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Review on Some Medicinal Plants with Hepato-protective Activities.

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Review Article

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ABSTRACT

Medicinal plants play an important role in the lives of rural people particularly in remote parts of developing countries with few health facilities. It is estimated that around 70,000 plants species from lichens to towering trees has been used for medicinal purpose. The present review provides the importance of the plants with hepatoprotective activity. There are many plants with this activity and some of them are mentioned in the review. 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 kinds of liver diseases in man and animals.

INTRODUCTION

Liver is considered to be one of the most vital organs that functions as a centre of metabolism of nutrients such as carbohydrates, proteins and lipids and excretion of waste metabolites. Additionally, it is also handling the metabolism and excretion of drugs and other xenobiotics from the body thereby providing protection against foreign substances by detoxifying and eli-minating them.Liver cell injury caused by various toxicants such as certain chemotherapeutic agents, paracetamol etc., chronic alcohol consumption and microbes is well-studied. Enhanced lipid peroxidation during metabolism of ethanol may result in development of hepatitis leading to cirrhosis. One of the important and well documented uses of plant-products is their use as hepatoprotective agents. Hence, there is an ever increasing need for safe hepatoprotective agent [1].

Aim of Work

Liver is a vital organ play a major role in metabolism and excretion of xenobiotics from the body.Liver cell injury caused by various toxic chemicals (certain antibiotic, chemotherapeutic agents, carbon tetrachloride (CCL4), thioacetamide (TAA) etc.), excessive alcohol con-sumption and microbes is wellstudied. The present review is aimed at compiling data on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models using modern scientific system.

HEPATOPROTECTIVE HERBS

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. The limiting factors that contribute to this eventuality are (i) lack of standardization of the herbal drugs; (ii) lack of identification of active ingredient(s)/principles(s); (iii) lack of randomized controlled clinical trials (RCTs), and (iv) lack of toxicological evaluation.

Drugs effective against a variety of liver disorders. The present review is aimed at compiling data based on reported works on promising A large number of plants and formulations have been claimed to have

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hepatoprotective activity. In India, more than 87 plants are used in 33 patented and proprietary multi ingredient plant formulations [2]. Inspite of the tremendous advances made, no significant and safe hepatoprotective agents is available in modern therapeutics. Therefore, due importance has been given globally to develop plant based hepatoprotective phytochemicals from medicinal plants that have been tested in hepatotoxicity models.

LIST OF PLANTS

AMARANTHUS TRICOLOR

AZADIRACHTA INDICA

BAUHINIA VARIEGATA

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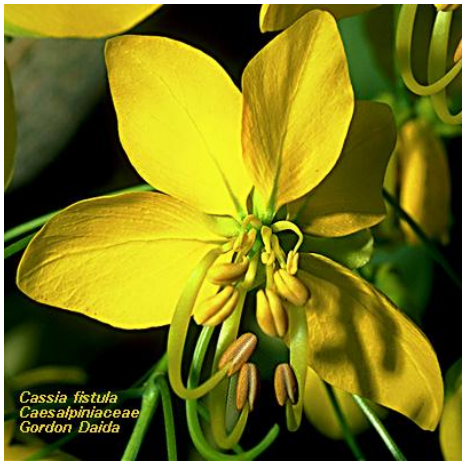
BOERHAAVIA DIFFUSA

CANNA INDICA



CASSIA FISTULA

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CURCUMA LONGA

DAUCUS CAROTA

ECLIPTA ALBA

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FICUS CARICA

LUPEOL OF MANGO PULP

MORINGA OLEIFERA

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PERGULARIA DAEMIA

SOLANUM NIGRUM

TAMARINDUS INDICA

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TRIDAX PROCUMBENS

TYLOPHORA INDICA

PLANT PROFILES

AMARANTHUS TRICOLOR

Family : Amaranthaceae
Synonym : Joseph's-coat, Amaranthus tricolor L.

Hepatoprotective activity

The ethanolic extract of leaves of *Amaranthus tricolor* L. (ATE) was tested for its efficacy against CCl_4-induced liver toxicity in rats. The hepatoprotective activity of ATE was evaluated via measuring various liver toxicity parameters, the lipid profile, and a histopathological evaluation. A sleeping time determination study and an acute toxicity test were performed in mice. The results clearly showed that oral administration of ATEat the dose of(50-100mg/kg), for three weeks significantly reduced the elevated levels of serum GOT, GPT, GGT, ALP, bilirubin, cholesterol, LDL, VLDL, TG, and MDA induced by CCl_4. Moreover, ATE treatment was also found to significantly increase the activities of NP-SH and TP in liver tissue. The prolongation of narcolepsy induced by pentobarbital was shortened significantly by the extract. The observed hepatoprotective effect appears to be due to the antioxidant properties of *amaranthus tricolor* [3].

AZADIRACHTA INDICA

Family : Meliaceae
Synonym : Antelaea azadirachta, Azadirachta indica A. Juss

Hepatoprotective activity

The effect of methanolic extract of *Azadirachta indica. indica* leaf on serum enzyme levels (glutamate

oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase) elevated by paracetamol induced hepatotoxicity in rats. It was interesting to observe that serum enzyme levels were much elevated in paracetamol induced animals than in those receiving a combination of paracetamol and lead extract.it is more effective as the oral dose of(40-50mg/kg). 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 [4].

BAUHINIA VARIEGATA

Family : Fabaceae
Synonym : Bauhinia variegata L.

Hepatoprotective activity

The alcoholic extract of the bark of the plant *bauhinia variegate* L.was known to produce the hepatoprotective activity. The hepatoprotective activity was investigated in carbon tetrachloride (CCl_4) intoxicated *Sprague-Dawley* rats. *Bauhinia variegata* alcoholic Stem Bark Extract (SBE) at different doses (100 and 200 mg/kg) were administered orally to male *Sprague-Dawley* rats weighing between 100-120 g. The effect of SBE on the serum marker enzymes, *viz*., AST, ALT, ALP and GGT and liver protein and lipids were assessed. The extract exhibited significant hepatoprotective activity. Hence, *B. variegata* appears to be a promising hepatoprotective agent [5].

BOERHAAVIA DIFFUSA

Family : Nyctaginaceae
Synonym : Red spiderling **,** Boerhavia diffusa L.

Hepatoprotective activity

The roots of *Boerhaavia diffusa* commonly known as 'Punarnava', are used for the treatment of various hepatic disorders.. The hepatoprotective activity of roots of different diameters collected in three seasons, rainy, summer and winter, was examined in thioacetamide intoxicated rats. The results showed that an aqueous extract as the i.v dose of (2 ml/kg) of roots of diameter 1–3 cm, collected in the month of May (Summer), exhibited marked protection of a majority of serum parameters, i.e. GOT, GPT, ACP and ALP, but not GLDH and bilirubin. the aqueous form of drug (2 ml/kg) administration has more hepatoprotective activity than the powder form; this is probably due to the better absorbtion of the liquid form through the intestinal tract.

CANNA INDICA

Family : Cannaceae
Synonym : Indian shot, *Canna indica* L.

Hepatoprotective activity

The hepatoprotective activity of methanol extract of aerial parts of *Canna indica* L. plant was evaluated against carbon tetrachloride induced hepatotoxicity. Extract at doses (100 and 200mg/kg) restored the levels of all serum parameters like SGPT, SGOT, TB which were elevated in CCl4 administrated rats. A 10% liver homogenate was used for estimation of catalase, GSH content, LPO level for *in vivo* antioxidant status of liver. All LPO, Reduced GSH, Catalase levels were observed normal in extract treated rats. Histopathology demonstrated profound necrosis, lymphocytic infiltration was observed in hepatic architecture of carbon tetrachloride rats which were found to obtain near normalcy in extract plus carbon tetrachloride administrated rats. This clearly suggests that methanol extract of aerial parts of *Canna indica* L. has liver protective effect against carbon tetrachloride induced hepatotoxicity [6].

CASSIA FISTULA

Family : Fabaceae
Synonym : Canafistula, Cassia fistula L.

Hepatoprotective activity

Hepatoprotective activity of the n-heptane extract of *Cassia fistula* leaves was investigated in rats by inducing hepatotoxicity with carbon tetrachloride:liquid paraffin (1:1). The extract has been shown to possess significant protective effect by lowering the serum levels of transminases (SGOT and SGPT), bilirubin and alkaline

phosphatase (ALP). The extract of *C. fistula* at a dose of 400 mg/kg administered orally is showed significant hepatoprotective activity which was comparable to that of a standard hepatoprotective agent [7].

CURCUMA LONGA

Family : Zingiberaceae
Synonym : Turmeric, Curcuma longa L.

Hepatoprotective activity

The hepatoprotective activity of the ethanol extract of the rhizome of Curcuma longa was investigated against paracetamol-induced liver damage in rats. At the dose of 600 mg/kg, paracetamol induced liver damage in rats as manifested by statistically significant increase in serum alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) and alkaline phosphatase (ALP). Pretreatment of rats with the ethanolic extract of Curcuma longa (100 mg/kg) prior to paracetamol dosing at 600 mg/kg statistically lowered the three serum liver exzyme activities. Moreover, treatment of rats with only the ethanolic extract of Curcuma longa (100 mg/kg) had no effects on the liver enzymes. This current results suggest that ethanolic extract of Curcuma longa has potent hepatoprotective effect against paracetamol-induced liver damage [8].

DAUCUS CAROTA

Family : Apiaceae
Synonym : Carrot, Daucus carota L.

Hepatoprotective activity

The effect of methanol extractof the roots of *daucus carota L.*on carbon tetrachloride (CCl_4) induced acute liver damage was evaluated. The increased serum enzyme levels (viz., glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, lactate dehydrogenase, alkaline phosphatase, sorbitol and glutamate dehydrogenase) by CCl_4-induction were significantly lowered due to pretreatment with the extract. The extract also decreased the elevated serum bilirubin and urea content due to CCl_4 administration. Increased activities of hepatic 5′-nucleotidase, acid phosphatase, acid ribonuclease and decreased levels of succinic dehydrogenase, glucose-6-phosphatase and cytochrome *P*-450 produced by CCl_4 were reversed by the extract in a oral dose of(200-400mg/kg). Results of this study revealed that carrot could afford a significant protective action in the alleviation of CCl_4-induced hepatocellular injury [9].

ECLIPTA ALBA

Family : Asteraceae
Synonym : Eclipta prostrata L.
Vernacular names : Tamil - karisalankanni

Hepatoprotective activity

The methanolic extract of fresh leaves of the plant Eclipta alba (Ea) was known to produce hepatoprotective activity. The hepatoprotective potential of the fraction prepared from alcoholic extract was studied in vivo in rats and mice against carbon tetrachloride induced hepatotoxicity. The hepatoprotective activity was determined on the basis of their effects on parameters like hexobarbitone sleep time, zoxazolamine paralysis time, bromosulphaline clearance, serum transaminases and serum bilirubin .it is effective as the oral dose of (10-80 mg/kg, p.o.) containing coumestan wedelolactone and desmethylwedelolactone as major components with apigenin, luteolin, 4-hydroxybenzoic acid and protocateuic acid as minor constituents exhibited maximum hepatoprotective activity and is the active fraction for hepatoprotective activity of Eclipta alba leave [10].

FICUS CARICA

Family : Moraceae
Synonym : *Ficus carica* Linn.

Hepatoprotective activity

The methanol extract of the leaves of *Ficus carica* Linn. was evaluated for hepatoprotective activity in rats with liver damage induced by carbon tetrachloride. The extract at an oral dose of 500 mg/kg exhibited a significant protective effect by lowering the serum levels of aspartate aminotransferase, alanine aminotransferase, total serum bilirubin, and malondialdehyde equivalent, an index of lipid peroxidation of the liver. These biochemical

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observations were supplemented by histopathological examination of liver sections. The activity of extract was also comparable to that of silymarin, a known hepatoprotective [11].

LUPEOL OF MANGO PULP

Family : Anacardiaceae
Synonym : Mangifera horsefieldii.

Hepatoprotective activity

Lupeol, a triterpene present in mango In the present study, chemopreventive properties of lupeol of mango pulp extract (MPE) were evaluated against 7,12-dimethylbenz(a)anthracene (DMBA) induced hepatotoxicity in Swiss albino mice. Lupeol as the oral dose of (25 mg/kg body weight, bw) or 1 mL of 20% w/v aqueous MPE/mouse were daily given for the effective hepatoprotective activity.

MORINGA OLEIFERA

Family : Moringaceae
Synonyms : Moringa oleifera Lam.

Hepatoprotective activity

The Hepatoprotective effect of Ethanolic leave Extract of *Moringo Oleifera* was tested on paracetamol induced hepatic injury on wistar rats. Fifteen (15) female adult wistar rats were divided into three (3) groups. Group I was the Control group that received distilled water only, group II was the negative control that received 1 g/kg of paracetamol on the 10th day, and group III received 500 mg/kg of theextract for duration of ten (10) days. Group III was pre-treated with 500 mg/kg of the ethanolic leave extractof *Moringa oleifera* before inducing the liver damage on the 10th day with 1 g/kg of paracetamol. Twelve (12)hr after administration, the rats were sacrificed and the liver was fixed immediately in Formalin. The liver tissues was processed and stained in Haematoxylin and Eosin (H&E).The histological observations showed that the leave extract of *Moringa oleifera* was hepatoprotective [12].

PERGULARIA DAEMIA

Family : Asclepiadaceae (Milkweed family)
Synonym : Asclepias daemia,Daemia extensa

Hepatoprotectiveactivity

The aqueous and ethanolic extracts obtained from aerial parts of *Pergularia daemia* were evaluated for hepatoprotective activity in rats by inducing liver damage by carbon tetrachloride. The ethanolic extract at an oral dose of 200 mg/kg exhibited a significant protective effect by lowering serum levels of glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase, total bilirubin and total cholesterol and increasing the levels of total protein and albumin levels. The activity may be a result of the presence of flavonoid compounds.

SOLANUM NIGRUM

Family : Solanaceae
Synonyms : Night shadingale ,Solanum nigrum L.

Hepatoprotective activity

The aqueous extract of whole plant of *solanum nigrum* (SNE) was effective against thioacetamide (TAA)-induced liver fibrosis in mice. It is administered as the dose of (0.2 or 1.0 g/kg). The extract reduced the hepatic hydroxyproline and α -smooth muscle actin protein levels in TAA-treated mice. SNE inhibited TAA-induced collagen (α1)(I), transforming growth factor-β1 (TGF-β1) and mRNA levels in the liver. Histological examination also confirmed that SNE reduced the degree of fibrosis caused by TAA treatment in mice. probably through the reduction of TGF-β1 secretion [13]. aqueous extract of SN (ASNE) also evaluated in CCl4 induced chronic hepatotoxicity in rats. Liver histopathology showed that ASNE 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. The effect was dependent on the concentration of plant extracts. These studies suggested that the observed hepatoprotective effect of these crude plant extract may be due to their ability to suppress the oxidative degradation of DNA in the tissue debris. Since the herb is commonly known as hepatoprotective agent and have shown these efficacy in protecting against both CCl4 and thioacetamide induced hepatic injury [13,14].

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TAMARNDUS INDICA

Family : Ceasalpiniaceae
Synonym : Tamarindus officinalis, Tamarindus occidentalis.

Hepatoprotective activity

Protective effect of *Tamarindus indica* Linn was evaluated by intoxicating the rats with paracetamol (1 g/kg p.o.) for seven days. The aqueous extracts of different parts of *Tamarindus indica* such as fruits, leaves (350 mg/kg p.o.) and unroasted seeds (700 mg/kg p.o.) were administered for 9 days after the third dose of paracetamol. Biochemical estimations such as aspartate transaminase, alanine transaminase, alkaline phosphatase, total bilirubin and total protein were recorded on 4 th and 13 th day. Liver weight variation, thiopentone induced sleeping time and histopathology were studied on 13 th day. Silymarin (100 mg/kg p.o.) was used as a standard. A significant hepatoregenerative effect was observed for the aqueous extracts of tamarind leaves, fruits and unroasted seeds as judged from the parameters studied [4].

TRIDAX PROCUMBENS

Family : Asteraceae
Synonym : Vranaropani

Hepatoprotective activity

The hepatoprotective activity of ethanolic extract of aerial parts of *Tridax procumbens* was investigated against d-Galactosamine/Lipopolysaccharide (d-GalN/LPS) induced hepatitis in rats. d-GalN/LPS induced hepatic damage was manifested by a significant increase in the activities of marker enzymes (aspartate transaminase, alanine transaminase, alkaline phosphatase, lactate dehydrogenase and gamma glutamyl transferase) and bilirubin level in serum and lipids both in serum and liver. Pretreatment of rats with a chloroform insoluble fraction from ethanolic extract of *Tridax procumbens* as the oral dose of(300mg/kg) will reversed these altered parameters to normal values. The biochemical observations were supplemented by histopathological examination of liver sections. Results of this study revealed that *Tridax procumbens* could afford a significant protection in the alleviation of d-GalN/LPS-induced hepatocellular injury [15].

TYLOPHORA INDICA

Family : Asclepiadaceae (milkwed family)
Synonym : Asclepias asthmatica.

Hepatoprotective activity

The methanolic extract of *Tylophora indica* leaves was screened for hepatoprotective activity in carbon tetrachloride induced hepatotoxicity in albino rats. The degree of protection was measured by estimating biochemical parameters like Serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, total protein and level of serum bilirubin (both total and direct). Hepatoprotective activity of methanolic extract at a dose of 200 mg/kg and 300 mg/kg body weight, i.p., *Tylophora indica* leaves (200 and 300 mg/kg) exhibited significant reduction in serum hepatic enzymes when compared to rats treated with carbon tetrachloride alone.

DISCUSSION

Popularity of herbal remedies is increasing globally and at least one quarter of patients with liver diseases use ethnobotanicals. More efforts need to be directed towards methodological scientific evaluation for their safety and efficacy by subjecting to vigorous preclinical studies followed by clinical trials to unravel the mysteries hidden in the plants. This approach will help exploring the real therapeutic value of these natural pharmacotherapeutic agents and standardized the dosage regimen on evidence-based findings to become more than a fashionable trend. Many herbals are on the market to support health, relieve symptoms and cure diseases. However, most of these products lack scientific pharmacological validation. In experimental hepatotoxicity models in laboratory or higher animals, several herbals exerted hepatoprotective/curative effects that warrants their clinical testing. Due to lack of scientificbased pharmacological data, most of the herbal formulations cannot be recommended for the treatment of liver diseases

In spite of the availability of more than 300 preparations for the treatment of jaundice and chronic liver diseases in Indian Systems of Medicine (using more than 87 Indian medicinal plants,) only four terrestrial plants have been scientifically elucidated while adhering to the internationally acceptable scientific protocols. In-depth studies have proved *solanm nigrum* to be antioxidative, antilipid peroxidative, antifibrotic, antiinflammatory,

immunomodulating and liver regenerative. *Indigofera tinctoria* has been shown to be hepatoprotective and capable of inducing an endogenous interferon *canna indica* is proved to be antiinflammatory, hepatoprotective and immunomodulatory. Extensive studies on *Phyllanthus amarus* have confirmed this plant preparation possessed antiviral against hepatitis B and C viruses, hepatoprotective and immunomodulating effects, besides antiinflammatory properties.

CONCLUSION

Chronic hepatic diseases stand as one of the foremost health troubles worldwide, with liver cirrhosis and drug induced liver injury accounting ninth leading cause of death in western and developing countries. Therapies developed along the principles of western medicine are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Therefore, treating liver diseases with plantderived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive.

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