ABSTRACT: Drug Induced hepatotoxicity is a common occurrence and one of the main reasons of drug withdrawal from the market after approval by a Federal Agency such as the FDA. The cause of hepatic injury can also be bacterial, parasitic or viral. Although the liver has a very high regenerative potential compared to other organs, acute liver failure has a high mortality rate. The drug-induced or other forms of liver damage such as viral hepatitis can also lead to long lasting chronic effects such as fibrosis resulting in cirrhosis or hepatocellular carcinoma. The mechanism of liver damage due to chemicals such as Paracetamol (Acetaminophen) or other agents such as viruses is complex and only partly understood. It appears that free radical injury is involved in liver damage although other mechanisms have also been described. At present there is no treatment for acute Hepatic failure and only supportive treatment is available. Viral hepatitis is also a major cause of morbidity and mortality in this part of the world. There is a vaccine available for Hepatitis B but it also provides only partial safety. The reason for being expensive is because it is made by Recombinant DNA Technology. The extracts of Withania somnifera have a very long history of use in traditional medicine such as the Ayurvedic system for more than 3000 years. The active ingredients of this plant are withanolides, which are steroidal lactones, have been shown to have adaptogenic and regenerative properties. The powdered roots of Withania somnifera showed curative property in the context of carbendazim-induced histopathological changes in the liver and kidney of rat. (Akbarsha, et al. (2000). In this review article, we will mention some Hepatoprotective natural compounds that are used in different parts of the world.

Keywords: Cytochrome P-450, Galactosamine, Glutathione peroxidase.

INTRODUCTION

The use of natural compounds has a very long history dating back to 4000-5000 yrs when there was no modern medical facility available. That era of human history can be considered as a golden era because not much people fell ill and most importantly people die of natural death, which is very difficult to see today. Today, there is lot of pollution and huge boom in the population caused a major problem of providing every individual their basic needs of life. This leads to poor living standards and hence leading to falling ill or death due to some disease or poverty.

Liver is an important organ of our body. It is the main metabolic machinery of our body. Most of the drugs are metabolized in the liver using the main enzyme system called as Cytochrome P450 system. It also has many isoenzymes which can be selective to different drugs or compounds. Unfortunately, in Third World countries all of the above said causes are prevalent and especially the viral one which is increasing day by day. It is due to poor sanitation and improper medical practice done here. At the present moment, there is no
hepatoprotective drug in Allopathic system of medicine. So, there is strong need to develop such medicine using the natural products, so that the precious lives of many patients can be saved. Also that developed drug should be cost effective so that poor population can purchase it. Here, we have reviewed some examples of Hepatoprotective natural compounds and about their possible pharmacological actions.

**Hepato-Protective Natural Compounds**

**Veronica amygdalina (Family Compositae):**
Is used in Nigerian folk medicine as a tonic and remedy against constipation, fever, high blood pressure, and many infectious diseases. The hepatoprotective and antioxidant effects of an aqueous extract of *V. amygdalina* leaves against acetaminophen-induced hepatotoxicity and oxidative stress in mice were evaluated. Activities of liver marker enzymes in serum (glutamateoxaloacetate transaminase, glutamate-pyruvate transaminase, lactate dehydrogenase, and alkaline phosphatase) and bilirubin levels were determined colorimetrically, while catalase activity, lipid peroxidation products, thiobarbituric acid-reactive substances (TBARS), iron, and total protein concentrations were measured in liver homogenate. Acetaminophen challenge (300 mg/kg, i.p.) for 7 days caused significant (*P* < 0.01) increase in the levels of bilirubin, liver enzymes, TBARS, and iron, while catalase activity and total protein level were reduced significantly (*P* < 0.01). Pre-administration of *V. amygdalina* resulted in a dose-dependent (50-100 mg/kg) reversal of acetaminophen-induced alterations of all the liver function parameters by 51. 9-84.9%. Suppression of acetaminophen-induced lipid peroxidation and oxidative stress by the extract was also dose-dependent (50-100 mg/kg). The results of this study suggest that *V. amygdalina* elicits hepatoprotectivity through antioxidant activity on acetaminophen-induced hepatic damage in mice (Iwalokun et al., 2006).

**Nigella sativa Land Urtica dioica L:** The seed of *Nigella sativa* L (NS), an annual Ranunculaceae herbaceous plant, has been used traditionally for centuries in the Middle East, Northern Africa, Far East and Asia for the treatment of asthma. *Urtica dioica* L (UD) is a plant belonging to the family Urticaceae. Its seeds are widely used in folk medicine in many parts of Turkey, especially in the therapy of advanced cancer patients. Fifty-six healthy male Wistar albino rats were used in this study. The rats were randomly allotted into one of the four experimental groups. All groups received CCl4 (0.8 mL/kg of body weight, sc, twice a week for 60 d). In addition, B, C and D groups also received daily i.p. injections of 0.2 mL/kg NS or/and 2 mL/kg UD oils for 60 d. Group A, on the other hand, received only 2 mL/kg normal saline solution for 60 d. Blood samples for the biochemical analysis were taken by cardiac puncture from randomly chosen-seven rats in each treatment group at beginning and on the 60th d of the experiment. NS and UD decrease the lipid peroxidation and liver enzymes, and increase the antioxidant defense system activity in the CCl4-treated rats (Kanter et al., 2005, Al-Ghamdi, 2003 and Mahmoud et al., 2002).

**Eucalyptus Maculata:** Eucalyptus maculata is one of several species of genus Eucalyptus indigenous to Australia and introduced to and cultivated in Egypt. The plant is considered as an indigenous source of medicine exhibiting an anti-asthmatic activity and is used in the treatment of chronic bronchitis. The chloroformic extract and pure phenolic isolates were evaluated for their antioxidant and hepatoprotective properties in mice and rats based on biochemical changes in serum and tissues as well as pathological changes in the liver and spleen. Acetaminophen (ACP) at a dose of 1 g/kg body weight produced 100% mortality in mice, while pretreatment of animals with the chloroformic extract (125 and 250 mg/kg) protected against the mortalities by 66%. Pretreatment of rats with either the chloroformic extract (250 mg/kg) or any of the pure isolates (20 mg/kg) significantly reduced the increase in serum level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) produced by ACP (640...
Pretreatment of animals with the chloroformic extract or its isolates also protected against ascorbic acid depletion in serum and kidney tissues induced by oral administration of paraquat (PQ) without modifying the serum level of glutathione (GSH) and glycogen content in liver tissue. The phenolic content of the chloroformic extract and the pure isolates produced an antioxidant activity which may be due to the formation of stable phenoxy radical in addition to its effect through vitamin C (Mohamed et al., 2005).

**Mangiferin and its derivatives: Bombax ceiba L.** (syn. B. malabaricum DC), commonly known as Simul, Simbal or Silk-cotton tree belongs to the family Bombacaceae. It is reputed as an important medicinal plant. Phytochemical studies on various parts of B. ceiba revealed that it is rich in phenolic compounds. While mangiferin, a xanthone, is present in large amounts in the leaves, and obtained directly from the extract. It has significant effect as a hypotensive agent and possesses hypoglycemic activity with negligible toxicity. Mangiferin, 2-b - D-glucopyranosyl-1,3, 6, 7-tetrahydroxy-9H-xanthen9-one, obtained directly from methanolic extracts of Bombax ceiba leaves in substantial amounts demonstrated strong antioxidant activity (EC50 5.8:i:0.96m g/ml or 13.74mM) using DPPH (2,2-diphenyl-1-picrylhydrazyl) assay comparable to rutin, commonly used as antioxidant for medical purposes. Mangiferin showed hepatoprotective activity against carbon tetrachloride induced liver injury further supporting the free radical scavenging property in the in vivo system. (Dar et al., 2005)

**Indigofera aspalathoides:** The alcoholic extract of stem of Indigofera aspalathoides was evaluated for its anti Hepato toxic activity against CC14-induced hepatic damage in rats. The activity was evaluated by using biochemical parameters, such as serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), total bilirubin and gamma glutamate transpeptidase (GGTP). The histopathological changes of liver sample were compared with respective control. The extract showed remarkable hepatoprotective effect (Rajkapoor et al., 2006).

**Silymarin, milk thistle (Silybium marianum):** Silymarin, derived from the milk thistle plant, Silybium marianum, has been used in traditional medicine as a remedy for diseases of the liver and biliary tract. In the present study, the effect of Hepato-protective drug silymarin on body weight and biochemical parameters, particularly, antioxidant status of ethanol-exposed rats was studied and its efficacy was compared with the potent antioxidant, ascorbic acid as well as capacity of hepatic regeneration during abstention. The production of reactive oxygen species (ROS) is considered to be a major factor in oxidative cell injury. The antioxidant activity or the inhibition of the generation of free radicals is important in providing protection against such hepatic damage.

Ethanol, at a dose of 1.6 g/kg body wt/day for 4 wks affected body weight in 16-18 week-old male albino rats (Wistar strain weighing 200-220 g). Thiobarbituric acid reactive substance (TBARS) level, super oxide dismutase (SOD), and glutathione-stransferase (GST) activities were significantly increased, whereas GSH content, and catalase, glutathione reductase (GR) and GPx (glutathione peroxidase) activities significantly reduced, on ethanol exposure. These changes were reversed by silybin and ascorbic acid treatment. It was also observed that abstinence from ethanol might help in hepatic regeneration. Silybin showed a significant hepatoprotective activity, but activity was less than that of ascorbic acid. Furthermore, preventive measures were more effective than curative treatment (Das et al., 2006).

**Lygodium flexuosum (L) Sw:** The hepatoprotective potential of Lygodium flexuosum (L) Sw. was evaluated in male Wistar rats against carbon tetrachloride-induced liver
damage in preventive and curative models. Toxic control and n-hexane extract-treated rats received a single dose of CCl4 (150 microL/100g, 1: 1 in com oil). Pre-treated rats were given n-hexane extracts at 200 and 100 mg/kg dose 48, 24 and 2 h prior to CCl4 administration. In post-treatment groups, rats were treated with n-hexane extract at a dose or 200 and 100 mg/kg, 2, 24 and 48 h after CCl4 intoxication. Rats pre-treated with Lygodium flexuosum remarkably prevented the elevation of serum AST, ALT, LDH and liver lipid peroxides in CCl4-treated rats. Rats treated with the extract after the establishment of CCl4 induced liver injury showed significant (p < or = 0.05) protection of liver as evidenced from normal AST, ALT, LDH and MDA levels. Hepatic glutathione levels were significantly (p < or = 0.05) increased by the treatment with the extracts in both the experimental groups. Histopathological changes induced by CCl4 were also significantly (p < or = 0.05) reduced by the extract treatment in preventive and curative groups. Phytochemical studies revealed the presence of saponins; triterpenes, sterols and bitter principles in Lygodium flexuosum-hexane extract which could be responsible for the possible hepatoprotective action. (Wills et al., 2006)

Hemidesmus indicus R. br: Treatment of rats with paracetamol and CCl4 produced a significant increase in the levels of serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), total and direct bilirubin. Rats pretreated with methanolic extract of roots of H. indicus (100 Silymarin, milk thistle (Silybium marianum); Silymarin, derived from the milk thistle plant, Silybium marianum, has been used in traditional medicine as a remedy for diseases of the liver and biliary tract. In the present study, the effect of Hepato-protective drug silymarin on body weight and biochemical parameters, particularly, antioxidant status of ethanol-exposed rats was studied and its efficacy was compared with the potent antioxidant, ascorbic acid as well as capacity of hepatic regeneration during abstention. The production of reactive oxygen species (ROS) is considered to be a major factor in oxidative cell injury. The antioxidant activity or the inhibition of the generation of free radicals is important in providing protection against such hepatic damage.

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**Rubia cordifolia Linn:** The hepatoprotective effects of rubiadin, a major constituent isolated from Rubia cordifolia Linn, were evaluated against carbon tetrachloride (CCl$_4$) induced hepatic damage in rats. Rubiadin at a dose of $50$, $100$ and $200$ mg/kg was administered orally once daily for 14 days. The substantially elevated serum enzymatic activities of serum glutamic oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (SALP) and gammaglutamyltransferase (gamma-GT) due to carbon tetrachloride treatment were dose dependently restored towards normalization. Meanwhile, the decreased activities of glutathione S-transferase and glutathione reductase were also restored towards normalization. In addition, rubiadin also significantly prevented the elevation of hepatic malondialdehyde formation and depletion of reduced glutathione content in the liver of CCl$_4$ intoxicated rats in a dose dependent manner. Silymarin used as standard reference also exhibited significant hepatoprotective activity on post treatment 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 rubiadin has a potent hepatoprotective action against carbon tetrachloride induced hepatic damage in rats (Rao et al., 2006).

**Cassia fistula Linn. leaf extract:** CCl$_4$ alone treatment ($0.1$ ml of liquid paraffin/100g body weight, ip) for 7 days followed by $0.1$ ml of CCl$_4$ (in liquid paraffin/100g body weight, ip) from day 8 till day 14, caused a 16 fold increase in lipid peroxidation and a $50\%$ reduction in catalase and glutathione reductase in liver tissue of rats accompanied by an increase in the activities of transaminases, alkaline phosphatase, lactate dehydrogenase and gamma - glutamyl transpeptidase in serum as compared to liquid paraffin treated control. Pretreatment of ethanolic leaf extract of *C. fistula* ($500$mg/kg body weight/day for 7 days) followed by CCl$_4$ treatment ($0.1$ ml/100g body weight from day 8 till day 14) completely reversed back lipid peroxidation and the activities of catalase and glutathione reductase in the liver tissue towards normalcy. This treatment also reversed the elevated levels of the enzymes in the serum. Ethanolic leaf extract alone treatment did not produce any change in all the parameters studied. The results suggest antioxidant and hepatoprotective properties of *C. fistula* during its pretreatment against CCl$_4$ induced hepatotoxicity (Pradeep et al., 2005).
**Alnus japonica:** The stem bark of the Betulaceae plant Alnus japonica, which is indigenous to Korea, has been used as a popular folk medicine for hepatitis and cancer. In this study, the antioxidant activity of the crude extract and the hepatoprotective activities on acetaminophen (AAP)-induced toxicity in the rat liver were evaluated. The effect of the methanol (AJM) and solvent traction of the stem bark of Alnus japonica (AJ) on AAP-induced hepatotoxicity in rats was investigated. In rat hepatocyte culture, pretreatment with AJM (50, 100, 150 and 200 µg/ml) significantly decreased the cytotoxicity of AAP in a dose-dependent manner. The pretreated with EtOAc and BuGH fraction led to an increase in free radical scavenging activity and a decrease in inhibition of lipid peroxidation, both superoxide dismutase and catalase prevent the hepatotoxicity by AAP in the treatment of A. japonica fraction. It was conclude that AJ is an important antioxidant in AAP-induced hepatotoxicity and that extract of AJM plays a hepatoprotective effects against AAP-induced cytotoxicity in cultured rat hepatocytes in vitro. Pending more evaluation for safety and efficacy, AJ can potentially be used in mitigating AAP-induced hepatotoxicity (Kim *et al.*, 2004).

**Crassocephalum crepidioides** (*C. crepidioides*, Japanese name; Benibanaborogiku): Is wildly distributed in the Okinawa Islands and is known in folk medicine for the treatment of acute hepatitis, fever, or edema. This plant is popular as an edible wild plant in Taiwan. Free radical scavenging and protective actions against chemically induced hepatotoxicity of Crassocephalum crepidioides were investigated. A water extract of *C. crepidioides* strongly scavenged superoxide anion, hydroxyl radical and also stable radical 1,1-diphenyl-2-picrylhydrazyl. Galactosamine (GaIN, 400 mg/kg) and lipopolysaccharide (LPS, 0.5m g/kg) induced hepatotoxicity of rats as seen by an elevation of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and of lipid peroxidation in liver homogenates was significantly depressed when the herbal extract was given intraperitoneally 1 and 15 h before GaIN and LPS treatment. Sirpilarly, carbon tetrachloride (CCI4) induced liver injury as evidenced by an increase in AST and an ALT activity in serum was also inhibited by the extract pretreatment. Isochlorogenic acids, quercetin and kaempferol glycosides were identified as active components of *C. crepidioides* with strong free radical scavenging action. These results demonstrate that *C. crepidioides* is a potent antioxidant and protective against GaIN plus LPS- or CCI4-induced hepatotoxicity (Aniya *et al.*, 2005).

**Aronia melanocarpa:** The fruits of Aronia melanocarpa are rich in anthocyanins – plant pigments with anti-inflammatory and antioxidant activity. Histopathological changes such as necrosis, fatty change, ballooning degeneration and inflammatory infiltration of lymphocytes around the central veins occurred in rats following acute exposure to CCI4 (0.2 ml kg⁻¹, 2 days). The administration of CCI4 increased plasma aspartate transaminase (AST) and alanine transaminase (ALT) activities induced lipid peroxidation (as measured by malondialdehyde (MDA) content in rat liver and plasma) and caused a depletion of liver reduced glutathione (GSH). NFJAM (5, 10 and 20 ml kg⁻¹, 4 days) dose-dependently reduced the necrotic changes in rat liver and inhibited the increase of plasma AST and ALT activities, induced by CCI4 (0.2ml kg⁻¹, 3rd and 4th days). NFJAM also prevented the CCI4-induced elevation ofMDA formation and depletion of GSH content in rat liver (Valcheva-Kuzmanova, 2004).

**Solanum trilobatum:** The whole plant of *S. trilobatum* was collected from and around Chennai. The plant was authenticated by Captain Srinivasa Murthy Drug Research Centre for Ayurveda, Arumbakkam, Chennai. Many hepatoprotective herbal preparations have been recommended in alternative systems of medicine for the treatment of hepatic disorders. No systematic study has been done on protective efficacy of *Solanum trilobatum* to treat hepatic diseases. Protective action of *Solanum trilobatum* extract (STE) was
Ahmad and Sharafatullah evaluated in an animal model of hepatotoxicity induced by carbon tetrachloride (CCI4). Wistar albino rats were divided into five groups. Group I was normal control group; Group II, the hepatotoxic group was given CCI4; Groups III-V received different doses of plant extract with CCI(4). Liver marker enzymes were assayed in serum and antioxidant status was assessed in liver tissue. Levels of marker enzymes such as alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) were increased significantly in CCI4 treated rats (group II). STE brought about a significant decrease in the activities of all these enzymes. Lipid peroxidation (LP) was increased significant in liver tissue in the CCI4 treated rats (group II) while the activities of glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD) were decreased. STE treatment led to the recovery of these levels to near normal. The present observations suggested that the treatment with S. trilobatum extract enhance the recovery from CCI4 induced hepatic damage due to its antioxidant and hepatoprotective property (Shahjahan et al., 2004).

Nymphaea stellata willd: Nymphaea stellata willd, a medicinal plant mentioned in Ayurveda for the treatment of liver disorders, has not been subjected to systematic scientific investigations to assess its hepatoprotective effects. Therefore, the present study was undertaken to investigate the hepatoprotective activity of extract of Nymphaea stellata willd., flower against carbon tetrachloride-induced hepatic damage in albino rats. The oral administration of varying dosage of extract of Nymphae stellata willd., flower to rats for 10 days afforded the good hepatoprotection against carbon tetrachloride-induced elevation in serum marker enzymes, serum bilirubin, liver lipid peroxidation and reduction in liver glutathione, liver glutathione peroxidase, glycogen, superoxide dismutase and catalase activity (Bhandarkar et al., 2004).

Limonium sinense: In the present study, the hepatoprotective action of Limonium sinense (Plumbaginaceae) was evident after carbon tetrachloride (CCI (4)) and beta-D-galactosamine (D-GaIN), respectively, challenge in rats. The plant materials were divided into two parts: (1) the roots extracted with water (WRE) and (2) the leaves extracted with methanol and fractionated with chloroform (CLE). Both WRE and CLE were extremely flavonoid-enriched extracts. In an CCI(4)-induced acute liver damage study, pretreatment with WRE at 300 mg/kg i.p. and CLE at 100 mg/kg i.p. significantly reduced the aminotransaminases levels of SGOT (p < 0.01) and SGPT (p < 0.01) previously increased by CCI( 4) intoxication. In D-GaIN-induced acute liver damage study, administration of WRE (300 and 500 mg/kg) or CLE (100 mg/kg) p.o. also significantly reduced the SGOT (p < 0.01) and SGPT (p < 0.01) levels previously increased by D-GaIN intoxication.

Furthermore, the serum triglyceride level was increased after pretreatment with WRE or CLE previously reduced by D-GaIN intoxication. All of the liver function profiles were confirmed to have improvement of liver lesion in histopathological observation. In an acute toxicity test on ICR mice, the LD(50) of WRE was 777.6 mg/kg i.p. An in vitro study showed that CLE possessed a more potent cytotoxicity to human hepatocellular carcinoma cells (Hep3B) (EC(50) = 43.1 micro glmL) than the other organic fractions, which were fractionated from methanol extracts of the leaves of L. sinense. The present results conclude that L. sinense possesses a hepatoprotective efficacy, and is relatively safe in rats. (Chaung SS et al., 2003)

Myristica fragrans: To evaluate the hepatoprotective activity of spices, 21 different spices were fed to rats with liver damage caused by lipopolysaccharide (LPS) plus d-galactosamine (D-GaIN). As assessed by plasma aminotransferase activities, nutmeg showed the most potent hepatoprotective activity. Bioassay-guided isolation of the active compound from nutmeg
was carried out in mice by a single oral administration of the respective fractions. Myristicin, one of the major essential oils of nutmeg, was found to possess extraordinarily potent hepatoprotective activity. Myristicin markedly suppressed LPS/D-GaIN-induced enhancement of serum TNF-alpha concentrations and hepatic DNA fragmentation in mice. These findings suggest that the hepatoprotective activity of myristicin might be, at least in part, due to the inhibition of TNF-alpha release from macrophages. However, further studies are needed to elucidate the hepatoprotective mechanism(s) of myristicin (Morita et al., 2003).

Combretum quadrangulare: Hepatoprotective effect of MeOH, MeOH-H2O (1:1) and H2O extracts of Combretum quadrangulare seeds were examined on D-galactosamine (D-GaIN)/tumor necrosis factor-alpha(TNF-alpha)-induced cell death in primary cultured mouse hepatocytes. The MeOH extract showed the strongest inhibitory effect on D-GaIN/TNF-alpha-induced cell death (IC50, 56.4 microgl/ml). Moreover, the MeOH extract also significantly lowered the serum glutamic pyruvic transaminase (sGPT) level on D-GaIN/lipopolysaccharide (LPS)-induced liver injury in mice. Bioguided separation of the MeOH extract led to the isolation of 38 compounds of various classes including triterpene glucosides, lignans and catechin derivatives. Among the isolated triterpene glucosides, lupane-type (1-3; IC50, 63.1, 59.8 and 76.2 microM, respectively) and ursane-type (11, mixture of 12 and 14; IC50, 30.2 and 34.6 microM, respectively) compounds exhibited strong hepatoprotective activity. 1,0-Galloyl-6-O-(4-hydroxy-3,5dimethoxy) benzoyl-beta-D-glucose (26; IC50, 7.2 microM), methyl gallate (28; IC50, 19.9 microM), and (-)-epicatechin (31; IC50, 71.2 microM) also had a potent hepatoprotective effect on D-GaIN/TNF-alpha-induced cell death in primary cultured mouse hepatocytes (Adyana et al., 2000, Banskota et al., 2000).

Apocynum venetum: The leaves of Apocynum venetum L. are used as a tea material in north China and Japan. A water extract (500 mg/kg/day, one week administration) of the leaves of A. venetum showed protective effects against carbon tetrachloride (CCl4, 30 microliters/mouse) or D-galactosamine (D-GaIN, 700 mg/kg)/lipopolysaccharide (LPS, 20 micrograms/kg)-induced liver injury in mice. Tumor necrosis factor-alpha (TNFalpha) secreted by LPS-stimulated macrophages is the most crucial mediator in the DGalN/LPS-induced liver injury model. The extract had no significant inhibition on the increase of serum TNF-alpha (1169 ± 132 pg/ml vs. 1595 ± 314 pg/ml of control), but exhibited a complete inhibition at the concentration of 100 micrograms/ml on TNF-alpha (100 ng/ml)-induced cell death in D-GaIN (0.5 mM)-sensitized mouse hepatocytes. Further activity-guided ITactionation resulted in the isolation of fifteen flavonoids viz. (-)epicatechin (1), (-)-epigallocatechin (2), isoquercetin (3), hyperin (4), (+)-catechin (5), (+)-gallocatechin (6), kaempferol-6'-O-acetate (7), isoquercetin-6'-O-acetate (8), catechin-[8,7-e]-4 alpha-(3,4-dihydroxyphenyl)-dihydro-2(3H)-pyranone (9), apocynin B (10), apocynin A (11), cinchonain Ia (12), apocynin C (13), apocynin D (14) and quercetin (15). All the compounds showed inhibitory effects on TNF-alpha-induced cell death with different intensities. The flavonol glycosides 3, 4, 7 and 8 and the phenylpropanoid-substituted flavan-3-0Is 11 and 12 showed potent inhibitory effects on TNF-alpha-induced cell death with IC50 values of 37.5, 14.5, 31.2, 55.1, 71.9 and 41.2 microM, respectively. In contrast, the clinically used 5 and its analogues 1, 2 and 6 showed apparent activity only at 80 microM. These flavonoids appeared to be the hepatoprotective principles of the leaves of A. venetum. The hepatoprotective effects exhibited by the extract and its constituents suggest a validation of the leaves as a tea material (Xiong et al., 2000).

CONCLUSION

In the light of the above cited examples of the Hepato protective compounds or plants we can suggest that there is a strong need to develop a
drug which can be used to protect or treat liver failure using anyone or combination of these compounds. As every one of us knows that there are Pros and cons attached to everything in this world, the main disadvantage of using these natural compounds is that they can be extracted in very little amounts using Kilograms of plant parts. But the advantage is that they are very cheap and have almost no side effects.

REFERENCES


