IJPSR (2020), Volume 11, Issue 9 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 06 December 2019; received in revised form, 26 February 2020; accepted, 11 March 2020; published, 01 September 2020

PRESENT SCENARIO OF HEPATOPROTECTIVE POTENTIAL OF MEDICINAL PLANTS: AN UPDATED REVIEW

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Keywords:

Hepatoprotective, Herbal, Hepatotoxicity, Liver, Ayurveda

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ABSTRACT: The liver is the principal site for metabolism and excretion in the body. The human liver metabolizes substances by various biochemical pathways, including oxidation, reduction, hydration, condensation, hydrolysis, conjugation or isomerization. Disorder of any of therefore mentioned process may lead to liver cell injury, what we call as hepatotoxicity, which in turn leads to many diseases. Such diseases are responsible for higher mortality rates worldwide. Hepatotoxicity can be due to medicines, chemicals, dietary disturbances, or herb induced liver damage *via* hepatotoxins. A number of herbal and herbomineral preparations are available in the Ayurveda, the traditional Indian medicine, which has been investigated for their hepatoprotective potential to treat different types of liver disorders. The use of natural elements to eliminate the root cause of the disease by restoring balance at the same time creates a healthy lifestyle to prevent the recurrence of imbalance. Herbal medicines have existed worldwide with long recorded history, and they were used in ancient Chinese, Greek, Egyptian, and Indian medicine for various therapies purposes. World Health Organization estimated that 80% of the word's inhabitants still rely mainly on traditional medicines for their health care. The subcontinent of India is well-known to be one of the major biodiversity centers with about 45,000 plant species. The present review is focused on different herbal plants that have the potential to cure the hepatotoxicity.

INTRODUCTION: The liver is the second largest (after the skin) organ in the human body and the largest gland (weighing an average of 1500 g). The liver is located in the upper right-hand portion of the abdominal cavity, beneath the diaphragm, and on top of the stomach, right kidney, and intestines. Shaped like a cone, the liver is a dark reddish-brown organ that weighs about 3 pounds.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.11(9).4189-00

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(9).4189-00

The liver is an organ only found in vertebrates which detoxifies various metabolites, synthesizes proteins, and produces biochemicals necessary for digestion [1, 2].

The liver is the most important organ that plays an important role in maintaining various physiological processes in the body. Liver damage is very common because the liver is a key organ in the detoxification process. Hepatotoxic chemicals damage liver cells primarily by producing ROS, some of which form covalent bonds with the lipid tissue. Due to excessive exposure to hazardous chemicals, sometimes the free radicals generated are so high that they overpower the natural defense system, leading to hepatic damage [3].

Hepatitis, a common disorder of varying severity, can lead to cirrhosis, liver failure, and death. If acute liver disorders are not promptly treated, the damage will go to chronic forms characterized by continuing hepatocellular necrosis and inflammation, usually with fibrosis, which tends to progress to cirrhosis and liver failure [4].

There are five main viruses, referred to as types A, B, C, D, and E. These five types are of the greatest concern because of the burden of illness and death. Liver injury or liver dysfunction is a major health problem that challenges not only health care professionals but also the drug regulatory agencies and the pharmaceutical industry. Despite enormous advances in modern medicine, there are no completely effective drugs that stimulate hepatic function, that offer complete protection of the organ, or that help to regenerate hepatic cells [5]. The aim of these alternatives being more effective and less toxic.

Herbal medicines have been used in the treatment of liver disease for a long time. In this context, therapeutic alternatives are limited. For this reason, there is a great need to find new drugs for the treatment of these pathologies.

There are potent indigenous herbal medicines available for the treatment of liver disorders in various parts of the world, and most of them have not yet been scientifically validated. If they are conducted, it could lead to the development of cost-effective drug. In the absence of a reliable liver protective drug in the modern system of medicine, a number of medicinal preparations in Ayurveda are recommended for the treatment of liver disorders. Natural remedies from medicinal plants are considered to be an effective and safe alternative treatment for liver diseases [6].

The plant-derived phytoconstituents (polysaccharides, proteins, and flavanoids, lignans, carotenoids, *etc*.) stimulate the immune system and maintaining hepatic diseases [7]. Flavonoids are phenolic compounds widely distributed in plants and have been reported to exert multiple biological effects, including antioxidant and free radical scavenging abilities [8]. There are a number of hepatoprotective herbs that have been reported. The present review is aimed at compiling data on promising phytochemicals from hepatoprotective herbs.

Hepatotoxicity Inducing Agents: Many xenobiotics like chemicals, drugs, household things, herbs and environmental factors are well-known to induce hepatotoxicity. Most significant for xenobiotic-induced liver injury, the centrilobular (zone-3) hepatocytes are the 1st sites of hemoprotein P450 accelerator activity, which regularly makes them at maximum risk of xenobiotic-induced liver injury. CCl_4, N-nitrosodiethylamine, Acetylaminofluorene, Galactosamine, d-Galactosamine/Lipopolysaccharide, TAA, Antitubercular drugs, PCM, Arsenic *etc*. have been shown to induce experimental hepatotoxicity in laboratory animals [9].

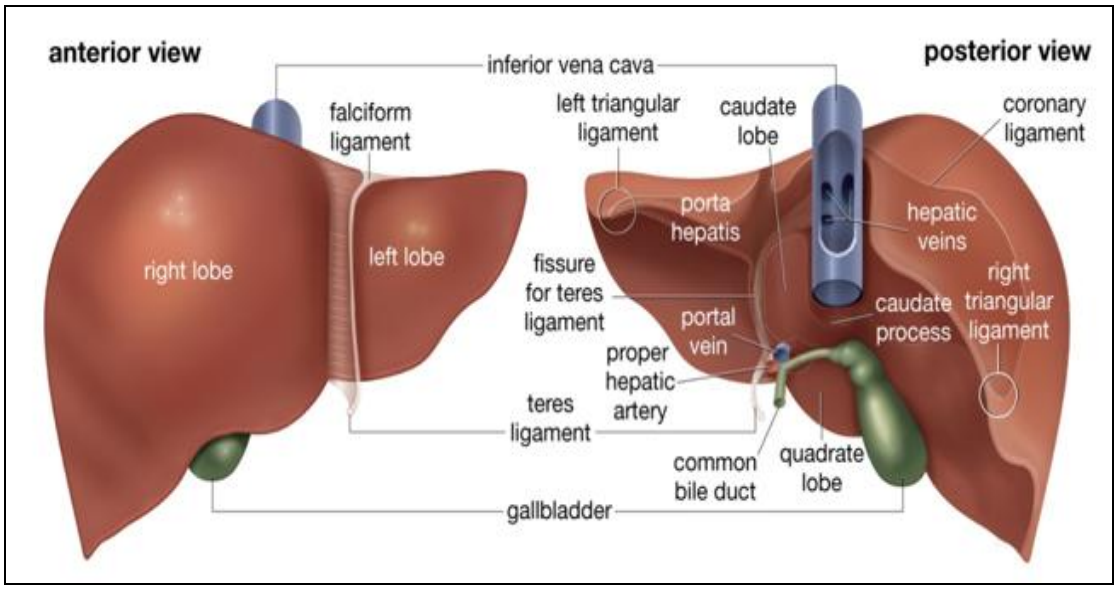

FIG. 1: ANATOMY OF LIVER

Model of Hepatotoxicity:

Thioacetamide Induced Hepatotoxicity Model: TAA, originally used as an antimycotic agent, is potent toxin bioactivated by hemoprotein P450 to sulfine (sulfoxide) and sulfene (sulfone) metabolites; it is known to induce liver cirrhosis of the liver in murine models that is caused by free radical-mediated super-molecule peroxidation. TAA administration results in liver harm in experimental rats by a marked increase alanine aminotransferase (ALT), aspartate aminotransferase (AST) in serum and malondialdehyde in the liver, conjointly centrilobular necrosis in internal organ design. TAA interferes with the movement of RNA from the nucleus to the protoplasm, which can cause membrane injury. A substance of TAA is chargeable for internal organ injury. TAA cut back the number of viable hepatocytes, likewise as rate oxygen consumption. Usually, TAA dosage is 100 - 300 mg/kg, administrated subcutaneous or intra-peritoneal. Future administration and/or high doses of TAA ends up in an organic chemistry modification, microscopic anatomy, and characteristic lesion in rat liver, which corresponds to cirrhosis of the liver-like patterns of micro-nodular liver cirrhosis in humans and associated protein-energy deficiency disease. Investigation on therapeutic principles ought to be done throughout TAA administration (prophylactic agents) or inside 2 months when the withdrawal of harmful agents (therapeutics) [10, 11].

Carbon Tetrachloride Induced Hepatotoxicity Model: CCl_4 is a strong hepatotoxin producing hepatic necrosis. Liver injury due to CCl_4 in experimental rats has been induced experimentally by many investigators. CCl_4 is metabolized by cytochrome P450 in endoplasmic reticulum and mitochondria with the formation of highly reactive trichloromethylperoxy free radicals, which initiate lipid peroxidation and finally cell necrosis. Administration of a single dose of CCl_4 to a rat produces, within 24 h, centrilobular necrosis and fatty changes. The development of necrosis is associated with the leakage of hepatic enzymes into serum. The toxic dose of CCl_4 is 0.1 - 3 ml/kg administrated intraperitoneally[12].

Paracetamol Induced Hepatotoxicity Model: PCM, a widely used analgesic and antipyretic drug, produces acute liver damage in high doses. PCM administration causes necrosis of the centrilobular hepatocytes characterized by nuclear pyknosis and eosinophilic cytoplasm followed by the large excessive hepatic lesion. The covalent binding of N-acetyl-P benzoquinoneimine, an oxidative product of PCM to sulphydryl groups of protein, result in degradation and lipid peroxidation of glutathione level and thereby, produces cell necrosis in the liver. The dose of PCM is 1 - 2 gm/kg administrated orally [13].

Chloroform Induced Hepatotoxicity Model: Chloroform has toxic effects similar to those of CCl4. Metabolism by microsomal cytochrome P450 is obligatory for the chloroform induced hepatic, renal, and nasal toxicity. It seems that the cytochrome P450-mediated oxidative metabolism of chloroform results in the formation of inorganic chloride (excreted in the urine), carbon dioxide (exhaled), phosgene, and some hepatic covalently bound carbon (either *via* free radical or phosgene formation). Extensive covalent binding to the kidney and liver protein has been found in direct relationship with the extent of hepatic centrilobular and renal proximal tubular necrosis [14].

Rifampicin Induced Hepatotoxicity Model: Patients on coincidental rifampicin medical care have associate accumulated incidence of liver disease. This has been postulated due to rifampicin-induced cytochrome P450 enzyme-induction, inflicting associate accumulated production of the toxic metabolites from acetyl hydrazine (AcHz). Rifampicin conjointly will increase the metabolism of isoniazid to isonicotinic acid and reducer, each of that is hepatotoxic. The plasma half-life of AcHz (a metabolite of isoniazid) is shortened by rifampicin, and AcHz is quickly reborn to its active metabolites by increasing the oxidative elimination rate of AcHz, which is said to the upper incidence of liver necrosis caused by isoniazid and rifampicin together. Rifampicin conjointly interacts with antiretroviral medicine and affects the plasma levels of those drugs also as the risk of hepatotoxicity [15].

Isoniazid Induced Hepatotoxicity Model: Isoniazid hepatotoxicity may be a common complication of antituberculosis medical care that ranges in severity from well elevation of serum transaminases to hepatic failure requiring liver

transplantation. This can be not caused by high plasma bactericide levels; however, it seems to represent an individual response. Isoniazid is metabolized to mono AcHz, which is additional metabolized to a toxicant product by haemoprotein P450 resulting in hepatotoxicity. Human genetic studies have shown that haemoprotein P4502E1 (CYP2E1) is concerned with antitubercular drug hepatotoxicity. The CYP2E1/c1 genotype is related to a better CYP2E1 activity and will result in a better production of hepatotoxins. Experimental Rodent studies showed that Isoniazid and Hydrazine induce CYP2E1 activity. Isoniazid has an inhibiting result on CYP1A2, 2A6, 2C19, and 3A4 activity. CYP1A2 is usually recommended to be concerned with reductant detoxification. Isoniazid will induce its own toxicity, presumably by the induction or inhibition of those enzymes [16].

Other Drugs Induced Hepatotoxicity Model: Few other drugs reported to cause hepatotoxicity are Glucocorticoids, Antibiotics (Amoxicillin, Ciprofloxacin, Erythromycin), Oral contraceptives and antifungals (Fluconazole, itraconazole) [17].

Drug Hepatotoxicity: A wide variety of chemicals produces clinical and pathological hepatic injury. Biochemical markers (*e.g.*, alanine transferase, alkaline phosphatase, and bilirubin) are often used to indicate liver damage. Liver injury is defined as a rise in either

a. ALT level more than three times of upper limit of normal (ULN),

b. ALP level more than twice ULN, or

c. Total bilirubin level more than twice ULN when associated with increased ALT or ALP[18, 19].

Mechanism of Liver Damage: The possible mechanisms of liver toxicity are due to excessive use of drugs and other xenobiotics in the context of hepatic physiology, metabolism, and cell biology. The important liver injury mechanisms can be a consequence of metabolism and/or direct cell toxicity of chemicals. These mechanisms include bile acid-induced liver cell injury during cholestasis, pathophysiological effects of mitochondrial dysfunction, and cell damage by reactive oxygen and nitrogen species. Theses is the importance of vascular (Kupffer cells, neutrophils) and intracellular generation of reactive oxygen by mitochondria and xenobiotic inducible enzymes (*e.g.*, CYP 4502E1) [20] **Table 1**.

TABLE 1: AN UPDATED REVIEW ON HEPATOPROTECTIVE POTENTIAL OF MEDICINAL PLANTS

S. no.	Scientific name	Part used	Extract	Active constituent	Hepatoprotective activity/study outcomes
1	*Abutilon indicum* [21]	Whole plant	Aqueous	β-sitosterol, p-β-D-Glucosyloxybenzoic acid, Caffeic acid	Activates antioxidative enzyme against CCl_3 (Inducer)
2	*Adhatodavasica* [22]	Leaves	Aqueous	Vasicine, vasicol, vasicinone, peganine, adhatodine, vasicolinone	Reduces elevated levels of SGOT and SGPT
3	*Aloe barbadensis* [23]	Aerial parts	Pet. ether, CHCl3, Methanol, Aqueous	Barbaloin, chrysophanol, glycoside aloe-emodin, glucose, galactose, mannose and galacturonic acid	Protects against increased lipid peroxidation and maintained glutathione contents by antioxidant property
4	*Amaranthus spinosus* [24]	Whole plant	Ethanol	Flavonoids, phenolic, steroids, terpenoids, lipids, saponins	Normalises serum biochemical parameter by antioxidant activity
5	*Anogeissus latifolia* [25]	Bark	Hydroalcoholic	Tannins, gallic acid, ellagic acid, lutin and quercetin	Reduces the ALT, AST, ALP levels and lipid peroxidation
6	*Apium graveolens* [26]	Seeds	Methanol, Pet. Ether, Acetone	Flavanoids, anthrons, xanthons tannins	Reduces the elevated serum transaminases, ALP, total protein and albumin
7	*Aspalathus linearis* [27]	Leaves	Aqueous	Flavanoids	Antifibrotic effect,

					anticirrhotic effect
8	*Asteracantha longifolia* [28]	Seeds	Methanol	Lupeol and stigmatsterol	Reduces serum phospholipid level
9	*Azadirachta indica* [29]	Leaves	Ethanol	Quercetin, rutin	Balances serum biochemical levels by antioxidant activity
10	*Arachniodes exilis* [30]	Rhizome	Ethanol	Polyphenols	Reduces the levels of SGPT and SGOT
11	*Artemisia absinthium* [31]	Stem, leaves	Aqueous	Flavonoid glycosides	Facilitates to maintain intracellular antioxidant levels
12	*Alchornea cordifolia* [32]	Leaf	Methanol	Saponins, tannins and flavonoids	Inhibits the elevated serum levels of ALT and total bilirubin
13	*Annona senegalensis* [33]	Root	Methanol	Steroids, flavonoids, terpenoids	Decreases the ALT and AST value
14	*Andrographis paniculata* [34]	leaves	Aqueous	Diterpenoids, andrographolide, flavones	Decreases the level of serum AST,ALT, LDH, ALP and total bilirubin
15	*Boerhaavia diffusa* [35]	Leaf	Aqueous, ethanol	Phenolic content, flavonoid content, vitamin C, vitamin E	Preserves antioxidant potential
16	*Butea monosperma* [36]	Flowers	Aqueous	Butein, butin, isobutrin, Iso-monospermoside	Prevents from oxidative potential by inducers
17	*Byrsocarpus coccineus* [37]	Leaf	Aqueous	Flavonoids and alkaloids	Rich in antioxidants and strongly inhibit lipid peroxidation
18	*Bupleurum chinense* [38]	Root	Hot water	Flavonoids and polysaccharides	Reduces the AST, ALT, ALP, LDH and increases the GSH, GR, GST and SOD
19	*Calotropis procera* [39]	Flowers	Hydroethanol	quercetin-3-rutinoside, flavonoids	Prevents the depletion of GSH levels
20	*Cassia fistula* [40]	Leaves	n-hexane	Phenolic compounds, cyaniding B2, biflavonoids, triflavonoids	Facilitates in lowering the serum transaminases, bilirubin and ALP
21	*Cistanche tubulosa* [41]	Fresh stems	Methanol	Kankanosides H1, H2 and I, phenylethanoid glycosides	Reduces TNF-alpha-induced cytotoxicity in liver cells
22	*Crossandra Infundibuliformis* [42]	Leaf	Pet. ether	Phytosterols, phenolic compounds, flavanoids	Decreases hepatocyte peroxidation and lipoprotein lipase in liver
23	*Carya illinoensis* [43]	Nut shells	Aqueous	Polyphenols, condensed tannins	Inhibits Fe^{2+} induced lipid peroxides
24	*Cyathea gigantean* [44]	Leaves	Methanol	Triterpenes, sterols, saponins and flavonoids	Reduces the elevated level of SGOT, SGPT, ALP and TB
25	*Crataeva nurvala* [45]	Stem bark	Ethyl acetate	Lupeol, lupeollinoleate	Scavenges peroxyl radicals by bolstering the levels of antioxidant enzyme system
26	*Decalepis hamiltonii* [46]	Root	Aqueous	Flavonoids	Inhibits lipid peroxidation
27	*Daucus carota* [47]	Seeds	Methanol	Flavonoids	Decreases SGOT, SGPT and ALP
28	*Emblica officinalis* [48]	Fruit	Hydro-alcohol	Tannins, Flavonoids, Saponins, Alkaloids, Phenol	Reverses serum enzyme activity *i.e.*, AST, ALT, ALP and bilirubin
29	*Enicostemma axillare* [49]	Whole plant	Ethyl acetate	Secoiridoid glycoside	Decreases the lipid peroxidation
30	*Euphorbia fusiformis* [50]	Tubers	Ethanol	Ellagic acid	Possesses antioxidative against oxidants

31	*Fumaria indica* [51]	Whole plant	Ethanol-water (50%)	Narceimine, (-)-tetrahydrocoptisine, bicuculine, and fumariline	Reduces the elevated levels of serum transaminases (SGOT, SGPT)
32	*Fumaria species* [52]	Whole plant	Ethanol	Total phenol and flavonoid	Decreases plasma or hepatic MDA
33	*Fumaria indica* [53]	Whole plant	Pet. ether, aqueous, methanol	Campesterol, Protopine, octacosanol, narceimine narlumidine	Reduces the serum biochemical indicators (AST, ALT, ALP and LDH)
34	*Ginkgo biloba* [54]	Leaves	Pet. ether	Polyprenols	Reduces the elevated level of MDA by possessing zthe antioxidant ability
35	*Graptopetalum Paraguayense* [55]	Whole plant	Aqueous	Gallic acid	Facilitates to maintain intracellular antioxidant levels
36	*Gardenia gummifera* [56]	Roots	Methanol	Flavonoids and phenols	Suppresses the elevated levels of serum AST, ALT, ALP, LDH and MAD
37	*Glycyrrhiza glabra* [57]	Roots	CCl_4	18 β-Glycyrrhetinic Acid	Reduces the elevated levels of LDH,GOT, GPT and MDA and increases the reduced levels of SOD and GSH
38	*Gentiana olivieri* [58]	Aerial parts	Ethyl acetate	Isoorientin	Decreases the MDA, transaminase levels in plasma and hepatic tissue
39	*Halenia elliptica* [59]	Whole plant	Methanol	Carotenoids, gallic acid	Strong free radical scavenging activity
40	*Heterotheca inuloides* [60]	Whole plant	Acetone, Methanol	Quercetin, Stigmasterol, b-sitosterol, kaempferol, Cadalen-15-oic acid	Inhibits lipid peroxidation
41	*Hippophae rhamnoides* [61]	Leaves	Aqueous, Hexane, Ethyl acetate	Gallic acid, myricetin, quercetin, kaempferol and isorhamnetin	Protects against hepatocytic necrosis, fatty changesand oxidative damage
42	*Hybanthus Enneaspermus* [62]	Whole plant	Aqueous	Saponins, tannins, flavonoids, anthraquinones, terpenoids	Reduces lipid peroxidation and scavenges free radicals
43	*Hibiscus esculentus* [63]	Dried pods	Ethanol	Flavonoids, tannins, sterols and triterpenes	Decreases elevated serum SGOT, SGPT, ALP, GGT, cholesterol and TG
44	*Hibiscus vitifolius* [64]	Root	Methanol	Sterols, glycosides, triterpenoids, mucilage and flavonoids	Reduces the levels of serum AST, ALT, ALP, LDH levels
45	*Litchi chinensis* [65]	Fruit	pulp Fruit juice	Vitamin C, phenolic contents	Anti lipid peroxidation, anti-apoptosis
46	*Luminetzera racemosa* [66]	Bark	Ethanol, Water	Flavonoids, alkaloid, polyphenol	Activates cytochrome-P 450 enzyme system in the liver
47	*Lycium chinense* [67]	Fruit	Ethyl acetate	Cerebrosides and pyrrole derivatives	Blocked the release of SGPT
48	*Momordica dioica* [68]	Leaves	Aqueous	Flavonoids	Free radical- scavenging Property
49	*Morus bombycis* [69]	Whole plant	Aqueous	2, 5-dihydroxy-4, 3'-di (β-d-glucOpyranosyloxy) -trans-stilbene	Antioxidant property
50	*Melothria heterophylla* [70]	Aerial parts	Ethanol	β-Sitosterol, glycosides, saponin and flavonoids	Antioxidant property
51	*Murraya koeniggi* [71]	Leaf	Aqueous	Tannins and the	Anti lipid peroxidative

				carbazole alkaloids	property
52	*Moringa oleifera* [72]	Stem bark	Pet. ether, CCl_4	Phenolic content and flavonoids	Antioxidant property
53	*Murraya koenigii* [73]	Leaf	Hydro-ethanol	Flavonoids	Decreases the levels of AST, AST and ALP
54	*Mallotus japonicas* [74]	Whole Plant	Water	Bergenin	Prevents the elevation of MDA and glutathione content in the liver
55	*Nymphae stellata* [75]	Flower	Hydro-alcohol	Sesquiterpene lactones, terpenoids, flavanones and steroids	Activates antioxidative enzymes and stabilizes hepatic membrane
56	*Nicotiana glauca* [76]	Leaves	Aqueous	Flavonoids and phenols	Reduces the ALP, ALT,AST and TB level
57	*Phyllanthus amarus* [77]	Leaf	Ethanol	Flavonoids, phenols, polyphenols and lignans,	Enhances level of GSH, SOD, CAT and reduces GST, LPO level in the liver
58	*Phyllanthus niruri* [78]	Leaves, fruits	Methanol, Aqueous	Lignans, phyllanthin, flavonoids, Glycosides and tannins.	Inhibits membrane lipid peroxidation, scavenges DPPH radical
59	*Piper chaba* [79]	Fruit	Aqueous acetone	Piperchabamides E, G, and H	Inhibits TNF-alpha in liver
60	*Pittosporum neelgherrense* [80]	Stem bark	Methanol	Flavonoids	Decreases levels of serum enzymes (SGOT and SGPT)
61	*Prunus armeniaca* [81]	Seed kernel	Ethanol	Flavonoids, vitamin-C and carotenoids	Anti-lipid zeroxidative and free radical scavenging
62	*Pleurotus eryngii* [82, 83]	Dried fruits	Water	Polysaccharides, lipids, peptide, sterols, and dietary fibre	Increases the activities of antioxidant enzymes SOD, CAT,GSH and prevents excessive lipid formation in liver
63	*Pistacia lentiscus* [84]	Leaves	Aqueous	Flavonoids and phenols	Reduces ALP, ALT, AST and TB level
64	*Phillyrea latifolia* [85]	Leaves	Aqueous	Flavonoids and phenols	Reduces ALP, ALT, AST and TB level
65	*Rosa laevigata* [86]	Fruit	Aqueous-ethanol	Flavonoids	Increases Procaspase-3, Procaspase-8, FasL in liver
66	*Spirulina platensis* [87]	Spirulina microalgae		β-carotene, riboflavin, α tocopherol, α--lipoic acid	Free radical scavenging properties and antioxidant activity
67	*Terminalia catappa* [88]	Leaves	Chloroform	Flavonoids (Keampferol, quercetin), tannins (punicalin, 4punicalagin, tercatin), saponins, phytosterols	Prevents the mitochondrial disruption, Intra mitochondrial Ca^{2+} overloadand suppresses Ca^{2+} ATPase activity
68	*Terminalia chebula* [89]	Fruit	Ethanol	Chebuloside II	Antioxidant and act as membrane stabilizer
69	*Thunbergia laurifolia* [90]	Leaves	Aqueous	Apigenin, casmosiin, horogenic acid	Decreases ALT and AST release in liver
70	*Trianthema Portulacastrum* [91]	Whole plant	Ethanol	Saponin and punarnavine	Stimulates hepatic regeneration
71	*Trichosanthes Cucumerina* [92]	Whole plant	Methanol	Phenolics and flavonoids	Reduces lipid peroxidation
72	*Talinum triangulare* [93]	Whole plant	Aqueous	Polysaccharides	Hydroxyl radical scavenging activity
73	*Trichilia emetic* [94]	Root	Aqueous	Polyphenols, flavonoids and tannins	Scavenges the reactive oxygen species
74	*Trigonellafoenum graecum* [95]	Seed	Polyphenolic	Polyphenolic compounds	Reduces LDH leakage and normalizes GSH/GSSG ratio
75	*Tilia argentea* [96]	Flowers	Methanolic	Flavonol glycoside	Inhibits SGPT, SGOT elevations and suppresses

					TNF-α production
76	*Viburnum tinus* [97]	Leaves	Aqueous, methanol	Flavonoids and biflavonoids	Antioxidative property, scavenges excessive nitrous oxide radicals
77	*Vitex negundo* [98]	Leaf	Ethanol	Flavonoids, Vitamin C	Reduces oxidative stress
78	*Vitex trifolia* [99]	Leaf	Aqueous and ethanol	Persicogenin, artemetin, luteolin, penduletin and chrysosplenol-D	Decreases the rise of serum enzymes and total protein level in liver
79	*Vitis vinifera* [100]	Leaves	Ethanol	Halimane-type diterpenes, vitetrifolins	Reduces MDA, AST, ALT and GSH levels of plasma and liver tissue
80	*Woodfordia fruticosa* [101]	Flowers	Pet. ether, Methanol, $CHCl_3$, ethanol and aqueous	Quercetin-3-O-6"galloy) β-d-galactopyranoside, myricetin-3-O-6"O-gallo yl) β-d-galactopyranoside	Antioxidant property
81	*Zanthoxylum armatum* [102]	Bark	Ethanol	Isoquinoline alkaloid, berberine, flavonoids and phenolic compounds	Increases the levels of antioxidant enzymes: SOD and catalase
82	*Zosima absinthifolia* [103]	Roots	Pet. ether	-deltoin and (+)-columbianadin	Inhibits TNF alpha

Pet. ether-Petroleum ether, CCl_4-Carbon tetrachloride, SGOT-Serum glutamic oxaloacetic transaminase, SGPT-Serum glutamate pyruvate transaminase, ALT-Alanine transaminase, AST-Aspartate aminotransferase, ALP-Alkaline phosphatase, LDH-Lactic acid dehydrogenase, GSH-Glutathione Peroxidase, GR-Glutathione reductase, GST-Glutathione S-Transferase, SOD-Superoxide dismutases, TB-Total bilirubin, MDH-. Malate dehydrogenase, MDA-Malondialdehyde, TG-Triglyceraldehyde, CAT-Catalase, LPO-Lipid peroxidation, DPPH-2,2-diphenylpicrylhydrazyl

DISCUSSION: The goal of ethnopharmacological studies on medicinal plants should not be restricted to find new prototype pure compounds as drugs. Active extracts, fractions, or a 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.

CONCLUSION: From this review study, it is clear that the medicinal plants play a significant role against various diseases. Different medicinal herbs and plants extracts have potent hepato-protective activity in various animal models. The hepatoprotective activity is probably due to the presence of flavonoids, phenolic compounds, polyphenols, *etc*. in all few herbal plants. The results of this study indicate that extracts of leaves and plant extracts of some medicinal plants have good potentials for use in hepatic disease. The present review study gives evidential explore the mechanism of action of medicinal plants against experimentally induced hepatotoxicity.

The predicted mechanism of action of various plant extracts may be attributed to antioxidant properties and the presence of flavonoids, to increase the reduced level of blood glutathione in experimental animal models, to increase total proteins, to inhibit lipid peroxidation and increase in the antioxidant enzymatic activity, to decrease the hepatic marker enzymes (AST, ALT, ALP, and arginase) and total bilirubin in plasma, to enhance antioxidative enzymes, including SOD, GPx, CAT and GST, to decrease MDA level, SGOT, SGPT, *etc*. Hence, the review study is concluded that the herbal drug possesses hepatoprotective activity, and it has been proved by different animal models that give many links to develop the future trials.

ACKNOWLEDGEMENT: I am grateful to my Ph.D. guide, Dr. Priya Jain, Faculty of Pharmacy, SAGE University, for giving me support to carry on my work.

CONFLICTS OF INTEREST: There are no conflicts of interest.

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How to cite this article:
Saiju P, Jain P and Chatterjee DP: Present scenario of hepatoprotective potential of medicinal plants: an updated review. Int J Pharm Sci & Res 2020; 11(9): 4189-00. doi: 10.13040/IJPSR.0975-8232.11(9).4189-00.