IJPSR (2011), Vol. 2, Issue 3 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 18 November, 2010; received in revised form 28 January, 2011; accepted 12 February, 2011

A REVIEW ON HEPATOPROTECTIVE ACTIVITY OF MEDICINAL PLANTS

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Keywords:

Phytomedicines,

Liver diseases,

Hepatitis,

Hepatoprotection,

Herbal drugs

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ABSTRACT

A phytotherapeutic approach to modern drug development can provide many invaluable drugs from traditional medicinal plants. Search for pure phytochemicals as drugs is time consuming and expensive. Numerous plants and polyherbal formulations are used for the treatment of liver diseases. However, in most of the severe cases, the treatments are not satisfactory. Although experimental evaluations were carried out on a good number of these plants and formulations, the studies were mostly incomplete and insufficient. The therapeutic values were tested against a few chemicals-induced subclinical levels of liver damages in rodents. Even common dietary antioxidants can provide such protection from liver damage caused by oxidative mechanisms of toxic chemicals. However, experiments have clearly shown that plants such as *Picrorrhiza kurroa, Andrographis paniculata, Eclipta alba, Silibum marianum, Phyllanthus maderaspatensis* and *Trichopus zeylanicus* are sufficiently active against, at least, certain hepatotoxins. Screening plants for antihepatitis activities remains in its infancy. *P.kurroa, E. alba, Glycyrrhiza glabra, A. paniculata* and *P. amarus* are likely to be active against Hepatitis B virus. In the case of severe liver damage, most of the liver cells die or turn into fibrotic state. In this case, the treatment should include in addition to the therapeutic agents, agents which can stimulate liver cell proliferation. For developing satisfactory herbal combinations to treat severe liver diseases, plants have to be evaluated systematically for properties such as antiviral activity (Hepatitis B, Hepatitis C, etc), antihepatotoxicity (antioxidants and others), stimulation of liver regeneration and choleretic activity. The plants with remarkable activities for each of the above properties have to be identified. Single plant may not have all the desired activities. A combination of different herbal extracts/'fractions is likely to provide desired activities to cure severe liver diseases. Development of such medicines with standards of safety and efficacy can revitalise treatment of liver disorders and hepatoprotective activity.

INTRODUCTION: Medicinal plants play a key role in the human health care. About 80% of the world population rely on the use of traditional medicine which is predominantly based on plant materials [1]. The traditional medicine refers to a broad range of ancient natural health care practices including folk/tribal practices as well as Ayurveda, Siddha, Amchi and Unani. These medical practices originated from time immemorial and developed gradually, to a large extent, by relying or based on practical experiences without significant references to modern scientific principles.

These practices incorporated ancient beliefs and were passed on from one generation to another by oral tradition and/or guarded literature. Although herbal medicines are effective in the treatment of various ailments very often these drugs are unscientifically exploited and/or improperly used. Therefore, these plant drugs deserve detailed studies in the light of modern science.

It is estimated that about 7,500 plants are used in local 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 hitherto unknown to the mainstream population. The classical systems of medicine such as Ayurveda, Siddha, Amchi, Unani and Tibetan use about 1,200 plants [2]. A detailed investigation and documentation of plants used in local health traditions and pharmacological evaluation of these plants and their taxonomical relatives can lead to the development of invaluable plant drugs for many dreaded diseases. Random screening of plants has not proved economically effective [3].

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

Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages in liver. Enhanced lipid peroxidation produced during the liver microsomal metabolism of ethanol may result in hepatitis and cirrhosis [4]. It has been estimated that about 90% of the acute hepatitis is due to viruses. The major viral agents involved are Hepatitis B, A, C, D (delta agents), E and G. Of these, Hepatitis B infection often results in chronic liver diseases and cirrhosis of liver. Primary liver cancer has also been shown to be produced by these viruses.

It has been estimated that approximately 14- 16 million people are infected with this virus in South East Asia region and about 6% of the total population in the region are carriers of this virus. A vaccine has become available for immunization against Hepatitis B virus. Hepatitis C and Hepatitis E infections are also common in countries of South East Asia region [5].

In the present work, authors had reviewed the articles of hepatoprotective activity of the medicinal plants and has arranged them in the systemic order as shown in **table 1**.

TABLE 1: HEPATOPROTECTIVE ACTIVITY OF THE MEDICINAL PLANTS

Name of the Plant	Source or Family	Plant parts used	Hepatotoxicity inducing agents	Extracts studied	Biochemical and Histopathological Parameters studied
Orthosiphon stamineus [6]	Lamiaceae	Leaves	Acetaminophen	Methanol extract	AST, ALT and ALP
Baliospermum montanum [7]	Euphorbiaceae	Roots	Paracetamol	Alcohol , chloroform extract	SGPT, SGOT and alkaline phosphate, Histopathological changes in liver.
Tridax procumbens [8]	Asteraceae	Leaves	Carbon tetrachloride	Ethanolic extract	Glutathione, superoxide dismutase and catalase
Glycyrrhiza glabra Linn. [9]	Fabaceae	Root powder	Carbon tetrachloride	Root powder mixed with animal feed	TBARS,CD,SOD,CAT,GST,GSH-Px, GSH, LIPID PEROXIDATION
Phyllanthus niruri [10]	Euphorbiaceae	Leaves and fruits	Carbon tetrachloride	Methanolic and aqueous	glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT), DPPH radical scavenging
Cochlospermum Planchoni [11]	Coclospermaceae	Rhizomes	Carbon tetrachloride	Aqueous	Total bilirubin Alkaline phosphatase Alanine aminotransferase
Saururus chinensis [12]	Saururaceae	Whole plant	Carbon tetrachloride	Ethanol	alanine aminotransferase (ALT), aspartate aminotransferase (AST), hyaluronic acid (HA), hepatic malondialdehyde (MDA) content, and superoxide dismutase (SOD) activity, total cholesterol (TC), triglyceride (TG), total lipoprotein (TP), albumin (ALB), hydroxypropyline (HYP), total antioxidant capacity (T-AOC), laminin (LN), type III collagen terminal peptide (PC-IIINP), and type IV collagen (IV-C), as well as with Histopathological changes of liver.
'Teng-Khia-U' [13] derived from the entire plants of *Elephantopus scaber L., E. mollis H.B.K.* and *Pseudoelephantopus spicatus (*Juss.*)* Rohr	Asteraceae	Whole plant	D-galactosamine (d-gain)- and acetaminophen (apap)	Aqueous	serum glutamate-oxalate-transaminase (sGOT) and the serum glutamate pyruvate- transaminase (sGPT)
FructusSchisandrae chinensis (LFS) with *Astragalus polysaccharides(APS)* [14]	Magnoliaceae	Dried fructus	Carbon tetrachloride	Ethanol	Alanine aminotransferase(ALT), asparate aminotransferase (AST), alkaline phosphatase (ALP) malondialdehyde (MDA), reduced glutathione (GSH) andcatalase (CAT), superoxidedismutase (SOD)
Cordia macleodii [15]	Boraginaceae	Leaves	Carbon tetrachloride	Ethanolic	Glutamate pyruvate transaminase (GPT), serum glutamate oxaloacetate transaminase (GOT), Alkaline Phosphatase (ALP) and total bilirubin
Arachniodes exilis [16]	Dryopteridaceae	Rhizomes	Carbon tetrachloride	Ethanol	Lipid peroxide, DPPH, ABTS, superoxide anion, hydroxyl radical and hydrogen peroxide, glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, malondialdehyde and superoxidedismutase
Momordica dioica [17]	Cucurbitaceae	Leaves	Carbon tetrachloride	Ethanolic and aqueous	serum glutamate oxaloacetate transaminase (AST), serum glutamate pyruvate transaminase (ALT), serum alkaline phosphatase (SALP) and total

					bilirubin, Histopathological examination of rat liver sections
Swertiamarin isolated from *Enicostemma Axillare* [18]	Gentianaceae	Whole plant	D-galactosamine	Ethyl acetate	ASAT (IU/l) ALAT (IU/l) ALP (IU/l) Triglycerides (mg/dl) Total cholesterol (mg/dl) Total bilirubin (mg/dl) Total protein (g/dl) Creatinine (mg/dl) Albumin (g/dl)
Asparagus racemosus [19]	Liliaceae	Whole plant	Γ-radiation	Crude extract and a purified aqueous fraction	Lipid peroxidation, protein oxidation
CGX,- a modified traditional Chinese herbal drug [20]	--	--	Carbon tetrachloride	Aqueous	alanine transaminase (ALT), aspartate transaminase (AST), and lactate dehydrogenase (LDH) in serum, and the malondialdehyde concentrations in liver tissue
Propolis- is a resinous hive product collected by honeybees from various plant sources [21]	--	--	D-galactosamine (d-galn):tumor necrosis factor-a (tnf-a)	Meoh and water extracts	1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging activity, cytotoxicity and hepatoprotective activity
Tephrosia purpurea L. and *Tecomella undulate* [22]	Fabaceae Bignoniaceae	Aerial parts of tephrosia purpurea and stem Bark of tecomella undulata	Thioacetamide	Aqueous–ethanolic extract	serum aspartate aminotransaminase, alanine aminotransaminase, gamma glutamyl, alkaline phosphatise, total bilirubin, liver glutathione
Cassia fistula [23]	Leguminosae	Leaf	Carbon tetrachloride	Methanol	Serum levels of transaminases (SGOT and SGPT), bilirubin and alkaline phosphatase (ALP).
Amalkadi Ghrita [24] *(AG),* a polyherbal formulation composed of *Emblica officinalis* (10 g), *Glycyrrhiza glabra* (10 g), and cow's ghee	--	--	Carbon tetrachloride	Crude drug	Serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP), and acid phosphatase (ACP). The serum levels of total proteins, bilirubin and histological studies.
Gentiana olivieri [25]	Gentianaceae	Aerial parts	Carbon tetrachloride	Ethanol	Plasma and hepatic tissue malondialdehyde formation, and liver tissue glutathione level, as well as plasma transaminase enzyme levels (aspartate transferase and alanine transferase).
Zhi-Zi-Da-Huang [26] is a classical traditional Chinese formula comprising four crude drugs: *Gardenia jasminoides* Ellis. *Rheum officinale Baill, Citrus aurantium L.* and *Semen Sojae Preparatum* with a ratio of 3:1:4:8 in weight.	--	--	Alcohol	Diethyl ether and water	Aspartate transaminase (AST), alanine transferase (ALT), reduced glutathione (GSH), malondialdehyde (MDA) and superoxide dismutase (SOD). The biochemical observations were supplemented by Histopathological examination.
Amaranthus spinosus [27]	Amaranthaceae	Whole plant	Carbon tetrachloride	Petroleum ether	serum enzymatic levels of serum glutamate oxaloacetate transaminase (AST), serum glutamate pyruvate transaminase (ALT), serum alkaline phosphatase (SALP) and total bilirubin Histopathological examination

Apium graveolens and *Hygrophila Auriculata* [28]	Apiaceae Acanthaceae	Seeds	Paracetamol and thioacetamide	Petroleum ether and methanol	serum transaminases (SGOT and SGPT), alkaline phosphatase, sorbitol dehydrogenase, glutamate dehydrogenase and bilirubin in serum, Histopathological
Boerhaavia diffusa [29]	Nyctaginaceae	Roots	Thioacetamide	Aqueous	GOT, GPT, ACP and ALP, but not GLDH and bilirubin
Clerodendrum inerme [30]	Verbenaceae	Leaves	Carbon tetrachloride	Ethanol	alanine amino transferase (ALT), aspartate amino transferase (AST), alkaline phosphates (ALP), triglycerides (TGL), total cholesterol (TC)
Zanthoxylum armatum [31]	Rutaceae	Bark	Carbon tetrachloride	Ethanolic	serum transaminases, alkaline phosphatase and total bilirubin and antioxidant enzymes: superoxide dismutase, catalase and glutathione
Gundelia tourenfortii [32]	Asteraceae	Fresh edible stalk	Carbon tetrachloride	Aqueous ethanol	Histopathological studies, ALT, AST and ALP, and bilirubin
Cassia occidentalis [33]	Caesalpiniaceae	Leaves	Paracetamol and ethyl alcohol	Aqueous-ethanolic extract	Serum transaminase (aspartate amino transferase and serum alanine amino transferase), alkaline phosphatase, serum cholesterol, serum total lipids and Histopathological alterations.
Kalanchoe pinnata Pers.[34]	Crassulaceae	Leaves	Carbon tetrachloride	Juice of the fresh leaves and ethanolic extract	Serum glutamyl oxalacetic acid transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT) alkaline phosphatase (ALKP), serum bilirubin (SBLN), Histopathological studies.
Luffa echinata [35]	Cucurbitaceae	Fruits	Carbon tetrachloride	Petroleum ether, acetone and methanolic extracts	Serum glutamic oxalacetic transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase (ALKP), total protein (TP) and total albumin (TA).
Phyllanthus amarus Schum. et. Thonn. [36]	Euphorbiaceae	Aerial part	Ethanol	Aqueous	Hepatotoxic parameters studied in vivo included serum transaminases (AST and ALT), serum triglyceride (STG), hepatic triglyceride (HTG), tumor necrosis factor alpha, interleukin 1 beta, together with Histopathological examination.
Schouwia thebica [37]	Arecaceae	Aerial parts	Carbon tetrachloride	Diethyl ether, chloroform, ethyl acetate, and n-butanol	ALT, AST, and GGT, and levels of glucose, triglycerides, and cholesterol in serum
Thunbergia laurifolia Linn. [38]	Acanthaceae	Leaves	Ethanol	Aqueous extract	Serum glutamyl oxalacetic acid transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT) alkaline phosphatase (ALKP), serum bilirubin (SBLN), Histopathological studies.
Thymoquinone, the active constituent of *Nigella sativa* [39]	Ranunculaceae	Seeds	Tert-butyl hydroperoxide	Aqueous-ethanolic extract	ALT and AST
Apium gra_eolens Linn. *Croton oblongifolius* [40]	Apiaceae. Euphorbiaceae	Seeds Aerial parts	Carbon tetrachloride	Petroleum ether, acetone and methanol	Serum transaminases (SGOT and SGPT), alkaline phosphatase, total protein and albumin
Woodfordia fruticosa Kurz [41]	Lythraceae	Flowers	Carbon tetrachloride	Petroleum ether, chloroform, ethyl alcohol and	Serum transaminases, alkaline phosphatase, bilirubin and triglycerides

				aqueous	
Piper chaba [42]	Piperaceae	Fruit	D-galactosamine (d-galn)/lipopolysaccharides	Aqueous acetone	Serum glutamic oxalacetic transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase (ALKP), total protein (TP) and total albumin (TA).
Nelumbo nucifera Gaertn [43]	Nelumbonaceae	Leaves	Carbon tetrachloride	Ethanolic	ALT and AST
Bupleurum kaoi [44]	Umbelliferae	Dried roots	Carbon tetrachloride	Ethanolic	Serum glutamyl oxalacetic acid transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT) alkaline phosphatase (ALKP), serum bilirubin (SBLN), Histopathological studies.
Cuscuta chinensis [45]	Convolvulaceae	Seeds	Acetaminophen	Aqueous and ethanolic	superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), and by reducing malondialdehyde (MDA)
Hygrophila auriculata [46]	Acanthaceae	Root	Carbon tetrachloride	Aqueous extract	Alanine transaminase, aspartate transaminase (AST), alkaline phosphatase (ALP), total protein and total bilirubin. Hepatic tissues were subjected to Histopathological studies
Halenia elliptica [47]	Gentianaceae	Whole plant	Carbon tetrachloride	Methanolic	Showed a significant decrease in ALT, AST, ALP, and total bilirubin, Histopathological studies
Laggera pterodonta [48]	Asteraceae	Whole herb	Ccl4, carbon tetrachloride; d-galn, d-galactosamine; dpph, 1,1-diphenyl-2-picrylhydrazyl radical	Ethyl alcohol and aqueous	Alanine transaminase, aspartate transaminase (AST), alkaline phosphatase (ALP), total protein and total bilirubin.
Equisetum arvense [49]	Equisetaceae	Aerial parts	Carbon tetrachloride	Methanolic	alanine transaminase, aspartate transaminase (AST), alkaline phosphatase (ALP), and Histopathological studies
Byrsocarpus coccineus Schum [50]	Connaraceae	Leaf	Carbon tetrachloride	Aqueous	ALT and AST and total protein
Euphorbia fusiformis [51]	Euphorbiaceae	Tubers	Rifampicin	Ethanol	Serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), gamma glutamyl transpeptidase (GGTP), alkaline phosphatase (ALP), total bilirubin and total protein
Phyllanthus amarus Schum. [52]	Euphorbiacae	Whole Plant except root	Aflatoxin b1-induced liver damage	Ethanolic	Thiobarbituric acid reactive substances (TBARS) and enhancing the reduced glutathione level and the activities of antioxidant enzymes, glutathione peroxidase (GPx), glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT).
Hypericum japonicum [53]	Clusiaceae	Whole Plant	Carbon tetrachloride and α-naphthyl-isothiocyanate (anit)-	Aqueous, petroleum ether and chloroform	AST, ALT and T-BIL levels in serum
Decalepis hamiltonii [54]	Asclepiadaceae	Roots	Carbon tetrachloride	Aqueous extract	Lipid peroxidation and protein carbonylation, and restoring the levels of antioxidant enzymes (SOD, CAT, GPx, GR, and GST) and glutathione, Histopathological observations

Trichosanthes cucumerina [55]	cucurbitaceae	Whole plant	Carbon tetrachloride	Methanolic	Alanine amino transferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP), total bilirubin (TB), total protein (TP) and albumin (ALB) levels were estimated in serum as well as the glutathione (GSH) and malondialdehyde (MDA) Histopathological changes
Vitis vinifera [56]	Vitaceae	Leaves	Carbon tetrachloride	Chcl3, etoac, n-buoh, and water	(plasma and liver tissue MDA [malondialdehyde], transaminase enzyme levels in plasma [AST-aspartate transaminase, ALT-alanine transferase] and liver GSH [glutathione] levels) Histopathological studies
Mallotus japonicas [57]	Euphorbiaceae	Cortex	Carbon tetrachloride	Water	serum enzymatic activities of alanine: aspartate aminotransferase, sorbitol dehydrogenase and g-glutamyltransferase
Ganoderma lucidum [58]	Polyporaceaes	Winter mushrooms	D-galactosamine	Aqueous juice	(AST, ALT) in serum and MDA, GSH, Histological examination
Pittosporum neelgherrense [59]	Pittosporaceae	Stem bark	Carbon tetrachloride (ccl4)-, d-galactosamine (d-galn)- and acetaminophen (apap)-	Methanolic	serum enzymes, glutamate oxaloacetate transaminase (SGOT), glutamate pyruvate transaminase (SGPT)
Rubia cordifolia Linn. [60]	Rubiaceae	Roots	Carbon tetrachloride	Aqueous etoh extract	Serum glutamic oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (SALP) and γ-glutamyltransferase
Aloe barbadensis Mill [61]	Liliaceae	Dried aerial parts	Carbon tetrachloride	Petroleum ether , chloroform and methanol	Serum transaminases, alkaline phosphatase, bilirubin and triglycerides. lipid peroxidation, glutathione, glucose-6-phosphatase and microsomal aniline hydroxylase and amidopyrine N-demethylase
Fumaria indica [62]	PAPAVERACEAE	Whole plant	D-galactosamine	Butanol	Histological studies, serum enzymes (SGOT, SGPT, ALP) and metabolites bilirubin, reduced glutathione (GSH) and lipid peroxidation
Cochlospermum vitifolium [63]	COCHLOSPERMACEAE	Bark	Carbon tetrachloride	Hexane, dichloromethane, methanol	Serum glutamic–pyruvic transaminase and alkaline phosphatase
Picrorrhiza rhizome [64]	Scrophulariaceae	Dried underground stem	Poloxamer (px)-407	Water	Body weight and gains, liver weight, serum aspartate transferase (AST) and alanine transferase (ALT) levels were monitored with serum low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride and total cholesterol levels. slight increase of liver weight, serum AST and ALT
Artemisia absinthium [65]	Asteraceae	Powdered aerial parts	Carbon tetrachloride and by injection of endotoxin (lps, 10µg, i.v.) In bcg-primed mice	Aqueous	The levels of aspartate aminotransferase (AST), alanineaminotransferase (ALT), tumor necrosis factor- (TNF-α) andinterleukin-1(IL-1)in mouse sera, as well as superoxide dismutase (SOD),

					glutathioneperoxidase (GPx) and malondialdehyde (MDA)
Lactuca indica [66]	Compositae	Aerial parts	Carbon tetrachloride	Methanolic	serum glutamic–pyruvic transaminase and alkaline phosphatase
Cassia tora [67]	Caesalpiniaceae	Leaves	Carbon tetrachloride	Ethyl acetate	Glutathione enzyme activities.
Carum copticum [68]	Apiaceae	Seed	Paracetamol And ccl4	Water	Serum glutamic–pyruvic transaminase and alkaline phosphatase serum alkaline phosphatase (ALP) and aminotransferases (AST and ALT).
Azadirachta indica [69]	Meliaceae	Leaf	Paracetamol	70% ethanol	(Glutathione peroxidase (GPx), glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT)
Mamoridca subangulata *Naragamia alata* [70]	Cucurbitaceae Meliaceae	Leaf, whole Plant	Paracetamol	10% aqueous suspension was prepared in 2% (w/v) gum acacia	Serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), gamma glutamyl transpeptidase (GGTP)
Phyllanthus Niruri [71]	Euphorbiacea	Leaves	Paracetamol	Petroleum ether and 50% ethanol	Serum glutamic oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (SALP) and γ-glutmyltransferase and Histopathological studies.
Orthosiphon stamineus [72]	Lamiacea	Leaves	Paracetamol	Methanol	SGOT, SGPT, ALP and lipid peroxides
Silybum marianum *Cichorium intybus* [73]	Asteraceae	Leaves	Thioacetamide	Chloroform	SGOT, SGPT, aminotransferase, alkaline phosphate and bilirubin
Sarcostemma brevistigma [74]	Asclepiadaceae	Stem	Carbon tetrachloride	Ethyl acetate	Serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase, total bilirubin and gamma glutamate transpeptidase (GGTP)
Cassia fistula [75]	Leguminosae	Seeds	Paracetamol	Methanolic	SGOT, SGPT, ALP and Billirubin
Piper longum [76]	Piperaceae	Fruits and roots powder	Carbon tetrachloride	Milk extract	SGOT, SGPT, ALP and Billirubin
Chamomile capitula [77]	Asteraceae	Fresh natural mature capitula	Paracetamol	Aqueous Ethanolic	Liver glutathione, Na+ K+- ATPase activity, serum marker enzymes, serum bilirubin, glycogen and thiobarbutiric acid
Calotropis procera [78]	Apocynaceae	Flowers	Paracetamol	70% EtOH	SGPT, SGOT, ALP, bilirubin, cholesterol, HDL and tissue GSH
Aerva lanata Linn [79]	Amaranthaceae	Coarse powder plant material	Paracetamol	Hydroalcoholic	Serum enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin.
Acacia confuse [80]	Leguminosae	Bark	Carbon tetrachloride	Hydroalcoholic	Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and malondialdehyde (MDA) in plasma, and cytochrome P4502E1 (CYP2E1) protein superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase(CAT) in

					erythrocytes
Kigelia africana, Calotropis procera, Hibiscus sabdariffa and *Alchornea cordifolia* [81]	Bignoniaceae Apocynaceae Malvaceae Euphorbiaceae	Leaves Leaves Calyces Leaves	Paracetamol	Distilled water	Lipid peroxidation product thiobarbituric reacting substances (tbars) superoxide dismutase (sod), catalase (cat), gluthathione peroxidase (gpx), and d-aminolevulinate dehydratase (d-ala-d) activities
Pterocarpus marsupium Roxb. [82]	Papilionaceae	Stem bark	Carbon tetrachloride	Methanol and aqueous	Total bilirubin, serum protein, alanine aminotransaminase, aspartate aminotransaminase, and alkaline phosphatase activities) and Histopathological studies of the liver.
Alocasia indica Linn. [83]	Araceae	Leaves	Paracetamol	Hydroalcoholic	Total bilirubin, serum protein, alanine aminotransaminase, aspartate aminotransaminase, and alkaline hosphatase
Capparis spinosa [84]	Capparidaceae	Root bark	Carbon tetrachloride	Ethanolic	Alanine transaminase and aspartate transaminase activities
Spondias pinnata [85]	Anacardiaceae	Stem heart wood	Carbon tetrachloride	Ethyl acetate and methanolic	SGPT, SGOT, ALP, Total bilirubin (TB).
Embelia ribes [86]	Myrsinaceae	Fruits	Paracetamol	Water	SGPT, SGOT, ALP, Total bilirubin (TB) and Histopathological studies
Juncus subulatus [87]	Juncaceae	Powdered tubers	Paracetamol	70% methanol	Serum Liver enzymes (AST, ALT and ALP), total protein, albumin, cholesterol, triglycerides, nitric oxide (NO), malondialdhyde (MDA) and total antioxidant capacity (TAC)
Phyllanthus polyphullus [88]	Euphorbiaceae	Leaves	Acetaminophen	Methanolic	Aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin, gamma glutamate transpeptidase (GGTP), lipid peroxidase (LPO) with a reduction of total protein, superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx) and glutathione S-transferase (GST).
Tylophora indica [89]	Asclepiadaceae	Leaf powder	Ethanol	Aqueous	Aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin,
Cleome viscose Linn. [90]	Capparidaceae	Leaf powder	Carbon tetrachloride	Ethanolic	Aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin and Histopathological studies.
Ricinus Communis [91]	Euphorbiaceae	Leaves	Carbon tetrachloride	Cold aqueous extract	Aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin and Histopathological studies
Picrorhiza Kurrooa [92]	Scrophulariaceae	Root and rhizomes	Alcohol-carbon tetrachloride	Ethanol	Glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase, alkaline phosphatase, glutamate dehydrogenase and bilirubin
Ocimum snctum [93]	Lamiaceae	Leaf	Paracetamol	Hydroalcoholic	Aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin and Histopathological studies

Acacia Catechu [94]	Leguminosae	Powdered pale catechu	Carbon tetrachloride	Ethyl acetate	SGPT, SGOT, Serum alkaline phosphatise and Bilirubin content
Ginkgo Biloba [95]	Ginkgoaceae	Dried extract	Carbon tetrachloride	Ethanolic	SGPT, SGOT, Serum alkaline phosphatise and Bilirubin content, Histopathological studies
Scoparia dulcis [96]	Scrophulariaceae	Whole plant	Carbon tetrachloride	Methanol, diethyl ether and petroleum ether	aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin and Histopathological studies
Plantago Major L. [97]	Plantaginaceae	Seeds	Carbon tetrachloride	Ethanolic	aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin
Ptrospermum acerifolium [98]	Sterculiaceae	Leaves	Carbon tetrachloride	Ethanol	aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP),
Vitex trifolia [99]	Verbenaceae	Leaves	Carbon tetrachloride	Ethanol and water	Total protein, Histopathological studies, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP),
Hoslundia opposite [100]	Lamiaceae	Stem	Carbon tetrachloride and paracetamol	Methanol and ethyl acetate	AST, ALT and Bilirubin
Trianthema decandra [101]	Aizoaceae	Leaves	Carbon tetrachloride	aqueous	AST, ALT and Bilirubin. Histopathological studies
Hibiscus esculentus Linn. [102]	Malvaceae	Roots	Carbon tetrachloride	Water	SGPT, SGOT, ALP, Total bilirubin (TB).
Aegle marmelos correa ex Roxb. [103]	Rutaceae	Pulp/seeds	Carbon tetrachloride	water	AST, ALT and Bilirubin. Histopathological studies
Tylophora indica [104]	Asclepidaceae	Leaves	Carbon tetrachloride	Methanolic	SGPT, SGOT, Serum alkaline phosphatise and Bilirubin content
Casuarina equisetifolia, *Cajanus cajan,* *Glycosmis pentaphylla,* *Bixa orellana,* *Argemone mexicana,* *Physalis minima,* *Caesalpinia bonduc* [105]	Casuarinaceae Fabaceae Rutaceae Bixaceae Papaveraceae Solanaceae Fabaceae	Plant materials	Carbon tetrachloride	Methanolic extract	SGPT, SGOT, AST, ALT AND Cholesterol.

CONCLUSION: The goal of ethnopharmacological studies on medicinal plants should not be restricted to find new prototype pure compounds as drugs. Active extracts, fractions or mixture of fractions/extracts may prove very effective drugs. Plant drugs (combinations or individual drug) for liver diseases should possess sufficient efficacy to cure severe liver diseases caused by toxic chemicals, viruses (Hepatitis B, Hepatitis C, etc.), excess alcohol intake, etc. A single drug cannot be effective against all types of severe liver diseases. Effective formulations have to be developed using indigenous medicinal plants, with proper pharmacological experiments and clinical trials. The manufacture of plant products should be governed by standards of safety and efficacy.

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