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Review Article

A Review of Plants with Remarkable Hepatoprotective Activity

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Abstract

Liver being vulnerable to exogenous substances makes disease associated with it a matter of worldwide concern. Several research thus focus on hepatoprotection .Preventive and therapeutic activity of plants as a hepatoprotective agent is a topic of interest for researchers. Hepatotoxic agents like carbon tetrachloride, paracetamol, isoniazide etc. increase the serum biomarkers of liver where ALT is more specific than AST in detecting liver injury. Drug-induced liver injury (DILI) wherein more than 900 drugs have been implicated in causing liver injury. Plant phenolics include simple phenols, phenolic acids, coumarins, lignans, flavonoids, diaryl-alkanoids, stilbenoids, proanthocyanins, tannins, and anthocyanins some alkaloids. The greater the content of alkaloids, flavonoids, and saponins in an extract, the higher the hepatoprotective activity possessed by the extract. This paper reviews some plants documented between the periods of 2011-2021 with remarkable heptoprotective activity and discusses the various hepatotoxic agents used, its mechanism and hepatoprotective agents present in the specific plant.

Keywords: Hepatoprotective plants, flavonoids, saponin, alkaloids,hepatotoxicity, drug induced liver injury, hepatotoxic agents

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INTRODUCTION

Liver which is the largest gland in the body is a multifunctioning organ, responsible for metabolism, detoxification, secretion, synthesis, storage and immunological functions. The liver is permanent susceptible to exogenous substances e.g. drugs, alcohol and environmental toxins, which can lead to liver disorders, such as hepatocellular, cholestatic (obstructive) and mixed type of the liver disorders[1].Liver diseases have become a global concern worldwide and deaths caused by liver diseases are rising each year at an alarming rate[2]. It is steadily increasing over the years and World Health Organisation (WHO) has projected in its World Health Statistics of 2020 to be the eleventh most important cause of death in the world by 2030 and may be the tenth most common cause of death in India by 2020.Plants have been used since ancient times in the treatment of liver diseases, several research has proven the preventive and therapeutic activity of plants as a hepatoprotective agent. People are becoming aware about the various benefits and preferring the alternative medicine, for their health. As in 2018, 170 WHO Member States have acknowledged their use of Traditional and complementary medicine. Ayurveda a time honoured Indian system of medical practice has multitude proven formulations for the treatment of liver diseases. The plants which protect the liver contain variety of active constituents like flavonoids, glycosides, monoterpenes, coumarins, lignans, essential oil, carotenoids, organic acids, alkaloids and xanthene[3].Here this paper reviews some incredible plants for their hepatoprotective activity taken from various documented literature from the period of 2011-2021.

Table 1: Plant Description

Name of the plant	Common name	Part of plant used	Type of extract
Cichorium Intybus and Cynara Scolymus[4]	Chicory / Kasani / Artichoke Ahtichoke	Cichorium intybus root and Cynara Scolymus leaves	Ethanolic extract
Foeniculum Vulgare[1]	Fennel /sauf	Seed	Ethanolic extract
Cordia Sebestena L.[5]	Geiger / Lal Lasoda	Fruit	Ethanolic extract

Curcuma Heyneana[6]	Temu Giring a variety of Turmeric	Rhizome	Ethanolic extract
Lobelia Alsinoides Lam.[2]	Chickweed/Bhujbhuja kharpatwar	Whole plant	Kalka Preparation
Three Varieties of the Passion Fruit (Passiflora Sp.)[7]	Passion Fruit	Peel of the fruit (red, yellow and purple)	Ethanolic extract
Phyllanthus fraternus[8]	Gulf leaf flower / Bhumiamlaki	Leaves	Aqueous Extract
Pavetta Indica LINN[9]	Indian Pellet shrub / Kankara	Leaves	Ethanolic Extract
Mimosa Pudica[10]	Shameplant/Chuimuhi	Leaves	Ethanolic Extract
Terminalia Coriacea[3]	Belong to Arjun Family	Leaves	Methanolic Extract
Bambusa Bambos[11]	Bamboo / Bans	Shoot extract	Methanolic Extract
Rosa Canina[12]	Dog Rose	Fruit	Ethanolic Extract
Garcinia Pedunculata[13]	Bor Thekera /tikul	Fruit	Aqueous Extract
Tetrapleura Tetraptera[14]	Aridan/Prekese	Fruit	Methanolic Extract
Feijoa Sellowiana[15]	Horn of plenty/pineapple guava'	Fruit	Ethanolic Extract
Piper Cubeba[16]	Tailed pepper, Java pepper.	Fruit	Ethanolic Extract
Feronia Limonia[17]	wood apple/elephant apple/ kowit	Fruit pulp	Ethanolic Extract
Solanum Xanthocarpum[18]	yellow-fruit nightshade, Thai green eggplant,kantakari	Fruit	Ethanolic Extract

HEPATOTOXICITY

Injury or damage to the liver caused by substances like drugs, herbal agents, industrial chemical agents or nutritional supplements. Liver being the vital site for metabolism and biotransformation it becomes highly susceptible to damage. More than 900 drugs have been implicated in causing liver injury and it is the most common reason for a drug to be withdrawn from the market[19].Drug-induced liver injury (DILI) represents a diverse set of responses that occur after exposure to any manufactured or naturally occurring chemical compound[20].The DILIrank dataset consists of 1,036 FDA-approved drugs that are divided into four classes where 192 Most DILI concern-, 278 Less DILI concern, 312 No DILI concern where there is confirmed causal relationship between a drug and liver injury and the last group 254 Ambiguous-DILI-concern where the causality remains undetermined. LiverTox is another dataset providing up-to-date, information on the diagnosis, cause, frequency, clinical patterns and management of liver injury attributable to prescription and non-prescription medications and selected herbal and dietary supplements.

Table 2: Types of DILI

Intrinsic DILI	Idiosyncratic DILI
It affects every individual at the same dose	It affects individuals with risk factors (risk of unpredictable interactions among genetic, non-genetic factors like age, sex, existing imumunocompromised diseases, daily dose, and metabolism factors.)
Predictable	Unpredictable
Dose dependent	Non–Dose-Dependent
E.g. Acetaminophen etc.	E.g. tyrosine kinase inhibitors,antitubercular drugs etc.

Table 3: Bio Chemical Classification of DILI[20, 21]

Hepatocellular	Cholestatic	Mixed Hepatocellular/Cholestatic Pattern
ALT 2 to 5 times >the upper limit of normal (ULN) and/or an ALT/ALP ratio> than 5	ALP 3 times >ULN and/or an ALT/ALP ratio < 2	ALT 2 to 5 times >the ULN and ALP 3 times> the ULN and/or an ALT/ALP ratio between 2 and 5.
hepatocyte necrosis, poor prognosis	bland cholestasis is the result of abnormal biliary secretion, with no hepatocellular damage	cholestasis with concomitant hepatic parenchymal damage

Hepatotoxic agents increase the serum levels of ALT(alanine transaminase),AST(aspartate aminotransferase), ALP (Alkaline phosphatase) TB(total bilirubin), DB(direct bilirubin) and TG (Serum Triglycerides),cholestrol,urea and decrease the serum levels of Albumin, GSH glutathione reductase and TP(total protein). ALT is more specific than AST in detecting liver damage as AST can be found not only in the liver but also in the heart, muscle, kidney as well as brain.[6]

Table 4: Description of Hepatotoxic Agent

Name of the plant	Hepatotoxicity inducing agent	Biochemical/Histopathological tests
Cichorium Intybus and Cynara Scolymus[4]	Paracetamol at 0.5 mg/kg bodyweight	Creatinine phosphokinase (CPK), Alanine Aminotransferase (SGPT or ALT), Aspartate Aminotransferase (SGOT or AST), Lactate Dehydrogenase (LDH), creatinine, Gamma-Glutamyl Transferase (GGT), Uric acid and weight
Foeniculum Vulgare[1]	Paracetamol at 2g/kg body weight	Aspartate amino transferase (AST), alanine amino transferase (ALT), Alkaline phosphatase (ALP), bilirubin.
Cordia Sebestena L.[5]	Simvastatin at 20 mg/kg body weight	SGOT(Serum glutamic oxaloacetic transaminase), SGPT (serum glutamic pyruvic transaminase), cholesterol, bilirubin, urea, albumin, total protein and red blood cells (RBC), white blood cells (WBC) haemoglobin (Hb), platelets and lymphocytes and liver histopathology study
Curcuma Heyneana[6]	Isoniazid at the dose of 50 mg/kg and rifampin at dose of 100 mg/kg body weight	Alanine transaminase (ALT) and aspartate transaminase (AST), livers were collected for histopathology study
Lobelia Alsinoides Lam.[2]	Carbon Tetrachloride 1:1 mixture in olive oil at 1.25 ml/kg bodyweight	AST), ALT, ALP, total bilirubin, total protein, albumin and total cholesterol, liver for histopathology study.
Three Varieties of the Passion Fruit (Passiflora Sp.)[7]	Paracetamol at 500mg/kg body weight	ALT, AST, Urea and Creatinine
Phyllanthus Fraternus[8]	Carbon Tetrachloride : Olive oil (dose not mentioned)	SGOT, SGPT, ALP, bilirubin, cholesterol, and total protein, liver tissues for histopathology study
Pavetta Indica LINN[9]	Paracetamol at 2000mg/kg bodyweight	SGOT, SGPT, Albumin, Globulin, Total bilirubin, direct bilirubin, total protein
Mimosa Pudica[10]	High fat diet (HFD) for 2 weeks and streptozotocin (STZ) (35 mg/kg body weight).-induced type 2 diabetic rats	Glucose, insulin, AST, ALT, ALP and LDH
Terminalia Coriacea[3]	Carbon Tetrachloride at 2ml/kg bodyweight	AST, ALT, ALP ,direct bilirubin, total bilirubin and Cholesterol, liver for histopathology study
Bambusa Bambos[11]	Carbon Tetrachloride at 1 mL/kg body weight	Aspartate Amino Transaminase (AST), Alanine Amino Transaminase (ALT), Alkaline Phosphatase (ALP) and Total Bilirubin
Rosa Canina[12]	Carbon tetrachloride 1 ml/kg body weight	aspartate aminotransferase (AST), alanine amino transaminase (ALT), alkaline phosphatase (ALP), albumin (ALB), total protein (TP) and malondialdehyde (MDA), histopathological study
Garcinia Pedunculata[13]	Paracetamol at 1 g/kg body weight	acute oral toxicity test ,ALT,AST,alkaline phosphatase, histopathological study
Tetrapleura Tetraptera[14]	Carbon tetrachloride at 0.75mg/kg body weight	ALT, AST, alkaline phosphatase, bilirubin, histopathological study, Measurement of Lipid Peroxide
Feijoa Sellowiana[15]	methylenedioxymethamphetamine(MDMA) at 10mL/Kg body weight	ALT, AST, glutathione reductase, histopathology study
Piper Cubeba[16]	Carbon tetrachloride at 1 ml/kg body weight	antioxidant potential tested by (DPPH) free radical scavenging activity, hydroxyl radical scavenging activity, nitric oxide radical scavenging activity and hydrogen peroxide radical scavenging activity, ALT, AST, ALP, TB, DB ,TG and Total proteins along with histopathology study Lipid Peroxidation (LPO), Reduced Glutathione (GSH) and Catalase Level (CAT) determination.
Feronia Limonia[17]	Paracetamol at 500 mg/kg body weight	AST, ALT, ALP, Total Bilirubin, Total cholesterol, Triglycerides & the body weight.
Solanum Xanthocarpum[18]	Carbon tetrachloride at 1 ml/kg body weight	Aspartate aminotransferase (AST), alanine aminotransferase (ALT), Serum alkaline phosphatise (SALP) and total bilirubin, antioxidant activities as lipid peroxidation (LPO), reduced glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) were screened along with histopathological studies.

1. Carbon tetrachloride- Out of 18 research papers reviewed 8 used Carbon tetrachloride (CCl_4) as the hepatotoxin in (1:1) ratio mixed in olive oil /liquid paraffin. The carbon tetrachloride administration causes oxidative damage.ROS causes membrane lipid peroxidation, cell and mitochondrial membrane degradation, endoplasmic reticulum dysfunction, and intracellular macromolecule damage[35], fibrosis, inflammation and fatty degeneration in the liver.

2. Paracetamol- Paracetamol also known as acetaminophen is the most common cause of DILI. It is the next frequent hepatotoxin used in the reviewed papers for inducing hepatotoxicity. Mitochondrial dysfunction is attributed as the main source of free radicals and oxidative stress in paracetamol hepatotoxicity .Increased activity of mitochondrial complex I, a site for free radical generation seen in paracetamol overdose is directly related degree of liver injury[22].

3. Methylenedioxymethamphetamine (MDMA) - MDMA or ecstasy is an amphetamine derivative which has been abused as a widespread recreational. Liver is a target organ for MDMA toxicity. MDMA is metabolized by cytochromes P_{450}2D, 2B and 3Aand reactive metabolites are readily oxidized to the corresponding o-qiuinones and reactive oxygen species (ROS) which results in hepatotoxicity[15].

4. Simvastatin- Statins can lead to idiosyncratic liver injury; More than 50 cases of liver injury have been reported in association with atorvastatin and simvastatin. Mortality from liver injury has only been associated with atorvastatin and simvastatin[23]. Mitochondrial dysfunction is one of the major factors that explain the mechanism of statin-induced hepatotoxicity. Another major reason for statin induced hepatotoxicity is that mitochondria or cytochromeP450-dependent metabolism act as Reactive Oxygen Species (ROS) generation systems and participate in cell death processes[24].

5. Isoniazid and rifampin- DILI may occur to the tuberculosis patients who consume INH for 6 to 9 months, RIF for 4 months, or a combination of INH and RIF for 4 months. INH along with RIF produces toxic metabolites or oxidants such as acetylhydrazine (AcHz) and hydrazine (Hz) which are oxidized by microsomal enzymes P450 especially CYP2E1 into radical metabolites. These metabolites cause hepatotoxicity[6].

6. High fat diet (HFD) and streptozotocin (STZ) - High fat diet (HFD) and streptozotocin (STZ) induced type 2 diabetes mellitus. Liver is an important organ for glucose homeostasis. In diabetes mellitus the liver damage is related to free radicals formation through glucose oxidation, decrease in antioxidant defence mechanism pathway, on-enzymatic glycation of protein and cytokine production. Chronic hyperglycaemia is a major reason for oxidative stress which leads to pathological changes in liver cell.

HEPATOPROTECTIVE ACTIVITY

Compounds which restore liver damage or act as boon for the liver are hepatoprotective agents. In the normal state, antioxidant defence systems such as SOD, catalase, and glutathione peroxidase enzymes eliminate the damaging free radicals[35]. There are several plants reported to have phytoconstituents which proves the hepatoprotective activity.

Table 5: Description of Hepatoprotective Agent

Name of the plant	Hepatoprotective agent
Cichorium Intybus Cynara Scolymus	Esculetin, Hydroxycinnamic acid, Caffeoylquinic acid, Dicaffeoylquinic acid, Chicoricacid[25], cichotyboside[26], flavonoids, saponins[4] Flavones, flavanones, flavonols, coumarins, and phenolic acids[4]
Foeniculum vulgare	d-limonene[1]
Cordia sebestena L.	Flavonoids[5]
Curcuma heyneana	Flavonoids, saponins, tannins,glycosides,steroids/triterpenoids, curcuminoid which comprises of comprises curcumin, demethoxycurcumin and bisdemethoxycurcumin[6]
Lobelia Alsinoides Lam.	Steroids, alkaloids, phenol and tannins[2]
Three Varieties of the Passion Fruit (Passiflora Sp.)	Alkaloids, flavonoids, steroids, triterpenoids, saponins, tannins, glycosides, and phenolic[7]
Phyllanthus Fraternus	Phenolic and flavonoid content[27]
Pavetta Indica LINN	Flavonoids and their glycosides, alkaloids, sterols, phenolics, lignins, terpenoids, coumarins,saponins,phenols[28]
Mimosa Pudica	Flavonoids, glycosides, terpinoids, alkaloids, phenol and tannin[10]
Terminalia coriacea	β – Sitosterol, Stigmasterol, 1H-Inden-1-one,2,3-dihydro-3,3,5,6,-tetramethyl, n-hexadecanoic acid, flavonoids and tannins[3]
Bambusa Bambos	Flavonoids, steroidal alkaloids, etc[11]
Rosa Canina	Flavonoids, phenolic acids, tannins, carotenoids[12]
Garcinia Pedunculata	Flavonoids, saponins, glycosides, steroids, alkaloids and phenols[13]
Tetrapleura tetraptera	Flavonoid,polyphenols,flavanol[29]
Feijoa sellowiana	polyphenols[15]

Piper cubeba	Essential oil, terpenoids, and flavonoids[30]
Feronia limonia	Flavonoids[17]
Solanum xanthocarpum	Flavonoids, steroidal alkaloids ,triterpenes, quercitrin, apigenin glycosides[18]

Plant phenolics include simple phenols, phenolic acids, coumarins, lignans, flavonoids,diaryl-alkanoids, stilbenoids, proanthocyanins, tannins, and anthocyanins some alkaloids. They protect against oxidative damage by donating hydrogen or electron to free radicals and aid in stabilizing cell membrane networks and inhibiting the formation and expression of inflammatory cytokines like tumor necrosis factor alpha (TNF-α), Transforming Growth Factor beta (TGF-β) and varieties of interleukins (IL-6, IL-2, IL-8)[31].

Flavonoids –Enhance the antioxidant functions of liver by increasing the level of superoxide dismutase, glutathione s-transferase and glutathione peroxidase, improve insulin sensitivity and inhibit hepatic stellate cell activation by regulating the activities of the enzymes such as heme oxygenase-1, cytochrome P450 and telomerase. Reduce inflammatory reaction by restraining the expression of tumor necrosis factor-α, interferon-γ and interleukin-6, and mediate apoptosis and autophagy by controlling the pathways of genes-p 53-genetics, nuclear factor κB and phosphatidylinositol 3-kinase/protein kinase B signaling, which provides an alternative way for the treatment of liver injury[32]. Three flavonoids, rutin, robinin and gossypetin 3-glucuronide 8-glucoside were isolated and characterized from TCLME(methanolic extract of T. coriacea leaves for the first time[33].

The administration of Piper cubeba ethanolic extract PCEE significantly scavenge reactive free radicals that diminish oxidative stress or damage of liver tissue and provoke the activities of the hepatic antioxidant enzymes. Down-regulated the CCl_4-induced proinflammatory cytokines TNFα and IL-6 mRNA expression ,while it upregulated the IL-10 and induced hepatoprotective effect by down-regulating mRNA expression of iNOS and HO-1 gene[30].A study conducted to assess Hepatoprotective effects and structure-activity relationship of five flavonoids against lipopolysaccharide/D-galactosamine induced acute liver failure in mice showed flavonoids activity on anti-oxidation, anti-inflammation, and anti-apoptosis. After lipopolysaccharide (LPS)/D-galactosamine (D-GalN) administration, five flavonoids inhibited oxidative activities with reducing nitric oxide synthase (iNOS), malondialdehyde (MDA), and improving catalase (CAT), superoxide dismutase (SOD), total antioxidant capacity (T-AOC), nuclear factor erythroid-derived 2-related factor 2 (Nrf2) and heme oxygenase-1 (HO-1). They reduced pro-inflammatory cytokines, prevented the phosphorylation of IKK, IκBα, and NF-κB/p65 in the NF κB signaling pathway. Also inhibited hepatocyte apoptosis through increasing Bcl-2/Bax ratio and suppressing the Caspase family proteins[34].

Esculetin-reduce the expression of inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Increased the amount of Nrf2 (which plays a role in resistance to oxidative stress) phosphorylation and simultaneously decrease the amount of its inhibitor Keap1.Esculetin induces antioxidant effects by inducing antioxidant enzymes, which is marked by a significant increase in SOD. Esculetin decreased neutrophil filtration[35].

Hydroxycinnamic acids (HCs) are phenolic compounds , subclass includes coumaric acid, ferulic acid, caffeic acid,cinnamic acid, chlorogenic acid. Caffeic acid can modulate the expression of kelch-like ECH associated protein-1 (Keap1), a hepatic carcinoma factor, by interacting with Nrf2 binding site and restraining it from binding to Keap1 and elevating the expressions of vital antioxidative signals like HO-1[31].

Chichoric acid-Activates nuclear factor-erythroid 2-related factor 2 (Nrf2) pathway with increasing the level of AMP-activated protein kinase (AMPK). Treatment led to improved protein levels of autophagy genes. The hepatoprotective impact of chicory was due to aversion of lipid peroxidation, supporting of endogenous antioxidant, and overexpression of genes encoding antioxidant enzymes, thus averting DNA damage[25]. Phenolic structures in the Cynara scolymus extract have a pivotal role in free radical mediated processes inhibition[4].Several studies prove the hepatoprotective activity of C.scolymus but failed in the reviewed comparison study, a concentration higher is believed to show hepatoprotection.

Curcumin-It exerts its protective and therapeutic effects in oxidative coupled

liver diseases by suppressing proinflammatory cytokines, lipid peroxidation products, hepatic stellate cells, and Akt activation. Curcumin improve oxidative stress induced expression of

Nrf2, SOD, CAT, and GSH. Curcumin acts as a free-radical scavenger over the activity of different kinds of ROS with its active phenolic pharmacophore, b-diketone and methoxy group[31]. Functional hydroxyl groups in flavonoids mediate their antioxidant effects by scavenging free radicals, also activate glutathione peroxidase system as protective enzyme and inhibit the enzymes which are involved in reactive oxygen species generation.curcumin stimulates antioxidant enzyme activity like glutathione peroxidase, superoxide dismutase and catalase. Curcumin is capable of scavenging oxygen free radicals such as superoxide anions and hydroxyl radicals which are important in initiation of lipid peroxidation. It shows hepatoprotection by two mechanisms, directly by stabilizing or delocalizing unpair electron or indirectly by stimulating antioxidant activity[6].

Saponins can directly protect hepatocytes from apoptosis through a mechanism of inhibition of the production of Tumor Nuclear Factor Alpha (TNFα). Alkaloids are found in abundance in almost all parts of plants and have activities in scavenging the reactive oxygen species[7].Ginsenoside Rb1, a major saponin in ginseng, exert antinflammatory response by inhibiting proinflammatory cytokines and alleviate signalling pathway[36].

Inhibitory effect of limonene on the expression of NF-κB and its upstream TNF-α, reduced infiltration of inflammatory cells, activation of the AMPK signaling pathway. Thus, Antioxidant, anti-inflammatory, and antiapoptotic property of limonene plays an important role[37].D-limonene present in F. vulgare increase concentration of reduced Glutathione (GSH) which binds with NAPQI (N-acetylp-benzoquinone imine). Its mechanisms against liver fibrosis may be related with inhibiting lipid peroxidation formation in liver tissue of liver fibrosis mice and reducing the collagen formation by suppressing protein expression of TGF-β_1, α-SMA, MMP-9 and TIMP-1[38].

Catechins are renowned for their powerful potential to scavenge various free radicals such as hydroxyl, peroxyl, superoxide, and other radicals. Antioxidant activity of catechins is mediated through different mechanisms. They are able to transfer an electron to bind a reactive radical, while they change to the more stable and less reactive phenoxyl radical. They are also able to chelate Cu^{2+} and Fe^{3+} ions, thus limiting free radicals generation. Indirectly, catechins exert an antioxidant effect by increasing the level of endogenous antioxidants such as glutathione reductase, catalase, and superoxide dismutase. Moreover, catechins are reported to have an inhibitory effect on xanthine oxidase that catalyzes the metabolism of purines into uric acid and reactive oxygen species[39].

Alkaloids demonstrate hepatoprotective activity through their action in decreasing CYP2E1 mRNA and therefore CYP2E1 activity[40].A study with steroidal alkaloid from S. saligna reduced liver inflammation by firstly reducing the T-cells multiplication and amount of IL-2 which change the entire inflammation reactions and as well non-cytotoxic, secondly acts as antioxidant and act as a free radicals scavenger which is produced by the hepatocytes[41].

RESULT

Table 6: Result Description

Name of the plant	Study model	Result
Cichorium Intybus Cynara Scolymus[4]	Broiler Chicken	Ethanolic extract of Cichorium intybus showed significant hepatoprotective effect by decrease in AST and GGT concentrations at 0.1% alcoholic extract compared to Cynara Scolymus which did not protect the liver against paracetamol induced injury, both decreased the mortality rate and significant gain in body weight was observed.
Foeniculum Vulgare[1]	Rabbit	Study result showed Foeniculum vulgare at 500 mg/kg as most hepatoprotective. Histopathological findings also supported the biochemical results.
Cordia Sebestena L. [5]	Wistar Albino Rats	Cordia sebestena fruit extract at dose of 400 mg/kg reversed liver deteriorations. Histopathological study revealed the regeneration of hepatocytes.
Curcuma heyneana[6]	Wistar Albino Rats	Administration of ethanol extract of C. Heyneana rhizome at the dose of 25, 125 or 625 mg/kg significantly inhibited the elevated liver biomarkers. Treatment with doses of 125, 625mg /kg did not show any sign of necrosis. Ethanol extract strongly scavenged DPPH.
Lobelia Alsinoides Lam. [2]	Wistar Albino Rats	Animals treated with the fine paste of L. Alsinoides at 2.16 g/kg showed best hepatoprotective activity.Histomorphologic evaluation showed hepatoprotective effect with scattered mitotic figures in the parenchyma, doses up to 2500 mg/kg are not toxic to rats, showed good anti-oxidant activity.
Three Varieties of the Passion Fruit (Passiflora Sp.) [7]	Albino Rats	The hepatoprotective activity and nephroprotective activity of purple passion fruit peel extract at 250 mg per kg of body weight was best compared to red and yellow peel extract.
Phyllanthus Fraternus[8]	Wistar rats	P. Fraternus reduced liver biomarkers best at 500 mg/kg body weight ,showed rising total protein levels and reduction of necrosis and sinusoids was observed in histopathological examination
Pavetta Indica LINN[9]	Albino Rats	No mortality up to 2000 mg/kg body weight. Ethanol extract of P. Indica exhibited significant hepatoprotective activity at 100mg/kg and 200mg/kg body weight.
Mimosa Pudica[10]	Wistar Rats	Mimosa Pudica leaves extract at 300 mg/kg of body weight showed Hepatoprotective activity by significantly restored liver markers.
Terminalia Coriacea[3]	Albino Rats	METC at 500 mg/kg, body weight treated rats exhibited maximum depletion of liver biomarkers. The histopathology study also showed the hepatic protection of extracts, No lethality was observed at 2000mg/kg.
Bambusa Bambos[11]	Wistar Rats	Methanolic shoot extract of b. Bambos at dosage 400 mg/kg per body weight showed best hepatprotection.
Rosa Canina[12]	Albino Wistar rats	R. Canina at doses of 500 and 750 mg/kg significantly reduced elevated levels of ALT, AST, ALP and MDA, increased the serum levels of ALB and TP histopathological studies supported the biochemical finding.
Garcinia Pedunculata[13]	Wistar albino rats	Acute oral toxicity study did not reveal any mortality in any dose up to 2,000 mg/kg,reduction in AST,ALT,alkaline phosphatase
Tetrapleura	Wistar rats and	The extracts decreased the elevation in the activities of the enzymes in the liver.

Tetraptera[14]	mice	They also protected against CCl4 induced lipid peroxidation at 100-500 mg/kg. The extracts reduced CCl4-liver induced necrosis in dose dependent manner.
Feijoa Sellowiana[15]	Albino Wistar rats	Dose dependently the results showed decrease in ALT, AST and GSH, necrosis in the liver parenchyma also decreased.
Piper Cubeba[16]	Swiss Albino mice and Wistar rats	Extract had significant dose-dependent antioxidant activity in all in vitro experiments, it attenuated ccl4 induced serum marker enzymes and total protein and histopathology result supported the same.
Feronia Limonia[17]	Albino rats	Treatment at 300 mg / kg of ethanolic extract of Feronia Limonia promoted body weight and showed significant hepatoprotective activity
Solanum Xanthocarpum[18]	Sprague-Dawley rats and Swiss albino mice	400 mg/kg body weight showed maximum reduction in hepatotoxicity induced serum levels and reduced the lipid peroxidation in the liver tissue and restored activities of defence antioxidant enzymes. GSH, SOD and catalase towards normal levels and histopathology study also supported the same.

DISCUSSION

All the plants reviewed have remarkable proven hepatoprotective potential due to various miraculous phytoconstituents. The greater the content of alkaloids, flavonoids, and saponins in an extract, the higher the hepatoprotective activity possessed by the extract. Flavonoids are polyphenol compounds that have been proven for hepatocytes protection from free radical scavenging activity[7]. Polyphenols are a group of compounds in plants with high antioxidant potential. This antioxidant activity is mainly due to their redox potential that allows them to neutralize free radicals, singlet oxygen or decomposing peroxides[29]. The *n*-hexane extract lowered thiobarbituric acid reactive substance (TBARS) more than the methanol extract[14], antiplasmodial effects of this plant might be correlated to his high phenolic content .Further research for active Phytoconstituents demonstrating hepatoprotective activity of C. Sebestena fruit is suggested [5]. The mechanism of the hepatoprotective action of the plant L. Alsinoides was uncertain from the study but is assumed to be due to the capacity of the plant derivatives to prevent lipid peroxidation by its free radical scavenging activity in the liver[2]. Bamboo is an under-explored plant with high therapeutic potential. Bambusa vulgaris have shown great antioxidant activity and presence of saponins, alkaloids, flavonoids, phenolics tannins, phytosterols, and triterpenoids[42].Investigations are required to characterize the active hepatoprotective agent and mechanism of action of Bambusa Bamboo[11].Several plants are under the research and several others are still undercover to be discovered for their possible hepatoprotective activity, this is the need of an hour as liver diseases are a growing threat.

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