

LIVER PROTECTION BY EDIBLE FRUITS – A REVIEW

T. Kalpana¹ and S. Gopinathan^{2*}

¹Ph.D. Scholar, Pharmaceutical Biotechnology Lab., Department of Biotechnology, Srimad Andavan Arts and Science College (Autonomous), Tiruchirappalli-620005, India.

²Director-Projects, Department of Biotechnology, Srimad Andavan Arts and Science College (Autonomous), Tiruchirappalli-620005, India.

Article Received on
08 March 2016,

Revised on 29 March 2016,
Accepted on 20 April 2016

DOI: 10.20959/wjpr20165-6165

Corresponding Author*Dr. S. Gopinathan**

Director-Projects,
Department of
Biotechnology, Srimad
Andavan Arts and Science
College (Autonomous),
Tiruchirappalli-620005,
India.

ABSTRACT

The liver plays a central role in transforming and clearing chemicals and is susceptible to the toxicity from the chemical agents. Hepatotoxicity implies chemical-driven liver damage. Certain drugs when taken in overdoses and sometimes even when introduced within therapeutic ranges may injure liver. In Indian traditional systems of medicine a number of medicinal herbs and their formulations are used to cure liver disorders. The consumption of some plant parts and fruits play a vital role in human health care. Recent scientific investigations have indicated that beneficial role of different plant parts and particularly fruits are attributed to the presence of diverse phytochemicals present within them. The present review is the compilation of investigations carried out and reported on some edible fruits, which are consumed by humans and are demonstrated as

hepatoprotective agents.

KEYWORDS: Liver injury, hepatotoxins, hepatoprotective agents, edible fruits, phytochemicals.

INTRODUCTION

The liver plays a pivotal role in the regulation of vital physiological functions such as metabolism, secretion of bile, storage of vitamins and detoxification of drugs and other toxins.^[1] The liver is also involved in the biochemical processes of providing nutrients, supplying energy, growth and reproduction. In addition, it aids in the metabolism of carbohydrates and fats.^[2] Additionally, it is the key organ of metabolism and continuous

excretion of various xenobiotics. The toxins absorbed from the intestinal tract gain access first to the liver by portal blood supply resulting in a variety of liver injuries and ailments. Thus liver diseases are remaining one of the major health problems which require immediate medical attention.^[3] Modern synthetic medicines have little to offer liver protection from toxins and other alleviation of other hepatic diseases, whereas the plant based natural preparations are much preferable drug for the treatment of liver damage and further, they protect the liver from other liver diseases.^[4]

Certain drugs when taken in overdoses and sometimes even when taken within therapeutic ranges may injure the liver. Other chemicals used in various industries, including food processing industries and drinking water treatment units and few herbal medicines can also induce hepatotoxicity. Chemicals that cause liver injury are called hepatotoxins. Till date, modern drugs which are available in the markets have not been able to serve as satisfactory medications for liver disorders because of their diverse side effects and high cost. It is therefore necessary to search for alternative drugs for the treatment of liver diseases to replace the currently available drugs of doubtful efficacy and safety. Herbal medicines, fruits, vegetables and other plant parts play an important role in the management of various liver disorders.^[5]

Man since time immemorial has been using herbs and other natural products as medicine to alleviate many diseases and also for developing immunity or resistance against some metabolic and degenerative diseases associated with aging. The Indian traditional systems of medicine such as Ayurveda, Siddha, and Unani are developed based up on the experiences in the use of plant products to combat common diseases. Medicinal plants which are mentioned in Ayurveda for liver ailments have drawn much attention as no reliable hepatoprotective drugs are available in modern medicine.^[6] Radhika and Yuvarani^[7] reviewed the hepatoprotective potential of different parts of some selected plants. They also suggested that the leading cause of liver disease in India is hepatitis viruses, which often leads to Fulminant Hepatic Failure. Research on natural hepatoprotective products opens up new vistas of therapeutic applications for hepatoprotection. Search for liver protectants has been evaluated as promising field of investigation and a number of formulations containing some plant products are being routinely used to cure hepatic damage. The consumption of fruits is more beneficial and demonstrated as hepatoprotective because of the phytochemicals present in the fruits. Since they provide nutrition as well as useful as drug and therefore they can be

considered as nutraceuticals. The present review is aimed to compile the scientific investigations reported on the use of fruits as hepatoprotective agents.

***Benincasa cerifera* Thunb.**

Benincasa cerifera (Cucurbitaceae), commonly known as “Winter Melon” or “Ash Gourd” or “Wax Gourd” is one of the best fruits having medicinal values and it is also used as vegetable. It is cultivated throughout the arid and semiarid regions of India and also on the hilly regions up to 1200 meter (MSL) altitude. In Ayurvedic system of medicine the fruit of *B. cerifera* is mentioned as “Kushmanda” and it is considered as diuretic (mutral), aphrodisiac (vrishya), and appetizer (dipana); used in acid reflux syndrome (Amlapitta), purpura (Raktapitta), emaciation (Kshaya), and mental disorder (Chetovikara). Thakkar *et al.*^[8] investigated the in-vivo antioxidant and hepatoprotective activities of *B. cerifera* fruit extract in alcohol induced liver damage in Wistar albino rats. The authors observed significant hepatoprotective activity by the extract. The liver function parameters such as serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), total bilirubin (TB), direct bilirubin (DB), triglyceride (TG) and total cholesterol (TC) were increased in alcohol intoxicated rats and they were decreased significantly near to normal level after the administration of *B. cerifera* fruit extract. Significant in-vivo antioxidant activity was also found with the fruit extract. The activity of in vivo antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) was decreased in diseased rats and the activity was significantly increased after the administration of fruit extract. The increased lipid peroxidation (LPO) in disease condition was significantly reduced by the fruit extract treatment. From this study it was concluded that *B. cerifera* fruit is an effective antioxidant as well as a hepatoprotective agent.

***Benincasa hispida* (Thunb.) Cogn. [synonym of *B. cerifera*]**

Anti-inflammatory drugs offer relief symptoms in the inflammatory diseases when the underlying cause of inflammation is unidentified. Since inflammation is also one of the pathological symptoms of liver damage, any drug having anti-inflammatory activity may be ideal as supportive drug to cure liver damage. A number of Cucurbitaceae plants have been shown to possess anti-inflammatory activity. Anti-inflammatory activity of petroleum ether and methanol extract of *B. hispida* fruit was reported by Rachchh *et al.*^[9] Both the extracts at the dose of 300 mg/kg body weight, produced dose dependent and significant inhibition of carrageenan- induced paw edema, histamine induced paw edema and cotton pellet induced

granuloma in rat model. In carrageenan- induced paw edema model, petroleum ether and methanol extracts showed maximum inhibition in inflammation (0.270 ± 0.063 , 0.307 ± 0.043 respectively) as compared to control group (1.27 ± 0.059) which were comparable with the treatment with standard reference drug, valdecoxib (0.247 ± 0.033). In histamine-induced paw edema, both the extracts showed maximum inhibition (62.86% and 54.84% respectively) as compared to control group, which were comparable with the standard drug, cetirizine (95.24%). Petroleum ether and methanol extracts showed slight reduction in granuloma tissue formation in cotton pellet implanted rats, which were not significant with that of standard drug, diclofenac sodium.

In Ayurveda, the fruit of *B. hispida* fruit is known as 'Kushmanda' and it is used to cure stomach ulcer (gastroprotective), heart diseases (angiogenic), free radical scavenging potential (antioxidant), bronchodilator (anti-asthmatic), prevention from usage of narcotics (opioid withdrawal benefit), antipyretic, antidiarrheal, antiobesity, CNS mediating agent (anorectic) and anti-Alzheimer's disease. Ghosh and Bhagel^[10] have investigated the phytochemicals present in the fruit extract of *B. hispida* and identified the compounds such as lupeol, β - sitosterol and their acetates, cucurbitacin, rhamnose, mannitol, triacontenol, fat, vitamin, glucose, adenine, trigonelline and histidine based on the TLC and HPTLC fingerprint analyses. The waxy layer of fruit skin contains pentacyclic triterpene, namely isomultiflorenol acetate. The chemical compounds such as hexanal and pyrazine are responsible for the aroma of the fruit. The researchers reported that treatment of fruit pulp extract of *B. hispida* markedly decreased the lipid peroxidation level, significantly increased the superoxide dismutase (SOD), catalase (CAT) activity and reduced glutathione level in different parts of the brain. This study showed the antioxidant property of extract of *B. hispida* and may be beneficial in the management of colchicine induced Alzheimer's disease in rat model due to its antioxidant properties.

Oxidative stress induced by free radicals is the main cause of many human diseases. Plant-derived antioxidant supplements can counter oxidative damage in cells. Samad et.al.^[11] investigated the effects of water extracts from dried seeds of *B. hispida* on *in vitro* antioxidant activity and correlated the activity to the content of total phenolic compounds and flavonoids. The levels of phenolic and flavonoid compounds were 81.3 ± 1.4 mg gallic acid equivalent /g and 486.8 ± 4.1 mg catechin equivalent /g dry mass, respectively. The *in vitro* antioxidant activity of *B. hispida* was estimated by DPPH (2,2-diphenyl-picrylhydrazyl

hydrate), ABTS (1, 2,2'-azinobis-[3-ethylbenzothiazoline-6-sulfonic acid]) and HRSA (hydroxyl radical scavenging activity) methods in a dose-dependent manner, with maximum inhibition of $79.8 \pm 0.2\%$, $82.3 \pm 1.9\%$ and $95.5 \pm 0.8\%$, respectively. Inhibition of linoleic acid oxidation and nitrite scavenging activity were maximum $73.2 \pm 1.0\%$ and $73.6 \pm 1.3\%$ at 6 days and 1-h incubation time, respectively. Based on the present investigation it is suggested that the dried seeds from *B. hispida* could be used as a source of natural antioxidant agent in the food industry.

***Coccinia grandis* Linn.**

Coccinia grandis (Cucurbitaceae) is a climber herb cultivated throughout India. In folklore medicine, the fruit is used to treat leprosy, fever, asthma, infective hepatitis, jaundice and sore throat. It is also used as expectorant and astringent. The alcoholic extract of the plant is used as hypoglycaemic and anti-oxidant agent. A polyphenolic compound isolated from the ethanol extract possesses anti-dyslipidimic activity.

Vadivu *et al.*^[12] have evaluated the hepatoprotective activity of the alcoholic extract of the fruits of *Coccinia grandis* against CCl_4 induced hepatotoxicity in rats. Treatment with 250 mg/kg of ethanolic fruit extract significantly reduced the levels of liver marker enzymes such as Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT), Alkaline phosphatase (ALP) total protein and direct bilirubin, indicating its hepatoprotective action. Assessment of liver function can be made estimating the activities of SGOT, and SGPT which are present in higher concentrations in cytoplasm. In hepatopathy, these enzymes leak into the blood stream and the activity is directly proportional to the extent of liver damage.

Histopathological reports also showed that *C. grandis* treatment markedly reduced the toxicity of CCl_4 and preserves the histo-architecture of liver tissues to normal conditions. The authors reported that the flavonoids present in the fruit exert multiple biological activities including antioxidant and free radical scavenging properties. The polyphenol compounds inhibit stellate cell activation by perturbing signal transduction pathway and cell protein expression. The administration of hepatoprotective agents may induce the hepatocytes to resist the toxic effect of CCl_4 . Therefore the hepatoprotective activity of the extract may be due to its antioxidant property exerted by flavonoids available in the fruits.

***Coccinia indica* Linn.**

Coccinia indica is an herb belongs to the family Cucurbitaceae contains resins, alkaloids. It is an anti-inflammatory agent, good laxative and used in many other medicinal applications. The aqueous fruit extract of *C. indica* against paracetamol induced hepatotoxicity in albino Wistar rats was carried out by Arun kumar and Eswar kumar.^[13] The aqueous extract of *C. indica* fruit was administered to the experimental animals in two different dosages (200mg/kg) and (400mg/kg) for 14 days. The histopathological studies and liver marker enzymes such as SGOT, SGPT and ALP confirmed that the 400mg/kg dosage of extract showed reduction of hepatic damage and lowered the necrosis process. Further, it improvised the normal architecture of liver cells and did not show any significant pathological manifestations. The elevation in the liver marker enzymes such as SGOT, SGPT ALP and the level of total bilirubin in paracetamol intoxicated rats was significantly high when compared to the healthy rats and the treatment with aqueous extract of *C. indica* reduced the activity of SGPT, SGOT, ALP and the level of total bilirubin in diseased animals which were comparable to the levels of the healthy rats. From the present investigation the researchers have concluded that the aqueous extract of *C. indica* possess significant hepatoprotective activity against paracetamol induced liver damage in rats.

***Cucumis trigonus* Roxb.**

C. trigonus (Cucurbitaceae) known as “Bitter Gourd” is indigenous to India and it is also growing in Ceylon, Malaya, North Australia, Afghanistan and Persia.^[14] In Indian traditional systems of medicine the fruit pulp of *C. trigonus* is used as expectorant, liver tonic, stomachic and purgative. In recent investigations the fruit pulp is proved to be useful in leprosy, jaundice, diabetes, bronchitis and amentia.^[15] Liver protective action of *C. trigonus* fruit extract was evaluated in an animal model study of liver damage induced by CCl₄ by Kalpana *et al.*^[16] The fruit was extracted in petroleum ether, chloroform, alcohol and water. The water and alcoholic extracts were found to be positive for the presence of steroids, triterpenoids, saponins and glycosides and petroleum ether extract was found to be positive for the presence of fat and fatty oil. Treatment with 300 mg/kg dose of *C. trigonus* alcoholic, chloroform and aqueous extracts markedly prevented CCl₄ induced elevation of ALT, AST and ALP activities and the level of bilirubin. But the petroleum ether extract did not protect rat liver against CCl₄ damage. According to the results, it is hypothesized by the researchers that steroids and triterpenoids present in the alcoholic extract could be responsible for the hepatoprotective activity.

***Garcinia pedunculata* Roxb.**

G. pedunculata is a medicinal plant commonly known as “Amlavetasa” and its fruit has been indicated for many ailments such as chronic catarrh, asthma, cough, bronchitis, fever and as cardiogenic.^[17] Ravi *et al.*^[18] evaluated the hepatoprotective activity of the fruit extract of *G. pedunculata* in paracetamol induced liver toxicity in rats. The preliminary phytochemical analysis of the fruit extract revealed the presence of flavonoids, saponins, glycosides, steroids, alkaloids and phenols. In the present study the paracetamol toxicity significantly increased the liver marker enzymes such as serum transaminases (SGOT and SGPT), alkaline phosphatase (ALP) and the elevation was decreased significantly after the administration of fruit extract when compared with reference drug. Histopathological studies has shown the mild to moderate regenerative effect of the extract and it might have possessed membrane stabilizing action and thus contribute the protection of structural integrity of the hepatocytes. It is further reported that the fruit extract of *G. pedunculata* has good antioxidant property.

***Litchi chinensis* Sonner.**

Litchi chinensis (Sapindaceae) is a small evergreen tree, grows up to 10-12 meter height with broad round – topped crown and glossy green foliage. Fruits are globose or oblong to ovate about 3.8 cm long by 2.5 cm diameter. Red when ripe and pericarp is dry, thin, brittle, sharply tuberculate, containing fleshy white translucent juice and seeds are having edible oil. Litchi fruit is claimed to possess liver tonic activity hence researchers select to establish scientific evidence for its traditional claim. Hepatoprotective activity of aqueous extract of *L. chinensis* fruit was evaluated by Souza *et al.*^[19] by using CCl₄ induced hepatic injury in adult Wistar rats. Qualitative phytochemical analysis of the alcoholic extract of *L. chinensis* fruit showed the presence of carbohydrates, flavonoids and tannins, proteins and amino acids. The alcoholic and aqueous extracts showed dose dependent activity. Both extracts at higher dose i.e., 500 mg/kg body weight produced a significant reduction in the activity of liver marker enzymes such as SGPT, SGOT, ALP and the level of bilirubin in the CCl₄ intoxicated rats, when compared with rats treated with reference drug (LIV-52). Histopathological examination of the liver tissues of CCl₄ intoxication showed intense inflammation, congestion in the sinusoids, pyknosis of nucleus and necrosis of the liver cells. Pre-treatment with LIV-52 and alcoholic and aqueous extracts of Litchi fruit have shown reduction in inflammation and significantly prevented degeneration of hepatocytes. The protective activity shown by the Litchi fruit extracts may be due to their antioxidant potential, which may be due

to the presence of flavonoids and also the fruit is known to be rich in vitamin C one of the well known antioxidant phytochemical.

***Momordica dioica* Roxb.**

M. dioica is a perennial climber with tuberous roots and is growing throughout India. Phytochemical investigation has revealed the presence of alkaloids and ascorbic acid in the fruits. Shankar *et al.*^[21] have studied the hepatoprotective activity of the fruits of *M. dioica* against CCl₄ induced hepatotoxicity in rats. The ethyl acetate and ethanolic extracts of *M. dioica* showed a significant hepatoprotective activity at the dose of 200 mg/kg of body weight. The CCl₄ treatment injured the liver in the animals and showed significant increase in the level of serum total bilirubin, and activities of ALP, AST and ALP along with a significant increase in total protein and after the treatment with fruit extracts the abnormalities in the biochemical parameters were brought back to normalcy. The phytochemical screening of ethanol extract showed positive results for steroids, triterpenoids and glycosides. The results of the present study suggested that *M. dioica* fruit extract possess potential hepatoprotective activity against CCl₄ induced hepatotoxicity possibly by its antioxidant activity.

***Morinda citrifolia* Linn.**

Morinda citrifolia is a small evergreen tree and it is native to Pacific Islands and growing in Polynesia, Asia and Australia. Its fruit is known as 'Noni' or 'Indian mulberry' and the fruit is 3-4 inches in diameter with a warty, pitted surface. *M. citrifolia* is one of the most important medicinal plants and it has been promoted for a wide range of medicinal uses to cure arthritis, burns, circulatory weakness, diabetes, cancer, skin inflammation and wounds.^[22-24] The fermented fruit juice of the *M. Citrifolia* was used to study the hypoglycaemic and hepatoprotective properties in diabetes-induced rats by Shivananda *et al.*^[25] The rats were randomly distributed into 4 groups of 6 rats in each group (control, diabetic experimental, diabetic standard, and diabetic untreated). Diabetes was induced by administration of streptozotocin (50mg/kg body weight). Fasting blood glucose, body mass, liver tissue glycogen contents and the extent of liver degeneration were assessed. Diabetic experimental animals were treated with *M. citrifolia* juice (2 ml/kg, twice a day) and standard reference hypoglycaemic drug, glibenclamide orally for 20 days. Both the treatment groups exhibited a significant reduction in blood glucose level of 150 mg/dl \pm 15.88 and 125 mg/dl \pm 3.89, respectively, as compared to diabetic untreated animals with fasting blood glucose of 360

± 15.81 mg/dl, ($P < .003$). On 10th day of experiment, diabetic experimental animals exhibited a decrease in body mass (10.2 g, 5.11%) which increased significantly by the 20th day (6 g, 3.0%, $P < .022$). Histological study of liver tissue obtained from untreated diabetic animals revealed significant fatty degeneration as compared to other three groups. The data of this study proved the hypoglycaemic and hepatoprotective activity of *M.citrifolia* fruit extract.

***Phoenix dactylifera* Linn.**

The botanical name of date fruit is *Phoenix dactylifera*. The hepatoprotective activity of aqueous extract of date fruit extract (ADE) against dichloro acetic acid (DCA) induced liver damage in rats was investigated by Amira el Arem *et al.*^[26] Oral administration of the ADE to male Wistar rats intoxicated with DCA at 0.5 and 2g/L as drinking water for 2 months, demonstrated a significant protective effect by lowering the activities of hepatic marker enzymes such as AST, ALT, LDH and GGT and the level of conjugated bilirubin and also by improving the histological architecture of the rat liver. ADE attenuated oxidative stress by decreasing the extent of hepatic TBARS (Thiobarbituric Acid Reactive Substances) formation, restoring the activities of antioxidant enzymes like SOD, CAT and GPx and also by reducing hepatic DNA fragmentation. The free radical scavenging activity of ADE was evaluated by using the DPPH assay method. The phytochemical analysis of the aqueous extract of date fruit revealed the presence of total carbohydrate, phenols, flavonoids and tannins. The different polyphenolic compounds are identified as gallic acid, chlorogenic acid, protocatechuic acid, ferulic acid, caffeic acid, syringic acid, m-hydroxybenzoic acid, coumaric acid, phenyl acetic acid and catechin. The present investigation on date fruit demonstrated that it protects rat liver from DCA- induced liver injury and suggested as a potential hepatoprotective agent.

***Piper longum* Linn.**

Piper longum is called as “Indian Long Pepper” and it is an important medicinal plant used in Ayurveda and Unani systems of medicine.^[27,28] Fruits of *P. longum* are ovoid, yellowish orange sunk in freshly spike. The fruits have warm taste and useful in asthma, bronchitis, tumours, spleen disorders, inflammations, leprosy, insomnia, jaundice, piles and tuberculosis. The root is used as laxative, antihelminthic and useful in abdominal pains and diseases of spleen.^[29] Ethanol extract of *P. longum* fruits and five different crude fractions, such as petroleum ether (40-60⁰), solvent ether, ethyl acetate, butanol and butanone were subjected to

preliminary qualitative chemical investigations. The ethanolic extract and all other fractions were screened orally for hepatoprotective activity in adult Wistar rats by using CCl₄ induced liver damage. Biochemical parameters such as SGOT and SGPT were analysed to determine the status of liver functions of the rats. The ethanol extract and its butanol fraction have shown marked decrease in both SGOT and SGPT activity and the activity was comparable to that of rats treated with LIV-52, the reference drug. Histopathological profile of the diseased rat liver showed intense centrilobular areas, whereas livers obtained from rats treated with ethanol extract and butanol fraction of fruits of *P. longum* showed significant signs of amelioration of CCl₄ induced liver injury as evident from the presence of normal hepatic cords, absence of necrosis and less degree of infiltration. Hepatoprotective action of fruits of *P. longum* may be due to its ability to induce microsomal enzymes, which accelerates the detoxification and excretion of CCl₄ or by inhibition of lipid peroxidation due to CCl₄ intoxication. The biochemical and histopathological observations of the present study reveals that ethanolic extract and butanol fraction of ethanolic extract of fruits of *P. longum* exert a protective action against CCl₄ induced hepatic damage.^[30]

***Pithecellobium dulce* Benth.**

Pithecellobium dulce belonging to the family Leguminosae and its fruit is called as 'Kodukkapuli' in Tamil, 'Jangal Jalebe' in Hindi and 'Manila Tamarind' in English. It is a small to medium sized, evergreen; spiny wood legume tree grows up to the height of 18 meter and found throughout in India and Pakistan. The plant is well known for its edible fruits and they have been consumed for various ailments. The hepatoprotective activity of *P. dulce* was evaluated against alcohol and paracetamol induced liver damage in rats by Kasarala Raju and Jagadeeshwar^[31] Phytochemical analysis of the fruit revealed the presence of alkaloids, flavonoids, glycosides, saponins, sterols and triterpenoids. In the present study alcohol and paracetamol treatment in rats resulted in enlargement of liver, which was evident by increase in the weight and volume of liver. The animals treated with ethanol and water extracts of *P. dulce* showed significant reduction on liver weight and liver volume compared to disease control animals. Rats treated with alcohol and paracetamol developed the significant hepatic damage which was observed as elevated serum levels of hepato-specific enzymes like AST and ALT when compared to normal healthy control animals. Animals treated with ethanol and water extracts of fruit of *P. dulce* showed significant effect on the amelioration of liver damage which was comparable with healthy control animals. The results

of the present research have clearly indicated that ethanol and water extracts of fruits of *P. dulce* are potential hepatoprotective agents.

***Prunus domestica* Linn.**

The fruit of the plant *P. domestica* which was claimed to possess hepatoprotective activity due to the presence of flavonoids, glycosides, alkaloids, phenolic compounds, terpenoids, protein and amino acids. Manoj *et al.*^[32] studied the hepatoprotective efficiency of methanol: ethanol (70:30) extract of *P. domestica* against paracetamol and CCl₄ induced hepatitis in rats. Alteration in the levels of biochemical marker enzymes of hepatic damage like SGPT, SGOT and ALP and total bilirubin and in vivo antioxidant enzymes like LPO, GSH, CAT and SOD were estimated in both treated and untreated animal groups. Administration of paracetamol (2g/kg) and CCl₄ (1.5ml/kg) has enhanced the levels of liver marker enzymes total bilirubin and direct bilirubin and tissue GSH. Treatment with extracts of *P. domestica* fruit at the dose levels of 150 mg/kg and 300mg/kg has brought back the altered levels of biochemical markers to the near normal levels in a dose dependent manner. The authors concluded that this effect may be due to the presence of polyphenols and other antioxidant chemicals in the extract of *P. domestica*.

***Scindapsus officinalis* (Roxb.) Schott.**

Scindapsus officinalis (Araceae) fruit is mentioned as 'Gaja peepal' in Ayurveda. The fruit is used as a raw drug of known properties in both Ayurvedic and Unani systems of medicine. The fruit is reported to be useful as a diaphoretic, carminative stimulant, antihelminthic, aphrodisiac, galactagogue, and appetizer and the decoction of fruit is useful in the treatment of diarrhoea, asthma and other infectious diseases. *S. officinalis* fruit pulp contains active secondary metabolites like flavonoids, tannins, glycosides, alkaloids, and terpenes. *S. officinalis* is pharmacologically proved for its antioxidant, antibacterial and antidiabetic activities. Hydro alcoholic extract (50% ethanol) of *S. officinalis* fruit was evaluated for its hepatoprotective potential by Shrivastava *et al.*^[33] Alteration in the activities of SGOT, SGPT and ALP, and levels of bilirubin and total protein, tissue GH, GSSG and MDA were noticed in both treated and untreated animal groups. The levels of SGOT, SGPT and ALP and bilirubin were enhanced whereas levels of total serum protein, and tissue MDA were increased and tissue level of GSH was significantly reduced in paracetamol treated animals. Pre treatment with hydro-alcoholic extract of *S. officinalis* fruit (at dose of 200mg/kg and 400 mg/kg b.w.) has brought back the altered biochemical markers to the near normal levels. The

histopathological study of the liver tissues showed liver necrosis in diseased condition and the significant recovery was noticed in the animals treated with fruit extract. Based on the improvement in the activities of serum marker and antioxidant enzymes, physiological parameters and normalcy of histopathological damages showed the hydro alcoholic extract of *S. officinalis* fruit possesses hepatoprotective activity and thus supports the traditional claim.

***Sesbania grandiflora* Linn. Pers.**

Sesbania grandiflora (Fabaceae) commonly known as “Sesbania” in English and “Agathi” in Tamil has been used as an highly nutritive vegetable in South East Asian countries. Ayurvedic practitioners use the fruit of *S. grandiflora* for alexetenic, laxative and intellectual stimulation properties and further it is prescribed for the ailments of anaemia, bronchitis, fever, pain, thirst, ozoena and quartan fever. Ramakrishnan *et al.*^[3] reported the hepatoprotective potential of *S. grandiflora* fruit. The petroleum ether extract of *S. grandiflora* fruit showed a significant dose dependent (100mg, and 200mg/kg P.O.) protective effect against thioacetamide and ranitidine induced hepatotoxicity in Wistar strain of albino rats. The degree of protection was measured by using biochemical parameters such as SGOT, SGPT and ALP, total bilirubin (TB), total cholesterol (TC) and total protein (TP). The level of SGOT, SGPT, ALP, TB, TC and TB were significantly elevated in the liver of animals intoxicated with thioacetamide. The pre-treatment with petroleum ether extract of *S. grandiflora* fruit exhibited inhibition of thioacetamide induced hepatic aberrations and best result was achieved with higher dose of the extract. The hepatoprotective effect of the *S. grandiflora* fruit extract was further confirmed by histopathological examination of the liver tissues of disease control, ranitidine treated and extract treated animal groups. The liver samples of ranitidine intoxicated rats showed dilatation of blood sinusoids, more number of inflammatory cells in the form of lymphocytes and some incidences of bile stasis. The histopathological profile of the liver tissues of the rats treated with ranitidine along with higher dose of the extract showed reduction in dilation of sinusoids, decreased number of Kupffer cells and lymphocytic infiltration which suggests hepatoprotective activity of the extract of *S. grandiflora* fruits.

***Averrhoa bilimbi* Linn.**

The plant *A. bilimbi* commonly known as ‘Bilimbi’, is a tropical tree reaches up to 5 to 10 metre in height. The uncooked bilimbi fruit is prepared to relish and served along with rice in natives of Kerala state of India. The hepatoprotective activity of *A. bilimbi* fruit extract in

Wistar strain of albino rats intoxicated with acetaminophen was evaluated by Thamizh selvam *et al.*^[34] the fruit extract was administered in two different doses (250 mg/kg and 500 mg/kg body weight). Silymarin was used as standard positive control at 100mg/kg body weight. The liver marker enzymes in the serum such as SGOT, SGPT and ALP were found to be increased about two fold in the acetaminophen intoxicated disease control animals as compared with healthy control animals. After the treatment with *A. bilimbi* fruit extract the diseased animals showed a significant decrease in the activities of SGOT, SGPT and ALP. It is concluded that the efficacy of the extract is found to be dose dependent, as there is a greater level of efficacy in the higher dose. The histopathological studies of liver tissues of disease control animals showed extensive areas of haemorrhage and necrosis in the liver parenchyma and vacuolated cytoplasm in hepatocytes. The extract treated groups showed improved and apparently normal architecture of the liver, glomeruli and myocardial tissues. All these biochemical diagnostic parameters and histological tissue analysis were evidence for the hepatoprotective activity of *A. bilimbi* fruit. It is assumed by the authors that the high contents of phenolic compounds, and flavonoids may be attributing to the medicinal property of the *A. bilimbi*.^[35]

Lagenaria siceraria

L. siceraria (Molina) Standley (synonyms: *L. leucantha* Rusby; and *L. vulgaris* Ser.) belongs to the botanical family of Cucurbitaceae. The fruit is called as “Bottle gourd” in English and “Lauki” in Hindi. It is an excellent fruit and having the essential nutritional constituents which are required for good health of humans. The plant is widely growing throughout India. It is a climbing or trailing herb, with bottle or dumb-bell shaped fruits. Traditionally, it is used as a vegetable and also as medicine in India, China, European countries, Brazil and Hawaiian island etc. In India, it is traditionally used as a cardio protective tonic, as well as general health tonic, and aphrodisiac, alternative, purgative, antiinflammatory and diuretic agent. It is also useful in stomach pain, ulcers, fever, pectoral cough, asthma and other bronchial disorders. Recently, the *in vitro* antioxidant activity of the epicarp and fresh juice of *L. siceraria* fruit have been reported. *L. siceraria* is considered as a good source of vitamin C, carotene, vitamin B-complex, zinc, flavonoids, triterpenoids, saponins, magnesium, pectin and also contain high choline level- a lipotropic factor, flavones C-glycosides. Kota *et al.*^[35] carried out the in-vivo antioxidant activity of ethanolic extract of fruit of *L. siceraria* (EELS) by using CCl₄ induced liver damaged rabbits. The authors reported that CCl₄ intoxication raised the levels of SGPT, SGOT, ALP, and bilirubin and reduced the total protein in

diseased rabbits as compared to the normal healthy animals. Elevation of such parameters suggests that toxic effect was able to reach the liver and induce detectable damages. The treatment with EELS significantly reduced the activity of liver marker enzymes (SGPT, SGOT, and ALP), bilirubin and significantly increased the total protein in CCl₄ intoxicated rabbits which is suggestive for the protection of the structural integrity of the hepatocytes membrane or regeneration of damaged liver cells by test drug. Antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and free radical scavenger i.e., reduced glutathione (GSH) are the protective agents for the biological systems from oxidative stress. This study showed the significant decrease in SOD, CAT and GSH activity in rabbits intoxicated with CCl₄ as compared to pre-treated animals. On the other hand, there was a significant increase in SOD, CAT and GSH activities in animals that treated with EELS as compared to the intoxicated animals. This improvement in the antioxidant status may explain the modulatory effect of EELS which involves the maintenance of antioxidant capacity and protected the hepatic tissue against oxidative stress. This results of the present study suggests that EELS is a potent antioxidant agent and protects the liver from carbon tetrachloride induced damage.^[36]

REFERENCES

1. Samir S. Hepatoprotective natural products. *Ethano Botanical Leaflets*, 2001; 12: 1-5.
2. Ahsan M. R, Islam K. M, and Bulbul. I.J. Hepatoprotective activity of Methanol extract of some medicinal plants against CCl₄ induced hepatotoxicity in rats, *Global Journal of Pharmacology*, 2009; 3: 116-122.
3. Ramakrishnan. S, Bhaskar Gopal. P. V.V. S. Srikantha reddy K, Ranjit Kumar P, Kumar K S, and Kumar I.L.N. Hepatoprotective activity of fruits of *S. grandiflora* L. Pers against thioacetamide and ranitidine induced hepatotoxicity in rats. *International Journal of Phytomedicines*, 2012; 4: 140-149.
4. Karan M. Vasisht K. and Handa. S.S. Anti hepatotoxic activity of *Swertia chirata* on CCl₄ induced hepatotoxicity in rats, *Phytotherapy Research*, 1999; 13: 24-30.
5. Dinesh K. Sivakumar V. Selvapriya B. Deepika. E. and Mohamed Sadiq A. Evaluation of hepatoprotective polyherbal formulation contains some Indian medicinal plants, *Journal of Pharmacognosy and Phytochemistry*, 2014; 1-5.
6. Gupta S.S. Prospects and perspectives of natural plant products in medicine. *Indian Journal of Pharmacology*, 1994; 26: 1-12.

7. Radhika J. and Yuvarani S. Role of medicinal plants in hepato protection. International Journal of Research Instinct, 2015; 2(1): 1-16.
8. Jalarambhai H. Thakkar, Hittesh Ravai, Rameshwar Patel and Nilesh Kanzaria. Investigation of hepatoprotective activity of *Benincasa cerifera* against alcohol induced hepatotoxic rats. Article ID: Inventi: Pep 17442/15, 2015.
9. Rachchh M. A, Yadav P. N, Gokani R.H and Jain S.M. Anti inflammatory activity of *B. hispida* fruit. International Journal of Pharmacy and Biosciences, 2011; 2(3): 98-106.
10. Kuntal Ghosh and Baghel M. S. A pharmacognostical and physiochemical study of *B. hispida* with Ayurvedic review. International Journal of Research in Ayurveda and Pharmacy, 2011; 2(6): 1664-1668.
11. Nadira Binte Samad, Trishna Debnath, Hai Lan Jin, Bo Ram Lee, Pyo Jam Park, Seung Yuan Lee and Beong Ou Lim. Antioxidant activity of *B. hispida* seeds. Journal of Food Biochemistry, 2012; 1-8.
12. Vadivu. R, Krithika. A, Biplale. C, Dedeepya. P, Shoeb. N and Lakshmi. K. S. Evaluation of hepatoprotective activity of the fruits of *Coccinia grandis* Linn. International Journal of Health Research, 2008; 1(3): 163-168.
13. Arun Kumar Sanapala and Eswar Kumar. K. Hepatoprotective activity of aqueous fruit extract of *Coccinia indica* against paracetamol induced hepatotoxicity in rats. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2013; 4 (1): 179-182.
14. Naik. V. R, Agshikar. N.V and Abraham. J.S. *Cucumis trigonus* Roxb. II. Diuretic activity. Journal of Ethnopharmacology, 1981; 3: 15-19.
15. Arya V.S. (ed). Indian Medicinal Plants, A compendium of 500 species, Orient Longman Ltd., Madras, 1994; 234-235.
16. Kalpana Patil, Shaikh Mohammed Imtiaz, Anoop Singh, Varsha Bagewadi and Shaikh Gazi. Hepatoprotective activity of *Cucumis trigonus* Roxb. fruit against CCl₄ induced hepatic damage in rats. Iranian Journal of Pharmaceutical Research, 2011; 10(2): 295-299.
17. Kagyung. R, Gajurel. P. R, Rethy. P. And Singh. B. Ethno medicinal plants used for gastrointestinal diseases by Adi Tribes of Dehang- Debang Biosphere Reserve in Arunachal Pradesh. Indian Journal of Traditional Knowledge, 2010; 9: 496-501.
18. Ravi Munduguru, Madhan Chakkravarthy Varadharajan and Ravi Shankar Basavaiah. Hepatoprotective activity of *Garcinia pedunculata*. A Journal of the Bangladesh Pharmacological Society, 2014; 9: 483-487.

19. Souza M, Singh R, Reddy P, Hukkeri V. and Byahatti V. Hepatoprotective activity of fruit pulp extract of *Litchi chinensis* Sonner. on CCl₄ induced hepatotoxicity in albino rats. International Journal of Alternative Medicine, 2006; 4(1): 1-5.
20. Shankar P. Prasanna Kumar B. R. and Mohammed Khallel. Hepatoprotective activity of *Momordica diocia* Roxb. fruits in CCl₄ induced hepatotoxicity in rats. Iranian Journal of Pharmaceutical Sciences, 2011; 7(4): 279-282.
21. Elkins R. Hawaiian (Noni) *Morinda citrifolia*, Woodland, Pleasant grove, Utah, USA, 1997.
22. Hirazumi A, Furusawa E, Chou S.C. and Hokama Y. Immuno modulation contributes to the anticancer activity of *Morinda citrifolia* (Noni) fruit juice. Proceedings of the Western Pharmacology Society, 1996; (39): 7-9.
23. Wang M. Y. and Su. C. Cancer preventive effect of *Morinda citrifolia* (Noni). Annals of the New York Academy of Sciences, 2001; 952: 161-168.
24. Shivananda Nayak. B, Julien R, Marshall, Godwin Isitor and Andrew Adogwa. Hypoglycaemic and hepatoprotective activity of fermented fruit juice of *Morinda citrifolia* (Noni) in diabetic rats. Evidence based Complementary and Alternative Medicine. Article ID 875293, 2011; 5.
25. Nayak B.S. Sandiford S. and Maxwell A. Evaluation of the wound healing activity of ethanolic extract of *Morinda citrifolia* (Noni) leaf. Evidence based Complementary and Alternative Medicine, 2009; 6(3): 351-356.
26. Amira el arem, Fatma Qhraiiri, Lamia Lahouar, Amira Thouri, Emna Behija Saafi, Amel Ayed, and Mouna Zekri. Hepatoprotective activity of date fruit extracts against Dichloroacetic acid- induced liver damage in rats. Journal of Functional foods, 2014; (9): 119-130.
27. Anonymous. The wealth of India – Raw materials Vol. VIII. Publication and Information Directorate, CSIR, New Delhi, 1981; 236.
28. Naddkarni K.H. Indian Materia Medica. Vol: I. Popular Prakashan, Bombay, 1976; 965.
29. Kirtikar K.R and Basu B.D. In: Indian medicinal plants, 2nd Edition, Vol: III. International Book distributors, Dehra Dun, 1987.
30. Jalalpure S. S, Patil. M.B, Prakash N.S, Hemalata. K. and Manvi. F. V. Hepatoprotective activity of fruits of *Piper longum* Linn. Indian Journal of Pharmacy Science, 2003; 65(4): 363-366.

31. Kasarala Raju and Jagadeeshwar K. Phytochemical investigation and hepatoprotective activity of ripe fruits of *Pithecellobium dulce* in Albino rats, Scholars Academic Journal of Pharmacy (SAJP), 2014; 3(6): 449-454.
32. Manoj Soni, Mohanty P.K and Jaliwala Y. A. Hepatoprotective activity of fruits of *Prunus domestica*. International Journal of Pharmacy and Biosciences, 2011; 2(2): 439-453.
33. Nikhil Shrivastava, Preeti Agarwal, Akanksha Khare, Sarlesh Rajput, Rajendra Singh Baghel, and Satyendra Singh Baghel. Hepatoprotective activity of *Scindapsus officinalis* fruit in paracetamol induced hepatotoxicity in rats. International Journal of Pharmaceutical Sciences and Research, 2013, 4 (4): 1598-1609.
34. Thamizh Selvam N., Santhi P. S., Sanjayakumar Y. R., Venugopalan T. N., Vasanthakumar K. G. and Swamy G. K. Hepatoprotective activity of *Averrhoa bilimbi* fruit in acetaminophen induced hepatotoxicity in Wistar albino rats. Journal of Chemical and Pharmaceutical Research, 2015, 7(1): 535-540.
35. Karunakar Kota, Sandhya Sharma, and Jameela Tahashildar. Amelioration of oxidative stress by ethanolic extract of the fruit of *Lagenaria siceraria* in rabbits consisting of carbon tetra chloride induced hepatotoxicity. World Journal of Pharmaceutical Research, 2016; 4(2): 648-660.