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A Review of Plants for Hepatic Disorders

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ABSTRACT

The liver is an important organ that aids in the anabolism and elimination of xenobiotics from the body. Liver malfunction is a serious public health problem which affects not only doctors and nurses, but also the pharmaceutical industry and a governing authority of drugs. Excessive alcohol use, toxic chemicals (particular antibiotics, chemotherapeutic drugs, carbon tetrachloride (CCL4), thioacetamide (TAA), and microorganisms all induce liver cell harm. In this scenario, the current synthetic medications to treat liver problems promote more liver damage.

As a result, herbal drugs have grown in popularity and are widely used. For a long time, plants have been utilized to treat hepatic illness. There are a variety of herbal preparations on the market. The goal of this review is to compile information on promising phytochemicals from medicinal plants that have been investigated in hepatotoxicity models utilising cutting-edge scientific methods.

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INTRODUCTION

The liver is a key organ that serves as a hub for the metabolism of nutrients such as carbohydrates, proteins, and lipids, as well as the excretion of waste metabolites.[1] It also manages the metabolism and excretion of pharmaceuticals and other xenobiotics from the body, protecting the organism against foreign chemicals through detoxification and elimination.[2] Bile is a substance secreted by the liver that aids digestion, among other things.[3] Chronic alcohol consumption, microorganisms, and liver cell injury induced by various toxicants such as some chemotherapeutic drugs, carbon tetrachloride, and thioacetamide are all well-studied.[4] Hepatitis and cirrhosis may occur as a result of increased lipid peroxidation during ethanol metabolism.[5] Plants have been used in the treatment of numerous diseases since the dawn of humanity.[6] Traditional Indian medicine, such as Ayurveda, Siddha, and Unani, is primarily focused on the utilisation of plant ingredients.[7] Because of their safety, efficacy, and cost effectiveness, herbal medications have grown in importance and popularity in recent years. In some circumstances, the therapeutic effectiveness of medicinal plants is influenced by their connection with other plants in their environment.[8] Hepatoprotective compounds are one of the most important and well-documented uses of plant products. As a result, there is a growing demand for safe hepatoprotective agents.[9]

Hepatoprotective Plants

Herbal-based treatments for liver problems have been used in India for a long time and have been popularised by major pharmaceutical companies all over the world[10]. Despite their widespread use, herbal medicines in general, and herbal medications for liver illnesses in particular, are still considered unsuitable therapy options for liver ailments[11]. The following limiting factors contribute to this eventuality: I lack of herbal drug standardisation; (ii) lack of active ingredient identification; (iii) absence of randomised controlled clinical trials (RCTs); and (iv) lack of toxicological evaluation. Natural therapies

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for liver disease treatment have a long history, beginning with Ayurvedic medicine and spreading to Chinese, European, and other traditional medicine systems.[12] The twenty-first century has seen a paradigm shift toward therapeutic evaluation of herbal products in liver disease models, combining the strengths of traditional medical systems with the modern concept of evidence-based medicinal evaluation, standardisation, and randomised placebo controlled clinical trials to support clinical efficacy.[13]

Hepatoprotective activity has been claimed for a variety of plants and preparations. It has been stated that around 160 phytoconstituents from 101 plants have liver-protective properties.[14] In India, 33 patented and proprietary multi-ingredient plant compositions use more than 87 plants. Despite great progress, no significant and safe hepatoprotective drugs are currently accessible in modern treatments. As a result, the development of plant-based hepatoprotective medications that are effective against a variety of liver disorders has received a lot of attention around the world. The goal of this review is to compile data from published studies on promising phytochemicals from medicinal plants that have been examined in hepatotoxicity models.[15]

Flacourtia Indica

The hepatoprotective effects of extracts from the aerial portions of Flacourtia indica (Burm. f.) Merr. were investigated. All extracts were observed to lower serum aspartate transaminase (AST), serum alanine transaminase (ALT), and serum alkaline phosphatase in rat models of paracetamol-induced liver necrosis (ALP).[16] At a single oral dose of 1.5g/kg of body weight, petroleum ether and ethyl acetate extracts showed the most significant reduction in serum levels of AST and ALT, with a reduction of 29.0 percent AST and 24.0 percent ALT by petroleum ether extract and 10.57 percent AST and 6.7 percent ALT level b Paracetamol-induced necrosis was also recovered well by petroleum ether and ethyl acetate extracts, according to histopathological analysis.[17]

The methanol extract, on the other hand, had no discernible effect on paracetamol-induced liver necrosis. Petroleum ether and ethyl acetate extract's hepatoprotective properties could be achieved through the suppression of microsomal drug metabolising enzymes. However, the dose utilised in this study is excessively high, and it is neither successful nor rational for a human dose. Ethyl acetate extract compared to paracetamol (3 g/kg of body weight) treated animals.[18]

Fig. 1: Flacourtia indica

Annona Squamosa

The hepatoprotective efficacy of Annona squamosa extracts (300 and 350 mg/kg bw) in an isoniazid + rifampicin-induced hepatotoxic model in albino Wistar rats was investigated. When compared to the hepatotoxic group, the therapy group had a substantial decrease in total bilirubin, a significant rise in total protein, and a significant decrease in ALP, AST, and ALT.[19] The hepatotoxic group had hepatocytic necrosis and inflammation in the centrilobular region, as well as portal triaditis, according to the histological findings. The therapy group had low inflammation and mild portal triaditis, with normal lobular architecture. Another study looked at the protective effect in hepatotoxicity caused by diethylnitrosamine.[20] The extracts of Annona squa-mosa were found to have a hepatoprotective effect in this investigation, suggesting that the plant extract could be an efficient treatment for chemical-induced liver damage.[21]

Fig. 2: Annona squamosa

Silybum Marianum

Polyphenolic extracts of Silybum marianum and Cichorium intybus were tested for their ability to protect rats from thioacetamide-induced hepatotoxicity.[22] The extracts were given to the rats at a dose of 25 mg kg-1 body weight, along with 50 mg kg body weight thioacetamide. In the groups treated with extracts and thioacetamide, activity

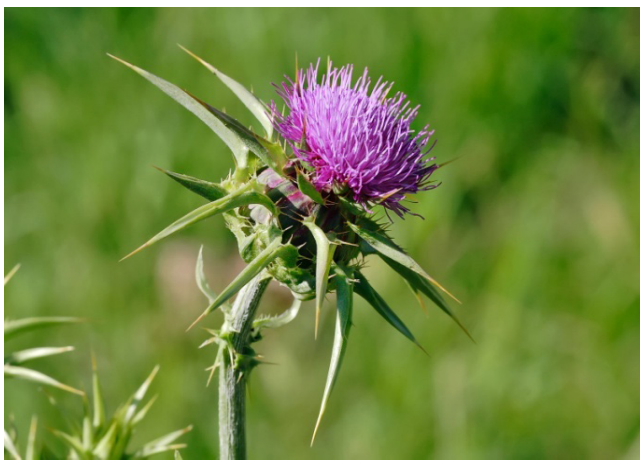

Fig. 3: Silybum marianum

of aminotransferases, alkaline phosphatase, and bilirubin decreased significantly when compared to the group treated alone with thioacetamide. The levels of Na+, K+, and liver weight did not differ substantially between the groups. Because of the presence of flavonoids and their antioxidant properties, this finding showed that Silybum marianum and Cichorium intybus extracts have a hepatoprotective impact on liver cells. [23]

Chamomile Capitula

The effect of an ethanolic extract of Chamomile recutita capitula (400 mg kg-1, P.O.) on blood and liver glutathione, Na+ K+-ATPase activity, serum marker enzymes, serum bilirubin, glycogen, and thiobarbutiric acid reactive substances against paracetamol-induced liver damage in rats was investigated to determine the possible mechanism of hepatoprotection. The extract of Chamomile recutita was found to have reversal effects on the levels of the above-mentioned parameters in paracetamol hepatotoxicity, implying that it has hepato-protective and/or hepato-stimulant activity.[24]

Fig. 4: Chamomile capitula

Coccinia grandis

The effects of an alcoholic extract of the fruits of Coccinia grandis Linn (Curcubitaceae) on CCl4-induced hepatotoxicity in rats were studied, as well as the levels of AST, ALT, ALP, total proteins, and total and direct bilirubin.[25] The alcoholic extract significantly (p0.05) lowered serum enzymes (AST, ALT, and ALP) and bilirubin activities, which were comparable to silymarin, at a dose level of 250 mg/kg, indicating its hepatoprotective activity.[26]

Wedelia calendulacea

The hepatoprotective potential of an ethanolic extract of *Wedelia calendulacea* L. (Asteraceae) was investigated in rats after they were exposed to CCl4-induced acute hepatotoxicity.[27] The use of an ethanolic extract of Wedelia calen-dulacea resulted in a dose-dependent reduction in CCl4-induced higher serum enzyme activity, as well as an increase in total proteins and bilirubin, indicating that the extract could aid in the recovery of normal liver function in rats. In CCl4-induced hepatic damage rats that received an ethanolic extract of Wedelia calendula-cea, the weight of organs such as the liver, heart, lung, spleen, and kidney increased compared to the CCl4-treated control group.[28]

Fig. 6: Wedelia calendulacea

Aegle Marmelos

The leaves of *Aegle marmelos*, also known as Bilva in ancient Sanskrit, were employed as a herbal treatment in the Indian system of medicine.[29] Using important marker biochemical indicators, the hepatoprotective efficacy of Aegle marmelos in rats with alcohol-induced liver injury was assessed. The findings revealed that Bael leaves have a strong hepatoprotective effect. Other researchers came to similar conclusions.[30]

Fig. 5: Coccinia grandis

Fig. 7: Aegle marmelos

Cassia Roxburghii

Cassia roxburghii DC seeds have been utilised in ethnomedicine for a variety of liver ailments because to their hepatoprotective properties. In rats, a methanolic extract of Cassia roxburghii restored the toxicity caused by the combination of ethanol and CCl4 in a dose-dependent manner. At doses of 250 mg/kg and 500 mg/kg, the extract has a similar impact to Liv-52®, a well-known plants-based hepato-protective formulation against hepatotoxins.[31]

Fig. 8: Cassia roxburghii

Orthosiphon Stamineus

The hepatoprotective effect of Orthosiphon stamineus methanol extract was tested in a paracetamol-induced hepatotoxicity rat model. Biochemical markers like AST, ALT, ALP, and lipid peroxides were measured in both the paracetamol-treated and control (untreated) groups. In a dose-dependent way, treatment with the methanolic extract of O. stamineus leaves (200 mg/kg) has hastened the recovery of the altered levels of biochemical markers to a near-normal profile. [32]

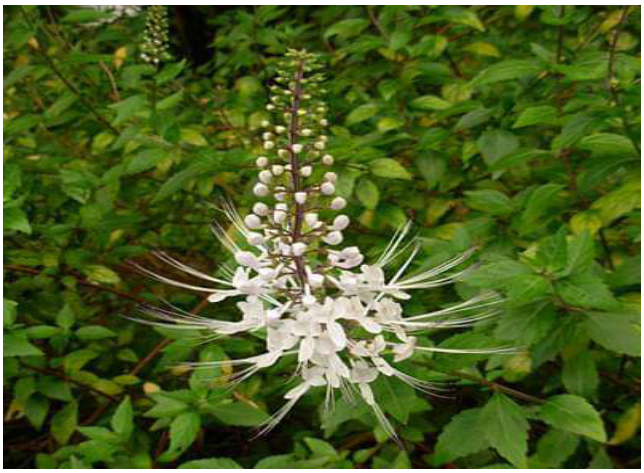

Fig. 9: Orthosiphon stamineus

Ficus Carica

In CCl4-induced liver damage rats, a methanolic extract of Ficus carica Linn. (Moraceae) leaves was tested for hepatoprotective efficacy. The extract had a significant protective effect at an oral dose of 500 mg/kg, as seen by decreased blood levels of AST, ALT, total serum bilirubin, and malondialdehyde equivalent, a measure of liver lipid peroxidation.[33]

Fig. 10: Ficus carica

Lepidium Sativum

In CCl4-induced liver injury in rats, the hepatoprotective activity of methanolic extract of Lepidium sativum at doses of 200 and 400 mg/kg was examined. All biochemical parameters were observed to be significantly reduced in groups treated with Lepidium sativum. In the Lepidium sativum-treated groups, the severe fatty alterations in the livers of rats produced by CCl4 were minimal.[34]

Fig. 11: Lepidium sativum

Sargassum Polycystum

In rats with D-galactosamine-induced hepatitis, the preventive effect of an ethanol extract of Sargassum polycystum was tested.[35] The D-galactosamine-induced elevations in the levels of diagnostic marker enzymes (AST, ALT, and ALP) in rats' plasma were significantly decreased (P0.05) after oral treatment of S. polycystum extract [125mg/kg bodyweight/day for 15 days]. It also possesses antioxidant efficacy against D-galactosamine-induced hepatitis, preventing lipid peroxidation and maintaining the hepatic enzymatic and non-enzymatic antioxidant defence systems at near-normal levels. S. polycystum's antihepatotoxic potential could be attributed to its anti-oxidant and membrane-stabilizing properties.[36]

Fig. 12: Sargassum polycystum

Solanum Nigrum

In mice, the effects of *Solanum nigrum* extract (SNE) on thioacetamide (TAA)-induced liver fibrosis were investigated. Throughout the experiment, mice in the three TAA groups were given distilled water and SNE (0.2 or 1.0 g/kg) through gastrogavage on a regular basis. In TAA-treated mice, SNE lowered hepatic hydroxyproline and -smooth muscle act protein levels. TAA-induced collagen (1)(I), transforming growth factor-1 (TGF-1) and mRNA levels in the liver were reduced by SNE.[37] SNE reduced the degree of fibrosis generated by TAA therapy, according to histological evaluation. TAA-induced hepatic fibrosis in mice is greatly reduced when SNE is given orally, most likely due to a decrease in TGF-1 production.[38]

The preventive effects of aqueous ex-tract of SN (ASNE) against liver damage in CCl4-induced chronic hepatotoxicity in rats were investigated in another investigation.The results demonstrated that ASNE treatment reduced CCl4-induced blood levels of hepatic enzyme indicators, superoxide, and hydroxyl radicals considerably. ASNE reduced the occurrence of liver diseases such as hepatic cells hazy swelling, lymphocyte infiltration, hepatic necrosis, and fibrous connective tissue proliferation generated by CCl4 in rats, according to histopathology. As a result, the findings of this study suggest that ASNE may protect the liver from CCl4-induced oxidative damage in rats, and that this hepatoprotective effect may be due to its modulation of detoxification enzymes as well as its antioxidant and free radical scavenging properties.[39]

In the reaction combination combining calf thymus DNA and a free radical producing apparatus, plant extracts of Solanum nigrum and Cichorium intybus protect DNA from oxidative damage to its deoxyribose sugar moiety.[40] The effect was proportional to the amount of plant extracts used. The effect of Cichorium intybus, on the other hand, was substantially stronger than that of Sola-num nigrum.[41] The observed hepatoprotective action of these crude plant extracts may be attributable to their ability to prevent the oxidative destruction of DNA in tissue debris, according to these investigations.[42]

Because these herbs are well known as hepatoprotective agents and have been found to protect against CCl4-induced liver injury, it is possible that their efficacy is due to their ability to scavenge free radicals.

Prostechea michuacana

The effects of methanol, hexane, and chloroform extracts of Prostechea michuacana (PM) on CCl4-induced liver damage in albino rats were investigated. The in vivo peroxidation generated by CCl4 was reduced by pre-treatment with methanolic extract, which showed a dose-dependent reduction in biochemical indicators of liver damage.[43] Similarly, the effects of pretreatment with PM extracts on paracetamol-induced hepatotoxicity, as well as the probable mechanisms involved, were investigated in rats after administration of PM extracts at 200, 400, and 600 mg/kg. Blood biochemical profiles were monitored to determine the level of protection.[44] The methanolic extract of orchid had a strong hepatoprotective effect, as seen by decreased serum enzyme activity and bilirubin levels.[45]

These findings revealed that a methanolic extract of PM could protect against paracetamol-induced lipid peroxidation, hence avoiding the harmful effects of paracetamols toxic metabolites. This hepatoprotective effect was similar to that of sylmarin.

Fig. 13: Solanum nigrum

Fig. 14: Prostechea michuacana

Extracts of hexane and chloroform had no discernible effect. The results suggested that the methanolic extract of PM could be a natural hepatoprotective agent.[46]

DISCUSSION

Herbal medicines are becoming increasingly popular around the world, with ethnobotanicals being used by at least a quarter of patients with liver problems. To unravel the mysteries concealed in the plants, more efforts should be put into thorough scientific evaluation for their safety and efficacy by subjecting them to rigorous pre-clinical investigations followed by clinical trials. This method will aid in the investigation of the true therapeutic potential of these natural pharmacotherapeutic substances, as well as the standardisation of dosing regimens based on evidence-based discoveries, allowing them to become more than a passing fad. Many herbals are available to help with health, symptom relief, and illness cure. The majority of these products, on the other hand, lack scientific pharmacological confirmation.

Several herbals showed hepato-protective/curative benefits in laboratory or higher animal hepatotoxicity models, indicating that clinical study is warranted. Most herbal formulations cannot be recommended for the treatment of liver problems due to a lack of scientifically supported pharmacological data.

Despite the fact that Indian Systems of Medicine have more than 300 preparations for the treatment of jaundice and chronic liver diseases (using more than 87 Indian medicinal plants), only four terrestrial plants have been scientifically elucidated while following internationally accepted scientific protocols. Sylibum marianum has been proven to be anti-oxidative, anti-lipid peroxidative, antifibrotic, anti-inflammatory, immunomodulating, and liver regenerative in investigations.

Glycyrrhiza glabra has been demonstrated to be hepatoprotective and capable of causing endogenous interferon to be produced. Picrorhiza kurroa has anti-inflammatory, hepatoprotective, and immunomodulatory properties. Extensive research on Phyllanthus amarus has revealed that it has antiviral activities against the hepatitis B and C viruses, as well as hepatoprotective and immunomodulating effects, as well as anti-inflammatory qualities.

CONCLUSION

Chronic hepatitis is one of the world's most serious health problems, with liver cirrhosis and drug-induced liver impairment accounting for the ninth greatest cause of mortality in both developed and developing countries. Therapies based on western medicine concepts are typically ineffective, have a high risk of side effects, and are prohibitively expensive, especially in developing countries.

As a result, treating liver illnesses with plant-derived chemicals that are readily available and do not require time-consuming pharmaceutical production appears to be very appealing. An attempt has been made in this review article to compile the reported hepatoprotective plants from India and abroad, which may be useful to health professionals, scientists, and scholars working in the field of pharmacology and therapeutics in developing evidence-based alternative medicine to cure various types of liver diseases in humans and animals.

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