Herbs as liver savers- A review

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Received 21 January 2010; Accepted 20 September 2010

Herbal medicines are in great demand in the developed world for primary health care due their efficacy, safety and lesser side effects. Recently, considerable attention has been paid to utilize eco-friendly and bio-friendly plant-based products. The current availability of high-tech methods allows researchers to optimize the effectiveness, standardization and clinical testing of these herbs to meet international standards. A wide group of medicinal plants and preparations had been used over centuries almost exclusively as antimicrobial, cytotoxic, antidiabetic, antiinflammatory, etc. In addition, numerous plants and polyherbal formulations are used in treatment of liver related disorders. However, for developing satisfactory herbal combinations to treat liver diseases plants needs to be evaluated systematically for its potency as antiviral, antihepatotoxicity, antioxidants, stimulation of hepatocytes regeneration and choleretic activity. Development and scientific studies have validated such herbal medicines or combinations confirming the biological efficacy and safety which revitalize treatment of liver disorders. The present review is systematically conducted to overview the plants like *Andrographis paniculata* Nees., *Eclipta alba* Hassk., *Lawsonia alba* Lam., *Picrorhiza kurroa* Royle ex Benth., and *Silybum marianum* Linn., proved as hepatoprotective and used as the ingredients of liver protection drugs in the last few decades. Nevertheless, much additional work is needed to open up new biomedical application of these plants.

**Keywords:** Antioxidant, Herbs, Hepatoprotective, Hepatotoxic, Liver disorders, Serum transaminases

**IPC code:** Int. cl. A61K 36/00, A61P 1/16

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**Introduction**

Medicinal plants play a key role in the human health care system. About 80% of the world population rely on traditional medicine which is predominantly based on plant materials. The traditional medicine refers to a broad range of ancient, natural health care practices including folk/tribal practices as well as Ayurveda, Siddha and Unani. It is estimated that about 7,500 plants are used in health traditions in, mostly, rural and tribal villages of India. Out of these, the real medicinal value of over 4,000 plants is either little known or unknown to the mainstream population. Health and well-being has been a subject of man’s primary concern since time immemorial. There has been resurgence of scientific interest in medicinal plants during the past few decades due to their importance in traditional system of medicine. Herbal medicines are in great demand in the developed world for primary health care because of their efficacy, safety and lesser side effects. A detailed investigation and documentation of plants used in health traditions and pharmacological evaluation of these plants and their taxonomical relatives can lead to the development of invaluable plant based drugs for many dreaded diseases. A large number of plants and purified natural substances have been screened for liver disorders.

Liver diseases are mainly caused by toxic chemicals, excess consumption of alcohol, infections and autoimmune disorder. Most of the hepatotoxic chemicals damage liver cells mainly by lipid peroxidation and other oxidative damages. Liver is the most important organ where drugs are structurally altered; resulting biologically inactive or active metabolites and some of these are toxic. Liver is exposed to drugs in higher concentration as whole of the drug pass through liver to reach systemic circulation. Thus, the liver is a vulnerable target of injury from various chemicals and drugs and disordered hepatic function is an important cause of abnormal drug handling. Further liver has capacity to recover from acute injury by hepatocellular regeneration with the production of new cells, which restore liver functions and normal tissue structure. Chronic liver injury, however often leads to fibrosis, scar formation and distortion of normal tissue architecture.
Supporters of herbal medicine claim that herbs may treat and prevent diseases. This adds to a deep belief that these treatments are safe as they are natural and fit into the image of a gentle and therefore, harmless alternative to conventional medicine. Herbal remedies support natural healing phenomena through blocking the progression of the degenerative pathological processes. Modern medicine offers limited success in providing effective cure and there is a severe need to develop new drugs capable of healing toxic liver damages. In traditional systems of medicine, plants were claimed to be effective and used successfully to alleviate multiple liver disorder. But, evidence for efficacy is sparse. In spite of limitations, a number of herbal show promising effects, either experimentally in cell culture (in-vitro models), animal studies (in-vivo models), or even in clinical trials.

In this regards, we systematically summarized reported scientific papers that describe evaluations of liver protective plants and critically appraised the evidence based as par to international standards for appropriate scientific study designs that could justify their use as hepatoprotective agents.

Clinically tested plants

*Silybum marianum* Linn. (Fam.-Asteraceae) has been used to treat liver diseases since 16th century. Major constituents of plant are flavonoids (silibinin, silidianin, silichristin and isosilibinin). Silibinin is the biologically most active compound. The pharmacological profile of silymarin has been well defined and hepatoprotective properties of silymarin were investigated both in-vitro and in-vivo models. Experimental studies demonstrated its antioxidant, free radical scavenging properties and improvement of the antioxidative defence by preventing glutathione (GSH) depletion and antifibrotic activity.

Pharmacologically tested plants

Aqueous extract of leaves of *Adhatoda vasica* Nees (Fam.-Acanthaceae), showed significant hepatoprotective effect at doses of 50-100mg/kg, p.o. on liver damage induced by D(+)-galactosamine (D(+)-GalN) (200mg/kg, i.p.) in Wistar rats (either sex). The extract possessed a potent antioxidant effect.

Aqueous extract of *Aloe barbadensis* Mill. (Fam.-Liliaceae) aerial parts at dose of 500mg/kg, p.o. was significantly capable of restoring integrity of hepatocytes indicated by improvement in physiological parameters, excretory capacity of hepatocytes and also by stimulation of bile flow secretion in male Wistar rats or Swiss Albino mice. Extract prevented the hepatic damage against carbon tetrachloride (CCl₄) (1ml/kg, p.o.) and significantly ameliorated the levels of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP).

Methanol seeds extract (250mg/kg, p.o.) of *Apium graveolens* Linn. (Fam.-Apiaceae) and aerial parts (200mg/kg, p.o.) of *Croton oblongifolium* Roxb. (Fam.-Euphorbiaceae) showed significant hepatoprotective activity against CCl₄ (1.5ml/kg, p.o.) induced hepatotoxicity in female Albino Wistar rats.

Fresh juice of tender leaves of *Azadirachta indica* A. Juss. (Meliaceae) (200mg/kg, p.o.) inhibited acetaminophen (APAP) (2g/kg, p.o.) induced lipid peroxidation and prevented depletion of sulfhydryl groups in liver cells of Albino rats (CF strain) of either sex. Pre-treatment with juice stabilized the significant increased serum enzyme levels.

Aqueous extract (100mg/kg, p.o.) of aerial parts of *Ballota glandulosisissa* Hub.-Mor & Patzak. (Lamiaceae) showed hepatoprotective effect against CCl₄ (0.8ml/kg, i.p.) induced hepatotoxicity in either sex of Sprague-Dawley rats and Swiss Albino mice. Treatment with plant extract significantly ameliorates the levels of serum maker enzymes elevated by the toxicant.

Latex of *Calotropis procera* Ait. (Asclepiadaecae) was evaluated for its hepatoprotective effect against CCl₄ (2ml/kg, s.c., in olive oil) induced hepatotoxicity in Wistar rats of either sex. Oral administration of aqueous suspension of dried latex at 5, 50 and 100mg/kg doses produced a dose-dependent reduction in the serum levels of liver enzymes. The dried latex treatment also normalized various biochemical parameters of oxidative stress.

Ethanol and aqueous extracts (250mg/kg, p.o.) of dried fruits of *Carica papaya* Linn. (Caricaceae) showed remarkable hepatoprotective activity against CCl₄ (1.25ml/kg, p.o.) induced hepatotoxicity in male Albino rats. Decrease in serum bilirubin after treatment with the extract in intoxicated group indicated the effectiveness of the extract in normal functional status of the liver. So, the result indicates that the ethanol and aqueous extracts of *C. papaya* possess significant hepatoprotective activity.

Treatment with aqueous leaves extract (250 and 500mg/kg, i.g.) of *Cassia auriculata* Linn. (Caesalpiniaecae) to ethanol (5ml/kg, 20%, i.g.) intoxicated male Wistar rats showed hepatoprotective effect when compared to unsupplemented ethanol.
intoxicated rats. Treatment with extract elevated the activities of superoxide dismutase (SOD) and catalase (CAT) and significantly lowered the levels of thiobarbituric acid reactive substances (TBARS), hydroperoxides, also reduced the levels of total bilirubin (TB), AST, ALT, ALP in serum and GSH in the liver\(^7\).

The effect of 50% ethanol extract (400mg/kg, p.o.) of Chamomile (Matricaria chamomilla Linn.) (Asteraceae) capitula flowers on blood and liver GSH, sodium potassium adenosine tri-phosphatase (Na\(^+\) K\(^+\) ATPase) activity, serum marker enzymes, serum bilirubin, glycogen and TBARS against APAP (200mg/kg, p.o.) induced damage in Albino rats (either sex) liver was studied to know possible mechanism of hepatoprotection. The extract prevented the toxic effects of APAP on the serum parameters and stimulated hepatic regeneration through an improved synthesis of protein or accelerated detoxification and excretion\(^8\).

The effect of various flavonoids (quercetin-3-methyl-ether, quercetin-3, 7-dimethyl-ether and kaempferol-3, 7-dimethyl-ether) isolated from leaves of Cistus laurifolius Linn. (Cistaceae) were assessed on lipid peroxidation, cellular GSH, serum AST and ALT enzyme levels in APAP (800mg/kg, p.o.) induced liver damage in male Swiss Albino mice. At dose level (114mg/kg, p.o.) quercetin-3, 7-dimethyl-ether showed potent antioxidative and hepatoprotective activity\(^9\).

Aqueous extract (200mg/kg, p.o.) of Cleome viscosa Linn. (Capparaceae) seeds showed protective effect against hepatotoxicity induced by CCl\(_4\) (0.5ml/kg, i.p.) in male Wistar Albino rats. The extract protected the rats from hepatotoxicity evidenced by significant reduction in serum enzymes AST, ALT, ALP, Y-glutamyl transpeptidase and lipid peroxidase and elevation in GSH\(^10\).

Ethanol extract (200mg/kg, p.o.) of Clerodendrum inerme Linn. (Verbenaceae) leaves when screened for its hepatoprotective activity in CCl\(_4\) (0.5ml/kg, i.p.) induced liver damage in either sex of Swiss Albino mice and Wistar Albino rats, significantly decreased the serum enzyme (ALT, AST, and ALP), Triglycerides (TGL), Total Cholesterol (TC) and significantly increased the GSH level. Moreover, pre-treated with the extract prevented the effect of hepatotoxicity\(^11\).

Cuscuta chinensis Lam. (Convolvulaceae) seeds ethanol extract showed significant hepatoprotective effect at dose levels, 125 and 250mg/kg, p.o. and potentiate significant reduction in levels of GSH, glutathione peroxidase (GPT) and ALP against APAP (835mg/kg, i.p.) induced hepatotoxicity in male Wistar Albino rats\(^12\).

The effect of ethanol extract (100 and 250mg/kg, p.o.) of whole plant of Eclipta alba Hassk. (Asteraceae) when administered to APAP (500mg/kg, p.o.) induced hepatic damaged Albino mice of either sex protected hepatotoxic action as evidenced by significant reduction in the elevated serum marker enzymes levels and also showed 38% reduction in serum ALT levels\(^13\).

The combined hepatoprotective effect of bi-herbal ethanol extract was evaluated against CCl\(_4\) (2ml/kg, p.o.) induced hepatic damage in male Albino Wistar rats. The ethanol extract (50mg/kg, p.o.) in ratio of (1:1) of Eclipta alba Hassk. (Asteraceae) leaves and Piper longum Linn. (Piperaceae) seed restored the substantially elevated serum marker enzymes towards normal. In addition, bi-herbal extract significantly decreased the liver weight of intoxicated rats\(^14, 15\).

Methanol extract (500mg/kg, p.o.) of Ficus carica Linn. (Moraceae) leaves exhibited a significant protective effect against liver damaged by CCl\(_4\) (1.5ml/kg, p.o., in olive oil) in male Wistar rats. Treatment with the extract significantly inhibited the elevation in serum AST, ALT levels and liver lipid peroxidation level\(^16\).

The essential oil (0.4ml/kg, i.p.) extracted from seeds of Foeniculum vulgare Mill. (Apiaceae) inhibited the hepatotoxicity induced by CCl\(_4\) (0.8ml/kg, i.p.) in male Sprague-Dawley rats with evidence of decreased levels of serum ALT, AST, ALP and TB\(^17\).

The glycyrrhizin isolate from liquorice (Glycyrrhiza glabra Linn.-Fabaceae) roots was investigated on acute hepatitis induced by lipopolysaccharide (LPS) and D (+) galactosamine (D(+)GalN) (mix 25ng LPS/20mg D(+)GalN, i.v.) in male BALB/c mice. Glycyrrhizin (50mg/kg, i.p.) inhibited the increased serum ALT levels. Moreover, glycyrrhizin also reduced the responsiveness of cells to IL-18 (a potent inflammatory cytokine that regulates autoimmune and inflammatory diseases produced by Kupffer cells, β-cells and dendritic cells) in the liver injury. Results suggested that glycyrrhizin inhibits the LPS/ D (+)GalN induced liver injury by preventing inflammatory responses and IL-18 production\(^18\).

The juice of the leaves (200mg/kg, p.o.) and ethanol extract (200mg/kg, p.o.) of Kalanchoe pinnata Lam. (Crassulaceae) were investigated...
against CCl$_4$ (2ml/kg, i.p., in liquid paraffin) induced hepatotoxicity in Wistar Albino rats of either sex. The study confirmed that juice is more effective hepatoprotective as compared to ethanol extract$^{39}$.

Ethanol extract of the bark of Lawsonia alba Linn. (Lythraceae) showed a significant hepatoprotective effect against CCl$_4$ (1 ml/kg, p.o.) induced oxidative stress in male Albino Wistar rats. Pre-treatment with extract at dose levels of 250 and 500 mg/kg, p.o. significantly lowered the serum transaminase GSH, GPT, lactate dehydrogenase (LDH) levels. In addition, extract inhibited the peroxidation of microsomal lipids in dose dependent manner$^{30}$.

Chloroform extract (200 and 400 mg/kg, p.o.) of aerial parts of Leucas lavandulaefolia Rees (Lamiaceae) exhibited a significant protection in D(+)GalN (400 mg/kg, i.p.) induced liver damaged in male Wistar rats. Treatment with extract showed significant decrease in serum AST, ALT, ALP, TB, LDH, TC levels when compared with intoxicated group$^{31}$.

The different extracts, petroleum ether, acetone and methanol (250 mg/kg, p.o.) of Luffa echinata Roxb. (Cucurbitaceae) fruit showed a significant hepatoprotective activity comparable to standard drug silymarin against CCl$_4$ (1 ml/kg, s.c.) induced hepatotoxicity in Wistar Albino rats$^{32}$.

Pretreatment with aqueous extract (100mg/kg, p.o) of fruits of Lycium chinense Mill. (Solanaceae) showed a significant protective effect by lowering the serum AST, ALT and ALP. In addition, pre-treatment with extract prevented the elevation of hepatic malondialdehyde (MDA) formation, the depletion of GSH content and catalase activity in the liver of CCl$_4$ (0.5 ml/kg, s.c.) intoxicated male Sprague-Dawley rats. The extract also displayed hydroxide radical scavenging activity in a dose dependent manner$^{33}$.

The n-hexane extracts (100 and 200 mg/kg, p.o) of fruits of Lygodium flexuosum Swartz. (Lygodiaceae) whole plant showed complete protection in D(+)-GalN (800 mg/kg, i.p.) induced liver injury in Wistar rats of either sex as evident by normal serum AST, ALT and LDH levels, hepatic GSH and MDA levels and also by normal histological index of liver in extract treated rats$^{34}$.

The hepatoprotective activity of aqueous extracts of leaves (500 mg/kg, fresh wt., 50mg/kg, dry wt., p.o.) of Momordica subangulata Blume (Cucurbitaceae) and whole plant suspension (500 mg/kg, p.o.) of Naragamia alata W&A (Meliaceae) were studied in APAP overdose (2 g/kg, p.o., in 40% w/v aqueous sucrose solution) induced liver damage in Wistar Albino rats. The extracts showed significant protective effects$^{35}$.

Combination of 70% ethanol extracts of the roots of Paeonia lactiflora Pall. (Paeoniaceae) and Astragalus membranaceus Bunge (Fabaceae) demonstrated more significant hepatoprotective activity than the herbs when used individually in liver fibrosis induced in male Sprague-Dawley rats with CCl$_4$ (1 ml/kg, s.c.). Moreover, administration of the combined extracts (40, 80 and 160 mg/kg, i.g.) significantly decreased the elevation of serum transaminase activities, hyaluronic acid, laminin and procollagen type III levels and contents of hydroxyproline in liver tissue by approximately 30-60%$^{36}$.

The n-hexane extract (200 mg/kg, p.o., in 5% Tween-80) of whole plant of Phyllanthus maderaspatensis Linn. (Euphorbiaceae) showed a remarkable and better hepatoprotective activity than standard drug silymarin against APAP (2 g/kg, p.o., in 40%w/v aqueous sucrose solution) induced hepatotoxicity in Charles Wistar rats as justified from the serum marker enzymes. Whereas, the aqueous and ethanol extracts showed moderate activity as compared to the n-hexane extract$^{37}$.

Alcohol extract (50%) in 100 mg/kg, p.o. dose and mixture of lignans, isolated from leaves of Phyllanthus niruri Linn. (Euphorbiaceae) showed significant hepatoprotective activity against APAP (500 mg/kg, p.o., in 0.9% saline) induced liver cell damage in Albino mice. The extract and lignans mixture completely prevented the toxic effects of APAP on the serum parameters by the stimulation of hepatic regeneration through an improved synthesis of protein or accelerated detoxification and excretion$^{38}$.

Ethanol extract (200 mg/kg, p.o., in Tween-80) of whole plant of Phyllanthus rheedii Wight (Euphorbiaceae) was pharmacologically analysed for its preventive effect in D(+)-GalN (800 mg/kg, i.p., in normal saline) induced liver damage in Wistar rats of either sex. The levels of serum parameters (ALT, AST, ALP and TB) and tissue parameters (LDH and TBARS) were decreased significantly in extract treated group when compared to intoxicated group$^{39}$.

Aqueous extract of roots of Platycodon grandiflorum (Jacq.) A. DC. (Campanulaceae) showed a protective effect against APAP (400 mg/kg, i.p., in saline) induced hepatotoxicity in male ICR mice. Hepatic GSH and glutathione-S-transferase (GST) activities were not affected by treatment with the extract alone. However, pre-treatment with the
extract protected the APAP induced depletion of hepatic GSH levels. This effect of the extract on cytochrome P450, 1A2 and 2 E1 (major isoenzymes involve in APAP bioactivation) were investigated. The protective effect was due to extract ability to block P450 mediated APAP bioactivation.

The ethanol extract (200 mg/kg, i.p.) of the oyster mushroom Pleurotus ostreatus (Jaqc.) Quelet (Pleurotaceae) on CCl₄ (2 ml/kg, i.p., in olive oil) induced liver damage in male Albino Wistar rats showed a significant hepatoprotective activity. Significant elevated levels of MDA and lowered levels of GSH were observed in intoxicated liver. In addition, extract treated group serum AST, ALT and ALP levels reverted towards normal, while the hepatic concentration of GSH, CAT, SOD and Gpx were significantly increased and MDA significantly lowered when compared to intoxicated untreated group.

Chloroform extract (200 and 400 mg/kg, p.o.) of leaves of Polygala arvensis Willd. (Polygalaceae) exhibited a significant protective effect when compared to standard drug silymarin (P<0.001) by normalizing the levels of serum AST, ALT, ALP, TB, LDH, TC, TGL, albumin and total proteins (TP) which were significantly (P<0.001) increased in male Wistar rats intoxicated with D(+)-GalN (400 mg/kg, i.p.).

Aqueous extract (5ml/kg, i.p.) of leaves of Rhodococcus vitis idaea (Linn.) Avrorin (Eriaceae) significantly inhibited the hepatotoxicity and oxidative stress induced by D(+)-GalN (700 mg/kg, s.c.) evident by an increase in serum alanine aminotransferase and GSH activities and lipid peroxidation in liver of male Wistar rats. The extract showed a potent antioxidant and protective property.

The different extracts ethanol, ethyl acetate and n-butanol (400 mg/kg, p.o.) of aerial parts of Schouwia thebica Webb. (Brassicaceae) showed significant hepatoprotective activity. These extracts significantly reduced the increased levels of serum ALT, AST, glucose, TGL and TC in CCl₄ (2.5 ml/kg, p.o., in corn oil) intoxicated male Sprague-Dawley rats. The activity was related to the presence of flavonoids in the extracts.

Treatment with the ethanol extracts (25 mg/kg, i.p.) of seeds of Silybum marianum Linn. (Asteraceae) and Cichorium intybus Linn. (Asteraceae) reduced the levels of enzymes activity (serum AST, ALT and ALP) and the level of TB in thioacetamide (50 mg/kg, i.p.) intoxicated Wistar male rats. Values of sodium, potassium and liver weight showed no significant difference. The protective effects of these extracts were due to the presence of flavonoids and their antioxidant potential.

The protective effects of chloroform extract (100 mg/kg, p.o.) Terminalia catappa Linn. (Combretaceae) leaves on CCl₄ (10ml/kg, i.p., in olive oil) induced liver damage in male ICR mice was studied. Serum AST and ALT activities increased remarkably (2.0-fold and 5.7-fold, respectively) after the CCl₄ injection. In addition, the liver lipid peroxidation level in intoxicated group showed 2.8-fold increase of that in the normal group. However, treatment with various concentrations of the extract (20, 50 and 100 mg/kg) blocked the above changes significantly in a dose dependent manner and the elevations in serum AST and ALT activities and liver lipid peroxidation level were inhibited almost completely.

The protective effect of ethyl acetate extract (25 mg/kg, i.p.) of aerial parts of Teucrium polium Linn. (Lamiaceae) showed potential anti-lipidperoxidative and antioxidant activities in female Albino Wistar rats with CCl₄ (3 ml/kg, i.p.) induced hepatotoxicity. The elevated levels of blood marker enzymes (GPx and SOD) and biochemical parameters (GSH and TBARS), returned towards normal in groups treated with silymarin (25 mg/kg, i.p.) and ethyl acetate extract which clearly manifest their anti-hepatotoxic effect.

Ethanol extract (100 and 200 mg/kg, p.o., in 50% w/v aq. sucrose solution) of leaves of Trianthema portulacastrum Linn. (Aizoaceae) showed a significant dose dependent protective effect against APAP (3 g/kg, p.o., 1 h after ethanol extract administration) and thioacetamide (100 mg/kg, s.c., 2% w/v solution in distilled water) induced hepatotoxicity in Wistar Albino rats of either sex. The degree of protection was measured using biochemical parameters like serum AST, ALT, ALP, TB and TP. The extract completely prevented the toxic effects of APAP and thioacetamide by stimulating the hepatic regeneration through an improved synthesis of protein or accelerated detoxification.

Ethanol extract (300 mg/kg, p.o.) of Tridax procumbens Linn. (Asteraceae) aerial parts was investigated against D(+)-GalN/LPS (300 mg/kg, i.p.) induced hepatic damage in male Wistar Albino rats by a significant increase in the activities of serum marker enzymes (AST, ALT, ALP, LDH and gamma glutamyl transferase), TB and lipids levels both in serum and liver. Pretreatment of extract afforded a significant protection against liver injury by maintaining these levels to nearly normal.
Alcohol (200 and 500mg/kg, p.o., in Tween-80) and aqueous (125 and 300mg/kg, p.o., in Tween-80) extracts of leaves of *Tylophora indica* (Burm.f.) Merrill, (Asclepiadaceae) showed protective effects on ethanol (3.76g/kg, p.o.) induced hepatotoxicity in male Wistar Albino rats. Pretreatment of extracts significantly prevented the physical (increased liver weight and volume), biochemical (increase in serum ALT, AST, ALP, TB, TC, TGL and albumin), histological (damage to hepatocytes) and functional (thiopentane induced sleeping time) changes in animals.

Some more medicinal plants (Plate 1) which are proved as hepatoprotective are described in Table 1. Most commonly used plants *Adhatoda vasica* Nees., *Aloe barbadensis* Mill., *Andrographis paniculata* Nees, *Azadirachta indica* A. Juss., *Eclipta alba* Hassak., *Lawsonia alba* Lam., *Picrorhiza kurroa* Royle ex Benth., *Silybum marianum* Linn. (are scientifically validated in experimental animal models and used by topmost companies as ingredients of herbal formulations for liver disorders for example., Amazon liver support, Bhumyamlaki, G-LIV-DS Syrup, Hepta-B, Hepato-guard, Livotone, Liv up, Livpar, Liv-52, Milk Thistle complex, Stimuliv, Tefroli, V- gel and Yakrit Plihantak Churna.

The present review is an attempt to systematically summarize the current scientific evidence regarding the medicinally valuable plants, herbal drugs and their constituents, especially in-regards to their presumed beneficial effect to protect liver and delineates the issues that need to be addressed to incorporate herbal medicine into the arsenal of therapies in the treatment of liver diseases. Plant drugs (combinations or individual drug) for liver diseases must possess sufficient efficacy to cure severe liver diseases caused by toxic chemicals, viruses (Hepatitis B, Hepatitis C, etc.) and excess alcohol intake.

**Conclusion**

In spite of tremendous strides in modern medicine, there is hardly any drug that stimulates liver functions, protect liver from damage or help regenerating hepatic cells. However, a number of drugs are employed in traditional system of medicine for liver affections and show promising...
Table 1—Some more plants proved to be hepatoprotective against various hepatotoxins

<table>
<thead>
<tr>
<th>Plant</th>
<th>Parts used</th>
<th>Extract</th>
<th>Dose</th>
<th>Toxicants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acalypha racemosa Wall. (Euphorbiaceae)</td>
<td>Leaves</td>
<td>Methanol extract</td>
<td>60 and 120mg/kg, p.o.</td>
<td>CCl₄ (1.5ml/kg, i.p.)</td>
</tr>
<tr>
<td>Actinidia deliciosa Chev. (Actinidiaceae)</td>
<td>Roots</td>
<td>Ethanol extract</td>
<td>60 and 120mg/kg, p.o.</td>
<td>CCl₄ (2ml/kg, s.c.)</td>
</tr>
<tr>
<td>Aegle marmelos Corr. (Rutaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>1g/kg, p.o.</td>
<td>EtOH (30%) (1ml/kg, p.o.)</td>
</tr>
<tr>
<td>Annona squamosa Linn. (Annonaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>350mg/kg, p.o.</td>
<td>INZ (100mg/kg, i.p.)</td>
</tr>
<tr>
<td>Aspalathus linearis (Brum. f) Dahlg (Theaceae)</td>
<td>Leaves</td>
<td>Aqueous extract</td>
<td>5ml/kg, p.o.</td>
<td>RFN (100mg/kg, i.p.)</td>
</tr>
<tr>
<td>Bauhinia variegate L. (Fabaceae)</td>
<td>Stem bark</td>
<td>Ethanol extract</td>
<td>100 and 200mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td>Berberis tinctoria Lesch. (Berberidaceae)</td>
<td>Leaves</td>
<td>Methanol extract</td>
<td>150 and 300mg/kg, p.o.</td>
<td>APAP (750mg/kg, p.o.)</td>
</tr>
<tr>
<td>Boswellia serrata Roxb. (Burseraceae)</td>
<td>Oleo gum resin</td>
<td>n-Hexane extract</td>
<td>87.5 and 175mg/kg, p.o.</td>
<td>APAP (2g/kg, p.o.)</td>
</tr>
<tr>
<td>Butea superba Roxb. (Fabaceae)</td>
<td>Stem bark</td>
<td>Ethanol extract</td>
<td>50 and 100mg/kg, p.o.</td>
<td>CCl₄ (0.1ml/kg, i.p.)</td>
</tr>
<tr>
<td>Cajanus indicus Linn. (Fabaceae)</td>
<td>Leaves</td>
<td>Protein fraction</td>
<td>2mg/kg, i.p.</td>
<td>APAP (300mg/kg, p.o.)</td>
</tr>
<tr>
<td>Careya arborea Roxb. (Myrtaceae)</td>
<td>Roots</td>
<td>Ethanol extract</td>
<td>100, 200 and 400mg/kg, p.o.</td>
<td>CCl₄ (0.2mg/kg, p.o.)</td>
</tr>
<tr>
<td>Cassia occidentalis Linn. (Fabaceae)</td>
<td>Roots</td>
<td>Aqueous extract</td>
<td>200mg/kg, p.o.</td>
<td>CCl₄ (2ml/kg, i.p.)</td>
</tr>
<tr>
<td>Careya arborea Roxb. (Myrtaceae)</td>
<td>Stem bark</td>
<td>Methanol extract</td>
<td>50, 100 and 200mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td>Camellia sinensis Linn. (Theaceae)</td>
<td>Leaves</td>
<td>Aqueous extract</td>
<td>50, 100 and 200mg/kg, p.o.</td>
<td>TAA (100mg/kg, s.c.)</td>
</tr>
<tr>
<td>Cichorium intybus Linn. (Asteraceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>50, 100 and 200mg/kg, p.o.</td>
<td>CCl₄ (3ml/kg, i.p.)</td>
</tr>
<tr>
<td>Commiphora opobalsamum Linn. (Burseraceae)</td>
<td>Aerial parts</td>
<td>Ethanol extract</td>
<td>250 and 500mg/kg, p.o.</td>
<td>CCl₄ (0.25ml/kg, i.p.)</td>
</tr>
<tr>
<td>Croton zehntneri Pax et Hoff. (Euphorbiaceae)</td>
<td>Leaves</td>
<td>Essential oil</td>
<td>30, 100 and 300mg/kg, p.o.</td>
<td>APAP (500mg/kg, p.o.)</td>
</tr>
<tr>
<td>Curculigo orchioides Gaertn. (Amaryllidaceae)</td>
<td>Rhizomes</td>
<td>Methanol extract</td>
<td>70mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, s.c.)</td>
</tr>
<tr>
<td>Curcuma longa Linn. (Zingiberaceae)</td>
<td>Rhizomes</td>
<td>Ethanol extract</td>
<td>200 and 100mg/kg, p.o.</td>
<td>INZ (50mg/kg, p.o.)</td>
</tr>
<tr>
<td>Diospyros malabarica (Desr.) Kostel. (Ebenaceae)</td>
<td>Bark</td>
<td>Methanol extract</td>
<td>200 and 300mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td>Enicostemma axillare Lam. (Gentianaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>0.66g/kg, p.o. and Roots</td>
<td>CCl₄ (0.7ml/kg, i.p.)</td>
</tr>
<tr>
<td>Epaltes divaricata Caso. (Asteraceae)</td>
<td>Whole plant</td>
<td>Aqueous extract</td>
<td>0.9g/kg, p.o.</td>
<td>CCl₄ (0.5ml/kg, i.p.)</td>
</tr>
<tr>
<td>Euphorbia antiquorum Linn. (Euphorbiaceae)</td>
<td>Aerial parts</td>
<td>Aqueous extract</td>
<td>100 and 200mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td>Ginkgo biloba Linn. (Ginkgoaceae)</td>
<td>Leaves</td>
<td>Dry extract</td>
<td>Ginkgolides (50mg/kg, i.p.)</td>
<td>CCl₄ (0.5ml/kg, i.p.)</td>
</tr>
<tr>
<td>Hyrophila spinosa T. Anders (Acanthaceae)</td>
<td>Roots</td>
<td>Aqueous extract</td>
<td>20mg/kg, p.o.</td>
<td>CCl₄ (2ml/kg, i.p.)</td>
</tr>
<tr>
<td>Ichnocarpus frutescens Linn. (Apocynaceae)</td>
<td>Whole plant</td>
<td>Chloroform extract Methanol extract</td>
<td>250 and 500mg/kg, p.o.</td>
<td>APAP (750mg/kg, p.o.)</td>
</tr>
<tr>
<td>Indigofera trita Linn. (Fabaceae)</td>
<td>Whole plant</td>
<td>Ethanol extract</td>
<td>200 and 400mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td>Launaea pinatifida Cass. (Asteraceae)</td>
<td>Leaves and roots</td>
<td>Ethanol extract</td>
<td>0.66g/kg, p.o.</td>
<td>CCl₄ (0.5ml/kg, i.p.)</td>
</tr>
<tr>
<td>Leucophyllum frutescens Berl. (Scrophulariaceae)</td>
<td>Aerial parts</td>
<td>Methanol extract</td>
<td>100 and 200mg/kg, p.o.</td>
<td>CCl₄ (2ml/kg, p.o.)</td>
</tr>
<tr>
<td>Momordica dioica Roxb. (Cucurbitaceae)</td>
<td>Roots</td>
<td>Ethanol extract</td>
<td>200mg/kg, p.o.</td>
<td>CCl₄ (0.4ml/kg, i.p.)</td>
</tr>
</tbody>
</table>

Contd.
hepato-protective activity. Since the evidence supporting the use of botanicals to treat chronic liver diseases is insufficient and only few of them are well standardised and free of serious side effects. Particularly with regard to adequately powered randomised-controlled clinical trials with well-selected end points are needed to assess the role of herbal therapy for liver diseases.

Pharmacological validation of each hepatoprotective plant should include efficacy evaluation against liver diseases induced by various agents, efficacy against viral hepatitis as well as liver damage induced by hepatotoxic chemicals by oxidative mechanisms or other mechanisms. Further, the plant drugs have to be evaluated for their effects on liver regeneration and bile secretion.

Table 1—Some more plants proved to be hepatoprotective against various hepatotoxins—Contd.

<table>
<thead>
<tr>
<th>Plant</th>
<th>Parts used</th>
<th>Extract</th>
<th>Dose</th>
<th>Toxicant/s</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Nelumbo nucifera</em> Gaertn. (Nymphaeaceae)</td>
<td>Flowers</td>
<td>Ethanol extract</td>
<td>200 and 400mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Nigella sativa</em> Linn. (Ranunculaceae)</td>
<td>Seeds</td>
<td>Ethanol extract</td>
<td>800mg/kg, p.o.</td>
<td>CCl₄ (1.15ml/kg, s.c.)</td>
</tr>
<tr>
<td><em>Ocimum sanctum</em> Linn. (Lamiaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>200mg/kg, p.o.</td>
<td>INZ (27 mg/kg/day)</td>
</tr>
<tr>
<td><em>Parkinsonia aculeata</em> Linn. (Fabaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>100, 200 and 300mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Pergularia daenio</em> Forsk (Asclepiadaceae)</td>
<td>Aerial parts</td>
<td>Ethanol extract</td>
<td>50, 100 and 150mg/kg, p.o.</td>
<td>CCl₄ (1.25ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Phoenix dactylifera</em> Linn. (Arecalesae)</td>
<td>Pits and flesh</td>
<td>Aqueous extract</td>
<td>10% of Basal diet</td>
<td>CCl₄ (0.2ml, 100g, i.p.)</td>
</tr>
<tr>
<td><em>Phyllanthus polyphyllas</em> Willd. (Euphorbiaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>200 and 300mg/kg, p.o.</td>
<td>APAP (750mg/kg, p.o.)</td>
</tr>
<tr>
<td><em>Pterocarpus santalinus</em> Linn. (Fabaceae)</td>
<td>Stem bark</td>
<td>Aqueous extract</td>
<td>40, 60 and 100mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, s.c.)</td>
</tr>
<tr>
<td><em>Punica granatum</em> Linn. (Punicaceae)</td>
<td>Peel</td>
<td>Powdered drug</td>
<td>3-Bromo-6-(4-chlorophenyl) -4-methylthio-2H-pyran-2-one</td>
<td>CCl₄ (0.7ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Raphanus sativus</em> Linn. (Brassicaceae)</td>
<td>Seeds</td>
<td>Ethanol extract</td>
<td>400mg/kg, p.o.</td>
<td>APAP (2mg/kg, p.o.)</td>
</tr>
<tr>
<td><em>Rhododendron arboreum</em> Sm. (Ericaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>400mg/kg, p.o.</td>
<td>TAA (400mg/kg, s.c.)</td>
</tr>
<tr>
<td><em>Ricinus communis</em> Linn. (Euphorbiaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>400mg/kg, p.o.</td>
<td>TAA (400mg/kg, s.c.)</td>
</tr>
<tr>
<td><em>Rubia cordifolia</em> Linn. (Rubiaceae)</td>
<td>Roots</td>
<td>Methanol extract</td>
<td>100mg/kg, i.p.</td>
<td>TAA (100mg/kg, s.c.)</td>
</tr>
<tr>
<td><em>Sarcostemma brevigistigma</em> Wight (Asclepiadaceae)</td>
<td>Stem</td>
<td>Ethyl acetate extract</td>
<td>650mg/kg, p.o.</td>
<td>CCl₄ (1.25ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Saponaria officinalis</em> Linn. (Caryophyllaceae)</td>
<td>Roots</td>
<td>Powdered drug</td>
<td>10% of Basal diet</td>
<td>CCl₄ (0.5ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Smilax chinensis</em> Linn. (Liliaceae)</td>
<td>Roots</td>
<td>Ethanol extract</td>
<td>100mg/kg, p.o.</td>
<td>APAP (750mg/kg, p.o.)</td>
</tr>
<tr>
<td><em>Solanum trilobatum</em> Linn. (Solanaceae)</td>
<td>Whole plant</td>
<td>Ethanol extract</td>
<td>250mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Swertia longifolia</em> Boiss (Gentianaceae)</td>
<td>Aerial parts</td>
<td>Ethanol extract</td>
<td>200mg/kg, p.o.</td>
<td>APAP (600mg/kg, i.p.)</td>
</tr>
<tr>
<td><em>Syzygium aromaticum</em> Linn. (Myrtaceae)</td>
<td>Flower buds</td>
<td>Ethanol extract</td>
<td>500mg/kg, p.o.</td>
<td>APAP (600mg/kg, i.p.)</td>
</tr>
<tr>
<td><em>Terminalia belerica</em> Roxb. (Combretaceae)</td>
<td>Fruits</td>
<td>Ethanol extract</td>
<td>200 and 400mg/kg, p.o.</td>
<td>EtOH (30%) (3ml/kg, p.o.)</td>
</tr>
<tr>
<td><em>Thespesia lampas</em> Dalz. (Malvaceae)</td>
<td>Roots</td>
<td>Ethanol extract</td>
<td>300mg/kg, p.o.</td>
<td>CCl₄ (3ml/kg, s.c.)</td>
</tr>
<tr>
<td><em>Tinospora cordifolia</em> Willd. (Menispermaceae)</td>
<td>Roots</td>
<td>Ethanol extract</td>
<td>200mg/kg, p.o.</td>
<td>INZ (50mg/kg, p.o.)</td>
</tr>
<tr>
<td><em>Trigonella foenum-graecum</em> Linn. (Fabaceae)</td>
<td>Seeds</td>
<td>Diethyl ether extract</td>
<td>0.5ml/kg, i.p.</td>
<td>TAA (0.8ml/kg, i.p.)</td>
</tr>
<tr>
<td><em>Urtica parviflora</em> Roxb. (Urticaceae)</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>250, 500 and 700mg/kg, p.o.</td>
<td>CCl₄ (1ml/kg, s.c.)</td>
</tr>
<tr>
<td><em>Vetiveria zizanioides</em> Linn. (Poaceae)</td>
<td>Roots</td>
<td>Methanol extract</td>
<td>300 and 500mg/kg, p.o.</td>
<td>EtOH (20%) (3.76g/kg, p.o.)</td>
</tr>
<tr>
<td><em>Vicia calcarata</em> Desf. (Fabaceae)</td>
<td>Aerial parts</td>
<td>Ethanol extract</td>
<td>Flavonoid-25 mg/kg, p.o.</td>
<td>CCl₄ (100mg/kg, p.o.)</td>
</tr>
<tr>
<td><em>Xylopia philodora</em> Mildbr. (Annonaceae)</td>
<td>Stem bark and leaves</td>
<td>Crude extract, Ether, 50, 100 and 250mg/kg, p.o. extract and Essential (Essential oil) 10% v/w oil of 2.5kg Stem bark, p.o.</td>
<td>CCl₄ (0.3ml/kg, i.p.)</td>
<td></td>
</tr>
<tr>
<td><em>Zizyphus mauritiana</em> Lamk. (Rhamnaceae)</td>
<td>Seeds</td>
<td>Ethanol extract</td>
<td>200mg/kg, p.o.</td>
<td>APAP (500mg/kg, p.o.)</td>
</tr>
</tbody>
</table>

cont
Therefore, the most effective drug for each kind of liver disease has to be selected by separate efficacy evaluations. Pharmacovigilance of plant based drugs be further improved and mechanisms of action must be elucidated. There is still lot of work to be done in order to achieve a reliable standardized products and to link it to a specific biological activity and therapeutic application.

Acknowledgement
The authors extend their sincere thanks to Shri Parveen Garg (Chairman, I.S.F. College Of Pharmacy, Moga) for his co-operation and for providing the required institutional facilities.

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