Review Article

A Review on Hepatoprotective Medicinal Plants

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ABSTRACT

The Liver is a vital organ involved in the maintenance of metabolic functions and detoxification of the exogenous and endogenous challenges like xenobiotic drugs, viral infections and chronic alcoholism. Liver diseases are a major worldwide health problem, with highly causing disorder in developing countries. They are mainly caused by chemicals and some drugs when taken in very high doses. Despite advances in modern medicine, there is no effective drug available that stimulates liver function, offer protection to the liver from damage or help to regenerate hepatic cells. There is urgent need, therefore, for effective drugs to replace supplement those in current use. Herbal remedies are focused in the pharmaceutical industry to evolve a safe route for liver disorders. Medicinal plants have been considered as important therapeutic aid for alleviating ailment of humankind. Herbal medicines have been used in the treatment of liver diseases for a long time. The present review is aimed at compiling data based on reported works on promising medicinal plants that have been tested for their hepatoprotective activity in different hepatotoxicity induced models. The biochemical and pathological mechanism of hepatotoxicity has been also discussed in present review.

Keywords: Detoxification, liver function, medicinal plants, hepatoprotective.

INTRODUCTION

Liver is most important organ, which plays a pivotal role in regulating various physiological processes in the body. [1] These functions include the synthesis of most essential serum proteins, regulations of nutrients, production of bile and metabolism of xenobiotics as the primary organ for detoxification of endogenous as well as exogenous compounds. Liver injury may follow the inhalation, ingestion or parental administration of a number of physiological and chemical agents. [2]

Chronic hepatic diseases stand as one of the foremost health trouble worldwide, with liver cirrhosis and drug induced liver injury accounting ninth leading cause of death in western and developing countries. Therapies developed along the principles of western medicine are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for developing world. Therefore, treating liver diseases with plant derived compounds which are accessible and do not require laborious pharmaceuticals synthesis seems highly attractive. [(3)] Liver diseases are a worldwide problem. Conventional drugs used in the treatment of liver diseases are sometimes inadequate and can have serious adverse effects like mild digestive problem, headache, nausea etc. It is necessary to search for alternative drugs and for treatment of liver disease to replace currently used drugs of doubtful efficacy and safety.

A large number of plants and formulations have been claimed to have hepatoprotective activity. Nearly 160 phytoconstituents from 101 plants have been claimed to possess liver protecting activity. In India, more than 87 plants are used and 33 patented and proprietary multi-ingredient plant formulations. In spite of the tremendous advances made, no significant and safe hepatoprotective agents are available in modern therapeutics Therefore, due importance has been globally to develop plant- based hepatoprotective drugs effective against a variety of liver disorders. [4]

Herbal therapies are free from side effects and toxicity, unlike allopathic medicines. Medicinal plants play a key role in the human health care. About 80% of the world population relies on the use of traditional medicine which is predominantly based on plant materials.

Though the liver is effective in the detoxification of foreign bodies, with its numerous but vital activities, the liver becomes a target organ for diseases; there are various causes of liver diseases, generally resulting from viral or protozoal infections, excessive use of alcohol, drugs and xenobiotics. [5]

Methodology

This review discussed pathology and biochemical mechanisms of hepatotoxicity which is an important tool for identification and characterization of liver injury. It also illustrates patterns of liver injury during hepatotoxicity. The present review is aimed at compiling data based on reported works on promising medicinal plants that have been tested for their hepatoprotective

activity in different hepatotoxicity induced models. Review describes the extract of plant, its dose and route of administration, model, biochemical estimation and its outcome and also reported antioxidant activity.

Pathology of Hepatototoxicity [6]

Mechanism of Hepatotoxicity

Pathology

Liver pathology serves as an important tool for identifying and characterizing liver injury whether or not clinic biochemical changes are also identified. Main patterns of liver injury during hepatotoxicity may include zonal necrosis, hepatitis, cholestasis, steatosis, granuloma, vascular lesions, and neoplasm, veno-occlusive diseases.

Zonal necrosis

This type of injury may be caused by exogenous substances like paracetamol and carbon tetrachloride. Such injury is largely confined to a particular zone of the liver lobule. It may manifest as a very high level of alanine aminotransferase and severe disturbance of liver function leading to acute liver failure.

Hepatitis

This type of liver injury shows hepatocellular necrosis associated with infiltration of inflammatory cells. It may be further characterized into three categories, namely, viral, focal and chronic. *Viral hepatitis*, where histological features are similar to acute viral hepatitis, may be caused by halothane, isoniazid, acetaminophen, bromfenac, nevirapine, ritonavir, troglitazone and phenytoin. *Focal hepatitis* where scattered foci of cell necrosis may accompany lymphocytic infiltration may be caused by aspirin. *Chronic hepatitis* is similar to autoimmune hepatitis clinically serologically and histologically. It may be caused by methyldopa, diclofenac, dantrolene, minocycline and nitrofurantoin. Among herbal remedies, *Larrea tridentata* and *Lycopodium serratum* leads to chronic hepatitis. Non-nucleoside reverse transcriptase inhibitors, especially viramune [nevirapine] are also associated with hepatitis and hepatic necrosis.

Cholestasis

This type of liver injury leads to impairment of bile flow, itching and jaundice. The angiotensin-converting enzyme [ACE] inhibitors, amoxicillin, chlorpromazine, erythromycins and sulindac to associated with etiology of cholestasis. It may be inflammatory, bland or ductal. *Inflammatory cholestasis* may be caused by allopurinol, carbamazepine. *Bland cholestasis* without any parenchymal inflammation may be caused by anabolic steroids and androgens, while *ductal cholestasis* showing progressive destruction of small bile ducts may be caused by chlorpromazine and flucloxacillin.

Steatosis

This type of liver injury may manifest as triglyceride accumulation which leads to either small droplet [microvesicular] or large droplet [macrovesicular] fatty liver. Aspirin, ketoprofen, tetracycline, nucleoside reverse transcriptase inhibitors and valproic acid and *Scutellaria* sp. plant may lead to microvesicular steatosis while acetaminophen and methotrexate may lead to macrovesicular steatosis.

Granuloma

Hepatic granulomas are associated with granulomas located in periportal or portal areas and show features of systemic vasculitis and hypersensitivity. Drugs like allopurinol, sulfonamides, pyrazinamide, phenytoin, isoniazid, penicillin and quinidine have been found to cause such injury.

Vascular lesions

Such condition is caused by injury to the vascular endothelium and may be caused by chemotherapeutic agents, anabolic steroids.

Neoplasm

Prolonged exposure to some medications and toxins like vinyl chloride, anabolic steroids, arsenic may cause neoplasms like hepatocellular carcinoma, angiosarcoma and liver adenomas.

Veno-occlusive

The hepatic vein becomes clogged, blocking off the blood supply to the liver. It is a non-thrombotic obliteration of small intra hepatic veins by sub endothelial fibrin associated with congestion and potentially fatal necrosis of centrilobular hepatocytes. The pyrrolizidine alkaloids have been associated with this type of severe liver disorder. Busulfan and cyclophosphamide also cause venoocclusive disease.

Biochemical Mechanism [6]

The hepatotoxic effects of chemical agents may involve different mechanisms of cytolethality. These mechanisms may have either direct effect on organelles like mitochondria, endoplasmic reticulum, the cytoskeleton, microtubules and nucleus or indirect effect on cellular organelles through the activation and inhibition of signalling kinases, transcription factors and gene-expression profiles. The resultant intracellular stress may lead to cell death caused by either cell shrinkage and nuclear disassembly [apoptosis] or swelling and lysis [necrosis]. Main mechanisms involved are listed below:

Direct effect of toxicant upon critical cellular systems

Hepatotoxicants can attack directly certain critical cellular targets like plasma membrane, mitochondria, endoplasmic reticulum, nucleus and lysosomes thus disrupting their activity. Various chemicals and metal ions bind to mitochondrial membranes and enzymes,

disrupting energy metabolism and cellular respiration. Many hepatotoxicants act as direct inhibitors and uncouplers of mitochondrial electron transport. Covalent binding of the drug to intracellular proteins cause a decrease in ATP levels leading to actin disruption and rupture of the membrane. The mushroom toxin, phalloidin also causes increase in plasma membrane permeability by binding to actin and disrupting the cell cytoskeleton. Toxicants like chlorpromazine, phenothiazines, erythromycin salts have direct surfactant effects on the hepatocyte plasma membrane. NAPQI forms a covalent adduct with mitochondrial proteins having thiol groups and plasma membrane proteins involved in calcium homeostasis.

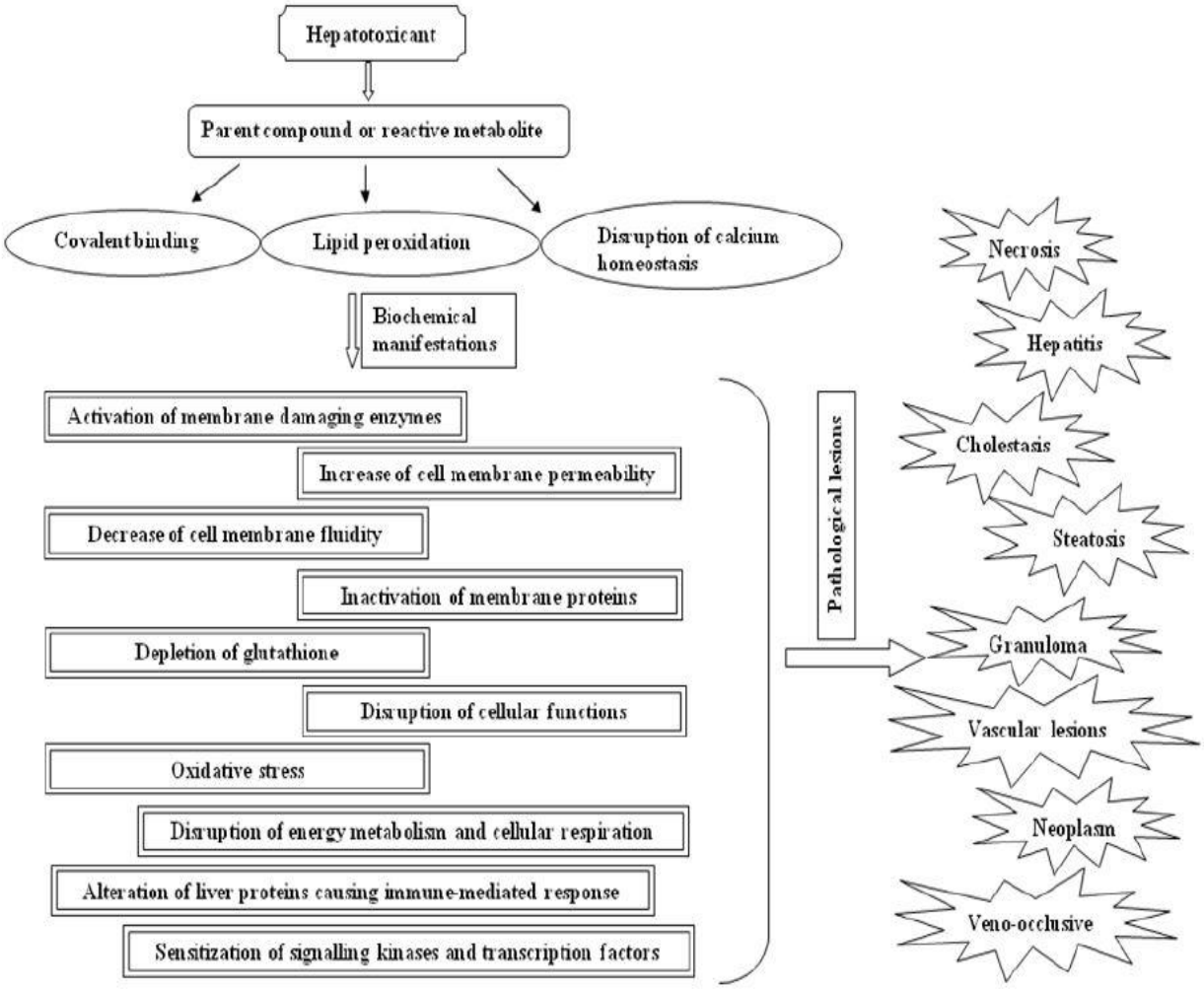

Figure 1: Biochemical and Pathological mechanism of hepatotoxicity.

Formation of reactive metabolites

Many hepatotoxicants like carbon tetrachloride, amodiaquine, acetaminophen, halothane, isoniazid, allyl alcohol and bromobenzene are metabolically activated to chemically reactive toxic metabolites which can covalently bind to crucial cellular macromolecules thus inactivating critical cellular functions. Glutathione provides an efficient detoxification pathway for most electrophilic reactive metabolites. However, many alkylating agents, oxidative stress and excess substrates for conjugation can lead to the depletion of glutathione thus rendering cells more susceptible to the toxic effects of chemicals. The reactive metabolites may also alter liver proteins leading to an immune response and immune-mediated injury.

Lipid peroxidation and redox cycling

These are involved in hepatotoxicity leading to cell death due to oxidative stress which is caused by an alteration in the intracellular pro oxidant to antioxidant ratio in favor of pro oxidants. Lipid peroxy radicals lead to increased cell membrane permeability, decreased cell membrane fluidity, inactivation of membrane proteins and loss of polarity of mitochondrial membranes. Metal ions like iron and copper participate in redox cycling while cycling of oxidized and reduced forms of a toxicant leads to the formation of reactive oxygen free radicals which can deplete glutathione through oxidation or oxidize critical protein sulfahydryl groups involved in cellular or enzymatic regulation or can initiate lipid peroxidation. Excessive consumption of ethanol contributes to free radical generation, lipid peroxidation and glutathione

depletion. Severe α-amanitin hepatotoxicity is also contributed by a peroxidative process. Halogentaed hydrocarbons, hydroperoxides, acrylonitrile, cadmium, iodoacetamide, chloroacetamide and sodium vanadate are also reported to exhibit hepatotoxicity due to lipid peroxidation.

Disruption of calcium homeostasis

Calcium is involved in a wide variety of critical physiological functions. Calcium homeostasis is very precisely regulated in the cell. Cytosolic free calcium is maintained at relatively lower concentration. The calcium concentration gradient between the inside of the cell and the extracellular fluid is maintained by an active membrane-associated calcium and magnesium effluxing adenosine triphosphatase [ATPase] enzyme system which is an important potential target for toxicants. Chemically induced hepatotoxicity may lead to the disruption of calcium homeostasis. Non-specific increases in permeability of the plasma membrane, mitochondrial membrane and membranes of smooth endoplasmic reticulum lead to disruption of calcium homeostasis by increasing intracellular calcium. Decline in available NADPH, a cofactor required by calcium pump may also disrupt calcium homeostasis. Disruption of calcium homeostasis may result in the activation of many membrane damaging enzymes like ATPases, phospholipases, proteases and endonucleases, disruption of mitochondrial metabolism and ATP synthesis and damage of microfilaments used to support cell structure

Biochemical Markers [6]

The hepatotoxins produce a wide variety of clinical and histopathological indicators of hepatic injury. Liver injury can be diagnosed by certain biochemical markers like alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP] and bilirubin. Elevations in serum enzyme levels are taken as the relevant indicators of liver toxicity whereas increases in both total and conjugated bilirubin levels are measures of overall liver function.

Enzyme Disease

- Aspartate aminotransferase - Diffuse liver cell necrosis e.g. (AST, SGOT) viral hepatitis, alcoholic liver disease, Acute myocardial infarction
- Alanine aminotransferase - More specific for diffuse liver (ALT, SGPT) cell damage than AST e.g. viral hepatitis
- Creatine kinase-MB (CK-MB) - Acute myocardial infarction, myocarditis Skeletal muscle injury
- Lipase - more specific for acute pancreatitis
- Amylase - Acute pancreatitis Sialadenitis
- Lactic dehydrogenase (LDH) - Acute myocardial infarction, Myocarditis, Skeletal muscle injury
- Cardiac troponin (CTn) - Specific for acute myocardial infarction

Hepatotoxicity can be characterized into two main groups, each with a different mechanism of injury shown in table no. **(1).**

ABBREVIATIONS

ALT - Alanine transaminase, AST - Aspartate aminotransferase, ALP - Alkaline phosphatase, LDH - Lactic acid dehydrogenase, GSH - Glutathione Peroxidase, GR - Glutathione reductase, GST - Glutathione S-Transferase, γ-GT-γ–glutamyl transpeptidase, SOD - Superoxide dismutase, TB - Total bilirubin, MDA - Malondialdehyde, TG - Triglyceraldehyde, CAT - Catalase, LPO - Lipid peroxidation, DPPH - 2,2-diphenylpicrylhydrazyl, SGOT - Serum glutamic oxaloacetic transaminase, SGPT - Serum glutamate pyruvate transaminase.

CONCLUSION

Marketed hepatoprotective formulations are used for the therapy which may cause side effects such as nausea, vomiting, headache, GIT problems, urinary retention etc. to overcome this, medicinal plants are utilized for hepatoprotection which has less side effects as compared to synthetic drugs. We believe that the medicinal plants have a potential hepatoprotective activity which can be used as adjuvant in therapy of various liver diseases. This review is to summaries explanatory data of medicinal plants having hepatoprotective activity with respect to its parts and extracts used highlighting the various studies done by other researchers using various experimental models.

The comprehensive information regarding these medicinal plants will be beneficial for further research. Since, the additional studies are required to isolate the exact active principles which are responsible for hepatoprotective activity as well as to reveal the mechanisms for its action of these medicinal plants.

Table 1: Biochemical markers of hepatotoxicity in blood plasma and serum.[6]

Biochemical Parameter	Tissue localization	Cellular Localization	Histopathological lesion	Reason of abnormality
Alanine aminotransferase	Primarily liver; trace amounts in skeletal muscles and heart.	Cytoplasm and mitochondria	Hepatocellular necrosis	Leakage from damaged tissues
Alkaline phosphatase	Liver, bile duct, bone, placenta, kidney and intestine	Cell membrane	Hepatobiliary injury and cholestasis	Overproduction and release in blood.
γ-Glutamyl transferase	Kidney, liver, bile duct, pancreas	Cell membrane	Hepatobiliary injury and cholestasis	Overproduction and release in blood
Total bilirubin	Direct (Liver, bile, small intestine, large intestine) Indirect (Reticuloendothelial cells of spleen, serum.	Extracellular fluid	Hepatobiliary injury and cholestasis	Decreased hepatic clearance
Urine bilirubin	Urine	-	Hepatobiliary disease	Leakage of conjugated bilirubin out of the hepatocytes into urine
Urobilinogen	Large intestine, urine	-	Hepatocellular dysfunction	An increase in unconjugated bilirubin, due to increased breakdown of RBCs, which undergoes conjugation, excretion in bile and metabolism to urobilinogen
Bile acids	Produced in liver, stored in gall bladder and released into the intestine	-	Hepatobiliary disease	Regurgitation into blood along with conjugated bilirubin
Prothrombin time	-	-	Hepatocellular dysfunction	Decreased synthetic capacity
Lactate dehydrogenase	Liver peroxisomes, muscles, kidney, heart	Mitochondria and sarcoplasmic reticulum	Hepatocellular necrosis	Leakage from damaged tissue
Sorbitol dehydrogenase	Liver, kidney, seminal vesicle, intestine	Cytoplasm, mitochondria	Hepatocellular necrosis	Leakage from damaged tissue
Glutamate dehydrogenase	Liver, kidney	Mitochondrial matrix	Hepatocellular necrosis	Leakage from damaged tissues
Total protein	Produced in liver and immune system	Blood plasma	Hepatic dysfunction	Decreased synthetic capacity
Albumin	Produced in liver	Blood plasma	Hepatic dysfunction	Decreased synthesis
Serum F protein	Liver, kidney	Primarily cytoplasm	Hepatocellular necrosis	Leakage from damaged tissue
Glutathione-Stransferase	Liver, kidney	Cytoplasm, mitochondrial, centrolobular cells	Early hepatocyte injury; Hepatocellular necrosis.	Readily released from hepatocytes in response to injury
Arginase I	Liver	Cytoplasm	Hepatocellular necrosis	Release from injured hepatocytes
Malate dehydrogenase	Liver, heart, muscle, brain	Cytoplasm, mitochondria	Hepatocellular necrosis	Leakage from damaged tissues
Purine nucleoside phosphorylase	Liver, muscle, heart	Cytoplasm of endothelial cells, kupferr cells, hepatocytes	Hepatocellular necrosis	Released into hepatic sinusoids with necrosis
Paraoxonase	Liver, kidney, brain, lung	Cytoplasm, microsomal, endoplasmic reticulum	Hepatocellular necrosis	Not a leakage enzyme; reduced hepatic synthesis and secretion

Table 2: Medicinal plants having potential Hepatoprotective activity.

Name of Plant & (Family)	Extract & plant Part used	Plant extract Dose & (Route of administration)	Animal used	Hepatotoxicity inducer drug, dose & (Route of administration)	Duration (Days)	Biochemical Estimation Significantly		Antioxidant activity significantly Elevated level as compared to control.	References
						Elevated level as Compared To control	Reduced level as compared to control		
Berberis Aristata (Berberidaceae)	Ethanolic extract of Stem	400 mg/kg (P. O.)	*Rat*	CCl4 1ml/kg (i.p)	7	-	SGOT, SGPT ALP, TB	–	(2)
Tamarindus Indica Linn. (Caesalpiniaceae)	-Aqueous extract of leaves and fruits -Aqueous extract of seeds.	350 mg/kg, (P.O.) 700 mg/kg (P. O.)	*Rat*	Paracetamol 1 gm/ kg. (P. O.) -CCl4 1ml/kg (i.p)	4 13	Total protein Total bilirubin	SGOT, SGPT ALP	–	(7)
Althaea officinalis Linn. (Malvaceae)	Ethanolic extract of root	100 mg/ kg (P. O.)	*Rat*	CCl4 1ml/kg (i.p)	7	-	SGOT, SGPT		(8)
Tridex Procumbens Linn. (Asteraceae)	Ethanolic extract of Whole plant	100 mg/kg, 200mg/kg, 300mg/kg, 400mg/kg (P. O.)	Rat	Paracetamol 1 gm/ kg. (i.p)	7	Total protein	SGOT, SGPT ALP Total bilirubin	LPO, SOD GT, CT, Glycogen level	(9)
Eclipta Alba (Asteraceae)	Aqueous extract of leaves	500 mg/kg (P. O.)	*Rat*	Paracetamol 2 gm/ kg. (P. O.)	7	Serum protein	SGOT,SGPT, ALP Serum bilirubin, Serum cholesterol, LDH, γ-GT, Serum Triglycerides.	-	(10)
Cissus quadrangularis Linn (Vitaceae)	Methanolic extract of stem	54 mg/kg (P. O.)	*Rat*	Isoniazide 50mg/kg (P. O.)	30		SGOT, SGPT ALP, Serum bilirubin.	LPO, SOD Glutathione, Catalase, MDA	(11)
Orthosiphon stamineus (Lamiaceae)	Ethanolic extract of leaves	100 mg/kg ,200 mg/kg (P. O.)	*Rat*	Thiacetamide 200mg/kg (i.p)	60	Total protein, Albumin	SGOT, SGPT ALP, Serum bilirubin	MDA	(12)

Bauhinia Purpurea (Fabaceae)	Methanolic extract of Leaves	50 mg/kg, 250 mg/kg, 500mg/kg (P.O.)	*Rat*	Paracetamol 250 mg/ kg. (P. O.)	7	Total phenolic content	SGOT, SGPT ALP.	DPPH Scavenging assay (In – Vitro)	(13)
Cucumis Trigonus Roxb. (Cucurbitaceae)	Ethanolic extract of fruit	100mg/kg, 250 mg/kg, 500mg/kg (P. O.)	*Rat*	Rifampicin + Isoniazide 50 mg/ kg (i.p)	21	Total protein, Albumin, Globulin, γ-GT	SGOT,SGPT, ALP, Total bilirubin.	LPO,SOD, MDA, Glutathione, peroxidation, Catalase, Reduced glutathione.	(14)
Mirabilis Jalapa L. (Nyctaginaceae)	Ethanolic extract of roots	250 mg/ kg (P. O.)	*Rat*	Paracetamol 2 gm/ kg. (P. O.)	14		SGOT, SGPT,ALP, Total bilirubin	-	(15)
Adansonia Digitata L. (Baobab)	Methanolic extract of fruit pulp	100 mg/kg 200mg/kg (i.p)	*Rat*	CCl4 2 ml/kg (i.p)	21		SGOT, SGPT,ALP, Bilirubin	-	(16)
Phyllanthus niruri (Phyllanthac eae)	Aqueous extract of Whole plant	1oo mg/ kg 50 mg/kg 25mg/kg (i.p)	*Rabbit*	Paracetamol 300 mg/ kg. (P. O.)	28	Protein, Albumin	SGOT,SGPT, Total bilirubin	-	(17)
Boerhaevia diffusa linn (Nyctoginaceae)	Ethyl acetate + Chloroform extract of root	100 mg/kg (P. O.) 200 mg/kg (P. O.)	*Rat*	CCl4 2 ml/kg (i.p)	7		SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin, Total cholesterol	LPO, SOD, Catalase,	(18)
Premna esculenta Roxb. (Verbenaceae)	Ethanolic extract of leaves	200 mg/kg 400 mg/kg (i.p)	*Rat*	CCl4 1 ml/kg (i.p)	7	Total protein, Albumin	SGOT,SGPT, ALP.	LPO, SOD, Catalase,	(19)
Ferula asafetida (Umbellifers)	Aqueous extract of	50 mg/kg, 100mg/kg -200 mg/kg (P. O.)	*Rat*	CCl4 1 ml/kg (i.p)	21	-	SGOT,SGPT, ALP, Cholesterol, Total bilirubin, Triglyceride.	LPO, SOD,	(20)
Vitex Negundo Linn (Lamiaceae)	Absolute ethanolic extract of leaves	300 mg/kg (P. O.)	*Rat*	Paracetamol 3 gm/ kg. (P. O.)	7	-	SGOT,SGPT, ALP,	-	(21)
Tephrosia Purpurea (Fabaceae)	Aqueous extract of Whole plant	75 mg/kg, 150 mg/kg (P. O.)	*Rat*	Paracetamol 1 gm/ kg. (P. O.)	7	-	SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin,	DPPH Scavenging assay (In – Vitro)	(22)

Senna alata Linn Roxb.) (Fabaceae)	Methanolic extract of leaves	400 mg/kg (i.p)	*Rat*	CCl4 2 ml/kg (i.p)	7	Total protein Albumin Globulin	Total bilirubin, Direct bilirubin,	-	(23)
Tagetes erecta Linn (Astraceae)	Ethanolic extract of roots	200 mg/kg, 400 mg/kg (P. O.)	*Rat*	Ethanol 3.76 gm/ kg (Twice in a day) (P. O.)	24	Total protein, Total Cholesterol	SGOT,SGPT, ALP, Total bilirubin, Total cholesterol	LPO, SOD, Catalase, Glutathione	(24)
Punica granatum (Lythraceae)	Aqueous extract of root and Peel	200 mg/kg, 400 mg/kg (P. O.)	*Rat*	CCl4 1 ml/kg (i.p)	1, 4	-	SGOT,SGPT ALP Total bilirubin.	-	(25)
Enhydra Fluctuans Lour (Asteraceae)	Ethanolic extract of aerial parts	200 mg/kg (P. O.)	*Rat*	CCl4 1 ml/kg (i.p)	10	Cholesterol, HDL,	SGOT,SGPT, ALP, Total Protein, Total bilirubin, Direct bilirubin, Cholesterol	-	(26)
Vetiveria zizanoides (Poaceae)	Ethanolic extract of Root	150 mg/kg 300 mg/kg (P. O.)	*Rat*	Paracetamol 3 gm/ kg. (P. O.)	10	-	SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin, Total cholesterol	LPO, SOD, Catalase, Glutathione	(27)
Clerodendron Inerme (Verbenaceae)	Ethanolic extract of leaves	200 mg/kg 400 mg/kg (P. O.)	*Rat*	Paracetamol 750 mg/ kg. (P. O.)	7	Total protein	SGOT,SGPT, ALP, bilirubin,	-	(28)
Bombax Ceiba (Malvaceae)	Aqueous extract of flowers	250 mg/kg, 500 mg/kg (P. O.)	*Rat*	CCl4 1 ml/kg (i.p)	7	Total protein, Triglyceride	SGOT,SGPT ALP, Total bilirubin, Albumine		(29)
Rumex Vesicarius Linn (Polygonaceae)	Methanolic extract of whole plant	100 mg/kg, 200 mg/kg (P. O.)	*Rat*	CCl4 1.5 ml/kg (i.p)	7	Total protein	SGOT,SGPT, ALP, Total bilirubin,	SOD, Catalase, MDA.	(30)
Jatropha Tanjorensis (Euphorbiaceae)	Methanolic extract of leaves	100 mg/kg, 200 mg/kg (P. O.)	*Rat*	CCl4 4 ml/kg (i.p)	14	Total protein, HDL	SGOT,SGPT, ALP, LDL, Albumine, VLDL Triglyceride, Total cholesterol,	-	(31)
Jatropha Gossypifolia (Euphorbiaceae)	Pet. Ether and methanolic extract of	200 mg/kg (P. O.)	*Rat*	CCl4 1 ml/kg (s.c)	7	Total protein, Total Cholesterol	SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin,	SOD, Catalase.	(32)

	Aerial parts.								
Bambusa arundinaceae (Graminae)	methanolic extract of Young shoot	50 mg/kg 100 mg/kg 200 mg/kg (P. O.)	*Rat*	Thiacetamide 100 mg/kg (S.C)	7		SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin.	LPO.	(33)
Santolina chamaecyparissus Linn (Astraceae)	Ethanolic extract of Whole plant	250 mg/kg (P. O.)	*Rat*	D – galactoamine 400 mg/kg (i.p)	14	Total protein.	SGOT,SGPT, ALP, Total bilirubin, LDH.		(34)
Plumbago zeylanica (Plubaginaceae)	Pet. Ether extract of roots	300 mg/kg (P. O.)	*Rat*	Paracetamol 400 mg/ kg. (P.O.)	7	Total protein	SGOT,SGPT, ALP, LDH, Triglyceride, γ-GT	-	(35)
Cassia tora (Leguminosae)	Ethanolic extract of leaves	600 mg/kg (P. O.)	*Rat*	CCl4 100 mg/kg (i.p)	21	Total protein	SGOT,SGPT	Catalase, LPO, Glutathione, SOD, Glutathione -S-Transferases.	(36)
Trichosanthes lobata (Cucurbitaceae)	Ethanolic extract of whole plant	200 mg/kg 400 mg/kg (P. O.)	*Rat*	Paracetamol 2 gm/ kg. (P. O.)	7	Total protein	SGOT,SGPT, ALP, Total bilirubin.	-	(37)
Corchorus depressus Linn (Tiliaceae)	Ethanolic extract of whole plant	200 mg/kg 400 mg/kg (P. O.)	*Rat*	CCl4 1 ml/kg (i.p)	7	Total protein.	SGOT,SGPT, ALP, Total bilirubin.	SOD, Catalase, Glutathione, MDA	(38)
Cicer arietinum (Fabaceae)	Ethanolic extract of seeds coat	500 mg/kg (P. O.)	*Rat*	CCl4 2 ml/kg (i.p)	6	-	SGOT,SGPT, ALP, Total bilirubin.	-	(39)
Euphorbia tirucalli (Euphorbiaceae)	Methanolic extract of Aerial parts	125 mg/kg 250 mg/kg (P. O.)	*Rat*	CCl4 1 ml/kg (i.p)	7	-	SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin, Total cholesterol, Triglyceride.	-	(40)
Vaccaria pyramidata (Caryophyllaceae)	Ethanolic extract of root	200 mg/kg 400 mg/kg (P. O.)	*Rat*	CCl4 1.25mg /kg (P.O.)	14	-	SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin, Triglyceride.	-	(41)
Polygala javana DC (Polygalaceae)	Ethanolic extract of whole plant.	100 mg/kg 200 mg/kg (P. O.)	*Rat*	CCl4 2.5 ml/kg (P.O)	14	Total protein, Albumin, Globulin.	SGOT,SGPT, ALP, Total bilirubin, Direct bilirubin.	LPO, SOD, Catalase, Glutathione Peroxidation.	(42)

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