alternative systems of medicine. These plants may offer new alternatives to the limited therapeutic options that exist at present in the treatment of liver diseases or their symptoms, and they should be considered for future studies. Conventional medicine is now pursuing the use of natural products such as herbs to provide the support that the liver needs on a daily basis. A more thorough review on various herbal products available in India and abroad as a hepatoprotectant is in near future.

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