Hepatoprotective Activity of Extracts and Chemically Defined Molecules from Herbal Drugs : Review#

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Abstract

Liver diseases have become one of the major causes of morbidity and mortality in man and animals all over the globe and hepatotoxicity due to drugs appears to be the most common contributing factor. About 20,000 deaths occur every year due to liver disorders. Hepatocellular carcinoma is one of the ten most common tumors in the world with over 2, 50,000 new cases each year. Plants have potent biochemical components of phytomedicine. Plant based natural phyto-constituents can be derived from any morphological part of the plant and may contain active components. The beneficial medicinal effects of plant materials typically result from the combinations of secondary products present in the plant. The medicinal actions of plants are unique to a particular plant species or groups and are consistent with this concept as the combination of secondary products in a particular plant is taxonomically distinct as such different types of drugs such as acetaminophen; chloroquinine and isoniazid are inducing hepatoxicity in the world. Herbal plants have been used traditionally by herbalists worldwide for the prevention and treatment of liver disease so. Herbal drugs were prescribed even when their biologically active compounds were unknown because of their effectiveness, few side effects and relatively low cost.

In this review, an attempt has been made to compile the reported hepatoprotective activity of plants from India and abroad and may be useful to develop evidence based medicine to cure different kind of liver diseases in man and animal.

Keywords: Hepatic disorder, Hepatoprotective herbs, Ayurvedic formulations

Introduction

Liver has a pivotal role in regulation of physiological processes. It is involved in several vital functions such as metabolism, secretion and storage. Furthermore, detoxification of a variety of drugs and xenobiotics occurs in liver. The bile secreted by the liver has, among other things, an important role in digestion. Liver diseases are among the most serious ailment. They may be classified as acute or chronic hepatitis (inflammatory liver diseases), hepatosis (non inflammatory diseases) and cirrhosis (degenerative disorder resulting in fibrosis of the liver). Liver diseases are mainly caused by toxic chemicals (certain antibiotics, chemotherapeutics, peroxides oil, aflatoxin, carbon-tetrachloride, chlorinated hydrocarbons, etc.), excess consumption of alcohol, infections and autoimmune/disorder.

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The liver functions as a great metabolic factory and is particularly concerned with metabolizing drugs, especially those given orally. It plays a key role in the metabolism of lipids, proteins and carbohydrates, as well as in immunomodulation. The sheer complexity and varied nature of its interactions continually expose it to a variety of toxins, therapeutic agents etc., making it susceptible to literally hundreds of diseases. Some of these diseases are rare; others are common, such as hepatitis, cirrhosis, pediatric liver disorders, alcohol related disorders, liver cancer, and weakened liver function on older people. Cirrhosis is the third leading cause of death in adults aged between 25 and 59, and seventh leading cause of death overall. It has been estimated that approximately 14 - 16 million people are infected with this virus in South East Asia region and about 6% of the total population in the region are carriers of this virus.

The situation in India is more serious so far as viral hepatitis is concerned. It is reported that one among every 25 Indians is a carrier of hepatitis B virus and fifth major cause of mortality of people in the age groups of 15-45 years. 1% of total adult death attributed in India is due to infection caused by hepatitis virus B. Besides, incidence 60% chronic liver diseases and 80% of primary liver cancer are due to residual effects of hepatitis B infection. With of lack of safe and effective treatment for liver diseases, researches have been turned towards alternative therapies with ethnic drugs of herbal origin used traditionally, especially in lights of new findings.

Treatment of liver diseases is still largely influenced by holistic approach in different system of medicines. The modern allopathic has very limited effective remedies. However much of remedies claims to be available in folk lore traditional system of medicine based on plants. More than 600 numbers of plants based commercial products are available in different parts of world market for the treatment of variety of liver diseases. In India alone there are more than 60 poly herbal preparations available in market.

In vivo and *in vitro* investigations established conclusively that many such plants species does posses prophylactic and therapeutic activity. Recent development of both *in vivo* and *in vitro* investigation procedure laid the foundation for scientific exploration of such plants species as well as helped in validating the folk lore claims. This is evident from the voluminous scientific publications on such investigations on traditional herbal remedies particularly in last two decades. Isolation of novel active phytoconstituents from many such plant species possessing significant potency of antihepatotoxic, will lead for further development of ideal remedies for various liver diseases.

Hence, there is an ever-increasing need for safe hepatoprotective agents. Herbal-based therapeutics for liver disorders have been in use in India for a

long time and popularized world over by leading pharmaceuticals. Despite the significant popularity of several herbal medicines in general, and for liver diseases in particular, they are still unacceptable as treatment modalities for liver diseases. The limiting factors that contribute to this eventuality are lack of standardization of the herbal drugs, identification of active ingredient(s)/ principles(s), randomized controlled clinical trials (RCTs) and toxicological evaluation.

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. About 600 commercial herbal formulations with claimed hepatoprotective activity are being sold all over the world. However, only a small proportion of hepatoprotective plants as well as formulations used in traditional medicine are pharmacologically evaluated for their safety and efficacy

Numerous plants and polyherbal formulations are used for the treatment of liver diseases. However, in most of the severe cases, the treatments are not satisfactory. Although experimental evaluations were carried out on a good number of these plants and formulations, the studies were mostly incomplete and insufficient. The therapeutic values were tested against a few chemicals-induced subclinical levels of liver damages in rodents. Even common dietary antioxidants can provide such protection from liver damage caused by oxidative mechanisms of toxic chemicals. However, experiments have clearly shown that plants such as *Picrorrhiza kurroa, Andrographis paniculata, Eclipta alba, Silibum marianum, Phyllanthus maderaspatensis* and *Trichopus zeylanicus* are sufficiently active against, at least, certain hepatotoxins.

Single plant may not have all the desired activities. A combination of different herbal extracts/fractions is likely to provide desired activities to cure severe liver diseases. Development of such medicines with standards of safety and efficacy can revitalise treatment of liver disorders and hepatoprotective activity.

The traditional medicinal plants species have been subjected in various experimental models of investigation and attempt has made to calibrate their therapeutical activity. The herbs used in hepatic disease have been extensively exploited all over the world and large numbers of the plant species has been documented as hepatoprotective antihepatotoxic, cholegoge and choleric. A diverse nature of chemical compounds has been identified from such plants species through bio-assay guided investigation. However, in some plant species the total extract or fraction of extract has reported to possess better and potent biological activity compared to isolated pure compound(s) from the

extracts. Plant derived extracts and chemically defined molecules are enumerated in Table 1 and 2.

Table 1: Plant Extracts with Hepatoprotective Activity

Family and Botanical name	Origin	Plant Parts used	Extracts Studied	Type of assay	Hepato-toxicity Inducing Agents	References
Acanthaceae *Acanthus ilicifolius* L.	India	Leaves	Alcohol	*In vivo*	CCl_4	Babu *et al*. (2001)
Andrographis lineata Nees	India	Leaves	Aqueous, methanol	*In vivo*	CCl_4	Sangameswaran *et al*. (2008)
Andrographis paniculata (Burm.f.) Nees	India	Leaves	Alcohol	*In vivo*	CCl_4	Rana and Avadhoot (1991)
Anisotes trisulcus (Forssk.)	Yemen	Whole plant	Ethanol	*In vivo*	CCl_4	Fleurentin *et al.* (1986)
Asteracantha longifolia L.	Sri Lanka	Whole plant	Aqueous	*In vivo*	CCl_4 and PCM	Hewawasam *et al*. (2003)
Hygrophila auriculata (K.Schum.) Heine	India	Seeds	Methanol	*In vivo*	PCM and Thioacetamide	Singh and Handa (1995)
Hypoestes triflora (Forssk.) Roem. and Schult	Rwanda	Leaves	Aqueous	*In vivo*	CCl_4	Van Puyvelde *et al*. (1989)
Rhinacanthus nasuta (L.) Kurz.	India	Root	Methanol	*In vivo*	CCl_4	Suja *et al*. (2003)
Adoxaceae *Viburnum tinus* L.	Southern Europe	Leaves	Aqueous-methanol	*In vivo*	CCl_4	Mohammed *et al*. (2005)
Aizoaceae *Trianthema portulacastrum* L.	India	Leaves	Ethanol	*In vivo*	PCM and Thioacetamide	Kumar *et al*. (2004)
Apiaceae *Apium graveolens* L.	India	Seeds	Methanol	*In vivo*	PCM and Thioacetamide	Singh and Handa (1995)
Carum copticum L.	Pakistan	Seeds	Aqueous-methanol	*In vivo*	CCl_4 and PCM	Gilani *et al*. (2005a)
Apocynaceae *Apocynum venetum* L.	China, Japan	Leaf	Aqueous	*In vivo*	CCl_4 and GAIN	Xiong *et al*. (2000)
Araliaceae *Acanthopanax senticosus* (Rupr. and Maxim.) Harms	Taiwan	Whole plant	Methanol	*In vivo*	CCl_4 and Acetami-nophen	Lin and Huang (2002)
Asclepiadaceae *Sarcostemma brevistigma* Wight	India	Stem bark	Ethyl acetate	*In vivo*	CCl_4	Sethuraman *et al*. (2003)
Asteraceae *Achyrocline satureioides* (Lam.) DC.	Argentina	Aerial parts	Aqueous	*In vivo*	Bromobenzene	Kadarian *et al*. (2002)

Family and Botanical name	Origin	Plant Parts used	Extracts Studied	Type of assay	Hepato-toxicity Inducing Agents	References
Artemisia absinthium L.	Pakistan	Aerial parts	Aqueous-methanol	*In vivo*	CCl_4 and Aceta-minophen	Gilani and Janbaz (1995a)
Artemisia maritima L	Pakistan	Aerial parts	Aqueous-methanol	*In vivo*	CCl_4 and Aceta-minophen	Janbaz and Gilani (1995)
Artemisia vulgaris L.	Pakistan	Aerial parts	Aqueous-methanol	*In vivo*	GAIN and LPS	Gilani *et al*. (2005b)
Bidens chilensis DC	Taiwan	Whole plant	Methanol	*In vivo*	CCl_4 and PCM	Chih *et al*. (1996)
Bidens pilosa L.	Taiwan	Whole plant	Methanol	*In vivo*	CCl_4 and PCM	Chih *et al*. (1996)
Cichorium intybus L.	India	Seeds	Alcohol	*In vivo*	CCl_4	Ahmed *et al*. (2003)
Crassocephalum crepidioides Benth	Japan	Whole plant	Aqueous	*In vivo* and *in vitro*	GAIN, LPS and CCl_4	Aniya *et al*. (2005)
Elephantopus mollis Kunth.	Taiwan	Whole plant	Aqueous	*In vivo*	Acetaminophen and GAIN	Lin *et al*. (1995b)
Elephantopus scaber L.	Taiwan	Whole plant	Aqueous	*In vivo*	Acetaminophen and GAIN	Lin *et al*. (1995b)
Flaveria trinervia (Spreng.) C.Mohr	India	Leaf	Methanol	*In vivo*	CCl_4	Umadevi *et al*. (2004)
Gundelia tourenfortii L.	Iran	Stalk	Hydro-alcoholic	*In vivo* and *in vitro*	CCl_4	Jamshidzadeh *et al*. (2005)
Pseudoelephantopus spicatus (Juss. Ex Aublet) Gleason	Taiwan	Whole plant	Aqueous	*In vivo*	Acetaminophen and GAIN	Lin *et al*. (1995b)
Wedelia chinensis (Osbeck) Merr.	Taiwan	Whole plant	Methanol	*In vivo*	CCl_4, Aceta-minophen and GAIN	Lin *et al*. (1994)
Wedelia calendulacea L.	India	Leaf	Ethanol	*In vivo*	CCl_4	Murugaian *et al*. (2008)
Balanophoraceae *Thonningia sanguinea* Vahl.	Ghana	Roots, leaves	Aqueous	*In vivo* and in vitro	GAIN and CCl_4	Gyamfi *et al*. (1999)
Bixaceae *Cochlospermum tinctorium* Perri ex Rich.	Mali	Rhizome	Ethanol and hydro-ethanol extract	*In vivo*	CCl_4	Diallo *et al*. (1992)
Bixa orellana L.	Bangla-desh	Seed	Methanol	*In vivo*	CCl_4	Ahsan *et al*. (2009)
Brassicaceae *Coronopus didymus* L.	India	Whole plant		Aqueous	*In vivo*	CCl_4 Mantena *et al*. (2005)

Family and Botanical name	Origin	Plant Parts used	Extracts Studied	Type of assay	Hepato-toxicity Inducing Agents	References
Burseraceae *Commiphora opobalsamum* (L.) Engl.	Saudi Arabia	Aerial parts	Ethanol	*In vivo*	CCl_4	Al-Howiriny *et al*. (2004)
Caesalpiniaceae *Bauhinia racemosa* Lam	India	Bark	Methanol	*In vivo*	CCl_4 and PCM	Gupta *et al*. (2004)
Capparidaceae *Cleome viscosa* L	India	Leaves	Ethanol	*In vivo*	CCl_4	Gupta *et al*. (2009)
Casuarinaceae *Casuarina equisetifolia* Forst	Bangla-desh	Leaves, bark	Methanol	*In vivo*	CCl_4	Ahsan *et al*. (2009)
Celasteraceae *Salacia reticulata* Wight	Sri Lanka, India	Root, stem	Aqueous, methanol	*In vivo*	CCl_4	Yoshikawa *et al*. (2002)
Chenopodiaceae *Beta vulgaris* L.	India	Root	Ethanol	*In vivo*	CCl_4	Agarwal *et al*. (2006)
Combretaceae *Combretum* Kurz.	Japan	Leaves	Methanol	*In vivo* and *in vitro*	GAIN	Banskota *et al*. (2003)
Terminalia arjuna L.	India	Bark	Aqueous	*In vivo*	CCl_4	Manna *et al*. (2006)
Terminalia belerica Roxb	India	Fruits	Ethanol	*In vivo*	CCl_4	Jadon *et al*. (2007)
Terminalia catappa L.	Okinawa Island	Leaves	Aqueous	*In vivo* and *in vitro*	GAIN and LPS	Kinoshita *et al*. (2007)
Terminalia chebula Reiz.	India	Fruits	Ethanol	*In vivo* and *in vitro*	Anti TB drugs	Tasduq *et al*. (2006)
Compositae *Ambrosia maritima* L.	Egypt	Whole plant	Aqueous-methanol	*In vivo*	Acetaminophen	Ahmed and Kharter (2001)
Crepis rueppellii (Sch.) Bip.	Yemen	Whole plant	Ethanol	*In vivo*	CCl_4	Fleurentin *et al*. (1986)
Eclipta alba Hassk.	India	Whole plant	Alcohol	*In vivo*	CCl_4	Singh *et al*. (1993)
Epaltes divaricata (L.) Cav.	India	Whole plant	Aqueous	*In vivo*	CCl_4	Hewawasam *et al*. (2004)
Convolvulaceae *Cuscutae semen* Lam.	Korea	Seeds	Aqueous	*In vivo*	DMN	Kim *et al*. (2007a)
Erycibe expansa Wall. and G.Don	Thailand	Stem	Methanol	*In vitro*	GAIN	Matsuda *et al*. (2004)
Crassulaceae *Kalanchoe pinnata* Pers.	India	Leaves	Juice of leaves, ethanol extract of marc	*In vivo* and *in vitro*	CCl_4	Yadav and Dixit (2003)

Family and Botanical name	Origin	Plant Parts used	Extracts Studied	Type of assay	Hepato-toxicity Inducing Agents	References
Cucurbitaceae *Luffa echinata* Roxb.	India	Fruits	Pet.ether, acetone, methanol	*In vivo*	CCl_4	Ahmed *et al*. (2002)
Cyperaceae *Cyperos scariosus* R.Br.	Indonesia, Pakistan	Tubers	Aqueous-methanol	*In vivo*	CCl_4	Gilani and Jambaz (1995b)
Ebenaceae *Diospyros malabarica* (Desr.) Kostel	India	Bark	Methanol	*In vivo*	CCl_4	Mondal *et al*. (2005)
Euphorbiaceae *Alchornea cordifolia* Schum and Thonn.	Nigeria	Leaves	Ethanol	*In vivo*	Acetaminophen	Olaleye *et al*. (2006)
Croton oblongifolius Roxb.	India	Aerial parts	Pet.ether, acetone, methanol	*In vivo*	CCl_4	Ahmed *et al*. (2002)
Emblica officinalis Gaertner	India	Fruits	Hydro-alcoholic	*In vitro*	Anti TB drugs	Tasduq *et al*. (2005)
Phyllanthus maderaspatensis L.	India	Whole plant	n-hexane	*In vivo*	CCl_4 and Thioacetamide	Asha *et al*. (2007)
Phyllanthus niruri L.	Brazil	Leaves	Aqueous	*In vivo*	PCM	Sabir and Rocha (2008)
Phyllanthus reticulatus Poir.	India	Aerial parts		Ethanol	*In vivo*	CCl_4 Das *et al*. (2008)
Fabaceae *Acacia catechu* (L.f.) Willd.	India	Bark	Ethyl acetate		*In vivo*	CCl_4 Ray *et al*. (2006)
Bauhinia variegata L. bark	India	Stem	Alcohol	*In vivo*	CCl_4	Bodakhe and Ram (2007)
Cajanus cajan L.	India	Leaves	Methanol	*In vivo*	Alcohol	Kundu *et al*. (2008)
Cassia fistula L.	India	Leaves	n-heptane	*In vivo*	CCl_4	Bhakta *et al*. (1999)
Cassia occidentalis L.	India	Leaves	Aqueous-ethanol	*In vivo*	PCM and ethyl alcohol	Jafri *et al*. (1999)
Glycine max (L.) Merr	Taiwan	Seed	Water	*In vivo*	Acetaminophen	Wu *et al*. (2001)
Phaseolus aureus Roxb.	Taiwan	Seed	Water	*In vivo*	Acetaminophen	Wu *et al*. (2001)
Phaseolus calcaratus Roxb	Taiwan	Seed	Water	*In vivo*	Acetaminophen	Wu *et al*. (2001)
Phaseolus radiatus L.	Taiwan	Seed	Water	*In vivo*	Acetaminophen	Wu *et al*. (2001)
Pterocarpus marsupium Roxb.	India	Stem bark	Methanol	*In vivo*	CCl_4	Mankani *et al*. (2005)
Trigonella foenum-graecum L.	India	Leaves	Ethanol	H2O2	CCl_4	Meera (2009)

Family and Botanical name	Origin	Plant Parts used	Extracts Studied	Type of assay	Hepato-toxicity Inducing Agents	References
Fumariaceae *Fumaria indica* (Hausskn.) Pugsley	India	Whole plant	Methanol, Pet.Ether, aqueous	*In vivo*	PCM, Rifampicin, CCl_4	Rao and Mishra (1997)
Fumaria parviflora Lam.	Pakistan	Shoots	Aqueous-methanol	*In vivo*	PCM	Gilani *et al*. (1996)
Gentianaceae *Enicostemma littorale* Blume.	India	Whole plant	Alcohol	*In vivo*	CCl_4	Senthilkumar *et al*. (2005)
Swertia japonica (Roem. and Schult.) Makino.	Japan	Whole plant	Butanol	*In vivo*	GAIN	Hase *et al*. (1997b)
Lamiaceae *Ocimum basilicum* L.	India	Leaves	Ethanol	H_2O_2	CCl_4	Meera *et al*. (2009)
Moraceae *Ficus carica* L.	India	Leaves	Methanol	*In vivo*	CCl_4	Krishna *et al*. (2007)
Ficus hispida L	India	Leaves	Methanol	*In vivo*	PCM	Mandal *et al*. (2000)
Moringaceae *Moringa oleifera* L.	Malaysia	Leaves	Hydro-alcoholic	*In vivo*	Acetaminophen	Fakurazi *et al*. (2008)
Myrtaceae *Careya arborea* Roxb.	India	Stem bark	Methanol	*In vivo*	CCl_4	Sambath *et al*. (2005)
Nyctaginaceae *Boerhaavia diffusa* L.	India	Roots	Aqueous	*In vivo*	Thioacetamide	Rawat *et al*. (1997)
Nymphaceae *Nymphaea stellata* Willd.	India	Flowers	Alcohol	*In vivo*	CCl_4	Bhandarkar and Khan (2004)
Oleaceae *Phillyrea latifolia* L.	Jordan	Leaves	Aqueous	*In vivo*	CCl_4	Janakat and Al-Merie (2002)
Ophioglossaceae *Helminthostachys zeylanica* (L.) Hook	India	Rhizomes	Methanol	*In vivo*	CCl_4	Suja *et al*. (2004)
Orchidaceae *Anoectochilus formosanus* Hayata	Taiwan	Whole plant	Aqueous	*In vivo* and *in vitro*	CCl_4	Wu *et al*. (2007)
Polygalaceae *Polygala arvensis* Willd.	India	Leaves	Chloroform	*In vivo*	GAIN	Dhanabal *et al*. (2006)
Rhamnaceae *Ventilago leiocarpa* Benth.	Taiwan	Bark	Methanol, ethanol, butanol and aqueous	*In vivo*	CCl_4	Lin *et al*. (1995a)
Ziziphus mauritiana Lam.	Nigeria	Leaves	Ethanol	*In vivo*	CCl_4	Dahiru *et al*. (2005)

Family and Botanical name	Origin	Plant Parts used	Extracts Studied	Type of assay	Hepato-toxicity Inducing Agents	References
Rubiaceae *Hedyotis corymbosa* (L.)Lam.	India	Whole plant	Methanol	*In vivo*	PCM	Sadasivan *et al*. (2006)
Mitracarpus scaber Zucc.	Mali	Whole plant	Methanol	*In vivo* and *in vitro*	CCl_4	Germano *et al*. (1999)
Morinda citrifolia L.	America	Whole plant	Methanol	*In vivo*	CCl_4	Wang *et al*. (2008)
Rutaceae *Aegle marmelos* (L.) Corr. Serr.	India	Leaves	Fine powder inphysio-logical saline	*In vivo*	Alcohol	Singanan *et al*. (2007)
Glycosmis pentaphylla Corr.	Bangla-desh	Leaves, bark	Methanol	*In vivo*	CCl_4	Ahsan *et al*. (2009)
Scrophulariaceae *Bacopa monniera* (L.) Pennell	India	Whole plant	Alcohol	*In vivo*	Morphine	Sumathy *et al*. (2001)
Picrorrhiza kurroa (Roule.) Sans	Himalayas	Rhizome, roots	Ethanol	*In vivo*	GAIN	Anandan and Devaki (1999)
Smilacaceae *Smilax regelii* Killip and Morton	Saudi Arabia	Roots	Ethanol	*In vivo*	CCl_4	Rafatullah *et al*. (1991)
Solanaceae *Nicotiana glauca* Graham.	Jordan	Leaves, flowers	Aqueous	*In vivo*	CCl_4	Janakat and Al-Merie (2002)
Solanum nigrum L	India	Fruits	Ethanol	*In vivo*	CCl_4	Raju *et al*. (2003)
Solanum pseudocapsicum Hassl.	Jerusalem	Leaves	Methanol	*In vivo* and *in vitro*	CCl_4	Vijayan *et al*. (2003)
Solanum trilobatum L.	India	Whole plant	Methanol	*In vivo*	CCl_4	Shahjahan *et al*. (2004)
Umbelliferae *Bupleurum kaoi* Liu (Chao et Chuang)	Taiwan	Leaves	Aqueous	*In vitro*	Acetamino-phen and CCl_4	Liu *et al*. (2006)
Daucus carota L.	Europe, Asia, Africa	Roots	Aqueous	*In vivo*	CCl_4	Bishayee *et al*. (1995)
Foeniculum vulgare	Turkey Miller	Seeds	Essential oil	*In vivo*	CCl_4	Ozbek *et al*. (2003)
Valerianaceae *Nardostachys jatamansi* D.C.	India	Rhizomes	Ethanol	*In vivo*	CCl_4	Ali *et al*. (2000)
Vitaceae *Rhoicissus tridentata*(L.f.) Wild and R.B. Drumm	South Africa	Roots	Aqueous	*In vivo*	CCl_4	Opoku *et al*. (2007)

Table 2: Chemically defined Molecules with Hepatoprotective activity

Chemical substance	Plant	Plant part	Class	References
3,4-di-O-caffeoylquinic acid	*Lactuca indica* L.	Aerial parts	Quinic acid	Kim *et al*. (2007b)
3,5-di-O-caffeoyl-muco-quinic acid	*Lactuca indica* L.	Aerial parts	Quinic acid	Kim *et al*. (2007b)
5-O-(E)-p-coumaroylquinic acid	*Lactuca indica* L.	Aerial parts (2007b)	Quinic acid	Kim *et al*.
α-Amyrin (Aubl.) March	*Protium heptaphyllum*	Trunk wood resin	Triterpene	Oliveira *et al*. (2005)
β-Amyrin (Aubl.) March	*Protium heptaphyllum*	Trunk wood resin	Triterpene	Oliveira *et al*. (2005)
Anastatin A	*Anastatica hierochuntica* L.	Whole plant	Flavonoid	Yoshikawa *et al*. (2003)
Anastatin B	*Anastatica hierochuntica* L.	Whole plant	Flavonoid	Yoshikawa *et al*. (2003)
18 β-glycyrrhetinic acid	*Glycyrrhiza uralensis* Fisch.	Rhizomes	Glycyrrhetinic acid	Shim *et al*. (2000)
Tetrahydroswer-tianolin	*Swertia japonica* Makino	Aerial parts	Xanthione	Hase *et al*. (1997b)
Gentiopicroside	*Swertia japonica* Makino	Aerial parts	Iridoid	Hase *et al*. (1997b)
Sweroside	*Swertia japonica* Makino	Aerial parts	Iridoid	Hase *et al*. (1997b)
Andrographolide	*Andrographis paniculata* (Burm.f) Nees	Aerial parts	Diterpene	Chander *et al*. (1995)
Erycibenin A	*Erycibe expansa*	Stem	Pterocarpane	Matsuda *et al*. (2004)
5,7,4´-trihydroxy-3´-Methoxyisoflavone	*Erycibe expansa*	Stem	Isoflavone	Matsuda *et al*. (2004)
Genistein	*Erycibe expansa* Wall. Ex G.Don.	Stem	Isoflavone	Matsuda *et al*. (2004)
Orobol	*Erycibe expansa* Wall. Ex G. Don.	Stem	Isoflavone	Matsuda *et al*. (2004)
Mangiferin	*Salacia reticulata* Abst.	Roots	Phenolic compound	Yoshikawa *et al*. (2002)
(-)-4´-O-methy-lepigallocatechin	*Salacia reticulata* Abst.	Roots	Phenolic compound	Yoshikawa *et al*. (2002)
Thymoquinone	*Nigella sativa* L.	Aerial parts	Quinone	Daba and Abdel-Rahman (1998)
Lithospermate B	*Salvia miltorhiza* Bunge	Roots	Caffeic acid	Hase *et al*. (1997a)

Chemical substance	Plant	Plant part	Class	References
Taxiresinol	*Enciostemma littorale*	Aerial parts	Tetrahydro-furan	Nguyen *et al*. (2004)
(7´R)-7´-hydroxylariciresinol	*Enciostemma littorale*	Aerial parts	Tetrahydro-furan	Nguyen *et al*. (2004)
Onitin	*Equisetum arvense* L.	Aerial parts	Phenolic compound	Oh *et al*. (2004)
Luteolin	*Equisetum arvense* L.	Aerial parts	Flavonoid	Oh *et al*. (2004)
Quercetin-3-O-β-D-glucuronopyranoside	*Saururos chinensis* (Lour.) Baill.	Aerial parts	Flavonol glycoside	Sung *et al*. (1997)
Quercetin-3-O-β-D-glucuronopyranosyl methyl ester	*Saururus chinensis* (Lour.) Baill.	Aerial parts	Flavonol glycoside	Sung *et al*. (1997)
Scropolioside-A	*Scrophularia koelzii* Pennell	Aerial parts	Iridoid glycoside	Garg *et al*. (1994)
3-(S)-3-_-Dglucopyrano-syloxybutanolide	*Goodyera schlechtendaliana* Reichb.*G. matsumurana* Schltr.*G. discolor* Kergawl	Whole plant	Aliphatic glycoside	Du *et al*. (2000)
3-(S)-3-_-D-glucopyranosyloxy-4-hydroxybutanoic acid	*Goodyera schlechten-daliana* Reichb.*G. matsumurana* Schltr.*G. discolor* Kergawl.	Whole plant	Aliphatic glycoside	Du *et al*. (2000)
Agathisflavone	*Canarium manii* King	Aerial parts	Biflavonoid	Anand *et al*. (1992)
(S)-bakuchiol	*Psoralea corylifolia* Babchi	Aerial parts	Monoter-penephenol	Hyun *et al*. (2001)
Monomethyl fumarate	*Fumaria indica* Pugsley	Whole plant	Fumaric acid	Rao and Mishra (1998)
Wighteone	*Cudrania cochinchinensis* (Lour.) Kudo et Masam.	Roots	Flavonoid	Lin *et al*. (1996)
Naringenin	*Cudrania cochinchinensis* (Lour.) Kudo et Masam.	Roots	Flavonoid	Lin *et al*. (1996)
Torilin	*Cnidium monnieri* (L.) Cusson	Aerial parts	Sesquiterpene	Oh *et al*. (2002)
Torilolone	*Cnidium monnieri* (L.) Cusson.	Aerial parts	Sesquiterpene	Oh *et al*. (2002)
Allicin	*Allium sativum* L.	Cloves	Allyl thiosulfinates	Vimal and Devaki (2004)
Kaempferol	*Rhodiola sachalinensis* A.Bor.	Roots	Phenolic compound	Song *et al*. (2003)

Chemical substance	Plant	Plant part	Class	References
Salidroside	*Rhodiola sachalinensis* A.Bor.	Roots	Phenolic compound	Song *et al*. (2003)
1-O-galloyl-6-O-(4-hydroxy-3,5-dimethoxy)benzoyl-β-d-glucose	*Combretum quadrangulare* Kurz	Seeds	Gallic acid	Adnyana *et al*. (2001)
Picroliv	*Picrorhiza kurroa* Royle ex Benth.	Aerial parts	Iridoid glycoside	Visen *et al*. (1991)
Indigtone	*Indigofera tinctoria* L.	Aerial parts	Aliphatic nitrocompound	Singh *et al*. (2001)
Acanthoic acid	*Acanthopanax koreanum* Nakai	Root bark	Diterpene	Park *et al*. (2004)
Myristin	*Myristica fragrans* Houtt.	Aerial parts	Cetyl ester	Morita *et al*. (2003)
Rutin	*Artemisia scoparia* Waldst. and Kit.	Aerial parts	Flavonoid	Janbaz *et al*. (2002)
Troxerutin	*Artemisia scoparia* Waldst. and Kit.	Aerial parts	Flavonoid	Zhang *et al*. (2009)
Neoandrographolide	*Andrographis paniculata* (Burm.f.) Wall. Ex Nees	Aerial parts	Diterpene	Chander *et al*. (1995)
5-0-methyl-(E)-resveratrol.3-0-β-D glucopyranoside	*Acer mono* Maxim.	Leaves	Stilbene glycoside	Yang *et al*. (2005)
5-0-methyl-(E)-resveratrol.3-0-_-Dapiofuranosyl-1->6)-β-D glucopyranoside	*Acer mono* Maxim.	Leaves	Stilbene glycoside	Yang *et al*. (2005)
Corilagin	*Terminalia catappa* L.	Leaves	Tannin	Kinoshita *et al*. (2007)
y-Amyrone	*Sedum sarmentosum* Bunge	Aerial parts	Triterpene	Amin *et al*. (1998)
3-epi-y-amyrin	*Sedum sarmentosum* Bunge	Aerial parts	Triterpene	Amin *et al*. (1998)
y-Amyrin	*Sedum sarmentosum* Bunge	Aerial parts	Triterpene	Amin *et al*. (1998)
18β-hydroperoxy-olean.12-en-3-one	*Sedum sarmentosum* Bunge	Aerial parts	Triterpene	Amin *et al*. (1998)
Rubiadin	*Rubia cordifolia* L.	Roots	Anthraquinone	Rao *et al*. (2006)
3,4,5-trihydroxy-benzoic acid	*Terminalia belerica* Roxb.	Fruit	Gallic acid	Jadon *et al*. (2007)
Kinsenoside	*Anoectochilus formosanus* Hay.	Whole plant	Furanone	Wu *et al*. (2007)

Discussion and Conclusion

The liver is the most important organ in the body. It has a pivotal role in regulation of physiological processes. It is involved in several vital functions such as metabolism, secretion and storage. Liver diseases are among the most serious ailments. They may be classified as acute or chronic hepatitis (inflammatory liver diseases), hepatosis (non inflammatory diseases) and cirrhosis (degenerative disorder resulting in fibrosis of the liver).

Modern society has innate knowledge about the herbal treatment of liver disease from many cultures. Research into plants traditionally used in the treatment of liver disease has significantly advanced in the past 15 years, and much of what has been discovered supports traditional knowledge. Considering the enormous biodiversity resources over the world's traditional system and the high incidence of liver complications, the present review extensively focuses on collection of data for different plants, which are available in India and all over the world. These medicinal plants claimed as liver protective agents are classified according to their biological source, phytoconstituents; part used and plants in formulations. People from India are still dependent on conventional therapies to treat liver complications. Because of their easy availability and low cost. Since large mass of populations used preferable herbal preparation, therefore there is need to be evaluate for their proportion, their dose and rational behind combination in different polyhedral preparation.

These herbal drugs have shown the ability to maintain the normal functional statues of the liver with or without fewer side effects. These are the reason that's why herbal hepatoprotectives are mostly preferred by medical practitioners.

It has been seen that herbal hepatoprotective drugs have less side effect or interaction as compared to synthetic medicine but in other hand scientific evidence from tests done to evaluate the safety and effectiveness of traditional hepatoprotective medicine products and practices is limited and further study of products and practices is needed.

Pharmacokinetic and toxicity studies have not disclosed any issues that could limit the therapeutic use of these drugs. Also the study is required to identify glycosides, flavonoids, triterpenes and phenolic compounds as classes of compounds with hepatoprotective activity.

Further studies including clinical trials need to be carried out to ascertain the safety of these compounds as a good alternative to conventional drugs in the treatment of liver diseases

Since the traditional system of medicine recommends various hetptoprotective agents and preparations to treat hepatic disorders. The management of lives disease is still challenges to modern medicine. The modern allopathic drugs have very little to offer for alleviation of hepatic ailments and some these drugs adversely affect the liver function. A phytotherapeutic approach to modern drug development provides many invaluable drugs from traditional medicinal plants. Search for pure phytochemical as drug is time consuming and extensive. Numerous plants and polyherbal formulations are being used for the treatment of liver diseases.

Today, unfortunately the herbal resources have declined rapidly because more than 80% of our total medicinal plants used by Indian pharmaceutical industry are collected from their wild sources and they are not being grown or domesticated so far. To meet their burgeoning demand is the need of the day. Moreover, our natural resource base of medicinal plants is being depleting day by day. Hence there is an urgent need to encourage field scale cultivation of prioritized medicinal plants through government initiatives before it's too late.

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