



SCREENING OF HEPATOPROTECTIVE ACTIVITY OF SOME HERBAL PLANTS: A REVIEW

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ABSTRACT:

The scientific basis for the statement that plants and their active constituents play an important role in the prevention diseases is continuously advancing. In this review article, an attempt has been made to compile the reported hepatoprotective plants from India and abroad and may be useful to the health professionals, scientists and scholars working the field of pharmacology and therapeutics to develop evidence based alternative medicine to cure different kind of liver diseases in man and animals.

KEY WORDS: Hepatoprotective, pharmacology, therapeutics, diseases.

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. It has a pivotal role in human metabolism. It secretes bile, prothrombin and fibrinogen, blood-clotting factors, and heparin, a mucopolysaccharide sulfuric acid ester that prevents blood from clotting within the circulatory system.¹

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. Plants have potent biochemical components of phytomedicine. Plant based natural constituents can be derived from any part of the plant like bark, leaves, flowers, roots, fruits, seeds, etc.² (i.e. any part of the plant may contain active components. The beneficial medicinal effects of plant materials typically result from the combinations of secondary products present in the plant. The medicinal actions of plants are unique to particular plant species or groups and are consistent with this concept as the combination of secondary products in a particular plant is taxonomically distinct³ Different types of drugs such as acetaminophen, chloroquine and isoniazid are inducing hepatotoxicity in the world. Isoniazid rifampicin, used for tuberculosis therapy, was associated with hepatotoxicity.⁴ Herbal plants have been used traditionally by herbalist worldwide for the prevention and treatment of liver disease. Herbal drugs were prescribed even when their biological active compounds were unknown because of their effectiveness, fewer side effects and relatively low cost.⁵

According to world health organization (WHO) more than 80% of the world's population relies on traditional medicines for their primary health care needs.⁶ In India, about 40 polyherbal commercial formulations reputed to have hepatoprotective action are being used. It has been reported that 160 phytoconstituents from 101 plants have hepatoprotective activity.^{7,8} Liver protective herbal drugs contain a variety of chemical constituents like phenols, coumarins, lignans, essential oil, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, alkaloids and xanthines.⁹ Modern medicines have little to offer for alleviation of hepatic diseases and it was chiefly the plant-based preparations, which were employed for their treatment of liver disorders. But there was not much drug available for

the treatment of liver disorders^{10, 11} Therefore; many folk remedies from plant origin were tested for its potential antioxidant and hepatoprotective liver damage in experimental animal model. Carbon tetrachloride (CCl₄) induced hepatotoxicity model is widely used for the study of hepatoprotective effects of drugs and plant extracts.^{12, 13}

Hepatoprotective Plants

Aerva lanata (Kapuri jadi)

The hepatoprotective activity of hydro alcoholic extract of *Aerva lanata* (Amaranthaceae) was evaluated against paracetamol induced liver damage in rats and the extract of *Aerva lanata* (600mg/kg) was administered orally to the animals with hepatotoxicity induced by paracetamol (3gm/kg). Silymarin (25mg/kg) was given as reference standard. All the test drugs were administered orally by suspending in 0.5% Carboxy methylcellulose solution. The plant extract was effective in protecting the liver against the injury induced by paracetamol in rats. This was evident from significant reduction in serum enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin. It was concluded from the result that the hydroalcoholic extract of *Aerva lanata* possesses hepatoprotective activity against paracetamol-induced hepatotoxicity in rats.¹⁴

Anisochilus carnosus (Kapurli)

Hepatoprotective effect of *Anisochilus carnosus* (Lamiaceae) was studied against CCl₄ induced hepatotoxicity in rats. Hepatotoxicity was induced in albino Wister rats of either sex by intraperitoneal injection of CCl₄. The ethanol extract of *A. carnosus* was administered to the experimental rats at two dose levels 200 and 400mg/kg body weight. The Hepatoprotective effect of the extract was evaluated by the assay of liver function biochemical parameters like Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamate Oxaloacetate Transaminase (SGOT), Alkaline phosphate (AP), Total bilirubin and Total Protein In these animals the toxic effect CCl₄ was controlled significantly as compared to the normal and standard drug silymarin treated groups.¹⁵

Chamomile capitula (Chamomile)

Hepatoprotective activity of aqueous ethanolic extract of *Chamomile recutita capitula* (Asteraceae) on blood and liver glutathione, Na⁺ K⁺- ATPase activity, serum marker enzymes, serum bilirubin, glycogen and thiobarbutiric acid

reactive substances against paracetamol induced damage in rats have been studied to find out the possible mechanism of hepatoprotection. It was observed that extract of chamomile has reversal effects on the levels of above-mentioned parameters in paracetamol hepatotoxicity. The extract of capitula of chamomile functions as a hepatoprotective agent and this hepatoprotective activity of chamomile may be due to normalization of impaired membrane function activity¹⁶

Coccinia grandis (Ivy Gourd)

The hepatoprotective effects of an aqueous leaf extract of *Coccinia grandis* (Cucurbitaceae) was studied on carbon tetrachloride (CCl₄) induced liver damage in albino rats. Toxicity was induced by using 30% CCl₄ suspended in olive oil (1.0 ml/kg body wt intraperitoneal) after every 72 hrs for 3 doses. The aqueous leaf extract at a dose of 250mg/kg was administered orally by intragastric tube for 10 days. Blood and liver tissue were collected for the assessment of serum marker enzymes such as ALT, AST and ALP. It was observed that the extract of *Coccinia grandis* was effective in protecting the liver against the injury induced by (CCl₄) in rats. The liver tissue was used for histopathological assessment.¹⁷

Cudrania tricuspidata (cudrang),

Phytochemical investigation of the MeOH extract of the root barks of *Cudrania tricuspidata* Bureau (Moraceae), as guided by hepatoprotective activity *in vitro*, furnished four isoprenylated xanthenes, cudratricusxanthone A (1), cudraxanthone L (2), cudratricusxanthone E (3), and macluraxanthone B (4). All of these compounds showed the significant hepatoprotective effect on tacrine-induced cytotoxicity in human liver-derived Hep G2 cells. Compounds 1, 2, and 4 also exhibited the significant hepatoprotective effect on nitrofurantoin-induced cytotoxicity in human liver-derived Hep G2 cell.¹⁸

Eclipta alba (Bhringaraja),

The effect of *Eclipta alba* (EA) (Asteraceae) extract was studied on paracetamol induced hepatic damage in mice. Treatment with 50% ethanol extract of *E. alba* (100 & 250mg/100g body weight) was found to protect the mice from hepato-toxic action of paracetamol as evidenced by significant reduction in the elevated serum transaminase levels. Histopathological studies showed marked reduction in fatty degeneration and centrilobular necrosis, in animals receiving different doses of *E. alba* along with paracetamol as compared to the control group. The study revealed that *Eclipta alba* have significant hepatoprotective activity.¹⁹

Flacourtia indica (Baichi)

The hepatoprotective activity of aqueous extract leaves of *Flacourtia indica* (Flacourtiaceae) was found against CCl₄ induced hepatotoxicity. Treatment of aqueous extract of *Flacourtia indica* leaves (250 & 500 mg/kg) exhibited a significant protective effect in experimental rats by altering the serum levels of AST, ALT, ALP, Total Protein, Total Bilirubin and liver TBARS. These biochemical observations were supported by histopathological study of liver sections. It has been concluded that the aqueous extract of the leaves of *Flacourtia indica* protects liver against oxidative damages and possess good hepatoprotective activity²⁰

Hedyotis corymbosa ('Parppatakapullu')

The hepatoprotective effect of the methanolic extract of the whole plant of *Hedyotis corymbosa* (Rubiaceae) was evaluated against paracetamol overdose-induced liver damage in Wistar rats. The methanolic extract of the plant

produced significant hepatoprotective effects as evidenced by decreased serum enzyme activities, SGPT, SGOT, SAKP and serum bilirubin and an almost normal histological architecture of the liver, in treated groups, compared to the controls. *Hedyotis corymbosa* shortened hexobarbitone-induced sleeping time in mice, besides showing significant antilipid peroxidant effect *in vitro*. The results thus support the use of *Hedyotis corymbosa* as a hepatoprotective agent.²¹

Launaea intybacea (bitter lettuce)

The hepato-protective activity of petroleum ether, chloroform, ethyl acetate and water extract of aerial parts of *Launaea intybacea* (Asteraceae) were evaluated in CCl₄-induced hepatotoxicity in albino rats. Silymarin (200mg/kg) was given as reference standard. The ethyl acetate and water extracts of aerial parts of *Launaea intybacea* had shown very significant hepatoprotection against CCl₄-induced hepatotoxicity in albino rats in reducing serum total bilirubin, direct bilirubin, SGPT and SGOT levels.²²

Leucas ciliata (Tufted Leucas)

Hepatoprotective activity of *Leucas ciliata* (Lamiaceae) extract was evaluated by carbon tetrachloride (CCl₄) induced liver damage model in rats. In hepatoprotective activity study, CCl₄ significantly increased the levels of serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP) and total bilirubin. Pretreatment of the rats with ethanolic extract of *L. ciliata* (100, 200 and 400mg/kg *po*) inhibited the increase in serum levels of SGPT, SGOT, ALP and total bilirubin and the inhibition was comparable with silymarin (100mg/kg *po*). The study revealed that *L. ciliata* leaves have significant hepatoprotective activity.²³

Orthosiphon stamineus (poonai meesai)

Hepatoprotective activity of methanol extract of leaves of *Orthosiphon stamineus* (Lamiaceae) against paracetamol-induced hepatotoxicity. Methanol extract showed presence of phenolic compound and flavonoids. The hepatoprotective activity of the methanol extract was assessed in paracetamol induced hepatotoxic Rats. Alteration in the levels of biochemical markers of hepatic damage like SGOT, SGPT, ALP and lipid peroxides were tested in both Paracetamol treated and untreated groups. Paracetamol (2g/kg) has enhanced the SGOT, SGPT, ALP and the Lipid peroxides in liver. Treatment of methanolic extract of *O. Stamineus* leaves (200mg/kg) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner. The result suggested that *O. Stamineus* methanol leaf extract possessed hepatoprotective activity.²⁴

Piper nigrum (Black pepper)

Hepatoprotective activity of *Piper nigrum* (piperaceae) *L.* root extracts was evaluated by carbon tetrachloride (CCl₄) induced liver damage model in rats. Among the three different extracts (water, ethanol and chloroform extract), ethanol extract exhibits the highest hepatoprotective activity ($p < 0.05$). When using the ethanol extract at a dose of 120-mg/ kg to treat the CCl₄-intoxicated rat, the activities of alanine transaminase (ALT) and aspartate transaminase (AST) in rat serum decreased to 65.7 and 84.5%, respectively. At the same time, the lipid peroxidation (MDA) decreased to 52.3% and glutathione (GSH) increased to 55.8% in the rats liver homogenate, as compared with those of the CCl₄ positive control rats. The hepatoprotective effect of ethanol extract was also supported by the histopathological observations. The findings indicated that the ethanol extract of

P. nigrum L. root was an efficient hepatoprotective agent against CCl₄-induced liver injury.²⁵

Sesamum indicum (Sesam)

The hepatoprotective activity of ethanol extracts of *Sesamum indicum* Linn. (Pedaliaceae) Seeds were evaluated against carbon tetrachloride (CCl₄) induced hepatic damage in rats. The extract at two different doses (400mg/kg and 700mg/kg) was administered orally once daily. The substantially elevated serum enzymatic level of Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT), alkaline phosphatase (ALP), Acid phosphatase (ACP), Total Protein, Albumin and Total Bilirubin were restored towards normalization significantly by the extract. The biochemical observations were supplemented with histopathological examination of rat liver sections. The results of this study strongly indicate the *Sesamum indicum* Linn. Seeds have potent hepatoprotective action against carbon tetrachloride induced hepatic damage in rats.²⁶

Spermacoce hispida (Shaggi button weed')

The hepatoprotective activity of the ethanolic extract of *Spermacoce hispida*. (Rubiaceae) Linn was studied 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 suggested that the use of ethanolic 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.²⁷

Tinospora cordifolia (Amrit)

The effect of *Tinospora cordifolia* (Menispermaceae) was evaluated against hepatosuppression induced by carbon tetrachloride (CCl₄). The evaluation markers used were serum marker enzymes viz. GOT, GPT, Alkaline phosphate, glucose, bilirubin, Triglycerides, γ GT, cholesterol, DNA, RNA and total protein. These biochemical parameters were significantly changed by the single dose of CCl₄. The treatment of *Tinospora cordifolia* significantly recovers all the serum and liver parameters like normal levels. However, silymarin was used as a reference standard for this study. The findings indicate that the hepatoprotective action of *Tinospora cordifolia* against hepatosuppression possibly involves CCl₄ bio activation through selective inhibitors of reactive oxygen species Hence *Tinospora cordifolia* indicating protection in liver may prove promising effect against liver disorders.²⁸

Wedelia calendulacea (Pilabhamgara)

The hepatoprotective activity of ethanolic extract of *Wedelia calendulacea* L. (Asteraceae) was studied by estimating serum enzyme activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), protein and bilirubin. The treatment with EEWC showed a dose-dependent reduction of CCl₄ 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.²⁹

CONCLUSION

Liver diseases have become one of the major causes of mortality all over the globe and hepatotoxicity due to drugs appears to be the most common contributing factor. About 20,000 deaths found every year due to liver disorders. Hepatocellular carcinoma is one of the ten most common tumors in the world with over 2, 50,000 new cases each year. In this review article, an attempt has been made to compile the reported hepatoprotective plants from India and abroad and may be useful to the health professionals, scientists and scholars working the field of pharmacology and therapeutics to develop evidence based alternative medicine to cure different kind of liver diseases in man and animals.

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