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Review Article

HEPATOPROTECTIVE ACTIVITY OF SOME MEDICINAL PLANTS: A REVIEW

Towseef Hassan [1]*, Veerakumar D [1], Insha Naseer [1], Anandhi N [2]
[1]Ph. D Research Scholars, Department of Zoology, Annamalai University, Annamalainagar, Tamil Nadu, India
[2]Ph. D Research Scholar, Department of Biochemistry and Biotechnology, Annamalai University, Annamalai Nagar, Tamil Nadu, India
*Corresponding Author Email: iamtowseef19@gmail.com

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ABSTRACT

Liver is an essential organ. Its plays a main function in metabolism and excretion of xenobiotics from the body. Moreover it is also coping with the metabolism and excretion of medicine and other xenobiotics from the frame there with the aid of supplying safety towards foreign substances by using detoxifying agents and putting them off. The most important capabilities of the liver are carbohydrate, protein, fat metabolism and detoxification, secretion of bile and storage of vitamins. In this examine, on line databases together with web of Science, Pub Med, Scopus, and Science Direct were looked for papers. Liver illnesses are first rate problem in worldwide. Liver damage or liver disorder is a major fitness troubles those demanding situations no longer most effective health care professionals but also the pharmaceutical industry and drug regulatory companies. Liver disease (Hepatic disease) is a term that impacts the cells, tissues, systems or factures of the liver. Liver cell harm resulting from various toxic chemical compounds (along with anti-biotic, chemotherapeutic retailers, thioacetamide and paracetamol and so forth.), excessive alcohol intake and microbes are nicely studied. A number of natural tablets show promising hepatoprotective activities in acute and chronic liver damage. In medication the natural products play an essential role because of their protection, efficacy and price effectiveness. Medicinal plants might also function as vital source of doubtlessly useful for the development of effective therapy to fight several liver troubles. In this review we centred on the number of medicinal plants for protective effect in liver diseases.

Keywords: Liver, Xenobiotics, Detoxification, Liver illnesses, Plant extracts

INTRODUCTION

The Greek word for liver is hepar, so medicinal phrases related to liver often begin with hepato or hepatic. The liver is the second largest organ in our body; weighing approximately 1.5 kg in adults, representing 2 % of the Total Body Weight (TBW). It is positioned beneath your rib cage at the proper aspect. It is located inside the proper upper quadrant of the stomach. It is protected by way of Glisson's capsule, a visceral continuation of the peritoneum. The liver is composed of two foremost lobes, right and left and 2 accent lobes, quadrate and caudate. The proper lobe is six times larger than left lobe. It plays remarkable functions in our body like bile production and excretion; excretion of Bilirubin, cholesterol, hormones, drugs, metabolism of proteins, fats and carbohydrates. It is involved with almost all the biochemical pathways for growth, fight against disease, nutrient supply, energy provision and reproduction. And it functions as a centre of metabolism of nutrients such as carbohydrates, proteins and lipids and excretion of waste metabolites. The bile secreted by the liver has, among other things, plays an important role in digestion. The liver also removes harmful substances from our blood. It is called as Detoxification (Cleansing). Consequently, renovation of a healthful liver is important for the overall properly being of a character.[1-5]

Medicinal plants play a key function inside the human fitness care. Approximately 80 % of the world populace is predicted on using conventional medicine that predominantly based on plant materials.[6] The traditional medicine refers to a vast variety of ancient herbal health care practices consisting of folk/tribal practices in addition to Ayurveda, siddha and Unani. Those medical practices originated from time immemorial and evolved step by step, to a massive extent, by depending or based totally on practical stories without considerable references to modern clinical principles. It is predicted that approximately 7,500 plants are utilized in local fitness traditions in, typically, rural and tribal villages of India. Out of these, the real medicinal cost of over 4,000 plants either little acknowledged or unknown to the mainstream population. The classical systems of drugs which include Ayurveda, Siddha, Amchi, Unani and Tibetan use about 1,200 plants.[7] A detailed research and documentation of flowers utilized in local fitness traditions and pharmacological evaluation of these plants and their taxonomical family can cause the improvement of invaluable plant drugs for plenty dreaded sickness. Random screening of plants has no longer proved economically effective.[8]

Herbal drugs are more broadly used than allopathic drugs as hepatoprotective drugs because they are less expensive, higher cultural acceptability, higher compatibility, with the human body and minimum facet results. These herbal drugs have shown the potential to hold the normal useful statues of the liver with or without fewer facet results.[9] The study of herbs dates back over 5000 years to the Sumerians, WHO delineated well-established meditative uses for such plants as laurel, caraway and thyme. Ancient Egyptian before 1000 B.C. used garlic, opium, castor oil, coriander, mint, indigo and different herbs for medication and therefore the old Testament also mentioned herb use and cultivation, as well as mandrake, vetch, caraway, wheat, barley and rye. Also, the employment

of seasoning medicine is often copied back to 2100 B.C. The age previous system of seasoning medication is being revived by regular apply for its long curative impact, straight forward availableness, natural means of healing and fewer facet effects.[10]

Therefore, there is precise hobby in growing new pills from plant resources, to deal with liver illnesses. In step with the World Health Organization, natural tablets from medicinal plants constitute a main part of the traditional medicinal drug gadget.[11] Recently in growing countries the utilization of medicinal plants has won prominence and popularity due to their protection, efficacy and cost effectiveness.[12]

Liver Functional Tests

The term "liver function tests" is actually a misnomer. The previous researchers identified and distinguished liver functions tests as mentioned below ;

Standard Liver Function Tests (LFT's) consist of the following enzymes[23]

1. Alanine Transaminase (ALT),
2. Aspartate Transaminase (AST),
3. Alkaline Phosphatase (ALP),
4. Gamma Glutamyl Transferase (GGT), Together with
5. Bilirubin,
6. Albumin,
7. Total Protein and
8. Globulin.

When considered together, these analytes open a diagnostic window into multiple organ systems. Doctors obviously appreciate this broad utility; LFTs comprise 32 % of all Biochemistry testing done by Clinipath Pathology.

Inducing Hepatoxicity in Animal models

Hepatotoxin is a toxic chemical substance which damages the liver. Toxic liver damage produced by means of drugs and chemical compounds may additionally virtually mimic any shape of evidently going on liver ailment. Several chemicals were recognised to set off hepatotoxicity. Carbon tetrachloride (CCl_4), Galactosamine, D-Galactosamine/lipo polysaccharide (GalN/LPS), Thioacetamide (TAA), Anti tubercular drugs, Paracetamol, Arsenic, Alcohol, Isoniazid, Rifampicin, Antibiotics, Epoxidizedoil, Aflatoxin and so on., are used to induce experimental hepatotoxicity. Most of the inorganic compounds producing hepatotoxicity are Phosphorus, Copper and Iron. The natural dealers encompass sure obviously happening plant toxins including pyrrolizidine alkaloids, Mycotoxins and Bacterial Toxins.

Carbon tetrachloride (CCl_4)

Liver injury because of CCl_4 in rats changed into 1st reported in 1936[13] and has been broadly and successfully used by many investigators.[14, 15]

Mode of Action CCl_4

Carbon tetrachloride is metabolized by way of Cytochrome P-450 in endoplasmic reticulum and mitochondria with the formation of CCl_3-O-, a reactive oxidative unfastened radical, which initiates lipid peroxidation.[16,17] Administration of a single dose of CCl_4 to a rat produces, within 24 h, a centrilobular necrosis and fatty changes. The poison reaches its most awareness in the liver within 3 h of management. Thereafter, the level falls and with the aid of 24 h there is no CCl_4 left inside the liver.[18] The development of necrosis is related to leakage of hepatic enzymes into serum. Dose of CCl_4 that induces hepatotoxicity stages from 0.1 to 3 ml/kg administered intra peritoneal.

Thioacetamide

Thioacetamide (TAA) was first introduced by Childs and Siegler in 1945. It was first used of decay of oranges and then as a fungicide.[19] Thioacetamide (TAA) is an organosulfur compound having formulation C_2H_5NS.[20] Several corporations and investigators studied the toxicity of thioacetamide like Fitzhugh and Nelson 1948.[21] It was suggested that a single dose of this hepatotoxic agent should produce centrilobular hepatic necrosis and that continual administration caused cirrhosis and hepatocarcinoma.

Mode of Action TAA

The mechanism behind its toxicity is related to its toxic metabolite thioacetamide (s-oxide) which is responsible for hepatic injury. It interferes with the movement of RNA from the nucleus to the cytoplasm which might also cause membrane harm. It reduces the quantity of viable hepatocytes as well as rate of oxygen consumption and also decreases the volume of bile and its content, that is, bile salts, cholic acid and deoxycholic acid. Inside the evaluation of liver damage with the aid of TAA, the enhanced activities of these serum marker enzymes observed in TAA treated rats study correspond to the extensive liver damage induced by TAA.[22,23]

Paracetamol (APAP)

Paracetamol is also called as Acetaminophen. It had been available since the 1950s as an over-the-counter product for ache and fever relief. APAP hepatotoxicity is the classical instance of direct liver damage. APAP has lengthy been recognized as potentially deadly due to dose-associated hepatic and /renal injury.[24] It produces acute liver damage in high doses. APAP overdose induces nephrotoxicity which happens in about 1–2 % of patients.[25]

Mode of Action Paracetamol

Paracetamol administration reasons necrosis of the centrilobular hepatocytes characterized by means of way of nuclear pyknosis and eosinophilic cytoplasm observed through massive excessive hepatic lesion. The covalent binding of N-acetyl-p-benzoquinone imine, an oxidative made of paracetamol to sulphydryl companies of protein, bring about lipid peroxidative degradation of glutathione degree and by this way of the usage it produces cellular necrosis inside the liver. Dose of Paracetamol is 1 gm/kg given by oral.[26] APAP toxicity is associated with extended stage of hepatocellular enzymes viz., AST, ALT, LDH and SALP into circulate.[27,28] APAP intoxication inhibits the activity of antioxidant enzymes (SOD, CAT, GPx, GR, G6PDH, AND GST).[27,29-31]

Alcohol

Alcohol is the most psychoactive substance used after caffeine. Continual alcoholism is a prime public health hassle and reasons sickness and toxicity. Accumulating proof advocate that intermediates of oxygen reduction can be related to the improvement of alcoholic disorder. [32] Alcoholic liver disorder is a worldwide health trouble which has three manifestations in shape of fatty liver/steatosis, alcoholic hepatitis and liver cirrhosis. At least 80 % of continual alcoholic clients can also

expand steatosis, 10-35 % alcoholic hepatitis and about 10 % liver cirrhosis. Intake of alcohol causes accumulation of reactive oxygen species (ROS) like superoxide, hydroxyl radical and hydrogen peroxide in the hepatic cells that oxidize the glutathione which leads to lipid peroxidation of mobile membranes, oxidation of protein and DNA resulting in hepatic harm. [33]

Mode of Action Alcohol

Alcohol administration causes oxidative strain ends in alcohol-mediated hepatotoxicity. To start with, in the liver alcohol is metabolized into the enormously poisonous acetaldehyde by means of the enzyme alcohol dehydrogenase. Acetaldehyde is then oxidized to acetate with the aid of acetaldehyde oxidase or xanthine oxidase giving upward push to ROS via cytochrome P450 2E1. Prolonged intake of alcohol increases nitric oxide (NO) degree which leads to formation of poisonous oxidant peroxy nitrite. Low ability of antioxidants in this case leads to harm of the cells of the hepatic cells and the cell organelles with the release of reactive aldehydes and ROS.[34] Alcohol consumption have a few blessings as increasing high density lipoprotein (HDL-C) causing safety against atherosclerosis.[35-37] Alcohol induces oxidative pressure which is known to purpose liver damage that is many biochemical metabolic reactions occur due to it. Some of those consist of redox reaction changes, production of reactive acetaldehyde, harm to the mitochondria of cells, cell membrane damages, hypoxia, effects on immune machine, altered cytokine manufacturing, and induction of CYP2E1 and mobilization of iron.[36-38]

Hepatoprotective Plants

A large variety of medicinal plants have been tested and determined to include active standards with curative house towards a ramification of sickness. Liver defensive plants contain a spread of chemical parts like phenols, coumarins, lignans, essential oil, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, alkaloids, and xanthines. Therefore a large range of plants and formulations have been claimed to have hepatoprotective activities so the improvement of plant based totally hepato protecting drugs has been given significance within the global market place.[39]

This review article has been offered to enumerate some plants which have hepatoprotective properties that are *Andrographis paniculata, Ageratum conyzoides, Alchemilla mollis*, *Euphorbia tirucalli* L., *Gardenia gummifera* Linn, *Butea monosperma, Ceriops decandra* (Griff.), *Macrothelypteris torresiana, Rhus oxyacantha, Polygonum orientale, Aquilaria agallocha.*

Andrographis paniculata

Andrographis paniculata (Burm. F.) Nees belonging to family Acanthaceae is the most popular traditionally recognised medicinal plant used for the remedy of array of sickness like viral fever, chicken pox, not unusual bloodless, diarrhoea, dysentery, eczema, epidemic encephalitis B, hepatitis, herpes zoster, mumps, ulcer, neurodermatitis, infection, pharyngolaryngitis, pneumonia, respiration infections.[40] The plant is widely used as a traditional remedy in nations like India, China, Hongkong, bites.[40,41] It is commonly known as Kalmegh or King of bitters cultivated in many regions of South Asian countries because of well-known medicinal value.[42] Inside the Ayurvedic machine of medicine, *A. paniculata* is frequently used in combination with other herbs and care merchandise for treating sufferers suffering from diverse physical and intellectual issues. It has been envisioned that *A. paniculata* is utilized in Indian structures of medication for a long term to deal with sufferers with liver illnesses.[44] Not only as a single agent it also used as a component of poly-herbal preparation to treat liver damages.[45] of *A. paniculata* were screened for hepato renal shielding activity against ethanol-induced toxicity in mice. Intraperitoneal pre treatment of mice with andrograholides (500 mg/kg body weight of mice) and arabinogalactan (125 mg/kg Body weight of mice) for 7 d, earlier than intraperitoneal injection of ethanol (7.5 mg/kg body weight) minimized toxicity as discovered by unique enzyme assay within the liver and kidney tissues, each andrograholides and arabinogalactan extensively (well known Silymarin whilst in comparison to the ethanol handled group.[46]

Ageratum conyzoides

Ageratum conyzoides, belongs to the family Asteraceae tribe Eupatoriae. Ageratum is derived from the Greek words 'a geras', meaning non-aging, referring to the longevity of the whole plant. Conyzoides on the other hand is derived from 'konyz' the Greek name of Inula helenium which the plant resembles. A large majority of the plants in the family are herbaceous while trees and shrubs are comparatively rare. *A. conyzoides* is a tropical plant that is very common in West Africa and some parts of Asia and South America. It is an annual branching herb which grows to approximately 1 m in height. The plant grows commonly in the proximity of habitation, thrives in any garden soil and is very common in waste places and on ruined sites. It has a peculiar odor likened in Australia to that of a male goat and hence its name 'goat weed' or 'billy goat weed'.[47-49]

The hepatoprotective activity of acetone and n-hexane extracts of *Ageratum conyzoides* in wistar rats following acetaminophen (APAP) induced hepatotoxicity. Single high dose exposure of APAP significantly ($p<0.05$) increased in ALT, AST, and GGT activity and levels of BUN, CR, unconjugated bilirubin and A/G ratio, whereas activity of LDH-P, total protein, albumin, globulin and conjugated bilirubin were significantly ($p<0.05$) reduced as compared to control. Pre-exposure with acetone and n-hexane extracts of *A. conyzoides* restore the values of ALT, GGT, LDH-P, albumin, unconjugated and conjugated bilirubin as compared to control whereas the AST, globulin, A/G ratio, BUN and CR levels are not restored by administration of plant extracts. It is evident from observations that acetone and n-hexane extracts of *A. conyzoides* was able to restore the levels of SGPT, SGOT, LDH and bilirubin as an indication of the stabilization of plasma membrane as well as repair of hepatic tissue damages caused by APAP.[50]

Alchemilla mollis

Alchemilla mollis (Buser) [Family- Rosaceae] Rothm, from the genus Alchemilla, is also used in traditional European medicine. "Herba Alchemillae", a commercial drug containing *A. mollis* extract, has astringent, diuretic, and antispasmodic effects; it is also used as a medicine for the treatment of wounds and the treatment of excessive menstruation in folk medicine.[51-53] *A. mollis* grows naturally and widely in Turkey, especially in north and north-eastern Anatolia.[54]

Alchemilla mollis Rothm aerial part and root methanolic-water extracts were evaluated for their hepatoprotective activity on carbon tetrachloride induced hepatotoxicity and hypoglycemic activity on alloxan-induced diabetic mice. None of the tested extracts exhibited effects on blood glucose levels. However hepatoprotective activity results have revealed that serum ALT levels were significantly lowered by both the aerial part and root extracts at doses of 100 mg/kg and 200 mg/kg. Histopathological examination showed that *A. mollis* aerial parts and roots induced significant recovery from cellular damage; when compared to the

carbon tetrachloride group, the most significant activity was observed with *A. mollis* aerial part extracts at a dose of 200 mg/kg. There is evidence of a hepatoprotective activity of A. *mollis* on the phenolic content of the plant, especially in the case of flavonoids, which have potent antioxidant properties.[55]

***Euphorbia tirucalli* L.**

Euphorbia tirucalli Linn belonging to Euphorbiaceae family. It is a flowering shrub or tiny tree indigenous to temperate regions. It has pencil like twigs from which it derives its vernacular name pencil tree.[56] *E. tirucalli* is broadly distributed in hotter parts of India and planted as a hedge plant in garden and along cultivated fields.[57] *E. tirucalli* is universally known as Aveloz. It is a native of Africa and America but has turn out to be acclimated and growing liberally in all parts of India particularly in the drier parts of Bengal and South India and basically grown-up in hedge. It is developed in Berar for shelter young mango plants from straight sunlight.[58-60]

Aqueous extract of *E. tirucalli* was tested against CCl_4 induced hepatic damage in rats. The extract was produced considerable hepatoprotective activity by decrease in levels of serum bilirubin, cholesterol, triglycerides and tissue lipid peroxidation. GSH level in tissue was increased.[61]

***Gardenia gummifera* Linn**

Gardenia gummifera (Rubiaceae) is well known for its medicinal properties in indigenous medicine in India. In Indian System of Medicine, the gum Dikamali is one of the important drugs.[62]
The hepatoprotective and antioxidant activity of methanolic extract of whole plant of *Gardenia gummifera* (GGME) was evaluated against paracetamol induced liver damage in rats. And the GGME fractionated based on polarity of solvents with toluene, ethanol, 2-butanone, n-butanol and petroleum ether. The substantially elevated serum enzymatic levels of Aspartate Aminotransferas (AST), Alanine Transaminase (ALT), Alkaline Phosphate

(ALP) and total Bilirubin were restored towards normalization significantly by the GGME in a dose dependent manner in paracetamol induced liver damage. The biochemical observations were supplemented with histopathological examination liver sections high protection against paracetamol induced hepatoxicity. Further investigation continued with GGME fractions, 2-Butanone Fraction (BTF) and n-butanol Fraction (BAF) substantially elevated serum enzymatic levels of AST, ALT, ALP and Total Bilirubin (TB) were restored towards normalization significantly The significant values showed with n-butanol fraction on pentobarbitone induced sleeping time in mice and the liver weight of paracetamol induced liver damaged in rats. Meanwhile, *in vitro* antioxidant activities such as DPPH scavenging assay was also screened which were also found significantly positive in a dose dependent manner. The results of this study strongly indicate that GGME and n-butanol fraction results potent hepatoprotective activity against paracetamol induced liver damage in experimental animals.[63]

Butea monosperma

Butea monosperma (Lam.) Taub. family Fabaceae is a subtropical Indian medicinal plant that finds an important place in traditional therapies. Its popular names are 'Flame of the forest' in English and 'Palash' in Hindi. It is widely distributed along Indo-Gangetic plains. It is commonly used in Indian folk medicine for many years due to its healing properties and for curing a number of health problems viz. wounds, liver disorders, neurodegeneration, osteoarthritis, diabetes, etc.[64, 65]
Hepatoprotective properties of ethyl acetate fraction (Beac) from *B. monosperma* bark in rat model. In preliminary antioxidant studies, Beac demonstrated pronounced superoxide scavenging (IC50 88.85 mg/ml) and anti-lipid peroxidation (IC50 131.66 mg/ml) potential. In animal studies, Beac showed protective effect against thioacetamide induced pathophysiology in liver of male Wistar rats. The levels of different parameters related to hepatic functions were altered by thioacetamide treatment (300 mg/g bw) in rats. The pre-treatment of rats with

Beac (50, 100 and 200 mg/kg bw) was able to normalize the biochemical markers viz. serum bilirubin, SGOT, SGPT, albumin and ALP along with liver anti oxidative molecules viz. SOD, CAT, GSH and GR. Results of histopathological and colorimetric studies revealed that Beac treatment also restored the markers of fibrosis i.e. collagen and hydroxyproline towards normal level. Beac considerably inhibited thioacetamide- induced expression of p-PI3K, p-Akt and p-mTOR in hepatocytes as revealed from immuno histochemical studies. This finding is the first evidence of inhibitory action of *B. monosperma* bark on these pro-carcinogenic proteins. HRMS analysis revealed the presence of quercetin, buteaspermin B and ononin in Beac fraction of *Butea monosperma*. From the results, it can be concluded that *B. monosperma* bark is a rich source of phytochemicals with *in vitro* and *in vivo* protective activities which deserves further mechanistic studies for its use as a hepatoprotective agent in the prevention of hepatic inflammation and its related malignancies.[66]

***Ceriops decandra* (Griff.)**

Ceriops decandra (Griff.) Ding Hou it is a mangrove plant [Family-Rhizophoraceae]. In folklore medicine, the bark and leaf parts of *C. decandra* are used as cure for ulcer and hepatitis.[67]

The hepatoprotective activity of plant parts (leaf, bark, collar, flower and hypocotyls) of *C. decandra*; *In vitro* antioxidant studies were carried out with DPPH, HRSA, NO, FRAP and LPO assays. The LD50 was calculated and *in vivo* hepatoprotective activity was carried out with the leaf extract, which was found to be the most potent. The *in vivo* hepatoprotective activity was performed as follows: Group 1, control animals; Group 2, carbon tetrachloride (CCl_4)-treated animals; Group 3, silymarin (100 mg kg−1 bw *p.o.*) treated animals; Groups 4, 5 and 6, *C. decandra* treatment groups (100, 200 and 400 mg kg−1 bw). Histopathological scores were calculated with standard protocols. Of the selected different plant parts, theleaf extract showed maximum antioxidant scavenging properties. A study of the oral acute toxicity found *C. decandra* extract to be non-toxic up to 2000 mg kg−1 bw. The *in vivo* hepatoprotective nature of the leaf extract was identified as dose dependent and the levels of SGOT, SGPT, ALP, bilirubin, CHL and LDH were found to be significantly decreased ($p < 0.05$) compared with hepatotoxin groups. Histopathological scores did not show any significant variations between control and high dose (400 mg kg−1 bw) of leaf extract-treated animals. Preliminary phytochemical analysis of the leaf extract revealed the presence of phenolic groups, alkaloids, triterpenoids, flavonoids, catechin and anthraquinone. In conclusion, the hepatoprotective nature of the *C. decandra* leaf extract might be due to the occurrence of unique secondary metabolites and their antioxidant scavenging properties.[68]

Macrothelypteris torresiana

Macrothelypteris torresiana (Gaudich), syn. Lastrea torresiana Moore (family: Thelypteridaceae) is a species of fern which is

native to tropical and subtropical region of the world. It is a robust fern with a short creeping rhizome.[69,70] In traditional medicine *M. torresiana* leaves and roots have a wide range of reputed medicinal application. The aerial parts are used for treatment of fever, pain, granulation, healing and reducing odor in chronic skin ulcer and inflammation by the tribes of Pakistan, India and China. It is also used in Chinese folk medicine for the treatment of edema for patient suffering from kidney problems.[71,72]

Hepatoprotective potential of ethanol extract from *M. torresiana* aerial parts (EEMTAP) and detect the polyphenolic compounds present in the extract using high performance thin layer chromatography (HPTLC). Hepatoprotective potential of EEMTAP was tested at doses of 300 and 600 mg/kg, per os (p.o.), on Wistar albino rats. The extract and silymarin treated animal groups showed significant decrease in activities of different biochemical parameters like serum glutamic oxaloacetic transaminase (SGOT), serum glutamate-pyruvate transaminase (SGPT), and alkaline phosphatase (ALP), which were elevated by carbon tetrachloride (CCl_4) intoxication. The levels of total bilirubin and total protein along with the liver weight were also restored to normalcy by EEMTAP and silymarin treatment. After CCl_4 administration, the levels of hepatic antioxidant enzymes such as glutathione (GSH) and catalase (CAT) were decreased whereas the level of hepaticlipid peroxidation (LPO) was elevated. The levels of these hepatic antioxidant enzymes were also brought to normalcy by EEMTAP and silymarin treatment. Histological studies supported the biochemical findings, and treatment with EEMTAP at doses of 300 and 600 mg/kg, p.o. was found to be effective in restoring CCl_4-induced hepatotoxicity in rats. A simple HPTLC analysis was conducted for the detection of polyphenolic compounds in EEMTAP, and the result revealed the presence of caffeic acid as phenolic acid and quercetin as flavonoid. The proposed HPTLC method is simple and concise and provides a good resolution of caffeic acid and quercetin from other constituents present in EEMTAP.[73]

Rhus oxyacantha

In Tunisia, the genus Rhus is represented by two species: [*Rhus oxyacantha* (Shousb). Ex. Cav = R. oxya. canthoides Dum. cours = *Rhus tripartita* (Ucria) Grande [=*R. tripartitum* (Ucria) D.C. = *Searsia tripartita* (Ucria) Moffet] and Rhus pentaphylla.[74] *Rhus oxyacantha* known locally as "Jdéri" is a Tunisian plant used in traditional medicine for the treatment of digestive diseases.[75,76] *Rhus oxyacantha* is not growing only in Tunisia but also it's very abundant in north Africa, especially in the steppes of desert, arid and semi-arid areas.[77,78] It also exists in Sicily and Western Asia steppes and is used in folkloric and traditional medicine of many countries situated in the cited areas.[77,79,80] In Arabian traditional medicine, different parts of *Rhus oxyacantha* plant, have been used for centuries to treat inflammatory conditions as well as gastrointestinal and cardiovascular disorders.[81]

The RE exhibited high total phenolic, flavonoid and condensed tannins contents. The antioxidant activity *in vitro* systems showed a significant potent free radical scavenging activity of the extract. The HPLC finger print of *R. oxyacantha* active extract showed the presence of five phenolic compounds with higher amounts of catechol and gallic acid. The *in vivo* results showed that a single intraperitoneal administration of DDT enhanced levels of hepatic markers (ALT, AST and LDH) in serum of experimental animals. It also increased the oxidative stress markers resulting in increased levels of the lipid peroxidation with a significant induction of SOD and GPx, metallothioneins (MTs) and a concomitant decrease of non protein thiols (NPSH) in liver. However, pre treatment of rats with RE at a dose of 150 and 300 mg/kg body weight significantly lowered serum transaminases and LDH in treated rats. A significant reduction in hepatic thiobarbituric reactive substances and a decrease in antioxidant enzymes activities and hepatic MTs levels by treatment with plant extract against DDT were observed. These biochemical changes were consistent with histopathological observations, suggesting marked hepatoprotective effect of RE with the two doses used. These results strongly suggest that treatment with ethyl acetate extract normalizes various biochemical parameters and protects the liver against DDT-induced oxidative damage in rats and thus help in evaluation of traditional claim on this plant.[82]

Polygonum orientale

Polygonum orientale L. (Family-Polygonaceae) has been used as medicine and food in Chinese herbal pharmacopeias.[83] Numerous natural products possess medicinal properties; for example, flavonoids are among the most well-known examples of powerful pharmaceutical ingredients found in plants. Phytochemical studies have shown abundant flavonoids in this plant such as taxifolin and quercetin. Phenolics such as gallic acid and protocatechuic acid were also identified.[84] The whole plant has been used in China for the treatment of various conditions such as arthritis, edema, dysentery, fractures, urticarial, and muscle injuries.[85]

Hepatoprotective activity of the ethanolic extract of *P. orientale* (POE) fruits against carbontetrachloride (CCl_4)-induced acute liver injury (ALI). Mice were pre treated with POE (0.1, 0.5, and 1.0 g/kg) or silymarin (0.2 g/kg) for 5 consecutive days and administered a dose of 0.175 % CCl_4 (ip) on the 5th day to induce ALI. Blood and liver samples were collected to measure anti oxidative activity and cytokines. The bioactive components of POE were identified through high-performance liquid chromatography (HPLC). Acute toxicity testing indicated that the LD50 of POE exceeded 10 g/kg in mice. Mice pre treated with POE (0.5, 1.0 g/kg) experienced a significant reduction in their serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), and alkaline phosphatase (ALP) levels and reduction in the extent of liver lesions. POE reduced the malondialdehyde (MDA), nitricoxide (NO), tumor necrosis factor-a (TNF-a), interleukin-1b (IL-1b), and interleukin-6 (IL-6) levels, and increased the activity of superoxide dismutase (SOD), glutathione peroxidise (GPx), and glutathione reductase (GRd) in liver. HPLC revealed peaks at 11.28, 19.55, and 39.40 min for protocatechuic acid, taxifolin, and quercetin, respectively. In summary, the hepatoprotective effect of POE against CCl4-induced ALI was seemingly associated with its antioxidant and anti-pro inflammatory activities.[86]

Aquilaria agallocha

Aquilaria agallocha belonging to the family thymelaeacea is known as Agarwood in English, Agar in Hindi and Aguru in Sanskrit.[87] Agarwood has been utilized for varied purposes all over the world for thousands of years. Its utilization has been reported in Ayurveda, Tibetan and traditional East-Asian medical practice including Susruta Samhita and Shahih Muslim.[88,89] Traditionally the bark, root and leaves of the heartwood of Agarwood are used for their medicinal properties like aphrodisiac, anodyne, acrid, astringent, aromatic, cardio tonic, bitter, carminative, fragrant and stimulant. Agarwood is also used as appetizer, carminative and mouth freshener and used to treat colic pain, toothache, severe pains and headache during the pregnancy.[90]

Group I animals were treated with 1% CMC for 8 days. Group II, III, IV and V animals were first treated with '1% CMC' 1 ml/kg/day, AAE 200 mg/kg/day, AAE 400 mg/kg/day and silymarin 100 mg/kg/day respectively for 7 days and then, orally

administered with PCM 3 g/kg b. wt. on 8th day in a single dose. 24 h after the last dosing by PCM, the blood was obtained through the retro-orbital plexus under light anesthesia and the animals were sacrificed. Hepatoprotective potential was assessed by various biochemical parameters such as ALT, AST, ALP, LDH, bilirubin, cholesterol, TP and ALB. Group IV rats showed significant ($p < 0.01$) decrease in ALT, AST, ALP, LDH, cholesterol, bilirubin, liver wt. and relative liver wt. levels while significant ($p < 0.01$) increase in final b. wt., TP and ALB levels as compared to group II rats. Hepatoprotective potential of AAE 400 mg/kg/day was comparable to that of standard drug silymarin 100 mg/kg/day. Results of the study were well supported by the histopathological observations. Compare to standard group.[91]

CONCLUSION

Notwithstanding super advances in current medication, hepatic disorder remains a worldwide fitness problem; for that reason the look for new medicines is still ongoing. Numerous formulations of medicinal plants are used to deal with liver disorders in Chinese ethno clinical exercise and conventional medication. A lot of these treatments act as radical scavengers, while others are enzyme inhibitors or mutagens. The hepatoprotective effect of the plants is likely because of the presence of flavonoids, alkaloids, terpenoids, glycosides and steroids. Energetic extracts, fractions or combination of fractions/extracts of flowers may also prove very powerful capsules. Plant extracts (combos or individual drug) for liver illnesses have to possess sufficient efficacy to remedy extreme liver sicknesses resulting from poisonous chemicals, viruses (Hepatitis B, Hepatitis C, and so on.), extra alcohol consumption, and repeated administration of medication like paracetamol, Rifampicin and Isoniazid. A single drug cannot be effective in opposition to all types of excessive liver sicknesses. Effective formulations should be advanced the use of indigenous medicinal plant life, with proper pharmacological experiments and clinical trials. The manufacture of plant products need to be ruled by using standards of protection and efficacy.

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