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Review Article

HEPATOPROTECTIVE HERBS: AN UPDATED REVIEW

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ABSTRACT

Liver diseases are becoming a serious global health problem and may be caused by many toxic substances, including chemotherapeutic drugs, thioacetamide, carbon tetrachloride, certain antibiotics, excessive alcohol consumption, and microbes. Therefore, having a healthy liver is vitally important for good health and well-being. The liver is an important organ, contributing to the metabolism of the body and that of xenobiotics. There are many toxic substances which could cause liver damage (certain antibiotics, chemotherapeutic drugs, carbon tetrachloride, thioacetamide, and microbes, are mostly responsible for liver cell damage). The synthetic drugs that are available at this point to deal with liver dysfunction causes additional harm to the liver. Hence, the use of herbal medicines has grown and become popular. The important medicinal herbs that can be used to treat liver diseases with the least impact on the kidneys have been described. Because of the hepatoprotective character, antioxidant-related characteristics and least harm to kidneys, features of the newly described medicinal plants can be used to develop new medicines for the prevention and treatment of liver diseases.

Keywords: Herbal drugs, Hepatotoxicity, Liver diseases, Medicinal plant, Factors

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INTRODUCTION

With an average adult weight of 1.4 kg, the liver is the heaviest gland in the human body (after the skin) and the second largest organ. It occupies the majority of the right hypchondiac and a portion of the epigastric regions of the abdominopelvic cavity and is located inferior to the diaphragm [1]. The liver plays a major role in the metabolism and excretion of drugs. Detoxicfying pharmaceuticals and xenobiotics in the liver via drug metabolizing enzymes (DMEs) is one of the significant processes involved in the restoration of homeostasis [2]. The liver accounts for 2 % to 3 % of normal body weight. It normally has four lobes, each defined in both morphological and functional annatomy. It is located underneath the right hemidiaphragm (right upper quadrant of the abdominal cavity) and has ligamentous attachments to the area. It is protected by the ribcage and is held in place by peritoneal reflections. Although the liver's ligamentous attachments are not true ligaments, they are avascular and continuous with the Glisson capsule or the liver's visceral peritoneum [3]. Hepatotoxicity refers to damage to the liver caused by chemicals. Drug-induced damage to the liver can cause acute and chronic liver disease. The liver is susceptible to the toxicity wrought by many other chemicals, and the liver's role to metabolize and excrete toxins is of paramount importance. Several drugs, including acetaminophen, can lead to harm to an organ by overtaking otherwise modest therapeutic dosages. The liver can also be damaged by other chemical agents, e. g., in factories or laboratories, naturally occurring compounds (e. g., microcystins), and herbal medicines. Substances that are harmful to the liver are also termed hepatotoxins [4]. The most common reason for drugs to be withdrawn from the market is liver damage; drug-induced liver damage has been linked to 900+drugs, and hepatotoxicity and drug-induced liver injury are also responsible for the failure of many compounds that are under investigation so that it is essential that new drug screening assays could use new stem cell-derived hepatocyte-like cells, which will determine hepatotoxicity much earlier in the drug developmental process. Subclinical liver damage occurs with the administration of chemicals and will typically only manifest as abnormal liver enzymes. Drug-induced liver damage is responsible for 50% of all cases of acute liver failures and 5% of all hospital admissions [5]. Most of these substances are absorbed through the gastrointestinal tract, but a smaller number though parenterally or absorbed through the skin or lungs immediately (inhalants). The majority of drugs and xenobiotics are lipophilic because they pass readily through the intestine and hepatocyte cell membranes. Metabolism in the hepatocyte alters drug structure in such a way that the drug is more hydrophilic, producing water soluble metabolites which are cleared in urine or bile. Drug metabolic pathways are divided into phase I pathways (oxidation, reduction, hydrolysis) mediated by various cytochrome P450 isozymes and phase II conjugation pathways (glucuronidation, acetylation, sulphation, methylation) mediated by various transferases. Highly polar drugs do not require metabolism. Some drugs may degrade spontaneously [6].

Genetic and nongenetic risk factors

Risk factors for susceptibility to drug-induced hepatotoxicity

- Toxic potential of drug: *such as* Reactive Metabolites, Acyl glucuronide, Mitochondrial effects
- *Genetic factors such as* drug metabolism, detoxification, transport
- Environmental factors such as ethanol and Age/Sex

Table 1: Therapeutic agents causing hepatotoxicity [7, 8]

Antimicrobial	Analgesics and anti-tuberculosis drug	Immunomodulator	Antiepileptics
Amoxicillin	NSAIDs	Interferon-beta	Phenytoin
Isoniazid	Rifampicin, Rifabutin	Interferon-alpha	Lamotrigine
Sulfamethoxazole	Pyrazinamide	Anti-TNF agents Azathioprine	Valproic Acid
Trimethoprim	Prothionamide	Cyclophosphamide	Carbamazepine

Table 2: Medicinal plants with hepatoprotective potentials

Name of the plant	Extract used	Hepatotoxicity-inducing agents	Biochemical and histopathological parameter studied	Hepatotoxicity-inducing agents
Phyllanthus Muellarianus (leaves) [9]	Aqueous	ALP, ALT, AST, ALB, TB, CAT	Acetaminophen	400 mg/kg
Picrorhizakurroa (Roots) [10]	Ethanol	SGOT, SGPT, ALP	CCl4	2.60 ml/kg
*Bauhinia Variegate (*Stem barks) [11]	Alcohol	AST, ALP, GGT, ALT	CCl4	100 and 200 mg/kg
Galium aparine (whole) [12]	Alcohol	ALT, AST, and ALP	CCl4	2 ml/kg
Ficus cordata (roots) [13]	Methanol/ethyl	LDH	CCl4	400 mg/kg
*Canna indica (*Aerial parts) [14]	Methanol	SGPT, SGOT, TB, CAT, GSH, LPO	CCl4	100 and 200 mg/kg
*Curcuma longa (*Rhizome)[15]	Ethanol	ALT, ALP, and AST	PCM	600 mg/kg
Dodonaeaviscosa (leaves) [16]	Methanol	AST, LDLC, ALT	Alloxan	500 mg/kg
*Ecliptaprostrate (*Fresh leaves)[17]	Methanol	ALT, AST, and serum bilirubin	CCl4	10 80 mg/kg
Boerhaviadiffusa (Roots)[18]	Ethanol	SGPT, SAP, TGs, and total lipid levels	Country-made liquor	200 and 400 mg/kg
Tylophora (leaves) [19]	Methanol	SGPT, ALP, SGOT	CCl4	200 and 300 mg/kg
*Tylophora (*Leaves) [20]	Methanol	SGPT, ALP, SGOT	CCl4	200 and 300 mg/kg
*Tridax Procumbens (*Aerial parts) [21]	Ethanol	AST, LDH, ALT, ALP, GGT, TB	d-GalN/lPS	300 mg/kg
Opuntia ficus-indica (Leaves) [22]	Aqueous	AST, ALT, Creatinine, Urea, Uric acid	CCl4	2, ml/kg
*Apium graveolens (*Seeds) [23]	Methanol	SGOT, SGPT, SALP	CCl4	250 mg/Kg
*Opuntia ficus-indica (*Stem) [24]	Aqueous	ALAT, ASAT, ALP, LDH, CHL	CPF	1500 mg/kg
*Agrimoniaeupatoria (*Aerial part) [25]	Aqueous	AST and ALT	Ethanol	100 and 300 mg/kg
*Vitis vinifera (*Leaves) [26]	Alcohol	AST and ALT	CCl4	125 mg/kg
Rheum palmatum (Aerial part) [27]	N/A	N/A	CCl_4/ethanol	25 and 100 mg/kg
*Ziziphus oenoplia (*Roots) [28]	Alcohol	SGOT, SGPT, SALP, SB, SOD, CAT, GST	INH and RIF	150 and 300 mg/kg
Corylus avellana (Leaves) [29]	Aqueous	GPT and GOT	CCl4 and acetaminophen	NA
Cinnamomum Cassia (Bark) [30]	Ethanol	TP, albumin, TB, direct bilirubin,	Dimethyl nitrosamine	40 mg/kg
Pistacia lentiscus (Gums) [31]	NA	AST, ALT and MDA, GSH, GPx, GST, GR, SOD	CCl4	NA
Punica granatum (Edible and Portion) [32]	Acetone	AST, ALT, and LDH	INH and RIF	400 mg/kg
Rosa damascene Mill (Flower) [33]	Aqueous	AST, ALT, ALP, LDH, ALBTB, urea and creatinine	Acetaminophen	250, 500 and 1000 mg/kg
Cucurbita maxima (Aerial parts) [34]	Methanol	SGPT, SGOT, ALP, TP, and TB	CCl4	250 and 500 mg/kg
Cynara (Root) [35]	Hydroalcohol	ALT, ALP, AST,	CCl4	900 mg/kg
Taraxacum Officinale (Roots) [36]	Hydroalcoholic acid	TBARS, GST, GSH, SOD, CAT, GR, and	Ethanol	250 mg/kg
Tragopogon Porrifolius (Edible root and shoot) [37]	Methanol	CAT, SOD and GSTAST, ALT	CCl4	250 mg/kg
Baliospermum Montanum (Root) [38]	Methanol	GOT, GPT, ALP, TB, TC, TB	TAA	2000 mg/kg
Tephrosia Purpurea (Aerial parts) [39]	Ethanol	AST, GSH, ALT, ALP, TB, GGT	TAA	500 mg/kg
Alchornea Cordifolia (leaves) [40]	Methanol	SGOT/AST, SGPT/ALT, ALP	CCl4	300 mg/kg
Glycosmis pentaphylla Corr. (Leaves, bark) [41]	Methanol	ALT/SGPT, AST/SGOT, CHL	CCl4	500 mg/kg
Wedelia chinensis L. (Leaves) [42]	Ethanol	AST, ALT, ALP, Protein	CCl4	200 mg/kg
Cassia fistula (Seeds) [43]	Methanol	SGOT, SGPT, ALP, and bilirubin	PCM	200 and 400 mg/kg
*Tylophora (*Leaves) [19]	Methanol	SGPT, ALP, SGOT	CCl4	200 and

CONCLUSION

New hepatoprotective drugs need to be discovered because current medications that treat liver diseases, particularly a viral hepatitis or any degree of chronic liver disease, do not serve the unmet needs of the patients and may have detrimental renal effects. Because liver function is of upmost importance to the human body, liver disease and liver injury is now ranked as one of the most impotent health issues in the world. The causes of liver injury primarily include excessive intake of alcoholic beverages, lack of dietary discipline, herbal supplement use, viral, bacterial and parasitic infections, autoimmune diseases, neoplastic processes, metabolic disorders, and substance abuse. For example 50% of people living in developing countries that have liver disease or any form of liver disease choose to use herbal medicine for treatment and therefore have tapped worldwide interest. The majority of herbal extracts that are available today have demonstrated great effect with mild effects on regulating the signs and symptoms associated with liver disease or liver injury. In the treatment of liver disease or the symptoms associated with liver disease, the herbs may have provided a new avenue to explore in the constrained options for medicinal measures.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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