

HERBAL AND AYURVEDIC LEADS FROM PRECLINICAL STUDIES HAVING HEPATOPROTECTIVE POTENTIAL - A REVIEW

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ABSTRACT

Liver disease is a major health problem worldwide, and it makes it necessary to develop new drug or formulation that help counteract or prevent these liver diseases. Liver plays a main role in the metabolism and excretion. Due to this reason, liver is exposed more to toxicity. In addition to it, there is still lack of some reliable hepatoprotective drug, which arose the scope for finding new drugs. There has been tremendous work done on herbal and ayurvedic formulation in invitro and invivo models to evaluate their hepatoprotective activity. In this study all the work done on 287 preclinical studies on hepatoprotective activity are review and were compiled. The drugs or formulation that show hepatoprotective potential in preclinical studies are the source of lead for researchers/medicals in treating the patients with liver disease and also for evaluating their safety and efficacy in the human trials.

KEYWORDS: Liver disease, hepatoprotective activity, leads, preclinical studies.

INTRODUCTION

Liver is the largest gland of the human body, situated at the right side of upper abdominal cavity. Hepatocytes which constitute 55-65% of the liver, plays vital functions like-

- Synthesis of protein
- Storage of protein
- Biotransformation of carbohydrates
- Cholesterol, bile salts and phospholipids synthesis
- Detoxification, modification, and excretion of the exogenous and endogenous substances
- Initiation of the formation and secretion of bile.
- Metabolizing of toxic chemicals and drugs.

As liver is the main site for metabolism of toxic chemicals and drugs, it is highly vulnerable to injury from them. The manifestation of this injury may vary from asymptomatic elevation to fulminant hepatic failure.

Several mechanisms are known, which initiate liver cell damage and also aggravate ongoing processes of injury. Mitochondria are consider as prominent targets for the hepatotoxicity of many drugs. The dysfunction of these vital cell organelles further results in impairment of the metabolism of energy and intracellular oxidant stress. Along with the excessive production of reactive oxygen species and peroxynitrite. In addition to the mitochondria, induction of the cytochrome P450 isoenzymes such as CYP2E1 also increased the oxidant stress and cell injury. Once function of hepatic cells are impaired, accumulation of bile acids causes the additional stress

and cytotoxicity. This cell injury, gut-derived endotoxin or a combination of both also activate the Kupffer cells and recruit neutrophils into liver. These inflammatory cells further initiate additional injury to liver. This injury leads to toxicities of liver known as hepatotoxicity.^[1]

These hepatotoxicity are induced by various drugs in animal models. These models are stated below that by which dose and for how much time it taken to do so.

Animal Models Of Hepatotoxicity^[2]

Carbon tetrachloride induced hepatotoxicity model

Animal used, Dose and route for inducing the toxicity

- Male Sprague-Dawley rats given CCl₄ 0.5 ml/kg i.p. for 3 days.
- Male Sprague-Dawley rats given CCl₄ 0.2 ml/100 g i.p. for 2 weeks.
- Male Wistar rats given CCl₄ 0.5 ml/kg i.p. twice a week for a period of 4 weeks.
- Male Wistar rats given CCl₄ 0.125 ml/kg i.p. for 7 days.
- Wistar strain albino rats given CCl₄ 1.0 ml/kg i.p. after every 72 h for 10 days.
- Male Wistar rats given CCl₄ 2 ml/kg, s.c. at every 72 h for 10 days.

These rats when given CCl₄ at the specific doses for the given time period induces hepatotoxicity.

Thioacetamide induced hepatotoxicity models

Animal used Dose and route for inducing the toxicity

- Male Wistar rats given Thioacetamide 200 mg/kg i.p. twice a week for 12 weeks.
- Male Wistar rats given Thioacetamide 300 mg/kg i.p. for 14 days.
- Wistar male rats given Thioacetamide 400 mg/kg i.p. for 2 weeks.

Diethyl nitrosamine (DEN) induce hepatotoxicity models

Animals of either sex were treated with diethyl nitrosamine having different concentration (50–200 mg/kg, i.p. for 4–12 weeks) of diethyl nitrosamine to induced hepatotoxicity.

Aflatoxin induced hepatotoxicity models

Animals of either sex were treated by different concentrations (200 lg/kg–6 mg/kg, p.o. for 2 days–52 weeks) of aflatoxin to induce hepatotoxicity.

PCM induced hepatotoxicity models

Animals of either sex were treated with different doses (3 mg/kg, p.o. for 7 days–3 weeks) of PCM to induce hepatotoxicity.

Cisplatin (anticancer drug) induced hepatotoxicity models

Animals of either sex are treated by different concentration (3.5–7 mg/kg i.p. for 1–5 days) of cisplatin to induce hepatotoxicity.

Erythromycin induced hepatotoxicity model

Animals of either sexes were treated by 100 mg/kg p.o. of erythromycin for 14 days to induce hepatotoxicity.

Isoniazid and Rifampicin induced hepatotoxicity

Wistar rats were treated with isoniazid (INH), co-administered with rifampicin (RIF) at 50–100 mg/kg i.p./o.p. dose for 10–28 days to induce hepatotoxicity.

Radiation-induced hepatotoxicity

Male wistar albino rats given single dose of whole body gamma rays (6 Gy) for 15 consecutive days, male sprague-dawley rats exposed to 5 Gy of c-radiation for 2 days and male wistar albino rats irradiated at an acute single dose level of 3 or 6 Gy for 7 days are used to induced hepatotoxicity.

Metal-induced hepatotoxicity

Male Wistar rats treated with mercury chloride (HgCl₂) (80 mg/l) as drinking water for 4 weeks, male albino rats given 5 mg/kg s/c injection of mercury (Hg) in the form of mercuric chloride for the 7days are used to induced hepatotoxicity.

Ethanol induced hepatotoxicity

Animal used, Dose of ethanol and route for inducing hepatotoxicity

- Male albino wistar rat treated with ethanol 7.9 g/kg p.o. daily for 45 days

- Wistar albino rats treated with ethanol 2.0 ml/100 g p.o. for 21 days
- Male albino wistar rats treated with ethanol 5 g/kg/day p.o. for 60 days
- Wistar female rats treated with ethanol 3.76 gm/kg twice a day p.o. for 25 days

Bile ducts ligation

In this model a midline abdominal incision and isolation of the common bile duct above the duodenum, and then, two ligatures were placed to proximal portion and one ligature was placed to the distal part of bile duct. Each biliary ducts from lobule is ligated separately to reduce the risk of biliary cysts. BDL stimulates proliferation of the biliary epithelial cells, which result in proliferation of bile ducts, cholestasis, portal inflammation, and fibrosis, causing secondary biliary cirrhosis, and then leads to the liver failure.

Portal vein ligation

Firstly laparotomy is performed with the upper abdominal incision. PVL was performed as the ligation of left portal vein which is leading towards the anterior lobe. Alongside length of the portal vein 10–20 gauge needle were held and 2–3 silk ligatures were tied around portal vein. The needle was then watchfully slipped out of ligatures allowing portal vein to open to the diameter equal to that of 20-gauge needle and then the abdomen was closed

Genetic model

• TGF-1 transgenic mice

The liver-specific over-expression of TGF-1 plays an essential role in the fibrogenesis of liver by activating the hepatic stellate cells (HSCs) to myofibroblasts and enhance synthesis of the extracellular matrix proteins.

• Bcl-xL/mice

Deletion of specific anti-apoptotic gene Bcl-xL-persistent apoptosis of hepatocytes is sufficient to stimulate the liver fibrosis.

• PDGF transgenic mice

Upregulation of TGF-b1 was reported to be responsible for the fibrogenesis of liver by overexpression of PDGF-A B, or C in PDGF family members.

• Abcb4/mice (Mdr2/mice)

Chronic cholangitis and severe biliary fibrosis occur in ABCB4-KO mice-due to absence of the phospholipid transporter in the bile which results in intoxication-based hepatocellular and injury of bile duct.

Hepatoprotective Leads

In modern science there is no reliable drug which can help in improving the condition. So many studies are conducted on herbal, ayurvedic drugs and formulation to note if they show some hepatoprotective potential. These studies are carried on different drug induced hepatotoxicity invivo model and isolated hepatocytes

models. A lot of drugs show hepatoprotective potential in these studies. These studies are reviewed and compiled in the (Table no 1) showing the model used in

the study, drug or formulation taken, species taken, dose and result of the study. These are the proven leads for hepatoprotective action in preclinical studies.

Table 1: Results of pre clinical studies conducted on drugs/plants/formulation for its hepatoprotective action.

S. no.	Hepatotoxicity model	Drug/plant/formulation evaluated	Dose	Species of the animal used	Result of the study
1.	Alcohol induced	<i>Rosmarinic acid</i> . ^[3]	10 mg/kg/ body wt	Rats	Prevent oxidant imbalance and liver injury
2.	CCl4 induced	<i>Tinospora cardifolia</i> Miers ^[4]		Albino rats	Decreased fibrosis and suppressed Kupffer cell function.
3.	Liquor induced	Ethanollic extract of roots of <i>Boerhavia diffusa</i> Linn ^[5]		Albino rats	Decreased serum alanine amino transferase, triglycerides, cholesterol and total lipid levels in both serum and tissues
4.	Thioacetamide, Galactosamine and CCl4 induced	Ursolic acid derive from <i>Punarnava leaves</i> ^[6]	5-20 mg/kg body wt.	Rats	Increased viability of rats hepatocytes
5.	Paracetamol induced	<i>Andrographolide</i> isolated from <i>Andrographis paniculata</i> Neesfor ^[7]		Exvivo preparation of isolated rat hepatocyte	Shows choleric effect that reduces cholestasis and diminished retention of toxic substance
6.	Hepatitis induced by CCl4	<i>Abhraka bhasma</i> ^[8]	10, 20, 30, 40 mg/kg/ body wt	Albino rats	Centrolobular necrosis reduced and counteracted the action of CCl4 on liver lipolytic enzymes
7.	CCl4 induced	<i>Panchagavya ghrita</i> ^[9]	150-300 mg/kg body wt	Albino rats	Shows significant decreased in levels of serum marker enzyme and reverse histopathological changes.
8.	Paracetamol induced	Six polyherbal formulation – <i>Liv.52</i> , <i>Livergen</i> , <i>Livokin</i> , <i>Octogenarian</i> , <i>Stimuliv</i> , <i>Tefroliv</i> ^[10]	2.6ml/kg/ day, 5.2ml/kg/ day	Swiss Albino rats	At 2.6ml/kg/day <i>Liv.52</i> and <i>Livergen</i> reversed toxicity and at 5.2ml/kg/day all these six polyherbal formulation shows marked beneficial
9.	CCl4 and Paracetamol given along with drugs	Methanolic extract of <i>Hemidesmus indicus R. Br</i> ^[11]		Wistar Albino rats	Shows significant less rise in levels of SGOT, SGPT, ALP and total bilirubin
10.	CCl4 induced	Ethyl acetate extract and two crude fractions- solvent ether and ethyl acetate of rhizome of <i>Cyperus Rotindus</i> ^[12]	100 mg/kg	Rats	Ethyl acetate extract at an oral dosage of 100 mg/kg show significant protection effect
11.	CCl4 induced	<i>Liv.52</i> and <i>Kumaryasava</i> ^[13]		Rats	<i>Liv.52</i> and <i>Kumaryasava</i> shows protective effect on hepatic enzyme

					induced due to CCl4
12.	In vitro and invivo model and CCl4 induced	Hydroalcoholic extract of <i>Cissampelos pareira</i> root ¹⁴		Invitro and rats	Shows significant reduction of elevated serum marker enzyme
13.	CCl4 induced and HepG2 cell line	<i>Punaravashthak</i> kwath ^[15]		Wistar rats and cell line	Supports hepatoprotective action in both HepG2 and CCl4 induced hepatotoxicity
14.	CCl4 induced and freshly isolated rat hepatocyte	Hydroalcoholic extract of <i>Cichorium intybus</i> ^[16]	50, 100, 200 mg/kg in rats and 60-600microg/ml, 1.5 mg/ml \$3.6mg/ml concentrate in isolated hepatocyte	Rats and isolated hepatocyte of rats	Protect liver at 50 and 100 mg/kg but in 200 mg/kg less effective and protect liver cells at 60-600micro/ml and >= 1.5mg/ml increase CCl4 induced cytotoxicity and above 3.6mg/ml is toxic itself.
15.	CCl4 induced	<i>Different extracts of Tinospora Cordifolia</i> ^[17]	200 mg/kg/ body wt	Wistar albino rats	Reduce the serum enzyme marker value.
16.	Paracetamol induced	<i>Eclipta Alba</i> extract ^[18]		Rats	Has significant hepatoprotective effect
17.	CCl4 induced	<i>Liverge</i> ^[19]		Rats	Show significant hepatoprotective effect
18.	CCl4 and Paracetamol induced	Polyherbal formulation F1 and F2 ^[20]	400mg/kg/ body wt	Albino rats	F1 and F2 both show prophylactic and therapeutic effects as hepatoprotective
19.	Isoniazid and rifampicin induced hepatitis	Ethanol extract of <i>Picrorrhiza Kurroa</i> ^[21]	50mg/ kg/day	Rats	Significantly prevented the antitubercular drug induced alterations.
20.	CCl4 induced	Extract of <i>Albino Averroha Carambola</i> fruit ^[22]		Albino mice	Significantly reduced serum liver enzymes and increased glutathine levels
21.	Acetaminophen induced	Ethanol extract of <i>Terminalia pallida</i> ^[23]	250mg/kg and 500mg/kg/ body wt	Rats	Shows hepato protective and antioxidant properties
22.	CCl4 induced	Aqueous extract of <i>E.divaricata</i> plant ^[24]		Male mice	Shows hepato protective abilities
23.	CCl4 induced	Methanol extract of <i>Ficus Carica</i> Linn. ^[25]	500mg/kg	Rats	Lower the serum enzyme marker
24.	Paracetamol induced	Ethanol extract of <i>Feronia limonia</i> Linn ^[26]	300mg/kg	Albino rats	Show hepato protective activity,
25.	CCl4 induced	Methanolic flower extract of <i>Nerium oleander</i> ^[27]	100, 200 and 400mg/kg	Rats	Shows maximum hepatoprotective activity at 400mg/ kg dose
26.	Paracetamol induced	Ethanol extract from the leaves of <i>Aerva lanata</i> and <i>Achyranthes aspera</i> ^[28]	200, 400mg/kg body weight	Rats	Shows hepatoprotective activity
27.	Invitro	<i>Eclipta Elba</i> extract ^[29]		Invitro assay	Shows hepatoprotective action
28.	Paracetamol induced	Aqueous extract of <i>Amarsnthus tricolor</i> Linn. ^[30]		Wistar albino rats	Shows hepatoprotective activity

29.	CCI4 induced	Ethanol extract of <i>Symplocos racemosa</i> ^[31]		Rats	Shows improvement in hepatoprotection, morphological and histopathological
30.	CCI4 induced	Vasicinone derived from <i>justicia adhtoda</i> ^[32]		Mice	Decreased serum enzyme markers
31.	d-galactosamine induced	Aqueous extract of <i>adhatoda vasica</i> ^[33]	50-100mg/kg	Rats	Shows significant hepatoprotection
32.	CCI4 and rifampicin induced	Hydroalcoholic extract of <i>Luffa acutangula</i> ^[34]		Rats	Shows antioxidant and hepatoprotection activity and inhibit lipid preoxidation
33.	d- galactosamine and thioacetamide induced	<i>Clear liv</i> ^[35]	800, 1000mg/kg	Wistar rats	1000mg dose show significant hepatoprotection
34.	CCI4 induced	Ethanol and ethylacetate extract of <i>Argyrea specios</i> ^[36]	200 and 400 mg/kg	Rats	Shows antioxidant and hepatoprotective activity
35.	Paracetamol induced	Ethanol extract of <i>Capparis brevispina</i> ^[37]	250 and 500mg/kg	Wistar rats	Shows significant hepatoprotective action
36.	Isoniazid and rifampicin induced	<i>Erythrina indica</i> ^[38]	100, 200mg/kg	Rats	Significantly prevent hepatotoxicity
37.	Paracetamol induced	Chloroform and methanol extract of <i>Ichnocarpus frutescens</i> (Linn.) ^[39]		Wistar albino rats	Antioxidant and hepatoprotective action shown
38.	CCI4 induced	Ethanol extract of <i>M. azedarach</i> (MAE) and <i>P. longum</i> (PLE) and their combination biherbal extract (BHE) ^[40]	50mg/kg	Albino rats	Combination of their extract shows more significant hepatoprotective action
39.	CCI4 and paracetamol induced	Hydroalcoholic extract of <i>Alocasia indicia</i> leaves ^[41]	250, 500mg/kg	Rats	Shows significant hepatoprotection
40.	Alcohol, CCI4 and paracetamol induced	<i>Jigrine</i> ^[42]		Rats	Shows antioxidant and hepatoprotective action comparable to <i>Liv.52</i>
41.	Paracetamol induced	<i>Tinospora cordifolia</i> (Willd.) Miers ex Hook. F., <i>Tinospora sinensis</i> (Lour.) Merrill and <i>Neem</i> (<i>Azadirachta indica</i> A. Juss.) ^[43]		Rats	<i>Tinospora sinensis</i> shows significant hepatoprotection than others
42.	Paracetamol induced	<i>Ocimum sanctum</i> leave extract ^[44]		Rats	Show partial hepatoprotection
43.	CCI4 induced	Aqueous extract of <i>Bombax ceiba flower</i> ^[45]	250, 500mg/kg	Rats	Show significant hepatoprotection
44.	CCI4 induced	Methanolic extract of <i>Mimosa pudica</i> leaves ^[46]	200mg/kg	Wistar albino rats	Shows comparable hepatoprotection to Silymarin
45.	Acetaminophen induced	Ethanol extract of <i>Acorus calamus</i> ^[47]	250, 500mg/kg/ body wt	Rats	Shows antioxidant and hepatoprotective action
46.	Paracetamol induced and invitro antioxidant assay	Methanol extract of <i>C. Ternatea</i> ^[48]	IC50 in vitro- 420microg/ml In mice - 200mg/kg	Invitro antioxidant and Mice	Shows hepatoprotection in both invitro and mice
47.	CCI4 induced	Petroleum ether, ethanol, water and chloroform		Invitro antioxidant assay	Show good antioxidant and hepatoprotection

		extract of <i>Oroxylum indicum Vent</i> ^[49]			
48.	Paracetamol induced	<i>Mamordica subangulata</i> and <i>naragamia alata</i> ^[50]	50mg/kg	Rats	<i>Mamordica</i> show hepatoprotection but <i>naragamia alata</i> don't
49.	CCI4 induced	Methanol extract of <i>Delonix regia</i> aerial parts ^[51]	400mg/kg	Wistar albino rats	Shows that it posses hepatoprotective action
50.	CCI4 induced	Polyherbal formulation composed of <i>Phyllanthus niruri</i> , <i>Eclipta alba</i> , <i>Cichorium intybus</i> , <i>Boerhaavia diffusa</i> , <i>Embelia ribes</i> , <i>Berberis aristata</i> and <i>Picrorhiza kurroa</i> ^[52]		Rats	Shows significant hepatoprotection
51.	Acetaminophen	<i>Satwa</i> prepared from three <i>Tionspora speciea</i> ^[53]		Rats	<i>T.cordifolia</i> -normalization of periportal hepatocytes whereas, <i>T.sinensis</i> showed prominent hepato-regenerative activity+increase in the normal hepatocytes and <i>Neem guduchi</i> -strikingly normal liver histology without any anatomically detectable anomalies
52.	CCI4 induced	Ethanol extract of <i>Euphorbia hirta</i> ^[54]	100, 300mg/kg	Rats	Shows hepatoprotection
53.	CCI4 induced and rat hepatocytes	Hydroalcoholic extract of <i>Anogeissus latifolia</i> bark ^[55]		In vitro and wistar rats	Shows hepatoprotection in both invitro and invivo
54.	Paracetamol induced	Petroleum ether and hydroalcoholic extract of <i>Pterospermum acerifolium</i> ^[56]	25, 50 mg/kg/ body wt	Albino rats	Both extracts have significant hepatoprotection
55.	Paracetamol induced	Three samples of <i>mandur bhasma</i> ^[57]		Rats	Shows significant different hepatoprotection of three samples
56.	CCI4 induced	Hydroethanolic extract of <i>Ipomoea digitata</i> Linn tuberous root ^[58]		Female wistar rats	Shows hepatoprotection
57.	CCI4 induced	Ethanol extract of <i>Ficus benjamina</i> ^[59]	250, 500 mg/kg/ bodywt	Rats	Show hepatoprotective action
58.	CCI4 induced	Chloroform extract of <i>Desmodium gangeticum</i> ^[60]		Rats	Shows significant hepatoprotective action
59.	CCI4 induced	Ethanol extract of <i>Premna corymbosa</i> leaves ^[61]	200, 400 ml/kg/ body wt	Wistar rats	Show significant hepatoprotection
60.	N-nitrosodiethylamine and CCI4 induced	<i>Embelin</i> ^[62]	50, 100mg/kg/ body wt	Rats	Shows chemopreventive and hepatoprotective activity
61.	Thioacetamide and allyl alcohol induced	<i>Sida rhombifolia ssp</i> ^[63]		Rats	Show potent hepatoprotection

62.	CCI4 induced and invitro	<i>Sapindus mukorossi</i> (<i>S. mukorossi</i>) and <i>Rheum emodi</i> (<i>R. emodi</i>) extracts ^[64]	<i>S. mukorossi</i> - 2.5mg/mL and <i>R. emodi</i> -3.0 mg/mL in rats	Male rats and primary hepatocytes	Shows hepatoprotective action in both invitro and rat
63.	CCI4 induced	Ethyl acetate fraction of <i>Tephrosia purpurea</i> ^[65]		Rats	Better hepatoprotection than Silymarin
64.	Paracetamol induced	Coumestans isolated form <i>W.calendulacea</i> leaves ^[66]		Albino rats	Show significant hepatoprotection
65.	Paracetamol induced	Alcohol, chloroform and aqueous extract of roots of <i>Baliospermum montanum</i> ^[67]		Albino rats	Alcohol and aqueous extract show significant hepatoprotection but chloroform extract show moderate activity
66.	CCI4 induced	Aqueous and ethanolic extract of <i>Garcinia indica</i> Linn fruit ^[68]	500mg/kg	Wistar albino rats	Show significant antioxidant and hepatoprotective action
67.	Invitro	<i>Calotropis gigantea</i> flower extract ^[69]		Invitro	Shows very good prophylactic and therapeutic hepatoprotective action
68.	CCI4 induced	Ethanolic extract of <i>Eclipta alba</i> ^[70]	200mg/kg	Albino rats	Show significant hepatoprotective action
69.	CCI4 induced	<i>Livshis</i> ^[71]	25-3200mg/kg	Male albino rats	Acute toxicity study show no toxicity upto 3200mg/kg and hepatoprotection at 50mg/kg is found
70.	CCI4 induced	Methanolic extract of <i>Curculigo orchoides</i> rhizomes ^[72]		Male rats	Shows hepatoprotective potential
71.	Paracetamol induced	<i>Somnathi tamra bhasma</i> ^[73]	67.5mg/kg/body wt	Albino rats	Show significant hepatoprotection
72.	Invitro assay and CCI4 induced	<i>Curcuma xanthorrhiza</i> ^[74]	125, 250 and 500mg/kg	Invitro assay and rat	Show hepatoprotective and antioxidant activity in both invitro and rats
73.	Paracetamol induced	<i>Andrographis Paniculata</i> powder extract ^[75]	500mg/kg	Rats	Show more hepatoprotection than <i>aeroliv</i>
74.	CCI4 induced	Ethanol extract of <i>Bacopa monnieri</i> L plants – <i>Bacoside A</i> ^[76]		Albino mice	Show significant hepatoprotection
75.	Anti- Tb drugs	<i>Liv. 52</i> ^[77]		Rats	Show antioxidant and hepatoprotective action
76.	D- galactosamine	Alcoholic extract of <i>Bacopa monniera</i> (BME) ^[78]		Rats	Show significant hepatoprotection
77.	CCI4 induced	Ethanol extract of <i>Swertia chirayita</i> Buch Ham and <i>Andrographis paniculata</i> ^[79]	200mg/kg	Swiss albino rats	<i>A.Paniculata</i> shows significant better hepatoprotection than <i>S. Chirayita</i>
78.	CCI4 induced	Ethanolic extract of <i>Jatropha gossypifolia</i> ^[80]	500mg/kg	Rats	Show significant oxidation and hepatoprotection
79.	CCI4 induced and invitro asaay	<i>C. album</i> extract ^[81]	450mg/kg	Rats and antioxidant invitro assay	Show significant results compare to Silymarin
80.	CCI4 induced	Ethanolic extract of	500mg/kg	Mice	Show significant

		<i>Aegle marmelos</i> ^[82]			hepatoprotection
81.	CCI4 induced	Ethanol extract of <i>Polygala rosmarinifolia</i> ^[83]		Rats	Show significant hepatoprotection
82.	CCI4 induced	Aqueous extract of <i>T. Cordifolia</i> ^[84]		Albino rats	Show significant hepatoprotection
83.	CCI4 induced	Alcohol extract of <i>Capparis sepiaria</i> Linn. (<i>Capparaceae</i>) stem ^[85]	100mg/kg	Albino rats	Show significant hepatoprotective activity
84.	CCI4 induced	<i>LIV-first</i> ^[86]	16.3mg/kg	Albino rats	Shows hepatoprotective action
85.	CCI4 induced and paracetamol induced	<i>Himoliv</i> ^[87]	0.5 and 1 ml/kg	Rats	Show significant hepatoprotective action compare to Silymarin
86.	Cadmium induced	<i>Moringa oleifera</i> ^[87]	500mg/kg	Wistar albino rats	Shown protection against cadmium induced hepatotoxicity
87.	Paracetamol induced and invitro antioxidant assay	Chloroform, ethyl acetate and methanol extract of <i>Smilax chinensis</i> ^[89]	100mg/kg	Rats and invitro antioxidant assay	Ethyl acetate extract had antioxidant and hepatoprotective action.
88.	Paracetamol induced	Hydroalcoholic extract of <i>Scindapsus officinalis</i> fruit ^[90]	200, 400mg/kg	Rats	Show significant hepatoprotection
89.	In vitro and invivo	Ethanol extract of <i>Bacopa monnieri</i> Linn ^[91]	300mg/kg/day	Invitro and invivo	Shows significant antioxidant and hepatoprotection
90.	Paracetamol induced	Ethanol extract of <i>Psidium guajava</i> ^[92]	Extract-200, 400mg/kg Phospholipid complex-100mg/kg	Albino rats	Phospholipid complex shows better activity than the plain extracts
91.	Anti Tb drugs induced	<i>Vasaguduchyadi kwatha</i> ^[93]		Albino rats	Show hepatoprotection due to it's membrane-stabilizing action and antioxidant property
92.	CCI4 induced and invitro	Crude hydro-alcoholic extract (CE) and its four fractions viz. methanol (MF), ethyl acetate (EF), n-Butanol (BF), and precipitated aqueous (PAF) of <i>A. racemosus</i> roots ^[94]		Rats and DPPH free radical scavenging assay	Show hepatoprotection in decreasing order of EF > MF > CE > BF > PAF
93.	Paracetamol induced	Extract of stem bark of <i>Ficus religiosa</i> Linn ^[95]	200mg/kg	Rats	Shows significant hepatoprotection. Methanolic extract shows more activity than other extract
94.	CCI4 induced	Warm aqueous extract of <i>Lawsini inermis</i> leaf, ^[96]		Wistar Albino rats	Shows anti lipid peroxidant and hepatoprotection effect
95.	Invitro	Aqueous extract of <i>P. Kurroa</i> , ^[97]		Different radical scavenging assays and then liver slice culture system induced hepatotoxicity by ethanol	Show antioxidant activity and significantly reduced lipid peroxidation

96.	Alcohol induced	<i>Bael</i> leaves, ^[98]		Albino rats	Shows significant hepatoprotection
97.	CCl4 induced	Ethanol extract of <i>Berberis coriacea</i> leaves, ^[99]	100, 200mg/kg	Male wistar Albino rats	Show hepatoprotection and no toxic effect up to dose of 2000mg/kg
98.	Isoniazid induced	Ethanol extract of <i>Jasminum grandiflorum</i> leaves (JG), ^[100]		Wistar Albino rats	Show significant hepatoprotection
99.	Paracetamol induced	<i>Arogyavardini rasa</i> , ^[101]		Rats	Shows significant hepatoprotection
100.	Ethanol induced	Liv. 52, ^[102]		Rats	Inhibit lipid peroxidation and significant hepatoprotection
101.	Paracetamol induced	Ethanol and water extract of <i>Macrotyloma uniflorum</i> , ^[103]	400mg/kg	Wistar Albino rats	Both extract show significant hepatoprotection
102.	CCl4 induced	Ethanol extract of <i>Berberis aristata DC</i> , ^[104]	100 and 300 mg/kg	Wistar Albino rats	Both dose shows significant hepatoprotection
103.	Country liquor induced	Ethanol extract of <i>ginger</i> ^[105]	200mg/kg	Rats	Shows significant hepatoprotection
104.	Paracetamol induced	<i>Withania somnifera</i> , ^[106]	500 mg/kg	Rats	Shows antioxidant and significant hepatoprotection
105.	CCl4 induced	Ethanol extract of <i>Melothria heterophylla</i> Lour Cogn, ^[107]	200 and 400mg/kg	Rats	Show hepatoprotection and antioxidant activity
106.	CCL4 induced	<i>Elephantopus scaber</i> Linn, ^[108]		Rats	Shows hepatoprotection
107.	CCl4 induced	Prak-20, ^[109]		Wistar albino rats	Shows hepatoprotection in three different studies
108.	Paracetamol induced	Ethanol extract of <i>Clerodendron inerme</i> leaves, ^[110]	200mg/kg	Swiss albino rats	Shows significant hepatoprotection and no mortality upto 2000mg/kg dose
109.	Invitro and CCL4 induced	Aqueous extract of the <i>Hygrophila Spinosa</i> (<i>K. Schum</i>) <i>Heine</i> (<i>syn. Asteracantha longifolia</i> <i>Nees, Acanthaceae</i>) stem, ^[111]		Antioxidant invitro using ferricthiocyanate (FTC) and thiobarbituric acid (TBA) methods. Rats	Show antioxidant and significant hepatoprotection
110.	CCL4 induced	Methanolic extract of <i>Plumeria alba</i> and <i>Aloevera</i> , ^[112]		Male wistar rats	Combination of both show significant hepatoprotection
111.	CCL4 induced	<i>C. trigonus</i> fruit extract, ^[113]		Albino wistar rats	Shows significant hepatoprotection
112.	CCl4 induced	Ethanol extract of <i>Anisochilus Carnosus</i> (<i>EEAC</i>) stem ^[114]	200 and 400mg/kg	Albino wistar rats	Shows significant hepatoprotection as compared to <i>Silymarin</i>
113.	CCL4 and ethanol induced	Ayush-Liv.04, ^[115]		Rats	Shows significant hepatoprotection
114.	Paracetamol induced	Aqueous extract of <i>Lawsonia inermis</i> . ^[116]		Rats	Shows significant hepatoprotection
115.	Paracetamol induced	Alcoholic and aqueous extracts of the aerial	200 and 400mg/kg	Mice	Shows significant hepatoprotection and

		parts of <i>Chenopodium album</i> , ^[117]			no toxicity upto 5g/kg in mice
116.	Invitro CCl4 induced liver slice	Hexane, ethanol (EtOH) and water (aq.) extract of <i>Mesua ferrea L. Stamen</i> , ^[118]		Ivitro antioxidant assay and liver slice culture	Hexane and ethanol extract show hepatoprotection
117.	CCL4 induced	Aqueous extract of <i>P. Niruri</i> ^[119]		Rats	Shows significant hepatoprotection and antioxidant activity with associated deleterious effects on kidney and testes
118.	CCl4 and paracetamol induced	Polyherbal formulation ^[120]	200 and 400mg/kg	Rats	Shows significant hepatoprotection at both doses in both models
119.	Paracetamol induced	Alcoholic extract of <i>Holostemma ada Kodien Shcult</i> ^[121]		Rats	Shows significant hepatoprotection
120.	Ethanol, CCL4 and galactosamine	<i>Livomynsh</i> ^[122]		Wistar rats	Shows significant hepatoprotection and antioxidant activity
121.	Paracetamol induced and invitro	<i>Oxalis corniculata L.</i> ethanolic extract ^[123]	500 µg/mL, po)	Wistar rats and invitro antioxidant free radical scavenging activity	Shows antioxidant and hepatoprotection potential
122.	Hexachlorocyclohexane – induced	<i>Andrographolide (ANDLE)</i> , extracted from <i>A paniculata</i> ^[124]		Mice	Shows significant hepatoprotection and antioxidant activity
123.	CCL4 induced	<i>Solanum trilobatum</i> extract (STE) ^[125]		Wistar Albino rats	Shows significant hepatoprotection and antioxidant activity
124.	Paracetamol induced	Methanolic extracts of <i>Andrographis paniculata</i> ^[126]	10 and 100 mg/kg	Mice	Shows hepatoprotection
125.	CCL4 induced invitro	Ethanol extract of <i>piper cubeba</i> fruit ^[127]		Invitro	Shows significant hepatoprotection and antioxidant activity
126.	Mercury induced	<i>Taurine</i> ^[128]		Rats	Shows significant hepatoprotection
127.	Rifampcin and isoniazid induced	Hydroalcoholic extract of <i>Ocimum gratissimum</i> leaves ^[129]	100 and 200mg/kg	Male wistar rats	Shows significant hepatoprotection
128.	CCl4 induced	<i>Superliv liq.</i> and <i>Repchol</i> ^[130]	5-10 ml/100 chicks/day	Broilera	Superliv liquid along with phytoadditive Repchol shows hepatoprotection
129.	CCl4 induced	Ethyl acetate extract of <i>Encostemma axillare (Lam). Raynal</i> ^[131]	100 and 200mg/kg	Rats	Shows hepatoprotection and antioxidant activity
130.	Thioacetamide induced	Ethanol extract of the rhizomes of <i>N. Jatamansi</i> ^[132]	800mg/kg	Rats	Show an increase in survival in rats intoxicated with LD90 dose of the hepatotoxic drug
131.	Iron overload induced	<i>Caesalpinia crista Linn.</i> (CCME) extract ^[133]		Mice	Shows hepatoprotection
132.	Paracetamol induced	Aqueous extract of <i>Phyllanthus emblica</i>		Wistar Albino rats	Shows hepatoprotection

		fruit ^[134]			
133.	CCL4 induced	<i>Boerhavia diffusa</i> extract ^[135]	100, 200 and 300mg/kg	Female Swiss albino mice	Shows hepatoprotection
134.	Paracetamol induced	Total extracts and steroidal saponins of <i>Solanum xanthocarpum</i> (Sx) and <i>Solanum nigrum</i> (Sn) ^[136]	100 and 200 mg/kg	Rats	Shows hepatoprotective and antioxidant effects of steroidal saponins of Sx and Sn greater than those of the total extracts
135.	CCL4 induced and invitro	HD-03/ES ^[137]	250, 500 and 1000mg/kg	Rats and invitro antioxidant using free radical scavenging activity	Shows significant hepatoprotection and antioxidant action
136.	CCl4 induced	Polyherbal formulation ^[138]	300mg/kg	Rats	Significant hepatoprotection
137.	Invitro and t-BHP induced	Ethanol extract of <i>Amorphophallus campanulatus</i> leaves ^[139]	1.0, 2.5, 5.0 and 7.5 µg	Invitro-Superoxide anion radical scavenging activity (SARSA), free radical scavenging activity (FRSA), ferrous ion chelation activity (FIC) and reducing power (RP) and was further carried out to assay the DNA damage and hepatoprotective activity	Shows significant hepatoprotection
138.	CCL4 and ethanol induced	Ethanol extract of <i>Ficus bengalensis</i> Linn leaves ^[140]	100, 200 and 400mg/kg	Rats	Shows significant hepatoprotection
139.	Isoniazid induced	Ethyl acetate extract of <i>Moringa oleifera</i> flower ^[141]		Rats	Shows significant hepatoprotection
140.	Rifampicin and isoniazid induced	<i>Hepatoplus</i> ^[142]	100mg/kg	Rats	Shows hepatoprotection equal to Liv.52
141.	Paracetamol induced	Aqueous and ethanol extract of <i>Helicanthus elastica</i> ^[143]	200 and 400mg/kg	Rats	Aqueous extract show more significant hepatoprotection at 200 mg/kg dose than Ethanol extract
142.	Acetaminophen induced	Aqueous and ethanol extract of <i>Pongamia pinnata</i> leaves ^[144]		Albino rats	Ethanol extract show significant hepatoprotection compared to aqueous extract
143.	CCl4 induced	Microspheres of NNDMA-curcumin ^[145]		Rats	Shows significant hepatoprotection by 12 µm size
144.	Acetaminophen induced	<i>Averrhoa bilimbi</i> fruit ^[146]	250 and 500 mg/kg	Wistar Albino rats	Show safety and efficacy on liver, kidney and heart
145.	Isoniazid and rifampicin induced	Methanol extract of <i>Adenanthera pavonina</i> ^[147]	100 and 200 mg/kg	Rats	Show hepatoprotection and antioxidant action

146.	Paracetamol induced	<i>Azadirachta indica</i> leaf extract ^[148]		Rats	Shows hepatoprotection
147.	Paracetamol and thioacetamide induced	Methanol extract of <i>Apium graveolens</i> and <i>Hygrophila auriculata</i> ^[149]		Rats	Show hepatoprotection
148.	Paracetamol induced	<i>Classia histula</i> leaf extract ^[150]	400mg/kg	Rats	Shows hepatoprotection
149.	Paracetamol and CCL4 induced	Methanolic extract of <i>Hemidesmus indicus</i> roots ^[151]	100-500mg/kg	Rats	Shows significant hepatoprotection
150.	d- Galactosamine	Chloroform insoluble fraction from ethanolic extract of <i>Tridax procumbens</i> ^[152]		Rats	Show significant hepatoprotection
151.	CCL4 induced	Ethanolic extracts of <i>Zanthoxylum armatum</i> DC bark ^[153]	100, 200 and 400 mg/kg	Male wistar rats	Significant hepatoprotection
152.	CCL4 induced	<i>Emblica officinalis</i> EO) and <i>Chyavanaprash</i> (CHY) extracts ^[154]		Rats	Shows significant hepatoprotection
153.	d- Galactosamine	Ethanol extract of <i>Picrorrhiza kurroa</i> ^[155]		Rats	Shows hepatoprotection
154.	CCL4 induced	<i>Kumari asav</i> , <i>kumari kalp</i> , <i>arogyavardhini</i> and <i>tamra bhasma</i> ^[156]		Albino rats	Shows hepatoprotection
155.	Aflatoxin B(1)-induced	Ethanolic extract of <i>Phyllanthus amarus</i> ^[157]	0.3g/kg	Mice	Shows antioxidant and hepatoprotection
156.	Invitro	<i>Hepatomed</i> ^[158]	3ml/100g	Cumene hydroperoxide (CHP) induced lipid peroxidation and reduced glutathione content in rat liver homogenate	Shows strong hepatoprotection with no adverse effects
157.	CCL4 induced and antioxidant assay	Aqueous extract of the <i>Hygrophila auriculata</i> roots ^[159]		Rats and Invitro by ferric hiocyanate (FTC) and thiobarbituric acid (TBA) methods	Shows hepatoprotection and antioxidant activity
158.	Galactosamine induced	Ethanol extract of <i>Ricinus communis</i> leaf ^[160]		Albino rats	Shows marked choleric activity and demonstrated an anticholestatic effect
159.	CCL4 induced	<i>Aloe barbadensis</i> petroleum ether, chloroform methanol and distilled water extract ^[161]		Mice	Distilled water extract only show hepatoprotection and this extract didn't show toxicity upto 2g/kgdose
160.	CCl4 induced and invitro	Methanolic and aqueous extracts of <i>azadirachta indica</i> leaves ^[162]		Male wistar rats	Shows potential hepatoprotection
161.	CCL4 induced	Methanolic and water extracts of <i>Ptreocarpus marsupium</i> wood Roxb. and <i>Butea frondosa</i> Koen. ex. Roxb.		Albino rats	Shows hepatoprotection

		leaves ^[163]			
162.	CCL4 induced	Alcoholic and aqueous extracts of <i>Nyctanthes arbor-tristis</i> leaves ^[163]	500mg/kg	Rats	Both extract show significant hepatoprotection
163.	Paracetamol induced	Hydroalcoholic extract of <i>Aerva lanata</i> ^[165]	600mg/kg	Rats	Shows hepatoprotection
164.	Anti Tb drugs	Ethanol extract of <i>M. oleifera</i> leaves ^[166]		Rats	Shows significant hepatoprotection
165.	CCL4 induced	Ethanol extract of <i>Eclipta alba</i> ^[167]	62.5-500mg/kg	Rats and mice	Shows hepatoprotection and didn't show any toxic effect upto 2g/kg dose
166.	CCL4 induced	Seed powder and aqueous extract of seeds of <i>Strychnos potatorum</i> ^[168]	100 and 200 mg/kg	Rats	200mg/kg dose show significant hepatoprotection
167.	CCL4 induced	<i>Rubiadin</i> , isolated from <i>Rubia cordifolia</i> Linn ^[169]	50, 100 and 200 mg/kg	Rats	Shows significant hepatoprotection
168.	Pyrogallol induced	<i>Livfit</i> ® ^[170]		Rats	Shows hepatoprotection by free radical scavenging property
169.	Anti Tb drugs induced and invitro	Hydroalcoholic extract of <i>Emblica officinalis</i> (fruit) ^[171]		Rats and in isolated hepatocyte	Shows hepatoprotection by stabilizing, antioxidative and CYP2E1 inhibitory effects.
170.	CCL4 induced	<i>Tinospora cordifolia</i> extract ^[172]	100mg/kg	Albino rats	Shows significant hepatoprotection
171.	CCL4 induced	Methanolic extract of whole plant of <i>Trichosanthes cucumerina</i> ^[172]	250 and 500mg/kg	Rats	Shows potential hepatoprotection
172.	CCL4 induced	<i>Bauhinia variegata</i> alcoholic Stem Bark Extract (SBE) ^[173]	100 and 200 mg/kg	Sprague-Dawley rats	Shows significant hepatoprotection
173.	CCl4 induced	Ethanol extract of <i>Hygrophila spinosa</i> and <i>Cassia accidentalis</i> ^[174]		Albino rats	Shows hepatoprotection
174.	CCL4 induced	Ethanol extract and four different fractions (CHCl ₃ , EtOAc, n-BuOH, and remaining water fraction) of <i>Vitis vinifera</i> L. leaves ^[176]	125mg/kg	Rats	Shows n-BuOH fraction in 83 mg/kg dose possess antioxidant and hepatoprotective activities
175.	CCL4 induced	Ethanol extract of <i>Portulaca oleracea</i> whole plant ^[177]		Rats	Shows significant hepatoprotection
176.	Anti-Tb drug induced	Ethanol extract of <i>Picrorhiza kurroa</i> rhizomes and roots (PK) ^[178]	50mg/kg/day	Rats	Shows hepatoprotection due to it's membrane stabilizing and antioxidant activity
177.	Paracetamol induced	Aqueous Ethanol Extract (AET) of mature <i>Rauwolfia serpentina</i> rhizome ^[179]		Rats	Shows hepatoprotection and antioxidant action
178.	Paracetamol induced	<i>Rohitaka ghrita</i> ^[180]	3.6-7.2g/kg	Wistar Albino rats	Shows significant

					hepatoprotection
179.	Paracetamol and rifampicin induced	Alcoholic and aqueous extract of <i>Trianthema portulacastrum</i> ^[181]		Rats	Shows significant hepatoprotection
180.	CCL4 induced	<i>Livobond</i> ^[182]	500 and 750mg/kg	Male Sprague-Dawley rats	Shows hepatoprotection and antioxidant action
181.	CCL4 induced	<i>Hepjaun syrup (HA-I)</i> and Modified Formulations ^[183]	500mg/kg	Rats	Shows significant hepatoprotection
182.	CCL4, paracetamol and thioacetamide induced	<i>Hepax</i> ^[184]		Rats	Shows significant hepatoprotection
183.	CCl4 induced and invitro antioxidant	<i>Justicia gendarussa</i> Burm. Methanol and distilled water extract ^[185]	300mg/kg	Antioxidant assay Albino rats	Methanol extract show significant hepatoprotection
184.	Paracetamol induced	Alcohol extract of <i>Caesalpinia bonducella</i> seeds ^[186]	100, 150 and 300mg/kg	Male albino rats	Show hepatoprotection at 300mg/kg dose
185.	Paracetamol, CCL4 and alcohol induced	Polyherbal hepatoprotective formulation (PHF)-containing spray-dried aqueous extracts of <i>Andrographis paniculata</i> Nees. (<i>Acanthaceae</i>), <i>Phyllanthus niruri</i> Linn. (<i>Euphorbiaceae</i>) and <i>Phyllanthus emblica</i> Linn. (<i>Euphorbiaceae</i>) ^[187]	100 and 200mg/kg	Rats	Shows significant hepatoprotection
186.	CCL4 induced	Extracts of <i>Ferula asafoetida</i> , <i>Momordica charantia</i> Linn and <i>Nardostachys jatamansi</i> ^[188]		Rats	Combination of these extract show significant hepatoprotection
187.	Paracetamol induced	Polyherbal formulation ^[189]		Rats	Shows significant hepatoprotection
188.	Paracetamol induced	Methanol and aqueous extracts of <i>Amorphophallus paeoniifolius</i> tubers ^[190]		Rats	Shows significant hepatoprotection
189.	Ibuprofen induced	Ethanol extract of <i>vitex negundo</i> leaves ^[191]	100 and 300 mg/kg	Male wistar albino rats	Show significant hepatoprotection at 300mg/kg dose
190.	Paracetamol, Galactosamine and CCL4 induced	<i>Iridoid</i> enriched fraction IF from the ethanol-Water extract of aerial parts (leaves and stems) of <i>Barleria prionitis</i> Linn. ^[192]		Mice	Show significant hepatoprotection and no toxicity upto 3000mg/kg
191.	CCL4 induced and invitro antioxidant assay	Methanol extract of <i>Ficus glomerata</i> ^[193]	250 and 500mg/kg	Rats and invitro antioxidant assay	Show hepatoprotection compared to <i>Silymarin</i>
192.	CCL4, paracetamol and rifampicin induced	Extracts of <i>Ficus glomerata</i> ^[194]		Albino rats	Petroleum ether extract against carbonetrachloride, total aqueous extract against paracetamol and methanolic extract against rifampicin-induced

					hepatotoxicities show similar hepatoprotection as of <i>Silymarin</i>
193.	Rifampicin induced	Petroleum ether extract of dried leaves of <i>Ficus carica</i> ^[195]		Rats	Show significant hepatoprotection
194.	CCL4 induced	Ethanol extract of leaves of <i>Rhododendron arboreum</i> ^[196]	40, 60 and 100mg/kg	Wistar rats	Show hepatoprotection and antioxidant activity
195.	CCL4 induced	Aqueous extract of <i>Boerhaavia diffusa</i> ^[197]	250 and 500 mg/kg	Male albino rats	Show hepatoprotection compared to <i>Silymarin</i>
196.	CCL4 induced and invitro	Alcoholic extract of <i>Premna serratifolia</i> Linn. leaves ^[198]	250mg/kg	Rats and EAC cell lines	Show hepatoprotection and antitumour activity
197.	Paracetamol induced	<i>Garcinia pedunculata</i> ^[199]		Rats	Shows significant hepatoprotection
198.	CCL4 induced	Methanol extract of <i>Smilax zeylanica</i> L roots and rhizomes ^[200]	200, 400 and 600 mg/kg	Wistar Albino rats	Shows significant hepatoprotection
199.	CCL4 induced	<i>Thespesia populnea</i> extracts ^[201]	60mg/kg and 500mg/kg	Rats	Ethanol extract of the stem bark was more active than n-hexane and water extracts, showing remarkable protection at a dose of 60 mg/kg b.wt.
200.	N-nitrosodiethylamine induced	Bacoside A isolated from <i>Bacopa monniera</i> Linn.) ^[202]	15mg/kg	Adult male albino rats	Shows hepatoprotection and antioxidant activity
201.	EAC tumor induced	Methanol extract of <i>Careya arborea</i> bark ^[203]	50, 100 and 200mg/kg	Mice	Show potent hepatoprotection and antioxidant action
202.	Paracetamol induced	Aqueous(AQS) and methanolic (MES) extract of <i>Sphaeranthus indicus</i> flower head ^[204]	300mg/kg	Rats	Shows hepatoprotection and antioxidant action
203.	Acetaminophen induced	Extracts of <i>Boerhaavia diffusa</i> leaves ^[205]		Rats	Aqueous and ethanol extract show hepatoprotection and antioxidant action
204.	Streptozotol induced	Methanol extracts of <i>P. marsupium</i> ^[206]	100 and 300 mg/kg	Rats	Show hepatoprotection and antioxidant action
205.	Paracetamol induced	Polyherbal Extract Containing <i>Andrographis Paniculata</i> , <i>Tinospora Cordifolia</i> and <i>Solanum Nigrum</i> ^[207]	500mg/kg	Swiss albino rats	Shows significant hepatoprotection
206.	CCL4 induced	Ethanol extract of aerial part of <i>Balanites aegyptiaca</i> ^[208]	100 and 200 mg/kg	Rats	Shows hepatoprotection and antioxidant action
207.	Paracetamol induced	<i>Mamordica subangulata</i> and <i>Naragamia alata</i> ^[209]	500mg/kg-wet/suspension leaves Ry-50mg/kg	Rats	Suspension of <i>mamordica subangulata</i> shows significant hepatoprotection
208.	Invitro	Ethanol extract of <i>B.scandens</i> leaves ^[210]	200 µg/ml	DPPH assay ORAC assay for antioxidant and	Shows hepatoprotection and antioxidant action

				MTT assay in BRL 3 A cell line for hepatotoxicity	
209.	CCL4 induced	<i>Amlakadi Ghrita (AG)</i> ^[211]	100 and 300mg/kg	Rats	Shows hepatoprotection compared to <i>Silymarin</i>
210.	Ethanol induced	<i>Phyllanthus amarus</i> and <i>Eclipta prostrata</i> leaves fine powder ^[212]		Albino rats	<i>Phyllanthus amarus</i> show slightly better hepatoprotection than <i>Eclipta prostrata</i>
211.	CCL4 induced	Ethanol extract of <i>Amaranthus spinosus</i> whole plant ^[213]	100, 200 and 400 mg/kg	Rats	Shows significant hepatoprotection at 400mg/kg dose
212.	CCL4 induced	Methanolic extract of <i>Stereospermum suaveolens</i> DC ^[214]	125, 250 and 500mg/kg	Albino rats	Shows hepatoprotection
213.	CCL4 induced	<i>Carduus acanthoides</i> , <i>C. nutans</i> , <i>Cichorium intybus</i> , <i>Fumaria asepalae</i> , <i>F. vailantii</i> , <i>Gentiana olivieri</i> and <i>Plantago lanceolata</i> ^[215]		Rats	<i>F. Vailantii</i> and <i>G. Oliveri</i> shows significant hepatoprotection
214.	Paracetamol induced	N-demethyl ricinine isolated from the <i>Ricinus communis</i> Linn leaves ^[216]	1.5- 12mg/kg	Rats	Shows more hepatoprotection than <i>Silymarin</i>
215.	Ethanol induced	<i>T cordifolia</i> , <i>T sinensis</i> and <i>Neem-Guduchi Satwa</i> ^[217]		Male wistar Albino rats	<i>T. cordifolia</i> and <i>Neem-Guduchi</i> show effect on lipid profile <i>T. bsinensis</i> show hepatoprotection and antioxidant action
216.	CCL4 induced	Herbal mixture ^[218]		Swiss albino mice	Shows similar hepatoprotection to <i>Liv.52</i>
217.	Paracetamol induced	Hydroalcoholic extract of <i>Abrus precatorius</i> seeds ^[219]	100, 200mg/kg	Rats	Shows significant hepatoprotection
218.	Ethanol induced	<i>Aegle marmelos</i> and <i>Eclipta alba</i> ^[220]		Rats	<i>Aegle marmelos</i> show more hepatoprotection than <i>Eclipta alba</i>
219.	CCL4 induced	<i>Luffa echinata</i> Roxb. (<i>Cucurbitaceae</i>) fruits extract ^[221]		Albino rats	Petroleum ether, acetone and methanolic extracts show significant hepatoprotective activity
220.	Alcohol induced	Alcoholic and aqueous extracts of <i>Tylophora indica</i> leaves ^[222]		Rats	Alcoholic extract shows greater hepatoprotection than aqueous. Alcoholic extract show no toxicity upto 5000mg/kg while LD50 of Aqueous was found to be 3162 mg/kg
221.	CCL4 induced	Ethanol extract of <i>Pterospermum acerifolium</i> leaves ^[223]	25mg/kg/day	Male wistar rats	Shows significant hepatoprotection

222.	CCL4 induced and invitro	Ethanol extract of <i>B.scandens</i> leaf ^[224]	2485 trolox eq/gm	Rats and BRL 3A cell line	Shows significant hepatoprotection and antioxidant action
223.	CCL4 induced	Hydroalcoholic extract of <i>Momordica charantia</i> Linn. Leaves ^[225]	100 and 200mg/kg	Wistar Albino rats	Show significant hepatoprotection
224.	CCL4 induced	<i>Kamilari</i> ^[226]	750mg/kg	Albino rats	Shows significant hepatoprotection
225.	CCL4 induced	Petroleum ether, chloroform, ethyl alcohol and aqueous extracts of the flowers of <i>Woodfordia fruticosa</i> ^[227]		Rats	Aqueous extract shows significant hepatoprotection
226.	Paracetamol induced	Aqueous extract of <i>Sphaeranthus indicus</i> whole plant ^[228]	400mg/kg	Rats	Shows significant hepatoprotection
227.	Paracetamol induced	Methanol extract of <i>Artocarpus lakoocha</i> fruit ^[229]		Mice	Shows significant hepatoprotection
228.	CCL4 induced	Ethanol extract of leaves of <i>Melia azedarach</i> and <i>Piper longum</i> seeds ^[230]	50mg/kg	Rats	Shows significant hepatoprotection
229.	CCL4 induced and invitro	Methanol extract of <i>Marsilea minuta</i> (<i>Marsileaceae</i>) ^[231]	200mg/kg	Rats and antioxidant invitro assay	Shows hepatoprotection and antioxidant activity
230.	CCL4 induced	Ethanol extract of <i>Melia azedarach</i> L leaves ^[232]	500mg/kg	Rats	Shows significant hepatoprotection
231.	Thioacetamide and gentamycin induced	Methanol and aqueous extract of <i>Phyllanthus amarus</i> seeds ^[233]	Methanolic-250mg/kg Aqueous-300mg/kg	Wistar rats	Methanol extract shows significant hepatoprotection than aqueous
232.	CCL4 induced and invitro	Isolated compounds from <i>TU</i> stem bark (TSB) ^[224]		Rats and HepG2 cells	Methanol extract shows significant hepatoprotection
233.	Galactosamine induced	<i>Swertiamarin</i> isolated from <i>Enicostemma axillare</i> Raynal ^[225]	100 and 200mg/kg	Rats	Show significant hepatoprotection
234.	Paracetamol induced	<i>Andrographis paniculata</i> and <i>Swertia chirayita</i> ^[226]	100-200mg/kg	Swiss albino rats	Shows significant hepatoprotection
235.	Streptozotin induced	Hydroalcoholic and aqueous extract of <i>Tamarindus indica</i> seeds ^[227]	100 and 200mg/kg	Rats	Hydroalcoholic extract show significant hepatoprotection than aqueous extract
236.	Ethanol induced	Aqueous extract of the roots of <i>Decalepis hamiltonii</i> ^[238]	50, 100 and 200mg/kg	Rats	Shows hepatoprotection and antioxidant activity
237.	CCL4 induced	<i>Tinospora cordifolia</i> , <i>Aloe Vera</i> and <i>Mangifera indica</i> plants extracts ^[238]		Wistar rats	<i>Aloe vera</i> shows significant hepatoprotection than other
238.	Acetaminophen induced	Emodin (1,3,8-trihydroxy-6-methyl anthraquinone), an active compound of <i>Ventilago madraspatana</i> Gaertn ^[240]	20, 30 and 40mg/kg	Rats	30mg/kg dose show optimum hepatoprotection
239.	Paracetamol and CCL4 induced	Ethanol extract of <i>C. Grandis</i> leaves ^[241]	150 and 300mg/kg	Rats	Show significant hepatoprotection and no toxicity upto

					3.2g/kg
240.	Alcohol induced	Alcoholic and aqueous extracts of aerial parts of <i>Chenopodium album</i> ^[242]	200 and 400mg/kg	Mice	Shows hepatoprotection at 400mg/kg dose and shows no toxicity upto 5g/kg
241.	Paracetamol induced and invitro	<i>Boswellia Serrata</i> extracts ^[243]		Rats and isolated hepatocytes	Shows hepatoprotection
242.	Paracetamol, thioacetamide and isoniazid	<i>HD-03</i> ^[244]		Rats	Shows significant hepatoprotection
243.	CCL4 induced	Aqueous extract of <i>Butea monosperma</i> flowers ^[245]	200, 400 and 800mg/kg	Rats	Shows significant hepatoprotection
244.	Paracetamol and isoniazid induced Invitro	Alcoholic extract of <i>Chonemorpha fragrans</i> (<i>C. fragrans</i>) root ^[246]		Rats and antioxidant invitro assay	Shows significant hepatoprotection and antioxidant
245.	Anti Tb drugs induced	<i>Anacyclus pyrethrum</i> Linn ^[247]	400mg/kg	Rats	Shows significant hepatoprotection
246.	Paracetamol induced	<i>PN kwath</i> ^[248]		Rats	Shows significant hepatoprotection.
247.	CCL4 induced	<i>Glycyrrhiza glabra</i> Linn. ^[249]		Sprague Dawley rats	Shows significant hepatoprotection
248.	CCI4 induced	<i>Prak-20</i> ^[250]	1.8gm/day	Wistar albino rats	Shows significant hepatoprotection
249.	CCI4 induced	Ethanol extract from <i>Corchorus depressus</i> ^[251]	50, 100, 200 µg/ml	Hep-G cell line	Show hepatoprotection and antioxidant activity
250.	CCL4 induced	Methanol extract of <i>Gymnosporia montana</i> leaves ^[252]		Liver cytoarchitecture	Show significant hepatoprotection
251.	Anti-Tb	Ethanol extract of <i>T. chebula</i> ^[253]			Shows hepatoprotection and antioxidant
252.	Paracetamol induced	Ethanol extract of the root of <i>P. odoratissimus</i> ^[254]	200 and 400 mg/kg	Male Wistar albino rats	400mg/kg show potent hepatoprotection than 200mg/kg
253.	Country liquor and paracetamol induced	Alcoholic extract of <i>P. emblica</i> and <i>quercetin</i> ^[255]	Extract at the dose of 100 mg/100 g and quercetin at the dose of 15 mg/100 g	Albino rats and mice	Shows significant hepatoprotection
254.	CCL4 induced	Methanol extract of <i>Clerodendrum infortunatum</i> Linn. (<i>MECI</i>) ^[256]	100 and 200mg/kg	Rats	Shows significant hepatoprotection
255.	CCL4 induced	<i>Coumarinolignoids</i> (cleomiscosins A, B, and C) isolated from the seeds of <i>C. viscosa</i> ^[257]	50mg/kg	Swiss albino rats	Shows significant hepatoprotection
256.	Ethanol induced	Ethanol extract of <i>Boerhaavia diffusa</i> root ^[258]	150mg/kg	Rats	Shows significant hepatoprotection
257.	CCL4 induced and invitro	<i>Randia dumetorum</i> leaf and bark ^[259]	400mg/kg	Male Wistar rats and DPPH, radical scavenging assay	Shows hepatoprotection action
258.	Thioacetamide induced	Aqueous extracts of <i>Convolvulus pluricaulis</i> leaves ^[260]	200, 400 and 600mg/kg	Rats	Shows significant hepatoprotection

259.	Acetaminophen induced	Aqueous extract of <i>Psidium guajava</i> leaf ^[261]	500mg/kg	Wistar albino rats	Show significant hepatoprotection and antioxidant action
260.	Paracetamol induced	Aqueous extract of <i>Psidium guajava</i> leaf ^[262]	500mg/kg	Rats	Show significant hepatoprotection
261.	CCL4 induced	Methanol extract of <i>Smilax zeylanica</i> L roots and rhizome ^[263]	200, 400 and 600mg/kg	Wistar albino rats	Shows significant hepatoprotection
262.	CCL4 induced and invitro	Methanol extract of <i>Justicia gendarussa</i> Burm ^[264]	300mg/kg	Rats and invitro assays	Shows significant hepatoprotection
263.	Thioacetamide and invitro induced	Ethyl acetate fraction (Beac) from <i>B. monosperma</i> bark ^[265]	300mg/kg	Male Wistar rats and invitro assay	Shows significant hepatoprotection
264.	CCl4 induced	<i>C. trigonus</i> fruit extracts ^[266]	300mg/kg	Female wistar albino rats	Shows significant hepatoprotection
265.	CCL4 induced	Ethanol extract of <i>Amaranthus tricolor</i> L. (ATE) leaves ^[267]		Rats and mice	Show significant hepatoprotection
266.	Paracetamol induced	Quercetin isolated from polyherbal hepatoprotective formulation ^[268]	50 and 100mg/kg	Rats	Shows significant hepatoprotection at 100mg/kg dose
267.	Acetaminophen induced	Withanolide-rich fraction (WRF) isolated from a methanolic extract of <i>Withania somnifera</i> roots ^[269]		Rats	Shows hepatoprotection
268.	Morphine induced	<i>Bacopa monniera</i> alcohol extracts ^[270]		Rats	Shows hepatoprotection action
269.	CCL4 induced	Ethanol extract of stem bark of <i>Bauhinia variegata</i> ^[271]	100, 200, 400 and 600mg/kg	Albino Wistar rats	100 and 200 mg/kg shows significant hepatoprotection
270.	CCL4 induced	Methanolic extract of <i>Hiptage bengalensis</i> (L.) kurz ^[272]	200 and 400mg/kg	Rats	Shows significant hepatoprotection and antioxidant action
271.	Paracetamol induced	Ethanol extract of <i>Sphaeranthus amaranthoides</i> whole plant ^[273]	400mg/kg	Rats	Show significant hepatoprotection
272.	Paracetamol induced	Aqueous extract of <i>Lawsonia inermis</i> ^[274]		Rats	Shows significant hepatoprotection
273.	D- Galactosamine induced	n-BuOH extract of <i>Swertia japonica</i> ^[275]		Mice	<i>Tetrahydroswertianolin</i> isolated shows strong hepatoprotection
274.	Paracetamol induced	Methanolic extract of <i>Syzygium jambos</i> (Alston) (Linn.) leaves ^[276]	100 and 200 mg/kg	Wistar albino	Shows hepatoprotection
275.	CCL4 induced	Ethanol extract of whole plant of <i>Andrographis paniculata</i> ^[277]		Albino rats	Shows hepatoprotection and antioxidant action
276.	CCl4 induced	Extract of <i>Nymphaea stellata</i> willd ^[278]		Albino rats	Shows good hepatoprotection
277.	CCL4 induced and invitro	Methanol extract of <i>S. xanthocarpum</i> leaves (SXAF) ^[279]	200mg/kg	Rats	Show potent hepatoprotection and antioxidant
278.	CCL4 induced	<i>Kumaryaasav</i> ^[280]	5.0	Wistar rats	Shows marked

			mL/Kg/day, 1.6 mL/Kg/day and 100 mL/Kg/day		hepatoprotection
279.	Sodium arsenite induced	Ethanol extract of <i>Pleurotus cornucopiae</i> ^[281]	400mg/kg	Rats	Shows significant hepatoprotection
280.	Paracetamol induced	Ethanol extract of <i>Curcuma longa</i> ^[282]	100mg/kg	Rats	Show potent hepatoprotection
281.	Paracetamol induced	Methanol extract of <i>Laurus nobilis</i> ^[283]	200 and 400mg/kg	Rats	Acts on liver as a potent scavenger of free radicals to prevent the toxic effects
282.	Anti -Tb drugs induced	<i>Hibiscus vitifolius</i> roots ^[284]	400mg/kg	Albino rats	Shows significant hepatoprotection and no toxicity upto 2000mg/kg
283.	Nitrobenzene induced	Ethanol extract of <i>Bacopa monnieri</i> ^[285]		Rats	Shows good hepatoprotection
284.	CCL4 induced	<i>Bauhinia racemosa</i> stem bark ^[286]		Rats	Shows significant hepatoprotection
285.	Paracetamol induced	Ethanol extract of <i>Trichosanthes lobata</i> ^[287]	200 and 400mg/kg	Male wistar rats	Shows significant hepatoprotection
286.	Paracetamol induced	Methanol extract of <i>Madhuca longifolia</i> flower ^[288]	100 and 200 mg/kg	Wistar albino rats	Shows significant hepatoprotection
287.	NAFLD induced	Water extract of <i>P. emblica L. fruit</i> ^[289]		Rats	Show significant hepatoprotection

SCOPE OF THE STUDY

- The leads which have showed the positive results for hepatoprotective activity can be used according to necessity in humans and their safety and efficacy can be further proven in the them
- So that a reliable, potent and safe hepatoprotective drug can be developed.

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