



E-ISSN: 2278-4136

P-ISSN: 2349-8234

www.phytojournal.com

JPP 2021; 10(3): 109-121

Received: 07-02-2021

Accepted: 15-03-2021

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Hepatoprotective effects of various medicinal plants: A systematic review

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Abstract

Various liver ailments (hepatitis, fatty liver, cirrhosis, liver cancer) are serious issues throughout the world, caused by viruses and hepatotoxic agents. The natural products play an important role in the discovery of many new drugs and active constituents. The medicinal plants and herbal preparations are used for the cure of various hepatic disorders. However, in severe cases the single medicinal plant is not so much satisfactory. These plants contain effective therapeutic agents such as alkaloids, glycosides, saponins, flavonoids, antioxidants and terpenes having hepatoprotective effects from the toxic agents.

Silbum marianum/milk thistle (Silymarin), *Glycyrrhiza glabra* (Glycyrrhizin), *Picrorhiza kurroa* (picrosides I and II), *Phyllanthus maderaspatensis* (β -sitosterol), *Andrographis paniculata* (Andrographolide), *Trichopus zeylanicus*, *Eclipta alba* and *Phyllanthus amarus* are sufficiently active against certain liver diseases.

Keywords: Hepatoprotective, hepatitis, medicinal plants, phytochemicals

Introduction

Liver is one the most important and largest organ of the body which plays an important role in the formation of hormones, serum proteins, clotting factors, cholesterol, bile, enzymes, detoxification of the toxic substances (certain drugs, alcohol), maintain homeostasis and metabolism of the various substances (carbohydrates, proteins and lipids). Deterioration of liver causes severe health problems. Hepatitis, fatty liver, cirrhosis and liver cancer are the major types of liver diseases. Cirrhosis and liver cancer are the most serious worldwide public health problems [1, 9].

Hepatitis is the inflammation of hepatocytes which is caused by viruses, chemicals/drugs and due to excessive use of alcohol. Viruses includes hepatitis A, B, C, D, E and G viruses. Among these viruses, hepatitis A, B, C and D are commonly occurring viruses. Common signs and symptoms of hepatitis are icterus (yellowish skin and eyes), nausea, vomiting, anorexia, fatigue, abdominal discomfort, tenderness in right hypochondriam region (RHR), fever, dark urine, myalgia and arthralgia [1-3]. Among these viruses the most dangerous virus is hepatitis B virus. Worldwide, approximately 240 Millions people have been effected from chronic hepatitis B virus. Chronic hepatitis B may causes liver cirrhosis, liver cancer. Liver cancer occurs due to damage of genetic material inside liver cells [2, 3].

From ancient time till nowadays herbal/medicinal plants are being used for the different diseases. In 2500 BC, Emperor Shen Nung circa wrote a Chinese book "Pen T' Sao," which contains 365 drugs of medicinal plants. Some medicinal plants of this book such as ephedra (Ephedrine, Pseudo ephedrine and Methyl ephedrine) cinnamon bark (Cinnamaldehyde, Camphor and Eugenol) are used nowadays. In 1550 BC, circa wrote a book "Ebers Papyrus" which shows 700 plants species used for therapeutic purposes [4].

Researcher confirmed in their research that herbal medicines are used for the various ailments of the liver [5-7]. Pharmacological properties of silybum marianum are antioxidant, anti-inflammatory, anti-lipid peroxidative, immunomodulating, antifibrotic and liver regenerating effects. It is used for toxic hepatitis, cirrhosis, fatty liver, viral hepatitis, radiation toxicity and ischemic injury of the liver. Picrorhiza kurroa has also good effects in the liver diseases [8]. Worldwide herbalist used different medicinal plants for prevention and treatment of liver diseases [10]. Many herbs have hepatoprotective effects while lot of plants are claimed to have liver healing properties drawn from various scientific researches [11, 12].

Hepatitis B and C are the most hazardous hepatitis as compared to the other types because hepatitis B virus has strong association with hepatocellular carcinoma while hepatitis C virus is strongly associated with liver cirrhosis(liver fibrosis) [13-20].

Aim of the study: The current systematic review focuses on ethanobotanical survey of medicinal plants used in the treatment of various hepatic disorders.

direct, scopus, midline databases, Handawi and Semantic scholars were searched for the terms of herbal medicine, natural products, medicinal plants, traditional medicines for hepatoprotective effects or hepatitis.

Methodology: Google scholar, PubMed, NCBI, Science

Table 1: The current study shows the systematic review of medicinal plants having hepatoprotective effects in various solvents (Methanol, Ethanol and Aqueous) and tabulated as below

S. No	Name of Plant	Family Name	Part used	Hepatotoxicity inducing agents	Extraction	Description of Biochemical Markers and Histopathological Parameters
1	<i>Orthosiphon Stamineus</i> (21)	Lamiaceae	Leaves	Acetaminophen	Methanol	Aspartate transaminase, ALT and Alkaline phosphatase
2	<i>Phyllanthus niruri</i> (22)	Euphorbiaceae	Leaves and fruits	CCl4	Methanolic and aqueous	Toxic effects of ccl4 reduced by the extract <i>Phyllanthus niruri</i> Which exhibit the reduction of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, DPPH (2, 2-diphenylpicrylhydrazyl).
3	<i>Cassia fistula</i> (23)	Leguminosae	Leaf	Carbon Tetrachloride	Menthol	Liver profile(SGPT, SGOT, serum bilirubin and (ALP)
4	a. <i>Apium graveonlens</i> b. <i>Hygrophila auriculata</i> (24)	a.Apiaceae b.Acanthaceae	Seeds	Thioacetamide and Acetaminophen	Menthol and petroleum ether	SGOT, SGPT, ALP, LDH, GLDH, S.bilirubin, histopathological studies.
5	<i>Luffa echinata</i> (25)	Cucurbits	Fruits	Carbon tetrachloride (CCL4)	Methanolic extracts, Petroleum ether and acetone	Serum glutamate oxaloacetate aminotransferase, serum glutamate pyruvate aminotransferase, alkaline phosphatase and serum albumin
6	<i>Croton oblongifolius</i> And <i>Apiumgra_ eolens</i> Linn. (26)	Euphorbiaceae or euphorbias Apiaceae/ Umbelliferae	Aerial parts Seeds	Carbon tetrachloride	Acetone, methanol and Petroleum ether	Estimation of liver aminotransferases (GOT and GPT), alkaline phosphatase, total protein and Albumin
7	<i>Halenia elliptica</i> (27)	Gentianaceae	All parts of the plant	Tetrachloromethane	Methyl alcohol	Significant decrease in alanine aminotransferase, aspartate aminotransferase, ALKP, serum bilirubin level, Histopathological evaluation
8	<i>Equisetum arvense</i> /horsetail (28)	Equisetaceae	Aerial parts	Carbon tet (CCl4)	Methanol extract	ALT, aspartate transaminase (AST), ALP, and Histopathology studies of liver tissues
9	<i>Trichosanthes cucumerina</i> (29)	Cucurbitaceae	Whole plant	CCL4	Methanolic	Serum ALT, AST, ALP, TB, TP and albumin (ALB), glutathione (GSH) and malondialdehyde (MDA) level were estimated. Evaluation of histopathological changes.
10	<i>Pittosporum neelgherrense</i> (30)	Pittosporaceae	Bark	Paracetamol, 2-amino-2-deoxy-D-galactose, Carbon tetrachloride (ccl4).	CH ₃ OH (Methanol)	Serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase.
11	<i>Aloe barbadensis mill</i> (31)	Liliaceae	Dried aerial parts	Tetrachloromethane (CCl ₄)	Trichloromethane, Petroleum ether and methanol	Serum transaminases (ALT and AST), ALKP, serum bilirubin, glucose-6-phosphatase, serum triglycerides or triacylglycerol level and glutathione level.
12	<i>Cochlospermum vitifolium</i> (32)	Cochlosperma-ceae	Bark	Carbon tetrachloride	Hexane (C ₆ H ₁₄), methylene chloride Methyl alcohol	Serum glutamic pyruvic transaminase and ALP
13	<i>Lactuca indica</i> (33)	Asteraceae / Compositae	Aerial parts	Carbon tetrachloride	Methanolic	SGPT and alkaline phosphatase
14	<i>Orthosiphon stamineus</i> (34)	Labiatae / Lamiacea	Leaves	Paracetamol	Methanol	Lipid peroxides, ALP, SGPT and SGOT.
15	<i>Cassia fistula</i> (35)	Fabaceae OR Leguminosae	Seeds	Paracetamol	Methanolic	Serum bilirubin, ALP SGOT and SGPT
16	<i>Pterocarpus marsupium</i> Roxb (36)	Papilionaceae	Bark(Stem)	Carbon tetrachloride (CTC) (perchloromethane)	Both Methanolic extract and	Total bilirubin, alkaline phosphatase, serum alanine and protein. Transaminases (ALT and AST) and Microscopic examination of

					aqueous extract used in the study	liver tissue.
17	<i>Spondias pinnata</i> (37)	Anacardiaceae	Stem	Carbon tetrachloride	C ₄ H ₈ O ₂ and Methanolic	SGPT or ALT, SGOT or AST, ALKP, serum bilirubin level in the blood.
18	<i>Juncus subulatus</i> (38)	Juncaceae	Powdered tubers	Paracetamol(PCM) (C ₈ H ₉ NO ₂)	70% methanol	Liver enzymes e.g ALT, AST, ALP), total albumin and protein level. serum cholesterol, triglycerides, nitric oxide (NO), malondialdehyde (MDA).
19	<i>Phyllanthus polyphullus</i> (39)	Euphorbiaceae	Leaves	Acetaminophen (C ₈ H ₉ NO ₂)	Methanolic	Aspartate transaminase. (AST), alanine amino transferase (ALT), (ALP) alkaline phosphatase, total bilirubin, gamma glutamyl. transferase, lipid peroxidase. (LPO) with a reduction catalase and glutathione S-transferase (GST).
20	<i>Scoparia dulcis</i> (40)	Scrophulari-aceae	Whole plant	Carbon tetrachloride	i.Methanol ii.diethyl-ether	Pathological studies of liver tissue, serum AST, alanine amino transferase (ALT), alkaline phosphatase (ALP) and total bilirubin
21	<i>Hoslundia opposita</i> (41)	Lamiaceae	Stem	Paracetamol and carbon tetrachloride	Methanol and ethyl Acetate	Serum AST, SGPT and Bilirubin
22	<i>Tylophora indica</i> (42)	Asclepidaceae	Leaves	Carbon tetrachloride	Methanolic	Serum GPT, GOT, ALP and Bilirubin
23	<i>a.Cajanus cajan, b.Caesalpinia bonduc, c.Argemone Mexicana, d.Casuarina equisetifolia, e.Glycosmis pentaphylla, f.Bixa orellana, g.Physalis minima,</i> (43)	a. Fabaceae b. Fabaceae c. Papaveraceae d. Casuarinaceae e. Rutaceae f. Bixaceae g. Solanaceae	Plant materials	Carbon tetrachloride	Methanolic extract	Serum (cholesterol, GOT and GPT)
24	<i>Tridax procumbens</i> (44)	Compositae	Foliage	Carbon tetrachloride	Ethanol extract	Catalase, Glutathione (N-(N-L-gamma-glutamyl-L-cysteiny) glycine and superoxide dismutase.
25	<i>Saururus chinensis</i> (Lour.) Baill (45)	Saururaceae	Whole plant	Carbon tetra-chloride	Ethanol	Lishu wang <i>et al.</i> conducted a study in 2009. The study suggested that ethanolic extract of <i>Saururus chinensis</i> effectively decreased the elevated level of hepatic enzyme (HA, SOD, AST, ALT, MDA, TAG, LP and ALB. Histopathological observation also suggested that the plant has antifibrotic effects against CCL4 toxicity.
26	<i>Schisandrae chinensis</i> (SC) (46)	Magnoliaceae	Dried fructus	CCL4	Ethanol	Significant decrease of liver enzyme (ALT, AST, ALP) due to use of ethanolic extract of <i>Schisandrae chinensis</i>
27	<i>Cordia macleodii</i> (47)	Boraginaceae	Leaves	CTC	Ethanol	Liver enzymatic activity Total bilirubin and serum [GPT, GOT and Alk. Phosphatase (ALP)]
28	<i>Arachniodes exilis</i> (48)	Dryopterid-aceae	Rhizomes	Perchloromethane	Ethanol	Evaluation of antioxidant effects of the extract (superoxide dismutase, DPPH, and H ₂ O ₂). Ser.GPT, GOT and malondialdehyde
29	<i>Momordica dioica.</i> (49)	Cucurbitaceae.	Leaves.	Tetrachloromethane	Aqueous solvent and ethanolic extract	Liver sections histopathological examination showed normal architecture. (AST), (ALT), total bilirubin and serum alkaline phosphatase (SALKP)
30	<i>Gentiana olivieri</i> (50)	Gentianaceae	Aerial parts	Ccl4	Ethanol	Estimation of malondialdehyde in liver tissue, and glutathione level, along with of plasma transaminase enzyme levels (SGPT/ALT and SGOT/AST)
31	<i>Clerodendrum inerme/ Clerodendrum inerme</i> (Linn.) Gaertn / <i>Nolkameria inermis</i> L. (51)	Verbenaceae	Leaves	Methane tetrachloride	C ₂ H ₅ OH	Ser. ALT, AST, alkaline phosphatase, triglyceride and total cholesterol level (TC)
32	<i>Zanthoxylum armatum</i> (52)	Rutaceae/ Rue family/ citrus family	Bark	Carbon tetrachloride	Extract of <i>Zanthoxylum armatum</i> in C ₂ H ₅ OH solvent	LFT along with antioxidant enzymes such as glutathione, superoxide dismutase, catalase

33	<i>Kalanchoe pinnata Pers (53)</i>	Crassulaceae/ stonecrop family or the orpine family	Leaves	Carbon tetrachloride or Ccl4	Ethanol extract and fresh juices of the leaves	Serum AspAT (SGOT), serum glutamyl pyruvate transaminase (SGPT) alkaline phosphatase (ALKP), serum bilirubin (SBLN) and histological studies of liver.
34	<i>Nelumbo nucifera Gaertn (54)</i>	Nelumbon-aceae	Leaves	Carbon tetrachloride	Ethanol	AL.transaminase and ASAT
35	<i>Bupleurum kaoi (55)</i>	Apiaceae	Power of dried Roots	Carbon tetrachloride	Ethanol	Microscopic examination of liver with Serum level of GOT, GPT, bilirubin (BLN) and alkaline phosphatase (ALKP)
36	<i>Euphorbia fusiformis (56)</i>	Euphorbiaceae	Ethanol extract of Tubers	Rifampicin	Ethanol	250 mg/kg oral dose has significant effects to decrease SGOT,SGPT, gamma glutamyl transpeptidase (GGTP), total bilirubin, alkaline phosphatase (ALP), and total protein in albino rats
37	<i>Phyllanthus amarus Schum. Et Thonn. (57)</i>	Euphorbiaceae	All parts of the plant are used except the root	AFB-1	Ethanol	Ethanol extract enhance the reduced level of glutathione. The oxidant activity of glutathione peroxidase, catalase, GST and superoxide dismutase (SOD) are inhibited.
38	<i>Azadirachta indica (58)</i>	Meliaceae.	Leaf	Paracetamol or Acetaminophen (C ₈ H ₉ NO ₂)	Ethanol extract(70%)	Significant lower the liver enzyme (Glutathione peroxidase (GPO), catalase (CAT), glutathione-S-transferase (GST),and superoxide dismutase (SOD)
39	<i>Phyllanthus Niruri (59)</i>	Euphorbiaceae.	Leaf of the plant	Paracetamol	Ethanol extract 50% and Petroleum ether	Serum SGOT, SGPT, SALP and γ -glutamyltransferase (GGT) level decreased after the use of <i>Phyllanthus Niruri</i> extract with the recovery histopathological effects of the liver due to paracetamol.
40	<i>Capparis spinosa (60)</i>	Capparidaceae/ caper family	Root bark	Carbon tetrachloride	Ethanol	Serum ALT and AST are reduced after use of ethanol extract of <i>Capparis spinosa</i>
41	<i>Cleome viscosa linn (61)</i>	Capparidaceae	Leaf powder	Carbon tetrachloride	Ethanol (C ₂ H ₆ O)	Important enzyme such as Aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) and total bilirubin are decreased by the use of <i>Cleome viscosa linn</i> extract. Histopathological analyses of liver samples shows hepatoprotective activity from Ccl4.
42	<i>Picrorhiza Kurrooa (62)</i>	Scrophulari-aceae	Root and rhizomes	Alcohol-carbon tetrachloride	Ethanol	12 mg/kg/ p.o dose lower the elevated level of serum GOT, GPT, acid phosphatase, alk. phosphatase, LDH and bilirubin level in the rat.
43	<i>Ginkgo Biloba (63)</i>	Ginkgoaceae	Dried extract	(CTC)	Ethanol	S.bilirubin level (total, direct and indirect) SGPT, SGOT, Serum alkaline phosphatase, and histopathological analysis confirm hepatoprotective effects of the plant extract
44	<i>Averrhoa carambola (64)</i>	Oxalidaceae	Fruit	Diethylnitrosamine (DNA) and Carbon tetrachloride(ccl4)	90% ethyl alcohol was used for the extraction	Hepatotoxicity was induced by DENA and CCL4 which was recovered by the <i>Averrhoa carambola</i> fruit extract in the following manner. The investigation exhibits that fruit extract of <i>Averrhoa carambola</i> has prophylactic role against hepatocellular carcinoma (HCC).
45	<i>Pterospermum acerifolium. (65)</i>	Sterculiaceae...	Leaves...	Carbon tetrachloride.	Ethanol.	25mg/kg/day dose reduced serum aspartate amino transferase (AST),(ALT) and alkaline phosphatase (ALP) level in the rats.
46	<i>Vitex trifolia (66)</i>	Verbenaceae	Leaves	Carbon tetra-chloride	Ethanol and water	Increased biomarker such as aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) due to ccl4 toxicity are Significant reduced after treated with ethanol and aqueous extract of <i>Vitex trifolia</i> . CCl ₄ induced hepatocellular injury is restored into normal architecture by using the extract of the plant
47	<i>Cochlospermum Planchoni (67)</i>	Coclosperm-aceae	Rhizomes/ creeping rootstalks/ rootstalks	Carbon tetrachloride (CTC) or Tetrachloromethane (TCM)	Aqueous	Increased liver enzyme (SGTP,SGOT, AKP) and total bilirubin are reduced due to use of aq. extract of <i>cochlospermum Planchoni</i>
48	'Teng-Khia-U' (Taiwan traditional medicine)	Asteraceae		(D- galN) or (2-	Water Extract of	Ser. glutamate-oxalate-transaminase and GPT level decreased after treatment and

	<i>a. E. mollis H.B.K. and b. Pseudo-elephantopus spicatus (Juss. ex Aubl.) Rohr c. Elephantopus scaber L., (68)</i>		Whole plant	Amino-2-Deoxy-Galactopyranose)and acetaminophen (AAP)	the plants	pathological changes of the liver improved after treatment
49	<i>Asparagus racemosus (69)</i>	Liliaceae	Whole plant	γ -radiation (range of 75–900 Gy)	Crude extract and a purified aqueous Fraction	Extract of the plant prevent liver damage from oxidative stress of lipid peroxidation
50	<i>A traditional Chinese herbal drug "CGX" which name meaning liver cleaning from the toxic substances (70)</i>	-----	-----	Carbon tetrachloride (CTC/ccl4)	Aqueous	CGX significantly decreased the catalase activity and glutathione content and it inhibit the TNF- α in liver tissue induced by ccl4
51	<i>a. Tephrosia purpurea (L.) pers And b. Tecomella undulate seem (71)</i>	a.Fabaceae b.Bignoniaceae	a.Aerial parts b.stem bark	Thioacetamide (C ₂ H ₅ NS)	a.Hydro-ethanolic b.Ethanolic extract	Extract of the plants decrease the serum aminotransaminase (GPT and GOP), GTT, ALP and total bilirubin along with improvement of glutathione level.
52	<i>Boerhaavia diffusa (72)</i>	Nyctaginaceae	Roots	Acetothioamide (CH ₃ CSNH ₂)	Aqueous	High level GOT, GPT and Bilirubin and ALP level are reduced after use of <i>Boerhaavia diffusa</i> aqueous extract
53	<i>Gundelia tourenfortii (L.) (73)</i>	Asteraceae	Dried powdered of foot stalks	Carbon tetrachloride	Hydroalcoholic	The histopathological study of liver section support that hydroalcoholic extract of <i>Gundelia tourenfortii (L.)</i> have hepatoprotective effects. SGOT, SGPT, ALP, and serum bilirubin level have significantly reduced.
54	<i>Cassia occidentalis (74)</i>	Caesalpini-aceae	Leaves	Paracetamol (C ₈ H ₉ NO ₂)and ethyl alcohol (C ₂ H ₅ OH)	Aqueous-ethanolic extract(50% v/v)	Histopathological alteration are restored with decrease level of Serum transaminases (asp. aminotransferase and alanine transaminase), alkaline phosphatase and serum cholesterol.
55	<i>Phyllanthus amarus(PA) (75)</i>	Euphorbiaceae	All parts of the plant except the underground parts	Ethanol	Aqueous	Increase level of serum transaminases level (AST and ALT), serum triacylglyceride (STAG), hepatic triglycerol is significantly decreased by use of (PA) extract. Histopathological studies confirm that extract of (PA) prevents liver injury.
56	<i>Thunbergia.laurif-olia Linn. (76)</i>	Acanthaceae	Leaves	Ethanol	Aqueous extract	Pornpen pramyothin <i>et al.</i> conducted the relevant study which demonstrate that Serum glutamyl oxaloacetic acid transaminase (SGOT), SGPT, Alk.phos and serum billirun level are significantly reduced. The study revealed that ethanolic extract of <i>Thunbergia laurifolia Linn</i> has hepatoprotective activity.
57	<i>Nigella Sativa(Thymoquinone) (77)</i>	Ranunculaceae	Seeds	Tert-butyl hydroperoxide(TBHP)	Aqueous-ethanolic extract	Thymoquinone prevent the release of ALT and AST from the liver cells by healing of hepatocytes
58	<i>Piper chaba (78)</i>	Piperaceae	Fruit	i.D-galactosamine (2-Amino-2-Deoxy-D-Galactose) ii.lipopolysaccharides	Aqueous acetone	The study explored that <i>Piper chaba</i> extract normalized the deteriorate enzyme of the liver (SGPT, Alk. phos and GOT) caused by the toxic agents.
59	<i>Cuscuta chinensis (79)</i>	Convolvulaceae	Seeds	(AAP or C ₈ H ₉ NO ₂)	Ethanolic And Aqueous	Antioxidant effects of the certain enzyme such as catalase, superoxide dismutase (SOD) and malondialdehyde (MDA) to prevent liver damage.
60	<i>Hygrophila auriculata (80)</i>	Acanthaceae	Root	CTC	Aqueous extract	<i>Hygrophila auriculata</i> Aqueous extract reduce the following enzyme of the liver. a.Alanine transaminase, b.aspartate transaminase (AST) c.alkaline phosphatase (ALP) d.total bilirubin. e.Investigation reveals normal histology of liver.
61	<i>Byrsocarpus coccineus Schum. & thonn. (81)</i>	Connaraceae	Leaf	CCl4 (Carbon-tetrachloride)	Aqueous	Ccl4 causes hepatolysis and increases serum ALT, AST and total protein, which are reduced with the help of <i>Byrsocarpus coccineus Schum. & thonn</i> extract.

62	<i>Hypericum japonicum</i> (82)	Clusiaceae	Whole Plant	Isothiocyanate (α -naphthyl-Isothiocyanate)($C_{11}NH_7S$) (Anit) and Carbon tetrachloride	chloroform, aqueous, petroleum ether solvents are used for extracts	<i>Hypericum japonicum</i> manifest potential effects against hepatotoxicity along with reduction of several liver enzyme.
63	<i>Decalepis hamiltonii</i> (83)	Asclepiad-aceae	Roots	Carbon tetrachloride	Aqueous extract	1. Significantly protective effects of liver toxicity with decrease liver marker enzyme (LDH, AST, ALT and AKLP). 2. Inhibition of lipid peroxidation and protein carbonylation. 3. Restoration antioxidant enzymes SOD, glutathione, GST, CAT, GPx.
64	Berginin is an important constituents of (<i>Mallotus japonica</i>) (84)	Euphorbiaceae	Cortex	Carbon tetrachloride	Water	Elevated serum enzyme (SGOT, SGPT, sorbitol dehydrogenase and GGT are restore towards normal values. Reduced activity of glutathione S-transferase and glutathione reductase was maintain by "Berginin".
65	<i>Ganoderma lucidum</i> (85)	Polyporaceae	Winter mushroom	(2-Amino-2-Deoxy-D-Galacto-pyranoside) OR $C_6H_{13}NO_5$	Aqueous juice	Serum (AST, ALT) and MDA, GSH and histological investigation reveals the hepatoprotective activity.
66	<i>Rubia cordifolia</i> Linn (86)	Rubiaceae	Roots	CCl_4	Aqueous ethanolic	After the use of aqueous ethanolic extract the serum glutamate oxaloacetate transaminase (SGOT), serum alkaline phosphatase (SALP), serum glutamate pyruvate transaminase (SGPT), and γ -Glutamyltransferase (G-glu-transpept) are reduced to normal level
67	<i>Picrorrhiza rhizome</i> (87)	Scrophulari-aceae	Dried rhizome	Poloxamer 407 (px-407)	Water/aqueous	AST, ALT, LDL, triglyceride (TG) and total cholesterol levels were observed to reduce after use of <i>Picrorrhiza rhizome</i>
68	<i>Artemisia absinthium</i> linn (88)	Asteraceae	Powder form of aerial parts	10 μ g carbon tetrachloride (CCl_4) injected i.v to mice to produce toxic effects	Aqueous	Reduced the following in the serum. a. aspartate transaminase (AST), b. alanineaminotransferase (ALT) c. TNF- α (tumor necrosis factor) d. interleukin-1(IL-1) e. superoxide dismutase (SOD)
69	<i>Carum copticum</i> L. (89)	Apiaceae/ Umbelliferae	Seeds	Acetaminophen And CCl_4 (Carbon tetrachloride)	Water	Aminotransferases (AST and ALT), and alkaline phosphatase (ALP)
70	a. <i>Mamoridca subangulata</i> And b. <i>Naragamia alata</i> (90)	a. Cucurbitaceae b. Meliaceae	a. Leaf and b. All parts of the plant	Paracetamol	2% (w/v) gum acacia is used for preparation of 10% aqueous suspension	γ GT, serum amino-transferases (GOT), and (SGPT)
71	<i>Chamomile recutita capitula</i> (91)	Asteraceae/ Compositae	Fresh natural mature Capitula	Paracetamol(Acetaminophen)(AAP)	Aqueous Ethanolic	Liver serum marker enzymes AST, ALT and bilirubin level are reversed to normal level by using chamomile extract and shows the antihepatotoxic effects.
72	<i>Aerva lanata</i> Linn (92)	Amaranth-aceae	Coarse powder plant material	Paracetamol (PCM) or Acetaminophen	Hydro-acholic	Serum ALT(IU), AST(IU), ALP and bilirubin level reduced by hydroalcoholic extract of <i>Aerva lanata</i> Linn.
73	Galic acid an active chemical constituents of (<i>Acacia confuse</i>) (93)	Leguminosae OR Fabaceae	Bark	Carbon tetrachloride	Hydro-alcoholic	Galic acid reduced the following substances. i. Malondialdehyde (MDA) ii. Aspartate transaminase (AST) iii. alanine aminotransferase (ALT) iv. (CYP2E1) v. SOD vi. Glutathione peroxidase (GPX) vii. Catalase (CAT).
74	a. <i>Calotropis procera</i> , b. <i>Kigelia africana</i> , c. <i>Alchornea cordifolia</i> and d. <i>Hibiscus sabdariffa</i> (94)	a. Apocynaceae b. Bignoniaceae c. Euphorbiaceae d. Malvaceae	Leaves of a, b, c and Calyces(d)	Paracetamol (AAP)	Distilled water	Normalized the serum GPT and GOT level along with the reduction of lipid peroxidation product activities (catalase (cat), superoxide dismutase, glutathione peroxidase (GTPO)

75	<i>Alocasia indica</i> Linn (95)	Araceae	Leaves	Acetaminophen (PCM)	Hydro-alcoholic	Extract of <i>Alocasia indica</i> Linn decrease serum transaminases enzyme along with ALPase and total bilirubin
76	<i>Embelia ribes</i> (96)	Myrsinaceae	Fruits	Paracetamol	Water	Elevated enzymes such as SGPT, SGOT, ALP, Total bilirubin (TB) caused by paracetamol toxicity are turn back to normal level. The relevant study exhibit hepatoprotective activity.
77	<i>Tylophora indica</i> (97)	Asclepiadaceae	powder of the leaves	Ethanol	Aqueous	<i>Tylophora indica</i> extract indicates the antihepatic activity with significantly turn down serum liver transaminases enzyme asp.TA, AlnTA, alkaline phosphatase (ALKP) and total bilirubin.
78	<i>Ricinus Communis. L</i> (98)	Euphorbiaceae	Leaves or Foliage	Carbon tetrachloride	Cold aqueous extract	The relevant study was conducted by M.V Natu <i>et al.</i> on the leaves of <i>Ricinus communis.linn</i> . The conclusion of the study described that the plant exhibited to recover the damage tissue of the liver and decreased the elevated level of liver biomarker such as asp.amino transferase, ALT, alk. phosphatase and total bilirubin.
79	<i>Ocimum snctum</i> (99)	Labiatae	Leaf	Acetaminophen (PCM)	Hydro-alcoholic	Hydroalcoholic extract of <i>Ocimum sanctum</i> normalized the necrotic lesion of the liver caused by PCM toxicity, with remarkable decrease of (AST), SGPT or alanine amino transferase (ALT), total bilirubin, alkaline phosphatase (ALP).
80	<i>Trianthema decandra L.</i> (100)	Aizoaceae martynov	Leaves	Carbon tetrachloride	Aqueous	<i>Trianthema decandra L.</i> extract reduce liver toxicity triggered by CCl ₄ and fall serum AST, ALT and Bilirubin upto regular level.
81	<i>Hibiscus esculentus</i> Linn (101)	Malvaceae	Roots	1,1,1,1-tetrachloro methane (CTC)	Water	Hepatic enzyme SGPT (7-56 IU), SGOT (5-40 IU), ALP (20-140 IU) and total bilirubin (TB) (0.1-1.2 mg/dl) are reduced to normal level with <i>Hibiscus esculentus</i> Linn therapy.
82	<i>Aegle marmelos(L.) correa Ex Roxb</i> (102)	Rutaceae	Pulp/seeds	(1,1,1,1-tetrachloro methane) or Carbon tetrachloride (CTC) or tetrachloro-methane	Water	Elevated level of AST, ALT and bilirubin are abated via aqueous extract of <i>Aegle marmelos correa ex Roxb</i> and the study reveals hepatoprotective effects
83	<i>Bauhinia purpurea</i> (103)	Fabaceae	Leaves	Paracetamol	Methanolic (CH ₃ OH)	Investigation reveals that ethanolic extract of <i>B.purpurea</i> remarkably reduced the AST and ALT level along with reduction of necrotic lesion/area of the liver caused by PCM.
84	<i>Elephantopus scaber</i> (104)	Asteraceae	Leaves of the plant in the month of October	Alcohol	Ethanol	The plant possess to reduce the serum biochemical profile of liver (AST, ALT, ALP, triglyceride,total bilirubin). The study also demonstrate antihepatic activity treated with ethanol extract.
85	Traditional Chinese formula(Zhi-Zi-Da-Huang 26)with 8:1:3:4 ratio of, i. Semen Sojae Preparatum ii. Rheum officinale Baill iii. Gardenia jasminoides Ellis. iv. Citrus aurantium L. (105)	-----	-----	Alcohol	Diethyl ether and water	The formula shows a significant reduction of transaminases and antioxidant substances such as glutathione, malondialdehyde (MDA) and superoxide dismutase (SOD).
86	Fermented Soybean (Nutrient Enriched Soybean Tempeh) 106	-----	-----	Alcohol	Cooled water extract	1000mg/kg weight material has lower the liver biomarker and also antioxidant properties.
87	<i>Laggera pterodonta</i> (107)	Asteraceae	All parts are used	Ccl ₄ (CTC), 2-Amino-2-Deoxy-D-Galactopyranose, (DPPH)	i. Ethyl alcohol ii. aqueous	Extract of the plant material decrease the level of transaminase beside with alkaline phosphatase (ALP) and total protein and bilirubin.
88	<i>Cassia tora</i> (108)	Caesalpini-aceae	Leaves	Carbon tetrachloride	Ethyl-acetate or ethyl-ethanoate (C ₄ H ₈ O ₂)	Exhibit antioxidant activity of glutathione to prevent liver cells from hepatolysis due to which the liver biomarker are reduced to normal.
89	<i>Sarcostemma brevistigma</i> (109)	Asclepiad-aceae	Stem	Carbon tetrachloride	Acetic acid ethyl ester (C ₄ H ₈ O ₂)	Important enzyme of the liver such as Serum glutamic oxaloacetic transaminase (SGOT), serum GPT, alkaline phosphatase(ALPase or

						Alk Phos), gamma glutamate trans-peptidase (GGTP) and total bilirubin are decreased via <i>Sarcostemma brevistigma</i> extract.
90	<i>Carissa opaca</i> (110)	Apocynaceae	Leaves	Carbon tetrachloride	Methanolic	The study indicated that the leaves extract has protective properties against ccl4 toxicity and significantly decrease the ALKP ant bilirubin level along with serum aminotransferases (GPT, GOT).
91	<i>Amaranthus spinosus</i> (111)	Amaranth-aceae	Whole plant	Carbon tetrachloride	Petroleum ether	i. <i>Amaranthus spinosus</i> extract indicates to normalize the damage tissue of liver caused by CCL4. ii. It also decrease aminotransferases, serum alkaline phosphatase (SALP) and total bilirubin which are deteriorate by carbon tetrachloride
92	<i>Terminalia chebula retzius</i> (112)	Combretaceae	Whole plant	<i>tert</i> -butylhydroperoxide-(<i>t</i> -BHP-)	Water	The study showed that extract of the plant remarkably reduced the changes(increase of liver enzyme) with prevention of liver injury via oxidative stress.
93	<i>Saponarin is an active constituent of Gypsophila trichotoma</i> Wend. (113)	Caryophyllaceae	Overground parts of plant material	PCM(paracetamol or acetaminophen)	80% methanol	In this study, saponarin has the ability to normalize the damage tissues of the liver to normal cellular architecture. It also exhibited the Antioxidant properties to reduce SOD, CAT, GST, GSH-Px.
94	<i>Propolis (a sticky hive substance collected by honeybees from several flower sources</i> (114)	-----	-----	D-galactosamine (2-Amino-2-Deoxy-Galactopyranoside) (ADGP) and alpha-tumor necrosis factor (tnf-a)	Wood alcohol (CH ₃ OH) and water extracts	Conclusion of the study are, i. Free radical scavenging activity ii. Successfully restore SGPT, SGOT and Alk. Phosphatase iii. Successfully alleviated hepatic injury stimulated by D-galactoseamine.
95	<i>Amalkadi Ghrita 24 (AG), is composed of cow's ghee and the following herbs. a. Glycyrrhiza glabra (10g) and b. Emblica officinalis(10g) (115)</i>	-----	-----	Ccl4	Crude drug	<i>Amalkadi Ghrita 24</i> mitigated the biochemical markers upto normal level. The study also demonstrated that AG restored the normal function and architecture of the liver
96	<i>Caesalpinia crista</i> Linn (synonyms of <i>C. bonducella</i> [L.]Roxb.)(116)	Fabaceae	Leaves	Liver Toxicity is induced by iron-Overload	100 g of powder was mixed in methanol : water (7 : 3)	The study concluded that <i>C. bonducella</i> [L.]Roxb extract has antioxidant activity. The ability of the plant material is to prevent the liver damage from iron overload by chelating mechanism.
97	a. <i>Bridelia ferruginea</i> Benth b. <i>Vernonia amygdalina</i> c. <i>Tridax procumbens</i> , d. <i>Ocimum gratissimum</i> . L and e. <i>Lawsonia inermis</i> (117)	a. Euphorbi-aceae b. Asteraceae/ Compositae/ sunflower family c. Compositae d. Lamiaceae e. Lythraceae	Leaves	2-Acetylamino-flourene(2-AAF)	100 g of leaves are soaked in 500ml of water	The leaves extract showed hepatoprotective effects against histopathological changes induced by 2-AAF.
98	(1) <i>Cichorium intybus</i> (2) <i>Silybum marianum</i> (118)	Asteraceae	Leaves	Thioacetamide(TAA)	Chloroform (CHCl ₃) OR Trichloromethane	1. The study explained that the leaves of <i>Cichorium intybus</i> and <i>Silybum marianum</i> (silymarin) decreased essential liver enzymes i.e SGOT, GPT, alkaline phosphate(ALK.phos) and bilirubin. 2. It has protective effects of liver tissues against TAA.
99	<i>Cuscuta australis</i> (119)	Convolvulaceae	Seed & stem of the plant	Acetaminophen(AAP)	Ethanollic extract	1. Histopathology The relevant study demonstrated that <i>Cuscuta australis</i> possess the ability to maintain the normal cytoarchitecture of the liver in the presence of paracetamol overdose. 2. Biomarkers A significant reduction of the liver injury marker (SGOT, SGPT, ALP and Billirubin, SOD and catalase) observed in this study.
100	<i>Boesenbergia rotunda</i> (120)	Zingiberaceae	Rhizome	Thioacetamide (CH ₃ CSNH ₂) (TAA)	Ethanollic extract	i. Microscopic examination was performed and observed the normal structure of the liver cells after the treatment of plant extract.

					ii. Extract of the <i>Boesenbergia rotunda</i> inhibit the release of the Reactive oxygen species to protect the liver injury and decrease the elevated biological markers.
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Conclusion

The use of synthetic medicines (allopathic) may cause severe side effects, having high cost. Hence liver complications are treating with medicinal plants (bioactive constituents) having least side effects and low cost. The current review article shows a detail of hepatoprotective medicinal plants. Medicinal plants contains alkaloids, glycoside, terpenes, flavonoids and saponins which are used in the healing of various ailments of liver. Extracts of medicinal plants open the ways for the discovery of new compounds (drugs). Medicinal plant (individual or in combinations) possess sufficient efficacy for the liver diseases caused by viruses and toxic chemicals.

Declaration of conflict of Interest

The authors hereby declare there is no conflict of interest with this submission.

Abbreviation

SGPT (Serum glutamate pyruvate transaminase), SGOT (Serum glutamate oxaloacetate transaminase), ALT (Alanine transaminase), AST (Aspartate transaminase), AspAT (Aspartate transaminase), AlnTA (Alanine transaminase), CCL4 or CTC (Carbon tetrachloride), AAP (Acetaminophen), PCM (Paracetamol), DPPH (diphenylpicrylhydrazyl), LFT (Liver function test), ALP or ALKP or (Alkaline phosphatase), LDH (Lactate dehydrogenase), GLDH (Glutamate dehydrogenase), GOT (Glutamic Oxaloacetic transaminase), GPT (Glutamic pyruvic transaminase), GPO or GSH-Px (Glutathione peroxidase), GSH (Glutathione), MDA (Malondialdehyde), LPO (Lipid peroxidase), SOD (Superoxide dismutase), TAA (Thioacetamide), TCM (Tetrachloromethane), LP (Lipoprotein), AFB-1 (aflatoxin B1), CYP2E1 (cytochrome P4502E1), TAG (Triacylglycerol), 2-AAF (2-Acetylaminoflourene), HA (Hyaluronic acid), CAT (Catalase), DENA (Diethylnitrosamine), GPx (Glutathione peroxidase), TG (Triglyceride), γ GT (Gamma-glutamyltransferase), TB (Total bilirubin), TP (total protein), ALB (Albumin), IU (International unit), AFB-1 (Aflatoxin B1), CTC (Carbon tetrachloride), C₂H₅OH (Ethanol), C₆H₁₃NO₅ (D-galactosamine), TBARS (Thiobarbituric acid reactive substances).

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