Review Article

A Comprehensive Review on Hepatoprotective Herbal Agents

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ABSTRACT

Herbal drugs are conventionally used in various parts of the world to alleviate different diseases. Many herbs have been proven to be efficient as hepatoprotective agents while many more are claimed to be hepatoprotective but be deficient in any such scientific substantiation to support such claims. The therapeutic values were tested against a few chemicals-induced subclinical levels of liver damages in rodents. Liver diseases are a major worldwide health problem, with high endemicity in developing countries. They are mainly caused by chemicals and some drugs when taken in very high doses. Liver is a vital organ play a major role in metabolism and excretion from the body. Natural remedies from medicinal plants are considered to be effective and safe alternative treatment for liver toxicity. There are several chemicals have been known to induce hepatotoxicity by producing reactive species which cause exhaustion in tissue thiol, lipid peroxidation, plasma membrane damage like carbontetrachloride, paracetomol, thioacetamide, antituberculer drugs, D-galactosamine, liposachharide and arsenic etc. The present review is designed to summarized the medicinal plants that have been tested in hepatotoxicity models using recent scientific system for protective effect in liver diseases.

Keywords: Liver, Hepatotoxicity, Hepatoprotective, Natural sources.

INTRODUCTION

Medicinal plants play a key role in the human health care. About 80% of the world population relies on the use of traditional medicine which is predominantly based on plant materials[1]. Liver damage is very common since liver has to detoxicate lot of many toxic substances. Most of the hepatotoxic chemicals damage liver cells, primarily by producing reactive species which form covalent bond with the lipids of the tissue[2]. The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamin. Thus, to maintain a healthy liver is a crucial factor for overall health and well being[3]. The bile secreted by the liver has, among other things, an important role in digestion[4]. The role played by this organ in the removal of substances from the portal circulation makes it susceptible to first and persistent attack by offending foreign compounds, culminating in liver dysfunction[5]. Liver diseases are mainly caused by toxic chemicals, excess consumption of alcohol, infections, and are sometime autoimmune[6]. Hepatotoxicity in most cases is due to free radical. Free radicals generated by the metabolism of toxicants initiate the toxicity cascade[7]. Paracetamol (PCM) also known as Acetaminophen, taken in overdose can cause severe hepatotoxicity and nephrotoxicity. PCM is activated and converted by cytochrome P450 enzymes to toxic metabolite NAPQI (N-acetyl-p-benzoquinoneimine) that causes oxidative stress and glutathione (GSH) depletion[8].

In view of severe undesirable side effects of synthetic agents, there is growing focus to follow systematic research methodology and to evaluate scientific basis for the traditional herbal medicines that are claimed to possess hepatoprotective activity[10]. The medicinal action of plants are unique to particular plant species or groups of plants and are consistent with this concept as the combination of secondary products in a particular plant is taxonomically distinct[11].

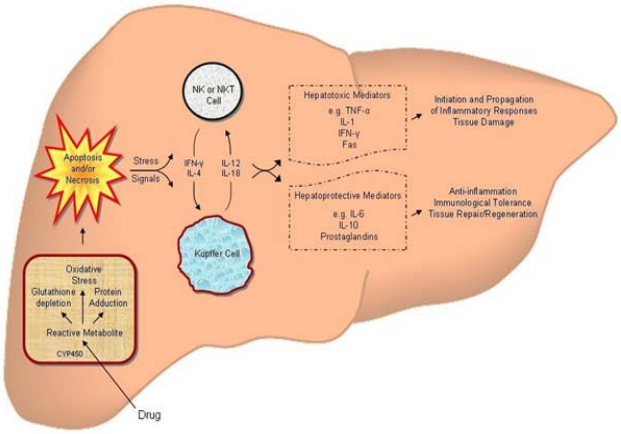

Figure 1: Mechanism of drug induced Liver injury[9].

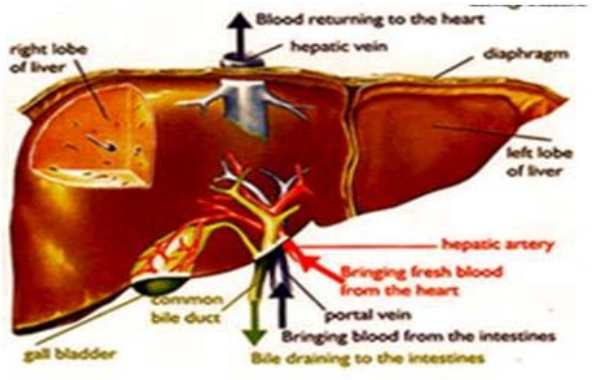

Figure 2: Anatomy and Physiology of Liver[12].

Table 1: Natural sources having hepatoprotective potential

Botanical name	Family	Part used	Extract used	Model used	Ref
Amorphophallus paeoniifolius	Araceae	Tubers	Methanol and aqueous	PIHT	13
Aerva lanata Linn.	Amaranthaceae	Whole plant	Hydroalcoholic	PIHT	14
Aegle marmelos	Rutaceae	Leaves	Ethanolic	CTCIHT	15
Andrographis paniculata (BURM.F) Nees	Acanthaceae	Leaves	Methanolic	PIHT	16
Alocasia indica (Linn.)	Araceae	Leaves	Hydroalcoholic	PIHT, CTCIHT	17
Annona squamosa Linn.	Annonaceae	Leaves	Alcoholic and water	IIHT, RIHT	18
Argemone mexicana (Linn).	Papaveraceae	Whole plant	Aqueous	CTCIHT	19
Abutilon bidentatum	Malvaceae	Aerial part	Aqueous methanolic	CTCIH, PIHT	20
Alangium salvifolium Linn.	Alangiaceae	Leaves	Aqueous and methanol	CTCIHT	21
Bauhinia purpurea Linn	Cesalpiniaceae	Leaves	Chloroform, alcohol and water	CTCIHT	22
Butea Monosperma Lam	Fabeceae	Stem bark	Methanolic	CTCIHT	23
Chenopodium album Linn.	Chenopodiaceae	Whole plant	Acetone and methanol	PIHT	24
Cassia fistula	Leguminosae	Fruit pulp	Aqueous	CTCIHT	25
Capparis sepiaria	Capparaceae	Stem	Alcoholic	CTCIHT	26
Calotropis gigantea	Ascelpiadaceae	Root, bark	Alcoholic	D-GIHT	27
Capparis brevispina DC.	Capparaceae	Stem bark	Ethanol	PIHT	28
Cyperus articulatus Linn.	Cyperaceae	Rhizome	Methanol	PIHT	29
Coccinia indica	Cucurbitaceae	Leaves	Diethylether	CTCIHT	30
Clerodendrum phlomidis Linn	Verbaneceae	Aerial part	Ethylacetate	PIHT	31
Curcuma xanthorrhiza Roxb.	Zingiberaceae	Rhizome	Ethanolic	EIHT	32
Canscora perfoliata Lam	Gentianaceae	Whole plant	Ethanol	CTCIHT	33
Cinnamomum zeylanicum L.	Lauraceae	Bark	Ethanolic	CTCIHT	34
Delonix regia	Caesalpiniaceae	Aerial part	Methanolic	CTCIHT	35
Enhydra fluctuans Lour	Asteraceae	Aerial part	Pet. ether, chloroform, ethanol	CTCIHT	36
Ecbolium viride (Forssk).	Acanthaceae	Roots	Methanolic	CTCIHT	37
Ficus benjamina Linn.	Moraceae	Leaves	Ethanolic	CTCIHT	38
Jatropha gossypifolia	*Euphorbiaceae*	Aerial parts	Petroleum ether, aqueous methanolic	CTCIHT	39
Launaea intybacea (Jacq) beauv	Asteraceae	Aerial parts	Ethylacetate	PIHT	40
Morus alba (Linn.)	Moraceae	Leaves	Petroleum ether, alcoholic chloroform, and water	CTCIHT	41
Oclmum sanctum	Lamiaceae	Leaves	Ethyl alcohol	PIHT	42
Ocimum gratissimum (L.)	Lamiaceae	Leaves	Methanolic	CTCIHT	43
Orthosiphon stamineus	Lamiaceae	Leaves	Methanolic	PIHT	44
Phyllanthus amarus	Euphorbiaceae	Leaves	Ethanol	EIHT	45
Phyllanthus niruri	Euphorbiaceae	Whole plant	Ethanolic	CTCIHT	46
Pterocarpus santalinus L.f.	Fabaceae	Stembark	Aqueou and ethanol	CTCIHT	47
Plumbago zeylanica Linn.	Plumbaginaceae	Aerial part	Methanolic	CTCIHT	48
Psidium guajava (Linn.)	Myrtaceae	Leaves	Aqueous	CTCIH, PIHT, TIHT	49
Phyllanthus emblica	Phyllanthaceae	Fruit	Aqueous	PIHT	50
Polyalthia longifolia	Leguminosae	Leaves	Methanol	PIHT	51
Santolina chamaecyparissus Linn	Asteraceae	Whole plant	Hydroalcoholic	D-GIHT	52
Solanum nigrum	Solanaceae	Whole plant	Water and methanol	CTCIHT	53
Rhododendron arboreum	Ericaceae	Leaves	Ethanolic	CTCIHT	54
Tecomella undulata	Bignoniaceae	Leaves	Methanol	EIHT, PIHT	55
Trichosanthes dioica Roxb.	Cucurbitaceae	Leaves	Ethanolic and aqueous	PIHT	56
Tephrosia calophylla	Leguminosae	Roots	Methanolic	CTCIHT	57
Tylophora indica (Linn.)	Asclepiadaceae	Leaves	Alcoholic and aqueous	EIHT	58

PIHT - Paracetamol induced hepatotoxicity, **CTCIHT** - Carbon tetra chloride induced hepatotoxicity, **EIHT** - Ethanol induced hepatotoxicity, **D-GIHT** - D-Galactosamine Induced hepatotoxicity, **TIHT**- Thioacetamide induced hepatotoxicity, **IIHT** - Isoniazid induced hepatotoxicity, **RIHT** - Rifampicin induced hepatotoxicity.

***Aerva lanata* Linn.**[14]

The hepatoprotective activity of hydroalcoholic extract of *Aerva lanata* against paracetamol induced liver damage in rats. The hydroalcoholic extract of *Aerva lanata* (600mg/kg) was administered orally to the animals with hepatotoxicity induced by paracetamol (3gm/kg). Silymarin (25mg/kg) was given as reference standard. All the test drugs were administered orally by suspending in 0.5% Carboxy methyl cellulose solution. The plant extract was effective in protecting the liver against the injury induced by paracetamol in rats.

***Andrographis paniculata* (BURM.F) Nees**[16]

The hepatoprotective activity of methanolic extracts of *Andrographis paniculata* was evaluated against paracetamol induced (500 mg/kg) hepatic damage in mice. The extracts at doses of 10 mg/kg and 100 mg/kg were orally administered at 24 and 72 hours time interval in each group. The results of the present study indicated that *Andrographis paniculata* possess hepatoprotective effects which could compromise the medicinal use of this plant in folk medicine.

Abutilon bidentatum[20]

Hepatoprotective activity of aqueous methanolic extracts of aerial parts of *Abutilon bidentatum* on carbon tetra chloride (CCl4) and paracetamol induced liver damage in rabbits. The results of this study strongly indicated that aerial parts of *A. bidentatum* had potent hepatoprotective action against CCl4 and paracetamol induced hepatic damage in rabbits.

***Butea Monosperma* Lam**[23]

The methanolic extract of stem bark of *Butea monosperma* Lam (MEBM) was studied for the hepatoprotective and antipyretic activities. Carbontetrachloride (1ml/kg, i.p) induced hepatotoxicity and Brewer's yeast (10ml/kg, s.c) induced pyrexia rat models were used. The 10 days treatment of MEBM (200 mg/kg and 400 mg/kg, p.o) showed significant hepatoprotective effect by dose dependent manner.

***Chenopodium album* Linn.**[24]

Hepatoprotective activities of dried whole plant of *Chenopodium album Linn,* acetone and methanol extracts, in ratio of (50:50) against paracetamol induced hepatic injury. Hepatic injury was achieved by injecting 2.5ml/kg oral route of pracetamol in equal proportion with dimethysulfoxide (DMSO). Acetone and Methanol extract at dose levels of 200 and 400 mg/kg offered significant. Acetone and Methanol extract at (400mg/kg, oral) showed significant hepatoprotective activity similar to that standard drug, silymarin.

Capparis sepiaria[26]

The hepatoprotective effect of the alcohol extract of *Capparis sepiaria* Linn. (Capparaceae) stem against carbon tetrachloride (CCl4)-induced toxicity was studied in albino rats. The rats were given daily pretreatment with alcohol extract of *C. sepiaria* (100 mg/kg) and the standard silymarin (25 mg/kg) orally for 7 days. The toxicant used on 7th day was CCl4 at a dose of 1.25 ml/kg as 1:1 mixture with olive oil. The extract produced significant reduction in the elevated levels of aspartate transaminase (AST), alanine transaminase (ALT), total bilirubin (TB) and rise of decreased total protein level when compared with the toxic control.

***Clerodendrum phlomidis* Linn**[31]

The hepato-protective activity of ethyl acetate extract of aerial parts of *Clerodendrum phlomidis* are evaluated in paracetamol-induced hepato toxicity in albino rats. Silymarin (200mg/kg) was given as reference standard. The ethyl acetate extract of aerial parts of *Clerodendrum phlomidis* have shown very significant against paracetamolinduced hepatotoxicity in albino rats in reducing serum total bilirubin, SALP, SGPT , SGOT levels and liver homogenates LPO, SOD, CAT, GPX, GST and GSH levels. The ethyl acetate extract of aerial parts of *Clerodendrum phlomidis* showed significant hepatoprotective activity.

Delonix regia[35]

The methanol extract of aerial parts of *D. regia* (400 mg/kg) was administered orally to the Wistar albino rats with hepatotoxicity induced by CCl4 (2 ml/kg, p.o.). Silymarin (50 mg/kg, p.o.) was given as reference standard. The plant extract was effective in protecting the liver against the injury induced by carbon tetrachloride in rats.

***Ficus benjamina* Linn.**[38]

The ethanolic extract of *Ficus benjamina* Linn. (250 and 500mg/kg) and isolated compounds (500mg/kg) was administered orally to the animals with hepatotoxicity induced by CCl4 (1.5 gm/kg). Silymarin (100mg/kg) was given as reference standard. The plant extract and both isolated compound was effective in protecting the liver against the injury induced by CCl4 in rats.

Oclmum sanctum[42]

Effect of *Ocimum sanctum* leaf extract was studied on paracetamol induced hepatic damage in rats. *O. sanctum* was found to protect the rats from hepatotoxic action of paracetamol as evidenced by significant reduction in the elevated serum enzyme levels. Histopathological studies showed marked reduction in fatty degeneration in animals receiving *O. sanctum* along with paracetamol as compared to the control group.

Rhododendron arboreum[54]

The hepatoprotective activity of pre-treatment with ethanolic extract of leaves of *Rhododendron arboreum* against carbon tetrachloride-induced hepatotoxicity in Wistar rat model. Liver damage was induced in experimental animals by administering CCl4. The ethanolic extract of *R. arboreum* (40, 60 and 100 mg/kg, p. o) was given for five days. Silymarin (100 mg/kg, po)

was given as the reference drug. The results indicate that leaves of *R. arboreum* possess hepatoprotective property possibly because of its reported anti-oxidant activity.

CONCLUSION

The rationale of pharmacological studies on medicinal plants is to come across new prototype pure compounds as drugs. The medicinal plants play an essential role aligned with various diseases. Various herbal plants and plants extracts have momentous hepatoprotective activity in animal models. The present study reveals plant extracts with hepatoprotective properties against toxic chemicals that cause liver injury, seeming to authenticate their use in folk medicine. These plants may offer new alternatives to the limited therapeutic options that exist at present in the treatment of liver diseases or their symptoms, and they should be well thought-out for future studies.

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