THERAPEUTIC PROPERTIES OF MEDICINAL PLANTS: A REVIEW OF THEIR DETOXIFICATION CAPACITY AND PROTECTIVE EFFECTS (PART 1)

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ABSTRACT

Modern research has shown that a wide range of plants can neutralize or detoxify toxins and protect respiratory, urinary, hepatic and neural systems from the toxic effects of drugs and chemicals. These plants included: Agrimonia eupatoria, Alhagi maurorum, Allium sativum, Alpinia galangal, Anchusa strigosa, Arctium lappa, Artemisia campestris, Asparagus officinalis, Astragalus hamosus, Bauhinia variegata, Benincas hispida, Brassica nigra, Brassica rapa, Bryonia dioica, Bryophyllum calycinum, Caesalpinia crista, Calendula officialis, Calotropis procera, Canna indica, Capparis spinosa, Capsella bursa-pastoris, Capsicum frutescens, Capsicum frutescens, Carthamus tinctorius, Carum carvi, Cassia occidentalis, Casuarina equisetifolia, Celosia cristata and Chenopodium album. This review will highlight the pulmonary, neuro-, hepato- and nephro-protective effects of these medicinal plants.

Key words: Pharmacology, toxicology, medicinal plant, protection, detoxification, liver, kidney, lung, nervous system.

INTRODUCTION

Detoxification is the process of purifying the body from compounds that have a detrimental effect on cell functions or structures. The need to cleanse and detoxify our bodies has grown as the number and quantity of poisonous compounds in the air, water, and food have increased. Modern research has shown that a wide range of plants can neutralize or detoxify toxins and protect respiratory, urinary, hepatic and neural systems from the toxic effects of drugs and chemicals [1-53]. This review will highlight the pulmonary, neuro-, hepato- and nephro-protective effects of the medicinal plants.

Agrimonia eupatoria

The hepatoprotective effects of Agrimonia eupatoria water extract (AE) was studied in chronic ethanol-induced liver injury in rats. Animals were treated orally with AE at 10, 30, 100, and 300 mg/kg/day. After chronic consumption of ethanol, serum aminotransferase activities and pro-inflammatory cytokines markedly increased, and those increases were attenuated by AE. The cytochrome P450 2E1 activity and lipid peroxidation increased after chronic ethanol consumption, while reduced glutathione concentration decreased. Those changes were attenuated by AE. Chronic ethanol consumption also increased the levels of Toll-like receptor 4 (TLR4) and myeloid differentiation factor 88 protein expression, inducible nitric oxide synthase and cyclooxygenase-2 protein and mRNA expression, and nuclear translocation of nuclear factor-kappa B, which was attenuated by AE. The results revealed that AE ameliorates chronic ethanol-induced liver injury, and that protection is likely due to the suppression of oxidative stress and TLR-mediated inflammatory signaling [54].

Alhagi maurorum

The hepatoprotective effect of Alhagi maurorum aerial parts ethanol extract was studied using Wistar albino rats. Liver injury induced in rats by carbon tetrachloride. The normal appearance of hepatocytes and correction of serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP) and total bilirubin, indicated a good protection of the extract from carbon tetrachloride hepatotoxicity. The results were compared with silymarin, the reference hepatoprotective drug [55]. Administration of 660 mg/kg of the ethanolic Alhagi maurorum extract to mice, showed a significant decrease in the level of transaminases in animals treated with a combination of...
ethanolic *Allaghi maurorum* extract plus carbon tetrachloride (CCl₄) or acetaminophen as compared to animals receiving CCl₄ or acetaminophen alone. Histopathological investigation also confirmed that, *Allaghi maurorum* extract protects liver against damage-induced either by carbon tetrachloride or acetaminophen [56, 57]. *Allaghi maurorum* extract (oral daily 100mg/kg body weight) in rats protect liver enzymes, oxidation status (MDA and GSH), fucosidase tumor marker and risk lipid ratio [58].

**Allium sativum**

Garlic administration (*Allium sativum*) has some beneficial effect in preventing heavy metal (nickel and chromium VI) induced alteration in lipid profile [59]. Metwally investigated the effect of treatment with garlic oil (*Allium sativum*) on some heavy metal (copper and zinc) toxicity in *Oreochromis niloticus*, the concentration of CuSO₄ was 300 mg/kg diet and ZnSO₄ 400 mg/kg diet. Garlic oil was added with concentration of 250 mg/kg diet, the experiment was extended for three months. Bioaccumulation of copper and zinc were recorded in treated fish as monitored by the significant (P<0.01) increase in serum and liver tissues concentrations, but they were decreased significantly after treatment with *Allium sativum*. Lipid profile, triglyceride (TG), cholesterol, very low density lipoprotein (VLDL), low density lipoprotein (LDL) showed significant increase [60]. The antihepatic toxicity of garlic was investigated experimentally in rats, CrCl₃ alone increased serum levels of AST and ALT. However, garlic inhibited the hepatotoxicity of CrCl₃, and the concomitant use of garlic and CrCl₃ decreased the levels of AST and ALT when garlic used in a dose of 60 and 120 mg /kg and CrCl₃ is 8 mg /kg [61]. Garlic decreased lead contents in tissues of lead exposed chicken and rats [62, 63]. The prophylactic efficacy of garlic (*Allium sativum*) to reduce tissue lead (Pb) concentration was evaluated experimentally in goats. The concomitant use of lead acetate and garlic dry powder reduced lead concentration considerably, which was indicating the potential activity of garlic against lead toxicity in goats [64].

**Alpinia galangal**

Qureshi, et al reported that the methanolic extract of *Alpinia galangal* reduced the cytological and biochemical changes induced by cyclophosphamide in mice [65].

**Anchusa strigosa**

The aqueous and ethanolic extracts of *Anchusa strigosa* were studied to inhibit aryl hydrocarbon hydroxylase activity (AHH) and 3-H-benzo [a] pyrene (3H-BP) binding to rat liver microsomal protein. The aqueous extracts showed no inhibitory effect while the ethanolic extracts exhibited strong inhibitory effect on both AHH and 3H-BP binding to the microsomal protein [66].

**Arctium lappa**

The chloroform extract fraction of the roots protected animals from chronic gastric ulceration by reducing gastric acid secretion via inhibition of gastric H⁺, K⁺-ATPase [67]. Oral administration of 100 mg/kg daily of *Arctium lappa* powder for 7 days in dextran sulfate induced colitis in mice prevented mucosal edema, submucosal erosions, ulceration, inflammatory cell infiltration and colon damage. In addition, immunohistochemistry analysis showed that the levels of the inflammatory cytokines, IL-6 and TNF-α were also decreased in *Arctium lappa* -treated groups [68]. Oral (1% in drinking water, or 400 mg/d) administration of inulin (one of the constituents of *A. lappa*) in rats was found to ameliorate DSS-induced colitis. It also induced an acidic environment (pH < 7.0) from the cecum to the left colon and increased lactobacilli counts. In addition, it increased the number of fecal bifidobacteria and lactobacilli in the cecal content of rats [69-70]. Burdock was shown to suppress the CCl₄ or acetaminophen-intoxicatated mice as well as the ethanol plus CCl₄-induced rat liver damage. The underlying hepatoprotective ability of burdock could be related to the decrease of oxidative stress on hepatocytes by increasing glutathione (GSH), cytochrome P-450 content and NADPH-cytochrome C reductase activity and by decreasing malondialdehyde (MDA) content, hence alleviating the severity of liver damage based on histopathological observations [71, 72].

**Artemisia campestris**

The anti-venomous activity of *Artemisia campestris* leaves extracts against the scorpion Androctonus australis garzonii and the viper Macrovipera lebetina venoms was examined. Assays were conducted by fixing the dose of extract to 3 mg/mouse, while the doses of venom were variable. A significant activity with respect to the venoms of scorpion Androctonus australis garzonii for the ethanolic extract was detected, and a significant neutralizing activity of the dichloromethane extract against the venom of a viper Macrovipera lebetina was obtained [73]. The effect of the aqueous dry leaves’ extract of *Artemisia campestris* on hemodynamic variations induced by Buthus occitanus tunetanus venom was assayed in pregnant and non pregnant rats. The results showed that the venom induced hypertension magnitude was much important in pregnant rats (maximal of 156% of baseline) than in cycling ones (maximal of 143.9% of baseline). When injected alone, the aqueous leaves extract of *A. campestris* induced a progressive significant diminishing of the mean arterial pressure. This effect did completely abolish the venom induced hypertensive shock, when envenomed rats were pretreated with the extract. The aqueous extract of *A. campestris* leaves prevented the induced hypertensive phase induced by the scorpion venom, probably mediated by adrenergic pathway [74].
**Asparagus officinalis**

The effects of cooked whole asparagus and its purified bioactive, rutin, were studied on colitis symptoms and disease progression in mice. C57BL/6 mice were fed a basal diet supplemented with 2% asparagus or 0.025% rutin for 3 weeks. Colitis was induced by 2% dextran sodium sulfate in drinking water for 7 days. Asparagus diet was determined to contain higher antioxidant capacities than rutin diet through antioxidant assays. During active colitis, consumption of asparagus alleviated some clinical symptoms (stool consistency, stool blood, and spleen hypertrophy) of colitis. In recovery, asparagus-fed mice were improving in terms of regenerating crypts, surface epithelial, and goblet cells, potentially due to its rutin content [75]. The protecting effect of asparagus on the rat liver injured by CCl4 (5%) poured into the stomach was investigated in rats. Compared with control, the contents of serum glutamic-pyruvic transaminase (SGPT) and malondialdehyde (MDA) were lower, and the content of liver superoxide dismutase (SOD) was higher in asparagus group [76].

**Astragalus hamosus**

The hepatoprotective activity of flavonoid rhamnocitrin 4'-β-D-galactopyranoside (RGP) obtained from leaves of *Astragalus hamosus* L. was documented against N-diethylnitrosamine (DENA)-induced hepatic cancer in Wistar albino rats [77]. The effects of rhamnocitrin 4'-β-D-galactopyranoside (RGP), isolated from *A. hamosus* were evaluated on isolated rat brain synaptosomes, prepared by Percoll reagent and on rat hepatocytes, isolated by two-stepped collagenase perfusion. In synaptosomes, RGP had statistically significant protective effect, similar to those of silymarin, on 6-hydroxydopamine-induced oxidative stress. These results correlate with the protective effects of kempferol and rhamnocitrin on oxidative damage in rat pheochromocytoma PC12 cells. In rat hepatocytes, the effect of RGP on two models of liver toxicity: Bendamustine and cyclophosphamide showed that the compound had statistically significant cytoprotective and antioxidant activity, similar to those of silymarin [78].

**Bauhinia variegata**

The antioxidant and nephroprotective effect in gentamicin-induced nephrotoxicity of the Ethanolic and aqueous extracts of root of *Bauhinia variegata* at a dose of 400 mg/kg bw was evaluated by gentamicin and cisplatin induced nephrotoxicity in rats. Both extracts showed nephroprotective activity in both gentamicin and cisplatin induced nephrotoxicity models as evident by decrease in serum creatinine, serum urea, urine creatinine and BUN levels in extract treated groups which was elevated by gentamicin and cisplatin in the respective models, which also confirmed by histopathological study [80]. The ethanolic extract of the stem of *B. variegata* showed chemoprevention against N-nitrosodiethylamine induced experimental liver tumor in rats. Ethanolic extract suppressed liver tumor induced by N-nitrosodiethylamine as revealed by decrease in N-nitrosodiethylamine induced elevated level of serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase, alkaline phosphatase, total bilirubin, gamma glutamate transpeptidase, lipid peroxidase, glutathione peroxidase and glutathione-S-transferase [27]. The ethanolic extract of the stem bark of *B. variegata* (at the dose of 100 and 200 mg/kg orally) showed hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in rats, it decreased the level of AST, ALT, ALP and GGT [81].

**Benincasa hispida**

The nephroprotective activity of hydro-alcoholic extract of *Benincasa hispida* whole fruit extract was investigated in paracetamol induced nephrotoxicity in rats. Treatment with hydro-alcoholic extract of *Benincasa hispida* whole fruit extract at doses of 200 and 400 mg/kg bw prevented the paracetamol-induced nephrotoxicity and oxidative impairments of the kidney, as evidenced by a significantly reduced in kidney weight, blood urea, blood creatinine, urinary glucose, urinary potassium level and also increased body weight, urine volume, urinary creatinine and blood total protein level. Hydro-alcoholic extract of *Benincasa hispida* whole fruit extract significantly increased the tissue GSH levels and reduced lipid peroxidation levels. Furthermore, it was confirmed by the histopathological observation that the degenerative changes caused by paracetamol were also restored by treatment with hydro-alcoholic extract of *Benincasa hispida* whole fruit extract [82]. It was also produced nephroprotective activity against mercury poisoning in rats [83].

**Brassica nigra**

The protective effect of the methanol extract of *Brassica nigra* leaves was investigated against D-galactosamine (D-GalN)-induced hepatic and nephrotoxicity in Wistar rats. The D-GalN-induced toxicity was evident from a significant increase (p < 0.001) in the serum and tissue inflammatory markers in toxic rats, when compared with the control (saline alone treated animals). The *Brassica nigra* pretreated groups (200 and 400 mg/kg bw) showed significant (p < 0.001) reduction in the D-GalN-induced toxicity as obvious from biochemical parameters. Histopathological observations confirm the
protective effect of *Brassica nigra* leaf extract by reduction in hepatic and renal tissue damage. Accordingly, the crude methanol extract of *Brassica nigra* leaf lacks inherent toxicity and exhibits hepatic and nephroprotective [84].

*Brassica rapa*

The effect of the aqueous extract of *Brassica rapa* chinensis was studied against bleomycin (BLM) induced pulmonary fibrosis. Aqueous extract of *Brassica rapa* chinensis (250, 500 mg/kg, po) showed significant protective effect against BLM induced pulmonary fibrosis in rats by normalizing the levels of glycoproteins (hexose, hexosamine and sialic acid) and improving the activity of Catalase (CAT) and Superoxide dismutase (SOD). The extract also improved pulmonary glutathione (GSH) content and depleted the lipid peroxidation levels in a dose dependent manner. The histopathological analysis also reveal the reversal of the lung architecture to near normal upon administration of plant extract [85]. The pre-treatment of rats with *Brassica rapa* juice protected the rats against CCl₄-induced hepatotoxicity. The treatment significantly reduced the serum GOT, GPT, alkaline phosphatase (ALP) and bilirubin level at a dose of 16 ml/kg bw. In addition, the juice was also replenished the lowered nonprotein sulphydryl (NP-SH) concentration in the liver tissue after CCl₄ treatment [12]. The juice administration (16 mL/kg bw) significantly lowered the phenobarbital induced sleeping, where the lower dose (8 mL/kg bw) showed an insignificant reduction in sleeping time in CCl₄-induced acute liver toxicity [86]. The protective effect of turnip root ethanolic extract (TREE) on early hepatic injuries was studied in alloxan-induced diabetic rats. TREE treatment groups received TREE (200 mg/kg) daily for 8 weeks through the gavage. TREE significantly decreased the levels of serum biomarkers of hepatic injury. Furthermore, it significantly decreased the lipid peroxidation and elevated the decreased levels of antioxidant enzymes in diabetic rats. The study also showed that histopathological changes were in agreement with biochemical findings [87]. The effect of aqueous extract of *Brassica rapa* chinensis (250, 500 mg/kg, po) against the oxidative stress induced by Tert-butyl hydroperoxide (t-BHP) in rats. The treatment with aqueous extract of *Brassica rapa* chinensis significantly combats the oxidative stress imposed by t-BHP in the hepatic tissues as evidenced by marked improvement in the antioxidant status and suppressing lipid peroxide levels. The results obtained were dose dependent with 500 mg/kg bw, dosage of *Brassica rapa* chinensis aqueous extract revealing more potential in curbing toxic insult of t-BHP [88]. The anti-fibrogenic and the therapeutic effect of turnip extracts was studied in thioacetamide (TAA)-induced liver fibrosis animal model. Anti-fibrogenic effect was demonstrated histopathologically and serologically after the animals fed with turnip extracts with synchronous TAA injections for 7 weeks. The animals fed with 20 mg/ml of turnip extracts showed the highest anti-fibrogenic effect [89]. The level of hepatic fibrosis induced by thioacetamide (TAA) was compared among TAA-turnip group, TAA group, and vehicle control group. Nodules-formed by TAA were observed; they were rarely shown in vehicle control group, observed in most area in TAA group, but only shown in periportal regions in TAA-turnip group. These results were confirmed through Masson’s trichrom stain; fibrous structures increased in TAA group (fibrosis score: 4) but significantly decreased in TAA-turnip group (fibrosis score: 2-3) [90]. Isorhamnetin 3-O-glucoside, which was contained together with isorhamnetin 3,7-di-O-glucoside in the plant leaves, suppressed increases in the plasma ALT and AST activities of mice with liver injury induced by the injection of carbon tetrachloride, but no suppression by isorhamnetin 3,7-di-O-glucoside was apparent. This result indicates that the release of glucose at the 7-position in isorhamnetin 3,7-di-O-glucoside was very important to mitigating liver injury [91]. The effect of the ethanol extract of the roots of *Brassica rapa* (EBR) to ameliorate cisplatin-induced nephrotoxicity was studied in terms of oxidative stress, as characterized by lipid peroxidation, reactive oxygen species (ROS) production, and glutathione (GSH) depletion in LLC-PK1 cells. Pretreatment of cells with EBR prevented cisplatin-induced decreases in cell viability and cellular GSH content. The effect of EBR was then investigated in rats given EBR for 14 d before cisplatin administration. A single dose of cisplatin (7 mg/kg, i.p.) caused kidney damage manifested by an elevation in blood urea nitrogen (BUN), serum creatinine, and urine lactate dehydrogenase (LDH) levels. Also, renal tissue from cisplatin-treated rats showed a significant increase in malondialdehyde (MDA) production, and in the activities of aldehyde oxidase (AO) and xanthine oxidase (XO). A significant decrease in the activities of antioxidant enzymes, such as, glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT) was observed in cisplatin-treated rats versus saline-treated normal group. In contrast, rats given EBR showed lower blood levels of BUN and creatinine, and of urinary LDH. Moreover, EBR prevented the rise of MDA production and the induction of AO and XO activities. This extract also recovered the reduced activities of GPx, SOD and CAT [92].

*Bryonia dioica*

The plant leaves extract was evaluated for its protective effect hepatotoxicity induced in rats with CCl₄. Single oral dose of 250mg/kg of different fractions extract was given to rats for 7 days. Serum activities of transaminases (ALT and AST) were used as the biochemical marker of hepatotoxicity. Histopathological changes in rat’s liver section were also examined. The results indicated that pretreatment of rats with Bryonia extract prior to induction of hepatotoxicity offered a hepatoprotective action [93].

*Bryophyllum calycinum*
The aqueous extract of the leaves possessed potent nephroprotective activity in gentamycin-induced nephrotoxicity in rats. The plant hydroalcoholic extract was also found to exert significant diuresis and antiuricilethic activity when given by oral and ip route to rats [94-96]. The plant was recorded as hepatoprotective. It was significantly lowers the enzyme SGOT, SGPT, SALP and SBLN which increased during liver injury. The juice of the leaves and the ethanolic extract of the marc left after expressing the juice were also found hepatoprotective against CCl₄-induced hepatotoxicity. It was also hepatoprotective at histopathological level [97-99]. The juice of the leaves and the ethanolic extract of the marc left after expressing were studied in rats against CCl₄-induced hepatotoxicity. It was found that they were effective hepatoprotective as evidenced by in vitro, in vivo and histopathological studies. The juice was found to be more effective than the ethanolic extract [100].

**Caesalpinia crista**

The alcoholic and aqueous extract of *Caesalpinia crista* was evaluated for protection against isoproterenol (85 mg/kg bw) induced myocardial infarction in albino rats. The heart damage induced by isoproterenol was indicated by elevated levels of the marker enzymes such as creatine kinase-isoenzyme (CK-MB), lactate dehydrogenase (LDH), serum glutamate oxaloacetic transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) in serum with increased lipid peroxide and reduced glutathione content in heart homogenates. Pretreatment with an ethanolic and aqueous extract of *Caesalpinia crista* at a dose of 400 mg/kg body wt, orally for 30 days, reduced significantly (p < 0.01) the elevated marker enzyme levels in serum and heart homogenates in isoproterenol-induced myocardial infarction. Histopathological observation revealed a marked protection by the extract in myocardial necrotic damage [101]. The hepatoprotective and antioxidant effect of the methanol extract of *Caesalpinia crista* was evaluated in albino rats. The methanolic extract of *Caesalpinia crista* at the doses of 50, 100 and 200 mg/kg and silymarin 25 mg/kg were administered to the CCl₄ treated rats. The effect of the methanol extract of *Caesalpinia crista* and silymarin on serum glutamyl pyruvate transaminase, serum glutamyl oxaloacetic acid transaminase, serum alkaline phosphatase, bilirubin, uric acid and total protein were measured in the CCl₄ induced hepatotoxicity in rats. Furthermore, the effects of the extract on lipid peroxidation (LPO), enzymatic antioxidant (superoxide dismutase and catalase), and non enzymatic antioxidant (glutathione (GSH), vitamin C and vitamin E) were estimated. The methanol extract of *Caesalpinia crista* and silymarin produced significant (p < 0.05) hepatoprotective effect by decreasing the activity of serum enzymes, bilirubin, uric acid, and lipid peroxidation and significantly (p < 0.05) increased the levels of SOD, CAT, GSH, vitamin C, vitamin E and protein in a dose dependent manner [102]. The ameliorating effect of *Caesalpinia crista* Linn. (CCME) extract on iron-overload-induced liver injury was investigated. CCME attenuated the percentage increase in liver iron and serum ferritin levels when compared to control group. CCME also showed a dose-dependent inhibition of lipid peroxidation, protein oxidation, and liver fibrosis. The serum enzyme markers were found to be less, whereas enhanced levels of liver antioxidant enzymes were detected in CCME-treated group. In presence of CCME, the reductive release of ferritin iron was increased significantly. Furthermore, CCME exhibited DPPH radical scavenging and protection against Fe⁴⁺-mediated oxidative DNA damage [103].

**Calendula officinalis**

The neuroprotective effect of *Calendula officinalis* Linn. flower extract (COE) on Monosodium glutamate (MSG)-induced neurotoxicity was evaluated in rats. Adult Wistar rats were administered systemically for 7 days with MSG and after 1h of MSG injection, rats were treated with COE (100 and 200 mg/kg) orally. At the end of the treatment period, animals were assessed for locomotor activity and were sacrificed; brains were isolated for estimation of LPO, GSH, CAT, TT, GST, Nitrite and for histopathological studies. MSG caused a significant alteration in animal behavior, oxidative defense (raised levels of LPO, nitrite concentration, depletion of antioxidant levels) and hippocampal neuronal histology. Treatment with COE significantly attenuated behavioral alterations, oxidative stress, and hippocampal damage in MSG-treated animals [104]. The neuroprotective effect of *Calendula officinalis* flower extract (COE) on 3-NP-induced neurotoxicity in rats was evaluated by observing behavioral changes, OS and striatal damage in rat brain. Adult female Wistar rats were pretreated with vehicle or COE (100 and 200 mg/kg) for 7 days, followed by cotreatment with 3-NP (15 mg/kg, intraperitoneally) for the next 7 days. At the end of the treatment schedule, rats were evaluated for alterations in sensory motor functions and short-term memory. Animals were sacrificed and brain homogenates were used for the estimation of lipid peroxidation (LPO), glutathione, total thiols, glutathione S-transferase, catalase and nitrite. A set of brain slices was used for the evaluation of neuronal damage in the striatal region of the brain. 3-NP caused significant alterations in animal behavior, oxidative defense system evidenced by raised levels of LPO and nitrite concentration, and depletion of antioxidant levels. It also produced a loss of neuronal cells in the striatal region. Treatment with COE significantly attenuated behavioral alterations, oxidative damage and striatal neuronal loss in 3-NP-treated animals [105]. The hepatoprotective effect of calendula flowers and/or thyme leave extracts on aflatoxins (AFs)-induced oxidative stress, genotoxicity and alteration of p53 bax and bcl2 gene expressions were evaluated. Animals treated with the extracts 1 week before AFs treatment showed a significant decrease in oxidative...
damage markers, micronucleated cells, DNA fragmentation and modulation of the expression of pro-apoptotic genes [106]. The hydroalcohol extract of the flowers, when given to CCl\textsubscript{4}-intoxicated liver in albino male Wistar rats at a dose of 10 ml/kg, resulted in a reduction of hepatocytolysis by 28.5 % due to reduction in glutamo-oxalate-transaminase (GOT) and glutamo-pyruvate-transaminase (GPT). Histoenzymology showed reduction of steatosis of lactate dehydrogenase (LDH), succinate dehydrogenase (SDH), cytochromoxidase (Cyox) and Mg\textsuperscript{2+}-dependent adenosine triphosphatase (ATPase) [107]. The hot water extract of C. officinalis flowers exhibited antihepatoma activity against five human liver cancer cells - HepG2/C3A, SK-HEP-1, HA22T/VGH, Hep3B and PLC/PRF/5 – with an inhibitory effect of 25–26% at a dose of 2000 µg/ml [108].

**Calotropis procera**

An aqueous ethanolic extract of *Calotropis procera* flowers was tested for its hepatoprotective effect against paracetamol-induced hepatitis in rats. Paracetamol (2000 mg/kg) has been reported to enhance SGPT, SGOT, ALP, bilirubin and cholesterol levels and reduce serum levels of HDL and the tissue level of GSH while treatment with an aqueous ethanolic extract of *C. procera* flowers (200 mg/kg and 400 mg/kg) restored the altered levels of biochemical markers to almost normal levels in a dose-dependent manner [109]. The possible hepatoprotective and nephroprotective activities of the ethanolic extract of *C. procera* root were investigated in female rats. Carbon tetrachloride (CCl\textsubscript{4}) was used for induction of hepatotoxicity and nephrotoxicity with significant (P<0.05) increase in the level of serum enzyme markers of hepatotoxicity and nonenzyme markers of nephrotoxicity. Administration of 150 and 300 mg/kg body weight (bw) of the ethanolic extract of *C. procera* root did not protect the liver and kidney from CCl\textsubscript{4} induced toxicity. Pretreatment with the extract rather potentiated the toxicity induced by CCl\textsubscript{4}. It is advised strongly that caution should be taken when ingesting alcoholic preparations of *C. procera* root [110].

The chloroform extract of *Calotropis procera* (100 and 200 mg/kg, po) showed remarkable hepatoprotective activity against paracetamol-induced hepatotoxicity as judged from biochemical parameters such as serum aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin, total protein, gamma glutamate transpeptidase (GGTP) and levels of lipid peroxides in liver, which was comparable to the activity exhibited by the reference standard Silymarin. Histopathological examination of the liver section of the rats treated with paracetamol showed intense centrilobular necrosis and vascuolisation. The rats treated with extracts with paracetamol showed sign of protection against paracetamol toxicity to considerable extent as evident from formation of normal hepatic cards and absence of necrosis and vascoles [111].

**Canna indica**

The hepatoprotective activity of methanol extract of aerial parts of *Canna indica* L. plant was evaluated against carbon tetrachloride induced hepatotoxicity. Extract at doses (100 and 200mg/kg) restored the levels of all serum parameters like SGPT, SGOT, TB which were elevated in CCl\textsubscript{4} administrated rats. A 10% liver homogenate was used for estimation of catalase, GSH content, LPO level for in vivo antioxidant status of liver. All LPO, Reduced GSH and catalase levels were observed normal in extract treated rats. Histopathology demonstrated profound necrosis, lymphocytic infiltration was observed in hepatic architecture of carbon tetrachloride rats which were found to obtain near normalcy in extract plus carbon tetrachloride administrated rats [112].

**Capparis spinosa**

Ethanolic root bark extract of *C. spinosa* (100, 200 and 400 mg/kg) afford significant dose-dependent protection against CCl\textsubscript{4} induced hepatocellular injury. 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 [113]. Treatment of the paracetamol-induced liver damage in rats with aqueous extract of *Capparis spinosa* (25, 50, 100, 200 mg/kg of body weight) for 7, 14, 21 days decreased alanine amino transferase, aspartate amino transferase activity, total bilirubin and creatinine levels in comparison with non treated group, as well as improving the damaged liver tissues with dose dependent manner [114].

**Capsella bursa-pastoris**

Capsaicin produces a protective effect in rat lung and liver by strengthening the pulmonary antioxidant enzyme defense system. Capsaicin treatment caused desensitization of the respiratory tract mucosa to a variety of lung irritants [116].

**Capsicum frutescens** and *Capsicum frutescens*

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**Carthamus tinctorius**

Hepatoprotective activity of methanolic extract of leaves of *Carthamus tinctorius* (MECT) was investigated against hepatotoxicity produced by administering a combination of two anti-tubercular drugs isoniazid and
rifampicin for 24 days by oral route in rats. MECT were administered at two graded dose (200 and 300 mg/kg po) 45 min after anti-tubercular challenge for 24 days. MECT, in all doses caused significant decrease in AST, ALT, ALP, and total bilirubin levels and elevated the level of GSH [117]. The potential protective effect of HSYA was investigated in liver fibrosis induced by carbon tetrachloride (CCl₄)-induced in rats. HSYA was given in a daily dose of 5 mg/kg intraperitoneally with concurrent CCl₄. CCl₄ treatment induced micronodular liver fibrosis with a pronounced deposition of collagen fibers. HSYA significantly reduced liver fibrosis. It down regulates α-smooth muscle actin (SMA), collagen α type 1, matrix metalloproteinases (MMP)-9, and tissue inhibitors of metalloproteinases (TIMP)-1 gene expression. This was accompanied by a decreased expression of transforming growth factor (TGF)-β1 and phosphorylation [118]. The effect of Safflower injection on the lipid peroxidation level and expression of heme oxygenase-1 of the rat liver with chronic hypoxia and hypercapnia was studied in rats. The activity of SOD of the liver in Safflower injection group was significantly higher than those in chronic hypoxia and hypercapnia for four weeks group, and the content of MDA was significantly lower. In chronic hypoxia and hypercapnia for four weeks group, there were multiple dispersed immunoreactivity cells in liver, the immunoreactivity cells were significantly decreased in Safflower injection group. Histological study revealed that there were many hepatocytes with obvious adipose degeneration. Hepatic pathological damage in Safflower injection group was lighter than that in chronic hypoxia and hypercapnia for four weeks group [119]. The protective effect of Hydroxysafflor yellow A (HSYA) was studied on inflammatory phase of bleomycin-induced pulmonary injury in mice. Three doses of HSYA (26.7, 40, 60 mg/kg/d) were intraperitoneally injected to mice consecutively for 1 week after bleomycin administration. It was found that HSYA attenuated the loss in body weight, the increase of myeloperoxidase activity and pathological changes of pulmonary inflammation caused by bleomycin. Treatment with HSYA also alleviated bleomycin-induced increase of mRNA level of tumor necrosis factor (TNF)-α, interleukin (IL)-1β and transforming growth factor (TGF)-β1 in lung homogenates. Moreover HSYA inhibited the increased activation of nuclear factor (NF)-κB and phosphorylation of p38 mitogen-activated protein kinases (MAPK) in lung tissue [120]. The effects of Safflor yellow (SY) was studied on rats of pulmonary fibrosis induced by bleomycin (BLM) and on differentiation of lung fibroblast into myofibroblast stimulated by transforming growth factor-β1 (TGF-β1). Two dose SY (intraperitoneal, 25, 50 mg/kg/d) were administered to rats treated by BLM consecutively for four weeks. SY alleviated the loss in body weight, the increase of hydroxyproline content in the lung tissues and pathologic changes of pulmonary fibrosis caused by BLM instillation. SY also prevented the increase of α-SMA positive cells and TGF-β1 expression induced by BLM. These effects were more significant with the using of high dose of SY. Moreover, SY (0.05, 0.25, 1.25 mg/ml) inhibited the expression of α-SMA during differentiation of lung fibroblast into myofibroblast stimulated by TGF-β1 [121]. The attenuated effect of Hydroxysafflor yellow A (HSYA) on acute lung injury (ALI) induced by lipopolysaccharide (LPS) administration was studied in mice. HSYA administration significantly attenuated inflammatory cell infiltration and alleviated pulmonary edema induced by LPS. Moreover, HSYA decreased NF-κB p65 nuclear translocation, inhibited proinflammatory cytokine TNF-α, IL-1β and IL-6 mRNA expression and promoted antinflammatory cytokine IL-10 gene expression following LPS injection. Pulmonary p38 MAPK phosphorylation was upregulated 4 h after LPS treatment, which could be suppressed by pretreatment with HSYA [122]. The pharmacological effect and mechanism of action of hydroxysafflor yellow A (HSYA) on acute lung injury (ALI) was studied in rats. HSYA alleviated pulmonary edema, reduce acidosis, keep PaO2 from descending, inhibit inflammatory cell infiltration, inhibit rat lung TNF-alpha and ICAM-1 mRNA expression and plasma IL-6 and IL-1beta level elevation [123].

**Carum carvi**

The renoprotective effect of aqueous extract of *Carum carvi* seeds was evaluated in experimentally induced diabetic nephropathy (DN) in rodents. The diabetic rats showed a variable increase in the serum levels of glucose, urea, creatinine, total urinary protein and microalbuminuric levels. Body weight decreased and urine volume increased in the diabetic groups. 30 and 60 mg/kg body weight of *Carum carvi* significantly decreased the levels of the biochemical parameters. High dose of *Carum carvi* aqueous seeds extract (60 mg/kg) showed renoprotection against STZ induced diabetic nephropathy in rats [124]. The renoprotective effect of *Carum carvi* essential oil (10 mg/kg of body weights orally) was also studied in diabetic rats. Diabetic rats showed an increase in the serum level of glucose, and decrease in glutathione peroxidase. 10 mg/kg body weight of *Carum carvi* oil significantly corrected these parameters. The morphological examination of untreated diabetic rats kidneys showed glomerular and tubular degeneration with massive cellular infiltration, hemorrhage in interstitial tissue and deformed renal tissue architecture. Whereas the kidney of *Carum carvi* essential oil treated rats showed marked improvement with minor pathological changes [125]. Essential oils of *Carum carvi* fruits were assayed for their hepatoprotective effect against carbon tetrachloride (CCl₄) damage. It exerted hepatoprotective effect and decreasing oxidative damage [126].

**Cassia occidentalis**

The nephroprotective activity of the 70%
hydroalcoholic extract of *Cassia occidentalis* was tested against gentamicin induced nephrotoxicity in rats. The degree of protection was determined by estimating urinary creatinine, urinary glucose, urinary sodium, urinary potassium, blood urea, serum creatinine levels and body weight of the animals. The in-vivo antioxidant activity was determined by estimating the tissue levels of GSH, SOD, catalase and lipid peroxidation. The treatment with hydroalcoholic extract of *Cassia occidentalis* (200 and 400 mg/kg body weight) markedly reduced gentamicin induced elevation of urinary sodium, potassium electrolytes, urinary glucose, blood urea and creatinine levels. It also increased the body weights. The comparative histopathological study of kidney exhibited almost normal architecture as compared to control group. The deterioration in the antioxidant parameter associated with gentamicin induced nephrotoxicity in rats was also attenuated by 70% hydroalcoholic extract of *Cassia occidentalis*. 70% hydroalcoholic extract of *Cassia occidentalis* showed a dose dependent increase in the level of GSH. However, 200 mg/kg showed 23.3% increase and 400 mg/kg showed 51.4.7% increase in GSH levels. treatment with 70% hydroalcoholic extract of *Cassia occidentalis* significantly elevated the SOD (p< 0.001) and catalase (p< 0.001) [127, 128]. The hepatoprotective effect of aqueous and aqueous-ethanolic extract (50% v/v) of leaves of *Cassia occidentalis* was studied on rat liver damage induced by paracetamol and ethyl alcohol by monitoring serum transaminase (aspartate aminotransferase and serum alanine amino transferase), alkaline phosphatase, serum cholesterol, serum total lipids and histopathological alterations. The extract of leaves of the plant produced significant hepatoprotection by restoring the liver functions [129, 130].

Chrysophanol isolated from *Cassia occidentalis* (50 mg/kg bw) and methanol fraction (COLMF) (200 mg/kg bw) were administered to rats with paracetamol induced hepatotoxicity for seven days. Oral administration of chrysophanol and COLMF significantly normalized the values of SOD, CAT, GPx, GSH, Vit-C and Vit-E. The elevated serum enzymatic levels of AST, ALT, ACP and ALP were significantly restored towards normalization by pre-treatment with chrysophanol and COLMF (p>0.05). The histopathological studies also confirmed the hepatoprotective nature of the extracts. The results of this study strongly indicate that *Cassia occidentalis* has potent hepatoprotective action against paracetamol induced hepatic damage in rats [131]. The antimitogenic potential of aqueous extract of *Cassia occidentalis* against the chromosomal aberrations (CA) produced in vivo by benzo[a]pyrene (B[a]P) and cyclophosphamide (CP) in mice was investigated. Male mice were treated with three doses of plant extract (50 mg/kg, 250 mg/kg and 500 mg/kg) for 7 days prior to the administration of single dose of mutagens (B[a]P 125 mg/kg oral; CP 40 mg/kg ip). The results indicated that *C. occidentalis* was not genotoxic per se and exerted no other toxic signs and symptoms in treated animals. The chromosomal aberrations produced by B[a]P and CP were significantly reduced (p<0.001) by *C. occidentalis* pre-treatment. Furthermore, animals treated with plant extract showed a reduced level of cytochrome P450 and elevated levels of glutathione S-transferase activity and glutathione content in the liver [132].

**Casuarina equisetifolia**

The nephroprotective activity of methanolic extract of *Casuarina equisetifolia* leaves was studied in gentamicin-induced nephrotoxicity in Wistar rats. Subcutaneous injection of rats with gentamicin (80 mg/kg body weight/day) for six consecutive days induced marked acute renal toxicity, manifested by a significant increase in serum urea, creatinine and uric acid levels, along with a significant depletion of serum potassium level. Also oxidative stress was noticed in the renal tissue as evidenced by a significant decrease in glutathione level, superoxide dismutase, glutathione-S-transferase activities, with a significant increase in malondialdehyde and nitric oxide levels when compared to control group. Administration of plant extract at a dose of 300 mg/kg once daily for 4 weeks restored normal renal functions and attenuated oxidative stress. *Casuarina equisetifolia* leaves extract ameliorates gentamicin-induced nephrotoxicity and oxidative damage by scavenging oxygen free radicals, decreasing lipid peroxidation and improving intracellular antioxidant defense [133]. The methanol extracts of *Casuarina equisetifolia* were studied for hepatoprotective activity against liver damage induced in Swiss albino rats by carbon tetrachloride (*CCL*_4). It was found that the methanol extract of *C. equisetifolia* at a dose of 500 mg/kg body weight exhibited moderate protective effect by lowering the serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and cholesterol to a significant extent. The hepatoprotective activity was also supported by attenuation of the histopathological changes associated with *CCL*_4 induced hepatotoxicity [134].

**Celosia cristata**

A new triterpenoid saponin, semenoside A, was isolated from *Semen Celosia cristatae*. The hepatoprotective activity of semenoside A with an oral dose of 1.0, 2.0 and 4.0 mg/kg, respectively, were investigated by carbon tetrachloride (*CCL*_4)-induced hepatotoxicity in mice. The results indicated that it had significant hepatoprotective effects (p < 0.01) [135]. Crystatain saponin exhibited significant hepatoprotective effect on carbon tetrachloride (*CCL*_4) - and N, N-dimethylformamide (DMF)-induced hepatotoxicity in mice, which were evidenced by significant decreases in the values of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) of serum and histopathological examinations compared to controls [136].
**Chenopodium album**

The antioxidant and hepatoprotective efficacy of *Chenopodium album* extract (300 mg/kg and 450 mg/kg) was evaluated in carbon tetrachloride (CCl₄) induced hepatotoxicity in rats. *Chenopodium album* extract was found to exhibit excellent antioxidant and free radical scavenging activity, when compared with ascorbic acid, in *in vitro* studies. *Chenopodium album* extract at a dose of 450 mg/kg showed inhibition of elevated biochemical parameters associated with induction of hepatotoxicity by CCl₄. It was also attenuated histopathologic effects of CCl₄ [137]. Alcoholic and aqueous extracts of the aerial parts of *Chenopodium album* at the doses of 200 and 400 mg/Kg were evaluated for hepatoprotective activity against paracetamol induced hepatotoxicity. The aqueous extract at a dose of 400 mg/kg was found to be more potent when compared to Silymarin. The alcoholic and aqueous extracts of *Chenopodium album* significantly restore physiological integrity of hepatocytes. Aqueous and alcoholic extract did not show any sign of toxicity up to oral dose of 5 g/Kg in mice [138]. The hepatoprotective activities of dried whole plant of *Chenopodium album* Linn, acetone and methanol extracts in ratio of (50:50), was also evaluated against paracetamol induced hepatic injury. Acetone and methanol extract at dose of 400mg/kg orally, showed significant (p<0.001) hepatoprotective activity, their effect was similar to the standard drug, silymarin [139].

**CONCLUSION**

The paper reviewed the pulmonary, neuro-, hepat- and nephro-protective effects of the medicinal plants to open the door for their utilization in medical applications as a result of effectiveness and safety.

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