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A REVIEW ON MECHANISTIC ASSESSMENT OF HEPATOTOXICITY AND MEDICINAL PLANTS WITH HEPATOPROTECTIVE POTENTIAL

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ABSTRACT: The liver is the most important organ in the body that plays a central role in the detoxification and excretion of many exogenous and endogenous compounds. Due to these functions, hepatic diseases continue to be among the main threats to public health, and that challenges health care professionals. Many liver diseases are chronic, meaning they last for years and may never go away. But even chronic liver diseases can usually be managed. The drugs that work on the liver are generally classified into two categories, one is antihepatotoxic agents, which generally antagonize the effects of any hepatotoxins causing any liver disease and another is hepatoprotective agents which prevent various types of liver infections prophylactically. Plants are the paramount source of herbal medicines. A plethora of data from the medicinal plants is available in literature. The present review is aimed at compiling data on promising herbs in concise manner, which are experimentally proved by the scientists as hepatoprotective.

INTRODUCTION: The liver is a large glandular organ that plays an important role in maintaining vital functions such as maintenance, performance, and regulating the homeostasis of the body. The human liver comprising two main lobes; the right lobe is larger than the left. The liver involved in almost all biochemical pathways like carbohydrate, fat, protein, hormone and drug metabolism, production of bile and bile acid, synthesis of clotting factors and plasma protein, storage of minerals, vitamins and glycogen **Fig. 1** [1].

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A liver normal function may alter by the number of factors such as viruses, alcohol, toxins and drug that can ultimately lead to hepatitis and cirrhosis [2]. Herbal drugs are still the mainstay of health care in several developing countries. The widely used herbal remedies and health care preparations as described in ancient texts such as the Vedas and the Bible are obtained from commonly used traditional herbs and medicinal plants.

The medicinal properties of these botanicals are being better understood and are attributable to the phytochemicals that specific plants contain. The efficacy and safety of herbal products, therefore, rely on the quality and proper identification of the raw material or the original plant source. According to Gurib-Fakim there are four basic ways in which plants that are used by tribal peoples are valuable for modern medicine:

Plants used as sources of direct therapeutic agents. Plants are also used as sources of starting points for the elaboration of semi-synthetic compounds. Plants can serve as sources of substances that can be used as models for new synthetic compounds. Plants can also be used as taxonomic markers for the discovery of new compounds [3].

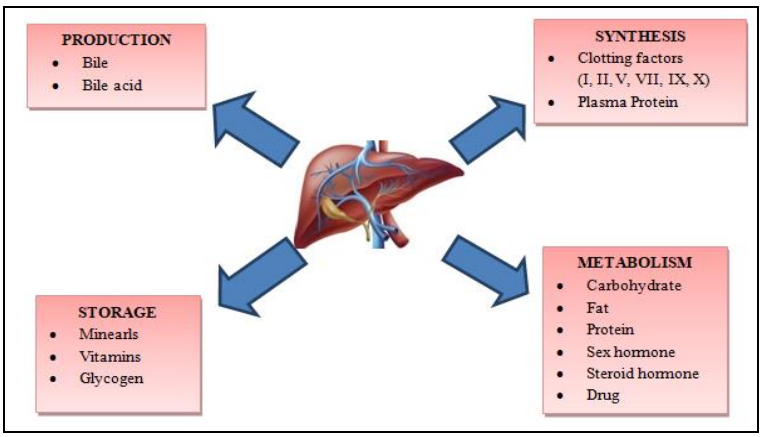

FIG. 1: DIFFERENT FUNCTIONS OF LIVER

METHODS: There is a plethora of medicinal plant data available that shows hepatoprotective activity. In the present article, we have searched and reviewed relevant studies on liver disease and hepatoprotective plants along with few isolated compounds through electronic searches of Pub med, Science Direct, Wiley, Scopus, Google Scholar, and EMBASE between the year 1992 and 2020. Based on this literature survey, the mechanism of liver diseases and medicinal plants with hepatoprotective potential are discussed in this review.

Diseases Associated with Liver Dysfunction: Liver disease is a general term that refers to any condition affecting your liver. These conditions may develop for different reasons, but they can all damage your liver and impact its function.

Liver dysfunction is broadly divided into two *i.e.*, hepatitis and cirrhosis [1]. Hepatitis can be caused by viruses, alcohol, toxins, and drugs that basically mean inflammation in a liver cell or hepatocytes. Viral hepatitis is an infection that occurs by different viruses, known as hepatitis A, B, C, D, and E. The characteristics features of viral hepatitis are shown in **Table 1**. Liver cell dysfunction leads to progressive cell death that initiates immunological reaction which is characterized by the release of signals.

The stimulation of the immune system activates the Kupffer cells and natural killer cells. These cells are responsible for the release of inflammatory mediators like cytokines, tumor necrosis factor (TNF-α), interferon-γ, and interleukin-1β that causes liver injury [4].

TABLE 1: CHARACTERISTICS FEATURES OF VIRAL HEPATITIS [1]

Characteristics	Hepatitis				
	A	B	C	D	E
Incubation Time (Days)	15-50	30-180	15-160	30-180	10-60
Transmission	Fecal/oral	Blood & Its fluid	Blood & Its fluid	Blood & Its fluid	Fecal/oral
Onset	Abrupt	Insidious	Insidious	Insidious	Abrupt

Overconsumption of alcohol leads to alcohol hepatitis that is the second most common cause of total human death every year. It consists of fatty liver, steatosis, alcoholic hepatitis, steatohepatitis, chronic hepatitis, liver fibrosis, and hepatocellular carcinoma. Ethanol is metabolized by enzymes catalyzed oxidative process. Alcohol dehydro-genase converts the alcohol into acetaldehyde after the chronic consumption of alcohol. The acetaldehyde is further metabolized to acetic acid by the enzyme acetaldehyde dehydrogenase, which is then converted to carbon-di-oxide and water molecules via a citric acid pathway. NADH is generated during the citric acid pathway triggers oxidative stress, which leads to the generation of reactive oxygen species (ROS), causing

peroxidation of lipid and decreasing the endogenous antioxidant. The active acetaldehyde induces fatty acid synthesis *via* an increase in NADH/NAD$^+$ ratio. This converts the glycerol to triglycerides and accumulates in the hepatocytes. This leads to disruption of the integrity of the cell. Other mechanisms of liver necrosis by ethanol chronic consumption include ATP depletion and intracellular Ca^{+2} accumulations [5]. The mechanism involved in alcohol-induced hepatitis includes shown in **Fig. 2**.

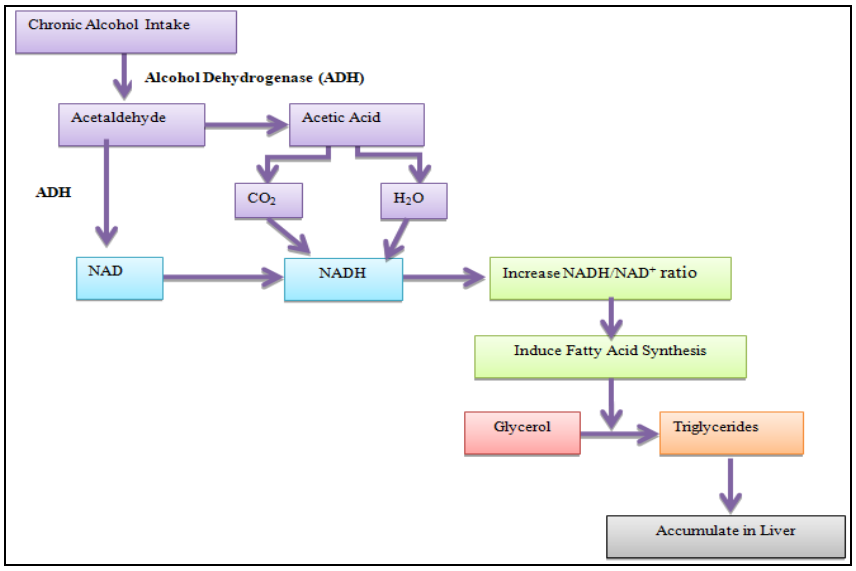

FIG. 2: MECHANISM OF ALCOHOL-INDUCED HEPATITIS

Drug-induced hepatitis is the major concern of acute liver failure and a major reason for liver transplantation. There are various pharmacological classes of drugs that cause liver injuries like anticancer, NSAIDs, anti-tuberculer, antiviral drugs and antibiotics. The liver metabolized the drug into inactive compounds via phase-II metabolism. The cytochrome P450 is the main enzyme system in the liver for the metabolism of drug metabolites. These metabolite bind ith the protein of cellular membrane to form an adduct. This adduct causes oxidative hepatocyte damage *via* a different mechanism like mitochondrial damage, ER stress, DNA damage, and bile acid accumulation. The injured hepatocyte release DAMPs molecules that stimulate the immune response. Activated immune systems release pro-inflammatory cells and sensitize T-lymphocytes, causing hepatocyte necrosis [2]. The mechanism or pathogenesis involved in drug-induced liver disease [6] is shown in **Fig. 3**.

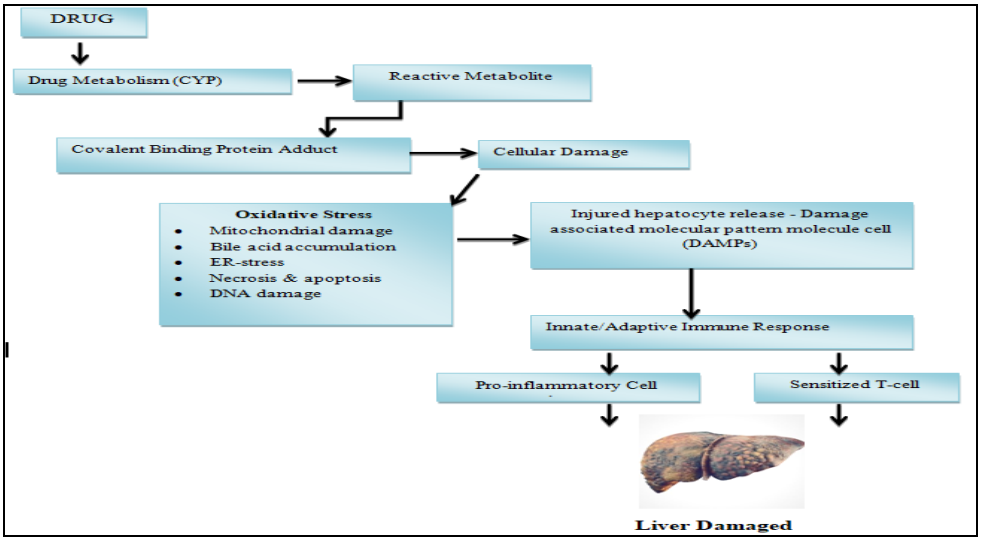

FIG. 3: PATHOGENESIS OF DRUG-INDUCED LIVER DISEASE

Cirrhosis is a formation of regenerative nodules in liver parenchymal cells by fibrous septa due to chronic liver injury. The mechanism behind liver cirrhosis includes the overproduction of insoluble collagen in the formation of connective tissues that reduces the hepatic blood flow and impairs the liver's metabolic function, and increased portal vein pressure [7, 8]. Cirrhosis is caused by a number of factors shown in **Fig. 4**.

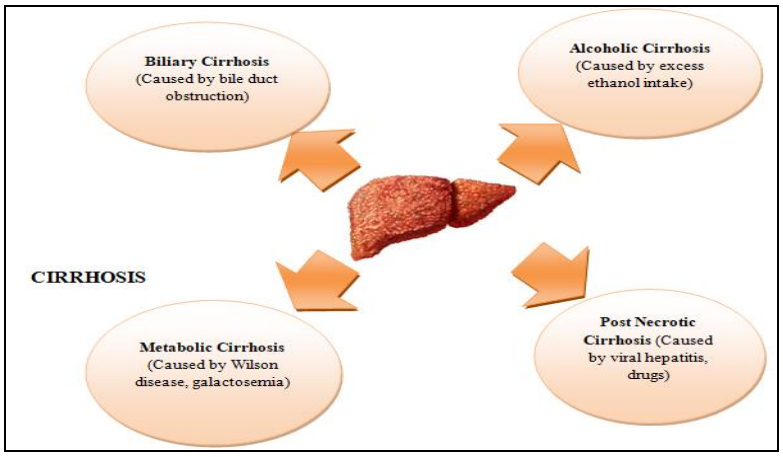

FIG. 4: CAUSES OF DIFFERENT TYPE OF CIRRHOSIS

Medicinal Plants with Hepatoprotective Activity: Liver failure due to inappropriate use of drugs such as paracetamol (PCM) and excessive alcohol consumption depends on age, gender, lifestyle, and nutritional deficiency. In addition, hepatotoxicity can also be caused by toxic substances such as thioacetamide (TAA), chemo-therapeutic agents such as carbon tetrachloride ($CC1_4$), some organic and inorganic compounds, aflatoxin, microbes, and viral infections. Several reports have shown that oxidative stress triggered by free radicals is the main causative agent of liver damage. Various mechanisms are involved in the toxicity of liver like generation of reactive oxygen species (ROS), increased lipid peroxidation and biochemical parameters, depletion of glutathione (GSH), and leads to alteration of membrane fluidity and permeability [9]. Folkloric plants play an indispensable role in improving the quality of life of rural dwellers, especially in developing countries where contemporary health facilities are not available to all. The plants are always being the starting material for the synthetic as well as for the semi-synthetic molecule. They are the rich source of bio active phyto-chemicals like alkaloids, glycosides, tannins, protein, carbohydrates, mucilage, flavonoids and phenolic compounds. The evaluation of efficacy and safety of medicinal plants as hepatoprotective are depended on the phytochemicals present in the extract. There is a need to prepare appropriate formulations of extracts and bioactive molecules to facilitate their physiological target and pharmacological activity. With increasing interest in traditional herbal medicines, the researchers are trying to explore the potential of herbal molecules as hepato-protective [10]. There is an abundance of research had been conducted on the plants and their isolated molecules to evaluate their hepatoprotective potential. Details of the most promising herbs having hepatoprotective potential in their different parts are discussed here. The results of the investigations of hepatoprotective activity conducted on many other plants are also summarized in **Table 2**.

TABLE 2: MEDICINAL PLANTS HAVING HEPATOPROTECTIVE ACTIVITY

S. no.	Name of Plant (Family)	Part of Plant (Extract, Dose)	Animal Used	Model of Hepato-Toxicity (Dose, Route)	Parameters Analysed
1.	*Abutilon indicum*[9, 10] (Malvaceae)	Root (Aqueous, 300 & 500 mg/kg) Flowers (Ethanol,	Albino rat Male wistar	Lead acetate (0.15%, p.o.) CCl_4	Decreased LPO level Increased CAT, SOD, GSH-Px level

		100, 250 & 500 mg/kg)	rat	(1 mL/kg, i.p.)	Improved histology Significantly decreased serum SGPT, SGOT, ACP, ALP, TB and DB level
2.	*Acacia catechu*[34] (Leguminosae) 	Seed & Bark (Ethanol, 400 mg/kg)	Female wistar rat	Acetaminophen 750 /kg, p.o.)	Decrease ALT, ALP, AST level Increased SOD, GSH, Decreased LPO level Histopathology showed normal structure of hepatocytes & absence of congestion
3.	*Achillea millefolium*[35,36] (Asteraceae) 	Whole plant (Methanol, 100 & 200 mg/kg) Flower (Luteolin, 250 and 500 mg/kg)	Male albino mice Mice	CCl_4 (0.2 %v/v, i.p.) CCl_4 1mL/kg, p.o.)	Decresed SGOT, SGPT and ALP level Improved the BSP removal rate Decresed SGOT, SGPT, ALP, TB, DB level Decresed thiopental induced sleeping time Improved histopathology
4.	*Adhatoda vasica*[37] (Acanthaceae) 	Whole plant (Ethyl acetate, 100 & 200 mg/kg)	Swiss albino rat	CCl_4 1 mL/kg, p.o.)	Decreased AST, ALT, ALP and TB level
5.	*Alangium salvifolium*[38] Wang (Alangiaceae) 	Leaves (Ethanol, 150 &300 mg/kg)	Female albino wistar rat	CCl_4 (1mL/kg, p.o.)	Significantly decreased SGPT, SGOT, ALP, TB, and ALB level Improved histopathology with reduced necrotic & fatty lobules
6.	*Allium Sativum*[39] (Amaryllidaceae)	Bulb (Ethanol, 20 mg/kg)	Male wistar rat	Ochratoxin A (OTA) (1 mg/kg, oral)	Decreased LPO, ALT, AST, LDH level Increased SOD and CAT activity

7.	 *Alpinia galangal*[40] (Zingeberaceae)	Rhizome & leaves (hydroalcoholic, 200 & 400 µg/mL)	Rat	D-galacto-samine (400 /kg, oral)	Decreased serum AST, ALT, ALP, TB and DB level
8.	 *Anacardium occidentale*[41] (Anacardiaceae)	Leaves (Methanol, 500 & 1000 mg/kg)	Wistar rat	CCl_4 (1 mL, oral)	Decresed ALT, AST, ALP level Improved Histopathology
9.	 *Argyreia nervosa*[42] (Linn.f.) (Convolvulaceae)	Root (Methanol, 200 & 400 mg/kg)	Albino wistar rat	CCl_4 (0.5 mL/kg, p.o.)	Decreased AST, ALT, ALP level Reversal of TP level
10.	 *Argyreia pilosa*[43] (Convolvulaceae)	Whole plant (Methanol, 200 mg/kg)	Albino wistar rat	PCM (0 g/kg, p.o.)	Decreased biochemical parameter like AST, ALP, ALT, TB and CHOL level Increased TP level
11.	 *Argyreia speciosa*[44] Burm.F. (Convolvulaceae)	Root (Ethanol, Ethyl acetate, 200 & 400 mg/kg)	Swiss albino mice	CCl_4 (0.7mL/kg, i.p.)	Decreased SGOT, SGPT, ALP, TB, DB, CHOL, level Improved necrosis, fatty lobules and hepatocytes degeneration

12.	 *Azima tetracantha*[45] Lam. (Salvadoraceae)	Leaf (Ethanol) 100 & 200 mg/kg	Wistar albino rat	CCl_4 (1mL/kg, s.c.)	Decreased AST, ALT, ALP, ACP and TB level
13	 *Bauhinia purpurea*[46,47] L. (Fabaceae)	Bark (Water, 50, 100 mg/kg)	Rat	Ethanol (1 g/kg, oral)	Increased antioxidant action (SOD, CAT, GSH-Px and GSH) Restored the SGOT, SGPT, TBRAS, TP, LPO level
14.	 *Bauhinia racemosa*[48] L. (Caesalpiniaceae)	Stem bark (Methanol, 50, 100 & 200 mg/kg)	Wistar albino rat	PCM (500 /kg, p.o.) CCl_4 (0 mL/kg, i.p.)	Decreased SGOT, SGPT, ALP, TB level Increased Total protein level
15.	 *Boswellia serrata*[49,50] (Burseraceae)	Leaf, Bark, Gum (Aqueous, 250, 500 & 750 mg/kg) Leaf (Pet. Ether and Ethanol, 250 mg/kg)	Male albino rat Albino rat	PCM (3 g/kg, p.o.) PCM (0 g/kg, oral)	Decreased serum ALT, AST and ALP level Decreased TB, SGPT, SGOT level Histopathology showed minimum necrosis, mild injury and swelling
16.	 *Brassica oleracea* L. var. Italica[51] (Brassicaceae)	Florets (Ethanol, 1 g/kg)	Rat	PCM (2g/kg, oral)	Decreased SGPT, SGOT, ALP level Histopathology showed normal structure with some inflammatory cells

17.	 *Brassica oleracea* L. var. capitata[52] Alef. F. alba DC. (Brassicaceae)	Florets (Essential oil, 146 mg/kg)	Male wistar rat	CCl_4 (0 g/kg, oral)	Increased LPO & CAT level Decreased ALP, GGT, ALT, TB level Improved histopathology
18.	 *Buchananiac lanzan*[53] Spreng (Anacardiaceae)	Bark (Methanol & Aqueous, 100, 200 & 400 mg/kg)	Rat	PCM (1g/kg, p.o.)	Decreased ALT, AST, ALP, TB, DB, ALB, CHOL, TG level
19.	 *Calotropis gigantea*[54,55] L. (Asclepiadaceae)	Aerial (Pet.ether, acetone, chloroform and methanol, 450 mg/kg) Stem (Ethanol, 250 & 500 mg/kg)	Wistar rat Rat	Acetaminophen (2 g/kg, oral) CCl_4 (1 mL/kg, s.c.)	Decreased SGPT, SGOT, ALP and TB level Decreased AST, ALT, LPO level Improved action of antioxidant (SOD, GSH-Px GSH and CAT)
20.	 *Calotropis procera*[56,57] (Ait) R.Br. (Asclepiadaceae)	Flower (Ethanol-70%, 200 & 400 mg/kg)	Albino rat & mice Wistar rat	CCl_4 (4 mL/kg, i.p.) PCM (2 g/kg, p.o.) Pentobarbitone (40 g/kg, i.p.)	Decreased serum SGPT, SGOT, ALP, TB, CHOL, TB HDL and DB level Increased TP level
21.	 *Cinnamomum tamala*[58](Laurels)	Leaves (Suspension, 200 & 400 mg/kg)	Albino wistar rat	PCM (2 g/kg, oral)	Decreased serum biochemical parameters (SGPT, SGOT, ALP, CHOL, TB and DB)

22.	 *Cissus quadrangularis*[59](Vitaceae)	Stem (Methanol, 500 mg/kg)	Wistar albino rat	Rifampicin 954 g/kg, p.o.)	Decreased liver AST, ALT, ALP and TB level
23.	 *Cuminum cyminum*[60](Umbelliferae)	Seeds (Aqueous, 100, 200 & 300 mg/kg)	Albino Sprague-dawley rat	Nimesulide (100 /kg, p.o.)	Decreased SGPT, SGOT, ALP and TB level
24.	 *Curcuma longa*[61](Zingiberaecae)	Rhizome (Aqueous, 500 mg/kg)	Wistar albino rat	Lead acetate (1g/kg, oral)	Decreased ALT, AST, ALP, LPO level Increased activity of SOD and GSH
25.	 *Cyclea peltata* (Poir.) Hook. F. &Thoms[62]. (Menispermaceae)	Root (Ethanol, 250 & 500 mg/kg)	Male wistar, Albino rat & Swiss albino mice	Acetaminophen (2.5g/kg, p.o.)	Decreased ALT, AST, ALP, TB and CHOL level Increased activity of MDA and GSH
26.	 *Citrus limon* L. Burm.[63,64] (Rutaceae)	Fruit (Ethanol, 150, 300 & 500 mg/kg) Fruit (Water,	HepG2 cell line Wistar rat	CCl_4 (1 mL/kg, i.p.) Carbofuran (1.6mg/kg, oral)	Decreased SGPT, SGOT, ALP, TB, DB and ALB level Increased GST, SOD, CAT and AchE liver level

		0.5 mL)			
27.	*Citrus hystrix*[65] (Rutaceae) 	Leaf (Methanol, 200 mg/kg)	Sprague-dawley rat, Swiss albino mice	PCM (2 g/kg, p.o.)	Increased antioxidant activity (SOD, CAT, GSH, GSH-Px) Decreased serum biochemical parameters Improve the oxidative damage
28.	*Citrus microcarpa*[66] Bunge (Rutaceae) 	Fruit peel (Ethanol, 4g/kg)	Male BFAD-Sprague-dawley rats	Acetaminophen (500 /kg, oral)	Significantly improved TB, DB, AST, ALT, ALP level and body weight
29.	*Crocus sativus*[67] (Iridaceae) 	Petals (Hydroalcoholic, 10 & 20 mg/kg)	Male wistar rat	Acetaminophen (600 /kg, oral)	Decreased ALT, AST, TB, and ALB level Increased TP level
30.	*Decalepis hamiltonii*[68] (Asclepiadaceae) 	Root (Aqueous, 50, 100 & 200 mg/kg)	Male wistar rat	Ethanol (1 g/kg, oral)	Significantly reduced AST, ALT, ALP and LDH level
31.	*Dioscorea villosa*[69] L. (Dioscoreaceae)	Root powder (Methanol, 10, 30, 50 µM)	HepG2 cell line	H_2O_2 (0.25 mM)	Increased percentage cell viability Restored their original morphology Increased GSH and ROS activity

32.	 *Dodonaea viscosa*[70,71] (Spindaceae) 	Whole plant (Methanol, 100 mg/kg) Leaves (Aqueous, Methanol, 500 mg/kg)	Male wistar rat Rabbit	CCl_4 (1mL/kg, i.p.) Alloxan monohydrate (80 g/kg, i.v.)	Reduced ALT, AST, ALP level Improved histopathology necrosis Decreased liver lipid and biochemical parameters (ALT, AST, LDL, HDL, TGs and TCHOL)
33.	*Elettaria cardamomum*[72,73] (Zingiberaceae) 	Dried fruit (Methanol, 100, 200 & 400 mg/kg) Seeds (Aqueous, 100 & 200 mg/kg)	Albino wistar rat Male albino rat	PCM (2 g/kg, oral) Gentamicin (80 g/kg, i.p.)	Decreased AST, ALT, ALP, TB level Improved histopathology Reduced elevated AST, ALT, TB, ALB level and lipid profile
34.	*Enicostemma axillare*[74] (LAM) Raynal (Gentianaceae) 	Aerial part (Aqueous & Ethanol, 100, 200 & 400 mg/kg)	Male albino wistar rat	Lanata camara (50 g/kg, oral)	Decreased SGOT, SGPT, ALB level Increased TP level
35.	*Ficus glomerata*[75] (Roxb) (Moraceae) 	unripe fruit (Ethanol, 100, 250 & 500 mg/kg)	Male albino wistar rat	PCM (500 mg/kg, p.o.) CCl_4 (0 mL/kg, i.p.)	Decreased SGPT, SGOT, ALP,ACP and TB level Improved fatty degeneration & ballooning of hepatocytes
36.	*Ficus religiosa*[76] L. (Moraceae)	Latex (Methyl alcohol, 300 mg/kg)	Male wistar rat	Cisplatin (7.5 mg/kg, i.p.)	Improved SOD & GSH level Decreased ALP, TP, TB, ALB, AST and ALT level

37.	 *Foeniculum vulgare*[77] Mill. (Umbelliferae) 	Seeds (Essential oil, 0.4 mL/kg)	Male 4560aradis-dawley rat	CCl_4 (0.8 mL/kg, i.p.)	Decreased AST, ALT, ALP and TB level
38.	*Garcinia indica* Choisy[78,79] (Clusiaceae/Guttiferae) 	Fruit rind (Aqueous, 400 & 800 mg/kg) Fruit (Aqueous, 400 & 800 mg/kg)	Wistar albino rat Wistar albino rat	Ethanol (5 g/kg, p.o.) CCl_4 (0 mL/kg, i.p.)	Significantly reduced ALT, AST, ALP level Increased TP level Incresaed antioxidant activity Centrilobular microvesicular and mild diffuse granular degeneration seen
39.	*Glycyrrhiza glabra*[80] (Papilionaceae/ Fabaceae) 	Root (Aqueous, 2 g/kg)	Rabbit	CCl_4 (0.25 L/kg, p.o.)	Improved serum biochemical parameters like ALT, AST, ALP, TB and TP
40.	*Guazuma Tomentosa*[81] (Malvaceae) 	Leaf (Ethanol, Dichloromethane, aqueous, 200 mg/kg)	Albino wistar rat	CCl_4 (50% v/v, s.c.)	Decreased serum SGOT, SGPT, ALP and TP level
41.	*Hedyotis corymbosa*[82] (Linn.) Lam. (Rubiaceae)	Whole Plant (Hydroalcoholic, 500 mg/kg)	Sprague-dawley rat	Isoniazid & rifampicin (50mg/kg, oral)	Significantly decreased ALT, AST, ALP and TB level

42.	 *Hibiscus rosa-sinensis*[83] L. Malvaceae)	Whole plant (Methanol, 100 & 200 mg/kg)	Wistar rat	Thioacetamide (300mg/kg, i.p.)	Decreased AST, ALT, LDH & LPO levels Increased GSH, CAT, GSH-Px and XO level
43.	 *Hibiscus vitifolius*[84] (Malvaceae)	Stem Bark (Acetate, 50 & 100 mg/kg)	Wistar albino rat	PCM (0 g/kg, p.o.)	Significantly decreased AST, ALT, ALP, TB and DB level
44.	 *Hydrolea zeylanica*[85] L. (Hydrophyllaceae)	Leaf (Methanol, 250 & 500 mg/kg)	Wistar albino rat	CCl_4 (0.1mL/kg, s.c.)	Decreased ALT, AST, ALP, TB, ALB and TP level
45.	 *Hyptis suaveolens*[86,87] L. Poit. (Lamiaceae)	Aereal part (Methanol, 50 mL/kg, 100 mg/kg) Leaves (Aqueous, 200 mg/kg)	Male wistar albino rat Rabbit	CCl_4 (1 mL/kg, oral) Acetaminophen (1000 kg, oral)	Decreased ALT, AST, ALP & LDH level Improved SOD, GSH level *In-vitro* study showed cytoprotective effect Significantly improved ALT, AST, CAT, TP, ALB and globulin level
46.	 *Indigofera suffruticosa*[88,89] (Mill.) (Fabaceae)	Leaves (Methanol, 50 mg/kg)	Swiss albino mice	PCM (300 /kg, oral)	Decreased AST, ALT, TB level Histopathology showed reduced tissue damage & increased organ regeneration rate

47.	 *Jasminum grandiflorum*[90,91] L. (Oleaceae) 	Leaves (Ethanol, 200 mg/kg) Leaf (Ethanol, 100 & 200 mg/kg)	Albino wistar rat Swiss albino rat	Isoniazid (54 g/kg, p.o.) PCM (400 /kg, oral)	Decreased AST, ALT level and lipid profile Decreased AST, ALP, ALP, TB, DB, LPO level Increased SOD level
48.	*Jatropha curcas*[92] L. (Euphorbiaceae) 	Leaf (Methanol, 300 mg/kg)	Rabbit	Cadmium chloride (1.25mg/kg, p.o.)	Decreased level of ALB, Globulin, AST, ALT and GGT Increased level of TP
49.	*Jatropha gossypifolia*[93] (Euphorbiaceae) 	Aerial part (Methanol Aqueous, 200 mg/kg)	Wistar albino rat	CCl_4 (0 mL/kg, s.c.)	Decreased serum SGOT, SGPT, TB, DB and CHOL level
50.	*Khaya grandifoliola*[94] C.DC. (Meliaceae) 	Stem Bark (CH2Cl2/CH3OH, 25 and 100 mg/kg)	Male wistar albino rat	CCl_4 (0.1mL/kg, i.p.)	Decreased ALP, AST, ALT level Increased TP level
51.	*Lanata camera*[95] (Verbenaceae)	Root (Aqueous, 250 mg/kg)	Wistar rat	CCl_4 (2 mL/kg, s.c.)	Significantly reduced SGPT, SGOT and TB level

52.	 *Leucas aspera*[96] Spreng (Lamiaceae)	Leaves (Ethanol, 200 & 400 mg/kg)	Wistar albino rat	Simvastatin (20 g/kg, p.o.)	Decreased SGPT, SGOT, ALP, TB, ALB level Histopathology showed improved tissue regeneration Increased TP level
53.	 *Leucas lavandulaefolia*[97] Rees (Labiatae)	Aerial Part (Ethyl Acetate, 400 mg/kg)	Male albino rat	CCl_4 (1.25 L/kg, oral)	Significantly decreased SGOT, SGPT, ALP and TB level
54.	 *Mammea Africana*[98] Sabine (Guttiferae)	Stem Bark (Ethanol-70%, 30-90 mg/kg)	Swiss albino rat	PCM (2g/kg, p.o.)	Decreased TB, DB, ALT, AST, ALP level Increased SOD, CAT, MDA, GSH level Histopathology showed marked tissue regeneration
55.	 *Melia azedarach*[99] L. (Meliaceae)	Leaves (Ethanol, 300 mg/kg)	Male albino rat	CCl_4 (1.25 L/kg, oral)	Decreased serum SGOT, SGPT, ALP and TB level
56.	 *Mentha arvensis*[100-101] L. (Lamiaceae)	Leaves (Ethanol, 100, 200 & 400 mg/kg)	Wistar albino rat	CCl_4 (1mL/kg, p.o.)	Decreased AST, ALT, ALP, TB, DB level Increased CAT, SOD and GSH level

57.	 *Mimusops elangi*[102, 103] (Sapotaceae) 	Fruit (Ethanol, 200 & 400 mg/kg) Bark (Methanol, aqueous, 200 mg/kg)	Wistar rat Male albino rat	D-Galactosamine (400 /kg, i.p.) CCl_4 (1 mL/kg, i.p.)	Decreased SGPT, SGOT, ALP, CHOL and TB level Reduced SGOT, SGPT, ALP, TB & DB level Histopathology showed improvement of necrotic tissue
58.	*Mimordica charantia*[104-105] L. (Cucurbitaceae) 	Leaves (Hydroalcoholic, 100 & 200 mg/kg) Leaves (Aqueous, 200 & 400 mg/kg)	Wistar albino rat Male wistar albino rat	CCl_4 (1 mL/kg, i.p.) CCl_4 (1 mL/kg, i.p.)	Decreased SGOT, SGPT, ALP & TB level Improved histopathology parameters Decreased ALT, AST, ALP, TB level Improvement of haematological parameters Mild to moderate improvement of tissue necrosis
59.	*Morinda citrifolia*[106](Rubiaceae) 	Fruit (Juice, 20 % v/v)	Female Sprague-Dawley rat	CCl_4 (0.25 L/kg, p.o.)	Decrease AST, ALT level Improved histopathology
60.	*Musa paradisiaca*[107-108] (Musaceae) 	Stem (Alcohol, aqueous, 250 mg/kg, 500 mg/kg) Fruit pulp (Methanol, 500, 1000 & 1500 mg/kg)	Wistar albino rat Adult wistar rat	CCl_4 (1 mL/kg, s.c.) PCM (1.2 g/kg, p.o.) CCl_4 (0mL, p.o.)	Decreased SGOT, SGPT, ALP, TB level Moderate change in tissue necrosis & fatty lobules Decreased ALT, AST, ALP level Treatment showed remarkable liver parenchyma preservation
61.	*Musa Sapientum*[109](Musaceae)	Central Stem (Aqueous, 25, 50 & 100 mg/kg)	Male wistar rat	CCl_4 (1.5 mL/kg, i.p.)	Reduced AST, ALT, ALP level Mild periportal inflammation with reduced steatosis

62.	 *Nigella sativa*[110-111] L. (Ranunculaceae) 	Seed (Aqueous, 500 mg/kg) Seed (Aqueous, 50 mg/kg)	Male rat Swiss albino mice	CCl_4 (4 mL/kg, p.o.) CCl_4 (1.9 mL/kg, oral)	Decreased SGOT, SGPT, TB level Reduced ALT, AST, ALP, LDH, TG, TC, HDL level Histopathology improved
63.	*Ocimum sanctum*[112] L. (Lamiaceae) 	Whole aerial part (Aqueous, 100, 200 & 300mg/kg)	Wistar albino rat	Lead (2.1mg/150g, oral)	Reduced AST, ALT, ALP, GGT, TB and tissue glycogen level Increased TP level
64.	*Otostegia persica*[113](Lamiaceae) 	Aerial part & root (Ethanol, 40, 80 & 120 mg/kg)	Male wistar rat	CCl_4 (0 mL/kg, i.p.)	Significantly decreased AST, ALT, ALP, TB, ALB level Increased SOD, GSH, CAT level Increased TP level
65.	*Oldenlandia umbellate*[114] (Rubiaceae) 	Whole Plant (Methanol, 50 & 100 mg/kg)	Albino rat	CCl_4 (0.25 mL/100 gm, oral)	Improved SGOT, SGPT, ALT, TB level and histopathology
66.	*Plumbago zeylanica*[115] L. (Plumbaginaceae)	Rhizome (Aqueous,	Male albino	CCl_4 (0.1mL/kg/day,	Significant improvement of biochemical parameters TP,

		1 g/kg)	wistar rat	i.p.)	CHOL, TB, AST and ALT
67.	*Polyalthia longifolia*[116] cv. Pendula (Annonaceae) 	Leaves (Ethanol, 400 mg/kg)	Male wistar albino rat	PCM (0 g/kg, oral)	Decreased ALT, AST and ALP level
68.	*Punica Granatum*[117] (Punicaceae) 	Leaf (Aqueous, 250 & 500 mg/kg)	Albino rat	CCl_4 (1mL/kg, i.p.)	Significantly reduced ALT, AST, ALP, TB level Increased TP level
69.	*Plectranthus amboinicus*[118](Lamiaceae) 	Leaves (Ethanol, 600 & 900 mg/kg)	Adult wistar rat	Rifampin (100mg/kg, i.p.) Pyrazinamide (350mg/kg, oral) Isoniazid (50 g/kg, i.p.)	Decreased ALT, AST, ALP level Increased MDA and GSH level
70.	*Quassia indica*[119] (Simarubiaceae) 	Leaves (Methanol, 200, 400, 800 & 1600 mg/kg)	Wistar albino rat	CCl_4 (1 mL/kg, i.p.)	Decreased serum SGOT, SGPT, TB, ALP level Histopathology showed normal hepatic globular
71.	*Rauwolfia serpentine*[120] (Apocynacea)	Rhizome (Aqueous ethanolic, 425 mg/kg)	Albino rat	PCM (200 /kg, p.o.)	Significantly decreased TBRAS, ALT, AST, ALP, TB level Increased Na-K-ATPase, SOD, GSH, CAT, GSHPx level

72.	 *Sapindus mukorossi*[121] (Sapindaceae)	Rhizome (Pet ether, benzene, chloroform & ethanol, 10, 50 & 100 µg/kg)	Male wistar rat	CCl_4 (100 /kg, p.o.)	Improved GSH, LDH and GPT level
73.	 *Sapindus trifoliatus*[122] (Sapindaceae)	Fruit pericarp (Ethanol & aqueous, 35mg/kg)	Male swiss albino mice	CCl_4 (0.1mL/kg, i.p.)	Decreased AST, ALT, ALP, TP and TB level
74.	 *Saraca ashoka*[123] (Roxb.) De Wilde (Caesalpiniaceae)	Stem bark (Methanol and hydroalcoholic, 200 & 400 mg/kg)	Wistar albino rat	CCl_4 (0.5 mL/kg, s.c.)	Decreased serum SGOT, SGPT and ALP level
75.	 *Scoparia dulcis*[124] L. (Scrophulariaceae)	Whole plant (Ethanol & aqueous, 500 mg/kg)	Sprague-dawley rat	CCl_4 (Inhalation twice a week)	Decreased ALT, AST, ALP and TB level significantly
76.	 *Sesbania grandiflora*[125-126] pers (Fabaceae)	Fruit (Pet. Ether, 400 mg/kg) Leaves (Aqueous, 250 & 500 mg/kg)	Wistar Albino Rat Wistar Albino rat	Ethanol (3.76 /kg, p.o.,) CCl_4 (1 mL/kg, i.p.)	Decreased biochemical markers like SGOT, SGPT, ALP, TB, DB, ALB Decreased SGPT, SGOT, ALP, TB, ALB and CHOL level Increased TP level

77.	 *Simarouba amara*[127] Aublet (Simaroubaceae)	Stem Bark (Aqueous, 100, 250 & 500 mg/kg)	Rat	CCl_4 (1 mL/kg, p.o.)	Increased MDA, CAT and SOD level
78.	 *Solanum torvum*[128](Solanaceae)	Leaf (Aqueous, 500, 1000 & 2000 mg/kg)	Wistar rat	NA	Improved ALT, AST, ALP, TP, ALB, plasma globulin and TB level
79.	 *Sphaeranthus amaranthoides*[114] Burm. (Compositae)	Whole plant (Methanol, 50 & 100 mg/kg)	Albino wistar rat	CCl_4 (0.25 mL/100g, oral)	Decreased liver biochemical markers like SGOT, SGPT, ALP and TB level
80.	 *Spinacia oleracea*[129] L. (Chinopodiaceae)	Leaves (Methanol, 100, 200 & 300µg/kg)	Wistar rat	CCl_4 (1.9mL/kg, i.p.)	Decreased ALT, AST and TB level
81.	 *Swertia chirayita*[130] (Gentianaceae)	Aerial part (Ethanol, 100, 200 mg/kg)	Female swiss albino mice	PCM (150mg/kg, oral)	Decreased SGOT, SGPT, ALP, TB, LPO level Restored GSH, GSH-Px level Histopathology showed reversal of pathological changes

82.	 *Solanum dulcamara*[131]L. (Solanaceae)	Whole plant (Hydroalcoholic, 200, 400 & 600 mg/kg)	Wistar albino rat	PCM (1 g/kg, oral)	Decreased SGPT, SGOT, TB, DB, ALP level Histopathology showed mild to moderate change in necrosis and fatty changes
83.	 *Solanum nigrum*[132] (Solanaceae)	Fruit (Hydroalcoholic, 250 mg/kg)	Wistar albino rat	CCl_4 (1.5 mg/kg, i.p.)	Decreased the elevated ALT, AST, TB, LPO level Increased TP level Restored SOD, GSH, LPO level Histopathology showed mild fatty changes and moderate centrilobular necrosis
84.	 *Solanum xanthocarpum*[133] (Solanaceae)	Fruit (Ethanol, 100, 200 & 400 mg/kg)	Sprague-dawley rat	CCl_4 (1.5 mL/kg, i.p.)	Decreased AST, ALT, ALP, TBL, LPO level Restored GSH, SOD, CAT level Improved histopathology
85.	 *Tephrosia purpurea*[134-135] L. (Fabaceae)	Root (Ethyl acetate, 25, 50 mg/kg)	Wistar albino rat	CCl_4 0.5 mL/kg, i.p.)	Reversal of elevated ALT, AST, ALP, TB, TG level Histopathology showed mild to moderate change in necrosis of hepatocytes
		Stem (Methanol, 75 & 150 mg/kg)	Wistar albino rat	CCl_4 (1.4 mL/kg, p.o.)	Decreased SGPT, SGOT, ALP, TB and DB level
86.	 *Terminlia belerica*[136] Roxb. (Combretaceae)	Fruits (Aqueous, ethanol, 200 & 400 mg/kg)	Wistar albino rat	Ethanol (2mL/100g/day, p.o.)	Reversal of AST, ALT, ALP, TB, DB, TP, ALB level, liver weight and volume

88.	 *Trichosanthes cucumerina*[139] L. (Cucurbitaceae)	Leaves (Ethanol, 150 mg/kg)	Albino rat	PCM (1 mg/kg, p.o.)	Decreased SGOT, SGPT, ALP, TB level Increased in total protein Histopathology showed mild degeneration of necrosis
89.	 *Trichosanthes lobata*[140] (Cucurbitaceae)	Whole plant (Ethanol, 200 & 400 mg/kg)	Female swiss mice, adult wistar albino rat	PCM (1 g/kg, oral)	Improved AST, ALT, ALP, bilirubin and TP level
90.	 *Taxus wallichiana*[141] (Taxaceae)	Leaves (Ethanol Methanol Ethyl acetate Chloroform Aqueous, 100, 300 mg/kg)	Wistar rat	CCl_4 (0 mL/kg, i.p.)	Decreased ALT, AST, LDH level Histopathology showed minimal fatty changes, necrotic tissue, very few number of cell infiltration
91.	 *Terminalia arjuna*[142] (Combretaceae)	Stem bark (Methanol, 25, 50, 100 mg/kg)	Goat liver slice	CCl_4	Reduced elevated ALT, AST, ALP and LDH level
92.	 *Thymus vulgaris*[143] (Lamiaceae)	Leaves (Essential oil, 125, 250 & 500 mg/kg)	Male Balb/c mice	Acetaminophe (250 /kg, oral)	Decreased ALT, AST, ALP and MPO level Histopathology showed improved hemorrhagic and necrotic areas

93.	 *Tinospora cordifolia*[144](Menispermaceae)	Leaf, stem, root (Pet.ether, ethanol, aqueous, 200 mg/kg)	Wistar albino rat	CCl_4 (0 mL/kg, oral)	Restored the elevated ALT, AST, ALP, TB level Histopathology showed absence of necrosis and vacuoles
94.	 *Valeriana wallichii*[145](Valerianaceae)	Root (Ethanol, 300, 500 mg/kg)	Charles foster rat	CCl_4 (1 mL/kg, p.o.)	Decreased ALT, AST, ALP level Improved histopathology
95.	 *Withania somnifera*[146-147] L. Dunal (Solanaceae)	Powder (Aqueous, 500 & 1000 mg/kg) Root (Methanol, 50, 100 & 200 mg/kg)	Rat Male wistar albino rat	PCM (900 /kg, i.p.) Acetaminophen (750 /kg, p.o.)	Reduced AST, ALT, ALP and TB level Increased GSH-Rd, SOD, CAT & TP level Histopathology showed mild degeneration of hepatocytes Inhibited TNF-α, IL-1β, COX-II and iNOS
96.	 *Zanthoxylum armatum*[148] DC (Rutaceae)	Whole Plant (Ethanol, 500 mg/kg)	Wistar albino rat	CCl4 (10 L/kg, i.p.)	Decreased liver inflammation, SGOT, SGPT, ALP level
97.	 *Zingiber officinale*[149](Zingiberaceae)	Rhizome (Ethanol, 250 500 mg/kg)	Rat	Thioacetamide (200 /kg, i.p.)	Improved percentage liver index Decreased ALB, Globulin, TB, ALP, ALT, AST, GGT level Increased TP level Partially preserved hepatocytes with small area of necrosis &

					fibrotic septa
98.	*Zizyphus lotus*[150] L. (Desf.) (Rhamnaceae) 	Fruit (Aqueous, 200 & 400 mg/kg)	Wistar rat	CCl_4 (1 mL/kg, i.p.)	Improved ALP, AST, ALT, TB, DB, TGs, VLDL, TCHOL, Creatinine, Urea, Uric acid and MDA level
99.	*Zizyphus spina-christi*[151] (Rhamnaceae) 	Fruit (Aqueous, 2.5, 5, 10, 15 % w/v)	Male Wistar rat	CCl_4 (0.2 mL/kg, s.c.)	Decreased ALT, AST, ALP level Increased SOD and GSH level
100.	*Zea mays*[152] L. (Poaceae) 	Husk (Ethanol, 187-748 mg/kg)	Male wistar rat	CCl_4 (1.5 mL/kg, i.p.)	Decreased serum ALT, AST, ALP, DB and TB level

***Acacia Catechu* Family *Leguminoseae*:** The ethanolic extract (250 mg/kg) of *Acacia catechu* bark was evaluated by Sheshidhar G Bannale *et al.* (2013) for hepatoprotective activity against paracetamol (250 mg/kg, p.o.) induced liver injury in albino wistar rat. Silymarin was taken as positive control for the study. The hepatoprotection was assessed by biochemical (SGOT, SGPT, ALP) and histological parameters. The result of the study revealed that ethanolic extract of *Acacia catechu* significantly reduced the elevated level of SGOT, SGPT and ALP. The histopathology showed central vein with normal hepatocyte and portal tract with mild congestion [11]. Further, the aqueous slurry of powder *Acacia catechu* (400 mg/kg) was analysed for the hepatoprotective activity against carbon tetra chloride (0.7 cc/kg, oral) induced hepatic injury in Wistar albino rat. Decreased level of biochemical parameters (SGPT, SGOT, TB, GGT, ALP) and histological results supported its hepatoprotective potential [12]. Jayashekhar *et al.* (1997) used ethyl acetate extract of *Acacia catechu* (250 mg/kg) and investigated hepatoprotective activity against CCl_4 induced toxicity (4 mL/kg, s.c. in olive oil) in albino rat. The result revealed that ethyl acetate extract significantly decrease the SGOT, SGPT, ALP and TB level. The histopathology showed slightly improvement in hepatocytes architecture [13].

***Adhatoda vasica* Family Acanthaceae:** The hepatoprotective activity of aqueous extract of *Adhatoda vasica* leaves was evaluated against CCl_4 (0.1 mL/kg, *i.p.*) induced hepatotoxicity in albino rats. Kumar *et al.* (2015) reported that aqueous extract at doses of 250 and 500 mg/kg showed significant decrease in serum biochemical parameters and total protein level was increased [14]. The ethanolic extract of *Adhatoda vasica* leaves was investigated by Chauhan *et. al.* (2008) for hepatoprotective activity. The extract was mixed with 1% gum tragacanth for oral administration in CCl_4 (0.1 mL/kg) induced liver injury in Wistar albino rat. The result revealed that plant extract significantly decreased the AST, ALT, ALP and TB level [15].

***Allium sativum* Family Amaryllidaceae:** The ethanolic extract of *Allium sativum* raw bulblets was evaluated for the hepato-protection against thioacetamide (50 mg/kg, s.c.) induced hepato-toxicity in Wistar albino rat. The study was conducted by Chinnala *et al.* (2018) at the dose of 200 and 400 mg/kg/p.o. A significant ($p<0.001$) reduction in elevated biochemical parameters like AST, ALP, ALT and TB confirmed the hepato-protective activity [16]. Tsai *et al.* (2019) evaluated the hepatoprotective activity of n-butanol and water fermented *Allium sativum* (200 & 500 mg/kg), against the CCl_4 (10 mL/kg, p.o.) induced liver toxicity. The results revealed that n-butanol and water extracts significantly reduced the serum AST, ALP and ALT level. The antioxidant parameters like hepatic MDA, GSH-Px and GSH-Rd level were increased and the reduced level of TNF-α and IL-1β showed the improvement in the histopathology [17].

***Azima tetracantha* Lam Family Salvadoraceae L** The anti-hepatotoxic effect of hydroalcoholic extract of *Azima tetracantha* leaves were evaluated against the ferrous sulphate (100 mg/kg, p.o.) induced liver toxicity in albino rat by Manikandaselvi *et al.* (2013). Various biochemical parameters like globulin, albumin, HDL, vitamin E, superoxide dismutase, LDL, VLDL, bilirubin, cholesterol, triglycerides, ALP, and TBARS were determined. The result of the study showed significant hepatoprotective activity [18]. Prakash *et al.* (2015) compared the hepatoprotective activity of *Azima tetracantha* leaf aqueous extract with silver nanoparticles (100, 200 & 300 µg/mL) through CCl_4 (1 % v/v, p.o.) induced liver toxicity. Biochemical variables such as protein, ALP, SGOT and SGPT were evaluated and results showed that extract with silver nanoparticles treated animals reversed the variables near to normal compared with *Azima tetracantha* leaf extract [19].

***Curcuma longa* Family Zingiberaecae:** Hepato-protective activity of ethanolic extract (250 & 500 mg/kg) of *Curcuma longa* rhizome was evaluated against the thioacetamide (200 mg/kg, i.p.) induced liver cirrhosis in Sprague-dawley rats. Salama *et al.* (2013) designed the study for 8 weeks. The hepatoprotective activity was evaluated by hepatic cytochrome P450 2E1, serum TGF-β1, and TNF-α. The result of the study revealed that the extract treated group improved the to pathological result, immune his to chemistry and liver biochemistry parameters compared to control group [20]. The ethanolic extract (0.187 mg/kg/day) of *Curcuma longa* rhizome was evaluated against the bleomycin (0.069 U/mL; 0.29 U/kg) induced chronic liver damage in males IRC mice. Bleomycin was injected intraperitoneally for a period of 4 weeks. Karamalakova *et al.* (2019) reported that crude drug extract significantly reduced the plasma bilirubin, gamma glutamyltranspeptidase (GGT) and lipid peroxidation level [21].

***Ficus religiosa* L Family Moraceae:** The aqueous and methanolic extract of *Ficus religiosa* at a dose of 200 mg/kg leaves were evaluated for the hepatoprotective activity on paracetamol (500 mg/kg, *i.v.*) and CCl_4 (1.5 mg/kg, oral) induced liver injury in Wistar rat. Selvan *et al.* (2017) reported that ALT and AST level was significantly decreased at the same dose [22]. The petroleum ether, ethyl acetate, methanolic and aqueous extract of stem bark of *Ficus religiosa* at a dose of 200 mg/kg was evaluated for the hepatoprotective activity against the paracetamol (2 g/kg, oral) induced liver toxicity in male Wistar albino rat. The hepatoprotective effect as assessed by Suryawanshi *et al.* (2011) revealed that biochemical variables like SGOT, SGPT, ALP, total bilirubin, and histological results improved by methanolic extract, significantly [23].

***Foeniculum vulgare* Mill Family Umbelliferae:** The hepatoprotective activity of hydroalcoholic

extracts (80%) (250 & 500 mg/kg) of Foeniculum vulgar seeds was evaluated against the paracetamol (2 g/kg, p.o.) induced toxicity in a rabbit model. Nazir *et al.* (2020) reported that hydroalcoholic extract significantly decreased the biochemical variables like AST, ALT, and ALP level, and the histopathology showed no evidence of fibrosis and steatosis [24]. Agrawal *et al*. (2018) used hexane and methanolic extract of *Foeniculum vulgare* seeds to evaluate hepatoprotective activity against CCl_4 (1 mL/kg, s.c.) induced liver injury in Wistar albino rat. Silymarin (100 mg/kg) was used as a standard drug. The hexane seed extract at dose of 400 mg/kg significantly reduced the biochemical variables like ALT, AST, ALP, and total & direct bilirubin [25].

***Glycyrrhiza glabra* Family Papilionaceae Fabaceae:** The hydro-methanolic (50%) root extract of *Glycyrrhiza glabra* was evaluated for the hepatoprotective potential against CCl_4 induced oxidative stress mediated hepatotoxicity in albino mice. CCl_4 (1.5 mL/kg) was injected i.p. for 7 days by Sharma *et al.* (2014). The result revealed that crude extract at doses of 300 and 600 mg/kg significantly decreased the LPO level and increased the GSH and CAT level [26]. The histopathology showed reduction in necrosis patterns. Huo et al. (2011), studied the hepatoprotective activity of aqueous extract (100, 150 & 300 mg/kg) of *Glycyrrhiza glabra* root against CCl_4 (2 mL/kg in 1:1 with groundnut oil, oral) induced liver injury in Wistar rat. After the treatment with the *Glycyrrhiza glabra* aqueous extract, the elevated level of serum biochemical parameters (AST, ALT and ALP) becomes inhibited. The result also showed that hydroxyproline and TNF-α increased levels also reversed [27]. The aqueous and ethanolic extract *Glycyrrhiza glabra* root was evaluated against CCl_4 (1 mL/kg, i.p. in olive oil) induced hepatopathy in male Wistar albino rat. The treatment dose was selected by Laylani *et al*. (2016) for both extracts (250 and 500 mg/kg). The result showed a significant reduction in AST, ALT, and improvement in SOD level [28].

***Melia azedarach* L Family Meliaceae:** The hepatoprotective activity of ethanolic extract of *Melia azedarachleaves* at the dose of 300 & 500 mg/kg was evaluated for the simvastatin (20 mg/kg, p.o.) induced liver injury in Wistar albino rat. Rao *et al.* (2012) reported a significant reduction in the serum SGPT, SGOT, ALP and TB level [29]. Ahmed *et al.* (2012) evaluated the hepatoprotective activity of Melia azadarach leaves ethanolic extract at the dose of 500mg/kg against the CCl_4 (1 mL/kg, p.o.) induced liver damage in Wistar albino rat. The study was designed for four days. The result of the study revealed that extract significantly decreased the level of SGOT, SGPT, and ALP level [30].

***Punica granatum* Family Punicaceae:** The study was planned by Khan *et al.* (2015), to investigate the hepatoprotective activity of ethanolic extract of *Punica granatum* peel at the dose of 200 & 400 mg/kg against the CCl_4 (1 mL/kg, i.p.) induced liver injury in Wistar albino rat. The results of biochemical analysis showed the decreased AST, ALT, ALP and TB level [31]. The histopathology showed a decrease in the extent of centrilobular necrosis. The further *in-vitro* study was also conducted on the hydroalcoholic, ethyl acetate and n-hexane (1-10000 µg/mL) extracts of *Punica granatum* seeds against CC_{l4} (100 mM) induced HepG2 cell line damage. Jamshidzadeh *et al.* (2012) reported that the percentage cell viability of HepG2 cells was increased by hydroalcoholic extract [32]. Khalil *et al*. (2004) was evaluated the aqueous extract (0.43 g/kg) of the rind of *Punica granatum* for hepato-protective activity against acetaminophen (0.5 g/kg, i.p.) induced liver damage in the male albino rat. The result showed decreased AST, ALT, and LDH levels. The histopathology showed a reduction in fatty droplets, vacuolization, and necrotic area after the treatment with extract [33].

CONCLUSION: Despite advances in pharmacology, the demerits associated with synthetic drugs have outshone the merits. The benefits of herbal treatments in human health is still a productive area of research and offer great confidence to researchers for finding the prevention tools for chronic disorders of human body. One major obstacle that might impair the potential use of traditional medicine as medicine of choice is the lack of standardization. The present paper is an attempt to review the hepatoprotective activities of traditional drugs reported in the recent literature. Isolation and characterization of the bioactive compounds from the active extract is a crucial step to find out the active principles within. There is a need to conduct experimental and clinically

controlled studies on plant extracts and bioactive compounds. It is anticipated that different studies on hepatoprotective activities of herbal drugs will open new avenues for further bio-prospection and will certainly lead to new pharmaceutical agents for the treatment of hepatic diseases.

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