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# A REVIEW ON HEPATOPROTECTIVE ACTION OF SELECTED TRADITIONAL HERBS

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**Abstract**
Herbal plants constantly prove themselves as the prime product for synthetic drugs. As of late herbs are staging a comeback solution to insidious and debilitating effects of synthetic drugs with hope of safety and efficacy. Nearly, 70% present day medications in India have been derived from Herbal products. In spite of remarkable strides in modern medicine, there are scarcely any drugs that stimulate hepatic function, protect liver from damage and help in regeneration of hepatic cells. In this scenario, herbal drugs are widely in use for its effectiveness, fewer side effects and relatively low cost. Although a number of plant drugs have been indicated in traditional literature for liver disorders, a simple and precise plant-based hepatoprotective drug is still an unmet medical need. So the present study précises our existing scientific information on selected herbs of Siddha literature for the treatment of manifestations caused by hepatic disorders.

**Keywords:** Herbs, Traditional medicines, Hepatoprotective drugs, Siddha.

## 1. INTRODUCTION

Liver is one of the vital organs in human body and is responsible for metabolic functions of carbohydrate, protein and fat, detoxification, bile secretion etc.[1,2] Any abnormal alterations in these functions can cause significant damage to the body.[3] Liver disease also known as Hepatic disease is a broad term that includes all the potential problems that may cause failure of liver to perform its functions. Many toxic chemicals (certain antibiotics, chemotherapeutics, peroxidised oil, aflatoxin, carbon tetrachloride, acetaminophen, chlorinated hydrocarbons, etc**.**), food, alcohol, infections such as parasites, viruses, fungi or bacteria and also autoimmune disorders can cause liver diseases such as hepatitis, inflammatory liver disease, jaundice, hepatosis (non-inflammatory liver disease, cirrhosis - a digestive disorder that is the result of liver fibrosis), liver cancer**,** etc.[4]Upon keen understanding of our body's natural ecosystem, majority of the diseases are chiefly due to the physiological burden of free radicals, causing imbalance in homeostatic phenomena between oxidants and antioxidants in the body resulting in liver anomalies such as cirrhosis, cholestasis, hepatitis, portal hypertension, hepatic encephalopathy, hepatic failure and certain tumours like hepatoma. Alternative medicines like Ayurveda, Siddha and Unani have been analysed to provide a holistic approach to treat hepatic disorders with success.[5]

Although acute hepatitis is spontaneously healed, treatment for chronic cases is recommended because of the likelihood of cirrhosis of the liver.[6]While comparing the use of chemical and herbal drugs, chemical drugs though beneficial has few but long-lasting side effects which are also

teratogenic while comparatively with that of herbal drugs that have lower side effects with very few or no complications and hence plant-derived medicinal products have increased global attention.[7]

Contemporary medicines have little to contribute for the liver disorders, it has been estimated that herbal drugs have a surprising role in the maintenance and performance of Liver functions. Recently, a worldwide upsurge in the preparation of medicinal plants and the isolation of their active compounds has emerged in health care and the present world seeks a blend between modern and traditional medicine.[8 -11]

**Pathophysiology of Kamalai (Hepatic disorders) in Siddha system**

The Siddha system of medicine is an oldest traditional system with enormous literary evidences of various medicinal herbs that have potent hepatoprotective activity. The Siddha system is based on the "*Tiridhosha* theory of disease" *Vatham, Pitham, Kabam*. The three humours are derived from "*Panchabootha*" by the combination of five bhoothas namely earth, water, fire, air and space. They are the fundamental principles of creation preservation and destruction in the universe. The *tridosha* theory is significant to be considered in health and disease. *Kamalai*which is also called as *Manjalnoi* in Siddha literature is a disease caused by increase of *Azhalkutram*(Pithahumour) in body. *Manjal*means yellow in Tamil Language and *Kamalai-KamamIllai* means lack of interest, because the person affected by this disease will lose interest / desire in food, objects and even day to day activities. It is also called "*Pithunoi*" which means the disease is due to increased *pitham*humour and *pithuneer* (probably bile/bilirubin).*Kamalai* is a disease mentioned in the Siddha literature characterized by pallor, yellowish discoloration of conjunctiva, tongue, lips, yellow coloured urine, vomiting, indigestion, fatigue and motion sickness irrespective of its etiology.[12]Hence this review article has been made with a focus on selected medicinal herbs complementing hepatoprotective action.

## 2. MATERIALS AND METHODS

The literature search was also performed in Siddha literature books Gunapadam Mooligaivaguppu (Materiamedica - herbal section) for hepatoprotective herbs and the herbs *Pongamiapinnata, Cedrusdeodara, Curcuma longa, Cosciniumfenestratum, Cinnamomumzeylanicum, Piper cubeba, Plumbagozeylanica, Cyperusrotundus* were filtered. The search terms included Hepatoprotection, anti-inflammation and antioxidant action. The search was carried out using various search engines such as Google scholar, Elsevier, Pubmedand Embase etc.

**Rationale of Hepatoprotective Herb**

- Biologically active compounds capable of significantly reducing levels of serum ALAT and ASAT, gamma-glutamyltranspeptidase (GGT), thiobarbituric acid-reactive substances (TBARS) tissue, conjugated dienes, lipid hydroperoxides, protein carbonyl content, bilirubin, ALP, lactate dehydrogenase (LDH), and phase I enzymes and phytocompounds that have potential to increase the activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GRx), glutathione-*S*-transferase (GST), alcohol dehydrogenase (ADH), and aldehyde dehydrogenase (ALDH) have been considered potential agents in reducing hepatic damage .
- Also, those herbs that have antioxidant properties, anti-inflammatory activity, stimulating liver cell regeneration and cell membrane stabilization to prevent hepatotoxic agents from entering hepatocyte are presently considered as hepatoprotective agents in herbal research arena.[13]
- Those herbs that promote the inhibition of Hepatocellular cancer cell line growth have also been indicated as hepatoprotective against Hepatic cancer.[14]

**Table-1. Medicinal herbs with potential pharmacological actions on Hepatoprotection**

| S.N | Ingredients | Phytochemicals | Potential Pharmacological actions |
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| 1. | *Pongamia pinnata* | Pongone, Galbone, Pongalabol, Pongagallone A and B and flavanoids[15] | Anti-inflammatory activity, antipyretic activity.[16] Showed in-vivo hepatoprotective activity in paracetamol-induced liver damage in albino rats[17] |
| 2. | *Cedrusdeodara* | Dihydroflavonol, Sesquiterpene, Himachalol, β-Himachalene, Allohimachalol, (+)-longborenol.[18] | Wood oil showed anti-inflammatory activity in carrageenan-induced inflammation at a dose of 50 mg/kg and 100 mg/kg, respectively.[19] |
| 3. | *Curcuma longa* | Ar-tumerone,Ociminearcurcumene, cineole,borneol,bornylacetate and curcumene.[20] | Showed high anti-inflammatory activity at a dose level of 100mg/kg when tested on the carrageenan rat paw model system[20] |
| 4. | *Cosciniumfenestratum* | Alkaloids, phenols, saponins,glycosides, flavonoids, triterpenoids, sterols and tannins[21] | Provide significant protection against CCl4 induced hepatotoxicity in rats.[21]. |
| 5. | *Cinnamomumzeylanicum* | Cinnamaldehyde, eugenol, linalool, safrole, pinene, phyllandrene, cymene[22] | Potent hepatoprotective agent against $CCl_4$ induced hepatotoxicity in rats[23] |
| 6. | *Piper cubeba* | Alkaloids, phenolic compounds, tannins, and flavonoids[24] | Protects the hepatocyte by impairing $CCl_4$-mediated lipid peroxidation and resulting in the prevention of the generation of free radical derivatives[25] |
| 7. | *Plumbagozeylanica* | Plumbagin, Naphthoquinone[26] | Restored the normal functional ability of the hepatocytes in Paracetamol induced liver injury[27]. |
| 8. | *Cyperusrotundus* | Calcium, caryophyllene, camphene, cyperol, cyperotundone, cyperolone, D-copadiene, D- sitosterol[28] | The activities of antioxidants enzymes glutathione peroxidase (GSH-Px) and glutathione –S-transferase (GST) were also concomitantly restored to near normal level by Aqueous extract of Cyperusrotundus supplementation to mercuric chloride intoxicated rats[28] |

## 3. DISCUSSION

### 1.*Pongaminapinnata:*

*Pongamia* is a genus having one species only *Pongamiapinnata* which belongs to family Leguminosae and subfamily Papilionaceae. It is a medium sized glabrous, perennial tree grows in the littoral regions of South Eastern Asia and Australia.[29]In traditional system of medicine various parts of the plant *Pongaminapinnata* are used as an active ingredient for the treatment of conditions like Rheumatoid Arthritis, Bronchitis, cough (Seed), Liver disorders, haemorrhoids (Bark), abdominal tumours, ulcers (Fruits), Diabetes (Flowers), constipation, dyspepsia, leprosy (Leaves).[30]

Literature shows that *Pongaminapinnata*has several pharmacological actions like anti hyperglycaemic activity, antimicrobial, anti-inflammatory, analgesic, antioxidant, antidiarrheal anti antiulcerogenic properties.[16,31]The chemical constituents of *Pongaminapinnata* contains flavones, flavans, chalcones, sesquiterpene, diterpene, triterpine, steroids, amino acid derivatives, saturated and unsaturated fatty acids along with beta s itosteryl acetate, galactoside, stigma sterol, its galactoside, sucrose and few other esters. It also contains 44.24% of Oleic acid, 29.64% of stearic acid and 18.58% of palmitic acid, trace amounts of hiragonic and octadecatrienoic acids and polyphenolics which are natural antioxidants.[32,33]Phytochemical studies revealed the presence of phenols and flavonoids that exhibit a significant hepatoprotective effect against hepatic damage induced by paracetamol. The results also demonstrated that the levels of SGPT, SGOT, ALP, and total bilirubin were reduced in rats treated with extract compared to intoxicated rats.[34]A study on healthy male Albino Wistar rats treated with PP aqueous extract observed partial reversal of lesions induced by Alloxan in the hepatocytes. The study also reported a significant decrease in SGPT, SGOT and bilirubin levels. A partial recovery and reversal in multifocal single cell necrosis was seen at low concentrations with *Pongamiapinnata* extract.[16] Histopathologicalexamination of liver tissue with IR induced hepatic reperfusion injury shows considerably less hepatocyte injury in rats with PP treatment. Free radicals are involved in the hepatic injury caused by ischemia and reperfusion. The prevention of free oxygen radicals that arise after hepatic IR and cause injury is seen when treated with *Pongamiapinnata* rich in flavonoids (Pongagallone A and B) which is known to be a strong antioxidant, breaking up free radicals.[35,36]

**2. *Cedrusdeodara***

*C. deodara* also known as Himalaya Cedar is a conifer tree which reaches up to 85 meters of height belongs to genus pinacea with basically tropical and subtropical worldwide distribution. The chemicals in wood are wikstromal, matairesinol, dibenzylbutyrolactol, 1,4-diaryl butane, benzofuranoid neo lingam, cedrin (6-methyldihydromyricetin), taxifolin, cedeodarin (6-methyltaxifolin), dihydromyricetin, cedrinoside, deodardione, diosphenol, limonenecarboxylic acid, (–)-matairesinol, (–)-nortrachelogenin, and a dibenzylbutyrolactollignan (4,4',9-trihydroxy-3,3'-dimethoxy-9,9'-epoxylignan). A new di-hydro flavonol named deodarin (3, 4, 5, 6-tetrahydroxy-8-methyl di-hydroflavonol) has been isolated from the stem bark. The phytocompoundsprotocatechuic acid, *2R*,*3R*-dihydromyricetin, massonianoside B and myricetin-3-*O*-β-D-glucopyranoside showed potent antioxidant activity and reduced the level of lipid peroxidation of liver homogenates in $CCl_4$-treated mice in the *in vivo* antioxidant assay.[37,38] Mechanistic studies in Molt-4 and HL-60 cell lines have confirmed that the *Cedrusdeodara*lignans can induce early Nitric oxide formation. Through this process the aspartic proteases are activated to generate peroxides and the resultant peroxides depolarize the mitochondrial membrane, leading to the cell apoptosis. In addition, the researchers also found that the total flavonoids extracted from the pine needles of *Cedrusdeodara* produced a dose-dependent inhibition of HepG2 cell growth, with the $IC_{50}$ value of 114.12 µg/ml indicating its effects in hepatocellular carcinoma cell lines.[14]

C. deodarais an evergreen conifer tree reaching unto 85 m in height with almost rough black, furrowed bark and spreading branches, shoots dimorphic, leaves 2-5,-5-8 cm needle like Triquetrous, sharp, pointed, flowers usually monoecious, but some trees or branches habitually Bear flowers of one sex. bitter, hot, slightly pungent, oleaginous in nature., Cedrusis a genus of Pinacea with basically tropical and subtropical worldwide distribution; the genus is comprised of trees which are sometimes cultivated either for their usefulness to traditional cultures or for ornamental purposes. Seeds are shed in season of winters. A tree of deodaracan live up to 600 years. Flowers appear in September and October. The best trees arefound on deep and drained soils. High atmospheric moisture is favourable. Shade is good for the growth, but young trees are prone to injury from frosts and cold wind. The chemical composition of plant is shown in

**3. Cyperusrotundus**

Cyperusrotundus (Family- Cyperaceae) common perennial weed with an elaborate underground system consisting of tubers, rhizomes and roots.[39] It has been claimed in the traditional literature against liver disorders.[40] Several studies have been performed on the hepatoprotective effects of *Cyperusrotundus*in Carbon tetrachloride ($CCl_4$) induced hepatotoxicity. It has been found that in $CCl_4$ induced hepatotoxicity the highly reactive trichloro free radical, attacks polyunsaturated fatty acids and produces hepatotoxicity by altering liver microsomes. A study by Suresh kumar and Mishra (2005) on $CCl_4$ induced hepatotoxic Wistar rats reported that $CCl_4$-induced liver peroxidation was inhibited significantly by *Cyperusrotundus* rhizome extract and the elevated levels of liver parameters such as SGOT, SGPT, ALKP, were significantly reduced. Moreover, the histopathological study of the treated rat organs showed no visible changes or mortality of the animals confirming the safety of the extract at selected dose regimen ranging from 100-1000 mg/kg.

The above facts were substantiated by another study by Parvez, Mohammad K et al 2019. Investigated the hepatoprotective, hepatitis B virus (HBV) inhibitory and hepatic CYP450 enzyme (CYP3A4) modulatory potential of *Cyperusrotundus* rhizome fractions in *in vitro* HepG2 cells (MTT assay), followed by *in vivo* evaluation in Wistar rats. The study results confirmed dose-dependent hepatoprotection in HepG2 cells. Further, oral administration of *C. rotundus* (100 and 200 mg/kg· bw/day) in $CCl_4$-injured rats, significantly normalized serum markers of healthy liver promising hepatoprotective and anti-HBV potential in experimental settings.Moreover, the histopathological study of the treated rat organs showed no visible changes or mortality of the animals confirming the safety of the extract at selected dose regimen ranging from 100-1000 mg/kg.[41, 42]

**4.Plumbagozeylanica**

*Plumbagozeylanica* L. is a South Asian medicinal herb of family Plumbaginaceae.[43]The species is distributed throughout most of the tropics and subtropics. *P. zeylanica* contains a variety of important chemical compounds such as naphthaquinones, alkaloids, glycosides, steroids, triterpenoids, tannins, phenolic compounds, flavanoids, saponins, coumarins, carbohydrates, fixed oils, fats and proteins.[44, 45, 46]The root, root barks, and seeds of *Plumbagozeylanica* are medicinally important parts. The root is the chief source of plumbagina yellow naphthoquinone pigment as the principle active compound.[47] RohitGoyal et al., 2012 performed a studyto investigate the hepatoprotective effects of standardized methanolic extract of *Plumbagozeylanica* root on paracetamol, CCl4 and alcohol induced hepatic injuries in rats which caused significant increase in serum markers of hepatic injury and decrease in tissue GSH and SOD levels. *Plumbagozeylanica* root possesses marked hepatoprotective potential through its oxidative, inflammatory and fibrotic effects. Moreover its safety was confirmed through liver histopathology study.The central vein dilation, infiltration and fatty degeneration in hepatotoxic and control groups were reversed with pre-treatment with methanolic extract of *Plumbagozeylanica* (100, 200 and 400 mg kg−1). Significant reversal of these toxic changes were dose dependently observed, as compared to hepatotoxicant control.[48]

Rajesh et al., (2009) conducted a study in methanolic extract of aerial parts of *P. zeylanica* to evaluate the hepatoprotective activity of CCl4-induced hepatotoxicity in wistar rats. The extract of aerial parts of *P. zeylanica* have shown very significant hepatoprotection against CCl4-induced hepatotoxicity in wistar rats by reducing serum total bilirubin, SGPT, SGOT and ALP levels. The hepatoprotective nature of the extract was also confirmed through the histopathological study.[49, 50] In another study byBinilEldhose et al. 2015, administration of thioacetamide (TAA) ) elevated the levels of ALT, AST, ALP and LDH in the blood circulation. Pre-treatment with *Plumbagoindica* crude methanolic extract reduced the elevated enzyme levels in serum plasma resulting from the stabilization of three enzymes, clearly showing a preventive effect of *Plumbagoindica* on thioacetamide (TAA)-induced liver damage. Also reduction in oxidative stress levels is the main mechanism of TAA action which were also

reversed on pre-treatment with *Plumbago zeylanica*.[51] Since formation of free radicals may contribute to oxidative damage, resulting in acute hepatitis, natural compounds that diminish free radical formation might be good candidates for the treatment of oxidative damage in cells and tissues.[52] In this aspect the plant *Plumbagozeylanica* can be considered as an effective antioxidant and hepatoprotective plant.

**5.Pipercubeba**

Cubeb (*Piper cubeba*) or tailed pepper is a flowering vine plant in the genus Piper belongs to the family Piperaceae. It is a perennial plant cultivated for its fruit and essential oil with round branches, climbing stem and rooting at the joints.[53] The dried fruits of cubebacontain essential oils like oxides 1,4- and 1,8-cineole, monoterpenes (sabinene 50%, α-thujene, and carene), sesquiterpenes (caryophyllene, copaene, α- and β-cubebene, δ-cadinene, germacrene) and alcohol cubebol which are traditionally used as expectorant, stimulant, carminative and appetite enhancers.[54,55]

Extensive evidence suggests that oxidative stress and inflammation as etiologic factors for liver, cardiovascular diseases and cancer.Enzymes like superoxide dismutase, glutathione peroxidise, catalase and certain endogenous antioxidants like α–tocopherol, uric acid, ascorbic acid and β–carotene act as a natural defence to oxidative stress protecting cells from free radicals damage and extensive lyses.A study conducted by GayatriNayak and Sahu (2011) claims that, the presence of phytochemical constituents especially polyphenols in ethanolic extracts of *Piper cubeba* showed high free radical scavenging activity when compared to Piper nigrum.[56]

The compound Carbon Tetrachloride CCl4 is much evident causing liver damage and necrosis by increasing lipid peroxidation in hepatocytes.[57] CC14 is metabolized by the enzyme cytochrome P450 into its reactive metabolites trichloromethyl (CCl3 +) free radicals and trichloromethylperoxy (CCl3OO) in the liver's endoplasmic reticulum. These metabolites increase lipid peroxidation leading to toxicity in the hepatocytes.Mansour AlSaid et al., analyzed the effect of Piper cubeba extract against carbon tetrachloride induced hepatotoxicity and oxidative stress in rats. CCl4 administration markedly increased the levels of SGPT, SGOT, GGT, and ALP in rats. Consequently the enzymes leak out of the hepatocytes by altered membrane integrity. These pathological changes were significantly low after treatment with *Piper cubeba* and silymarin. This current study indicates that *Piper cubeba*andsilymarinsignificantly treat the CCl4-induced hepatocyte injuries.[58]

**6. Cinnamon (Cinnamomumzeylanicum)**

Cinnamon (*Cinnamomumzeylanicum* L., Lauraceae) is an evergreen tree that grows wild in the tropical parts of the world likeIndia, Sri Lanka, Indochina and Madagascar. The inner bark of the tree has been used in ethno-medicine and culinary purposes. In addition, cinnamon is widely being used in traditional herbal medicine to treat various health conditions.[59]Kwshvari et al. 2013 proposed the major chemical composition of cinnamon essential oil is cinnamaldehyde (96.8%), while α- murolene (0.11%), α-capaene (0.2%), ρ- methoxy-cinamaldehyde (0.6%) and δ- cadinen (0.4%) are present in smaller parts. ElBaroty et al. (2010) analysed that cinnamon oil contains 45.13% cinnamaldehyde, 8.21% cinnamyl alcohol, 7.47% Eugenol and 5.23% methyl eugenol approximately.[60]

Increased serum levels of ALT, AST and ALP occur as a result of enzyme leakage from the hepatocytes at the instance of tissue damage in CCl4-treated animals. This condition is most likely associated with hepatonecrosis.[61] Administration of cinnamon extract significantly lowered or normalized the levels of these biomarker enzymes which indicatesits efficacy in preventing liver damage. The functioning of hepatocytes are markedly altered by the levels of ALP. Reduction in serum ALP levels stabilized the biliary dysfunction during chronic hepatic injury induced with CC14 in rats. Diminished levels of total protein and albumin also indicate liver damage in CC14 treated rats. Stimulation of protein synthesis and increasing the levels of total serum protein to normal indicates the

hepatoprotective action of cinnamon extract.[62]In a similar study the efficacy of oral administration of 200mg/kg ethanolic cinnamon extract and water extract given once daily for a week was analysed in rats treated with CC14. The results indicate that ethanolic extract has more potent hepatoprotective action than water extract against CC14 by lowering the levels of malondialdhyde (MDA) and increasing the levels of antioxidant enzymes superoxide dismutase and catalase (SOD and CAT).[63]

**7. Cosciniumfenestratum**

*Cosciniumfenestratum* commonly called as tree turmeric belongs to the family Menispermaceae. It widely grows in the Western Ghats (India) and Sri Lanka.[64] The chemical composition of the stem has berberine, sitosterol, ceryl alcohol, hentriacontane, oleic acid, palmitic acid and saponin along with some resinous material.[65]A preliminary phytochemical screening of *C. fenestratum* revealed the presence of berberine and phenolic compounds. Hence the current study suggests that *C. fenestratum* exhibits a hepatoprotective mechanism on cellular antioxidant defence by preventing oxidative damage in streptozotocin –nicotinamide induced diabetes.[66,67]*C. fenestratum* extract exhibits hepatoprotective activity in hepatic damage by fighting oxidative stress. A study was conducted on the evaluation of antioxidant activity with the alcoholic stem extract of *C. fenestratum* in ratswithstreptozotocin-nicotinamide induced type-2 diabetes. Diabetic rats treated with alcoholic extract of *C.fenestratum* showed a significant increaseof enzymatic antioxidants catalase, glutathione peroxidase, glutathione synthetase, peroxidase, superoxide dismutase and non-enzymatic oxidants like ascorbic acid, ceruloplasmin and tocopherol. The study suggests that the antioxidant activity of *C.fenestratum* could be due to the presence of phenolic compounds and berberine.[20]The major active ingredient is berberine, an isoquinoline alkaloid with several bioactivities (Birdsall and Kelly, 1997).[68]

The drug is used in treating various conditions of *kapha* and *vata*, inflammations, ulcers, wounds, burns,abdominal disorders, jaundice, skin diseases, diabetes, fever and general weakness.[69]Kong et al (2004) observed that berberine increases the expression of low-density lipoprotein receptor (LDLR) in hepatocytes via an extracellular signal regulated kinase (ERK)-dependent pathway. Their observations also revealed that berberine significantly decreases blood cholesterol, triglyceride and LDL cholesterol (LDLC) in hyperlipidaemia and elevated LDLR expression in patients with hepatitis B virus (HBV).[70,71] Recent study by Janbaz and Gilani (2000) demonstrated the effectiveness of oral dose of berberine (4 mg/kg) against acetaminophen and carbon tetrachloride (CCl4) induced hepatotoxicity.They proposed that it inhibited the activities of microsomal drug metabolizing enzymes, CYPs. Surprisingly, it was believed that berberine has a selective curative effect on acetaminophen compared to CCl4 induced hepatotoxicity. This theory was supported by further study reports that acetaminophen toxicity is mainly due to the oxidative stress and can be treated by antioxidants.[72, 73]

Hepatoprotective action of methanol extract of *Cosciniumfenestratum* stem (MEC) was analysed in rats with carbon tetrachloride-induced hepatopathy. Hepatotoxic rats were treated with MEC 60mg/kg body weight daily once orally for a period of 90 days. Anti-hepatotoxic effect was assessed by the serum levels of biomarker enzymes like aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, glucose 6 phosphate dehydrogenase gamma glutamyltranspeptidase and lactate dehydrogenase. The concentrations of total proteins, total lipids, triglycerides, phospholipids and cholesterol in serum, liver and kidney were also estimated. There was a significant decrease of the serum biomarkers to a normal level in carbon tetrachloride-treated rats when co-administered with MEC.[74]

**8. *Curcuma longa***

The genus *Curcuma* commonly called as Haldi is a well-known spice in India. It has more than 200 species and sub species across the world. It is an aromatic erect rhizomatous herb with large leaves, intense camphoraceous odour and externally used on sprain and bruises. Turmeric is native to Central

India and North-East.[75] The phytochemical constituents rhizomes are identified to have 30 components, among which 97.48% of the oil, with camphor (28.3%), ar-turmerone (12.3%), (Z)-ocimene (8.2%), ar-curcumene (6.8%), 1, 8-cineole (5.3%), elemene (4.8%), borneol (4.4%), bornyl acetate (3.3%) and curcumene (2.82%) as major elements.[76]*Curcumin*, the chrome orange-yellow compound present in turmeric rhizomes is known to have antioxidant properties. Chirangini evaluated the extracts of Crude methanol rhizomes of 11 species with curcumin as a reference indicator using sulphur free radical reactivity. MohitMangla et al., (2010) observed the anti-oxidant activity of the rhizomes of methanolic extract using DPPH (1,1-diphenyl-2-picrylhydrazyl) free radical scavenging assay. To evaluate the Inhibitory concentration IC 50 of the herb a graph was plotted between concentration and the percentages of inhibition. The IC 50 values of the extract and ButylatedHydroxytoluene was found as 862.35 µg and 46.25 µg respectively for 2 ml of 500 µm concentration of DPPH. This indicates that methanolic*Curcuma longa* extract had moderate Inhibitory concentration compared to ButylatedHydroxyltoluene.[77] Themethanolic rhizome extracts comprised of 37.64 mg and 44.33 mg of total phenol respectively with Tannic acid equivalents/g dry material. It was found that *Curcuma* have higher strengths of superoxide, ABTS [2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid)] and DPPH radical scavenging activities. IndrajitKarmakar et al.(2011) studied the effect of methanolic extract of *Curcuma longa* rhizome (MECC) on RNS (Reactive Nitrogen Species) and ROS (Reactive Oxygen Species) with in vitro methods using 1, 1-diphenyl-2-picrylhydrazil radical, nitric oxide, hydrogen peroxide, hydroxyl radical, superoxide anion, peroxynitrite and hypochlorus acid. Total phenol and lipid peroxidation were also analyzed by standard assay method. The extract was found to exhibit dose dependent antioxidant activity.[78, 79]

## 9. CONCLUSION

Herbs have been used since time memorial for the treatment of various diseases. Various researchers have explored several herbs for their hepatoprotective activities. Hepatoprotective plants are important for the discovery of drugs since they are cost effective, have fewer side effects, are more potent, and effective. Therefore this review work on hepatoprotective herbs will contribute to the benefit of the populations needing herbal treatment for liver diseases and also towards reducing the side effects of synthetic drugs.

**Conflict Of Interest**

The authors declare that there is no conflict of interest

## 10. REFERENCES

1. P. Pushpangadan. Development of phytomedicines for liver diseases. Indian Jour. of Pharmacol. 1999; 31; 166-175.
2. Ahsan R, Islam K.M., Musaddik A, Haque E. Hepatoprotective Activity of Methanol Extract of Some Medicinal Plants Against Carbon Tetrachloride Induced Hepatotoxicity in Albino Rats. Global Jour. of Pharmacol. 2009; 3; 116-122.
3. Sharma A, Chakraborti K.K., Handa S.S. Anti-hepatotoxic activity of some Indian herbal formulations as compared to silymarin. Fitoterapia.1991; 62; 229-235.
4. Subramonium, A. Thomas D, Leoutsakas D, Zabransky T and Kumar M: Hepatitis C in HIV infected individuals: cure and control, right now. Journal of the International AIDS Society 2011; 14: 1-8.
5. Nadkarni A. (2007). Indian MateriaMedica. 2nd Edition. Vol I. Bombay Popular Prakashan, Mumbai, 629.
6. Ni YH and Chen DS: Hepatitis B vaccination in children. The Taiwan experience. Pathologiebiologie 2010; 58: 296-300.

7. Rabiei Z, Bigdeli MR and Lorigooini Z: A review of medicinal herbs with antioxidant properties in the treatment of cerebral ischemia and reperfusion. Journal of Babol University of Medical Sciences 2015; 17(12): 47-56.
8. Govind P and Pandey SP: Phytochemical and toxicity study of *Emblicaofficinalis* (Amla). Int Res J Pharm 2011; 2(3): 270-272.
9. Jassim SAA and Naji MA: Novel antiviral agents. a medicinal plant perspective. Journal of Applied Microbiology 2003; 95: 412-427.
10. Karan M, Vasisht K, Handa S.S. Anti-hepatotoxic activity of Swertiachirata on carbon tetrachloride induced hepatotoxicity in rats. Phytotherapy Res.1999; 13; 24-30.Chatterjee TK. Medicinal plants with hepatoprotective properties. In: Herb.Opt. 2000; 3; 135.
11. Amit Roy , DayanandaBhoumik, Ram Kumar Sahul , Jaya Dwivedi3 Medicinal Plants Used in Liver Protection - A Review UK Journal of Pharmaceutical and Biosciences Vol. 2(1), 23-33, 2014.
12. KuppusamyMuthaliar, Siddha Maruthuvam, (1st Edn. 1954), Tamilnadu Siddha medical council, Chennai, 2nd Edn. 1987.
13. Madrigal-Santillán E, Madrigal-Bujaidar E, Álvarez-González I, et al. Review of natural products with hepatoprotective effects. *World J Gastroenterol*. 2014;20(40):14787-14804.
14. Shi X, Liu D, Zhang J, Hu P, Shen W, Fan B, Ma Q, Wang X. Extraction and purification of total flavonoids from pine needles of Cedrusdeodara contribute to anti-tumor in vitro. BMC Complement Altern Med. 2016; 16:245.
15. Rahul DeoYadav, S. K. Jain, ShashiAlok , S. K. Prajapati and AmitaVerma.Pongamiapinnata: an overview. IJPSR, 2011; Vol. 2(3): 494-500.
16. Singh RK, Pandey BL. Anti-inflammatory activity of seed extracts of *Pongamiapinnata* in rats. Indian Journal of Physiology and Pharmacology 1996; 40: 335-358.
17. HarleenKaur ,Mohanjit Kaur, Amarjeet Singh, Bimlesh Kumar. Hepatoprotective potential of aqueous and ethanolic stem-bark extracts of pongamiapinnata against paracetamol induced hepatotoxicity in rats. IJPSR, 2014; Vol. 5(10): 4275-4280
18. Dwaipayan Sinha. A review on phytochemical, ethnobotanical, pharmacological, and antimicrobial importance of Cedrusdeodara (Roxb. Ex D. Don) G. Don. International Journal of Green Pharmacy • Jan-Mar 2019 • 13 (1) | 1.
19. BhupendraSahu, RameshrooKenwat, ShashikantChandrakar. Medicinal Value of Curcuma cassia roxb: An Overview. UK Journal of Pharmaceutical and Biosciences Vol. 4(6), 69-74, 2016.
20. B.K. Manjunatha, Syed Murthuza, Sudharshan S.J, Divakara R. Phytochemical Investigation and Hepatoprotective Activity of CosciniumFenestratumColebr., A Rare Endangered Spp., from Western Ghats of India. Paripex-indian journal of research · February 2013.
21. Thomas J, Kuruvilla KM. Cinnamon. Handbook of Medicinal Spices. (2nd edn), CRC Press, Washington, DC, USA. 2012; 1: 182-196.
22. Eidi A, Mortazavi P, Bazargan M, Zaringhalam J. Hepatoprotective activity of cinnamon ethanolic extract against CCI4-induced liver injury in rats. EXCLI J. 2012 Aug 20; 11:495-507. PMID: 27547174; PMCID: PMC4990741.
23. Nirmalanithya R, Sainandhini R. Screening and evaluation of secondary metabolites present in piper cubeba. Asian J Pharm Clin Res, Vol 12, Issue 12, 2019, 81-83.
24. Lin HM, Tseng HC, Wang CJ, Lin JJ, Lo CW, Chou FP.Hepatoprotective effects of Solanumnigrum Linn extract against CCl(4)-induced oxidative damage in rats.*ChemBiol Interact. 2008 Feb 15; 171(3):283-93.*
25. Manu Pant, AnkitaLal, Swati Rana, Anju Rani. Plumbagozeylanica .: a mini review. International Journal of Pharmaceutical Applications. Vol 3, Issue 3, 2012, pp 399-405.
26. N. Kanchana and A.Mohamedsadiq. Hepatoprotective effect of plumbagozeylanica on paracetamol induced liver toxicity in rats. Int J Pharm PharmSci, Vol 3, Issue1, 151154.

27. Pushpendrakumarjain, Debajyoti Das. Pharmacognostic comparison of bacopamonnieri, cyperusrotundus, and emblicaofficinalis. Innov J AyruvedicSci, Vol 4, Issue 4, 2016, 16-26.
28. AhlemBahia ,YoucefNeciba. Hepatoprotective and Antioxidant Activity of Aqueous Extract of Cyperusrotundus Rhizome Against Mercuric Chloride Induced Oxidative Stress in Rats. Int. J. Pharm. Sci. Rev. Res., 27(1), July – August 2014; Article No. 21, Pages: 117-123.
29. Sangwan, Savita& Rao, D. & Sharma, R. (2009). A Review on PongamiaPinnata (L.) Pierre: A Great Versatile Leguminous Plant. Nat Sci. 8.
30. Kaur H, Kaur M, Singh A and Kumar B: Hepatoprotective potential of aqueous and ethanolic stem-bark extracts of *Pongamiapinnata* against paracetamol induced hepatotoxicity in rats. Int J Pharm Sci& Res 2014; 5(10): 4275-80. doi: 10.13040/IJPSR.0975-8232.5(10). 4275-80.
31. Brijesh, S., Daswani, P.G., Tetali, P. *et al.* Studies on *Pongamiapinnata* (L.) Pierre leaves: understanding the mechanism(s) of action in infectious diarrhea. *J. Zhejiang Univ. - Sci. B* **7,** 665–674 (2006).
32. Shameel S, Usmanghani K, Ali MS, Ahmad VU. Chemical constituents from the seeds of Pongamiapinnata (L.) Pierre. Pak J Pharm Sci. 1996 Jan;9(1):11-20. PMID: 16414771.
33. Al Muqarrabun LM, Ahmat N, Ruzaina SA, Ismail NH, Sahidin I. Medicinal uses, phytochemistry and pharmacology of Pongamiapinnata (L.) Pierre: a review. J Ethnopharmacol. 2013 Nov 25;150(2):395-420. doi: 10.1016/j.jep.2013.08.041. Epub 2013 Sep 7. PMID: 24016802.
34. AbhaySubhashMorajhar, BhagyashreeHardikar and Bharatbhushan Sharma, 2015. Hepatoprotective Effects of Crude Extracts of Pongamiapinnata in Alloxan Induced Diabetic Albino Wistar Rats. International Journal of Zoological Research, 11: 37-47.
35. Behera, Saiprasanna&Babu, S &Ramani, Roja& Choudhury, Prasanta. (2012). Studies on Hepatoprotective Activity of Hydroalcoholic leaf extract of PongamiaPinnata against I/R Induced Hepatic Reperfusion Injury. International Journal of Pharmacy and Biological Sciences. 2. 15-30.
36. Kumar, S."PhytochemistryAnd Pharmacological Studies f PongamiaPinnata (Linn.) Pierre." (2011).***2.***
37. Amit Sharma, Bharat Prashar and Pankaj Arora,Cedrusdeodara: A Medicinal Herb. Der PharmaChemica( 2018) Volume 10, Issue 4.
38. Yan-Ping Wu, Xue Liang, Xiao-Yan Liu, Kai Zhong, Bo Gao, Yi-Na Huang, Hong Gao, Cedrusdeodara pine needle as a potential source of natural antioxidants: Bioactive constituents and antioxidant activities, Journal of Functional Foods, Volume 14,2015,Pages 605-612.
39. The Wealth of India, Raw Materials, Vol. 11,Publication and Information Directorate, CSIR, New Delhi, 1950, 424.
40. Suresh Kumar, S V. (2005). 2. Hepatoprotective activity of rhizomes of Cyperusrotundus Linn against carbon tetrachloride-induced hepatotoxicity. S.V. Suresh Kumar and S.H. Mishra. Indian Journal of Pharmaceutical Sciences, 67(1), 2005, 84-88.. Indian Journal of Pharmaceutical Sciences. 67. 84-88.
41. Suresh Kumar, S V & Mishra, S.H. (2005). Hepatoprotective activity of rhizomes of Cyperusrotunduslinn against carbon tetrachloride-induced hepatotoxicity. Indian Journal of Pharmaceutical Sciences. 67. 84-88.
42. Parvez, Mohammad K et al. "The *in vitro* and *in vivo* anti-hepatotoxic, anti-hepatitis B virus and hepatic CYP450 modulating potential of *Cyperusrotundus*." *Saudi pharmaceutical journal: SPJ : the official publication of the Saudi Pharmaceutical Society* vol. 27,4 (2019): 558-564. doi:10.1016/j.jsps.2019.02.003.
43. Vijver LM et al. [1971] Antibacterial Activity in Roots of PlumbagozeylanicaPlanta Med. 20: 8-13.
44. Ravikumar VR et al. [2011] Phytochemical and antimicrobial studies on Plumbagozeylanica (L) (Plumbaginaceae). International Journal of Research In Pharmacy and Chemistry. 1(2): 185-188.

45. Ming Y et al. [2011] Chemical constituents of Plumbagozeylanica. Advanced Materials Research. 308-310:1662-1664
46. Krishnaswamy M et al. [1980] Plumbagin: a study of its anticancer, antibacterial and antifungal properties. Indian Journal of Experimental Biology 18(8):876-877.
47. Mir M A, Kumar A, Chauhan R, Ashraf M. W. Screening of stem extracts of Plumbagozeylanica for phytochemical, antimicrobial and anti-arthritis activity. Biomed Pharmacol J 2020: 13 (4).
48. RohitGoyal and PyareLal Sharma. Possible Mechanism of Plumbagozeylanica in Prevention of Hepatic Damage in Wistar Rat. American Journal of Pharmacology and Toxicology, 2012, 7 (3), 101-108.
49. Yuvaraj D. Mandavkar* and Sunil S. Jalalpure. A comprehensive review on Plumbagozeylanica Linn. African Journal of Pharmacy and Pharmacology Vol. 5(25), pp. 2738-2747, 30 December, 2011.
50. Rajesh Kumar, Sushil Kumar, &Patra, Arjun & JAYALAKSHMI, S.. (2009). Hepatoprotective activity of aerial parts of Plumbagozeylanicalinn against carbon tetrachloride-induced hepatotoxicity in rats. International Journal of Pharmacy and Pharmaceutical Sciences. 1.
51. BinilEldhose, Vicente Notario, JayeshKuriakose, M.S. Latha. Hepatoprotective effect of Plumbagoindica root extract on thioacetamide-induced liver damage in rats. Journal of Pharmacognosy and Phytochemistry 2015; 4(2): 97-101.
52. Pradeep HA, Khan S, Ravikumar K, Ahmed MF, Rao MS, Kiranmai M, Reddy DS, Ahamed SR, Ibrahim M. Hepatoprotective evaluation of Anogeissuslatifolia: in vitro and in vivo studies. World J Gastroenterol 2009; 15:4816-4822.
53. T GayatriNahak and R.K. Sahu Phytochemical Evaluation and Antioxidant activity of Piper cubeba and Piper nigrum. Journal of Applied Pharmaceutical Science 01 (08); 2011: 153-157
54. Amol P. Pachpute1 *, Tushar A. Deshmukh. Antioxidant and hepatoprotective activity of an ethanol extract of piper cubeba fruits Int. J. Res. Dev. Pharm. L. Sci. February-March, 2013, 2(2), 321-329.
55. Lawless and Julia. The illustrated encyclopaedia of essential oils: the complete guide to the use of oils in aromatherapy and herbalism, Element Books. (1995). several studies have been conducted to investigate the antioxidant effect of Piper cubeba.
56. Sies H., Stahl W. Vitamin E and C, beta carotene and *other carotenoids as antioxidants. Am J ClinNutr. 1995; 62:13115S-21S. Pietta P.G.* Flavonoids as antioxidants. J Nat Prod. 2000; (63):1035-42.
57. L. W. D. Weber, M. Boll, and A. Stampfl, "Hepatotoxicity and mechanism of action of haloalkanes: carbon tetrachloride as a toxicological model," Critical Reviews in Toxicology, vol. 33, no. 2, pp. 105–136, 2003.
58. Mansour AlSaid,1 Ramzi Mothana,1 Mohammad Raish,2 Mohammed Al-Sohaibani,3 Mohammed Al-Yahya,1 Ajaz Ahmad,4 Mohammed Al-Dosari,1 and Syed Rafatullah1. Evaluation of the Effectiveness of Piper cubeba Extract in the Amelioration of CCl4-Induced Liver Injuries and Oxidative Damage in the Rodent Model. BioMed Research International Volume 2015, Article ID 359358, 11 pages.
59. Kim MK, Lee HS, Kim ET, Won NH, Chi YM, Kim BC. Protective effect of aqueous extract of Perillafrutescens on tert-butyl hydroperoxide induced oxidative hepatotoxicity in rats. Food ChemToxicol 2007; 45:1738-44).
60. Kwshvari, M; S. Asgary; A. Jafarian-dehkordi; S. Najafi and S. M. GhoreyshiYazdi (2013). Preventive effect of cinnamon essential oil on lipid oxidation of vegetable oil. ARYA Atheroscler, 9(5):280-286.
61. Naik SR, Panda VS. Hepatoprotective effect of Ginkgoselect P phytosome in rifampicin induced liver injury in rats: evidence of antioxidant activity. Fitoterapia 2008; 79: 439-45 Ree KR,

Spector WG. Reversible nature of liver cell damage due to carbon tetrachloride as demonstrated by the use of phenergan. Nature 1961; 190:821-2).

62. Akram Eidi1*, Pejman Mortazavi2, Maryam Bazargan3, Jalal Zaringhalam4. Hepatoprotective activity of cinnamon ethanolic extract against ccl4-induced liver injury in rats. Excli Journal 2012; 11:495-507.
63. Moselhy SS, Ali HK. Hepatoprotective effect of cinnamon extracts against carbon tetrachloride induced oxidative stress and liver injury in rats. Biol Res. 2009; 42(1):93-8.
64. Varier PS. Cosciniumfenestratum; Indian Medicinal Plants, Compendium of 500 species; Hyderabad, India: Orient Longman Ltd; 1994. pp. 191–193.
65. The Wealth of India: CosciniumFenestratum, Publication Information and Directorate; India: CSIR; 1950. p. 360.
66. K.V. Tushar, Satheesh George, A.B. Remashree and Indira Balachandran, 2008. *Cosciniumfenestratum* (Gaertn.) Colebr.-A Review on this Rare, Critically Endangered and Highly-Traded Medicinal Species. *Journal of Plant Sciences, 3: 133-145.*
67. Punitha IS, Rajendran K, Shirwaikar A, Shirwaikar A. Alcoholic stem extract of Cosciniumfenestratum regulates carbohydrate metabolism and improves antioxidant status in streptozotocin-nicotinamide induced diabetic rats. *Evid Based Complement Alternat Med*. 2005;2(3):375-381.
68. Birdsall, T. and G. Kelly. "Berberine: Therapeutic Potential of an Alkaloid Found in Several Medicinal Plants." *Alternative Medicine Review* 2 (1997): 94-103.
69. Warrier, P.K., V.P.K. Nambiar and C. Ramankutty, 1994. Indian Medicinal Plants, a Compendium of 500 species. Orient Longman Limited, 160, Anna. Salai, Madras, 2: 191-193.
70. Kong W, Wei J, Abidi P, et al. Berberine is novel cholesterol-lowering drug working through a unique mechanism distinct from statins. Nat Med 2004; 10(12): 1344-1351. 36.
71. Zhao W, Xue R, Zhou ZX, Kong WJ, Jiang JD. Reduction of blood lipid by berberine in hyperlipidemic patients with chronic hepatitis or liver cirrhosis. Biomed Pharmacother 2008; 62(10):730-731.
72. Janbaz KH, Gilani AH. Studies on preventive and curative effects of berberine on chemical-induced hepatotoxicity in rodents. Fitoterapia 2000; 71(1):25-33. 29.
73. Harman AW. The effectiveness of antioxidants in reducing paracetamol-induced damage subsequent to paracetamol activation. Res CommunChemPatholPharmacol 1985; 49(2):215-228.
74. Venukumar MR, Latha MS. Effect of Cosciniumfenestratum on hepatotoxicity in rats. Indian J Exp Biol. 2004 Aug; 42(8):792-7.
75. Baghel SS, Baghel RS, Sharma K, Sikarwar I. Pharmacological activities of Curcuma longa. Int J Green Pharm 2013; 7:1-5.
76. Pandey, A.K. and Chowdhury, A.R. (2003), Volatile constituents of the rhizome oil of *Curcuma longa* Roxb. from central India. Flavour Fragr. J., 18: 463-465. https://doi.org/10.1002/ffj.1255.
77. Mangla, Mohit&Shuaib, Mohd& Jain, Jainendra&Kashyap, Minakshi. (2010). In-vitro evaluation of antioxidant activity of Curcuma longa Roxb. Int J Pharm Sci Res. 1.
78. Karmakar I, Dolai N, Bala A, Saha P, Sarkar N, Haldar PK. Scavanging activity of C. caesia rhizome against reactive oxygen and nitrogen species. Orient Pharm Exp. Med Springer 2011; 221-28.
79. Krishnaraj, Mannangatti&Manibhushanrao, K & N, Mathivanan. (2010). A comparative study of phenol content and antioxidant activity between non-conventional Curcuma longa Roxb. and Curcuma amadaRoxb. International Journal of Plant Production. 4. 169-174.