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Medicinal plants as hepatoprotective agents in Indian systems of medicine: A review

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ABSTRACT

Liver is a most important organ of the body. It plays an important role to maintaining various physiological processes in the body. It is involved in several vital functions, such as metabolism, secretion and storage. It plays a central role in the detoxification and excretion of many exogenous and endogenous compounds. Hence, any injury or impairment of its function has grave implications for the health of the affected person. Many more drugs or therapies are available for the treatment of hepatic disorders, but still there is a need for the novel drug discovery which can target multiple disease pathways. In the 21st century has a great that paradigm shift towards therapeutic evaluation of herbal products. The use of herbal products has a great role in the treatment of liver diseases and has no side effects. There are a number of hepatoprotective plants have been reported. In this review article, effort has been taken to collect and compile the details of hepatoprotective plants, which will be helpful in the field of Indian system of medicines.

Keywords: Hepatoprotetive plants, Liver, Indian systems of medicine.

INTRODUCTION

Liver is a paramount organ of the body and is strategically positioned to perform its task of maintaining the body's metabolic homeostasis. It is susceptible to persistent attack by offending agents like chemicals and other toxins. It has been estimated that approximately 14-16 million people are infected with hepatitis B virus in South East Asia region and about 6% of the total population in the region are carriers of this virus[1]. About 20,000 deaths occur every year due to liver diseases (World Health Organization). Hepatocellular carcinoma is one of the ten most common tumors in the world with over 2, 50, 000 new cases each year.[2]

Ayurveda is a traditional Indian medicinal system being practiced for thousands of years. It has been estimated that more than 750,000 species of higher plants exist on earth from which many more plants have been used in traditional system of medicine. The World Health Organization estimates that about three quarters of the world's population currently use herbs and other forms of the traditional medicines to treat their diseases, as they are cheap and easily available.[3] Faith in these traditional systems of medicine is relat0ed to cultural practices and belief. Review has introduced hepatoprotective medicinal plants that are used mainly for the treatment of liver disorders.

HEPATOPROTECTIVE MEDICINAL PLANTS:

Traditional herbal drugs are wonderful remedies for the treatment of various devastating disorders[4]. Various herbs *viz Andrographis paniculata*[5], *Cyperus longurs*[6] and *Asteracantha longifolia*[7] are known to possess therapeutic efficacy of cure liver diseases. Several hundred plants have been examined for use in a wide variety of liver disorders. Following are the few important hepatoprotective plants.

Taraxacum officinale: It is commonly known as Dandelion, has been widely used as a folkloric medicine for the treatment of liver and kidney disorders.[8]

Wilkstroemia indica: W. indica is a Chinese herb and has been evaluated in patients suffering from hepatitis B. A dicoumarin, daphnoretin are the active constituents of the herb. The drug has shown to suppress HbsAG in Hep3B cells. It activates protein kinase C.[9]

Tephrosia purpurea: In animal models, it offered protective action against carbon tetrachloride and D-galalactosamine poisoning[10]. The roots, leaves and seeds contain tephrosin, deguelin and quercetin.

Glycyrrhiza glabra: It is extensively used in Japan for the treatment of patients with liver diseases. A significant reduction of serum aminotransferases and suggested that long-term usage of glycyrrhizin prevents development of hepatocellular carcinoma in chronic hepatitis.[11]

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Phyllanthus niruri / Phyllanthus amarus: Phyllanthus niruri and Phyllanthus amarus are known to possess hepatoprotective activity[12]. Geetha et al., (1992) found improved liver function in patients treated with Phyllanthus amarus bringing about a significantly faster normalization of biochemical changes than control groups[13].

Bupleurum falcatum: The crude drug, saiko from the roots of Bupleurum falcatum has been widely used in oriental medicine for the treatment of hepatobiliary diseases. Active components responsible for the alleviation of liver dysfunction have been identified to be a mixture of saikosaponins[14].

Schizandra chinensis: The seed extract of Schisandra chinensis was investigated in the rats for its therapeutic effect on phase 1 hepatic drug metabolism against CCl_4 intoxication. Data suggested Schisandra chinensis as a promising agent for the improvement of Phase 1 oxidative metabolism in liver damaged by CCl_4 [15].

Andrographis paniculata: Andrographis paniculata is popularly known as Kalmegh and grows wildly in India. Hepatoprotective effect of Kalmegh has been reported to be quite significant against acute hepatitis induced by carbon tetrachloride, paracetamol and D-galactosamine as is evident from morphological, biochemical and functional parameters[16].

Picrorhiza kurroa: Picrorhiza kurroa, a well reputed Indian medicinal plant popularly known as kutki has been extensively worked up for hepatoprotective activity in a wide varitey of experimental models by a number of researchers [17, 18].

Artemisia scoparia / Artemisia iwayomongi: Extract from Artemisia iwayomongi inhibits liver fibrosis induced by carbon tetrachloride in rats[19]. The study supports the folkloric use of the plant Artemisia scoparia in liver damage due to the presence of this compound[20].

Boerhaavia diffusa Linn.: Boerhaavia diffusa abundantly occurs as a weed throughout India. The choloroform and methanolic extract of the roots and aerial parts of Boerhaavia diffusa exhibited hepatoprotective activity against carbon tetrachloride, paracetamol and D-galactosamine intoxication in experimental rats[21].

Eclipta alba: Eclipta alba exhibited antihepatotoxic activity against carbon tetrachloride, D-galactosamine and phalloidin induced toxicity against rat hepatocytes[22]. The study shows that hepatoprotective activity is due to the regulation of hepatic microsomal drug metabolising enzymes.

Wedelia calendulacea: The active constituent wedelolactone isolated from Wedelia calendulacea is known to possess significant hepatoprotective activity[23]. The leaves of Wedelia calendulacea afforded a significant protection against paracetamol induced hepatocellular injury[24].

Apium graveolens: Hepatoprotective activity of Apium graveolens was monitored for several liver function tests. Researchers confirmed the hepatoprotective potential of methanolic extract of Apium graviolens[12].

Garcinia kola: Kolaviron (active constituent of Garcinia kola) recoupe the CCl_4 induced liver damage[25]. Kolaviron also protects erythrocyte membrane from free radical attack on both lipids and proteins[26].

FEW OTHER HEPATOPROTECTIVE PLANTS:

Hepatoprotective plants	References
Terminalia belerica Roxb.[36]	Jadon *et al*., (2007)
Tinospora cordifolia[37]	Bishayi *et al*., (2002)
Aphanamyxis polystachya[38]	Gole and Dasgupta (2002)
Atractylodes macrocephala[39]	Wu *et al.,* (2001)
Cynara scolymus[40]	Speroni *et al.,* (2003)
Tridaxprocumbens[41]	Saraf *et al.,* (1992)
Trianthema portulacastrum[42]	Sarkar *et al*., (1999)
Zingiber officinale[43]	Nakatani (2000)
Indigofera tinctoria[44]	Singh *et al*., (2001)
Cistanche desesticola[45]	Xiong et al., (1998)
Pueraria lobata[46]	Arao *et al.,* (1998)
Tribulus terrestris[47]	Li *et al.,* (1998)
Boehmeria nivea, Var nivea[48]	Lin *et al*., (1998)
Cajanus indicus[49]	Datta *et al.,* (1999)
Ficus racemosa[50]	Mandal *et al*., (1999)
Phyllanthus fraternus[51]	Padma and Setty, (1999).
Trichopus zeylanicus[52]	Subramoniam *et al.,* (1998)
Cassia fistula[53]	Bhakata *et al.,* (2001)
Emblica officinalis[54]	Jose and Kuttan, (2000)
Arctium lappa[30]	Lin *et al*., (2002)

Curcuma longa: Hepatoprotective activity of Curcuma longa and curcuminoids against carbon tetrachloride and galactosamine induced liver damage has been reported[27]. Curcumin also has been found to inhibit the activity of glutathione-s-transferase[28].

Pistacia lentiscus: Aqueous extract of Pistacia lentiscus showed marked antihepatotoxic activity by reducing the activities of ALP, ALT, AST and the level of bilirubin[29].

Arctium lappa: Arctium lappa significantly improved various pathological and biochemical parameters, which were disturbed by ethanol and CCl_4 induced liver damage[30].

Carica papaya: Ethanolic and aqueous extract of Carica papaya was evaluated for its antihepatotoxic activity against CCl_4 induced liver damage. The activity was measured by using biochemical parameters such as AST, ALT, ALP, total bilirubin and GGT[31].

Myristica fragrans: Myristica fragrans possess potent hepatoprotective activity[32]. Myristicin markedly suppressed LPS/D-GalN-induced enhancement of serum TNF-alpha concentrations and hepatic DNA fragmentation in mice.

Gentiana olivieri Griseb.: Hepatoprotective effect of Gentiana olivieri Griseb. against carbon tetrachloride induced hepatic damage in rats has been evaluated. Results of biochemical tests and histopathological examination confirmed the hepatoprotective potential of Gentiana olivieri[33].

Foeniculum vulgare: The hepatotoxicity produced by CCl_4 was inhibited by essential oil of Foeniculum vulgare with evidence of decreased levels of ALT, AST and bilirubin[34].

Aquilegia vulgaris L.: Ethanolic extract of Aquilegia vulgaris L. showed significant reduction in the barbiturate induced sleeping time which was prolonged by CCl_4 in mice was observed indicating protective effect on microsomal drug metabolizing enzymes[35].

WELL KNOWN HERBAL PRODUCTS AND THEIR COMPOSITIONS :

Herbal Products	Compositions
Liv-52[71] M/S The Himalaya Drug Co., Makali, Bangalore.	Punarnava, Vidanga,Haritaki, Parpata Guduchi, Bringaraj, Daruharidra, Chitraka, Amlaki
Livotone[72] M/S East India Pharm. Works., Calcutta	Kalmegh, Ajmod, Talmakhana, Raktarohida, Methi, Kurchi
Stimuliv[73] M/S Francho - Indian Pharma-ceuticals Ltd. Bombay	Kalmegh, Bringaraj, Pitpapra
Tefroli[74] (M/S TTK Pharm Madras)	Kalmegh, Bringaraj, Sarponkha,Tulsi, Harde
Hepatogard[75] M/S Surajmani Enterprises A-1, Daman, Somnath Road , Dabhei Daman	Kutki, Kalmegh, Bhumyamlaki, Punarnava, Neem, Triphala, Bringaraj, Sunti, Pippali
Livomyn[76] M/S Charak Pharmac-euticals (India) Ltd. Samalkha	Vasaka, Brhati, Rohituk, Punarnava, Bhumyamlaki, Katuki, Guduchi

HEPATOPROTECTIVE PLANTS WITH THEIR ACTIVE CONSTITUENTS

Name of the plant	Active constituents
Eclipta alba	Wedelactone and dimethyl wedelactone
Andrographis paniculata	Andrographolide
Garcinia kola	Kolaviron
Silybum marianum	Silybin
Picrorhiza kurroa	Picroside I; Picroside II; Kutkoside
Schizandra chinensis	Gomishins; Schisandrin A; Wuweizisu C
Glycyrrhiza glabra	Glycyrrhizn; Glycyrrhetinic acid
Bupleurum falcatum	Saikosaponins
Sedum sarmentosum	Sarmentosins
Anacardium occidentalis	Catechin
Eucalyptus spp.	Ursolic acid
Curcuma long	Curcumin
Sida cordifolia	Fumaric acid
Wedelia calandulacea	Wedelactone
Myristica fragrans	Myristicin
Camellia sinensis	Catechins
Phylanthus niruri	Hypo-phyllanthin
Taraxacum	Taraxecerin and taraxcin
Cichorium intybus	Cichorin
Wilkstroemia indica	Daphnoretin
Artemisia scoparia	Rutin

SOME MORE PLANTS EVALUATED FOR LIVER PROTECTION:

Plants / Authors	Toxicants	Parameters
Trianthema portalacastrum L.[55] (Kumar *et al*., 2004)	Acetaminophen, Thioacetamide	AST, ALT, ALP, bilirubin and protein content.
Bupleurum kaoi Liu.[56] (Wang *et al*., 2004)	CCl_4	AST, ALT, LPO, antioxidative enzymes and histopathology.
Salvia officinalis[57] (Lima *et al*., 2004)	Tert-butyl hydroperoxide	Cell viability, LDH leakage, LPO and glutathione status.
Hypericum androsalmum[58] (Valentao *et al*., 2004)	Tert-butyl hydroperoxide	LDH, LPO, GSH and GSSG.
Acanthopanax koreanum[59] (Nan *et al*., 2004)	D-galactosamine	AST, ALT, TUNEL and DNA fragmentation assay.
Helminthostachys zeylanica L.[60] (Suja *et al*., 2004)	CCl_4	AST, ALT, choleretic activities, hexobarbitone induced sleeping time, LPO *in vitro* and histopathology.
Nymphaea stellata Willd.[61] (Bhandarkar & Khan, 2004)	CCl_4	Serum marker enzymes, LPO, GSH, glutathione peroxidase, bilirubin, glycogen, SOD and catalase activity.
Phyllanthus maderaspatensis Linn.[62] (Asha *et al*., 2004)	Acetaminophen	Choleretic activity, serum marker enzumes, *in vitro* hydroxyl radical scavenging activity and LPO.
Rosa damascene[63] (Achuthan *et al*., 2003)	CCl_4	AST, ALT, ALP, LPO and hydroxyl peroxide radical.
Zingiber officinale[64] (Bhandari *et al*., 2003)	Country-made liquor (CML)	AST, ALT, ALP, GTP and lipid peroxidation.
Sesbania gradiflora[65] (Pari and Uma, 2003)	Erytromycin estolate	AST, ALT, LPO, TG, bilirubin, cholesterol, pospholipids and hydroperoxides.
Astercantha longifolia[7] (Hewawasam *et al*., 2003)	Acetaminophen CCl_4	AST, ALT, ALP, GSH and histopathology.
Salvia miltiorrhiza[66] (Lee *et al*., 2003)	CCl_4	AST, ALT, LDH, GSH and GST activity.
Rhodiola sachalinensis[67] (Nan *et al*., 2003)	CCl_4	AST, ALT, Albumin, hydroxylproline, TBARS and histopathology.
Angelia archangelica[68] (Yeh *et al*., 2003)	Ethanol	AST, ALT, Cytochrome c test and *in vitro & in vivo* LPO.

Cleome viscose[69] (Rastogi *et al*., 2003)	Acetaminophen CCl_4	AST, ALT, ACPase, ALPase, albumin, GSH, glutathione reductase and histopathology.
Utrica dioica & *Nigella sativa*[70] (Turkdogan *et al*., 2003)	CCl_4	Immunohistochemical and histopathological examinations.

Paederia foetida, a herbs used as food in north east region of India, has shown promising hepatoprotective activity.[77-79] Chanda and coworkers reported its hepatoprotective activity against H. pyrolli.[80-81]

CONCLUSION:

Hepatic diseases are one of the foremost health problems in recent years. Therefore, treating liver diseases with plant derived compounds, which are more accessible. Considering the enormous biodiversity resources of Indian traditional system and the high incidence of liver complications, the present review focused on collection of data of the hepatoprotective herbal plants, which are available in India. This review article may be useful to the health professionals, scientist and scholars working the field of pharmacology and therapeutics to develop evidence based alternative medicine to cure different kinds of liver diseases in man and animals.

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