

A Comprehensive Review on Hepatoprotective Activity of the Selected Medicinal Plants

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Article history:

Received June 28th, 2016;
Approved July 15th, 2016;
Available online: Aug 2st,
2016.

Keywords:

Xenobiotics,
Hepatoprotective,
Detoxifying, Herbal drugs.

Abstract

Liver is considered to be one of the most vital organs that functions as a centre of metabolism of nutrients such as carbohydrates, proteins, lipids and excretion of waste metabolites. Additionally, it is also handling the metabolism and excretion of drugs and other xenobiotics from the body thereby providing protection against foreign substances by detoxifying and eliminating them. Hepatic disease (Liver disease) is a term that affects the cells, tissues, structures, or functions of the liver. A number of herbal drugs show promising hepatoprotective activities in acute and chronic liver damage. In recent years most of the people are showing interest in traditional system of medicine, and most of the products are making with natural or herbal products, from tooth paste to medicine. In medicine the natural products play an important role because of their safety, efficacy and cost effectiveness. Medicinal plants may serve as a vital source of potentially useful new compounds for the development of effective therapy to combat a variety of liver problems. The aim of this review is to elucidate the list of hepatoprotective medicinal plants.

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Introduction

Herbal drugs are more widely used than allopathic; drugs as hepatoprotective because of them are inexpensive, better cultural acceptability, better compatibility, with the human body and minimal side effects. These herbal drugs have shown the ability to maintain the normal functional statuses of the liver with or without fewer side effects. The liver plays an astonishing array of vital functions in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction. Therefore, maintenance of a healthy liver is essential for the overall well being of an individual. Liver cell injury caused by various toxicants such as certain chemotherapeutic agents, carbon tetrachloride, thioacetamide etc., chronic alcohol consumption and microbes is well-studied. Among the many diseases that can affect the liver the most common is 'viral hepatitis' (Inflammation of liver caused by viral infection). Hepatitis can be caused by drugs, viruses, bacteria, mushrooms, parasites like amoebas or giardiasis. Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. Several Indian medicinal plants have been extensively used in the Indian traditional system of medicine for the management of liver disorder. The use of natural remedies for the treatment of liver diseases has a long history and medicinal plants and their derivatives are still used all over the world in one form or the other for this purpose. Scientific evaluation of plants has often shown that active principles in these are responsible for therapeutic success. A large number of medicinal plants have been tested and found to contain active principles with curative properties against a variety of diseases. Liver protective plants contain a variety of chemical constituents like phenols, Coumarins, Lignans, essential oil, monoterpenes, carotinoids, glycosides, flavonoids, organic acids, lipids, alkaloids and xanthenes. Therefore a large number of plants and formulations have been claimed to have hepatoprotective activity so the development of plant based hepato protective drugs has been given importance in the global market. This review article has been presented to enumerate some plants that have hepatoprotective properties such as *Abelmoschus moschatus*, *Ageratum conyzoides*, *Ardisia solanacea*, *Arisaema leschenaultia*, *Callicarpa macrophylla*, *Capparis spinosa*, *Cassia auriculata*, *Chenopodium album*, *Chrysophyllum albidum*.

1. *Abelmoschus moschatus*

The *Abelmoschus moschatus* seed belong to family Malvaceae is cultivated in most places of India. The roots, leaves (rarely), and seeds of ambrette are considered valuable traditional medicines. The bitter, sweet, acrid, aromatic seeds are used as a tonic and are considered aphrodisiac, ophthalmic, cardiogenic, digestive, stomachic, constipating, carminative, pectoral, diuretic, stimulant, antispasmodic, deodorant, and effective against intestinal complaints, stomatitis; and diseases of the heart, allays thirst and checks vomiting. It also shows protective mechanism in Respiratory troubles and asthma Antispasmodic Itch [1] antioxidant, antimicrobial and free radical scavenging activity [2]. Alcoholic extract of *Abelmoschus moschatus* seed contains Flavonoid, Total phenol compounds, Nitrogenous compound and Resins while aqueous extract contains only Flavonoid, Total phenol compounds, and Nitrogenous compound other compound such as Alkaloids, Saponine, Tannins, Glycosides are absent.

The seed etanolic as well as aqueous extract of *Abelmoschus moschatus* was studied for the hepatoprotective activity against paracetamol induced hepatotoxicity. Paracetamol induce hepatotoxicity was evaluated by an increase ($P < 0.05$) in serum AST, ALT, ALP activity and bilirubin level Paracetamol hepatotoxicity was manifested by an increase ($P < 0.05$) lipid peroxidation, depletion of reduced glutathione (GSH) and catalase activity in liver tissue. Administration of etanolic as well as aqueous plants extract. [300mg/kg body weight of rat] protects the paracetamol

induced lipid peroxidation, restored altered serum marker enzymes and antioxidant level towards normal. The ethanolic extract was found more significant than the aqueous extract [3].



Fig: 1 *Abelmoschus moschatus*

2. *Ageratum conyzoides*

Ageratum conyzoides (AC) has been used in various parts of Africa, Asia, and South America for curing various diseases. [4], as purgative, febrifuge, for ophthalmia, colic, treatment of ulcers, and wound dressing. The antienteralgic and the antipyretic properties of the plant were also reported. In some African countries, the plant has been popular use for skin diseases, wound healing, mental and infectious diseases, headaches and dyspnea, [5] and used in traditional medicine for its anti-asthmatic, antispasmodic and haemostatic effects, [6] uterine troubles, pneumonia by rubbing them on the chest of the patient.[7] consist of Mono and Sesquiterpenes [8-10], Chromene, Chromone, Benzofuran, and Coumarin, Flavonoids[11], Triterpene and Sterols [11-15], Cardiovascular Activities [16-18], Analgesic and Anti-inflammatory Activities [19], Antibacterial and Wound Healing Properties[21-22] Radioprotective Activity[23], Anthelmintic and Nematicidal Activity [24], Insecticidal activity [25].

The methanolic extract of aerial parts of *Ageratum conyzoides* was used for evaluation of the hepatoprotective activity against ccl4 induced hepatotoxicity wstar albino rats at the doses of 200 and 400mg/kg with standard drug silymarin (100mg/kg,p.o) were administered three times at 12h intervals and then CCl₄ (1ml/kg) was administered to all the groups except normal control for 2 days. The hepatoprotective activity was assessed by using various biochemical parameters like SGOT, SGPT, ALP, γ -GT, TP and total bilirubin along with histopathological studies were observed after 36h of CCl₄ treatment and the methanolic extract shows significant protection against ccl4 induced hepatocellular injury [26].



Fig: 2 *Ageratum conyzoides*

3. *Ardisia solanacea*

Ardisia solanacea is a species of the genus *Ardisia* [27] found throughout tropical and subtropical regions of the world. Several of those species have been used as ornamental plants, medicines and food. This plant has stimulant and carminative properties. The plant is applied in the treatment of diarrhea, dysmenorrhea, gout, mental disorder, rheumatic arthritis, skin sore and vertigo. Roots have antibacterial activity. Other species of the *Ardisia* have been reported for their cytotoxic, thrombolytic and antioxidant properties.

The hepatoprotective activity was investigated with o alcoholic extract of *Ardisia solanacea* leaves against carbon tetrachloride (CCl₄) induced hepatotoxicity. Alteration in the levels of biochemical markers of hepatic damage like SGOT, SGPT, ALP, Billirubin and Protein were tested in both CCl₄ treated and untreated groups. CCl₄ (1ml) has enhanced the SGOT, SGPT, ALP and Total Billirubin where decrease in total protein level in liver. Treatment of alcoholic extract of *Ardisia solanacea* (200mg/kg) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner. The study suggested that *Ardisia solanacea* alcoholic leaf extract possessed hepatoprotective activity [28].



Fig: 3 *Ardisia solanacea*

4. *Arisaema leschenaultia*

Arisaema leschenaultii (B.) AL. (Family Araceae) is commonly known as Dhei or Cobra Lilly. It is widely distributed over the greater part of India on the hills of Assam, Karnataka, Kerala and Tamilnadu. Different parts of plant are traditionally used in Ayurveda for the treatment of urinary diseases, colitis, eczema, purging, gonorrhoea, piles, haemorrhoids, syphilis, roundworm, fistula and sinus [29]. The whole plant of this species has been reported to show antiseptic property in buffaloes, used as abortifacient and contraceptives for pig and cattle and also reported the method of preparing contraceptives from this plant.

Evaluate the hepatoprotective potential of ethanolic extract of *Arisaema leschenaultii* blume tuber against experimentally induced hepatotoxicity models in swiss albino mice. Silymarine was given as reference standard. The ethanolic extract of tuber of *Arisaema leschenaultii* blume have shown very significant hepatoprotection against paracetamol induced hepatotoxicity in swiss albino mice in reducing serum total bilirubin, SALP, SGPT, SGOT levels and liver homogenates LPO, SOD, CAT,GSH levels[30].

Fig: 4 *Arisaema leschenaultia*

5. *Callicarpa macrophylla*

Callicarpa macrophylla Vahl. (Fam. Verbenaceae) erect shrub which is globally distributed across [31]. The plant is used in Ayurveda and other folk medicines for the treatment of different diseases and disorders such as tumour, polydipsia, diarrhoea, diabetes, dysentery, fever and as a blood purifier. Glycosides, steroids, flavonoids, fatty acids, fixed oils etc. are present in the plant. The present study was designed to evaluate the pharmacognostical parameters of the stem of the plant. The stem of *C. macrophylla* consists of Glycosides, Flavonoid, Tannins, Carbohydrates.

Evaluates the hepatoprotective activity of the aqueous alcoholic (60%) extract of the aerial parts of *Callicarpa macrophylla* (Verbenaceae) against Paracetamol and carbon tetrachloride induced hepatotoxicity. Hepatoprotective activity of the extract was studied against Paracetamol (3 g/kg b.w./p.o. 3 days) and carbon tetrachloride (2 ml/kg, b.w. /S.C. 4 days) induced hepatotoxicity. Standard drug was used for hepatoprotection (Silymarin 25 mg/kg, b.w./p.o.). Treatment of animals with hydro-alcoholic extract of aerial parts of *C. macrophylla* significantly ($p < 0.05$) decreased the levels of SGOT in serum which is an indicative of hepatoprotective activity. Also brought down was the level of serum glutamic pyruvic transaminase (SGPT) significantly ($p < 0.05$ in 200 mg/kg b.w. and $p < 0.01$ in 100 mg/kg b.w. doses). Other than these parameters, the level of Bilirubin (Total and Direct) and histopathological studies were also indicative of hepatoprotective property of the plant extract. In conclusion, it is observed that hydro-alcoholic extract of aerial parts of *C. macrophylla* possess hepatoprotective property which was evident by biochemical parameters and histopathological reports [32].

Fig:5 *Callicarpa macrophylla*

6. *Capparis spinosa*

Capparis spinosa (CS) is a plant belonging to the Capparidaceae family. According to ethnopharmacological data collected in the southeastern region of Morocco, CS is alleged to possess a hypoglycaemic effect, which has been experimentally demonstrated [33-35]. Furthermore, it has been reported that some species of the genus *Capparis* possess molluscicidal activity [36], chonroprotective effect [37] and in vitro antitumour effect [38]. Protective action of *C. spinosa* ethanolic root bark extract was evaluated in this study in an animal model of hepatotoxicity, which was induced by carbon tetrachloride. Healthy male mice 30-35 g body weight, 6-8 week old) were

divided into 7 groups. Group 1 was normal control group; Group 2, the hepatotoxic group was given CCl₄; Group 3 was administered olive oil (vehicle); Groups 4-6 received different doses of ethanolic root bark extract (100, 200 & 400 mg/kg) with CCl₄; Group 7 was administered overdose of the extract (800 mg/kg). The parameters studied were alanine transaminase and aspartate transaminase activities and duration of sleep. The hepatoprotective activity was also supported by histopathological studies of liver tissue. Results of the biochemical studies of blood samples of CCl₄ treated animals showed significant increase in the levels of serum enzyme activities, reflecting the liver injury caused by CCl₄. whereas blood samples from the animals treated with ethanolic root bark extracts showed significant decrease in the levels of serum markers, indicating the protection of hepatic cells. The results revealed that ethanolic root bark extract of *C. spinosa* could afford significant dose-dependent protection against CCl₄ induced hepatocellular injury [39].



Fig: 6 *Capparis spinosa*

7. *Cassia auriculata*

Cassia auriculata L. commonly known as tanner's cassia, also known as “avaram” in Tamil language is a shrub belongs to the Caesalpiniaceae family. The shrub is especially famous for its attractive yellow flowers which are used in the treatment of skin disorders and body odour. It is widely used in traditional medicine for rheumatism, conjunctivitis and diabetes. It has many medicinal properties. Its bark is used as an astringent, leaves and fruits have anthelmintic property, seeds used to treat eye troubles and root employed in curing skin diseases [40]. It is also used for the treatment of ulcers, leprosy and liver diseases [41]. The antidiabetic, hypolipidemic [42] hepatoprotective effects of *Cassia auriculata* have been reported. The flower and leaf extract of *Cassia auriculata* is shown to have [43] Anti diabetic [44] Hepatoprotective [45] Antibacterial [46] Antipyretic [47] Antioxidant [48] Anthelmintic potential [49] Diuretic [50] Antiulcer and antioxidant activities.

The aqueous (100 mg/kg p.o.), methanolic (100 mg/kg p.o.) and petroleum ether (50 mg/kg p.o.) extracts of the flowers of *Cassia auriculata* Linn, (Caesalpinaceae) were tested for their hepatoprotective activity against paracetamol induced hepatotoxicity in albino rats. Silymarin at a dose of 25 mg/kg i.p. was used as standard. The degree of protection was measured by using biochemical parameters like serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase (ALP), direct bilirubin and total bilirubin. The histopathological studies were also conducted. The aqueous and methanolic extracts of the flowers showed a significant hepato protective activity comparable with those of the standard (Silymarin)[51].



Fig: 7 *Cassia auriculata*

8. *Chenopodium album*

Chenopodium album Linn. (Chenopodiaceae) is an annual shrub distributed throughout the world and is used as folk medicine. It has been found to have flavonoids (phenolic amide), saponins (cinnamic acid amide), alkaloids (chinalbin, apocortinoid, xyloside), phenols and lignans as active phytoconstituents. It has been found to have antipyretic, antinociceptive [52] and sperm immobilizing activity [53]. This plant has also been used to treat various nutritional deficiencies. It was also shown to have sedative and refrigerant properties and people have used the poulticed leaves to soothe burns. The tender shoots are eaten raw in salads or with curd. They are also cooked as vegetables and are also used as fodder [54]. It is evaluated for its Hepatoprotective [55-56] Spasmolytic, analgesic [57] Antimicrobial anthelmintic [58] Anti-inflammatory [59] and anticancerous (breast cancer) [60] efficacy. Hepatoprotective activities of dried whole plant of *Chenopodium album* Linn, in acetone and methanol solvent mixture extracts, (in 1:1 ratio) against paracetamol induced hepatic injury was studied. Hepatic injury was achieved by injecting 2.5ml/kg of paracetamol in equal proportion with dimethylsulfoxide (DMSO) through oral route. Acetone and Methanolic extract at dose levels of 200 and 400 mg/kg offered significant ($P < 0.001$) changes. Hepatoprotective action by reducing the serum marker enzymes like serum glutamate oxaloacetate (SGOT), serum glutamate transaminase (SGPT). They have also reduced the elevated level of serum alkaline phosphatase (ALP), serum acid phosphatase (ACP) and serum bilirubin. Reduced enzymic and nonenzymic antioxidant levels and elevated lipid peroxide level were restored to normal by administration of methanol and acetone extract of *Chenopodium album* Linn. Histopathological studies further confirmed the hepatoprotective activity of these extracts when compared with Paracetamol treated control groups. The result obtained were compared with silymarin (100mg/kg; oral), the standard drug. In conclusion Acetone and Methanol extract at (400mg/kg, oral) showed significant $p < 0.001$ hepatoprotective activity similar to that of the standard drug, Silymarin. [61].



Fig: 8 *Chenopodium album*

9. *Chrysophyllum albidum*

Chrysophyllum albidum G. belongs to the sapotaceae family and used in folklore in the treatment of yellow fever, malaria, diarrhea, vaginal and dermatological infections. The bark is used for the treatment of malaria and yellow fever, while the leaf is used as an emollient and for the treatment of skin eruption, stomachache and diarrhea [62]. The cotyledons from the seeds of *C. albidum* are used as ointments in the treatment of vaginal and dermatological infections, fruit pulp is rich in vitamin C and iron and an excellent source of raw material for industries [63]. Tannins, flavonoids, terpenoids, proteins, carbohydrates and resins are the phytochemicals that Eleagnine, tetrahydro-2-methylharman and skatole have been isolated from this plant and eleagnine was the main compound responsible for its antimicrobial activity [64]. The seed cotyledon has been reported to possess anti-hyperglycemic and hypolipidemic effects [65].

The leaf extract of *Chrysophyllum albidum* was studied for hepatoprotective activity against rats with induced liver damage by carbon tetrachloride (CCl₄). The rats were divided into five groups of eight rats per group. Animals of group A served as normal and were given only vehicle (distilled water) for 7 days. Animals of group B (positive control) were administered with vehicle on the first four days, and with the vehicle and CCl₄ on the fifth, sixth and seventh day. The animals of groups C, D and E were respectively administered with 500, 1000 and 1500 mg/kg of extract & distilled water for the first four days, and with distilled water, extract and CCl₄ on the last three days. Animals were subsequently anaesthetized and blood samples were collected for alanine amino transferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP), total bilirubin, total protein and albumin assays; liver organ was isolated and processed for histopathological studies. The results showed that the levels of AST, ALT, ALP and total bilirubin were significantly higher in rats treated with CCl₄ indicating liver injury, while these parameters were reduced significantly ($p < 0.05$) after treatment of rats with the extract. The hepatoprotective activity of *C. albidum* was also supported by histopathological studies of liver tissue. The liver tissue of rats in the group treated with CCl₄ showed marked centrilobular fatty degeneration and necrosis while the groups treated with plant extract showed signs of protection against this toxicant as evidenced by the absence of necrosis [66].



Fig: 9 *Chrysophyllum albidum*

10. *Clitoria ternatea*

Clitoria ternatea (Family- Leguminosae, previously known as Papilionaceae), a perennial twining herb, Various parts of *C. ternatea* have been reported to have tranquilizing property, anti-inflammatory, analgesic, antipyretic, and immunomodulatory activities [67]. The flavonol glycoside present in roots is reported to have antibacterial activity [68]. Considering the high economical and

pharmacological importance of secondary metabolites of this plant, industries are deeply interested in utilizing this plant in tissue culture technology. *C. ternatea* has been reported to have hepatoprotective [69], antihyperlipidemic [70] and immunoinhibitory activities. The organic solvent extracts of *C. ternatea* could be used as antimicrobial agents for the control of infectious diseases.

The hepatoprotective activity of *C. ternatea* against experimentally induced liver injury was evaluated. The hepatoprotective effect against paracetamol-induced liver toxicity in mice with the methanolic extract of *C. ternatea* leaf was measured by monitoring the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin along with histopathological analysis. The results of the paracetamol-induced liver toxicity experiments showed that mice treated with the ME of *C. ternatea* leaf (200 mg/kg) showed a significant decrease in ALT, AST, and bilirubin levels, which were more elevated in the paracetamol group ($p < 0.01$). *C. ternatea* leaf extract therapy also showed protective effects against histopathological alterations. Histological studies supported the biochemical findings and a maximum improvement in the histoarchitecture was seen. The hepatoprotective effect of *C. ternatea* leaf extract was confirmed against the hepatotoxicant, paracetamol [71].



Fig: 10 *Clitoria ternatea*

11. *Givotia moluccana*

The *Givotia moluccana* is belongs to Euphorbiaceae family is Commonly in dry deciduous belt, in the slopes in forest deciduous trees branch lets white stellate tonentose. The plant parts are used as Bark Rhumantism, Fruit- skin diseases, Seed-Dandruff and psoriasis, Stem-stem and bark paste is applied and leaves are used as bandage during deep cuts, leaves and Root-Medicinal activity Alkaloids, Carbohydrates, Proteins & Amino acids, Flavonoids, Phenolics /Tannins.

Natural remedies from medicinal plants are considered to be effective and safe alternative treatment for liver injury. The present study was conducted to evaluate the hepatoprotective activity of aqueous ethanolic extract of aerial parts of *Givotia moluccana* L. in wistar rats. The study was conducted using the popular inducing agent carbon tetrachloride (0.1 ml/kg) in 1% olive oil and silymarin (20 mg/kg, p.o.) was used as reference standard in the respective model to treat for 21 days. The effect was estimated by measuring the enzymatic levels. The aqueous ethanolic extract of aerial parts of *Givotia moluccana* L. has shown very significant hepatoprotection against CCl₄-induced hepatotoxicity in wistar rats. This was evidenced by marked reduction in marker enzymes in the serum. Hepatotoxicity might be defined as any chemical agent that can be produced injury to the liver. Liver is involved with almost all the biochemical pathways to growth, fight against disease, nutrients supply, energy provision and reproduction. The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamin [72].



Fig: 11 *Givotia moluccana*

12. *Hibiscus cannabinus*

Phytochemical screening of this plant revealed the presence of phenolics, tannin, saponin, alkaloids and steroids. The plant also has rich fibre content, which serves as a good material in the paper industry. *H. cannabinus* has been reported to be anodyne, aperitif, aphrodisiac, fattening, purgative, and stomachic, as well as a folk medicine for bilious conditions, bruises.

In the present study the hepatoprotective activity of a daily oral dose (1.6g kg⁻¹) of aqueous leaf extract of *H.cannabinus* was investigated over a two week period in albino rats. Liver damage in rats was induced using carbon tetrachloride and paracetamol. This was confirmed by increased plasma transaminases activities, total bilirubin concentration and thiobarbituric acid reactive substance. Histopathological examinations substantiated this liver damage with fatty deposits, severe inflammation and severe necrosis. The aqueous leaf extract of *H. cannabinus* showed a significant ($p<0.05$) hepatoprotective activity against this damage in lowering the plasma transaminases and bilirubin concentration significantly ($p<0.05$) absents of necrosis in liver cells of rats pretreated with extract indicated a protective effect. The extract also inhibited lipid peroxidation, suggesting a possible mechanism of action. The result obtained confirm the hepatoprotective activity of *H.cannabinus* [73].



Fig: 12 *Hibiscus cannabinus*

13. *Khaya senegalensis*

Dry zone mahogany (*Khaya senegalensis*) is a medicinal plant which contains scopoletin, scoparone, limonoid, tannins, saponins and sterol. Its stem, bark and leaves are used for the treatment of several human and animal diseases such as an antisickling agent. The liquid preparation obtained by boiling the plant material in water and extracting drugs by straining the preparation is given as remedy for malaria, which can also used as an anthelmintic, emetic, emmenagogue agent and in jaundice treatment.

The hepatoprotective effect was tested in rats against carbon tetrachloride (CCl₄) induced toxicity. Hepatoprotective extracts was given intraperitoneally one hour before injection of CCl₄ (800mg/kg I.P) and compared with silymarin, a standard hepatoprotective agent Methanolic extract of the bark of *Khaya senegalensis* showed a hepatoprotective effects against CCl₄- induced hepatotoxicity, which was evidenced by the significant decrease in ALT, AST and ALP. The methanolic extract of the bark of *Khaya senegalensis* possessed strong hepatoprotective effect and protects liver against oxidative damages [74].



Fig: 13 *Khaya senegalensis*

14. *Lannea Coromandelica*

Lannea coromandelica Houtt. Merrill.(Anacardiaceae) Bark & leaves of *Lannea coromandelica* is commonly used in treating ulcerative stomatitis, dyspepsia, general debility, gout, cholera, diarrhoea, dysentery, sore eyes, leprosy, sprains, bruises, wound, elephantiasis, eruptions, snakebite, stomachache and vaginal troubles. The presence of phenolic compounds, flavonoids, triterpenoids, tannin, alkaloids was confirmed and their pharmacological study revealed anti-inflammatory, antimicrobial, wound healing, hypotensive, aphrodisiac, anticancerous activities.

Hepatoprotective activity of *Lannea coromandelica* bark extract (LCBE) at different doses (400 and 200 mg/kg) was investigated on thioacetamide induced hepatotoxicity in rats. Thioacetamide caused elevation of serum concentration of AST, ALT, ALP, serum bilirubin and also reduced serum concentration of total protein, albumin, sodium, potassium in animals as compared to control. Whereas, serum bilirubin, cholesterol, sugar and LDH content were varied with the treatments but showed higher with the only ethanolic extract at dose of 400 mg/kg. The hepatoprotective activity of the alcoholic bark extract of *L. coromandelica* might be due to the presence of phenolic groups, terpenoids and alkaloids. [75].



Fig: 14 *Lannea coromandelica*

15. *Nauclea latifolia*

Nauclea latifolia (family: Rubiaceae) commonly known as pin cushion tree is a straggling shrub or small tree native to tropical Africa and Asia. Different parts of this plant are commonly prescribed traditionally as a remedy for diabetes mellitus. The plant is also used in the treatment of

ailments like malaria, gastrointestinal tract disorders, sleeping sickness, prolonged menstrual flow, and hypertension and as a chewing stick.

Hepatoprotective effect of the ethanol extract of *Nauclea latifolia* (NL) leaf was studied in Wistar albino rats model by applying Acetaminophen as the toxicity inducer and silymarin was used as the standard drug. Levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were increased and the levels of total protein and albumin were decreased in the treated rats. NL leaf extract at (400 mg/kg, bw) dose decreased the elevated levels of the transaminases and restored the normalcy of total protein (TP) and albumin significantly. The activities of catalase (CAT), glutathione Peroxidase (GPx) and superoxide dismutase (SOD) were decreased in hepatotoxic rats but administration with NL leaf extract increased the levels of these enzymes. Histopathological studies showed the restoration of Acetaminophen induced liver damaged with NL administration. From this study it can be concluded that the NL leaf showed significant hepatoprotective action [76].



Fig: 15 *Nauclea latifolia*

Discussion

Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. The use of natural remedies for the treatment of drug- induced hepatotoxicity has a long history. CCl_4 is bio-transformed by the cytochrome *P*450 system in the endoplasmic reticulum to produce trichloromethyl free radical ($\cdot\text{CCl}_3$). This freeradical then combines with cellular lipids and proteins in the presence of oxygen to form a trichloromethyl peroxy radical, which may attack lipids on the membrane of endoplasmic reticulum faster than trichloromethyl free radical. Thus, trichloromethyl peroxy free radical leads to elicit lipid peroxidation, the destruction of Ca^{2+} homeostasis, and finally results in cell death. Generally the hepato protective agent appears to inhibit lipid peroxidation and enhance antioxidant enzyme levels in addition to the free radicals scavenging action. The efficacy of any hepato protective agent is dependent on its ability to minimize the harmful effects caused by a hepatotoxin and maintain the normal liver physiology (77). In the results of CCl_4 -treated group, the biochemical parameters revealed the change in the levels of different enzymes indicating that CCl_4 induces damage to the liver. This is usually accompanied by the elevation in the levels of different liver enzyme markers (AST, ALT and ALP) in serum which is the direct reflection of the alterations in the hepatic structural integrity (78). Liver injury by toxicants causes cellular leakage and loss of functional integrity (79). ALT is a cytoplasmic enzyme found in very high concentration in the liver and an increase of this specific enzyme indicates hepatocellular damage, while AST is less specific than ALT as an indicator of liver function (80). The elevated levels of ALT and AST in CCl_4 -treated group was significantly reduced upon treatment with the plant extracts. Histological findings also support the biochemical investigations. The liver cells of CCl_4 treated group revealed marked sinusoidal dilation and centrilobular fatty degeneration. The incidence of liver damage was reduced

after the treatment with the plant extract. Some phytochemicals that are linked with hepatic protective activity of these plants are the compounds like flavonoids, triterpenoids, saponins and alkaloids which are known to possess hepatoprotective property (81-84). Phenolic antioxidants such as flavonoids and tannins are considered to be the promising therapeutic agents for free radical pathologies due to their scavenging ability with ROS. Many enzymes are involved in scavenging peroxide free radicals (catalase, glutathione peroxidase, glutathione-s-transferase, glutathione reductase and superoxide dismutase) which have recently received much attention in connection with antioxidant property. Catalase is the enzyme which is very efficient in decomposing hydrogen peroxide and disproportionates hydrogen peroxide into water and oxygen. The liver catalase activity is depressed in all hepatotoxic animals which is in correlation with the impairment of free radical scavenger system. The studies in the extract treated rats revealed that their Catalase levels were brought back to normal. SOD has been reported as one of the most important enzymes in the enzymatic antioxidant defense system. It scavenges the superoxide anion to form hydrogen peroxide and thus diminishing the toxic effect caused by this radical. Glutathione is one of the most abundant tripeptide, non-enzymatic biological antioxidant present in the liver. It removes free radical species such as hydrogen peroxide, superoxide radicals and maintains membrane protein thiols. It is also a substrate for glutathione peroxidase (GPx). Decreased level of GSH is associated with an enhanced lipid peroxidation was observed in CCl₄ treated rats. Glutathione peroxidase is thought to be the key enzyme in defense against oxidative damages. Glutathione peroxidase levels were also relatively low in hepatoma. The diminished enzyme activities along with excess radical production may lead to many of the observed deranged properties of hepatotoxic cells. The enzyme level was brought back to normal levels in the treated animals. Glutathione-s-transferase is an enzyme which catalyses the glutathione conjugation with electrophilic compounds bio-transformed from xenobiotics including aflatoxins. They can prevent initiation of hepatotoxicity process by inactivating or detoxifying. The enzyme levels in liver were reverted back nearer to normal values in phyto extract treated animals. Glutathione reductase level is also lowered in hepatotoxic animals. The results from treated animals exhibited no significant change in lipid peroxide and antioxidant levels when compared with the values obtained in control animals. The reversal of increased serum enzymes in CCl₄-induced liver damage by the extract may be due to the prevention of the leakage of intracellular enzymes by its membrane stabilizing activity. This is in agreement with the commonly accepted view that serum levels of transaminases return to normal with the healing of hepatic parenchyma and the regeneration of hepatocytes [20]. The preliminary phytochemical studies for different plant species reveal the presence of flavanoids in their extracts with different solvents and the observed antioxidant and hepato protective activity of *these species* may be due to the presence of flavanoids.

Conclusion

Hepatotoxicity is a prime concern for patients as well as doctors, scientists and drug development agencies. However researchers have revealed several mechanisms and also the effecting factors that might be used in diagnosis of liver diseases. Medication has its own limitations with regard to their effectiveness, adverse effects and cost, plant derived compounds are an effective alternative for the treatment of liver diseases. Available literature and traditional medicinal survey illustrates that herbal drug containing different phytochemicals can have hepatoprotective property which may be due to the individual or combined effects of these phytochemicals. The exact bioactive compounds responsible for the hepatoprotective property need to be isolated and characterized for further investigation. Several Pharmaceutical companies and regulatory agencies have larger amount of pre and post clinical trial data which demonstrates the value of medicinal plants and their role in the cure of liver disorders and it was proved clinically for their safety and efficacy. This

paper discusses the causes of hepatic diseases and the underlying mechanisms of hepatoprotection using medicinal plants and the future prospects related to the isolation of bioactive phytochemical compounds can increase the efficacy in disease treatment and cure.

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