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Medicinal plants in the protection and treatment of liver diseases

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Abstract

Hepatic dysfunction is globally a major health catastrophe that challenges the health care professionals. The existing synthetic drugs to treat liver diseases have not given much pronounced outcomes. So, conventional herbal plants have become progressively more popular and their utilization is more prevalent. The current review is assemblage of few promising medicinal plants used in the protection and treatment of various liver diseases. Extracts of plants ground significant alteration in liver marker enzymes against diverse hepatotoxic agents.

Introduction

The liver plays vital role in maintenance, performance, regulation of homeostasis, secretions of bile, storage of vitamins (Ahsan et al., 2009) and detoxification in the body. It participates in all the biochemical pathways to growth, immune system, nutrient supply, energy provision and reproduction (Ward and Daly, 1999). So, the proper functioning of liver is essential for the healthy living of an individual. Hepatic diseases escort to liver damage. A major contributory factor is the enlarge alcohol utilization in developed countries (Nadeem et al., 1997). Starvation, blood deficiency, communicable diseases and accessibility of over-the-counter hepatotoxic drugs are the most recurrent factors of liver cell injures in developing countries (WHO Bulletin, 1992). Hepatic cell injury caused by various toxicants like chemotherapeutic agents, anti tuberculosis drugs, carbon tetrachloride, paracetamol, chronic alcohol consumption and pathogenic microbes are well reported (Priya et al., 2010). Drugs such as paracetamol, carbon tetrachloride, thioacetamide and isoniazid catabolize the radicals, bring on lipid peroxidation, damage the membranes of liver cells and organelles, cause the inflammation and necrosis of hepatocytes and leads to the liberation of cytosolic enzymes into the systemic transmission (Singh et al., 1998).

The most common disease of the liver is jaundice can be presented as yellow coloration of eye sclera, skin and mucous membrane due to increase amount of bilirubin in body, having prehepatic, hepatic or post-hepatic causes (Tortora and Grabowski, 2002). Enlargement of liver (hepatomegaly) can occur due to increased accumulation of blood in liver, inflammation, pathogenic infection, cysts and increased size of hepatocytes, infiltrative disorders or microhepatic causes. Increased ammonia level in brain causes hepatic encephalopathy. When normal hepatic parenchyma is replaced by fibrosis or regenerative nodules, cirrhosis is formed. This may occur due to alcoholism or viral hepatitis. Carcinoma or bile stone sclerosing cholangitis can cause obstructive jaundice and bile duct obstruction can cause secondary biliary cirrhosis. They may be metabolic disorders include hereditary hyperbolic rubinemias and intermediate metabolism of liver, carbohydrates, proteins and heavy metals. Congenital metabolic disorders include: congenital hyperbilirubinemia, Gilbert syndromes, Rotor syndrome, Dubin-jhonson syndrome and

Table I: Classification of hepatotoxins and mechanism of action

Category of agent	Mechanism (UNOS)	Histological lesion	Examples (Avijeet et al., 2008)
Intrinsic toxicity Direct Indirect	 Membrane injury Interference with specific metabolic pathways leads to structural injury	 Necrosis and /or stenosis Necrosis and or stenosis	 CCl_4 , $CHCl_3$ Thioacetamide, paracetamol, ethanol, tetracycline
Host idiosyncrasy Hypersensitivity	Drug allergy	Necrosis or cholestetosis	Sulphonamides, iproniazid, halothane, paraaminosalicylate, isoniazid, pyrazinamide, rifampicin

alpha 1 antitrypsin deficiency. Aquired metabolic disorder may be due to food, beverages, toxins, drugs or alcohol. Hepatomegaly, alcoholic hepatitis and cirrhosis are the reasons of excessive alcohol intake (Dalia and Nagalakshrni, 2000).

All forms of liver injuries (microbiologic, toxic, circulatory or traumatic injury) lead to liver necrosis. Necrosis could be diffuse, zonal or focal (**Table I**). Other liver diseases include followings:

- Anemia, hemolytic anemia can cause decrease oxygen availability to liver cells and lead to their death.
- Infection: bacteria, viruses and fungi can cause liver problem.

1. Infectious disease includes canine hepatitis, canine herpes virus, feline infectious peritonitis, leptospirosis, abscesses histoplasmosis, histoplasmosis, coccidiomycosis and toxoplasmosis. HAV, HBV, HCV, HDV, HEV hepatotroipc viruses that cause acute attacks.
2. Hepatitis A virus can cause acute, self-limited disease that is transmitted orally.
3. Hepatitis B and C viruses are transmitted by exchange of body fluids such as blood transfusion and sexual contacts.
4. Hepatitis D is a viroid that causes inflammation along with HBV.
5. Hepatitis E is transmitted by enteric route and cause self-limited disease.
6. HBV-HDV cause chronic hepatitis. Methyldopa, nitrofurantoin, ketoconazole and paracetamol cause drug-induced hepatitis.

Medicinal herbal formulations belong to the conventional systems of medication have been considered as liver protective agents from so long. All following plants have momentous hepatoprotective potential all along with other activities.

Lepidium sativum belongs to family Brassicaceae, is commonly known as garden grass and also has hepatoprotective potential against carbon tetrachloride (**Figure 1)**. **Figure 2** has presented *Vaccinium procyanidins*, its hepatoprotective action against two hepatotoxins tetradecanoylphorbol acetate, carbon tetrachloride and D-galactosamine. **Figure 3** has presented the one medicinal plant (*Ficus carica*: family Umbelliferaceae) with mechanism of action as hepatoprotective agent (Poumale et al., 2008).

Various edible herbs also approved because of their activities in protection and treatment of liver diseases. They have shown their hepatoprotective action by various means. For example: fruit of *Allium sativum* belongs to family Liliaceae, is used most commonly in Indian Subcontinent foods and recognizes by the name of "Garlic: Lehsan". It has hepatoprotective potential due to its organosulphur components which is clearly depicted by **Figure 4**. Like this, roots of *Glycyrrhiza glabra* belongs to family Fabaceae, commonly known as "Malathi" has proved hepatoprotective action due to glycyrrhetinic acid and liqourice as major chemical constituents against hepatotoxins carbon tetrachloride and D-galactosamine N and viral and non viral heaptitis by controlling oxidative stress and hepatic phase I and phase II metabolism shown in **Figure 5**.

Thus the objective of the current review is intended to sum up the maximum medicinal plants those have been using and proved for the protection and treatment of liver **Table II**.

Alteration in liver markers: The consequences of hepatoprotective activity of extract of medicinal plants are considerable decline in liver marker enzymes: Total bilirubin (TB), direct bilirubin (DB), alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lipid profile, lactate dehydrogenase (LDH), gamma-glutamyltransferase (γ-GT), thiobarbituric acid reactive substances (TBARS) and markers for oxidative defense namely malondialdehyde (MDA), accompanied by significant enhance in the level of total protein (TP), glutathione (GSH), total thiols (TT), conjugated dienes (CD), superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), glutathione-S-transferase (GST) and glutathione peroxidase (GSH-Px) in treatment group as compared to the hepatotoxic group and these also estored the depleted liver thiol levels significantly.

Analysis of **Table II** indicates that there are compiled 112 Asian herbs which have been reported for their

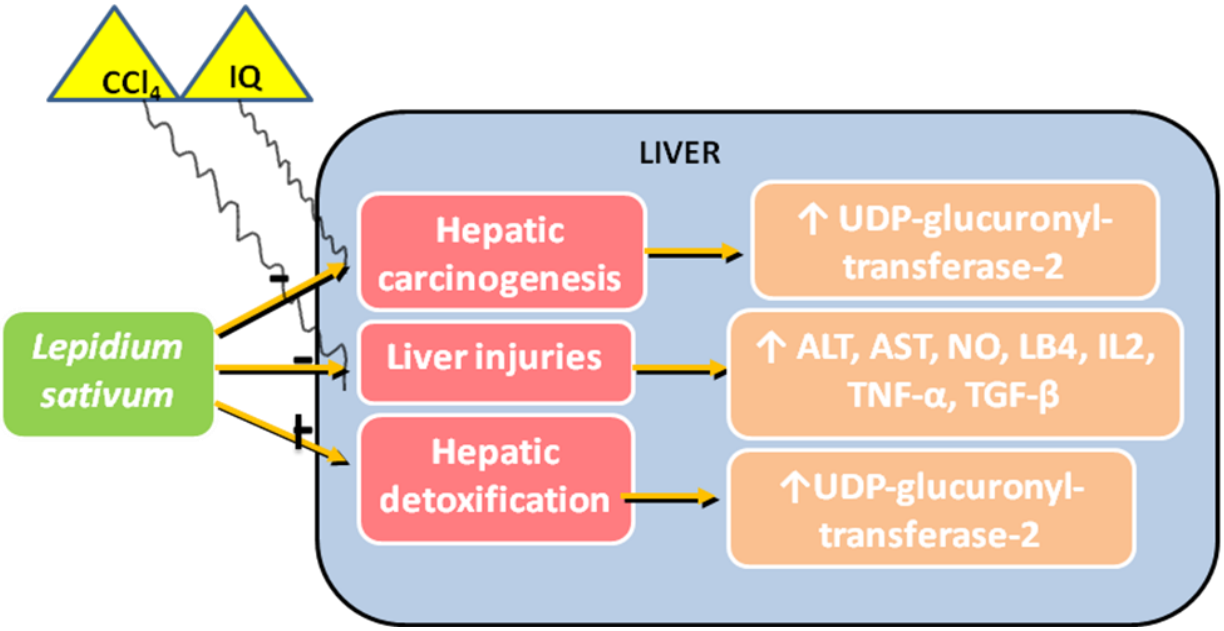

Figure 1: *Lepidium sativum* juice and powder has hepatoprotective activity against carbon tetrachloride (CCl_4) and 2-amino-3-methylimidazole-4, 5-quinoline (IQ). These hepatotoxins disturb the liver regular mechanisms. Plant juice inhibits the hepatocarcinogenesis via increasing the UDP-glucuronyl-transferase-2 and carcinogen detoxification, inhibits the liver injury via inhibiting the AST, ALT, nitric oxide (NO), leukotriene B4, interleukin 2 (IL-2), tumor necrosis factor α (TNF-α) and transforming growth factor β (TGF-β) and increases the hepatic detoxification via up regulating the glucuronyltransferase-2 (Afaf et al., 2008)

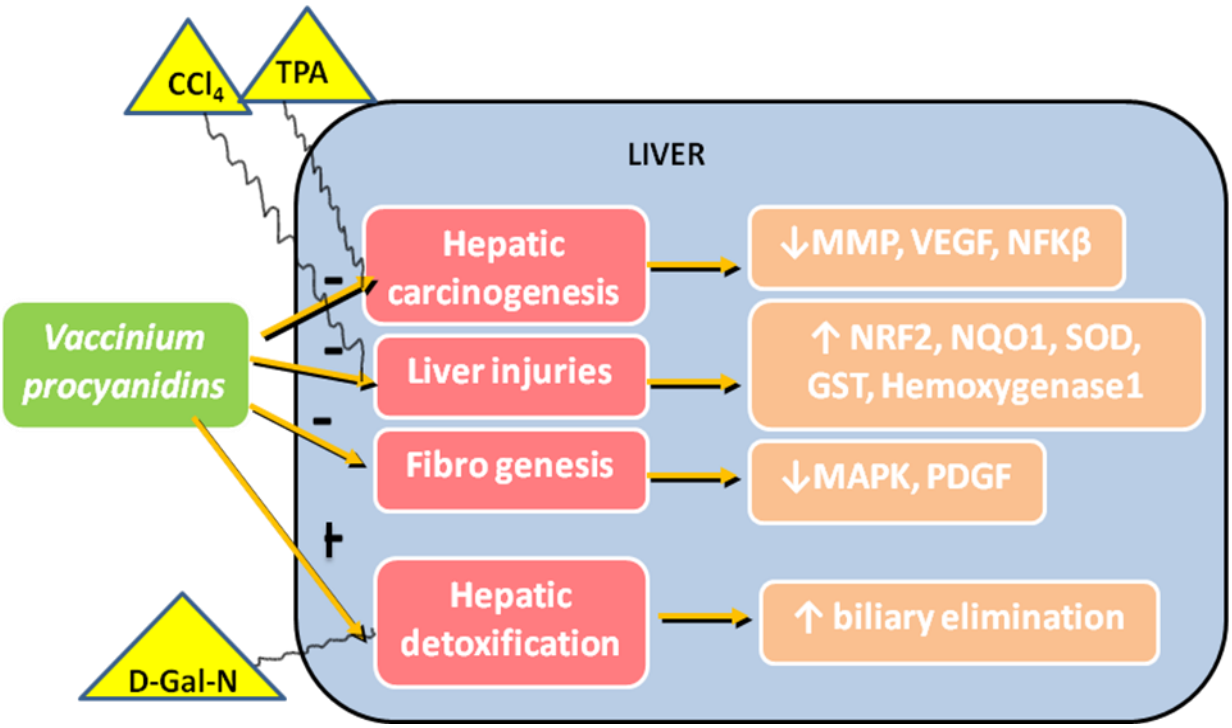

Figure 2: *Vaccinium procyanidins* inhibits the liver injury via increasing the nuclear factor 2 (NRF-2), NADPH dehydrogenase quinine 1 (NQO1), superoxide dismutase (SOD), glutathione-S-transferase (GST) and hemoxygenase 1, viral hepatitis, fibrogenesis via inhibiting the mitogen activated protein kinase pathways (MAPK) and platelet derived growth factor (PDGF), hepatocarcinogenesis via inhibiting matrix metalloproteinase (MMP), vascular endothelial growth factor (VEGF), nuclear factor kappa light chain enhancer of B cells (NF-ǩB), increases the hepatic detoxification and biliary elimination against hepatotoxins like carbon tetrachloride (CCl_4) and D-galactosamine N (Gressner et al., 2012)

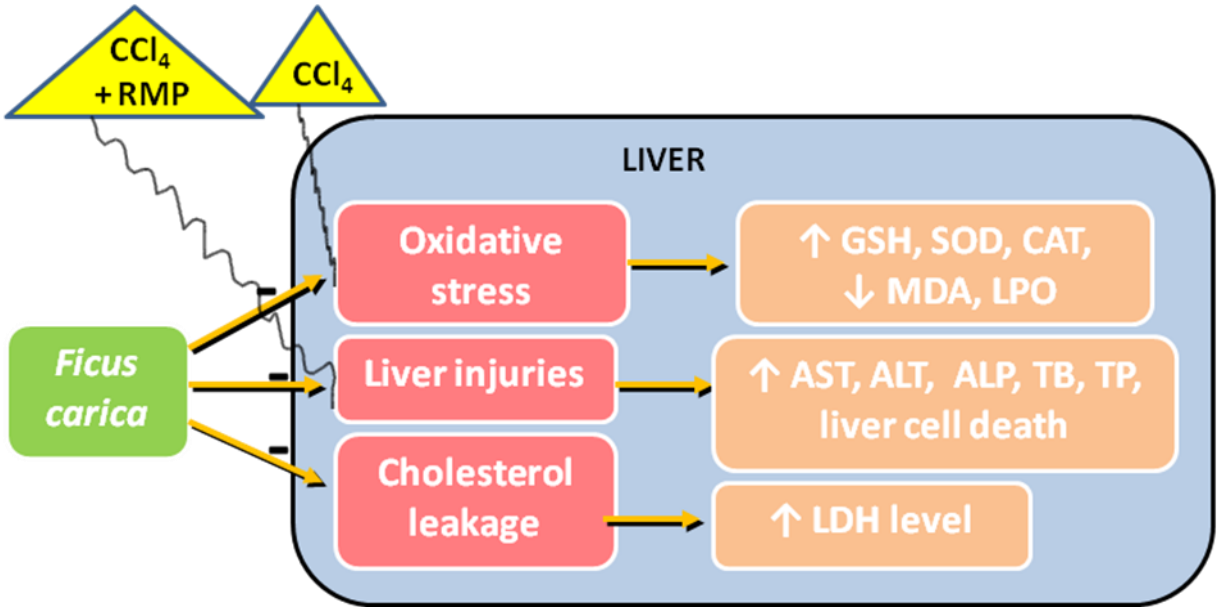

Figure 3: *Ficus carica* prevents the liver cell death and LDH leakage by increasing AST, ALT, ALP, TB and MDA levels and decreasing oxidative stress parameters (GSH, SOD, CAT), those were perturbed by CCl_4 and Rifampicin hepatotoxins (Poumale et al., 2008)

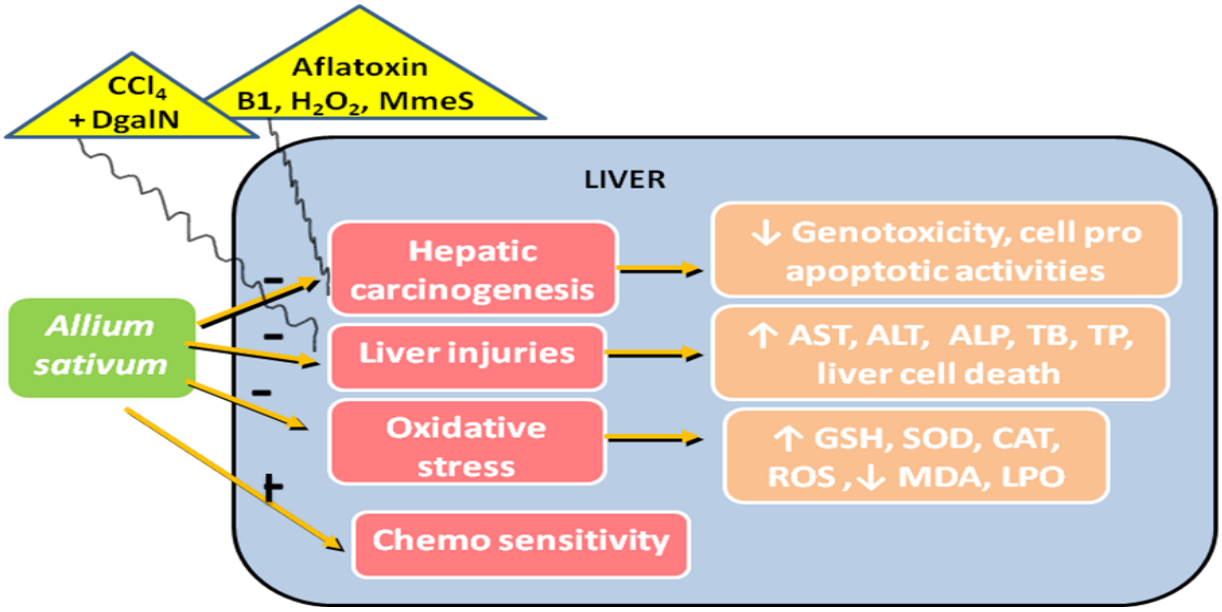

Figure 4: *Allium sativum* (Family Liliaceae) has shown hepatoprotective potential due to its organosulphur components including: allicin, diallyl sulphide, diallyl disulphide, S-allyl cysteine and allyl marcaptan. These constituents inhibits the hepatocarcinogenesis via inhibiting the genotoxicity, cell proapoptotic activities and increasing the chemosensitivity against carcinogens, aflatoxin B1, H_2O_2, methyl methanesulfonate (MmeS), bezno-a-pyrene and dimethylnitrosamine. Allicin inhibits the steatosis via inhibiting total serum cholesterol. Its oil and allicin has negative potential against hepatotoxins like CCl_4, D-gal-N, Ethanol and heavy metals via inhibiting the AST, ALT, ALP, MDA and ROS and increasing the GSH, SOD, CAT and GPx levels in intrahepatic tissues (Ilyas et al., 2011)

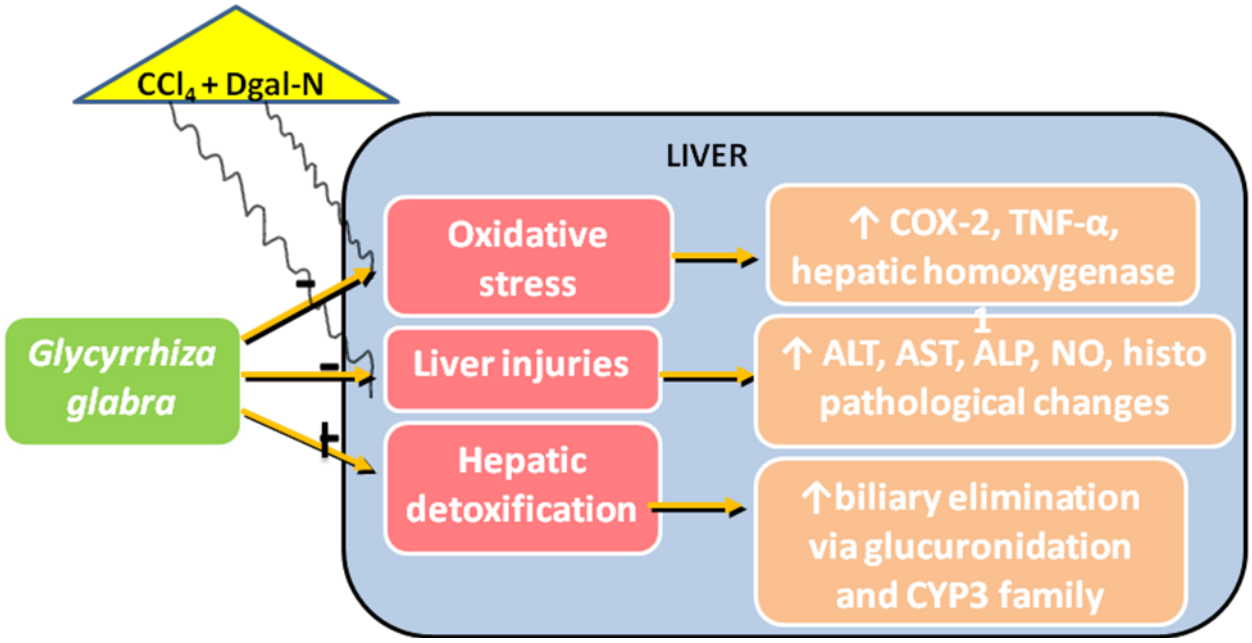

Figure 5: *Glycyrrhiza glabra* (Family: Fabaceae) has hepatoprotective action due to glycyrrhetinic acid and liqourice by inhibiting the liver injuries and inflammation via controlling the oxidative stress parameters and increasing the hepatic detoxification via increasing the cytochrom phase I and glucuronidation phase II metabolism which become affected by hepatotoxins carbon tetrachloride and D-galactosamine N (Al-Razzuq et al., 2012)

hepatoprotective activity against hepatotoxins. Among these 35 plants have proved their hepatoprotective activity against paracetamol, in which 17 studies were conducted on rats, 15 on mice and 3 on rabbits. 53 botanical herbs have shown their potential for protection and treatment of liver against carbon tetrachloride (inorganic substance), in which rat has been used as biological animal in 45, mice in 5 and rabbit in 3 studies. Anti-tuberculosis drugs (isoniazid, rifampicin, pyrazinamide etc) also act as hepatotoxin. In **Table II**, 7 plants have proved their activity against them and all studies were conducted on rats. Thioacetamide, an organosulphur compound has ability to destroy the hepatocyte. Five plants were reported against this hepatotoxin, in which 4 studies were conducted on rats and 1 on mice. Other hepatotoxins which become the reason of high magnitude of liver marker enzymes include D-galactosamine/ lipopolysaccharide (3 studies conducted: 2 on rat and 1 on mice), ethanol (3 plants studies on rats), γ-hexachlorocyclohexane by *Aloe vera* on mice, di-methylnitrosamine on rat, alloxan on rabbit, n-heptane on rat, bile duct ligation on rat and tacrine (centrally acting anticholinesterase) on human liver-derived Hep G2 cells. Among all listed plants, for only few acute toxicity studies were conducted. For example, *Aloe barbadensis* did not show any sign of toxicity up to oral dose of 2 g/kg in mice (Chandan et al., 2007) and *Euphorbia fusiformis* ethanol extract single dose LD_{50} was found to be 10,000 mg/kg body weight when administered orally in mice (Anusuya et al., 2010).

Botanical herbs have been used for protection and treatment of liver diseases due to the presence of chemical constituents. For example, polyphenolic compounds have an important role in stabilizing lipid oxidation and are associated with antioxidant activity. Phenyl propanoids include phenolic compounds; those have shown remarkable effects on carbon tetrachloride-induced toxic indications in rats while eugenol and acetyleugenol from *Syzygium aromaticum* (Myrtaceae) exhibit cholagogue activity in biological models which increase the contractile activity and promote the discharge of bile from the liver and the gall bladder. Coumarin derivatives like 7-hydroxy, 7-s- hydroxy, 4-hydroxy, 4,7-dihydroxy and 4,7-dimethyl-5-hydroxy coumarin, coumarin-3-carboxylic acid and dicoumarol has ability to stimulate choleresis in rats (Vonk et al., 1978). Family Compositae (*Artemisia abrotanum*, *Cichorium intybus*) produce poly phenolic compounds and all those chemical compounds which have hydroxyl group at C-7 are become able to exerting a strong choleretic action (Dey et al., 2013). Silymarin is a most potent hepatoprotective compound and a mixture of isomeric flavolignans- silybin, silydianin and silychristen. It produces its defensive mechanism by competitively blocking the binding of phalloidin to receptors on the membrane of liver cell and obstructing the α-amanitin to infiltrate through the membrane into the cell nucleus (Valan et al., 2013). Essential oil also has shown its protective potential on liver histology, liver metabolic and serum profile. Myrtaceae, Umbelliferae, Labiatae and Rosaceae families increase the bile secretion and organic

Table II: Reported medicinal plants having hepatoprotective potential

SL. No.	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
1	*Abutilon bidentatum (Malvaceae)*	Leaves, Flowers	Aqueous methanol	PCT and CCl_4	Rabbit	↓ SGPT, SGOT, ALKP and DB	Yasmin et al., 2011
2	*Aegle marmelos (Rutaceae)*	Leaves	Ethanol	CCl_4	Mice	↓ SGPT, SGOT, ALP and DB	Sumitha and Thirunalasundari 2011
3	*Aerva lanata (Amaranthaceae)*	Leaves	Hydro-alcoholic	PCT	Rat	↓ levels of AST, ALP, DB and serum TB	Vertichelvan et al., 2000
4	*Allium sativum (Liliaceae)*	Fruit	No extract	INH	Rat	↓ AST, ALP, SGPT, SGOT and DB	Ilyas et al., 2011
5	*Alcea rosea (Malvaceae)*	Aerial parts	Aqueous methanol	PCT	Mice	↓ levels of AST, ALP, DB and serum TB	Hussain et al., 2014
6	*Aloe barbadensis (Liliaceae)*	Aerial parts	Chloroform, ether and petroleum	CCl_4	Mice	↓ AST, ALP and ALT levels. Restored depleted liver thiols	Chandan et al., 2007
7	*Aloe vera (Liliaceae)*	Leaves	Aqueous	gamma-hexachlorocyclohexane (Lindane)	Mice	↓ AST, ALP and ALT levels. Restored depleted liver thiols	Etim et al., 2006
8	*Amaranthus caudatus (Amaranthaceae)*	Whole plant	Methanolic extract	PCT	Rat	↓ ALT, AST, DB, TB and MDA level. ↑ ALB, GSH, TT, TP and CT levels	Kumar et al., 2011
9	*Amaranthus spinosus (Amaranthaceae)*	Whole plant	Ethanol	CCl_4	Rat	↓ ALT, AST, DB, TB and MDA level. ↑ ALB, GSH, TT, TP and CT levels	Zeashan et al., 2008
10	*Annona squamosa (Annonaceae)*	Leaves	Aqueous ethanol	INH	Rat	↓ TB, ALP, AST, ALT and γ-GT and ↑ TP level	Kaleem et al., 2006
11	*Arachniodes exilis (Dryopteridaceae)*	Rhizome	Ethanol	CCl_4	Mice	↓ AST, ALT, ALP and CHL. ↑ antioxidant enzyme activities of SOD, CAT, MDA and GSH	Zhou et al., 2010
12	*Asparagus racemosus (Liliaceae)*	Whole plant	Crude aqueous	PCT	Rat	↑ LPO, ↓ GSH and SOD	Om et al., 2011
13	*Baliospermum montanum (Euphorbiaceae)*	Leaves	Alcohol, Chloroform	Thioacetamide	Mice	↓ in SGOT , SGPT and CHL level	Kumar and Mishra, 2012
14	*Berberis lyceum (Berberidaceae)*	Bark	Alcohol	CCl_4	Rat	↓ TB, ALP, AST, and ALT levels	Khan et al., 2011
15	*Bixa orellana (Bixaceae)*	Seed	Methanol	CCl_4	Rat	↓ in SGOT , SGPT and cholesterol level	Ahsan et al., 2009
16	*Boerhaavia diffusa (Nyctaginaceae)*	Roots	Aqueous	Thioacetamide	Rat	↓ TB, ALP, AST, and ALT and ↑ TP	Rawat et al., 1997
17	*Bombax ceiba (Bixaceae)*	Flowers	Methanol	INH, RMP	Rat	↓ TB, ALP, AST, and ALT and ↑TP	Ravi et al., 2010
18	*Bupleurum kaoi (Umbelliferae)*	Roots	Ethanol	Dimethyl nitrosamine	Rat	↓ SGOT , SGPT, ALP, AST and ALT	Yen et al., 2005

Table II: Reported medicinal plants having hepatoprotective potential (Cont.)

SL. No.	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
19	*Butea monosperma (Fabaceae)*	Flowers	Aqueous	PCT	Rabbit	↓ ALP, AST and ALT	Maaz et al., 2010
20	*Cajanus cajan (Fabaceae)*	Whole plant	Methanol	CCl_4	Rat	↓ SGOT , SGPT and CHL level	Sing et al., 2011
21	*Calotropis procera (Apocynaceae)*	Flower	Aqueous alcohol	PCT	Rat	↓ SGPT, SGOT, ALP, bilirubin and LDLP, ↑ serum levels of HDL and tissue level of GSH.	Setty et al., 2007
22	*Carica papaya (Caricaceae)*	Fruit	Aqueous ethanol	CCl_4	Rat	↓ SGOT , SGPT, ALP, AST, ALT and LDH levels	Sadeque and Begum, 2010
23	*Carissa opaca (Apocynaceae)*	Leaves	Methanol	CCl_4	Rat	↓ lipid peroxidation (TBARS), AST, ALT, ALP, LDH and γGT levels	Sahreen et al., 2011
24	*Carissa spinarum (Apocynaceae)*	Roots	Ethanol	PCT and CCl_4	Rat	↓ SGOT , SGPT, ALP, AST, ALT and LDH levels	Hegde and Joshi, 2010
25	*Cassia fistula (Leguminaceae)*	Leaves	Ethanol	N-heptane	Rat	↓ ALP, AST, ALT, LDH and γ-GT	Bhakta et al., 2001
26	*Cassia occidentalis (Caesalpiniaceae)*	Leaves	Aqueous ethanol	PCT	Rat	↓ SGOT , SGPT, ALP, AST, ALT and LDH levels	Rani et al., 2010
27	*Casuarina equisetifolia (Casuarinaceae)*	Leaves and Bark	Methanol	CCl_4	Rat	↓ SGOT , SGPT and cholesterol level	Ahsan et al., 2009
28	*Cestrum nocturnum (Solanaceae)*	Leaves	Aqueous ethanol	PCT	Mice	↓ SGOT , SGPT, ALP, AST, ALT and LDH levels	Qadir et al., 2014
29	*Chamomile recutita (Asteraceae)*	Flower	Methanol	CCl_4	Rat	↑ Conc. of glutathione in Liver & blood and Na+K+ATPase activity. ↓ ALT, AST, ALP, TB and liver glycogen levels	Gupta et al., 2006
30	*Chenopodium murale (Chenopodiaceae)*	Whole plant	Aqueous methanol	PCT	Mice	↓ ALP, AST, ALT and TB levels	Saleem et al., 2014
31	*Cinnamomum tamala (Lauraceae)*	Leaves	Methanol	PCT	Mice	↓ SGOT, SGPT, ALP, lipid profile, TB and ↑ TP	Selvam et al., 2010
32	*Clerodendron inerme (Verbenaceae)*	Leaves	Ethanol	PCT	Rat	↓ SGOT, SGPT, SALP, TB and ↑ TP levels	Haque et al., 2011
33	*Coccinia grandis (Curcubitaceae)*	Leaves	Aqueous, Ethanol	CCl_4	Rat	↓ SGOT, SGPT, ALP, TB and CHL levels	Sunilson et al., 2009
34	*Cocculus hirsutus (Menispermaceae)*	Aerial parts	Methanol	Bile duct ligation	Rat	↓ ALT, AST, LDLC, HDL TC and STG. ↑ antioxidant enzyme activities of SOD, CAT, GSH-Px and GST	Thakare et al., 2009
35	*Cochlospermum planchoni (Coclospermaceae)*	Rhizome	Aqueous	CCl_4	Rat	↓ ALP, AST and TB levels	Nafiu et al., 2011
36	*Convolvulus arvensis (Convolvulaceae)*	Whole plant	Ethanol	PCT	Mice	↓ ALP, AST, ALP and TB levels	Ali et al., 2013

Table II: Reported medicinal plants having hepatoprotective potential (Cont.)

SL. No.	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
37	*Cordia macleodii (Boraginaceae)*	Leaves	Ethanol	CCl_4	Rat	↓ SGPT, SGOT, ALP and TB levels	Qureshi et al., 2009
38	*Cuscuta chinensis (Convolvulaceae)*	Seeds	Aqueous ethanol	PCT	Rat	↑ antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH	Yen et al., 2007
39	*Cyathea gigantea (Cyatheaceae)*	Leaves	Methanol	PCT	Rat	↓ SGPT, SGOT, ALP,TB, TP and reverse the hepatic damage	Kiran et al., 2012
40	*Decalepis hamiltonii (Asclepiadaceae)*	Roots	Aqueous	Ethanol	Rat	↓ ALT, AST, LDLC, HDL TC and STG. ↑ SOD, CAT, GSH-Px, GST, and GSH	Srivastava and Shivanand appa, 2006
41	*Dodonaea viscose (Sapindaceae)*	Leaves	Methanol	Alloxan	Rabbit	↓ ALT, AST, LDLC, HDL TC and STG	Ahmad et al., 2011
42	*Eclipta alba (Asteraceae)*	Whole plant	Ethanol	PCT	Mice	↓ ALT level, fatty degeneration and centrizonal liver necrosis	Tabassum et al., 2004
43	*Emblica officinalis (Phyllanthaceae)*	Leaves	Ethanol	CCl_4	Rat	↓ ALT, AST, LDLC, HDL TC and STG	Jose and Kuttan, 2000
44	*Equisetum arvense (Equisetaceae)*	Aerial parts	Methanol	Tacrine	Hep G2 cells	↓ AST, ALT, TP, TB and ALP levels	Oh et al., 2004
45	*Eucalyptus maculata (Myrtaceae)*	Leaves	Chloroform	PCT	Rats and Mice	↓ AST, ALT and ALP	Mohamed et al., 2005
46	*Euphorbia fusiformis (Euphorbiaceae)*	Tubers	Ethanol	RMP	Rat	↓ AST, ALT, ALP, SGPT and SGOT	Anusuya et al., 2010
47	*Feronia elephantum (Rutaceae)*	Fruit	Aqueous	CCl_4	Rat	↓ ALT, AST, billirubin level and ↑ TP levels	Kamat et al., 2003
48	*Ficus cordata (Moraceae)*	Roots	Methanol/ ethylacetate	CCl_4	Rat	Prevent liver cell death and LDH leakage	Donfack et al., 2011
49	*Foeniculum vulgare (Apiaceae)*	Leaves and fruit	Ethanol	CCl_4	Rat	↓ AST, ALT, ALP, SGPT and SGOT	Ozbek et al., 2003
50	*Galium aparine (Rubiaceae)*	whole plant	Alcohol	CCl_4	Rat	↓ALP, AST, and ALT levels	Khan et al., 2011
51	*Glycosmis pentaphylla (Rutaceae)*	Leaves and bark	Methanol	PCT	Mice	↓ in SGOT , SGPT and cholesterol level	Nayak et al., 2011
52	*Glycyrrhiza glabra (Fabaceae)*	Roots	Aqueous	CCl_4	Rabbit	↑ antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH	Al-Razzuqi et al., 2012
53	*Gundelia tourenfortii (Asteraceae)*	Stalk	Hydro alcoholic	CCl_4	Rat	↓ALP, AST, TB and ALT levels	Jamshidzadeh et al., 2005
54	*Halenia elliptica (Gentianaceae)*	Whole plant	Methanol	CCl_4	Rat	↓ SGOT, SGPT, ALP, AST and TB levels	Huang et al., 2010

Table II: Reported medicinal plants having hepatoprotective potential (Cont.)

SL. No.	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
55	*Haloxylon salicornicum (Chenopodiaceae)*	Aerial parts	Ethanol	CCl_4	Rabbit	↓ SGOT, SGPT, ALP and TB levels	Ahmad and Erum, 2011
56	*Hemidesmus indicus (Apocynaceae)*	Roots	Methanol	INH and RMP	Rat	↓ ALP, AST, TB and ALT	Prabhakaran and Rangasamy, 2000
57	*Hygrophila auriculata (Acanthaceae)*	Roots	Aqueous	CCl_4	Rat	↓ AST , ALT, ALP, TB and CHL levels	Dhanaraj et al., 2012
58	*Hypericum japonicum (Clusiaceae)*	Whole plants	Aqueous	CCl_4	Mice	↓ SGPT, SGOT, AST , ALT and ALP levels	Wang et al., 2008
59	*Hyptis suaveolens (Lamiaceae)*	Leaves	Aqueous	PCT	Rabbit	↓ TP and TB levels	Babalola et al., 2011
60	*Ipomoea staphylina (Convolvulaceae)*	Levaes	Hydro-alcohol	CCl_4	Rat	↓ALP, AST, ALT, SGPT, SGOT and CHL levels	Bag and Mumtaz, 2013
61	*Kohautia grandiflora (Rubiaceae)*	Leaves	Aqueous	PCT	Rat	↓ AST , ALT, ALP, TB and TP	Garba et al., 2009
62	*Laggera pterodonta (Asteraceae)*	Whole plant	Ethyl alcohol	CCl_4	Rat	↓ AST , ALT, ALP, TB and TP	Wu et al., 2007
63	*Launaea procumbens (Asteraceae)*	Whole plant	Methanol	CCl_4	Rat	↓ ALT, AST, ALP, LDH, LDL, HDL, TC and Triglycerides levels	Khan et al., 2012
64	*Lepidium sativum (Brassicaceae)*	Whole plant	Methanol	CCl_4	Rat	↓ AST , ALT, ALP, TB and TP	Afaf et al., 2008
65	*Luffa echinata (Cucurbitaceae)*	Fruit	Petroleum, acetone and methanol	CCl_4	Rat	↓ SGOT, SGPT, ALP and AST levels	Ahmed et al., 2001
66	*Malva parviflora (Malvaceae)*	Whole plant	Methanol	PCT	Mice	↓ ALP, AST, TP and ALT	Mallhi et al., 2014
67	*Momordica dioica (Cucurbitaceae)*	Leaves	Aqueous methanol	CCl_4	Rat	↓ ALP, AST, TP and ALT	Jain et al., 2008
68	*Mimosa Pudica (Mimosaceae)*	Leaves	Methanol	CCl_4	Rat	↓ AST , ALT, ALP, TB and TP. ↓ SGOT, SGPT	Rajendran et al., 2009
69	*Moringa oleifera (Moringaceae)*	Roots, flowers	Methanol	INH, RMP, PZA	Rat	↑ Antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH. ↓ AST , ALT, ALP, TB and TP. ↓ SGOT, SGPT	Pari and Kumar, 2002
70	*Nigella sativa (Ranunculaceae)*	Seeds	Alcohol	Galactosa-mine/ lipo-polysaccharide	Rat	↓ALP, AST, TB, TP and ALT	Gani and John, 2013
71	*Ocimum gratissium (Lamiaceae)*	Fresh leaves	Methanol	CCl_4	Rat	↓ ALT, AST and ALP levels	Friday et al., 2012
72	*Ocimum sanctum (Lamiaceae)*	Leaves	Alcohol	PCT	Rat	↓ SGPT, SGOT, ALT, AST and ALP	Lahon et al., 2011

Table II: Reported medicinal plants having hepatoprotective potential (Cont.)

SL. No.	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
73	*Orthosiphon stamineous (Lamiaceae)*	Leaves	Methanol	PCT	Rat	↓ SGPT, SGOT, LPO, ALT, AST and ALP	Maheswari et al., 2008
74	*Parkinsonia aculeata (Fabaceae)*	Leaves	Ethanol	PCT	Rat	↓ SGOT, SGPT, LDH, ALP, TB and ↑ TP levels	Shah and Deval, 2011
75	*Phoenix dactylifera (Arecaceae)*	Fruits	Methanol	Thioaceta-mide	Rat	Ameliorated the increased level of MDA and decline of GSH and amelioration of ALT, ALP and AST	Okwuosa et al., 2014
76	*Picrorhiza kurroa (Scrophulariaceae)*	Roots rhizomes	Ethanol	CCl_4	Rat	↓ALP, AST, ALT, SGPT, SGOT and CHL levels	Arsul et al., 2011
77	*Piper chaba (Piperaceae)*	Fruit	Aqueous acetone	Galactosa-mine/lipo-polysaccha-ride	Mice	↓ALP, AST, ALT, SGPT and SGOT levels	Matsuda et al., 2009
78	*Pistacia integerrima (Anacardiaceae)*	Bark	Ethyl acetate	PCT	Rat	↓ ALP, AST, and ALT levels	Joshi and Mishra, 2010
79	*Plumbago zeylanica (Plumbaginacea)*	Aerial parts	Methanol	PCT	Rat	↓ serum TB, SGPT, SGOT and ALP levels	Kanchana and Sadiq, 2011
80	*Phyllanthus emblica (Euphorbiaceae)*	Fruits	Aqueous	PCT	Rat	Significant ↑ TBC and less necrosis	Malar and Mettilda, 2009
81	*Phyllanthus niruri (Euphorbiaceae)*	Leaves, fruits	Aqueous methanol	PCT	Mice	↑ Antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH.	Tabassum and Agrawal, 2005
82	*Phyllanthus polyphyllus (Euphorbiaceae)*	Leaves	Methanol	PCT	Mice	↓ ALP, AST, ALT, SPGT and SGOT levels. ↑ Antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH.	Srirama et al., 2012
83	*Physalis minima (Solanaceae)*	Whole plant	Methanol	CCl_4	Rat	↓ SGPT, SGOT, LPO, TP, ALT, AST and ALP	Ahsan et al., 2009
84	*Plantago major (Plantaginaceae)*	Whole plant	Methanol	CCl_4	Rat	↓ TB, TP, SGPT, SGOT, AST and ALP levels	Turel et al., 2009
85	*Pterospermum acerifolium (Sterculiaceae)*	Leaves	Ethanol	CCl_4	Rat	↓ALP, AST, ALT, SGPT, SGOT and CHL levels	Kharpate et al., 2007
86	*Rheum emodi (Polygonaceae)*	Roots	Petroleum benzene, chloroform	CCl_4	Rat	↓ serum TB, TP, SGPT, SGOT, AST and ALP levels	Ibrahim et al., 2008
87	*Rosa damascene (Rosaceae)*	Fruit	Aqueous methanol	CCl_4	Rat	↓ SGPT, SGOT, LPO, TP, ALT, AST and ALP levels.	Achuthan et al., 2003
88	*Rubia cordifolia (Rubiaceae)*	Roots	Methanol	Thioactami de	Rat	↓ ALP, AST, ALT , SPGT and SGOT levels	Babita et al., 2007
89	*Rumex dentatus (Polygonaceae)*	Whole plant	Aqueous-methanol	PCT	Mice	↓ ALP, AST, TB and ALT levels	Saleem et al., 2014
90	*Sarcostemma brevistigma (Asclepiadaceae)*	Stem	Ethyl acetate	CCl_4	Rat	↓ AST, ALT, ALP, TP, SGOT and TB levels and liver necrosis.	Singh and Mehta, 2003

Table II: Reported medicinal plants having hepatoprotective potential (Cont.)

SL. No.	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
91	*Saururus chinensis (Saururaceae)*	Whole plant	Ethanol	CCl_4	Rat	↓ AST, ALT, ALP and CHL. ↑ antioxidant enzyme activities of SOD, CAT, MDA and GSH.	Wang et al., 2009
92	*Schouwia thebica (Arecaceae)*	Aerial parts	Diethyl ether, chloroform	CCl_4	Rat	↓ ALT, AST, SGPT, SGOT, levels of glucose, triglycerides and CHL	Awaad et al., 2006
93	*Scoparia dulcis (Scrophulariaceae)*	Leaves	Ethanol	CCl_4	Mice	↓ SGPT, SGOT, ALP, AST, TB and ALT levels	Tsai et al., 2010
94	*Silybum marianum (Asteraceae)*	Whole plant	Ethanol	CCl_4	Rat	↓ AST, ALT, ALP and CHL. ↑ antioxidant enzyme activities of SOD, CAT, MDA and GSH.	Ramadan et al., 2011
95	*Spondias pinnata (Anacardiaceae)*	Stem wood	Ethyl acetate, methanol	CCl_4	Rat	↓ SGPT, SGOT, CHL, AST, ALT, ALP, TP and TB levels.	Rao and Raju, 2010
96	*Solanum nigram (Solanaceae)*	Fruit	Ethanol	CCl_4	Rat	↓ AST, ALT, ALP, TP and TB levels	Raju et al., 2003
97	*Stachytarpheta indica (Verbenaceae)*	Whole plant	Ethanol	CCl_4	Rat	↓ SGPT, SGOT, CHL, AST, ALT, ALP, TP and TB levels.	Joshi et al., 2010
98	*Suaeda fruticosa (Amaranthaceae)*	Leaves	Aqueous methanol	PCT	Rabbit	↓ SGPT, SGOT, AST, ALT, ALP, TP and TB levels.	Rehman et al., 2013
99	*Tecomella undula (Bignoniaceae)*	Aerial parts	Aqueous ethanol	PCT	Rat	↓ ALP, AST, ALT, SPGT and SGOT levels . ↑ Antioxidant enzyme activities of SOD, CAT, GSH-Px, GST and GSH.	Singh and Gupta, 2011
100	*Tephrosia purpurea L (Fabaceae)*	Aerial parts	Aqueous ethanol	Thioaceta-mide	Rat	↓ ALP, AST, ALT, SPGT and SGOT levels. Ameliorated the increased level of MDA and decline of GSH and amelioration of ALT, ALP and AST	Khatri et al., 2009
101	*Terminalia chebula (Combetraceae)*	Fruit	Ethanol	RIF, INH, PZA	Rat	↓ AST, ALT, ALP, TP and TB levels	Tasduq et al., 2006
102	*Thunbergia laurifolia (Acanthaceae)*	Leaves	Aqueous	Ethanol	Rat	↓ SGOT, SGPT, AST, ALP and TB levels	Pramyothin et al., 2005
103	*Thymus linearis (Lamiaceae)*	Leaves	Aqueous and ether	PCT and CCl_4	Mice	↓ SGOT, SGPT, ALT, AST, ALP and TB levels	Alamgeer et al, 2014
104	*Trianthema decandra (Aizoaceae)*	Leaves	Aqueous	CCl_4	Rat	↑ GSH, SOD, CAT levels. ↓ SGPT, SGOT, AST, ALT, ALP, TP and TB	Balamurugan and Muthu-samy, 2008
105	*Trichodesma sedgwickianum (Boraginaceae)*	Leaves	Ethanol	CCl_4	Rat	↑ GSH, SOD, CAT levels. ↓ AST, ALT, ALP, TP and TB levels.	Saboo et al., 2013
106	*Tridax procumbens (Asteraceae)*	Aerial parts	Ethanol	Galactosa-mine/ lipopolysa-ccharide	Rat	↑ GSH, SOD, CAT levels. ↓ AST, ALT, ALP, TP and TB levels.	Ravikumar et al., 2005

Table II: Reported medicinal plants having hepatoprotective potential (Cont.)

SL. No.	Botanical plant (Family)	Parts used	Extract	Hepatotoxic agent	*In vivo* models	Remarks about liver marker enzymes	References
107	*Tylophora indica (Asclepiadaceae)*	Leaf powder	Aqueous alcohol	Ethanol	Rat	↓ AST, ALT, ALP, TP and TB levels	Gujrati et al., 2007
108	*Vernonia amygdalina (Compositae)*	Leaves	Aqueous	PCT	Mice	↓ SGOT, SGPT, LDH, ALP, DB and TB, TBAR and iron. ↑ CAT and TP	Iwalokun et al., 2006
109	*Viola odorata (Violaceae)*	Leaves	Aqueous methanol	PCT	Mice	↓ SGOT, SGPT, TB, AST, ALP, ↑ CAT, GSH levels	Qadir et al., 2014
110	*Vitex trifolia (Verbenaceae)*	Leaves	Aqueous ethanol	CCl_4	Rat	↓ tissue necrosis, SGPT, SGOT, CHL, AST, ALT, ALP, TP and TB levels	Manjunatha and Vidya, 2008
111	*Vitis vinifera (Vitaceae)*	Roots	Ethanol	CCl_4	Rat	↓ SGOT, SGPT, TB, AST, ALP levels. ↑ CAT and GSH levels	Sharma et al., 2012
112	*Zanthoxylum armatum (Rutaceae)*	Bark	Ethanol	CCl_4	Rat	↓ SGOT, SGPT, TB, AST, ALP, ↑ CAT, GSH levels	Verma et al., 2010

components to protect the liver by producing essential oils through choleretic activity. Umbelliferae has also ability to regenerate the hepatocytes by decreasing the liver damage and tissue necrosis.

Various diterpenoids, triterpinoids and sesquiterpenoids mostly from Lauraceae, Acanthaceae, Compositae families have active components β-eugenol and hinesol exhibited significant liver protecting effects by decreasing the SGPT and SGOT levels. Curcurbitiacin B, a triterpene compound obtained from Cucurbitaceae family has shown it's inflammatory and choleretic activity in biological models. Active constituents: glycyrrhizin and glycyrrhetic acid from of *Glycyrrhiza glabra* (Fabaceae) prevent the cirrhosis in rats (Al-Razzuq et al., 2012). Carotenoids include crocin and crocetin isolated from the fruits Rubiaceae family increase the bile secretion when administered into rabbits. Extracts from Scrophulariaceae, Rubiaceae and Plantaginaceae families produce glycosides like picroside I and picroside II, acubin, iridoid and geniposidic acid have shown liver protective effects against liver intoxication by carbon tetrachloride in mice. Saponins like saikosaponin D and saikosamponin A are produced by Leguminosae, Polygonaceae, Caryophyllaceae and Arleaceae families protect the liver in rabbits from hepatotoxin like carbon tetrachloride and inhibit the deposition of lipid peroxides in the liver of rats. Catechin, quercetin, kaempferol, narringenin, isohelichrysin, luteolin stachyrin, α-tocopherol (vitamin E) belong to flavonoid group of compounds. All families like Compositae, Liliaceae, Euphorbiaceae, Scrophulariaceae, Labiatae etc have flavonoids as their major constituents and that's why having potent potential for protection and treatment of liver diseases correlating with radical scavenging activity by donating hydrogen atom [H^+]. Flavonoids also have ability to scavenge the superoxide anion and hydroxyl radicals and terminate chain radical reactions (Kumar et al., 2011).

Conclusion

The purpose of clustering maximum plants having potential for treatment and protection of liver against various hepatotoxic agents is to develop an encyclopedia. Although we know the traditional hepatoprotective and antioxidant plants those are easily available in their crude form but their use in this form is so difficult or some time useless to cure the disease. So, still there is a strong need to develop some effective agents based on plant principles.

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