



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. Liver injury induced by toxins is more common nowadays. Herbal remedies are focused in the pharmaceutical industry to evolve a safe route for liver disorders. Therefore, hepatoprotective natural products such as *Jatropha curcas*, *Foeniculum vulgare*, *Trigonella foenum graecum*, *Eclipta alba*, *Garcinia mangostana* Linn is reviewed.

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 (1). Therefore, maintenance of a healthy liver is essential for the overall well being of an individual. Liver cell injury caused by various toxicants such as certain chemotherapeutic agents, carbon tetrachloride, thioacetamide etc., chronic alcohol consumption and microbes is well-studied. Since time immemorial, mankind has made the use of plants in the treatment of various ailments. The Indian Traditional Medicine like Ayurveda, Siddha and Unani are predominantly based on the use of plant materials. Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. 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 agent (2). 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 (3). 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 possess strong antioxidant activity (4-6).

Hepatoprotective natural products

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 (7). Development of plant based hepato protective drugs has been given importance in the global market. 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 hepato-toxicity models. The hepato protective activities of *Jatropha curcas*, *Foeniculum vulgare*, *Trigonella foenum graecum*, *Eclipta alba*, *Garcinia mangostana* Linn is reviewed.

Jatropha curcas

Jatropha curcas Linn (Family: Euphorbiaceae), is an evergreen shrub, indigenous to America, but cultivated in most parts of India. This evergreen plant is common in waste places throughout India, especially on the Coromandel Coast and in Travancore; in the southern parts it is cultivated chiefly for hedges in the Konkan, and also in Malay Peninsula.[8] Leaves are regarded as antiparasitic, applied to scabies; rubefacient for paralysis, rheumatism; also applied to hard tumours. Leaves also show antileukemic activity.[9] Compounds that have been isolated from *Jatropha curcas* leaves include the flavonoids apigenin and its glycosides vitexin and isovitexin, the sterols stigmasterol, α -D-sitosterol and its α -D-glucoside.[10 - 13]. Methanolic fraction of leaves of *Jatropha curcas* (MFJC) was evaluated against hepatocellular carcinoma induced by Aflatoxin B1 (AFB1). Marked

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increase in lipid peroxide levels and concomitant decrease in enzymic antioxidants levels were observed in carcinoma induced rats, while methanolic fraction of *Jatropha curcas* treatment reversed the conditions to near normal levels. Liver histopathology showed that MFJC reduced the incidence of liver lesions, lymphocytic infiltrations and hepatic necrosis induced by AFB1 in rats. These results suggest that MFJC could protect liver against the AFB1-induced oxidative damage in rats (14).

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.(15). 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 cisanethole (16, 17). 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 (18)

Trigonella foenum graecum

Fenugreek (*Trigonella foenum graecum*) is an annual herb that belongs to the family Leguminosae. It has a long history as both a culinary and medicinal herb. The seeds of fenugreek are commonly used as a spice in food preparations due to the strong flavour and aroma. The seeds are reported to have restorative and nutritive properties (19).

Fenugreek seeds have antioxidant activity and have been shown to produce beneficial effects such as neutralization of free radicals and enhancement of antioxidant apparatus (20). The protective effect of a polyphenolic extract of fenugreek seeds (FPEt) against ethanol (EtOH)-induced toxicity was investigated in human Chang liver cells. EtOH treatment suppressed the growth of Chang liver cells and induced cytotoxicity, oxygen radical formation and mitochondrial dysfunction. Incubation of FPEt along with EtOH significantly increased cell viability in a dose-dependent manner, caused a reduction in lactate dehydrogenase leakage and normalized GSH/GSSG ratio. The findings suggest that the polyphenolic compounds of fenugreek seeds

can be considered cytoprotective during EtOH-induced liver damage. (21).

Eclipta alba

Eclipta alba Hassk. (Bhringaraja, Family: Compositae) is a perennial shrub which grows widely in moist tropical countries. Different uses have been reported for this shrub. It is used as alterative, anthelmintic, expectorant, antipyretic, antiasthmatic, tonic, deobstruent in hepatic and spleen enlargement, in skin diseases and as a substitute for Taraxacum (a popular liver tonic) (22, 23). Recently Chandra, have observed a significant anti-inflammatory activity of the powder in rats (24). It has been reported to be useful in liver ailments (25) & has been shown to possess hepatoprotective activity against carbon- tetrachloride induced liver cell damage in animals (26). The effect of *Eclipta alba* (EA) extract was studied on paracetamol induced hepatic damage in Mice. Treatment with ethanol extract of *E. alba* was found to protect the mice from hepato-toxic action of paracetamol as evidenced by significant reduction in the elevated serum transaminase levels (27).

Garcinia mangostana Linn

Garcinia mangostana Linn. commonly known as "mangosteen", is a tropical evergreen tree and is an emerging category of novel functional foods sometimes called "superfruits" presumed to have a combination of appealing subjective characteristics, such as taste, fragrance and visual qualities, nutrient richness, antioxidant strength (28) and potential impact for lowering risk of human diseases (29). The pericarps of *G. mangostana* have been widely used as a traditional medicine for the treatment of diarrhea, skin infection and chronic wounds in South East Asia for many years (30). These are the nature's most abundant sources of xanthenes, which are the natural chemical substances possessing numerous bio-active properties that help to maintain intestinal health, neutralize free radicals, help and support joints and cartilage functions and promotes immune systems (31). These are extracted from the rind of mangosteen containing 95% xanthenes also isoflavones, tannin and flavonoids (32). Treatment of hepatocellular carcinomas (liver cancer) with chemotherapy has generally been disappointing and it is most desirable to have more effective new drugs. The investigators extracted and purified 6 xanthone compounds from the rinds (peel) of the fruit of *Garcinia mangostana*, mangosteen fruit. The investigators tested this extract on 14 different human liver cancer cell lines. Several chemotherapeutic agents (drugs) were included in the study for comparison. The results showed that one of the xanthone derivatives which could be identified as garcinone E has potent cytotoxic effect (kill cells) on all liver cancer cell lines as well as

on the other gastric and lung cancer cell lines included in the screen. The investigators suggested that garcinone E may be potentially useful for the treatment of certain types of cancer (33).

Discussion

Popularity of herbal remedies is increasing globally and at least one quarter of patients with liver diseases use ethnobotanicals. 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 hepato-protective/curative effects that warrants their clinical testing. Due to lack of scientific-based pharmacological data, most of the herbal formulations can not be recommended for the treatment of liver diseases. (34).

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 an hepato protectant is in near future.

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