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Review Article

Hepatoprotective Activity - A Review

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Abstract

Liver diseases are a major problem of worldwide proportions and liver damage is very common since liver has the capacity to detoxicate toxic substances. In this review some of the plants with their extract studied for protective effect in liver diseases were summerised. The varios isolated compounds studied herein are Andrographolide, neo-andrographolide, bacoside-A, colchicine, populnin, naringenin, echinacoside, kolaviron, ternatin, indigtona, rubiadin, bacicalein, baicalin, wogonin, punicalagin, punicalin for their hepatoprotective activity. There are several chemicals have been known to induce heptotoxicity by producing reactive species which cause depletion in tissue thiol, lipid peroxidation, plasma membrane damage like carbontetrachloride, paracetomol, thioacetamide, antituberculer drugs, D galactosamine, liposachharide and arsenic etc.
Key Words: *Hepatoprotective, Heptotoxicity, Medicinal plants, Antioxidants*

1.Introduction

The Greek word for liver is *hepar,* so medicinal terms related to liver often start with hepato or hepatic. Liver plays a pivotal role in metabolism, secretion and storage and is sometimes referred as the " great chemical factory" of the body, because the body depends on the liver to regulate, synthesize, store and secrete many important proteins, nutrients, chemicals and to purify and clear toxins or unnecessary substances from the body[1]. The bile secreted by the liver, among other things, plays an important role in digestion. The risk of the liver intoxication has recently increased by the higher exposure to environmental toxins, pesticides and frequent use of chemotherapeutics.

Liver damage is always associated with cellular necrosis, increase in tissue lipid peroxidation and depletion in the tissue glutathione (GSH) levels. In addition, serum levels of many biochemical markers like serum glutamate oxaloacetate transaminase (SGOT/AST) and serum glutamate pyruvate transaminase (SGPT/ALT) triglycerides, cholesterol, bilirubin and alkaline phosphatase are elevated [2,3].

The following are some of the liver diseases that are commonly observed.

a) Necrosis
b) Cirrhosis
c) Hepatitis- may be of viral, toxic or deficiency type.
d) Hepatic failure - Acute or chronic
e) Liver disorders due to impaired metabolic function. Generally the disorders associated with fat (liposis) and bilirubin (jaundice) metabolisms are very commonly seen.
1. Disorders associated with fat metabolism: Fatty Liver

2. Disorders associated with bilirubin metabolism: jaundice or which may be of different types based upon mechanisms of action and etiology.

i. Hemolytic/Pre-hepatic jaundice.

ii. Obstructive (post-hepatic / cholestatic jaundice)

iii. Hepatogenous/ hepatic jaundice/cholestasis.

In these three conditions there occurs unconjugated hyperbilirubinaemia.

iv. Hereditary jaundice or pure cholestasis: Gilbert's syndrome, Dubin Johnson syndrome and Crigler-Najjar syndrome etc, Rotor's syndrome are some of the hereditary jaundice types.

f) Chemical/Drug induced hepatotoxicity: Generally may be hepatitis, jaundice and carcinogenesis.

1.1. Hepatotoxicity

Hepatotoxin is a toxic chemical substance which damages the liver. Toxic liver injury produced by drugs and chemicals may virtually mimic any form of naturally occurring liver disease. Hepatoprotective effect was studied against chemicals and drugs induced hepatotoxicity in rats like alcohol, carbon tetrachloride, galactosamine, paracetamol, isoniazid and rifampicin, antibiotics, peroxidised oil, aflatoxin etc.

Severity of hepatotoxicity is greatly increased if the drug is continued after symptoms develop. Among the various inorganic compounds producing hepatotoxicity are arsenic, phosphorus, copper and iron. The organic agents include certain naturally occuring plant toxins such as pyrrolizidine alkaloids, myotoxins and bacterial toxins.

Liver injury caused by hepatotoxins, such as carbon tetra chloride (CCl_4), ethanol and acetaminophen, is characterised by varying degrees of hepatocyte degeneration and cell death via either apoptosis or necrosis. The generation of reactive intermediate metabolites from the metabolism of hepatotoxins and the occurrence of reactive oxygen species (ROS) during the inflammatory reaction, account for a variety of pathophysiologic pathways leading to cell death, such as covalent binding, disordered cytosolic calcium homeostasis, GSH depletion, onset of mitochondrial permeability transition (MPT) and associated lipid peroxidation. The metabolism of hepatotoxins by cytochrome P-450 enzyme subtypes is a key step of the intoxication; therefore, enzyme inhibitors are shown to minimize the hepatotoxin-associated liver damage. Moreover, substantial evidence exists that MPT is involved in ROS-associated hepatocellular injury and new findings offer a novel therapeutic approach to attenuate cell damage by blocking the onset of MPT. Thus, oxidant stress and lipid peroxidation are crucial elements leading to hepatotoxin-associated liver injury. In addition to specific treatment for a given hepatotoxin, the general strategy for prevention and treatment of the damage includes reducing the production of reactive metabolites of the hepatotoxins, using anti-oxidative agents and selectively targeting therapeutics to Kupffer cells or hepatocytes for on-going processes, which play a role in mediating a second phase of the injury[4] .

1.2. Evaluation of hepatoprotective activity:

A review of literature reveals that several chemical substances and drugs having specific actions on liver are used as hepatotoxins in experimental animals to simulate ideal diseased conditions. The hepatoprotective activity can be most easily evaluated /screened with the aid of several model systems of liver damage in experimental animals.

In all test model systems, conditions for liver damage are implemented and an attempt is made to counteract this toxicosis with the substance/preparation under test. The magnitude of the protective effect can be measured by estimating the enzyme activities and the rate of survival and can be verified histologically. The available methods are *in vivo*, *ex vivo* and *in vitro* methods[8]. All these methods are used to study the protective or curative effects of any compound under test. In order to test for hepatoprotective activity the test substance and the hepatotoxin are administered simultaneously whereas in case of antihepatotoxic or curative activity the test substance is generally administered after induction of hepatotoxicity

a. *In vitro* methods: Hepatocytes are generally isolated by using *in-situ*, two step recirculating collagenase perfusion technique. These are then seeded in small containers and exposed to test samples and toxins. After a specified time period, the degree of toxicity or protection is assessed by viability tests and enzyme levels such as GOT and GPT. By employing primary culture hepatocytes using CCl_4, galactosamine, thioacetamide, ethanol, paracetamol (PCML) etc. as hepatotoxins several hepatoprotective screening models have been devised. These have a number of advantages over *in vivo* methods such as their ability to dispose numerous samples at a time, low cost with a small size, little variation and reproducibility of results. The major disadvantage is that sometimes it may not reflect the events which occur in animals.

b. Ex- *vivo* models: In this model, after completion of preselected *in vivo* test protocol hepatocytes are isolated and the percentage of viable cells and biochemical parameters are determined as liver function tests. These methods are somewhat better correlated to clinical models than *in vitro* or *in vivo* methods.

c. *In vivo* methods: This method is used not only to study the nature of the given compound but also to study the mechanism of the toxicant. Hepatotoxicity is produced in experimental animals by the administration of known dose of hepatotoxins like CCl_4, galactosamine, thioacetamide, ethanol and paracetamol etc., which produce marked measurable effects, the magnitude of which can be measured by carrying out various liver function tests viz. morphological, metabolic or functional, biochemical and histopathological determinations. Although it is a very convenient laboratory method, reproducibility of results is rather poor. The compounds having hepatoprotective claims are also evaluated in general for their choleretic or anticholestatic activity in order to know whether the liver disorder is due to an abnormality of bilirubin metabolism or not. Choleretics are those agents which increase the out puts of bile by stimulating the liver where as anticholestatics are those which correct the retention and accumulation of bile due to intrinsic and extrinsic factors in the liver. These activities are evaluated by studying bile flow content in conscious and anaesthetized animals for 5 hours.

1.3.Experimental modelS for hepatoprotective screening:

Several chemical reagents and drugs which induce liposis, necrosis, cirrhosis, carcinogenesis and hepatobiliary dysfunctions in experimental animals are classified as hepatotoxins. The following are some of the experimental models explained by employing some of the important hepatotoxins.

1. CCl_4 model: A number of CCl_4 models are devised depending upon its dosage through different routes of administration.

a) Acute hepatic damage: Acute liver damage, characterized by ischemia, hydropic degeneration and central necrosis is caused by oral or subcutaneous administration of CCl_4 (1.25ml/kg). The maximum elevation of biochemical parameters are found to be 24 hours after the CCl_4 administration normally administered as 50% v/v solution in liquid paraffin or olive oil[9] .

b) Chronic reversible hepatic damage: Administration of CCl_4 (1ml/kg S.C.) twice weekly for 8 weeks produces chronic, reversible liver damage [10].

c) Chronic, irreversible hepatic damage: Administration of CCl_4 (1ml/kg S.C.) twice weekly for 12 weeks simulates chronic, irreversible liver damage[11].

2.Thioacetamide model:Thioacetamide (100mg/kg s.c.) induces acute hepatic damage after 48 hrs of administration by causing sinusoidal congestion and hydropic swelling with increased mitosis[12].

3.D-galactosamine model: D-galactosamine (800mg/kg i.p.) induces acute hepatotoxocity after 48 hrs of administration with diffused necrosis and steatosis**[13]**.

4 .Paracetamol model: Paracetamol induces acute hepatotoxicity depending upon its dosage through different routes of administration, such as

a. Paracetamol (800mg/kg i.p.) induces centrilobular necrosis without steatosis [14].

b.Paracetamol at a single dose of 3g/kg p.o. stimulates acute hepatic damage. It takes 48 hrs to induce the toxicity[15].

5.Chloroform model: It produces hepatotoxicity with extensive central necrosis, fatty metamorphosis, hepatic cell degeneration and necrosis either by inhalation or by subcutaneous administration (0.4-1.5ml/kg)[16] .

6.Ethanol model: Ethanol induces liposis to a different degree depending upon its dose, route and period of administration as follows:

a. A single dose of ethanol (1ml/kg) induces fatty degeneration[17].

b. Administration of 40%v/v ethanol (2 ml/100g/day p.o.) for 21 days produces fatty liver[18].

c. Administration of country made liquor (3ml/100 g/day p.o.) for 21 days produces liposis[19].

1.5. Hepatoactive medicaments: The literature review reveals that a large number of drugs of plant origin are endowed with hepatoprotective claims either directly or indirectly. In recent years, the usage of herbal drugs for the treatment of liver diseases has increased all over the world[36]. The herbal drugs are believed to be harmless and free from serious adverse reactions, as they are obtained from nature and are easily available. Also, the limited therapeutic options and disappointing therapeutic success of modern medicine including herbal preparations[37] .

In recent years many researchers have examined the effects of plants used traditionally by many folklore remedies from plant origin have long been used for the treatment of liver diseases[38] indigenous healers and herbalists to support liver function and treat diseases of the liver. In most cases, research has confirmed traditional experience and wisdom by discovering the mechanisms and mode of action of these plants as well as reaffirming the therapeutic effectiveness of certain plants or plant extracts in clinical studies. Several hundred plants have been examined for use in a wide variety

of liver disorders. Just a handful has been fairly well researched [39]

There are about 600 commercial herbal formulations, which are claimed to have hepatoprotective activity and many of them are being sold in market all over the world. In India, about 40 patented polyherbal formulations representing a variety of combinations of 93 herbs from 44 families are available[40]. It has been reported that 160 phytoconstituents from 101 plants possess hepatoprotective activity[41] . Liver protective herbal drugs contain a variety of chemical constituents like phenols, coumarins, lignans, essential oil, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, alkaloids and xanthone derivatives[40]. Studies carried out in China and Japan resulted in the isolation of a hepatoprotective lignan, gomishin from the fruits of Chinese medicinal plant *Schizandra chinensis*. Gomishin is used for the treatment of chronic hepatitis. Studies carried out at Tropical Botanic Garden and Research Institute (TBGRI) have shown that *Trichopus zeylanicus*, *Phyllanthus maderaspatensis* and *P. kozhikodianus* are extremely active against paracetamol-induced liver damage in rats [42,43,44]. A recent report indicates that fumaric acid obtained from *Sida cordifolia* has significant anti-hepatotoxic activity in rat[45]. Ursolic acid which occurs in many plants also showed promising hepatoprotection against paracetamol and CCl_4 induced liver damage in rats[46,47] .Some of the reported constituents with pharmacologically/therapeutically proved claims may be enlisted as silymarin, (+)- catechin, saikosaponins, curcumin, glycyrrhizin, picroside I and II gomisin etc[48] , acetyl bergenin [49] and kolaviron[50] . Most commonly used plants in herbal formulations in India and scientifically validated in experimental animals are *Andrographis paniculat*)[51], *Boerhaavia diffusa*, *Eclipta alba*, *Picrorrhiza kurroa*[52] , Cichorium intybus, Tinospora cordifolia[53] .

Some of the polyherbal formulations are verified for their hepatoprotective action against chemical induced liver damage in experimental animals[54,55,56] : Liv.52[40,57], Liv.42, Liver cure, Tefroli [51,58], Livol , Hepatomed[59] , Jigrine[40] , Stimuliv[44] , Koflet[40] and Icterine[60] .

Antioxidants can protect experimental animals and humans from oxidant mediated liver damages. This effect can be seen even in certain common vitamins, spices and vegetables (e.g. Vitamin-E and turmeric). Efficacy of the traditional and new herbal products should be tested by standard experimental methods. Also, there should be adequate data from *in vivo* and *in vitro* studies to validate the therapeutic potential claimed[61].

Several plants have been reported to have hepatoprotective acvity among those, a few plants tested against different experimental models are listed in below table.

2 . List of hepatoprotective activity having medicinal

Plants:

Botanical Name	Family	Plant Parts Used	Screening Methods	References
Acacia catechu	Leguminosae	Powdered pale catechu	Carbontetra chloride induced	62
Acacia confuse	Leguminosae	Bark	Carbon tetra chloride	63
Aegle marmelos Correa	Rutaceae	Leaves	Paracetamol Induced	64
Aerva lanata	Amaranthaceae	Coarce powder Plant	Paracetamol Induced	65
Alchornea cordifolia	Euphorbiaceae	Leaves	Paracetamol Induced	66
Alocasia indica Linn	Araceae	Leaves	Paracetamol Induced	67
Aloe barbadensis	Liliaceae	Dried aerial parts	Carbontetra chloride	68
Amaranthus spinosus	Amaranthaceae	Whole plant	Carbontetra chloride	69
Amaranthus caudatus Linn	Amaranthaceae	Whole plant	Carbontetrachloride Induced	70
Anisochilus carnosus Linn	Lamiaceae	Stems	Carbontetrachloride Induced	71
Apium graveolens	Apiaceae	Seeds	Paracetamol and thioacetamide	72
Arachiodes exilis	Dryppteridaceae	Rhizomes	Carbontetra chloride	73
Argemone mexicana	Solanaceae	Plant material	Carbontetra chloride	74
Asparagus racemosus Linn	Asparagaceae	Roots	Paracetamol induced	75
Azadirachta indica	Meliaceae	Leaf	Paracetamol Induced	76
Azitetracantha	Salvadoraceae	Leaves	Paracetamol induced	77

Baliospermum montanum	Euphorbiaceae	Roots	Paracetamol induced	78
Boerhaavia diffusa	Nyctaginaceae	Roots	Thioacetamide	79
Bupleurum kaoi	Umbelliferar	Dried roots	Carbontetra chloride	80
Byrsocarpus coccineus	Connaraceae	Leaf	Carbontetra chloride	81
Bixa orellana	Bixxaceae	Plant material	Carbontetra chloride	82
Cajanus cajan Linn	Leguminosae	Pigeon pea leaf	D-galactosamine	83
Cajanus scarabaeoide	Fabaeceae	Whole plant	Paracetamol induced	84
Carissa carindas Linn	Apocyanaceae	Root	Carbontetrachloride Induced	85
Carum copticum	Apiaceae	Seed	Carbontetra chloride, paracetamol	86
Calotropis procera	Asclepediaceae	Root bark	Carbontetrachloride Induced	87
Cassia fistula	Leguminosae	Leaf	Carbontetrachloride Induced	88
Cassia tora	Caesalpiniaceae	Leaves	Carbontetra chloride	89
Cassia Occidentalis	Caesalpiniaceae	Leaves	Paracetamol and Ethyl alcoho	90
Chamomile capitula	Asteraceae	Fresh natural mature capitula	Paracetamol	91
Clerodendrum inerme	Verbenaceae	Leaves	Carbontetra chloride	92
Clitoria ternatea Linn	Fabaceae	Leaves	Paracetamol induced	93
Cleome viscose Linn	Capparidaceae	Leaf powder	Carbon tetra chloride	94
Cochlospermum planchoni	Coclospermaae	Rhizomes	Carbontetra chloride	95
Cichorium intybus	Asteraceae	Leaves	Thioacetamide	96
Cordia Macleodii	Boraginaceae	Leaves	Carbontetra chloride	97
Cuscuta chinensis	Convolvulaceae	Seeds	Acetaminophen	98
Decalepis hamiltonii	Asclepiadaceae	Roots	Carbontetra chloride	99
Elephrantopus scaber Linn	Asteraceae	Whole plant	D-galactosamine and acetaminophen	100
Equisetum arvense	equisetaceae	Aerial parts	Carbontetra chloride Induced	101
Embelia ribes	myrsinaceae	Fruits	Paracetamol induced	102
Enicostemma axillare	Gentianaceae	Whole plant	D-galactosamine	103
Euphorbia fusiformis	Euphorbiaceae	Tubers	Rifampicin	104
Ficus religiosa Linn	Moraceae	Stem bark	Paracetamol induced	105
Fructus schisandrae	Magnoliaceae	Dried fructus	Carbontetra chloride Induced	106
Fumaria indica	Papaveraceae	Whole plant	D-galactosamine	107
Ganoderma lucidum	Polyporaceae	Winter mushrooms	D-galactosamine	108
Ginkgo biloba	Ginkgoaceae	Dried extract	Carbontetra chloride Induced	109
Glyrrhiza glabra	Fabaceae	Root powder	Carbontetra chloride Induced	110
Gracinia indica Linn	Clusiaceae	Fruit rind	Carbontetrachloride Induced	111
Gmelina asiatica Linn	Verbenaceae	Aerial parts	Carbontetrachloride Induced	112
Gundelia tourenfortii	Asteraceae	Fresh edible stalk	Carbontetra chloride Induced	113
Halenia elliptica	Gentianaceae	Whole plant	Carbontetra chloride Induced	114
Hibiscus Sabdariffa	Malvaceae	Leaves	Paracetamol induced	115
Hibiscus esculentus	Malvaceae	Roots	Carbontetra chloride Induced	116
Hypericum japonicum	Clusiaceae	Whole plant	Carbontetra chloride Induced	117
Hygrophila auriculata	Acanthaceae	Root	Carbontetra chloride Induced	118

Hyptis suaveolens Linn	laminaceae	leaves	Acetaminophen induced	119
Hoslundia opposite	Lamiaceae	Stem	Carbontetra chloride And paracetamol Induced	120
Juncus subulatus	Juncaceae	Powdered tubers	Paracetamol induced	121
Kalanchoe pinnata	Crassulaceae	Leaves	Carbontetra chloride Induced	122
Lawsonia alba	Lythraceae	Whole plant	Carbon tetrachloride	123
Lactuca indica	Compositae	Aerial parts	Carbontetra chloride Induced	124
Luffa echinata	Curcubitaceae	Fruits	Carbontetra chloride Induced	125
Laggera pterodonta	Asteraceae	Whole herb	Carbontetra chloride And D-galactosamine Induced	126
Mallotus japonicas	Euphorbiaceae	Cortex	Carbontetra chloride Induced	127
Mamoridca subangulata	Cucurbitaceae	Leaf	Paracetamol induced	128
Melia azhadirecta Linn	Piperaceae	Leaves	Carbontetrachloride, silymarin induced	129
Morinda citrifolia Linn	Rubiaceae	Fruit	Streptozotocin induced	130
Myoporum lactum Linn	myoporaceae	Leaves	Carbontetrachloride Induced	131
Myrtus communis Linn	Myrtaceae	Leaves	Paracetamol induced	132
Nelumbo nucifera	Nelumbonaceae	Leaves	Carbontetrachloride Induced	133
Nigella sativa	Ranunculaceae	Seeds	Tert –butyl hydroperoxide	134
Ocimum sanctum	Lamiaceae	Leaf	Paracetamol induced	135
Orthosiphan stamineus	Lamiaceae	Leaves	Acetaminophen	136
Phyllanthus amarus schum	Euphorbiaceae	Aerial part	Ehanol	137
Phyllanthus amarus	Euphorbiaceae	Whole plant except root	Aflatoxin b1 induced liver damage	138
Physalis minima	Solanaceae	Plant material	Carbontetra chloride	139
Phyllanthus niruri	Euphorbiaceae	Leaves and fruits	Carbontetrachloride Induced	140
Phyllanthus polyphullus	Euphorbiaceae	Leaves	Acetaminophen	141
Picrorhiza kurrooa	Scrophulariaceae	Root and rhizomes	Alcohol –carbon tetra chloride	142
Picrorrhiza rhizome	Scrophulariaceae	Dried underground stem	Poloxamer(PX)-407	143
Piper chaba	Piperaceae	Fruit	D-galactosamine	144
Piper longum	Piperaceae	Fruits and roots	Carbontetra chloride	145
Pittosporum neelgherrense	Pittospoaceae	Stem bark	Carbontetra chloride, D-galactosamine and acetaminophen Induced	146
Plantago major	Plantaginaceae	Seeds	Carbontetra chloride	147
Pterocarpus marsupium	Papilionaceae	Stem bark	Carbontetra chloride	148
Ptrospermum acerifolium	Sterculiaceae	Leaves	Carbontetra chloride	149
Ricinus communis	Euphorbiaceae	Leaves	Carbon tetrachloride	150
Rubia cordifolia	Rubiaceae	Roots	Carbontetra chloride	151
Sarcostemma brevistigma	Asclepiadaceae	Stem	Carbontetra chloride	152
Saururus chinensis	Sauruaceae	Whole plant	Carbontetra chloride	153
Scoparia dulcis	Scrophulariaceae	Whole plant	Carbontetra chloride	154
Schouwia theebica	Arecaceae	Aerial part	Carbontetra chloride	155
Solanum nigram Linn	Solsnaceae	Fruits	Carbontetrachloride Induced	156

Tecomella undulate	Bignoniaceae	Stem bark	Thioacetamide	157
Tephrosia purpurea Linn	Fabaceae	Aerial parts	Thioacetamide	158
Thunbergia laurifolia	Acanthaceae	Leaves	Ethanol	159
Tridax procumbens	Asteraceae	Leaves	Carbontetrachloride Induced	160
Tylophora indica	Asclepiadaceae	Leaf powder	Ethanol	161
Vitex trifolia	Verbenaceae	Leaves	Carbontetrachloride Induced	162
Vitis vinifera	Vitaceae	Leaves	Carbontetrachloride Induced	163

3. Conclusion

Despite tremendous advances in modern medicine, hepatic disease remains a worldwide health problem; thus the search for new medicines is still ongoing. Numerous formulations of medicinal plants are used to treat liver disorders in Chinese ethno medical practice and traditional medicine. Many of these treatments act as radical scavengers, whereas others are enzyme inhibitors or mitogens .

The goal of ethnopharmacological studies on medicinal plants should not be restricted to find new prototype pure compounds as drugs. Active extracts, fractions or mixture of fractions/extracts may prove very effective drugs. Plant drugs (combinations or individual drug) for liver diseases should possess sufficient efficacy to cure severe liver diseases caused by toxic chemicals, viruses (Hepatitis B, Hepatitis C, etc.), excess alcohol intake,and repeated administration of drugs like paracetamol, ,Rifampicin and Isoniazid. A single drug cannot be effective against all types of severe liver diseases. Effective formulations have to be developed using indigenous medicinal plants, with proper pharmacological experiments and clinical trials. The manufacture of plant products should be governed by standards of safety and efficacy.

Various herbal plants and plants extracts have significant hepatoprotective activity in animal models was proved by research .The hepatoprotective activity of the plants probably due to the presence of flavonoids,alkaloids,terpenoids,glycosides and steroids.

References

1. Garba, S.H., Sambo, N., and Bala, U., T he effect of the aqueous extract of Kohautia grandiflora on paracetamol induced liver damaga in albino rats., *Nigeria journal of physiological Sciences*., 24(1):17-23(2009).
2. Mossa, J.S., Tariq, M., Mohsin, A., Aqeel, A.M., al-Yahya, M.A., al-Said MS., et al., Am J Chin Med., 19:223(1991).
3. Mascolo N., Sharma, R., Jain SC., Capasso F., *JEthnopharmacol* 22:211(1998).
4. Jian, Wu, Åke Danielsson, Mark, A.Z., Toxicity of hepatotoxins: new insights into mechanisms and therapy., 8(5):585-607(1999).
5. Fry, J.R., Bridges, J.K.L., *Rev.Biochem.Toxicol.*, 203-247(1979).
6. Grayer, R.J., Harborne, J.B., A survey of antifungal compounds from higher plants (1982-93), Phytochem.,37:19-42(1994).
7. Homberg, J.C., Abuat, N., Hetmy-Khalills., Bloue, M., Powlet J., Danan G., Benhamou J.P. Hepatology, page no.722-727(1985).
8. Visen, P.K.S, Annual report of ICMR Centre for advanced Pharmacological research on traditional remedies, Division of pharmacology, Central Drug Research Institute, Lucknow, 192-197(1993).
9. Rage, N., Dahanukar, S., and Karandikar, SM., Indian drugs, 27:18(1989).
10. Saraf, S., and Dixit., V.K., Fitoterapia., 62(6):534-536(1991).
11. Pathak, A.K., Saraf, S., and Dixit, V.K., Fitoterapia, 62:307(1991).
12. Saraf, S., Dixit, V.K., Thripati, S.C., and Patnaik, G.K., Fitoterapia, 63:414(1992).
13. Kiso, Y., Thokkin, M., Hikino, H., Assay method for antihepatotoxic activity using galactosamine-induced cytotoxicity in primary cultured hepatocytes. J.of Natural Prod., 46:841-847(1983).
14. Rachmilewitz, M., Rosin, A., and Doljanski, L., Observations on the mitotic reaction induced in the livers of rats by thiourea, Amer. J. Pathology, 26(5):937-949(1950).
15. Handa, S.S., and Anupama, S., Hepatoprotective activity of andrographolide against galactosamine and paracetamol intoxication in rats. Indian J.of Medical Research, 92(B):276-283(1990a).
16. Goldschmidt, S., Var, H.M., Ravdin IS: The influence of the foodstuffs upon the susceptibility of the liver to injury by chloroform, and the probable mechanism of action of them. J.of Clinical investigation, 80:277-289(1939).
17. Goodell, J.P.B., Hawkins., W.B., and Hanson, PC: Methionine protects against mepharsen liver injury in protein depleted dogs,

J.of Experimental Medicine, 79:625-632(1944).

18. Thripati, S.C., Patnaik, G.K., and Dhawan, B.N., Hepatoprotective activity of Picroliv against alcohol-carbon tetrachloride induced damage in rats, Indian J. Pharmacology, 23:143-148(1991).
19. Gulati, R., Agarwal, S., and Agarwal, S.S., Hepatoprotective activity of Boerhaavia diffusa Linn. Against country made liquor induced toxicity in albino rats fed on controlled calorie diet, Indian J. of Pharmacology, 23:264-266(1991).
20. Singleton V.L., Rossi J.A. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. Am. J. Enol. Vitic 16:144-158(1965).
21. Chen, C.C., Chen, Y.P., Hsu, H.Y., Chen, Y.L., Chem. Pharm. Bull. 32:166(1984).
22. Boyd, E.H. and Bereczky, .M., Liver necrosis from paracetamol., Br.J.Pharmacol., 26:606-614(1996).
23. Clark, R., Thompson, R.P.H., Borirackanyavat, V., Widoop, B., Davidson, A.R., Goulding, R., and Williams, R., Hepatic damage and death from overdose of paracetamol , Lancet, 1:66-69(1974).
24. Kaufman, D., Kelly, J.P., Rosenberg, L., Anderson, T.E., and Mitchell, A.A., Recent Patterns of medication use in the ambulatory adult population of the United States: the Slone Survey. JAMA., 287:337-44(2002).
25. Ray, S.D., Mumaw, V.R., Raje, R.R., Fariss, M.W., Protection of acetaminophen induced hepatocellular apoptosis and necrosis by cholesteryl hemisuccinole pretreatment, J. Pharmacol.Exp. Ther. 279:1470-1483(1996).
26. Savides, M.C., and Oehme, F.W., Acetaminophen and its toxicity., J. Appl. Toxicol., 3(2):95-111(1983).
27. Grahame-smith, D.G., Azonson, J.K., The drug therapy of gastro intestinal , hepatic and biliary disorders Chapter 23 In: Oxford Textbook of Clinical Pharmacology and Drug Therapy, Oxford University Press, Oxford.1st Edition, page no. 383-385(1984).
28. Jaeschke, H., Knight, T.R., and Bajt, M.L., The role of oxidant stress and reactive nitrogen species in acetaminophen hepatotoxicity., Toxicol. Let., 144:279-88(2003).
29. Josephy, P., The molecular toxicology of acetaminophen. Drug Metab. Rev., 37:581-94(2005).
30. Sarada, S., Madhanvankutty, K., Secretion of small and large intestine Chapter 5 In:Textbook of Human Physiology, S Chand & Company Ltd., New Delhi , 4th Edition page no. 182(1990).
31. Sood, R., Enzymology Chapter 21 In:Medical Laboratory Technology- Methods and Interpretation, Jaypee Brothers medical Publishers(p) Ltd., New Delhi, 4th edition, page no. 493-494, 504-505, 508-510, 513-514(1994).
32. Young, D., Effect of pre analytical variables on clinicallaboratory tests, 2nd Edn, American Association for Clinical Chemistry Press, Washington(1997).
33. Kaplan, A., Lavernel, L.S., In: Clinical Chemistry; Interpretation and techniques, 2nd edition, Lea and Febiger, Philadelphia, 219-296(1983).
34. Harshmohan., The liver , biliary tract , and exocrine pancreas, In: Textbook of Pathology, Jaypee Brothers Medical Publishers (P) Ltd. New Delhi , 4th Edition, page no. 22-24 ,569-630(2002).
35. Willard, R., Faulkner, meites, S., Selected methods for the small clinical chemistry laboratory, 9:113-118(1982
36. Gilroy, D.W., Lawrence, T., Perretti, M. and Rossi, A.G., Inflammatory resolution: new opportunities for drug discovery. Nature Reviews 3: 401-416 (2004).
37. Silva, E.G., Behr, G.A., Zanotto-Filho, A., et al. Antioxidant activities and fee radical scavenging potential Bauhinia microstachya (RADDI) MACBR. (Casalpinaceae) extracts linked to their polyphenol content. Biol Pharm Bull 30(8): 1488-96(2007).
38. Luper, S.,A review of plants used in the treatment of liver disease, Alternative Med. Rev., 3/4:178-189(1999).
39. Scott Luper, N.D., A review of plants used in the treatment of liver disease: part-I. Alternative Med. Rev., 3(6):410(1998).
40. Sharma, A., Chakraborti, K.K., and Handa, S.S., Antihepatotoxic activity of some Indian herbal formulation as compared to silymarin, Fitoterapia., 62:229(1991).
41. Handa, S.S., Sharma, A., Chakraborti, K.K., Natural products and plants as liver protecting drugs., Fitoterapia.,57:307-51(1986).
42. Asha, V.V., Pushpangadan, P., Preliminary evaluation of antihepatotoxic activity of Phyllanthus maderaspatensis, P. kozhikodianus and Solanum indicum. Fitoterapia 1998.
43. Subramoniam, A., Evans, D.A., Rajasekharan, S., Pushpangadan, P., Hepatoprotective activity of Trichopus zeylanicus extract against paracetamol induced hepatic damage in rats. Indian J Exp Biol. 36:385-9(1998).
44. Asha, V.V., Ethnobotany, pharmacognosy and ethnopharmacology of hepatoprotective agents employed by the folk practitioners and tribal physicians of South lndia.Ph.D.Thesis, University of Kerala. (1996).
45. Kumar, R.J., David, G.L., and Krupadanam, M., Phenolic constituents from the pods of Bauhinia vahlii., Fitoterapia., 61:456-460(1990).
46. Shukla, B., Visen, P.K.S., Patnaik, G.K., Tripathi, S.C., Srimal, R.C., Dayal, R., Dobhal, P.C., Hepatoprotective activity in the

rat of ursolic acid isolated from Eucalyptus hybrid. Phytotheraphy Res. 6: 74-9(1992).

47. Saraswat, B., Visen, P.K.S., Dayal, R., Agarwal, D.P., Patnaik, G.K., Protective action of ursolic acid against chemical-induced hepatotoxicity in rats. Indian J Pharmacol 28: 232-9(1996).
48. Wagner, H., Hikino, H., and Farnsworth, N.R., Economic and medicinal plant Research, vol. 2, Academic press, London.39, 22(1998).
49. Lim, H., Kim, M.K., Lim, Y., Cho, Y.H., and Lee, C.H., Inhibition of cell-cycle progression in HeLa cells by HY52, a novel cyclin-dependent kinase inhibitor isolated from Bauhinia forficata. Cancer Letters, 233(1):89-97(2006).
50. Olukoya, D.K., Idugbmi, T., Antibacterial activity of some medicinal plants from Nigeria, J.Ethnopharmacol.,39:69-72(1993).
51. Handa, S.S., Sharma, A., Chakraborti, K.K., Natural products and plants as liver protecting drugs., Fitoterapia.,57:307-51(1986).
52. Balandrin, M.F., Klocke, J.A., Wurtele, E.S., Bollinger, W.H., Natural Plant Chemicals: Sources of industrial and medicinal materials. Science 288:1154-6(1985).
53. Cox, P.A., The ethnobotanical approach to drug discovery: Strengths and limitations. In: Ethnobotany and the search for new drugs. Ciba Foundation symposium, 184, Chichester, John Wiley and Sons. 25-41(1994).
54. Doreswamy, R., Sharma, D., Plant drugs for liver disorders management. Indian Drugs 32:139-44(1995).
55. Katuria, M., Singh, L.N., Hepatoprotective effect of Liv. 52 and Kumaryasawa on CCl4 induced hepatic damage in rats. Indian J Exp Biol. 25:655-7(1997).
56. Farooq, S., Ahmad, I., Pathak, G.K., In vivo protective role of Koflet (an ayurvedic preparation) against cellular toxicity caused by CCl_4 and fly ash. J Ethnopharmacol. 58:149-56(1997).
57. Singh, B., Saxena, A.K., Chandan, B.K., Anand, K.K., Suri, O.P., et al. Hepatoprotective activity of verbenalin on experimental liver damage in rodents. Fitoterapia. 69:135-41(1998).
58. Chrungo, V.J., Reen, R.K., Singh, K., Singh, J., Effects of silymarin on UDP-glucuronic acid and glucuronidation activity in the rat isolated hepatocytes and liver in relation to D-galacto-seamine toxicity. Indian J Exp Biol, 35:256- 63(1997).
59. Sudhir, S., Budhiraja, R.D., Protective effect of Witthferin against an experimental model of hepatitis. Indian J Pharmacol 23:16-20(1991).
60. Doreswamy, R., Sharma, D., Plant drugs for liver disorders management. Indian Drugs 32:139-44(1995).
61. Medicinal plants in India, Indian J Med Res., 120:9(2004).
62. P. Jayasekhar, P.V. Mohanan*, K. Rathinam, Hepatoprotective Activity of Ethyl Acetate Extract of Acacia Catechu, Indian Journal of Pharmacology ,;Vol-29:Pg No. 426-428 1997.
63. Yu-Tang Tung, Jyh-Horng Wu, Chi-Chang Huang, Hsiang-Chi Peng, Ya-Ling Chen, Suh-Ching Yang, Shang-Tzen Chang, protective effect of Acacia Confusa Bark extract and its active compound gallic acid against carbon tetrachloride-induced chronic liver injury in rats, Food and Chemical Toxicology,,Pg No.03-21 ,2009.
64. Ramnik Singh, Harwinder Singh Rao, Hepatoprotective Effect Of The Pulp/Seed Of Aegle Marmelos Correa Ex Roxb Against Carbontetrachloride Induced Liver Damage In Rats, International Journal Of Green Pharmacy, Pg No-232-234 Oct-17 2010.
65. Manokaran S, Jaswanth A, Sengottuvelu S , Nandhakumar J, Duraisamy R, Karthikeyan D And Mallegaswari R, hepatoprotective activity of Aerva Lanata Linn. against paracetamol induced hepatotoxicity in rats, Research J. Pharm. And Tech. 1(4): Oct.-Dec. 2008.
66. M. Tolulope Olaleyea, B, B.T. Joa O Rochaa, Acetaminophen-induced liver damage in mice: Effects of some medicinal plants on the oxidative defence system, Experimental and Toxicologic Pathology 59 , 319–327 ,2009.
67. Wahid A Mulla, Vijay R Salunkhe & Satish B Bhise, Hepatoprotective activity of hydroalcoholic extract of leaves of Alocasia Indica (Linn.), Indian Journal Of Experimental Biology, ,Vol-47,Pg No.816-821 October 2009 .
68. B.K. Chandan, A.K. Saxena, Sangeeta Shukla, Neelam Sharma, D.K. Gupta, K.A. Suri, Jyotsna Suri, M. Bhadauria, B. Singh, Hepatoprotective Potential of Aloe Barbadensis Mill. Against Carbon Tetrachloride Induced Hepatotoxicity, Journal of Ethnopharmacology 111 560–566 (2007).
69. Hussain Zeashan A, G. Amresh A, Satyawan Singh B, Chandana Venkateswara Rao A, Hepatoprotective Activity Of Amaranthus Spinosus In Experimental Animals, Food And Chemical Toxicology 46 3417–3421 (2008).
70. Bagepalli Srinivas, Ashok Kumar, Kuruba Lakshman, Paresandra Avalakondarayppa Arun Kumar, Gollapalle Lakshminarayana Shastry Viswanpha, Veeresh, Prabhakar Veerapur, Boreddy, Shivanadpea, Thippeswamy, Bachappaa,Manoj. Hepatoprotective activity of methanol extracts of Amaranthus caudatus Linn. Against paracetamol-induced hepatic injury in rats, Journal of Chinese Integrative Medicine , 9(2), 194-200 ,2011.
71. Venkatesh P, Dinakar A, Senthilkumar N, Hepatoprotective activity of an ethanolic extract of stems of Anisochilus carnosus against carbon tetrachloride induced hepatotoxicity in rats, International Journal of Pharmacy and Pharmaceutical Sciences 3(1), 243-245,2011.
72. Bahar Ahmed, Tanveer Alam, Manoj Varshney, Shah Alam Khan, hepatoprotective activity of two plants belonging to the

apiaceae and the euphorbiaceae family, journal of ethnopharmacology 79 ,313–316,2002.

73. Daonian Zhoua B, Jinlan Ruana, Yaling Caia, Zhaemoi Xionga, Weifua, Anhua Weia, anti- antioxidant And Hepatoprotective Activity of Ethanol Extract of Arachniodes Exilis (Hance) Ching, Journal of Ethanopharmacology 232–237, 129 (2010).
74. Md. Rajib Ahsan, Km Monirul Islam, Israt Jahan Bulbul, Md. Ashik Musaddik, Ekramul Haque, Hepatoprotective Activity Of Methanol Extract Of Some Medicinal Plants Against Carbon Tetrachloride-Induced Hepatotoxicity In Rats, European Journal Of Scientific Research, , Vol.37(2), 302-310, 2009.
75. Fasalu Rahiman, Rupesh Kumar M, Tamizh Mani T, Mohamed Niyas K, Satya Kumar B, Phaneendra P, Surendra B, Hepatoprotective activity of "Asparagus racemosus root" on liver damage caused by paracetamol in rats, Indian Journal of Novel Drug Delivery, 3(2), 112-117, 2011.
76. R.R. Chattopadhyay, M. Bandyopadhyay, Possible Mechanism Of Hepatoprotective Activity Of Azadirachta Indica Leaf Extract Against Paracetamol-Induced Hepatic Damage In Rats :part III,indian J Pharmacol,june 2005,vol 37,ap no.184-185 , 2011.
77. Arthika S, Shanthammal Y, Sheryl Igal1 N, Elankini P, Pramod Reddy G, Gaidhani SN, Ganesan R, Hepatoprotective activity of the ethanolic extract of Azima tetracantha against paracetamol-induced hepatotoxicity in wistar albino rats, Journal of Advances in Pharmacy and Healthcare Research, 1(2), 14-20,2011.
78. Raju Ratan Wadekar, Radhika Sachin Supale, Kunal Mahesh Tewari, Kalpana S.Patil, Sunil Satyappa Jalalpure, Screening of Roots of Baliospermum Montanum For Hepatoprotective Activity Against Paracetamol Induced Liver Damage In Albino Rats, International Journal Of Green Pharmacy,, 220-223, July 2010.
79. K.S. Rawat A S. Mehrotra A, S.C. Tripathi B, U. Shome , Hepatoprotective Activity Of Boerhaavia Diffusa L. Roots - A Popular Indian Ethnomedicine, Journal Of Ethnopharmacology 56 61- 66, (1997).
80. Be-Jen Wang,, Chu-Ting Liu, Chin-Yin Tseng, Chien-Ping Wu, Zer-Ran Yu, Hepatoprotective And Antioxidant Effects Of Bupleurum Kaoi Liu (Chao Et Chuang) Extract And Its Fractions Fractionated Using Supercritical CO2 On Ccl4-Induced Liver Damage, Food And Chemical Toxicology 42 ,609–617, (2004).
81. Abidemi J. Akindele, Kenneth O. Ezenwanebe, Chidozie C. Anunobi, Olufunmilayo O. Adeyemi, Hepatoprotective And In Vivo Antioxidant Effects of Byrsocarpus Coccineus Schum. and Thonn. (Connaraceae), Journal of Ethnopharmacology 129 46–52, (2010).
82. Md. Rajib Ahsan, Km Monirul Islam, Israt Jahan Bulbul, Md. Ashik Musaddik, Ekramul Haque, Hepatoprotective Activity Of Methanol Extract Of Some Medicinal Plants Against Carbon Tetrachloride-Induced Hepatotoxicity In Rats, European Journal Of Scientific Research , Vol.37(2), 302-310, 2009.
83. Oluseyi Adeboye Akinloye, Moshood Olajire Olaniyi, Hepatoprotective effect of Cajanus cajan on tissue defense system in D-galactosamine-induced hepatitis in rats, Turk J Biochem, 36(3), 237–241, 2011.
84. Suman Pattanayak, Siva Sankar Nayak, Durga Prasad Panda, Subas Chandra Dinda, Vikas Shende, Amol Jadav, Hepatoprotective activity of crude flavonoids extract of Cajanus scarabaeoides (L) in paracetamol intoxicated albino rats, Asian J Pharm Biol Res, 1(1), 22-27, 2011.
85. Balakrishanan N, Balasubaramaniam A, Sangameswaran B, Bhaskar VH, Hepatoprotective activity of two Indian medicinal plants from Western Ghats-Tamil nadu, Journal Of Natural Pharmaceuticals, 2(2), 92-98, 2011.
86. A.H. Gilani A, , Q. Jabeen A, M.N. Ghayur A, K.H. Janbaz B, M.S. Akhtar C, Studies On The Antihypertensive, Antispasmodic, Bronchodilator And Hepatoprotective Activities Of The Carum Copticum Seed Extract, Journal Of Ethnopharmacology 98 127–135 , (2005).
87. S. Ramachandra Setty A, Absar Ahmed Quereshi A, A.H.M. Viswanath Swamy B,Tushar Patil A, T. Prakash A, K. Prabhu A, A. Veeran Gouda A, Hepatoprotective activity of Calotropis procera flowers against paracetamol-induced hepatic injury in rats, Fitoterapia 78 451–454, (2007).
88. Chaudhari N. B., Chittam K. P., Patil V. R., Hepatoprotective Activity Of Cassia Fistula Seeds against paracetamol-induced hepatic injury in rats, Arch Pharm Sci & Res Vol 1 No 2 218 - 221 October 2009
89. Muniyappan Dhanasekarana, Savarimuthu Ignacimuthua, Paulagastianb, Potential Hepatoprotective Activity Of Ononitol Monohydrate Isolated From Cassia Tora L.On Carbontetrachloride Induced Hepatotoxicity In Wistar Rats, Phytomedicine 16 891–895, (2009).
90. M.A. Jafri A,*, M. Jalis Subhani A, Kalim Javed A, Surender Singh B, Hepatoprotective Activity Of Leaves Of Cassia Occidentalis Against Paracetamol And Ethyl Alcohol Intoxication In Rats, Journal Of Ethnopharmacology,2001.
91. Ajay Kumar Gupta and 2Neelam Misra, hepatoprotective activity of aqueous ethanolic extract of Chamomile Capitula in paracetamol intoxicated albino rats, American Journal of Pharmacology and Toxicology 1 (1): 17-20, 2006.
92. N. Gopal A, S. Sengottuvelu B, Hepatoprotective Activity of Clerodendrum Inerme against CCL4 Induced Hepatic Injury In Rats, Fitoterapia 79 24–26, (2008).
93. Kuppan Nithianantham, Murugesan Shyamala, Yeng Chen, Lachimanan Yoga Latha, Subramanion L. Jothy, Sreenivasan Sasidharan, Hepatoprotective potential of Clitoria ternatea leaf extract against paracetamol induced damage in mice, Molecules, 16, 10134-10145, 2011.

94. Nishant Kumar Gupta,Vinod Kumar Dixit, Evaluation Of Hepatoprotective Activity Of C;Eome Viscose Linn. Extract.,Indian Journal Of Pharmacology, Feb,Vol-41,Pg No.-36-40 , 2009.
95. Roseline Aliyu A'b, Z.S.C. Okoye A, W, Thomas Shier *B, The Hepatoprotective Cytochrome P-450 Enzyme Inhibitor Isolated From The Nigerian Medicinal Plant Cochlospermum Planchonii Is A Zinc Salt, Journal Of Ethnopharmacology 48 89-97, (1995).
96. H. Madani, M. Talebolhosseini, S. Asgary and G. H. Naderi, Hepatoprotective activity of Silybum marianum And Clchorium Intybus against Thioacetamide In Rats, Pakistan Journal of Nutrition, ,Vol-7(1),Pg No.-172-176, 2008.
97. Naseem N. Qureshi A, Bhanudansh S. Kuchekar B, Nadeem A. Logade A, Majid A. Haleem A, Antioxidant And Hepatoprotective Activity of Cordia Macleodii Leaves, Saudi Pharmaceutical Journal, ,Vol-17, 299– 302 , 23 May 2009.
98. Feng-Lin Yen, Tzu-Hui Wu, Liang-Tzung Lin, Chun-Ching Lin, Hepatoprotective And Antioxidant Effects Of Cuscuta Chinensis Against Acetaminophen-Induced Hepatotoxicity In Rats, Journal Of Ethnopharmacology 111 ,123–128, (2007).
99. Anup Srivastava, T. Shivanandappa , Hepatoprotective Effect Of The Root Extract Of Decalepis Hamiltonii Against Carbon Tetrachloride-Induced Oxidative Stress In Rats, Food Chemistry 118 411–417, (2010).
100. Fei Yana,1, Qiao-Yanzhanga,1, Leijiaoa, Tinghana, Hongzhanga, Lu-Pingqina, Rahman Khalid, Synergistic Hepatoprotective effect of Schisandrae Lignans With Astragalus Polysaccharides On Chronic Liver Injury In Rats, Phytomedicine 16, 805–813,2009.
101. Hyuncheol Oh, Do-Hoon Kim, Jung-Hee Cho, Youn-Chul Kimc, Hepatoprotective and Free Radical Scavenging Activities Of Phenolic Petrosins and Flavonoids isolated from Equisetum Arvense, Journal Of Ethnopharmacology 95 (2004) 421–424.
102. Nahid Tabassum, Shyam S. Agrawal, hepatoprotective activity of Emebelia ribes against paracetamol induced acute hepatocellular damage in mice, Experimental Medicine, , Vol-10, 43-44, 200.
103. V. Jaishree, Shrishailappa Badami, Antioxidant and hepatoprotective effect of Swertiamarin from Enicostemma Axillare against D-Galactosamine Induced Acute Liver Damage in Rats, Journal Of Ethnopharmacology 130 ,103–106, (2010).
104. N. Anusuya, K. Raju, S. Manian, Hepatoprotective and Toxicological Assessment of an Ethnomedicinal Plant Euphorbia Fusiformis Buch.-Ham.Ex D.Don, Journal Of Ethnopharmacology 127 ,463–467, (2010).
105. Kavita Suryawanshi, Sanjay Khakre, Ashish Chourasia, Chaurasiya PK, Pawar RS, Deenanath Jhade, Hepato-protective activity of stem bark extracts of Ficus religiosa Linn in rats, International Journal of Biomedical Research 2(8), 466-475, 2011.
106. Fei Yana,1, Qiao-Yanzhanga,1, Leijiaoa, Tinghana, Hongzhanga, Lu-Pingqina, Rahman Khalid, Synergistic Hepatoprotective effect of Schisandrae Lignans With Astragalus Polysaccharides On Chronic Liver Injury In Rats, Phytomedicine 16 , 805–813, 2009.
107. Anshu Rathia, Arvind Kumar Srivastava, Annie Shirwaikarc, Ajay Kumar Singh Rawata, Shanta Mehrotrad, Hepatoprotective Potential of Fumaria Indica Pugsley Whole Plant Extracts, Fractions and an isolated Alkaloid Protopine, Phytomedicine 15 , 470–477, 2008.
108. Yanling Shi, Jie Sun, Hui He, Hui Guo, Sheng Zhang Hepatoprotective Effects Of Ganoderma Lucidum Peptides Against D-Galactosamine-Induced Liver Injury in Mice, Journal of Ethnopharmacology 117 , 415–419, 2008.
109. K. Ashok Shenoy,S.N.Somayaji,K.L.Bairy,Hepatoprotective Effects Of Ginko Biloba Against Carbontetrachloride,Induced Hepatic Injury In Rats,Indian Journal Of Pharmacology, Vol-33,Pg No.260-266,2001.
110. M.G.Rajesh,M.S.Latha, Protective Activityof Glycyrrhiza Glabra Linn. On Carbantetrachloride-Induced Peroxidative Damage, Indian Journal Pharmacol, Vol 38, 284-287, , October 2004.
111. Amol Bhalchandra Deore, Vinayak D Sapakal, Nilofer S Naikwade, Antioxidant and Hepatoprotective activity of Garcinia indica Linn fruit rind, Pharmacie Globale International Journal of Comprehensive Pharmacy , 2(6), 1-5, 2011.
112. Merlin NJ and Parthasarathy V, Antioxidant and Hepatoprotective activity of chloroform and ethanol extracts of Gmelina asiatica aerial parts, Journal of Medicinal Plants Research , 5(4), 533-538,2011.
113. Akram Jamshidzadeh, Fatema Fereidooni, Zohreh Salehi, Hossein Niknahad, Hepatoprotective activity of Gundelia tourenfortii, Journal of Ethnopharmacology 101, 233–237,2005.
114. Bouang, Xiaoquanban, Jingshenghe, Hongzeng, Pengzhang, Youweiwang, Hepatoprotective and antioxidant effects of the methanolic Extract from Halenia Elliptica, Journal Ofethnopharmacology Xxx, Xxx–Xxx,2010.
115. M. Tolulope Olaleyea, B, B.T. Joa O Rochaa, Acetaminophen-induced liver damage in mice: Effects of some medicinal plants on the oxidative defence system, Experimental and Toxicologic Pathology 59 ,319–327, 2008.
116. J.Anbu Jeba Sunilson, P.Jayaraj, M. Syam Mohan, A. Anitha Gnana Kumara, R. Varatharajan, Antioxidant And Hepatoprotective Effect Of The Roots Of Hibiscus Esculentus Linn., International Journal Of Green Pharmacy, , Pg No-200-20, Oct-17 20103.
117. Ning Wang , Peibo Li, Yonggang Wang, Wei Peng, Zhong Wu, Suiyi Tan,Shaoling Liang, Xiao Shen, Weiwei Su, Hepatoprotective Effect of Hypericum Japonicum Extract And Its Fractions, Journal Of Ethnopharmacology 116 ,1-6,(2008).
118. P. Shanmugasundaram, S. Venkataraman, Hepatoprotective And Antioxidant Effects of Hygrophila Auriculata (K. Schum) Heine Acanthaceae Root Extract, Journal of Ethnopharmacology 104 , 124–128,2006.

119. Babalola O, Ojo E, Oloyede F, Hepatoprotective activity of aqueous extract of the leaves of Hyptis suaveolens (L.) on acetaminophen induced hepatotoxicity in rabbits, Research Journal of Chemical Sciences, 1(7), 85-88, 2011.
120. Pete A. Akah,Gasmir L.Odo,Hepatoprotective Effect Of The Solvent Fractions Of The Stem Of Hoslundia Opposite Vahl (Lamiaceae) Against Carbontetrachloride And Paracetamol. international Journal of Pharmaceutical Sciences and Research ISSN: 0975-8232 Available online on www.ijpsr.com 515 Induced Liver Damage In Rats, International Journal Of Green Pharmacy, , Pg No.54-58, Oct-17 2010.
121. Ayman F. Abdel-Razika*, Abdel-Samid I. Elshamya, Mahmoud I. Nassara, Salah M. El-Kousyb, Hanaa Hamdyc, Chemical Constituents And Hepatoprotective Activity Of Juncus Subulatus ,Pg No.70-84, 2009.
122. N.P. Yadav, V.K. Dixit, Hepatoprotective Activity of Leaves of Kalanchoe Pinnata Pers, Journal of Ethnopharmacology 86 , 197–2022003.
123. M. Mujeeb, V. Aeri,, P. Bagri, S. A. Khan, Hepatoprotective Activity Of Methanolic Extract Of Tylophora Indica(Burm.F,) Merill. Leaves, International Journal Of Green Pharmacy, Pg No-125-127, Oct-17 2010.
124. Ki Hyun Kim,A Young Ho Kimb And Kang Ro Leea,*, Isolation Of Quinic Acid Derivatives And Flavonoids From The Aerial Parts Of Lactuca Indica L.And Their Hepatoprotective Activity In Vitro, Bioorganic & Medicinal Chemistry Letters 17 6739–6743, (2007).
125. Bahar Ahmed, Tanveer Alam, Shah A. Khan, Hepatoprotective Activity Of Luffa Echinata Fruits, Journal of Ethnopharmacology 76 , 187–189, 2001.
126. Yihang Wu A,B, Leixiang Yang B, Fang Wang C, Xiumei Wu D, Changxin Zhou B, Shuyun Shi B, Jianxia Mo B, Yu Zhao B, Hepatoprotective And Antioxidative Effects Of Total Phenolics From Laggera Pterodonta on chemical-induced injury in primary cultured neonatal rat hepatocytes, Food and Chemical Toxicology 45, 1349–1355,2007.
127. Hwa-Kyung Lim, Hack-Seang Kim, Hong-Serck Choi, Seikwan Oh, Jongwon Choi , Hepatoprotective Effects of Bergenin, A Major Constituent of Mallotus Japonicus, on Carbon Tetrachloride-Intoxicated Rats, Journal of Ethnopharmacology 72 , 469–474, 2000.
128. V.V.ASHA, Preliminary Studies On The Hepatoprotective Activity Ofmamordica Subangulata And Naragamia Alata, Indian Journal Of Pharmacology ; Vol-33,Pg No. 276-279, 2001.
129. Rajeswari H, Vasuki R, Samudram P, Geetha,2002.
130. WHO, Regional Office For The Western Pacific, Research Guidelines For Evaluating The Safety And Efficacy Of Herbal Medicines, Manila, WHO, 1993.
131. Pushpangadan P. Role of Traditional Medicine in Primary Health Care. In: Iyengar PK, Damodaran VK, Pushpangadan P, Editors. Science for Health. Published By State Committee On Science, Technology And Environment, Govt. Of Kerala, 1995.
132. Aszalos A, Editor. Antitumor Compounds of Natural Origin. Boca Raton, CRC Press, 1982.
133. Bo Huang, Xiaoquan Ban, Jingsheng He, Jing Tong, Jun Tian, Youwei Wang, Hepatoprotective And Antioxidant Activity Of Ethanolic Extracts Of Edible Lotus (Nelumbo Nucifera Gaertn.) Leaves, Food Chemistry 120, 873–878, 2010.
134. Mohamed Hesham Daba, Mohamed S. Abdel-Rahman, Hepatoprotective Activity of Thymoquinone in Isolated Rat Hepatocytes, Toxicology Letters 95, 23–29, 1998.
135. R.R. Chattopadhyay, S.K. Sarkar, S. Ganguly, C. Medda, T.K. Basu, Hepatoprotective Activity Of Oclmum Sanctum Leaf Extract Against Paracetamol Induced Hepatic Damage In Rats, Indian Journal Of Pharmacology ; Vol-24:Pg No. 163-165,1992.
136. Delhi, 1997:45-7 J.H.Chin,A.H.Hussin And S.Ismai,Anti-Hepatotoxicity Effect of Orthosiphon Stamineus Benth Against Acetaminophen-Induced Liver Injury In Rats By Enhancing Hepatic GST Activity, Pharmacognosy Research, March-April ,Volume-1, 53-58,2000.
137. Pornpen pramyothin, Chanon ngamtin, Somlak Poungshompoo, Chaiyo Chaichantipyuth, Hepatoprotective Activity of Phyllanthus Amarus Schum. Et. Thonn.Extract In Ethanol Treated Rats: In Vitro And In Vivo Studies, Journal Of Ethnopharmacology 114 , 169–173, 2007.
138. Farah Naaz, Saleem Javed , M.Z. Abdin, Hepatoprotective Effect of Ethanolic Extract of Phyllanthus Amarus Schum. Et Thonn. on Aflatoxin B1-Induced Liver Damage in Mice, Journal of Ethnopharmacology 113 (2007) 503–509. ats: Part III, Indian J Pharmacol,June Vol 37, Pg No. 184-185 International Journal of Pharmaceutical Sciences and Research ISSN: 0975-8232 Available online on www.ijpsr.com 513,2005.
139. Md. Rajib Ahsan, Km Monirul Islam, Israt Jahan Bulbul, Md. Ashik Musaddik, Ekramul Haque, Hepatoprotective Activity Of Methanol Extract Of Some Medicinal Plants Against Carbon Tetrachloride-Induced Hepatotoxicity In Rats, European Journal Of Scientific Research , Vol.37(2), 302-310, 2009.
140. Nahid Tabassum, Sushma Chattervedi, S. S Aggrawal, Nissar Ahmed, Hepatoprotective Studies On Phyllanthus Niruri On Paracetamol Induced Liver Cell Damage In Albino Mice, Experimental Medicine, October-December,Vol-12,Pg.No-211-212,2005.
141. Rajkapoor B, Venugopal Y, Anbu J, Harikrishnan N,Gobinath M* And Ravichandran V, Protective Effect Of Phyllanthus Polyphyllus On Acetaminophen Induced Hepatotoxicity In Rats, Pakisthan Journal Of Pharmaceutical Sciences, , Vo.21, Pg

No.57-62, January 2008.

142. S. C. Tripathi, G, K. Patnaik And B. N. Dhawan, Hepatoprotective Activity Of Picroliv Against Alcohol-Carbon Tetachloride Induced Damage In Rat, Indian Journal Of Pharmacology ,Vol-23,Pg No.143-148, 1991.

143. Hyeung Sik Lee, Hyo Chan Ahn, Sae Kwang Ku, Hypolipidemic Effect Of Water Extracts Of Picrorrhiza Rhizoma In PX-407 Induced Hyperlipemic ICR Mouse Model With Hepatoprotective Effects: A Prevention Study, Journal Of Ethnopharmacology 105 ,380–386, (2006).

144. Hisashi Matsuda A, Kiyofumi Ninomiya A,B, Toshio Morikawa A,B, Daisuke Yasuda A, Itadaki Yamaguchi A,Masayuki Yoshikawa A,*, Hepatoprotective Amide Constituents From The Fruit Of Piper Chaba : Structural Requirements, Mode Of Action, And New Amides, Bioorganic & Medicinal Chemistry 17, 7313–7323, 2009.

145. Jagruti A. PATEL & Urvi S. SHAH, hepatoprotective activity of Piper Longum Traditional Milk extract on carbon International Journal of Pharmaceutical Sciences and Research ISSN: 0975-8232 Available online on www.ijpsr.com 514 tetrachloride induced liver toxicity in wistar rats, vol. 8,, pp. 121-129, 2009.

146. S. Shyamal, P.G. Latha, V.J. Shine, S.R. Suja, S. Rajasekharan, T. Ganga Devi, Hepatoprotective Effects Of Pittosporum Neelgherrense Wight&Arn., A Popular Indian Ethnomedicine, Journal of Ethnopharmacology 107 , 151–155, 2006.

147. Idris Torel, Haneli Ozbek, Remzi Erten, Ahmet Cihat Oner, Nureddin Cengiz, Orhan Yilmaz, Hepatoprotective and anti inflammatory activities of Plantago Major L., Indian Journal of Pharmacology, Vol-41,Pg No.120-124, June 2009.

148. K. L. Mankani, V. Krishna, B. K. Manjunatha, S. M. Vidya, S. D. Jagadeesh Singh, Y. N. Manohara, Anees-Ur Raheman, K. R. Avinash, Evaluation of hepatoprotective activity of stem bark of Pterocarpus marsupium Roxb., Indian J Pharmacol , Vol 37 ,Pg No. 165-168, June 2005.

149. S. Kharpate, G. Vadnerkar, Deepthi Jain and S. Jain, Evaluation of Hepatoprotective activity of ethanol extract of Ptrospermum Acerifloium Ster leaves, Indian Journal Of Pharmaceutical Sciences, Vol-69, Pg No.850-852, Nov-Dec 2007.

150. M. V. Natu. Suraj Agarwal. S. L. Agarwal And S. Agarwal, Protective Effect Of Ricinus Communis Leaves In Experimental Liver Injury. Indian Journal Of Pharmacology, Vol- 9 (4),Pgno.265-268, 1977.

151. Guntupalli M. Mohana Rao, Chandana V. Rao, Palpu Pushpangadan, Annie Shirwaikar, Hepatoprotective Effects Of Rubiadin, A Major Constituent Of Rubia Cordifolia Linn., Journal Of Ethnopharmacology 103, 484–490, 2006.

152. Nirmal K. Neoliya, Yogendra N. Shukla, Mamta Mishra, Hepatoprotective Activity of Sarcostemma Brevistigma Against Carbontetrachloride-Induced Hepatic Damage In Ratscurrent Science, Vol. 84, No. 9, 10 May 2003.

153. Lishu Wanga,B, Dongyan Chenga, Haisheng Wanga, Lin Dia, Xuefeng Zhoub, Tunhai Xuc, Xianwen Yangb, Yonghong Liub,*, The Hepatoprotective And Antifibrotic Effects Of Saururus Chinensis Against Carbontetrachloride Induced Hepatic Fibrosis In Rats, Journal Of Ethnopharmacology 126 , 487–491, 2009.

154. T. K. Praveen, S.D. Harmaraj, Jitendra Bajaj, S. P. Dhanabai, S.Manimaran, M.J.Nanjan, Rema Razdan, Hepatoprotective activity of petroleum ether, diethyl ether and methanol extract of Scoparia Dulcis L. Against CCL4-Induced Acute Liver Injury In Mice, Indian Journal Of Pharmacology, Vol-41,Pg No.110-114, June 2009.

155. Amani, S. Awaad, A D. J. Maitlandb And G. A. Solimanc, Hepatoprotective Activity Of Schouwia Thebica Webb, Bioorganic & Medicinal Chemistry Letters 16 , 4624–4628. 2006.

156. Gupta Amartya K, Ganguly Partha, Majumder Upal K, Ghosal Shibnath, Hepatoprotective & antioxidant effect & stereoidal saponins of solanum of Solanum xanthocarpum & Solanum nigrum in paracetomol induce hepatotoxicity in rats, Pharmacologyonline, 1, 757-768,2009.

157. Amit Khatria, Arun Gargb, Shyam S. Agrawal C, Evaluation of Hepatoprotective Activity Of Aerial Parts of Tephrosia Purpurea L. And Stem Bark of Tecomella Undulate, Journal Of Ethnopharmacology 122 , 1–5,2009 .

158. Arjun H. Banskota A, Yasuhiro Tezuka A, I Ketut Adnyana A, Kiyoshi Midorikawa A, Katsumichi Matsushige A, Dejair Message B, Alfredo A.G. Huertas B, Shigetoshi Kadota A,, Cytotoxic, Hepatoprotective And Free Radical Scavenging Effects of Propolis From Brazil, Peru, The Netherlands And China, Journal Of Ethnopharmacology 72, 239–246,2000.

159. Pornpen Pramyothin , Hemvala Chirdchupunsare, Anudep Rungsipipat, Chaiyo Chaichantipyuth C, Hepatoprotective Activity Of Thunbergia Laurifolia Linn Extract In Rats Treated With Ethanol: In Vitro And In Vivo Studies, Journal of Ethnopharmacology 102 , 408–411, 2005.

160. Reddipalli Hemalatha, Anti-Hepatotoxic and Anti-Oxidant Defense Potential of Tridax Procumbens, International Journal of Green Pharmacy, 164-169, July 2010.

161. Vipul Gujrati,Nilesh Patel, Venkat N.Rao, K.Nandakumar, T.S. Gouda, Md.Shalam, S.M.Shanta Kumar, Hepatoprotective Activity Vof Alcoholic And Aqueous Extracts Of Leaves Of Tylophora Indica(Linn.) In Rats, Indian Journal Of Pharmacology, Vol-39,Pg No.43-47, Feb-2007.

162. B. K. Manjunatha And S.M. Vidya, Hepatoprotective activity of Vitex Trifolia against CCl4 induced hepatic damage, Indian Journal Of Pharmaceutical Sciences, Vol-70(2), Pg. No.-241-245, April 2008.

163. Didem Deliorman Orhan , Nil¨Ufer Orhan, Ender Ergun, Fatma Ergun,, Hepatoprotective Effect Of Vitis Vinifera L. Leaves On Carbontetrachloride-Induced Acute Liver Damage In Rats, Journal of Ethnopharmacology 112 , 145–151, 2007.