

## Pharmacological Appraisal of Herbal Medicines in treating Hepatic Diseases with Recent Advances: A review

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### ABSTRACT

Liver is the most vital organ of the body, which perform fundamental role in the regulation of diverse processes, such as metabolism, secretion, storage, and detoxification of endogenous and exogenous substances. Due to these functions, hepatic diseases continue to arise as main problem for mankind worldwide. Despite advances in modern medicine, there are no completely effective drugs that stimulate hepatic function, that offer complete protection of the organ, or that help to regenerate hepatic cells. The use of natural remedies for the treatment of liver disease has a long history, starting with the *Ayurvedic* treatment. Among several novel approaches, probiotics, development of a human recombinant single chain antibody and bone marrow transplant based therapy could also be a hope for the treatment of liver diseases in future.

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**Keywords:** Liver, Hepatic cells, *Ayurvedic*, Liver diseases



## **INTRODUCTION**

Liver plays a crucial role in distinguish functions of the body such as metabolism, secretion, storage, and detoxification of endogenous and exogenous substances. Liver diseases are major health problem worldwide due to unhealthy diet, pollution, environmental toxicants, infections and sedentary lifestyle (Rao et al., 2013). Synthetic drugs and food chemicals metabolize in the liver produces hazardous metabolites and free radicals that cause oxidative stress. Liver cell injury also caused by various toxicants such as chemotherapeutic agents, carbon tetrachloride, thioacetamide, chronic alcoholism and microbes. Treatment options for common liver diseases such as cirrhosis, fatty liver, and chronic hepatitis are often limited in efficacy, carry the risk of adverse effects and are often too costly, especially for the developing world. The effectiveness of treatments such as interferon, colchicine, penicillamine and corticosteroids are inconsistent and the incidence of side-effects profound. Physicians and patients are in need of effective therapeutic agents with a low incidence of side-effects (Ghosh et al., 2011). Medicinal plant based drugs are consider as a potent therapeutic agent to

reduce oxidative stress and helps in treatment of liver diseases. They contain various phytomolecules like flavonoids, tannin, steroids and phenolic compounds, which are helpful in free radical scavenging, reduce oxidative stress, and regeneration of hepatocytes (Sagar et al., 2014).

## **HEPATOTOXICITY**

Hepatotoxicity is the main reasons behind withdrawal of drug from the market. Fifty percent of all acute liver failures and 5% of all hospital admissions are associated with drug-induced hepatotoxicity. Liver damage is associated with cellular necrosis, increase in tissue lipid peroxidation and depletion of reduced glutathione levels. In addition, serum levels of biochemical markers like AST, ALT, ALKP, total bilirubin, are increased in liver disease. Liver diseases pose a serious challenge to international public health (Howida and Seif, 2016). Hepatotoxicity involves chemically-driven liver damage. Certain drugs and xenobiotics, when taken in overdoses and sometimes even when introduced within therapeutic ranges, may injure the liver cells. Other chemical agents, such as those used in laboratories and industries, natural chemicals (e.g., microcystins) and herbal remedies can also induce hepatotoxicity. Chemicals that

cause liver injury are called hepatotoxins. More than 900 drugs have been reported to cause liver injury and it is the most common reason for a drug to be withdrawn during post marketing surveillance. Chemicals often cause subclinical injury to liver which manifests only as abnormal liver enzyme tests. Drug induced liver injury is responsible for 5% of all hospital admissions and 50% of all acute liver failures. More than 75 percent of cases of idiosyncratic drug reactions result in liver transplantation or death (Pandit et al., 2012).

#### **HERBAL MEDICINAL PLANTS WITH HEPATOPROTECTIVE POTENTIAL**

These days the market for herbal medicines is growing rapidly worldwide since the virtues of herbal medicines are being recognized (Bent and Ko, 2004). However many doctors and scientists are expressing doubts about the safety profile of herbal medicines owing to lack of scientific data and compositional analyses that support its effect and stability as well (Bent 2008). Drugs from medicinal plants are considered to be effective and safe alternative for liver diseases. There are many potent herbal formulations used by people across the globe for the treatment of liver disorders but most of them have not yet scientifically validated. If these herbal

formulations will be scientifically validated in near future, it could lead to the development of cost effective medicines (Jamal et al., 2009). In the absence of reliable herbal formulation in current allopathic system of medicines, a number of medicinal and preparations in *Ayurveda* are recommended for the treatment of liver disorders (Karthikeyan and Deepa, 2010). The herbal medicines are considered to be of great importance among different rural or tribal communities in many developing countries (Gosh, 2003). According to World Health Organization (WHO) 80% of world's population depends on traditional medicines for the treatment of various diseases (WHO, 2002). The Indian traditional medicines is based on various systems such as *Ayurveda*, *Siddha* and *Unani* etc, which are still in use to provide primary health care, particularly to the rural folk throughout the globe, the traditional knowledge system has gained primary importance in context with conservation, sustainable development, and search for new utilization pattern for plant resources. Traditional medicines system includes the knowledge, skills and practices based on theories, beliefs and experiences of folk communities to maintain their health problems. The indigenous communities have

their own traditional medicine system with different medicinal plants and many traditional therapies for incurable diseases. A large number of wild and cultivated plants are being used by the traditional practitioners for the treatment of various ailments, thus a considerable amount of information on medicinal plants is available with these communities. Despite of tremendous advances, no significance and safe hepatoprotective medicines are available in modern therapeutics. 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 (Handa et al., 1986).

### **NOVEL APPROACHES IN LIVER DISEASE**

Among several novel approaches, probiotics appear interesting and reasonable option acting on gut-liver malfunction through the modulation of diet- based obesogenic, and inflammatory intestinal microbiota. Well conducted, controlled studies with probiotics are able to interact with gut microbiota, alone or in combination with other therapeutic measures (i.e. multiple targeted therapies ignoring the immunotherapeutic based approach). It also appears fully justified even

in children non alcoholic fatty liver disease (Gratz et al., 2010). Another proposed novel approach is the development of a human recombinant single chain antibody that actively binds to surface of myofibroblast. This antibody solely binds to myofibroblast in fibrotic mouse livers, that type of conjugation result in stimulation of myofibroblast apoptosis, the antibody binds with greater specificity and efficacy than the free compound. The antibody also reduces the side effect of liver macrophage. These data reveals that specifically stimulating the apoptosis of myofibroblast using a targeting antibody has beneficial in the treatment of liver diseases (Douglass et al., 2010). Bone marrow is a transplantable source of hepatic progenitors, various parameters supervising the success of bone marrow derived mesenchymal stem cell based therapy could also be a hope for the treatment of liver diseases in future (Kakinuma et al., 2003; Kallis et al., 2007).

### **CONCLUSION**

Present review emphasize on, degeneration of hepatocytes and liver injury due to consumption of certain synthetic drugs and xenobiotics such as acetaminophen, anti-TB drugs, thioacetamide, CCl<sub>4</sub>, D-galactosamine

and nimesulide are more common. This study also reports some novel approaches such as use of probiotics, development of a human recombinant single chain antibody and bone marrow transplant based therapy which could be a better option for treating liver disease in future. Herbal drugs could offer a novel alternatives to the limited therapeutic options that exist for the treatment of liver diseases.

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Table 1: List of medicinal plants use as liver protectants

Plants with botanical name	Family	Common name	Plant part used	Extract	Activity reported	Type of model	Sources
<i>Garcinia mangostana</i> Linn	Guttiferae	Mangostana	fruit	Ethanol	Hepatocellular carcinomas, antioxidants, diarrhea, skin infection, and chronic wound	Paracetamol	(Moongkarndi et al., 2004; Chaverri et al., 2008)
<i>Berberis Aristata</i>	Berberidaceae	Daruharidra	Root	Aqueous	Hepatoprotection, jaundice, and antioxidant.	Carbon tetrachloride	(CSIR, 1985; Gilani et al., 1999)
<i>Tinospora Cordifolia</i>	Menispermaceae	Guduchi	Stem	Aqueous	Hepatoprotective activity, jaundice, hepatitis B & E, anti-inflammatory, anti-arthritis, anti-osteoporotic activity, anti-allergic, anti-hyperglycemic, anti-pyretic, antioxidant, diuretic and cardioprotective activity	Carbon tetrachloride	(Upadhyay et al., 2010; Lal et al., 2007)
<i>Boerhavia Diffusa</i>	Nyctaginaceae	Punarnava	Root	Aqueous	GOT, GPT, ACP and ALP, but not GLDH and bilirubin	Thioacetamide	(Chandan et al., 1991)
<i>Morinda citrifolia</i>	Rubiaceae	Noni	fruit	Juice	Hepatic steatosis, ALP, AST, ALT, TC, TG, LDL, VLDL and HDL levels	Carbon tetrachloride	(Shivananda et al., 2011)
<i>Eclipta alba</i>	Compositae	False daisy	Hassk	Ethanol	Serum transaminase levels, liver tonic, anti-inflammatory, anthelmintic, expectorant, antipyretic, and in skin diseases	Carbon tetrachloride	(Chopra et al., 1996; Khin et al., 1978)
<i>Sargassum polycystum</i>	Phaeophyceae	Boto-boto	Whole plant	Ethanol	Hepatic lipid peroxidation, AST, ALT, ALP, and antioxidant	D-galactosamine	(Meena et al., 2008)
<i>Cichorium intybus</i>	Asteraceae	Chicory	Root	Ethanol	Liver tonic, gall protective,	Chlorpromazine	(Vetrivel et al., 2009)
<i>Polygala arvensis</i>	polygalaceae	Mirdoi	Leaves	Chloroform	Normalizing the levels of ASAT, GOT, ALAT, GPT, ALP, TB, LDH, TC, TGL and TP	D-galactosamine	(Dhanabal et al., 2006)
<i>Pterospermum acerifolium</i>	Sterculiaceae	Kanak champa	Leaves	Ethanol	AST, ALT and ALP	Carbon tetrachloride	(Kharpate et al., 2007)

<i>Sida acuta</i> Burm. f.	Malvaceae	Wireweed	Root	Methanol	Hepatoprotective potential, liver lipid peroxidation, stomachic, diaphoretic, antipyretic, cooling, astringent, tonic, and also in disorders of blood & bile	Paracetamol	(Kirtikar and Basu, 1975; Sreedevi et al., 2009)
<i>Rubia cordifolia</i> Linn	Rubiaceae	Madder	Root	Aqueous ethanolic extract	SSGOT, SGPT, SALP and $\gamma$ -glutamyltransferase	Carbon tetrachloride	(Adwankar et al., 1980; Guntupalli et al., 2006)
<b><i>Wedelia chinensis</i> Merrill</b>	Asteraceae	Bhringraj	Leaves	aqueous ethanolic extract	anti-hepatotoxic, osteoporosis, anti-inflammatory, wound healing, treat skin problems, dermatitis, eczema and acne	Carbon tetrachloride	(Meena et al., 2011; Martin et al., 2003)
<b><i>Citrullus colocynthis</i> L.</b>	Cucurbitaceae	bitter apple	Fruit & seeds	ethanolic extract	Powerful hepatic stimulant, hydragogue cathartic, strong laxative, constipation, edema, bacterial infections, cancer and diabetes.	Paracetamol	(Dar et al., 2012; Gaithi et al., 2004)
<b><i>Scutellariae radix</i></b>	Labiatae	Huang Qin	whole plant	aqueous ethanolic extract	liver diseases	carbon tetrachloride, H <sub>2</sub> O <sub>2</sub> -induced injury	(Chen et al., 2013)