A REVIEW OF HEPATOPROTECTIVE NATURAL PRODUCTS

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ABSTRACT
The maintenance of a healthy liver is essential for the overall well being of an individual. Because liver is a vital organ which can’t replace and were it plays a major role in metabolism and excretion of xenobiotics from the body, Liver injury or liver dysfunction is a major health problem that challenges not only health care professionals but also the pharmaceutical industry and drug regulatory agencies. Liver cell injury caused by various toxic chemicals such as certain antibiotic, chemotherapeutic agents, paracetamol, carbon tetrachloride, thioacetamide etc., excessive alcohol consumption and microbes are well studied. The available synthetic drugs to treat liver disorders in this condition also cause further damage to the liver. Hence, Herbal drugs have become increasingly popular and their use is wide spread. Herbal medicines have been used in the treatment of liver diseases for a long time. A number of herbal preparations are available in the market. 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.

Keywords: Liver, liver disease, hepatotoxicity, hepatoprotective activity, natural products.

INTRODUCTION
The liver plays an astonishing array of vital functions in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction. And it functions as a centre of metabolism of nutrients such as carbohydrates, proteins and lipids and excretion of waste metabolites. The bile secreted by the liver has, among other things, plays an important role in digestion. Therefore, maintenance of a healthy liver is essential for the overall well being of an individual.

Liver cell injury caused by various toxics such as certain chemotherapeutic agents, carbon tetrachloride, thioacetamide, chronic alcohol consumption and microbes are common. Enhanced lipid per oxidation during metabolism of ethanol may result in development of hepatitis leading to cirrhosis. Since time immemorial, mankind has made the use of plants in the treatment of various ailments. 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. Hence, there is an ever increasing need for safe hepatoprotective agents. In spite of tremendous strides in modern medicine, there are hardly any drugs that stimulate liver function, offer protection to the liver from damage or help regeneration of hepatic cell. Many formulations containing herbal extracts are sold in the Indian market for liver disorders.

But management of liver disorders by a simple and precise herbal drug is still an intriguing problem. Several Indian medicinal plants have been extensively used in the Indian traditional system of medicine for the management of liver disorder. Some of these plants have already been reported to posses’s strong antioxidant activity.

HEPATOPROTECTIVE NATURAL PRODUCTS
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. Despite the significant popularity of several herbal medicines in general, and for liver diseases in particular, they are still unacceptable treatment modalities for liver diseases. Hence development of plant based hepatoprotective drugs has been given importance in the global market. 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 formulations. In spite of the tremendous advances made, no significant and safe hepatoprotective agents are available in modern therapeutics. Therefore, due importance has been given globally to develop plant-based hepatoprotective drugs effective against a variety of liver disorders. The present review is aimed at compiling data based on reported works on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models. Hence the present review is aimed at collecting and compiling data based on reported works on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models.
Curcuma longa or turmeric is a member of Zingiberaceae family which is a perennial herb with short and thick rhizomes. Tumeric has been used extensively in traditional Chinese medicine and Ayurvedic medical system. Curcuma longa contains approximately 2% volatile oil, composed mainly of α- and β-turmerone, monoterpenes (Leung and Foster 1996), 5% curcuminooids, mainly curcumin, minerals, carotene and vitamin C. The active constituent of Curcuma longa is Curcumin, which is the yellow pigment of turmeric. The hepatoprotective activity of the ethanol extract 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 enzyme 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 result suggests that ethanolic extract of Curcuma longa has potent hepatoprotective effect against paracetamol-induced liver damage in rats.

Foeniculum vulgare

Fennel (Foeniculum vulgare Mill. family Umbelliferae) is an annual, biennial or perennial aromatic herb, depending on the variety, which has been known since antiquity in Europe and Asia Minor. The leaves, stalks and seeds (fruits) of the plant are edible. 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 transanethole, fenchone, methylchavicol, limonene, α-pinene, camphene, β-pinene, β-myrcene, α-phellandrene, 3-carene, camphor, and cisanethole. Hepatoprotective activity of Foeniculum vulgare (fennel) 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.
Swertia Chirata

Simultaneous treatments with S. Chirata (Gentianaceae), (in different doses, viz, 20, 50, and 100 mg/kg body wt daily) and (CCl4) cause improvement at both biochemical and histopathological parameters compared to that of (CCl4) treatment alone but it was most effective when S. chirata was administered in a moderate dose (50 mg/kg body wt)19,20.

Picrohiza kurroa

Administration of picroliv, a standardized fraction of alcoholic extent of Picrohiza kurroa (Scrophulariaceae) (3–12 mg/kg/day for two weeks) simultaneously with P. berghel infection showed significant protection against hepatic damage in Mastomys natalensis. The increased levels of serum glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase, lipoprotein-X (LP-X) and bilirubin in the infected animals were marked reduced by different doses of picroliv. In the liver, picroliv decreased the levels of lipid peroxides and hydroperoxides and facilitated the recovery of superoxide dismutase and glycogen21,22.

Azadirachta indica

Effect of A. indica leaf (meliaceae) extract on serum enzyme levels (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase) elevated by paracetamol in rats was studied with a view to observe any possible hepatoprotective effect of this plant. 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. The antihepatotoxic action of picroliv seems likely due to an alteration in the biotransformation of the toxic substances resulting in decreased formation of reactive metabolites23.

Andrographis paniculata

Antihapatotoxic activity of the Andrographis paniculata (acanthaceae) methanolic extract (equivalent to 100 mg/kg of andrographolide) and 761.33 mg/kg ip, of the andrographolide free methanolic extract (equivalent to 861.33 mg/kg of the methanolic extract) of the plant, using CCl4-intoxicated rats. Biochemical parameters like serum transaminases–GOT and GPT, serum alkaline phosphatase, serum bilirubin and hepatic triglycerides were estimated to assess the liver function. The results suggest that andrographolide is the major active antihepatotoxic principle present in A. paniculata24.

Flacourtia indica

The extracts 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 of 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.

Wedelia calendulacea

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 calendulaecae 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 group26.

Prostechea michuacana

Methanol, hexane and chloroform extracts of Prostechea michuacana (PM) were studied against CCl4-induced hepatic injury in albino rats. Pretreatment with methanolic extract reduced biochemical markers of hepatic injury levels demonstrated dose-dependent reduction in the in vivo peroxidation induced by CCl4. Likewise, pretreatment with extracts of PM on paracetamol-induced hepatotoxicity and the possible mechanism involved in this protection were also investigated in rats after administering the extracts of PM at 200, 400 and 600mg/kg. The degree of protection was measured by monitoring the blood biochemical pro-files. The methanolic extract of orchid produced significant hepatoprotective effect as reflected by reduction in the increased activity of serum enzymes, and bilirubin. These results suggested that methanolic extract of PM could protect paracetamol-induced lipid peroxidation thereby eliminating the deleterious effects of toxic metabolites of paracetamol. This hepato-protective activity was comparable with sylmarin. Hexane and chloroform extracts did not show any apparent effect. The findings indicated that the methanolic extract of PM can be a potential source of natural hepatoprotective agent27.
Aegle marmelos

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 rats using essential marker biochemical parameters. The results indicated that, the Bael leaves have excellent hepato-protective effect. Similar findings were also reported by other workers.

DISCUSSION

Popularity of herbal remedies is increasing globally and at least one quarter of patients with liver diseases use ethno botanicals. 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 herbal 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 scientific-based pharmacological data, most of the herbal formulations cannot be recommended for the treatment of liver diseases.

CONCLUSION

In this review article, effort has been taken to collect and compile the details regarding a few hepato protective natural products, which will be useful to the society to venture in to a field of alternative systems of medicine. A more thorough review on various herbal products available in India and abroad as a hepato protectant is in near future.

REFERENCES


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Mr. Fasalu rahiman o.m graduated from Rajiv Gandhi University of health sciences, Bangalore, Karnataka, India and doing post graduation from the same university. At post graduation level taken specialization in pharmacology, and doing master thesis in “hepatoprotective activity”.