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A Review on Hepatoprotective Activity of Some Medicinal Plants

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ABSTRACT

Liver is a vital organ play a major role in metabolism and excretion of xenobiotics from the body. Liver injury or liver dysfunction is a major health problem that challenges not only health care professionals but also the pharmaceutical industry and drug regulatory agencies. Liver cell injury caused by various toxic chemicals (certain anti-biotic, chemotherapeutic agents, carbon tetrachloride (CCL4), Thioacetamide (TAA) etc.), excessive alcohol consumption and microbes is well-studied. Herbal medicines have been used in the treatment of liver diseases for a long time. A number of herbal preparations are available in the market. The present review is aimed at compiling data on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models using modern scientific system.

Keywords: Herbal drugs, Liver Injury, Carbon tetrachloride (CCL_4), Hepatotoxicity.

INTRODUCTION

Man since time immortal has been using herbs (or) plant products as medicine for developing immunity against cold, fever, pain etc. Nature always stands as golden mark to amplify the outstanding phenomenon of symbiosis.

Traditional medicines using herbal drugs exists in every part of the world. Global estimates indicate that over $3/4^{th}$ of the 5 billion world population cannot afford the products of Western Pharmaceutical Industry and rely upon the use of traditional medicines derived from plants Kokate CK (1996).

Every country develops its own medicinal system, which includes China, Egypt and India. Thus, the Indian medicinal system came into existence. Raw materials are obtained from plant sources in the form of crude drugs such as dried herbal powders (or) extracts (or) mix of products (Ramarao AV, 1990). Siddha, Unani and Tibb are traditional health care systems which have been flourishing for many centuries. The use of traditional medicines include:

(i) Medication by use of medicinal plant, minerals, animal material.
(ii) Non-medication: acupuncture and yoga.

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With the development of Chemistry and Western Medicine, the chemical constituents of many species have been isolated and in some cases, duplicated in the form of synthetic drugs. Herbal derived substances remain the basis for a large proportion of the commercial medications used today for the treatment of heart diseases, high BP, pain, asthma and other illness. Today, a great number of modern drugs were derived from natural sources and 25% of all prescriptions contain one (or) more active ingredients from plants.

Methods of inducing hepatoxicity in animal models

A. Carbontetrachloride induced method

Animal model

The animals were divided into four groups comprising of six albino rats in each group using randomization technique and treated with the extract for sixteen days to assess the hepato protective potential of the plant. The first group (vehicle control) received vehicle for all the days. The second group was keptas toxin control and given only the carbon tetrachloride treatment. The third group received extract in the dose of 200mg/kg p.o. and the fourth group received the silymarin in the dose of 200mg/kg p.o, as a reference material for the study. All the animals except the vehicle control received carbon tetrachloride all 16th day of the treatment.

Collection of blood samples

The animals were sacrificed by cervical dislocation after 48 hours of carbontetrachloride administration. The blood samples were collected by cardiac puncture sin heparinized microfuge tubes. The blood samples thus collected were immediately centrifuged at 2200rpm for 15 minutes. When serum clearly separated out, the serum was analyzed for SGPT, SGOT and SALP levels using enzopak reagent kits by the method proposed by Reitman and Frankel.

Histopathological studies

The livers were dissected out immediately, washed with ice cold saline and 10% homogenates in 1.15%(w/v) KCl were prepared. The homogenates were centrifuged at 7000g for10 min at 4^{o}C and the supernatants were used for the assays of LPO, SOD, CAT, GPX, GST and GSH.

B. Anti tubercular inducing method

Animal model

Albino rats of either sex were selected and divided into five groups of six animals each. The animals were pretreated twice daily with vehicle (0.1% CMC), extract (250 and 500mg/kg, silymarin (100mg/kg) orally, 1h before Anti Tubercular drugs administration. All the animals except normal control group received Anti Tubercular drugs (combination of isoniazid, rifampicin, pyrazinamide, ethambutol) twice daily for a period of 28 days.

Collection of blood samples

On the 28^{h} day, the animals were anaesthetized using anesthetic ether and blood collected by cardiac puncture. The levels of SGOT, SGPT (Anita Pal et al., 2011), total bilirubin (Mihir Y et al., 2009), cholesterol, triglycerides, total proteins and albumin were estimated as per standard procedures. Immediately after collection of blood, the animals were euthanized with an over dosage of ether, livers were removed and kept in cold conditions. It was cross chopped with surgical scalpel into fine slices in chilled 0.25M sucrose, quickly blotted on a filter paper. The tissue was minced and homogenized in 10mM Tris-HCl buffer, pH 7.4(10%w/v) with 25strokes of tight Teflon pestle of glass homogenizer at a speed of 2500 rpm. The clear supernatant was used for oxidative stress markers assays like lipid peroxidation, Reduced Glutathione (Moran M.S et al., 1979), Superoxide dismutase (ArunK, 2011)and Catalase (Slater T F, 1971).

Histopathological studies

Histopathology of liver was carried out by a modified method of Luna (VipulGujrati et al., 2007). In brief, the autopsied livers were washed in normal saline and fixed in 10% formalin for 2h followed by bovine solution for 6h. The livers were then paraffin embedded and 5µ thick microtome sections were made, processed with alcohol-xylene series and stained with haematoxylin. It was then studied under light microscope for any histological protection or damage (Samuel Udem et al., 2011).

C. D-galactosamine induced method:

Hepatoprotective activity

Animals were divided in five groups of six rats each. Group 1 served as normal control and received. In Group 2 rats Liver damage was induced by administration of D -galactosamine at dose of 400-mg/kg i.p. on 14th day. Group 3 rats were treated with Silymarin (25 mg/kg p.o.) was used as positive standard. Group 4 rats were pretreated with extract at a dose of 200 mg/kg orally as a fine suspension in 0.6% Sodium carboxy methyl cellulose (CMC) for 14 days prior to the administration of D - galactosamine. Group 5rats were pretreated with extract at a dose of 400 mg/kg orally as a fine suspension in 0.6% sodium carboxy methyl cellulose (CMC) for 14 days prior to the administration of D - galactosamine.

Evaluation of serum enzymes

The serum levels aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma glutamyltransferase (γ-GT) and levels of bilirubin were assayed.

Histopathological studies

The livers were removed from the animals and the tissues were fixed in 10% formalin for at least 24 h. Then the paraffin sections were prepared and cut into 5 µ M thick sections. The sections were then stained with Haematoxylin– Eosin dye and were studied for Histopathological changes, i.e. necrosis, fatty changes, ballooning degeneration, and lymphocyte infiltration (Adewusi EA &Afolayan AJA, 2010).

Paracetamol induced method

Animal model

Swiss albino mice of either sex (30 animals) were divided into five groups comprising six mice in each group. Group I (control) received only distilled water. Group II (positive control) received 250 mg/kg by paracetamol suspension only. Group III received paracetamol suspension 250 mg/ kg body weight (b.w) + extract 250 mg/kg b.w of animals. Group IV received paracetamol suspension 250 mg/kg b. w+ 500 mg/kg. Group V received paracetamol suspension 250 mg/kg + silymarin 100 mg/kg. The extract was administered 3 h after the administration of paracetamol suspension. All the treatments were given orally by means of a gastric tube.

Collection of blood samples

The treatments were continued for 7 days and on the eighth day all animals were sacrificed under light ether anesthesia and blood collected without the use of anti-coagulant for serum preparation. The blood samples were collected by direct cardiac puncture and allowed to stand for 10 min before being centrifuged at 2,000 rpmfor 10 min and the serum was collected using rubber micropipette. The levels of alkaline phosphatase (ALP) was analyzed by the method of Wright et al., alanine aminotransferase (SGPT) and aspartate aminotransferase

(SGOT) were analyzed according to Reitman and Frankel.

Histopathological studies

The liver tissue was fixed in 10 % formalin and 5µ sections were cut, stained with haematoxylin and eosin and observed under light microscope (Manokaran et al, 2008).

Plants with Hepatoprotective activity

Research investigations conducted on several plant products used as liver protectives is well documented. Hepatoprotective effect of some of these lik e *Amaranthuscaudatus*Linn,*Aervalanata,Anisochiluscarn osus Linn,Aphanamixispolystachya,Asparagus racemosus Linn,Amaranthusspinosus,Azimatetracantha,Cajanuscaj an Linn,Veronica officinalis,Vitextrifolia,Clitoriaternatea Linn,* against Ccl_4 and galactosamine induced hepatic injury.

A liver disease is always associated with cellular necrosis, increases in tissue lipid peroxidation and depletion in the tissue GSH levels. In addition, serum levels of many biochemical markers like SGOT, SGPT, triglycerides, cholesterol, bilirubin, alkaline phosphatase are elevated. Inspite of phenomenal growth of modern medicine,there are few synthetic drugs available for the treatment of hepatic disorders. However there are several herbs or herbal formulations claimed to have possess beneficial activity in treating hepatic disorders (Austin DF, 2004).

Inspite of tremendous strides in modern medicine, there are hardly many drugs that stimulate liver function, offer protection to the liver from damage (or) help regeneration of hepatic cells. However, there are number of drugs employed in traditional system of medicine for liver infections**.**

About 600 commercial preparations with claimed liver protecting activity are available all over the world. About 100 Indian medicinal plants belonging to 40 families are used for herbal formulation. A few reports on the hepatoprotective activity are cited here, e.g. *Apiumgraveolens* Linn. (Umbelliferae), *Boerhaaviadiffusa* Linn.(Nyctaginaceae), *Euphorbia antisyphilitica*(Euphorbiaceae), *Rubiacordifolia* (Rubiaceae), *Solanum lyratum* (Solanaceae),*Tylophoraindica* (asclepiadaceae) (William M Lee, 1995).

In India, about 40 polyherbal commercial formulations reputed to have hepatoprotective action are being used. It has been reported that 160 phytoconstituents from 101 plants have hepatoprotective activity.Liver protective herbal drugs contain a variety of chemical constituents like phenols, coumarins, lignins, essential oil, monoterpenes, carotenoids, glycosides, flavanoids, organic acids, lipids, alkaloids and xanthenes. Plant extracts of many crude drugs are also used for the treatment of liver disorders. Extracts of different plants of about 25 plants have been reported to cure liver disorders**.** Several Indian medicinal plants have been extensively used in the Indian traditional system of medicine for the management of liver disorder. Some of these plants have already been reported to posses strong antioxidant activity (Achuthan, CR, 2003).

Trigonellafoenumgraecum

Shaileyee Das(2014) had evaluated the hepato-protective activity of methanol extract of seeds of *Trigonellafoenumgraecum* (TFG) in CCl4 induced toxicity in Wistar albino rats.The different solvents like pet.ether and methanol extracts are used,the methanol extract showed significant.There is decrease in SGOT, SGPT and serum bilirubin level were analysed.

Morchellaesculenta

R.Ravikumar et al., (2014) had evaluated the hepato-protective activity of Ethanolic extract of Morel mushroom of *Morchellaesculenta* in ccl4 induced hepatotoxicity in Wistar albino rats. The results showed ethanolic extract of the mycelim of Morchellaesculenta also significantly reduced the increase in serum ALP levels, extract reduced the increase in serum ALP levels to almost normal level.

Leptadenia pyrotechnica

Sangh Partap et al.,(2014) conducted research to evaluated hepato-protective activity of Methanolic extract of whole plant of *Leptadenia pyrotechnica* against paracetamol induced rats.The elevated serum level like SGOT, SGPT, ALP and Total bilirubin were found to be restored towards normal.

Morus nigra

Tauqeer Hussain Mallhi et al., (2014) had evaluated the hepato-protective activity of methanolic extract of leaves of *Morus nigra* against paracetamol induced rats. The results showed aqueous methanolic extract of the Morus nigra significantly reduced liver enzymes (ALT, AST, ALP) and total bilirubin induced by paracetamol and the results are comparable to silymarin.

Cyclea peltata

Varghese Jancy Shine et al., (2014) had evaluated the hepatoprotective and antioxidant properties of alkaloid extract of *Cyclea peltata* (C. peltata) against paracetamol/carbon tetra chloride induced liver damage in Wistar rats. The results showed that pretreatmentwith alkaloid extract of C. peltata caused significant reduction of serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase, serum alkaline phosphatase, serum cholesterol, liver malondialdehyde levels. The reduced glutathione, catalase, superoxide dismutase levels in liver were increased with alkaloid extract of C.peltatatreatment.These results were almost comparable to silymarin and normal control.

Coldenia procumbens

R.Ganesan et al., (2013) had investigated the hepatoprotective activityof*Coldenia procumbens Linn* whole plant chloroform Extract.It was extracted successively with chloroform and methanol in a Saxhlet apparatus and tested for antihepatotoxic activity on rats with of D-Galactosamine (D-GalN) orally. The

parameters assessed were serum levels of Serum Glutamic Oxaloacetate Trasaminase (SGOT), Serum Glutamic Pyruvate (SGPT), Trasaminase (SGOT), Alkaline Phosphatase (ALP), total protein, albumin, globulin, total cholesterol, total bilirubin and blood sugar changes in liver. There was significant reversal of biochemical changes induced by D-Galactosamine treatment in rats by chloroform extract treatment, indicating promising hepatoprotective activity.

Erythroxylum monogynum

Sabeena Hussain Syed et al., (2013) investigated the hepatoprotective activity of methanolic extract of leaves of *Erythroxylum monogynum* (E. monogynum) on paracetamol induced hepatotoxity in rats. The elevated serum levels like serum glutamic pyruvic transaminase,serum glutamic oxaloacetate transaminase,alkaline phosphatise and total bilirubin were found to be restored towards normal.

Z. officinale

Daleya Abdulaziz Bardi et al., (2013) had determined the hepatoprotective activity of ethanolic extract of rhizomes of *Z. officinale*(ERZO) against thioacetamide-induced hepatotoxicity in rats.These results showed that hepatoprotective activity($p<0.05$)against inducers, as indicated by an improvement in liver functions test.It concluded that Z.officinale rhizome possess hepatoprotective activity.

B. purpurealeaves

F. Yahya et al.,(2013) investigated the hepatoprotective activity of methanolic extract of *B. purpurealeaves* (MEBP) was inducing hepatotoxicity against paracetamol- (PCM-) induced liver toxicity in rats. Hepatotoxic rats pretreated with silymarin or MEBP exhibited significant decrease ($P< 0.05$) in ALT and AST enzyme level.

M. Malabathricum

Siti Syariah Mamat et al., (2013) determine the hepatoprotective activity of methanol extract of *M. Malabathricum* leaves (MEMM) against the paracetamol-induced liver toxicity in rats model. MEMM exerted significant ($p < 0.05$) and high antioxidant activity in which high TPC was recorded; while in the hepatotoxicity study, the extract exhibited significant hepatoprotective effects against the paracetamol-induced hepatotoxic model. The results observed for serum liver enzymes (ALT, ALP and AST) as well as the microscopicobservations and microscopic scoring supported the hepatoprotective potential of MEMM.

Eichhornia crassipes

G. Dineshkumar et al., (2013) had to evaluated the hepatoprotective activity of methanolic extract of *Eichhornia crassipes* against CCl4 induced albino rats and concluded that methanolic extract showed significant reduction in serum glutamic-pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP) and bilirubin when compared with silymarin used as a standard drug.

Desmodium adscendens

Joanna Magielse et al., (2013) had evaluated the hepatoprotective activity of aqueous decoction of *Desmodium adscendens*(Fabaceae) leaves and twigs against chemically-induced(D-pinitol) liver damage in rats. Enzyme levels of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP), which are among the usual biomarkers for liver damage,the significant decrease of AST and ALT was observed for the D. Adscendens decoction.

Ficus ingens

Abd El Raheim M. Donia et al., (2013) investigate the chemical constituents and hepatoprotective effect of whole plant of *Ficus ingens*(Miq.) Miq.(Moraceae) extract against carbon tetrachloride-induced acute liver damage in male Wistar albino rats. SC injection of CCl4to rats showed significant elevation of liver marker enzymes (ALT, AST, ALP and LDH) in their serum after 24 h of intoxication. The ethanol extract of F. Ingens to take different doses 100,200&400mg/kg. The results showed 400mg/kg is significant.

Echinopsgalalensis

Hossam M. Abdallah et al., (2013) had investigated the hepatoprotective activityof the flowering aerial parts of *Echinops galalensis* (Asteraceae) . The effect of the methanol extract of E. galalensis, its fractions as well as compounds on human hepatoma cell line (Huh7) was evaluated according to aspartate aminotransferase (AST), alanine transaminase (ALT), superoxide dismutase (SOD) activities and malondialdehyde (MDA) level before and after exposure of the cells to carbon tetrachloride (CCl4). The protective effect of E. galalensis was suggested to be mediated, at least partly, by its antioxidant activity.

Melastoma malabathricum

Farah Hidayah Kamisan et al., (2013) determine the hepatoprotective activity of a methanol extract of *Melastoma malabathricum* leaves (MEMM) using two established rat models by induction of hepatotoxicity either using paracetamol or carbon tetrachloride.The methanol extract ofMelastomamalabathricumleaves (MEMM) on aspartate transaminase (AST) and alanine transaminase (ALT) levels in paracetamol (PCM)- and CCl4-induced hepatotoxicity in rats.The results showed MEMM exhibited a significant ($p<0.05$) hepatoprotective activity.

Spinaciaoleracea L

Nilesh Kumar Jain et al., (2012) had investigate the in vitro and in vivo hepatoprotective effects of *Spinacia oleracea* L. (Chenopodiaceae)seeds on carbon tetrachloride (CCl4)-induced hepatic toxicity.In the in vitro studies, different extracts (i.e. petroleum ether, ethanol and aqueous)and fractions derived from ethanol

extract (i.e. chloroform, ethyl acetate and n-butanol)of Spinaciaoleracea seeds were screened at a concentration of 100g/mLagainst carbon tetrachloride (CCl4)-toxicity in rat hepatocyte culture. In vivohepatoprotective activity was assessed in rats intoxicated with CCl4. The results showed elevated levels of AST, ALT, ALP and LDH due to CCl4 intoxication were significantly ($P< 0.001$)prevented with SOBF treatment when compared with CCl4 control rats.

Alchornea cordifolia

Patience O Osadebe et al., (2012)had investigate the hepatoprotective and antioxidant activities of *Alchornea cordifolia* (A. cordifolia) leaf extract carbontetrachloride induced hepatotoxicity. Various fraction solvents i.e.,methanol,ethyl acetate and chloroform extracts were used .Among these extracts ethyl acetate and chloroform fractions,at a dose of 300mg/kg, produced significant($p<0.05$) when compared to normal. There is decrease In SGOT,SGPT, ALT, AST and TB.Methaol leaf extract showed antioxidant activities.

Ziziphusoenoplia(L.)Mill(Z.oenoplia)

Ch V Rao et al., (2012) had evaluated the hepatoprotective activity of *Ziziphusoenoplia* (L.) Mill (Z.oenoplia) root extract against antitubercular drugs induced hepatotoxicity. The anti-tubercular drugs used are Isoniazid(INH)and rifampicin(RIF).Ethanolic(50%) were used,the ethanolic extract showed significant when compared to normal . The serum levels of glutamic oxaloacetic transaminase (SGOT), glutamate pyruvate transaminase(SGPT), alkaline phosphatase(SALP), and bilirubin were estimated along with activities of superoxide dismutase, catalase.

Hibiscus vitifolius

Anbu Jeba Sunilson John Samuel et al., (2012) had evaluated the hepatoprotective activity of *Hibiscus vitifolius* root extract against anti tubercular drug induced hepatotoxicity. The antitubercular drugs used are Isoniazid, rifampicin, pyrazimide. Different extracts i.e., petroleumether, $CHCL_3$, methanol and aqueous extract were used. Among the 4 extracts, the methanol extract showed significant different when compared to normal.There is decrease in AST,ALT,ALP,LDH,TB, DB, increase in TC,TP and albumin.

Hedyotis corymbosa

Ramesh Kr.Gupta et al., (2012) had evaluated the hepatoprotective potential of methanolic extract of *Hedyotis corymbosa*aginst D-galactosamine induced hepatotoxicity in rats.The results showed that there is dose dependent prevetion in decreased serum levels of hepatic ezymes, reduction in lipid peroxidation and restores the activities of antioxidant enzymes towards normal.

M.paradisiaca

Nirmala M. et al., (2012) had investigated the hepatoprotective activity of stem of *M.paradisiaca* in CCL_4&PCM induced hepatotoxicity models in rats. Both alcoholic and aqueous extracts were demonstrated by using and experimentally induced hepatotoxicity models pretratment with alcoholic extract (500 mg/kg)more significantly reduced and alcoholic and aqueous extract (250 mg/kg)reduce to the less extent, the elevated of SGOT &SGPT, ALP&bilirubin.

Marrubium vulare L

Amita Verma et al., (2012) studied antihepatotoxic activity of *Marrubium vulare* L. through silico methods. The results stated that the Vulgarin exhibited a significant antihepatotoxic activity by decreasing the elevated levels of serum enzymes like SGOT,SGPT,ALP,total protein levels when compared to silymarin against CCL_4 induced toxicity in rats.

Cinnamomum zeylanicum

Akram Eidi et al., (2012) conducted research to evaluate hepatoprotective activity of *Cinnamomum zeylanicum* against CCL_4 induced rats .Upon administration of plant extract,there is significant reduction in CCL_4 toxicity on ALT,ALP etc.and increase in SOD and catalase enzymes. Histopathological studies also supporte that Cinnamon extract markedly reduced the toxicity of CCL_4 and preserved histoarchitecture of liver tissue to normal.

Lawsonia inermis

R. Selvanayaki et al., (2012) had evaluated the hepatoprotective activity of aqueous extract of *Lawsonia inermis* against paracetamol induced liver damage in rats.The results showed significant reduction in serum enzymes alkaline aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), Acid Phosphatase (ACP), Protein and Bilirubin.

FagoniaindicaBurm

I.M. Bagban et al., (2012) had investigated the hepatoprotective activity of the methanolic extract of *FagoniaindicaBurm*. on CCl4 induced hepatotoxicity in albino rats. Methanolic extract of Fagonia indica (MEFI)in different doses (200mg/kg and 400mg/kg b.w., p.o).The degree of protection was determined by measuring levels of biochemical marker like SGOT, SGPT, ALP, Bilirubin (Total & Direct)and Cholesterol.

Amorphophallus paeoniifoliustubers

Pramod J Hurkadale et al., (2012) studied the hepatoprotective activity of methanol and aqueous extracts of *Amorphophallus paeoniifoliustubers* against paracetamol induced liver damage in rats. The results showed significant reduction in the values of sGOT, sGPT, sALPandsB ($P<0.01$)almost comparable to the silymarin and Liv-52.

Solanum xanthocarpum

Talib Hussain et al., (2012) hadassessed the hepatoprotective effect of *Solanum xanthocarpum* (S. xanthocarpum)fruit extract against antitubercular drug-induced liver toxicity in rats.The three antitubercular

drugs [isoniazid (I) 7.5mg/kg, rifampicin (R) 10mg/kg and pyrazinamide (P) 35mg/kg] given orally as suspension for 35days in rats.By used ethanolic extract,the results showed sign ificantly (P<0.05-P<0.001)and dose-dependently prevented drug induced increase in serum levels of hepatic enzymes. Furthermore, S. xanthocarpumsignificantly (upto P<0.001)reduced the LPO in the liver tissue and restored activities of defence antioxidant enzymes GSH, SODandCATtowards normal levels.

Cyathea gigantea

P Madhu Kiran et al., (2012) had investigated the hepatoprotective activity of methanolic leaf extract of *Cyathea gigantea* (C. gigantea)against paracetamol induced liver damage in rats. The results showed treatment with methanolic leaf extract of C. giganteareduced the elevated levels of SGOT, SGPT, ALP, TB and also reversed the hepatic damage towards normal.

Mollugo nudicaulis

Sundaraj Rajamanikandan et al., (2012) had evaluated the hepatoprotective effect of ethanol extract of *Mollugo nudicaulis* (M. nudicaulis) against perchloroethylene-induced hepatotoxicity in wister albino rats. The results showed revealed that the extract significantly (P<0.05) restored the serum levels of AST, ALT, ALP, bilirubin and significantly (P<0.05) increased the antioxidant enzymes SOD, CAT, GPx, GST, GSH, vitamin Cinperchloroethylene-induced rats to its normaly.

Nerium oleander

Kumar Gaurav Singhal et al., (2012) investigated the antioxidant and hepatoprotective activity of methanolic flower extract of *Nerium oleander* against CCL_4 induced hepatotoxicity in rats.The extract showed potent activities on reducing power, Lipid peroxide, DPPH,ABTS, Superoxide amine etc. The elevated serum levels like SGOT,SGPT,AST,ALT and ALP and total bilirubin were found to be restored towards normal.

Table.1 Review of Plant Used In the Treatment of Liver Disease

S.No	Plant name(family)	Part used	Extract	Experimental model	Reference
1	*Amaranthuscaudatus*Linn (Amaranthaceae)	Whole plant	Methanol extract	CCL4 induced hepatotoxicity	Kuruba lakshman et al.,
2	*Aervalanata* (Amaranthaceae)	Whole plant	Petroleum ether extract	CCl4 induced hepatotoxicity	Nevin K G et al.,
3	*Anisochiluscarnosus Linn*(Lamiaceae)	stems	Ethanol	CCl4induced hepatotoxicity	Venkatesh et al.,
4	*Aphanamixispolystachya* (Meliacae)	Leaves	Ethanolic extract	CCl4 induced hepatotoxicity	Mukul k Gole et al.,
5	*Asparagus racemosus Linn*(Asparagaceae)	Roots	Ethanolic extract	Paracetamolinduced hepatotoxicity	Fasalurahimomom et al.,
6	*Amaranthusspinosus* (Araliacae)	Whole plant	(50%) Ethanolic Extract	CCL4 induced hepatotoxicity	Zeashan H et al.,
7	*Azimatetracantha* (salvadoracaeae)	Leaves	ethanolic extract	paracetamol induced hepatotoxicity	Arthika et al.,
8	*Aegicerasconiculatum* (Aegicerataceae)	stems	n-hexane,ethyl acetate	CCL4-induced hepatotoxicity	Roome T et al.,
9	*Cajanuscajan Linn*(Leguminosae)	Pigeon pea leaf	ethanol extract	D-galactosamineinduced hepatotoxicity	Oluseyeadeboyeakinloye et al.,
10	*Withaniafrutescens* (solanaceae)	Leaves	ethanoIic extract	CCL4-induced hepatotoxicity	Montilla MP et al.,
11	*Cajanusscarabaeoides Linn*(Fabaceae)	Whole plant	n-butanol,ethanolextract	paracetamol induced hepatotoxicity	Sumanpattanayak et al.,
12.	*Veronica officinalis*(scrophulariaceae)	herba	Pressed juice	Ccl4-induced hepatotoxicity	Rusu MA et al.,
13.	*Carissa carindas Linn*(Apocyanaceae)	Root	Ethanol	Carbon tetrachloride-induced hepatotoxicity	Balkrishnan et al.,
14.	*Vitextrifolia*(verbenaceae)	leaves	Aqueous&ethanolic extract	Carbon tetrachloride-induced hepatotoxicity	Manjunatha BK et al.,
15.	*Clitoriaternatea Linn*(Fabaceae)	Leaves	Methanol	Parcetamol hepatotoxicity	Yengchen et al.,
16.	*Ficusreligiosa*Linn (Moraceae)	Stem bark	Methanol	Paracetamol induced	Kavithasuryawanshi et al.,

17.	*Garciniaindica*Linn (Clusiaceae)	Fruit rind	Ethanol	Carbon tetra chloride induced	AmolBhalchandra Deore et al.,
18.	*Hyptissuaveolens*linn (Lamiaceae)	leaves	Aqueous	Acetaminophen induced	Babalola et al.,
19.	Meliaazhadirecta Linn (piperaceae)	leaves	ethanol	Carbon tetra chloride,silymarin	H.rajeswary et al.,
20.	*Morindacitrifolia*Linn (Rubiaceae)	Fruit	Aqueous	Streptozotocin induced	Shiva nandanayak et al.,

CONCLUSION

It has been encouraging to witness the recent discoveries in HBV infection with insights into the existence of genotype subgroups, mutant variants, knowledge regarding host, viral and environmental factors on the disease course, as well as advances in new treatment modalities. However, despite the much progress in understanding the natural history of HBV infection, we still have a long way to go before we can conquer hepatitis B infection. For instance, more studies are needed to clarify whether there is an association between genotype, mutant variants and the development of hepato cellular carcinoma. In the HBeAg-positive sub group, there still lacks a consensus on how to manage these patients when they present with signs of mild liver disease activity with alanine amino transferees less than two fold increase; future studies with longer follow-up may help us gain knowledge about the HBV behaviour in these individuals. There is much more to be understood about mutations and their impacts on the clinical course and long-term outcome of hepatitis B infection. For instance, it has been suggested that mutations can arise from vaccine-induced antibodies and this renders the immune response generated by the vaccination ineffective. Therefore, mutations may play a key role in the difficulties of managing hepatitis B infection. Hence, further research and understanding in this sector may bring exciting new information and better understanding of the natural history of HBVand supplement our existing armamentarium to combat this persistent worldwide prevalent disease.

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