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ANTIOXIDANT PROPERTY OF PLANT AN INDICATION FOR HEPATOPROTECTIVE ACTIVITY

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Received on 27-08-2012

Accepted on 15-09-2012

Abstract

Liver, the largest organ in the body is being evolved to maintain the body's internal milieu and also protect itself from the challenges it faces during its functioning. Since it is involved in the biochemical conversions of various endogenous and exogenously administered/ingested substances, there is a possibility of generation of various highly reactive species of free radicals. However, it has an inbuilt system like tissue glutathione (GSH), etc to scavenge them off. In spite of this the free radicals generated by some hepatotoxins like CCl_4 may overpower the protective mechanism of the liver and cause hepatic damage. Though the modern medicinal system has grown phenomenally, the drug for treating hepatic disease is still a dream. Hence, people are looking at the traditional systems of medicine for remedies to hepatic disorders.

Keywords: Anti-oxidant activity, Hepatoprotective activity, Liver, Medicinal plants.

Introduction

The liver is the most important organ in the body. It plays a pivotal role in regulating various physiological processes and also involved in several vital functions, such as metabolism, secretion and storage. It has great capacity to detoxicate toxic substances and synthesize useful principles^{1,2}. It helps 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. In addition, it aids metabolism of carbohydrate, protein and fat, detoxification, secretion of bile and storage of vitamins³. The role played by this organ in the removal of substances from the portal

circulation makes it susceptible to first and persistent attack by offending foreign compounds, culminating in liver dysfunction⁴.

Liver diseases remain one of the major threats to public health and are a worldwide problem⁵. They are mainly caused by chemicals like acetaminophen (in large doses), excess consumption of alcohol, infections and autoimmune disorders. Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages^{6,7,8}.

Damage to cells caused by free radicals is believed to play a central role in the aging process and in disease progression. Antioxidants are our first line of defense against free radical damage, and are critical for maintaining optimum health and wellbeing⁹.

Oxidative stress plays an important role in many diseases including liver diseases¹⁰. The production of oxidative stress can be controlled by the antioxidant systems in living organisms. However, the over production of oxidative stress can lead to damage in DNA, cell membrane, protein and cellular membranes and consequently induces degeneration, destruction and toxicity of various molecules¹¹ and causes muscular dystrophy, cancer as well as liver diseases. Currently, many synthetic antioxidant drugs (BHT, TBHQ) have been used in drug composition. However, these synthetic drugs can cause many side effects and then lead to many potential health problems. In this connection, herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. Herbal based therapeutics for liver disorders have been practiced in India for a long time and popularized globally by leading pharmaceutical companies¹². Liver protective plants contain a variety of chemical constituents like phenols, coumarins, monoterpenes, glycosides, alkaloids and xanthenes¹³.

Recent findings indicate that the hepatitis could be handled effectively if the drug possesses antioxidant and anti-inflammatory property. As the liver protection and proliferation of hepatocytes accelerate in the presence of Antioxidants. Hence the hepatoprotective potency of the plant could be attributed to its antioxidant property¹⁴.

In this work, we review the literature related to plants having antioxidant and hepatoprotective activity. These findings provide greater chances and flexibility in helping researchers identify plants having antioxidant and hepatoprotective potential.

Plants Having Hepatoprotective and Antioxidant Activity

Lumnitzera racemosa (Combretaceae)

L. racemosa (Combretaceae), a mangrove species found on the coast of India and in Andaman and Nicobar islands is known for its great economic importance¹⁵. Ravikumar and Gnanadesigan evaluated the hepatoprotective and in vitro antioxidant activity of *Lumnitzera racemosa* leaf extract. The preliminary phytochemical analysis of the plant part extracts showed the presence of reducing sugars, protein, phenolic groups, alkaloids, triterpenoids and tannins. Study reveals that the ethanolic leaf extract of *L. racemosa* possesses significant hepatoprotective effect in the CCL₄ intoxicated models. The in vitro assays such as DPPH radical scavenging assay, superoxide radical scavenging assay, hydroxyl radical scavenging assay, lipid peroxide radical scavenging assay suggest the ability of the *L. racemosa* leaf extract to reduce the biological oxidative stress. The hepatoprotective effect of the plant extract might be attributed to the presence of unique chemical classes such as alkaloids, terpenoids and alkaloids and in vitro antioxidant properties. Hence, the hepatoprotective effect of the leaf extract may be achieved by the scavenging free radical activity of the oxidative stress¹⁶.

Myristica malabarica (Myristicaceae)

The plant *Myristica malabarica* L. (Myristicaceae) is known for many medicinal properties such as indigestion, ulcers, wounds, aphrodisiac, as rejuvenator, in treating inflammation, cough, diarrhea, dropsy, liver disorders, paralysis, rheumatism, urinary calculi, vomiting¹⁷, also used in bronchitis, fever, burning sensation, to relieve pain in muscles, sprains and sores¹⁸. The plant contains many active constituents viz. 7, 4-dimethoxy-5 hydroxyl isoflavone, biochanin A, prunetin, 1, 3-diarylpropanol and alpha- hydroxyldihydrochalcone¹⁹, 2-acylresorcinol, diarylnonanoids, malabaricone C²⁰, malabaricone A, Malabaricones A-D, diarylnonanoids²¹. The antioxidant activities of the ethanol extract, its benzene and chloroform fraction from seed aril of *Myristica malabarica* (Myristicaceae) were assessed to validate the hepatoprotective potency of this plant. The extract and the fractions showed scavenging of 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical and inhibition of ABTS radical *in vitro*. Antioxidant activities of the extracts were also demonstrable *in vivo* by the inhibition of the carbon tetrachloride induced formation of lipid peroxides in the liver of rats by pretreatment with the extracts. CCl₄ - induced hepatotoxicity in rats was judged by the raised serum enzymes,

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aspartate transaminase, alanine transaminase and alkaline phosphatases was prevented by pretreatment with the extracts/fractions, demonstrating the hepatoprotective action. Among the tested extracts benzene fraction recorded highest efficiency in protecting liver damage induced by toxic effect of CCl₄ followed by crude ethanolic extract and chloroform fraction. The liver protection and proliferation of hepatocytes accelerate in the presence of antioxidants. In the present study it was evident that, the benzene fraction and the crude ethanol seed aril extract has potent antioxidant activity. Hence the hepatoprotective potency of the plant could be attributed to its antioxidant property²².

***Leucas ciliata* (Lamiaceae)**

Leucas ciliata (Lamiaceae) commonly known as Burumbi is a shrub which is frequently distributed along the ghats and in planes along forest edges in Ahmednagar, Dhule, Kolhapur, Mumbai, Satara, Sindhudurg and Thane regions of Maharashtra in India. Traditionally *L. ciliata* is used for wound healing and as antidote for snakebite²³. In Chinese medicine it is used for its antibacterial and antifungal activity²⁴. Preliminary phytochemical analysis of *L. ciliata* leaves indicated presence of relatively high levels of flavonoids. Several flavonoids have been reported to possess antioxidant and hepatoprotective properties²⁵. In the study of hepatoprotective activity, after treatment with CCl₄ there is a significant increase in levels of SGOT, SGPT, ALP, Bilirubin and also an increase in liver weight as compared to the normal control were observed. While in the groups of rats pretreated with silymarin the levels of SGOT, SGPT, ALP and Bilirubin were significantly lower. The groups of rats pretreated with *L. ciliata* extract, demonstrated dose dependent inhibition of elevation of the biochemical parameters. In the present study four methods were used for evaluation of antioxidant activity. The DPPH radical scavenging method and nitric oxide radical scavenging method were for direct measurement of radical scavenging activity. Reducing power method and Iron Chelation method indirectly evaluate the antioxidant activity. *L. ciliata* demonstrated dose dependent antioxidant activity comparable with Ascorbic acid. In all the methods. *L. ciliata* has strong antioxidant activity and this activity may be responsible for the hepatoprotective activity against carbon tetrachloride induced liver damage²⁶.

***Urtica dioica* (Urticaceae)**

Urtica dioica (Urticaceae) is a traditional Ayurvedic herb and also known as Vrishchhiyaa-shaaka. It is also known as Bichu Butti in Hindi and Punjabi, Anjuraa in Unani, Shisuun in folk language (Kumaon) and Stinging Nettle in English.

The plant is used traditionally as diuretic, emmenagogue, blood purifier and as anthelmintic. It is also used in nephritis, haematuria, jaundice and menorrhagia²⁷. The herb is also claimed to possess diuretic and natriuretic effects along with antidiabetic and antihypertensive activity²⁸. Preliminary phytochemical screening showed the presence of phytosterols, saponins, flavanoids, tannins, hydrolysable tannins, phenolic compounds, and proteins and amino acids. The antioxidant, hepatoprotective, and anthelmintic activities of methanol extract of leaves of *Urtica dioica* were investigated in the present study. Hepatoprotective potential of the extract was evaluated against CCl₄- induced hepatic injury in Wister rats. In addition, reducing power assay, determination of total antioxidant activity, DPPH radical scavenging activity and nitric oxide scavenging activity were investigated to evaluate the *in vitro* antioxidant activity of the extract. The results indicated significant antioxidant activity of the extract comparable to standard antioxidant compounds like α -tocopherol, ascorbic acid and BHA (Butylated hydroxyanisole). Significant hepatoprotective profile was also observed with maximum hepatoprotection at the dose of 400 mg/kg as suggested by decreased level of serum ALT, AST, ALP and total bilirubin levels towards normalization. Pretreatment of animals with the extract at all the dose level resulted a significant decrease in malonyldehyde (MDA) level as well as a significant increase in superoxide dismutase (SOD) level clearly indicating inhibition of lipid peroxidation and improvement of antioxidant defense enzyme system²⁹.

***Zingiber chrysanthum* (Zingiberaceae)**

Zingiber chrysanthum is a herb with a leafy stem about 1-1.5 meters long, a rhizomatous root stock and fine red and whitish flowers. It grows wildly distributed in the throughout tropical and subtropical parts of Tarai in the Kumaun and Garhwal regions of the state of Uttarakhand state in India³⁰. The plants of family Zingiberaceae occupy an important place in traditional Indian texts for their antispasmodic, anti-inflammatory, antioxidant, anthelmintic, hepatoprotective and antidiarrhoeal activities³¹. Chemical constituents of *Zingiber chrysanthum* are 1, 8- cineole (42%), alpha-fenchyl acetate (15%), alpha-terpineol (6%) and camphene (6%) as active principles in the essential oil of *Zingiber chrysanthum* rhizome³². Study was carried out to evaluate the hepatoprotective and antioxidant properties of acetone and methanol extracts of *Zingiber chrysanthum* rhizomes in mice. A significant increase in the levels of serum cholesterol, total proteins, bilirubin, albumin, urea, glucose, triglycerides and enzymic activity of AST, ALT and alkaline phosphatase as

well as histopathological changes in liver indicated a hepatotoxic effect of CCl₄ in mice. An improvement in biochemical parameters indicated a hepatoprotective effect in mice treated with AEZC and MEZC. The antioxidant potential of AEZC and MEZC was evaluated in terms of reducing power activity, from Fe³⁺ to Fe²⁺, 2, 2-diphenyl -1-picrylhydrazyl (DPPH) radical scavenging ability and the effect on the chelation activity of Fe²⁺ in comparison with, the synthetic and natural antioxidants. Butylated hydroxytoluene (BHT) was used as synthetic antioxidant and gallic acid and catechin were used natural antioxidants for reference. Both extracts showed significant antioxidant activity. The results of this study show that both AEZC and MEZC extracts have a hepatoprotective and antioxidant potential effect in mice with CCl₄- induced hepatotoxicity³³.

***Gmelina asiatica* (Verbenaceae)**

Gmelina asiatica popularly known as Nilakkumil in Tamil and Gopabhandra in Sanskrit is a large straggling shrub found in South India. The roots are used against gonorrhoea, catarrh of the bladder, rheumatism and as a blood purifier.

Gmelina asiatica is claimed to be useful in rheumatism, since it possess anti-inflammatory activity³⁴. The root of the plant also has potent hypoglycemic activity³⁵. *Gmelina* species is reported for its hepatoprotective activity³⁶. In the ethnobotanical claims, the aerial parts of the plant are used for the treatment of jaundice and other hepatic diseases by the folk tribes of Tamil Nadu State, India. In present study, the hepatoprotective activity of chloroform and ethanol extracts of *Gmelina asiatica* Linn. (Verbenaceae) aerial parts were evaluated against carbon tetrachloride (CCl₄) induced hepatic damage in rats. The extracts at dose of 400 mg/kg were administered orally once daily. The substantially elevated serum enzyme levels of aspartate aminotransferase (AST), alanine transaminase (ALT), serum alkaline phosphatase (SALP) and total bilirubin were restored towards normalization significantly by the extracts. Silymarin was used as standard reference and exhibited significant hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in rats. The biochemical observations were supplemented with histopathological examination of rat liver sections. The results of this study strongly indicate that *Gmelina asiatica* aerial parts have potent hepatoprotective action against carbon tetrachloride induced hepatic damage in rats. Ethanol extract was found more potent hepatoprotective. Meanwhile, *in vivo* antioxidant and free radical scavenging activities were also screened which were positive for both chloroform and ethanol extracts. This study suggests that possible mechanism of this activity may

be due to free radical-scavenging and antioxidant activities which may be due to the presence of flavonoids in the extracts³⁷.

***Tridax Procumbens* (Asteraceae):** *Tridax procumbens* Linn. (Asteraceae), a herb found throughout India is employed as indigenous medicine for a variety of ailments including jaundice³⁸. It is commonly used in Indian traditional medicine as anticoagulant, antifungal and in dysentery³⁹. Hepatoprotective activity of *Tridax procumbens* L. a medicinal herb commonly used in folklore system for wound healing and also against jaundice, was evaluated against paracetamol induced hepatic damage in male albino rats. Paracetamol induced hepatic damage was well manifested by significant increase in the activities of Alanine aminotransferase, Aspartate aminotransferase, Alkaline phosphatase in serum and enhanced lipid peroxidation. On the other hand, the activities of Superoxide dismutase and Catalase in liver tissue were lowered. Consequent to paracetamol induced hepatic injury, the Serum Bilirubin level was increased. Paracetamol toxicity, also resulted in, significant reduction in total serum protein and the hepatic glutathione and glycogen contents. The oral administration of varying doses of ethanolic extract of *Tridax procumbens* L. for the period of 7 days reversed these altered parameters to normal levels indicating the antioxidative and hepatoprotective efficacy of *Tridax procumbens* L. against paracetamol induced liver injury⁴⁰.

***Garcinia indica* (Clusiaceae)**

Garcinia indica Linn belonging to family Clusiaceae commonly called as 'Kokum' is found in Maharashtra and particular in Konkan, Goa and the western region of India. Fruits of *Garcinia indica* Linn have been suggested in the Indian system of medicine for a number of diseases. These include its usefulness as an infusion, in skin rashes caused by allergies, to relieve sunstroke, remedy for dysentery, an appetizer, liver tonic, to allay thirst and as a cardiogenic. The outer rind of the fruits of *Garcinia indica* Linn has been shown to be antioxidant activity⁴¹. The fruit rind contains polyisoprenylated benzophenones, garcinol, its isomer isogarcinol, xanthochymol, and isoxanthochymol⁴². The present study was undertaken to investigate antioxidant and hepatoprotective effect of aqueous and ethanolic extract of *Garcinia indica* Linn fruit rind. The aqueous and ethanolic extract of *Garcinia indica* Linn were studied for their antioxidant and hepatoprotective effects on carbon tetrachloride induced liver toxicity on Wistar albino rats. The study reveals that *Garcinia indica* Linn aqueous and ethanolic fruit rind extract significantly reduced level of serum biomarkers and

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restored near normal levels in CCl₄ induced hepatotoxic experimental rats. Aqueous and ethanolic extract produced significant antioxidant as well as hepatoprotective activity. The effect of aqueous extract was comparable to that of standard drug, silymarin⁴³.

***Momordica dioica* (Cucurbitaceae)**

Momordica dioica Roxb. genus is a native of tropical regions on Asia with extensive distribution in China, Japan, South East Asia, Polynesia besides tropical Africa and South America. As many of the species of this genus have been found to grow wildly in India, Bangladesh, Srilanka, Myanmar, Malay, etc. It contains Lectins, proteins, triterpenes and vitamins. The fruit contains a high amount of vitamin C⁴⁴. The fruit is rich in ascorbic acid and contains iodine. The fruit also contains alkaloid, flavonoids, glycosides and amino acids⁴⁵. In present study, the hepatoprotective activity of ethanolic and aqueous extracts of *Momordica dioica* Roxb. leaves were evaluated against carbon tetrachloride (CCl₄) induced hepatic damage in rats. The extracts were administered orally once daily. The substantially elevated serum enzymatic levels of serum glutamate oxaloacetate transaminase (AST), serum glutamate pyruvate transaminase (ALT), serum alkaline phosphatase (SALP) and total bilirubin were restored towards normalization significantly by the extracts. Silymarin was used as standard reference and exhibited significant hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in rats. The biochemical observations were supplemented with histopathological examination of rat liver sections. The results of this study strongly indicate that *Momordica dioica* Roxb. leaves have potent hepatoprotective action against carbon tetrachloride induced hepatic damage in rats. Ethanolic extract was found more potent hepatoprotective. Meanwhile, in vivo antioxidant and free radical scavenging activities were also screened which were positive for both ethanolic and aqueous extracts. This study suggests that possible mechanism of this activity may be due to free radical-scavenging and antioxidant activities which may be due to the presence of flavonoids in the extracts⁴⁶.

***Amorphophallus campanulatus* roxb. (Araceae)**

Amorphophallus campanulatus Roxb. belonging to family Araceae, locally known as Ol Kachu, is a perennial herb with rounded tuberous root stock (corm). The plant is widely distributed in Bangladesh, India and Africa. The tuberous roots of the plant have been used traditionally for the treatment of piles, abdominal pain, tumors, enlargement of spleen,

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asthma and rheumatism. The tuberous roots of the plant have also been reported to possess tonic, stomachic and appetizer properties. Antibacterial, antifungal and cytotoxic activities of tuberous roots extract were also reported. Chemical constituents of *Amorphophallus campanulatus* roxb. tubers are alkaloids, carbohydrates, proteins, amino acids, phenolic compounds, glycosides and flavonoids. In the present study, the hepatoprotective activity of ethanolic and aqueous extracts of *Amorphophallus campanulatus* (Roxb.) tubers were evaluated against carbon tetrachloride induced hepatic damage in rats. The extracts were administered orally once daily. The substantially elevated serum enzymatic levels were significantly restored towards normalization by the extracts. Silymarin was used as a standard reference and exhibited significant hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in rats. The biochemical observations were supplemented with histopathological examination of rat liver sections. The results of this study strongly indicate that *Amorphophallus campanulatus* (Roxb.) tubers have potent hepatoprotective action against carbon tetrachloride induced hepatic damage in rats. The ethanolic extract was found hepatoprotective more potent than the aqueous extract. The antioxidant activity was also screened and found positive for both ethanolic and aqueous extracts. This study suggests that possible mechanism of this activity may be due to free radical scavenging potential caused by the presence of flavonoids in the extracts⁴⁷.

***Phyllanthus niruri* (Euphorbiaceae)**

Phyllanthus niruri L (Euphorbiaceae), an annual and field weed that is widespread in temperate and tropical climates⁴⁸. *P. niruri* is a small erect annual herb growing up to 30 - 40 cm in height and indigenous to the Amazon rainforest and other tropical areas, including South East Asia, Southern India and China⁴⁹. It is popularly used in Asia, Africa and South America as a stomachic, aperitive, antihyperglycemic, antispasmodic, anti-hepatotoxic, antiviral, antibacterial, laxative, diuretic, carminative, in the management of diabetes, constipation, fever including malaria, jaundice, hepatitis B, dysentery, gonorrhoea, syphilis, tuberculosis, cough, influenza, diarrhoea, vaginitis, tumors and kidney stones⁵⁰. Antioxidant activity and hepatoprotective potential of *Phyllanthus niruri* were investigated. Methanolic and aqueous extract of leaves and fruits of *P. niruri* showed inhibition of membrane lipid peroxidation (LPO), scavenging of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical and inhibition of reactive oxygen species (ROS) in vitro. Antioxidant activity of the extracts were also demonstrable in vivo by the inhibition of the carbon tetrachloride (CCl₄) - induced formation

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of lipid peroxides in the liver of rats by pretreatment with the extracts. CCl₄ - induced hepatotoxicity in rats, as judged by the raised serum enzymes, glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT), was prevented by pretreatment with the extracts, demonstrating the hepatoprotective action of *P. niruri*⁵¹.

***Azadirachta indica* (Maliaceae)**

Azadirachta indica (Maliaceae) is known for its several medicinal values. The leaves, seeds, roots and bark of the plant possess bitter active principles in different constituents. The efficacy of *Azadirachta indica* extract against malarial, bacterial and viral infections had been reported. The plant also has insecticidal properties. Moreover, the antifertility and hypotensive with minimal negative chronotropic effects of *Azadirachta indica* had been reported. The bitter principles of *Azadirachta indica* are also known to increase the flow of saliva and gastric juice as a result of which the plant is used as stomachics. *Azadirachta indica* lowered blood glucose level and attenuated gastric ulcerogenesis. In present study we evaluated the hepatoprotective and antioxidant activity of methanolic and aqueous extracts of neem leaves against CCl₄ induced hepatotoxicity in isolated rat hepatocytes. Assessment of antihepatotoxic activity was done by *In vitro* studies involved isolation of hepatocytes and examination of the effect of toxicants along with the test samples. Antioxidant activity was determined by measuring the glutamyl pyruvate transaminase (GPT), reduced glutathione (GSH), alkaline phosphate level (ALP), asparatate transminase activity (AST) and enzyme activity. The result reveals that the plant contains both the antioxidant and hepatoprotective activity⁵².

***Thespesia lampas* (Malvaceae)**

Thespesia lampas Dalz & Gibs belongs to the Malvaceae family, vernacularly known as “*Ranbhendi*” is found as a wild herb growing during monsoon on the hills in a throughout India and also in Eastern Tropical Africa. In the folk medicine, this plant has been considered to be hepatoprotective and traditionally root paste used to cure jaundice in Korku tribe of Amravati district of Maharashtra and also in Nepal⁵³. The roots of this plant are reported for anti-diabetic, anti-hyperlipidaemic, hepatoprotective, antioxidant and anthelmintic activity⁵⁴. Flowers contain quercetin and some protocatechuic acid. The stems of the plant are used as a folk remedy and it is traditionally used in the treatment of inflammation, acidity, bleeding nose, bronchitis, cough, dysentery, fever, sun stroke, urinary complaints, anthelmintic, carbuncle. *T. lampas* stems showed antimicrobial activity and reported for presence of gossypol. In the ethnobotanical

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claims, the stems are used for the treatment of jaundice and other hepatic diseases by the folk tribes of Trimbakeshwar Hills, Maharashtra state, India⁵⁵. *Thespesia lampas* Dalz & Gibs is an important folk medicinal plant was evaluated for hepatoprotective and antioxidant activity against carbon tetrachloride (CCl₄) induced hepatic damage in rats. In the present study, the *T. lampas* stem extracts were administered orally once daily for nine days and on seventh day after one hour of drug administration CCl₄ was given orally. After 24 h of ninth day, they were sacrifice and their livers were dissected for biochemical and histopathological studies. The extracts showed significant hepatoprotective and antioxidant effect by lowering the serum levels of transaminases (SGOT and SGPT), alkaline phosphatase (ALP), bilirubin, protein, cholesterol and triglyceride as compared to silymarin as a standard hepatoprotective agent. The extracts showing increased levels of superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH) and decreased level of lipid peroxidation (LPO). The biochemical observations were supplemented with histopathological examination of rat liver sections. The results of *T. lampas* stems extract showed significant protection to the liver against carbon tetrachloride induced damages. Study suggested that among comparative significance of various extracts, the methanolic extract of *T. lampas* stems having better efficacy and significant activity⁵⁶.

Mesua ferrea (Clusiaceae)

Mesua ferrea belonging to family Clusiaceae commonly called Ceylon ironwood, Indian rose chestnut, Cobra's saffron or Nagkesar. The plant is named after the heaviness of its timber and cultivated in tropical climates for its form, foliage and fragrant flowers. It is native to tropical Sri Lanka but also cultivated in Assam, in southern Nepal, in Indochina and the Malay Peninsula. The seed oil of this tree found to be astringent, digestant anti poisonous, antimicrobial, anti-inflammatory, antipyretic and anthelmintic in many cases. In India, it is known for its use in fever, itching, nausea, leprosy, skin disorders, erysipelas, bleeding piles, metrorrhagea, menorrhagea, excessive thirst, and sweating. Study was carried out to evaluate the antioxidant activity of dried flower methanolic extract of *Mesua ferrea* in male Wister rat. Methanolic extract of *Mesua ferrea* linn was taken in 3 graded doses and were evaluated for their antioxidant activity and hepatoprotective effects. Rats were artificially inoculated with *Staphylococcus aureus* (ATCC 43300) in drinking water on the onset of experiment. After 24 h of bacteria inoculation, the methanolic extract was administered daily for 1 week. After 1 week, rats were sacrificed for their liver. The effect of *Mesua* extract was studied on antioxidant profile of

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liver. ALT, AST, CPK, Creatinine and urea profile were analyzed with standard procedures. Administration of *Mesua ferrea* flower extract in all the doses caused a significant increase in biochemical parameters and posed a hepatoprotective effect however in 100 mg/kg of BW, the effect was significant. CAT, SOD, GPx, and GR were measured for evaluation of antioxidant activity and found significantly higher activity in *Mesua* fed rats than control. AAT and AST showed a significant decrease in *Mesua* fed groups of Wister Rats. This investigation demonstrated the potent antioxidant activity of *Mesua ferrea* flower extract⁵⁷.

***Ichnocarpus frutescens* (Apocynaceae)**

The plant *Ichnocarpus frutescens* (linn). R.Br. belonging to Family Apocynaceae is a large much branched twining shrub, young branches are finely fulvous-tomentose. It is locally called Botilai and the plant is used by the local peoples of Mohuda, Berhampur, Orissa, India for simple fevers and to treat liver disorder. The whole plant is used as a tribal medicine in atrophy, bleeding gums, cough and dysentery. Stalk and leaves in decoction is used in the treatment of skin eruptions. A decoction of the roots of Colocynth, Anantamul, Sariva (Sanskrit) and Hedyotis biflora prepared in the usual way is administered with the addition of powdered long pepper and bdellium in chronic skin diseases, syphilis, loss of sensation and hemiplegia. The present study is aimed at evaluating the hepatoprotective effect of chloroform and methanol extract (CEIF and MEIF) of whole plant of *I. frutescens* (Linn.) by paracetamol-induced liver damage in rats. The chloroform and methanolic extracts of *I. frutescens* were studied for their hepatoprotective and antioxidant effects on paracetamol induced acute liver damage on Wistar albino rats. The degree of protection was measured by using biochemical parameters such as serum glutamate oxalate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP), bilirubin and total protein. Further, the effects of both extracts on lipid peroxidation (LPO), glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) were estimated. CEIF and MEIF at a dose level of 250mg/kg and 500mg/kg produce significant hepatoprotection by decreasing the activity of serum enzymes, bilirubin, and lipid peroxidation, while they significantly increased the levels of Glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) in a dose dependent manner. The effects of CEIF and MEIF were comparable to that of standard drug, Silymarin. From this study, it can be concluded that the chloroform and methanol

extract of *I. frutescens* is not only an effective hepatoprotective agent, but also possesses significant antioxidant activity⁵⁸.

***Irvingia gabonensis* (Irvingiaceae):** *Irvingia gabonensis*, commonly known as ‘African mango’ or ‘bush mango’ is a tree that grows to 15–40 m, with a slightly buttressed bole. *Irvingia gabonensis* occurs in the wild lowland forest, 2-3 trees are often found together and, in some areas, larger groups have been reported. It is largely distributed in Africa and it possesses edible fruits largely used in traditional and modern medicine for the treatment of a variety of illnesses; it also has industrial applications. In Cameroon, where the plant is locally known as ‘Kaka’, the stem bark is used to treat hunchback and infections. The *in vitro* hepatoprotective effect of the methanolic extract from *Irvingia gabonensis* on CCl₄- induced liver cell damage as well as the possible antioxidant mechanisms involved in this protective effect were investigated. The phytochemical investigation of this methanolic extract led to the isolation of seven compounds identified as: 3-friedelanone, betulinic acid, oleanolic acid, 3, 3’, 4’-tri-*O*-trimethylellagic acid, methyl gallate, hardwickiic acid and 3- β -acetoxyursolic acid. The hepatoprotective activity of these compounds was tested *in vitro* against CCl₄-induced damage in rat hepatoma cells. Compounds oleanolic acid, 3- β -acetoxyursolic acid, methyl gallate and betulinic acid showed significant hepatoprotective activity as indicated by their ability to prevent liver cell death and LDH leakage during CCl₄ intoxication. In addition, 2, 4-dinitrophenyl-1 picrylhydrazyl (DPPH) radical scavenging activity, the β -Carotene-Linoleic Acid Model System (β -CLAMS), the Ferric-Reducing Antioxidant Parameter (FRAP) and microsomal lipid peroxidation assays were used to measure the antioxidant activity of the crude extract and isolated compounds. Compared with compounds 3-friedelanone, betulinic acid, 3, 3’, 4’-tri-*O*-trimethylellagic acid and hardwickiic acid, compounds oleanolic acid, methyl gallate and 3- β -acetoxyursolic acid showed significant antioxidant effects involving radical scavenging action, inhibition of microsomal lipid peroxidation, β -CLAMS and FRAP assays. These results suggest that the protective effects of the crude extract of *Irvingia gabonensis* against CCl₄-induced hepatotoxicity possibly involve the antioxidant effect of these compounds⁵⁹.

Licorice (Fabaceae)

Licorice has been used as a medicinal plant for thousands of years. Licorice has been used in Chinese folk medicine for the treatment of various disorders. Licorice has the biological capabilities of detoxication, antioxidation, and

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antiinfection. The active component of licorice, glycyrrhizic acid, is hydrolyzed *in vivo* to glycyrrhetic acid, which is responsible for most of its pharmacological properties. In ancient Chinese medicine and during Roman times, licorice was also recommended to cure sterility in women. Licorice has held claim for therapeutic use for fevers, liver ailments, dyspepsia, gastric ulcers, sore throats, asthma, bronchitis, Addison's disease and rheumatoid arthritis and has been used as a laxative, antitussive and expectorant. Among its most consistent uses are as a demulcent for the digestive system, to treat coughs, to soothe sore throats, and as a flavoring agent. In this study, we evaluated the antihepatotoxic effect of licorice aqueous extract (LE) on the carbon tetrachloride (CCl₄)-induced liver injury in a rat model. Hepatic damage, as revealed by histology and the increased activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) activities, and decreased levels of serum total protein (TP), albumin (Alb) and globulin (G) were induced in rats by an administration of CCl₄ (1:1 in groundnut oil). Licorice extract significantly inhibited the elevated AST, ALP and ALT activities and the decreased TP, Alb and G levels caused by CCl₄ intoxication. It also enhanced liver super oxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px), glutathione reductase (GR), Glutathione S-transferase (GST) activities and glutathione (GSH) level, reduced malondialdehyde (MDA) level. Licorice extract still markedly reverses the increased liver hydroxyproline and serum TNF- α levels induced by CCl₄ intoxication. The data of this study support a chemopreventive potential of licorice extract against liver oxidative injury⁶⁰.

***Calotropis procera* (Asclepiadaceae)**

Calotropis procera Decne. (*Asclepiadaceae*) is an evergreen poisonous shrub. It is naturally and widely spread in different areas of Saudi Arabia. It grows commonly around farms, agricultural areas, and in the sandy warm parts especially in the western coastal plain (Tehama plain)⁶¹. *Calotropis procera* possesses flavonoids, alkaloids, cardiac glycosides, tannins, sterols and triterpenes. Flowers of *C. procera* possess anti-inflammatory, antipyretic, analgesic, antimicrobial properties and larvicidal activity. The latex of the plant was reported to possess analgesic and wound healing activity. The roots are reported to have anti-fertility and anti-ulcer activities. The flowers are reported to contain flavonoids, quercetin-3-rutinoside, sterols, etc. However, there are no reports regarding the hepatoprotective and anti-oxidant activity of the flowers of this plant. Flavonoids are reported

to possess anti-oxidant and hepatoprotective properties. Hepatoprotective activity of 70% ethanolic extract of flowers of *C. procera* was studied against CCl₄ induced hepatic injury in albino rats and mice. In addition, antioxidant activity was studied by *in vitro* models. Pre-treatment with 70% ethanolic extract (CPA) reduced the biochemical markers of hepatic injury like serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase, alkaline phosphatase, bilirubin, cholesterol, HDL and tissue glutathione (GSH) levels. Similarly pretreatment with CPA reduced the CCl₄ induced elevation in the pentobarbitone sleeping time. Histopathological observations also revealed that pretreatment with CPA protected the animals from CCl₄ induced liver damage. CPA demonstrated dose dependant reduction in the *in vitro* and *in vivo* lipid peroxidation induced by CCl₄. In addition it showed dose dependant free radical scavenging activity. The results indicate that flowers of *C. procera* possess hepatoprotective property possibly because of its anti-oxidant activity. This property may be attributed to the quercetin related flavonoids present in the flowers of *Calotropis procera*⁶².

Discussion

Many hepatotoxicants including carbon tetrachloride, nitrosamines, and polycyclic aromatic hydrocarbons required metabolic activation, especially by liver cytochrome P450 enzymes to form reactive, toxic metabolites that in turn produces liver injury in experimental animals and humans. It is commonly recognized that reactive oxygen species (ROS) are involved in a variety of physiological and pathological processes, including cellular signal transduction, cell proliferation, differentiation and apoptosis, as well as ischemia – reperfusion, injuries, inflammation and many neurodegenerative disorders. In healthy individuals, ROS production is continuously balanced by natural antioxidant defense system. Oxidative stress is a process where the physiological balance between pro-oxidants and antioxidants is disrupted in favor of the former, ensuing in potential damage for the organism. Carbon tetrachloride (CCl₄) is frequently used as a chemical inducer of experimental tissue damages. Transient tissue disorders after the administration of CCl₄ is believed to be induced by the trichloromethyl radical ($\cdot\text{CCl}_3$). This free radical induces an adverse reaction by forming other free radicals after its administration in the early stage between intracellular uptake and transformation into storage types. Many biological substances such as membrane lipids, proteins, and nucleic acids are known to be injured by trichloromethyl radicals. Dietary antioxidant intake may be an important strategy for inhibiting or delaying the oxidation

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of susceptible cellular substrates, and is thus relevant to disease prevention in many paradigms. Phenolic compounds such as flavonoids, phenolic acids, diterpenes and tannins have received attention for their high antioxidative activity. Converging evidence from both experimental and epidemiological studies have demonstrated that cereals, vegetables, and fruits contain a myriad of phenolic compounds.

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