



Medicinal Plants with Hepatoprotective Activity: A Review

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Abstract

The liver is essential organ of dominant importance involved in the safeguarding of metabolic functions and detoxification of the exogenous and endogenous substances. Impaired liver function affects the different homeostatic mechanisms, with potentially serious consequences. The potentially reactive oxygen species (ROS) are continuously generated inside the human body as a result of the exposure to exogenous chemicals. Under normal conditions, the ROS generated are detoxified by the antioxidant defences leading to equilibrium between these two processes. To prevent the damage caused by ROS, living organisms have developed an antioxidant defence system that includes the presence of nonenzymatic antioxidants and enzymes. Thus, the use of antioxidants in the prevention and cure of various diseases is expanding, and there is considerable interest in the study of the antioxidant activities of molecules.

Thus, the discovery of the substitute therapeutic means for the treatment of the liver disease is required. The treatment with less side effects and minimum possible dosage regimen should be the aim. Plants have played an important role in the discovery of novel and useful drugs used in modern medicine. The present review elaborates different plants used for the treatment of the hepatoprotective activity by using different models of hepatotoxicity.

Keywords

Liver, Plants, Antioxidant, Hepatoprotective Activity and Hepatotoxicity

INTRODUCTION:

The liver is the largest organ in the body, contributing about 2 percent of the total body weight, or about 1.5 kg in the average adult human. The basic functional unit of the liver is the *liver lobule*, which is a cylindrical structure several millimetres in length and 0.8 to 2 millimetres in diameter. The human liver contains 50,000 to 100,000 individual lobules [1].

The liver is essential organ of dominant importance involved in the safeguarding of metabolic functions and detoxification of the exogenous and endogenous substances like xenobiotics, drugs, viral infections and chronic alcoholism. Impaired liver function affects the different homeostatic mechanisms, with potentially serious consequences. About 20,000 deaths occur every year due to liver diseases.

Hepatocellular carcinoma is one of the ten most common tumours in the world with over 2,50,000 new cases each year. Although viruses are the main cause of liver diseases, excessive drug therapy, environmental pollution and alcoholic intoxication are not uncommon [2].

The potentially ROS such as superoxide radical (O_2^-), hydrogen peroxide (H_2O_2) and hydroxyl radical ($OH^\cdot$), are continuously generated inside the human body as a consequence of the exposure to exogenous chemicals in our environment and/or to a number of endogenous metabolic processes involving redox enzymes and bioenergetic electron transfer. Under normal circumstances, the ROS generated are detoxified by the antioxidant defences leading to equilibrium between these two processes. However, owing to ROS overproduction and/or inadequate antioxidant defences, this equilibrium is hampered, thus favouring a surge of ROS that culminates in oxidative stress. The ROS readily attack and induce oxidative damage to several biomolecules including proteins, lipids, lipoproteins and DNA, contributing to the development of various diseases such as atherosclerosis, diabetes, cancer, neurodegenerative diseases, hepatic diseases and the ageing process [3].

To prevent the damage caused by ROS, living organisms have developed an antioxidant defence system that includes the presence of nonenzymatic antioxidants (e.g. glutathione, uric acid, bilirubin, and vitamins C and E) and enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). It has been proposed that in addition to these natural antioxidant systems, other synthetic or natural ROS scavengers may reduce the incidence of free radical-mediated diseases. Thus the use of antioxidants in the prevention and cure of various diseases is expanding, and there is considerable interest in the study of the antioxidant activities of molecules [3].

Although medicinal plants are rarely used as antioxidants in traditional medicine, their claimed therapeutic properties could be due, in part to their capacity for scavenging oxygen free radicals, which may be involved in many diseases.

Thus, the discovery of the substitute therapeutic means for the treatment of the liver disease is required. The treatment with less side effects and minimum possible dosage regimen should be the aim. Plants have played an important role in the discovery of novel and useful drugs used in modern medicine. There are number of drugs of plant origin

which are useful, with life saving capacity and providing immediate therapeutic benefit. Plants have been a source for various drugs since longer time, and drugs from the plant source has less side effects. Thus, the plants can be used as a huge source for the treatment of the hepatic ailments.

Hepatotoxins and their mechanism of action:

In this review the authors mainly concentrated on hepatotoxins like Carbon Tetrachloride, Paracetamol.

Carbon Tetrachloride:

CCl_4 is a potent liver toxicant and its metabolites such as trichloromethyl radical ($CCl_3^\cdot$) and trichloromethyl peroxy radical ($CCl_3O_2^\cdot$) which attacks the polyunsaturated fatty acids of the membrane endoplasmic reticulum which cause severe damage in vital organs like liver by termination of movement of large quantities triglycerides from the liver to the plasma leading to fatty liver. The excessive generation of free radicals in CCl_4 induced liver damage will provokes a massive increase of lipid peroxidation in liver. These free radicals induce hepatotoxicity by binding with lipoproteins leads to peroxidation of lipids in endoplasmic reticulum which results in the loss of intracellular metabolic enzymes [4] and abnormal increase in the liver enzymes followed by hepatocellular necrosis. There is influx of monocytes into the liver during the CCl_4 induced hepatotoxicity causing an increase of Reactive Oxygen Species (ROS) synthesis and the rise in Kupffer cell leukotriene production in the liver leading to imbalance between cytoprotective and cytotoxic prostanoids [5].

Acetaminophen/ Paracetamol:

Paracetamol (PCM) is an analgesic and antipyretic drug which, when taken in at toxic doses, becomes a potent hepatotoxic substance by damaging renal tubules and causing hepatic necrosis and is lethal to experimental animals and humans. Its overdose can cause liver function failure, centrilobular hepatic necrosis and even death in experimental animals as well as human [6].

The mode of action of paracetamol on the liver is by covalent binding of its toxic metabolite, n-acetyl-p-benzoquinone-amine to the sulfhydryl group of protein resulting in cell necrosis and lipid peroxidation. Due to liver injury caused by paracetamol overdose, the transport function of the hepatocytes gets disturbed resulting in the leakage of the plasma membrane, thus causing an increase in serum enzyme levels [7].

Table No. 1: Hepatoprotective medicinal plants with their mode of action/Observation in Carbon Chloride treated Hepatotoxicity

Botanical name	Family	Parts used	Type of extract	Observation / mode of Action
<i>Alpinia oxyphylla</i> [8]	Zingiberaceae	Fruits	Ethanol	Flavonoids and other phenolic compounds may be partially responsible for the pharmacological effect of hepatoprotection.
<i>Beta vulgaris</i> [9]	Amaranthaceae	Roots	Ethanol	Showed significant dose dependent hepatoprotective activity.
<i>Boschniakia rossica</i> [10]	Orobanchaceae	Whole plant	Ethanol	Phenylpropanoid glycoside and iridoid glucoside may exhibits protective effect on CCl ₄ -induced acute hepatic injury by reducing oxidative stress
<i>Camellia sinensis</i> [11]	Theaceae	Packets	Hot water extraction and ethanol precipitation	Strong antioxidant activity against free radicals and afford significant protection against CCl ₄ induced oxidative liver injury in mice
<i>Cassipourea filiformis</i> [4]	Lauraceae	Whole plant	Chloroform	Protects from hepatocyte degradation, centrilobular necrosis, vacuolization and fatty infiltration thus shows dose dependent hepatoprotection.
<i>Clerodendrum inerme</i> [12]	Verbenaceae	Leaves	Ethanol	Showed significant decrease in the serum enzymes Alanine transaminase (ALT), Aspartate aminotransferase (AST) and Alkaline phosphatase (ALP) thus seems to possess hepatoprotective activity
<i>Cocculus hirsutus</i> [13]	Menispermaceae	Leaves	Ethanol	Ethanolic extract has potent hepatoprotective activity on carbon tetrachloride induced hepatocellular destruction in rats
<i>Corchorus depressus</i> [14]	Tiliaceae	Whole plant	Ethanol	It has potent cytoprotective effect against CCl ₄ induced toxicity in HepG2 cell line and which may be attributed to decrease in CCl ₄ induced reactive oxygen species levels and resultant oxidative stress.
<i>Ecballium elaterium</i> [15]	Cucurbitaceae	Fruits	--	Its hepatoprotective and anti-inflammatory effect was confirmed on a model of acute liver damage.
<i>Eclipta alba</i> [16]	Asteraceae	Leaves	Aqueous	The study indicates that the leaf extract of <i>E. alba</i> has potential restorative effect on CCl ₄ induced hepatotoxicity in male albino rats.
<i>Eryngium maritimum</i> [17]	Apiaceae	Seeds	Methanol	The obtained results highlighted the potential use of <i>E. maritimum</i> as a source of bioactive compounds with hepatoprotective and nephroprotective advantages.
<i>Fagonia indica</i> [18]	Zygophyllaceae	Whole plant	Methanol	Methanolic extract showed hepatoprotective activity against CCl ₄ induced hepatotoxicity and this might

<i>Fagonia schweinfurthii</i> [19]	Zygophyllaceae	Whole plant	Ethanol	be due to the presence of flavanoid and tannins. Results of this study revealed that ethanolic extract has significant hepatoprotective activity. This effect may be due to the ability of the extract to inhibit lipid peroxidation and increase in the antioxidant enzymatic activity.
<i>Cichorium glandulosum</i> [20]	Asteraceae	Roots	Ethanol	Results suggest that ethanolic extract is potent hepatoprotective agent that could protect liver against the acute injury and this ability might be attributed to its antioxidant potential.
<i>Garcinia indica</i> [21]	Clusiaceae	Fruits	Methanol	Results of this study revealed that <i>Garcinia indica</i> could afford a significant protection in the alleviation of CCl ₄ induced hepatocellular injury by free radical scavenger intercepting those radicals involved in CCl ₄ metabolism by microsomal enzymes.
<i>Gentiana veitchiorum</i> [22]	Gentianaceae	Whole Herb	Methanol	<i>G. veitchiorum</i> can protect the liver against CCl ₄ induced damage in mice, and this hepatoprotective effect was due at least in part to its ability through scavenging CCl ₄ associated free radical activities.
<i>Ginkgo biloba</i> [23]	Ginkgoaceae	Leaves	Acetone–Methanol	The results obtained in this study indicate that extract is able to inhibit CCl ₄ induced hepatotoxicity in rats. By scavenging free radicals, it inhibits lipid peroxidation and augments cellular antioxidant defense system.
<i>Glycyrrhiza inflata</i> [24]	Fabaceae	Roots and Rhizomes	Ethanol	Studies indicated that extract remarkably attenuated CCl ₄ induced acute liver injury in mice. These compounds could be promising hepatoprotective natural agents.
Green tea [25]	--	Leaves	Methanol	Hepatic tissue damage induced with CCl ₄ was improved with the treatment of extract. These results suggested that it possesses hepatoprotective properties against the effect of CCl ₄ .
<i>Hybanthus Enneaspermus</i> [26]	Violaceae	Whole plant	Aqueous	The present study results demonstrate the protective, curative and antioxidant effects of <i>H. enneaspermus</i> aqueous extract used against CCl ₄ induced hepatotoxicity in rats.
<i>Hyptis suaveolens</i> [27]	Lamiaceae	Areal parts	Methanol	This study shows that <i>H. suaveolens</i> methanol extract can be proposed to protect liver against CCl ₄ induced oxidative damage. The effect might be

<i>Juniperus Phoenicea</i> [28]	Cupressaceae	Berries	Aqueous	correlated with its antioxidant and free radical scavenger effects. The results of the present investigation indicate that <i>J. Phoenicea</i> possesses hepatoprotective activity and this effect was may be due to its antioxidant properties. <i>L. chinensis</i> extract were able to restore the viability of cells treated with CCl ₄ . Therefore, it possesses hepatoprotective activity, corroborating with ethno pharmacological use, and does not lead to acute toxicological effects. The hepatoprotective and antioxidant activities of the bark extract might be due to the presence of unique chemical classes such as flavonoids, alkaloids & polyphenols. It was suggested that the hepatoprotective effects of the extract might be related to antioxidative activity and expressional regulation of CYP2E1. It significantly reduces CCl ₄ induced acute hepatotoxicity by down regulating the expression of pro-inflammatory cytokines in rats. Results indicate that it has a profound protective effect against acute CCl ₄ induced hepatotoxicity in rats, which may be due to its free radicals scavenging effect, inhibition of lipid peroxidation, and its ability to increase antioxidant activity The extract scavenged 2,2-diphenyl-1-picrylhydrazyl (DPPH) and did not produce acute toxicity in mice at 2000 mg/kg. In conclusion, was confirmed the hepatoprotective potential of <i>M. robusta</i> by its antioxidant effects
<i>Litchi chinensis</i> [29]	Sapindaceae	Leaves	Hydroethanolic	<i>Mentha arvensis</i> possesses hepatoprotective effect against CCl ₄ induced liver damage in rats as evidenced by biochemical & histological parameters. The involvement of archidonic acid and purine metabolism in hepatoprotection has not been reported previously and may provide new therapeutic targets and/or options for the treatment of liver injury.
<i>Luminetzera racemosa</i> [30]	Combretaceae	Bark	Hydroethanolic	
<i>Lycium chinense</i> [31]	Solanaceae	Fruits	Aqueous	
<i>Lygodium flexuosum</i> [32]	Lygodiaceae	Whole plant	<i>n</i> - hexane	
<i>Mangifera Indica</i> [33]	Anacardiaceae	Stem bark	Aqueous	
<i>Maytenus robusta</i> [34]	Celastraceae	Leaves	Methanol	
<i>Mentha arvensis</i> [35]	Lamiaceae	Leaves	Ethanol Chloroform Aqueous	
<i>Muntingia calabura</i> [36]	Muntingiaceae	Leaves	Methanol	

<i>Nymphaea pubescens</i> [37]	Nymphaeaceae	Flower	Aqueous Methanol Chloroform	Glutathione and superoxide dismutase (SOD)-levels were restored towards normal in the liver of CCl ₄ treated rats, indicating the hepatoprotective role, which was found to contain a fair amount of flavonoids, phenolics, and saponin constituents.
<i>Panax ginseng</i> [38]	Araliaceae	Root		Exhibited strong hepatoprotective effect on the CCl ₄ induced acute liver injury, which was related to anti-oxidative and anti-inflammatory capabilities
<i>Mentha piperita</i> & <i>Petroselinum crispum</i> [39]	Labiatae & Apiaceae	Leaves	Aqueous	The results of this study show that peppermint, parsley and their mixture oils led to the protective effect against CCl ₄ hepatotoxicity. The results may be attributed to its antioxidant content and free radical scavenger effects.
<i>Periploca hydaspidis</i> [40]	Asclepiadaceae	Whole plant	Methanol	The altered levels of various parameters provoked by CCl ₄ toxicity restored towards the control level by the methanol extract of <i>P. hydaspidis</i> in a dose dependent manner. These results suggested the presence of antioxidant and anti-inflammatory phyto-constituents.
<i>Phoenix dactylifera</i> [41]	Arecaceae	Seeds	Aqueous	The <i>Phoenix dactylifera</i> seeds could be a promising candidate for protection against the CCl ₄ - induced liver intoxication, and this hepatoprotective effect might be attributed to the antioxidant and free radical scavenging activities
<i>Phyllanthus Urinaria</i> [42]	Phyllanthaceae	Whole plant	Ethanol /water	The results suggested that the potential hepatoprotective effects of PUL in attenuating CCl ₄ -induced hepatotoxicity could be partially attributed to regulating L-carnitine, taurocholic acid, and amino acids metabolism, which may become promising targets for treatment of liver toxicity
<i>Schisandra chinensis</i> [43]	Schisandraceae	Bee pollen	Ethanol	It has strong antioxidant activities and significant protective effect against acute hepatotoxicity induced by CCl ₄ and has been supported by the evaluation of liver histopathology in mice. The hepatoprotective effect may be related to its free radical scavenging effect, increasing antioxidant activity and inhibiting lipid peroxidation.
<i>Sesbania grandiflora</i> [44]	Fabaceae	Flowers	Ethanol & Aqueous	The ethanolic and aqueous extracts <i>S. grandiflora</i> flower have significant action on the liver of CCl ₄ induced hepatotoxicity animal models.

<i>Sida cordata</i> [45]	Malvaceae	Leaves	Ethanol & water mixture	The result of the study strongly indicates the protective effect against CCl ₄ induced acute liver toxicity in rats and thereby scientifically supports its traditional use.
<i>Phyllanthus amarus</i> [46]	Phyllanthaceae	Whole plant	Ethanol	The combination of silymarin and <i>Phyllanthus amarus</i> showed synergistic effect for hepatoprotection. May be due to higher availability of phyllanthus lignans particularly phyllanthin in the ethanolic extract.
<i>Spinacia oleracea</i> [47]	Chenopodiaceae	Seeds	Ethanol	The result of the present study indicates the significant hepatoprotective activity, and hence suggests its use as potential therapeutic agent in liver diseases.
<i>Spondias mombin</i> [48]	Anacardiaceae	Leaves & Stem	Methanol	This study provides preliminary evidence supporting the potential therapeutic benefit of <i>S. mombin</i> in xenobiotic-induced hepatotoxicity.
<i>Swertia chirayita</i> & <i>Andrographis paniculata</i> [49]	Gentianaceae & Acanthaceae	Whole plant	Ethanol	Since results of biochemical studies conclude that the ethanol extract of <i>A. Paniculata</i> showed significant better hepatoprotective as compare to <i>S. Chirayita</i> .
<i>Syzygium samarangense</i> [50]	Myrtaceae	Leaves	Methanol	<i>Syzygium samarangense</i> is a good candidate for further evaluation as an antioxidant and liver protecting drug. Due to presence of antioxidant molecules in leaf extract.
<i>Terminalia bellirica</i> [51]	Combretaceae	Fruits	Aqueous acetone	The results were found comparable with that of standard drug in all the parameters. The above findings suggest the therapeutic potential of the plant in alleviating hepatic oxidative stress and tissue damage; hence the traditional use of the plant in this regard stands justified.
<i>Teucrium polium</i> [52]	Lamiaceae	Aerial parts	Aqueous	Pretreatment with extract or Vit C improved the biochemical analyses, hematological parameters, and antioxidant defense system. Significantly reduce the hematoxicity and oxidative stress induced by CCl ₄ in rats.

Table No. 2: Hepatoprotective Medicinal Plants in Acetaminophen/Paracetamol Treated Hepatotoxicity

Plant	Family	Part used	Type of extract	Observation/Mode of action
<i>Acacia catechu</i> [53]	Fabaceae	Seeds & bark	Ethanol	Recovered liver from Acetaminophen induced damage by reducing oxidative stress and by increasing antioxidant defence signals
<i>Aegle marmelos</i> [54]	Rutaceae	Leaves	Ethanol	Exerts hepatoprotective activity through its antioxidant and anti-inflammatory properties which was enhanced by piperine.
<i>Amorphophallus paeoniifolius</i> [55]	Araceae	Tubers	Methanol and Aqueous	Showed significant reduction in the values of Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Oxaloacetate Transaminase (SGPT), & ALP. The hepatoprotective activity was confirmed by histopathological examination of the liver tissue of control and treated animal.
<i>Folium Syringae</i> [56]	Oleaceae	Leaves	Ethanol	Significantly reduced the toxicity induced by acetaminophen
<i>Passiflora subpeltata</i> [57]	Passifloraceae	Leaves	Acetone	Due to its alleviation of cellular antioxidant enzymes like catalase, SOD, Glutathione (GSH), Glutathione S-transferases (GST) and inhibition of lipid peroxidation shows strong hepatoprotective activity
<i>Selaginella lepidophylla</i> [58]	Selaginellaceae	Whole plant	Alcoholic & Aqueous	Exhibited significant hepatoprotective activity against Paracetamol and CCl ₄ induced hepatotoxicity in rats.
<i>Aquilaria agalloch</i> [6]	Thymelaeaceae	Leaves	Ethanol	Exhibited comparable protective potential against Paracetamol induced hepatotoxicity in rats as demonstrated by significant decrease in AST, ALT, ALP, Lactate dehydrogenase (LDH), cholesterol, bilirubin and increase in ALB, TP concentration, and prevention histopathological changes in liver
<i>Azadirachta indica</i> [59]	Mahogany	Leaves	Fresh Juice	Protects the liver from paracetamol induced hepatic damage by acting as an antioxidant.
<i>Cichorium intybus</i> & <i>Bougainvillea spectabilis</i> [60]	Asteraceae & Nyctaginaceae	Shoots & seeds	--	Prevented the paracetamol-induced rise in serum enzymes. Prevented CCl ₄ -induced prolongation in pentobarbital sleeping time confirming hepato protectivity

<i>Citrus hystrix</i> and <i>Citrus maxima</i> [61]	Rutaceae	Leaves	Methanol	The leaf extracts restored the liver function markers and hepatic antioxidants to the normal level than elevated levels noticed on paracetamol control & Reversal of hepato architecture has also been registered
<i>Cyathea gigantea</i> [62]	Cyatheaceae	Leaves	Methanol	Reduced the elevated levels of SGOT, SGPT, ALP, TB and also reversed the hepatic damage towards normal which further supports hepatoprotective activity
<i>Desmodium gangeticum</i> [63]	Fabaceae	Leaves	Ethanol	Serum ALT, ALP, AST, LDH, GGT was found to decrease & significantly attenuated the hepatotoxicity as an indirect target of paracetamol in an animal model
<i>Ecbolium viride</i> [64]	Acanthaceae	Roots	Ethanol	Shows hepatoprotective activity against paracetamol-induced hepatotoxicity in rats and it may be due to their antioxidant property
<i>Erythroxylum monogynum</i> [65]	Erythroxylaceae	Leaves	Methanol	Restored the elevated levels of serum markers as compared to toxic group which is confirmed by the histopathological changes observed.
<i>Flacourtia indica</i> [66]	Salicaceae	Aerial parts	Petroleum ether, Ethyl acetate & Methanol	Found to reduce SGOT, SGPT & Serum Alkaline Phosphatase (SAP) through the inhibition of microsomal drug metabolizing enzymes.
<i>Garcinia cola</i> [67]	Guttiferae	Seed		There was a significant reduction in the liver enzymes SGOT and SGPT and histology scores. Can protect against paracetamol-induced lethality and hepatotoxicity in rats
<i>Marrubium vulgare</i> [68]	Lamiaceae	Whole plant	Methanol	The toxic effects of paracetamol were significantly controlled in the extract treated groups which was manifested by the restoration of serum biochemical parameters to near normal levels
<i>Melia azedarach</i> [69]	Meliaceae	Leaves	Methanol	Has potent hepatoprotective activity against Paracetamol induced liver damage in rats, may be due to its antioxidant property
<i>Morinda Tinctoria</i> [70]	Rubiaceae	Leaves	Aqueous and Methanol	Both aqueous and methanol extracts of leaves of <i>M. tinctoria</i> have significant effect at higher dose of 150mg/kg.b.w.
<i>Passiflora leschenaultia</i> [71]	Passifloraceae	Leaves	Acetone	It attenuates acute paracetamol induced hepatic injury in rats. Probably this action is due to multiple mechanisms involving the

				elimination of the free radicals and thus inhibiting the elevation of serum biochemicals due to the presence of major phytochemical compounds
<i>Phoenix dactylifera</i> [72]	Arecaceae	Leaves	Aqueous and Methanol	Exerts protective effects against PCM- induced hepatotoxicity via scavenging free radicals and restoring hepatic antioxidant enzymes
<i>Phyllanthus niruri</i> [73]	Phyllanthaceae	Leaves	Aqueous	Crude aqueous extracts demonstrated the high efficacy in free radical scavenging, inhibition of reactive oxygen species and lipid peroxidation, which may be associated with treatment of different diseases, among which liver disease is the most important
<i>Emblica officinalis</i>	Phyllanthaceae	Fruits		The study validates that polyherbal formulation has a good hepatoprotective activity.
<i>Terminalia chebula</i>	Combretaceae	Fruits		
<i>Terminalia bellirica</i>	Combretaceae	Fruits		
<i>Picrorhiza kurroa</i>				
<i>Tinospora cordifolia</i>	Plantaginaceae	Rhizomes		
<i>Swertia chirata</i>	Menispermaceae	Stem		
<i>Azadirachta indica</i>				
<i>Adhatoda vasica</i> [74]	Gentianaceae Meliaceae	Herb Bark		
<i>Rhodiola imbricate</i> [7]	Acanthaceae Crassulaceae	Stem Bark Rhizomes	Acetone	It significantly protected the hepatic cells from damage. The HPLC analysis revealed the presence of some important phenolic compounds which could be responsible for the hepatoprotective activity
Silymarin & <i>Nigella sativa</i> [75]	Ranunculaceae	Seeds	Aqueous	The synergistic effect of silymarin and N. sativa extract is the most powerful in reducing the toxicity induced by APAP and improving the liver functions and antioxidant capacities of mice.
<i>Solanum xanthocarpum</i> & <i>Juniperus communis</i> [76]	Solanaceae & Cupressaceae	Fruits	Ethanol	Combined administration of lower doses significantly potentiated hepatoprotective effect which was significant as compared to their effect per se. The results clearly indicated hepatoprotective potential against AZM and PCM induced liver toxicity due to their synergistic antioxidant Properties

<i>Sphaeranthus indicus</i> [77]	Asteraceae	Roots	Ethanol and Aqueous	The expressions of different proteins spots were confirmed. These identified proteins involved in many cellular activities like maintain cellular integrity, iron transport, free radical scavenging activity and β oxidation of fatty acids. Therefore, the plant extracts could be used safely as food supplement for antioxidant activities enhancements.
<i>Terminalia paniculata</i> [78]	Combretaceae	Bark	Ethanol	It altered the levels of biochemical parameters and showed significant hepatoprotective activity.
<i>Teucrium stocksianum</i> [79]	Labiatae	Aerial parts	Ethanol	<i>T. stocksianum</i> significantly ameliorated all the paracetamol-induced signs of liver damage.
<i>Trianthema portulacastrum</i> [80]	Aizoaceae	Leaves	Ethanol	The plant extract completely prevented the toxic effects of paracetamol and thioacetamide on the serum parameters. A significant hepatoprotective activity of the Ethanol was shown.
<i>Tylophora villosa</i> [81]	Asclepiadaceae	Leaves	Ethanol	It showed therapeutic effect against paracetamol-induced hepatotoxicity in mice (<i>Mus musculus</i>)

CONCLUSION:

This review discussed different medicinal plants species which possesses the hepatoprotective activity. In addition, many of the species contains the phenols, phytosterols, saponin and flavanoid glycosides. However, the ranking of the overall hepatoprotective activity cannot be determined because the different experimental methods used for the different studies. Hence, we have focused here the different medicinal plants belonging to different families used as a hepatoprotective by discussing their mode of action. To make the herbal therapy more effective, it is very necessary to isolate the chemical entity responsible for the action and to identify the structure and the function relationship for the purpose of improved usefulness and pharmacokinetic profile. Prevention of the liver diseases is our interference and the successful completion of these proven strategies should be the focus of our efforts. These efforts will lead to the safer and the cost-effective drugs for the people suffering from the liver diseases, the number which is increasing day by day.

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