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REVIEW ON POTENTIAL PLANT BASED DRUGS FOR HEPATOPROTECTIVE ACTIVITY

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ABSTRACT

Liver diseases are becoming a common problem nowadays because of the increase in environmental pollutants, toxins, indiscriminate usage of medications, life style modifications and many more reasons. The review summarizes the hepatoprotective activity of *Eucalyptus Maculata, Swertia chirata, Indigofera aspalathoides, Curcuma longa, Terminalia chebula, Nigella sativa, Ocimum sanctums, Glycyrrhiza glabra, Foeniculum vulgare and Camellia sinensis.* Studies on these medicinal plants have shown promising results in hepatoprotective activity.

Keywords: Herbal drugs, Hepatoprotective, D-galactosamine, medicinal plants.

INTRODUCTION

Metabolic activity of liver can be enhanced by some herbal drugs. The toxins absorbed from the intestine tract gain access first to the liver, results in a variety of liver ailments. Liver cell injury can be caused by various toxicants such as carbon tetrachloride, thioacetamide, chronic alcohol consumption and microbial infection etc. Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. The Indian Traditional Medicine like Ayurveda, Siddha and Unani are predominantly based on the use of plant materials. The association of medical plants with other plants in their habitat also influences their medicinal values in some cases. One of the important and well documented uses of plant products is their use as Hepatoprotective agents.

Examples of hepatoprotective herbal plants:

***Eucalyptus Maculata*:** *Eucalyptus Maculata* belongs to the family Myrtaceae. The plant is considered as an indigenous source of drugs exhibiting an anti-asthmatic activity and is used in the treatment of chronic bronchitis. The chloroformic extract and pure phenolic isolates were evaluated for their antioxidant and Hepatoprotective properties in mice and rats based on biochemical changes in serum and tissues as well as pathological changes in the liver and spleen. *E. maculata* extract has inhibitory effect of free radical activity which may be due to the formation of stable phenoxyl radical in addition to its effect through vitamin C. Acetaminophen (ACP) at a dose of 1 g/kg body weight produced 100% mortality in mice, while pretreatment of animals with the chloroformic extract (125 and 250 mg/kg) has reduced the mortality rate by 66%. Pretreatment of rats with either the chloroformic extract (250 mg/kg) or any of the pure isolates (20 mg/kg) significantly reduced the increase in serum level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) produced by ACP.

***Swertia chirata*:** *Swertia chirata* belongs to the family Gentianceae. Due to the effect of hepatotoxic substance like ethanol, drugs, chemicals and others microbs, serum aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), and alkaline phosphatase (ALP) and bilirubin level are increased, but liver glycogen and serum cholesterol levels are decreased. Histologically it causes hepatocytic necrosis especially in the centrilobular region. Treatments with *S. chirata* at different doses, viz. 25, 50, and 100 mg/kg body wt daily, causes improvement in both biochemical and histopathological parameters compared to CCl_4 hepatotoxicity but the activity was maximum when given in a moderate dose 50 mg/kg body wt.

***Indigofera aspalathoides*:** *Indigofera aspalathoides* belongs to the family Papilionaceae. Commonly known as *Shivanar vembu* is distributed throughout the Southern India. The whole plant has been traditionally used for cooling, demulcent and odematous tumors used in the form of decoction for leprosy and cancerous affections. The ashes are used in preparations against hair infection. The stem is traditionally used for various skin disorders and cancer. Methanol extract of *Indigofera aspalathoides* stem also possess Hepatoprotective activity. The alcoholic extract of stem, root and leaves of Indigofera aspalathoides was evaluated for its anti hepatotoxic substances activity against d-galactosamine or corbontetrachloride induced hepatic damage in rats. The activity was demonstrated by using biochemical parameters, such as serum glutamate pyruvate transaminase (SGPT), serum

glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), total bilirubin and gamma glutamate transpeptidase (GGTP). The histopathological changes of liver sample were compared with respective control. The extract showed remarkable Hepatoprotective effect.

Curcuma longa*: Curcuma longa* belongs to the family Zingebaraceae. It is also known as Turmeric, a rhizome of a herb known for its medicinal properties and is a more acceptable and viable option for a common man. It protects the liver from a number of toxic compounds such as acetaminophen, carbontetrachloride and galactosamine. Turmeric's Hepatoprotective effect is mainly a result of its antioxidant properties as well as its ability to decrease the formation of pro inflammatory cytokines. Sodium curcuminate, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, and bilirubin as well as by increasing bile solubility, therefore, possibly preventing and treating cholelithiasis. Curcumin has choleretic activity that increases bile output and solubility, which may be helpful in treating gallstones.

Terminalia chebula: *Terminalia chebula* belongs to the family Combretaceae also known as 'King of Medicine'. It protects the liver from a number of toxic compounds such as carbon tetrachloride, galactosamine and, acetaminophen. A mixture of chebulic acid (CA) and its minor isomer, neochebulic acid with a ratio of 2:1 isolated from ethanolic extract of *T. chebula* fruits showed strong Hepatoprotective activity, Ethanol extract *T. chebula* was found to prevent the Hepatotoxicity caused by the administration of rifampicin, isoniazid and pyrazinamide (combination) in sub-chronic model (12 weeks). Protective effects of an aqueous extract of *T. chebula* fruit on the tetra-butyl hydroperoxide-induced oxidative injury was observed in cultured rat primary hepatocytic and rat liver have also been documented. *T. chebula* in an herbal formulation (HP-1) showed Hepatoprotective activity against carbon tetrachloride induced toxicity in rat hepatocytes.

Nigella sativa: *Nigella sativa* belongs to the family Ranunculaceae. It is a widely used medicinal plant throughout the world. It was reported that *N. sativa* (0.2 mL/kg) intraperitoneally relieves the deleterious effects of ischemia reperfusion injury on liver. Biochemical parameters like the serum aspartate aminotransferase, alanine aminotransferase lactate dehydrogenase levels and total antioxidant capacity (TAC), total oxidative status (TOS) and oxidative stress index (OSI) were determined in hepatic tissue in rats with hepatic ischemia. Results suggested that *N. sativa* treatment protects the rat liver against hepatic ischemia reperfusion injury. *N. sativa* administration protects hepatic tissue from deleterious effects of toxic metals such as lead, and attenuates hepatic lipid peroxidation following exposure to chemicals such as carbon tetrachloride. Cadmium (Cd) causes alteration of the cellular homeostasis and oxidative damage. The protective role of TQ on the hepatotoxicity of Cd with special reference to its protection against perturbation of non enzymatic and enzymatic antioxidants was investigated.

Ocimum sanctum: *Ocimum sanctum* belongs to the family Lamiaceae. Hepatoprotective activity of *Ocimum sanctum* leaves extract was evaluated in experimentally induced chronic lead toxicity in male wistar rats. The antioxidant enzymes and histopathological examination, immunohistochemical staining and ultrastructural examination of liver were estimated. Lead residue in liver was also measured. Tulsi significantly minimized the gross and histopathological changes and also reduces the apoptosis in hepatocytes. By the end of experiment in *Ocimum* treated animals the liver almost coming to its normal appearance. This experiment suggests that the *Ocimum sanctum* exhibited significant Hepatoprotective effect on lead induced hepatic damage in rats. In another study, Wistar strains of Albino rats were induced using lead for hepatotoxicity and the aqueous extract of *O. sanctum* were administered to the animals orally for a period of 21 days.

Glycyrrhiza glabra: *Glycyrrhiza glabra* belongs to the family Fabaceae. Chronic hepatitis (viral as well as non-viral) is a slowly progressive liver disease that may evolve into cirrhosis with its potential complications of liver failure or hepatocellular carcinoma. Current therapy with the alpha-interferon is directed as viral clearance, but sustained response is only achieved in 20-40% of patients without cirrhosis and is less than 20% in patients with cirrhosis who have greatest need of therapy. In Japan glycyrrhizin has been used for more than 60 years as treatment for chronic hepatitis under the name of Stronger Neo- Minophagen C (SNMC) clinically as an anti-allergic and antihepatitis agent. Glycyrrhizin induced a significant reduction in serum aminotransferases and improved the liver histology when compared with the placebo. It has also been implicated that long-term usage of glycyrrhizin prevents development of hepatocellular carcinoma in chronic hepatitis C. In vitro studies have indicated that glycyrrhizin modifies the intracellular transport and uppresses hepatitis B virus (HBV) surface antigen (HbsAg).

Foeniculum vulgare: Fennel (*Foeniculum vulgare*) belongs from Umbelliferae family, it is an annual, biennial or perennial aromatic herb, depending on the variety, the leaves, stalks and seeds (fruits) of the plant are edible[32]. *Foeniculum vulgare* is an aromatic herb whose fruits are oblong, ellipsoid or cylindrical, straight or slightly curved and greenish or yellowish brown in colour. Volatile components of fennel seed extracts by chromatographic analysis include trans-anethole, fenchone, methylchavicol, limonene, α-pinene, camphene, β-pinene, β-myrcene, α-phellandrene, 3-carene, camphor, and cis-anethole. Hepatoprotective activity of *Foeniculum vulgare* essential oil was studied using a carbon tetrachloride-induced liver fibrosis model in rats. The hepatotoxicity produced by chronic carbon tetrachloride administration was found to be inhibited by *Foeniculum vulgare* essential oil with evidence of decreased levels of serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bilirubin.

Camellia sinensis: *Camellia sinensis* belongs from Theaceae family. The leaves of *Camellia sinensis* are thermogenic, appetizer, digestive, carminative, diuretic, and useful in cardiodynia, hemorrhoids, inflammation and abdominal disorders. It has been previously reported that the leaves have used to treat the cancer of duodenum, lung, liver and mammary gland. Catechins in combination with antioxidants with vitamin E are hypothesized to offer Hepatoprotective defense against enzymes such as superoxide, dismutase and catalase. A number of catechins (flavanols) especially epigallocatechin gallate, epigallocatechin, epicatechin gallate and epicatechin which have been identified as active components which are responsible for antioxidant property, and also have the ability to stabilize cell membranes. The aqueous extract of *Camellia sinensis* (100 mg and 200 mg/Kg) were administered orally to the animals with CCl4 induced hepatotoxicity. The extract shows significant reduction in serum hepatic enzymes and liver lipid peroxide which were increased by carbon tetrachloride.

CONCLUSION

A collection of botanical medicines such as *Eucalyptus maculata*, *Curcuma longa*, *Camellia sinensis*, *Glycyrrhiza glabra*, *Terminalia chebula*, *Swertia chirata***,** *Indigofera aspalathoides***,** *Ocimum sanctum***,** *Foeniculum vulgare* and *Nigella sativa*, are the best-researched plants for the treatment of liver disease, with many human therapeutic trials available to the practicing physician to assess their potential effectiveness. The goal of ethnopharmacological studies on medicinal plants should not be restricted to find new prototype of pure compounds as drugs. Active extracts, fractions or mixture of extracts may prove very effective drugs. Plant drugs (combinations or individual drug) for liver diseases should possess sufficient efficacy to cure severe liver diseases caused by toxic chemicals, viruses (Hepatitis B, Hepatitis C etc) excess alcohol intake, etc. A single drug cannot be effective against all types of severe liver diseases. Effective formulations have to be developed using indigenous medicinal plants, with proper pharmacological experiments and clinical trials. The manufacture of plant products should be governed by standards of safety and efficacy.

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