www.ijrps.pharmascope.org

ISSN: 0975-7538
Review Article

Hepatoprotective Role of Herbal Plants – A Review

Deepak Kumar Mittal*, Deepmala Joshi, Sangeeta Shukla

Reproductive Biology and Toxicology Laboratory, School of Studies in Zoology, Jiwaji University, Gwalior - 474011 (MP), India

ABSTRACT

Liver plays a pivotal role in regulating various physiological processes such as metabolism, secretion and storage. It also plays an important role in removing harmful substances and toxins that enter the body. Liver cell injury caused by various toxic chemicals (Paracetamol, Carbon tetrachloride (CCl_4), Alcohol, D-galactosamine, Thioacetamide, etc.), excessive alcohol consumption and microbes are well-studied. The available synthetic drugs to treat liver disorders in this condition also cause further damage in the liver. Hence, Herbal drugs have become increasingly popular and their use is wide-spread. Herbal medicines have been used for the treatment of liver diseases for a long time. A number of herbal preparations are available on the market. The present review is aimed at compiling data on promising from medicinal plants that have been tested in hepatotoxicity models using the modern scientific system. Latest trends have shown increasing demand of phyto drugs and thus India, with its traditional background.

Keywords: Herbal Plants; Carbon tetrachloride; Paracetamol; Alcohol; Hepatotoxicity

INTRODUCTION

Nature has been a source of medicinal treatment for thousands of years. India is sitting on a gold mine of well-recorded and traditionally well-practiced knowledge of herbal medicines. This country is perhaps the largest producer of medicinal herbs and is rightly called the botanical garden into the world. There are very few medicinal herbs of commercial importance, which are not found throughout this country. It is generally estimated that over 6000 plants in India are in use in traditional, folk and herbal medicines, representing about 75% of the medicinal needs of the third-world countries (Dubey *et al.,* 2004, Rajshekharan, 2002). Medicinal herbs have been in use in one form or another, under indigenous systems of medicines like *Ayurveda, Siddha* and *Unani*. Considerable research on pharmacognosy, chemistry, pharmacology and clinical therapeutics has been carried out on these plants, which are now significant sources of pharmaceutical drugs. Latest trends have shown increasing demand of phyto drugs and thus India, with its traditional background, needs to increase its share on the world market.

Medicinal herb is a biosynthetic laboratory, for chemical compounds like glycosides, alkaloids, resins, oleoresins, etc. There is an urgent need to evaluate the therapeutic potentials of the drugs as per WHO guidelines. Ironically, few Indian products are available in a standardized form, which is the minimum requirement for introducing a product in the Western market (WHO, 2002).

* Corresponding Author
Email: deepakmittal05@gmail.com
Contact: +91-9425771967
Received on: 26-11-2011
Revised on: 16-02-2012
Accepted on: 23-02-2012

Hepatoprotective Herbal Plants

Polygonum Bistorta (Linn.): *Polygonum bistorta* Linn. (bistort or common bistort, PB) is a herbaceous flowering plant belonging to family *Polygonaceae*. This tall perennial herb grows in moist, shady areas of higher ground in the North of India (Punjab, Kashmir, Sikkim and Himmalyan Region), England, Southern Scotland, Europe, central Asia and west of the Rockies in North America, It flowers in May and June. The plant may be propagated by division of the root stock. The rhizome is odorless, but powerfully astringent in taste, as it contains tannin to the extent of 21 percent.

Preliminary study has been conducted on *Polygonum bistorta* and its aqueous ethanolic extracts were screened for anti-inflammatory activity. Before the induction of carrageenan rat paw oedema, administration of its extract (100 and 200 mg kg^{-1}, *p.o.*) suppresses both the maximal oedema response and the total oedema response (Duwiejua *et al*., 1994).The The The chloroform and hexane fractions and their subfractions were evaluated for their cytotoxic activity against P338 (Murine lymphocytic leukemia), *Hep* G2 (Hepatocellular carcinoma), *J82* (Bladder transitional carcinoma), *HL60* (Human leukemia), *MCF7* (Human breast cancer) and *LL2* (Lewis's lung carcinoma) cancer cell lines in culture (Manoharan *et al.,* 2007). They synergize the cytotoxicity of chemotherapeutic drug in

human by modulating drug efflux pathway (Naus *et al*., 2007). Smolarz *et al.,* 2007 demonstrated that ethanolic extracts from the roots of *Polygonum aviculare* L. showed an inductory activity on apoptosis in human leukemic Jurkat cells.

Picrorhiza kurroa (Benth.)**:** *Picrorhiza kurroa* (Pk), a known hepatoprotective plant and is an important remedy by Jivek, Charak and Vagbhatt in ancient Ayurvedic literature. The plant has been described as significantly useful in jaundice. In a double-blind trial, in the late seventies, Arogya-wardhani with its principal ingredient Pk (50%) was shown to significantly reduce serum bilirubin and transaminases in patients with viral hepatitis by some of the current authors. Experimentally, Pk has been shown to have the pharmacodynamic and biodynamic actions. Anti-necrotic effect in carbon tetrachloride induced damage in rats, and rabbits reduce fatty infiltration and lipid deposits in galactosamine and paracetamol-induced hepatic damage (Mogre *et al.,* 1981), reverses the loss in body weight in alcohol treated rats improves food intake in CCl_4 induced liver damage (Pilankar, 1981), enhances the levels of DNA, RNA, protein, inhibition of lipid peroxidation antiviral effects on vaccinia viruses (Singh *et al.*, 1982) and anti-inflammatory effects in carrageenin oedema and inhibition of experimental passive cutaneous anaphylaxis (Kamble *et al.,* 2008; Thyagarajan *et al.,* 2002).

Trichosanthes cucumerina (Linn.)**:** It is one agent among the major constituents of important Ayurvedic preparations. It is used as blood purifier, appetizer, digestive, germicidal, aphrodisiac, hypoglycemic, anti-inflammatory activities and liver disorders (Kumar *et al.,* 2007).

Urtica urens (Linn.)**:** *U. urens* treatment decreased the CCl_4 dependent elevated lipid peroxidation and serum LDH, ALT and AST activities. Furthermore, *U. urens* protected the inhibitory effect of CCl_4 on CYP2E1 catalyzed aniline 4-hydroxylase activities (Sen *et al.,* 2007; Chrubasik *et al.*, 2007).

Fumaria indica (Hausskn.)**:** Whole plants of *Fumaria indica* (Fumariceae) were studied for their hepatoprotective activity against CCl_4, APAP and rifampicin-induced hepatotoxicities in albino rats. It showed similar reductions in the elevated levels of serum biochemical liver markers in a manner similar that of silymarin indicating it as a potential hepatoprotective agent (Rathi *et al.,* 2008; Rao *et al.*, 2007).

Solanum nigrum **(**Linn.)**:** *Solanum nigrum* is an herbal plant that has been used as hepatoprotective and anti-inflammation agent in Chinese's medicine (Lin *et al.,* 2008) Ethanol extract of *Solanum nigrum* was investigated for its hepatoprotective activity against CCl_4-induced hepatic damage in rats. The activity was evaluated using biochemical parameters such as AST, ALT, ALP and total bilirubin (Kuppuswamy *et al*., 2003).

Vitis coignetiae (Linn.)**:** The methanol extracts of the Oriental medicinal plant *Vitis coignetiae* showed hepatoprotective activity in the *in vitro* assay method using primary cultured rat hepatocytes (Oshima *et al.,* 1995).

Polygala arvensis (Linn.)**:** The chloroform extracts of *Polygala arvensis*, exhibited significant protection by normalizing the levels of AST, ALT, ALP, total bilirubin, LDH, total cholesterol, triglycerides, albumin, total protein against D-Gal (400 mg/kg) (Dhanabal *et al.,* 2006).

Taraxacum officinale (Weber)**:** Traditionally, *T. officinale* has been used as a remedy for jaundice and other disorders of the liver and gallbladder, and as a remedy for counteracting water retention. Oral administration of extracts from the roots has been shown to act as a cholagogue, increasing the flow of bile (Chen *et al.,* 1996). The extracts of *T. officinale* have demonstrated antitumor, hypoglycemic, diuretic, antibacterial and nitric oxide regeneration activity (Sumanth and Ahmed, 2008).

Cichorium intybus (Linn.)**:** *Cichorium intybus* is a popular Ayurvedic remedy in the treatment of liver diseases. It is commonly known as kasni and is part of polyherbal formulations used for the treatment of liver diseases. In preclinical studies, an alcoholic extract was found to be effective at chlorpromazine induced hepatic damage in adult albino rats. A bitter glucoside, Cichorin ($C_{32}H_{34}O_{19}$) has been reported to be the active constituent of the herb (Zafar and Ali, 1998; Srinivas and Shalini, 1991; Bahar *et al.,* 2008).

Glychyrrhiza glabra (Linn.)**:** *Glychyrrhiza glabra*, commonly known as licorice contains triterpene saponin, known as glycyrrhizin, which has potential hepatoprotective activity. It belongs to a group of compounds known as sulfated polysaccharides. Several studies carried out by Japanese researchers have shown glycyrrhizin to be for anti-viral, and it has been potential for therapeutic use in liver disease (Selvam *et al.,* 1995). It reduces experimental hepatitis and cirrhosis, promotes the regeneration of liver cells. Favourable results have been reported in children suffering from cytomegalovirus after treating with glycyrrhizin (Hamza, 2007; Rajesh and Latha, 2004a).

Wilkstroemia indica (Linn.)**:** *W. indica* is a Chinese herb and has been evaluated in patients suffering from hepatitis B. *A dicoumarin*, daphnoretin is the active constituent of the herb. The drug has shown to suppress HbsAG in Hep3B cells. It is said to an activator of protein kinase C (Datta *et al.,* 1999).

Curcuma longa (Linn.)**:** Like silymarin, turmeric has been found to protect animal livers from a variety of hepatotoxic substances, including CCl_4 (Hamza, 2007), D-Gal, pentobarbitol, 1-chloro-2, 4-dinitrobenzene, 7 4-hydroxy-nonenal, (Selvam *et al.,* 1995) and APAP.

Table 1: Recent plants investigated for hepatoprotection

S. no.	Plants	Hepatotoxicants	Parameters	References
1	*Bauhinia racemosa*	Paracetamol and CCl_4	AST, ALT, SALP, TP, Albumin, Bilirubin, LPO, GSH, SOD and Catalase.	Gupta *et al.*, 2004b
2	*Ichnocarpus frutescens (Linn.)*	Paracetamol	AST, ALT, TP, SALP, Bilirubin, LPO, GSH, SOD and Catalase.	Dash *et al.,* 2007
3	*Ginkgo biloba*	CCl_4	AST, ALT, Albumin, and plasma antioxidants.	He *et al.,* 2006
4	*Chamomile capitula*	Paracetamol	Serum markers enzymes, LPO, GSH and ATPase	Gupta and Misra, 2006
5	*Ventilago madrespatana*	CCl_4	AST, ALT, SALP, LPO, GSH, Acid, Alkaline PO4, ATPase, SDH, Protein and Glycogen	Bhadauria *et al.,* 2007
6	*Hibiscus sabdariffa*	CCl_4	AST, ALT, LPO and total protein	Dahiru *et al.,* 2003
7	*Pterocarpus santalinus*	CCl_4	AST, ALT, LPO, Bilirubin, protein and Histopathology	Manjunatha, 2006
8	*Sarcostemma brevistigma*	CCl_4	AST, ALT, ALP, Total Bilirubin and GGT	Sethuraman *et al*., 2003
9	*Momordica Cymbalaria Fenzl*.	CCl_4	AST, ALT, ALP, bilirubin, total protein, cholesterol, triglyceride, GSH, CAT and SOD and Histopathology.	Koneri *et al*., 2008
10	*Leucophyllum frutescens*	CCl_4	AST and ALT	Balderas-Renteria *et al.,* 2007
11	*Foeniculum vulgare*	CCl_4	AST, ALT, ALP and bilirubin	Ozbek *et al.,* 2004
12	*Pisonia aculeata L.*	CCl_4	AST, ALT, ALP, GGT, bilirubin, LPO, SOD, CAT, GPx and GST	Palanivel *et al.,* 2008
13	*Rosmarinus tomentosus*	Thioacetamide	AST, ALT, GDH, TD, ALP, GGT and G-6-pase	Galisteo *et al.,* 2006
14	*Hygrophila spinosa and cassia occidentalis*	CCl_4	AST, ALT and GGT	Usha *et al.,* 2007
15	*Lupinus termis*	Aflatoxin-Bl	Histopathology	Saber *et al.,* 2006
16	*Phyllanthus niruri*	Paracetamol	AST, ALT and Bilirubin	Iqbal *et al.*, 2007
17	*Limonium sinense*	CCl_4 and D-galactosamine	AST, ALT and Electron microscope	Tang *et al.,* 2007
18	*Alchornea cordifolia*	Paracetamol	AST, ALT, Bilirubin and cholesterol	Olaleye *et al.,* 2006
19	*Ficus carica* Linn.	CCl_4	AST, ALT, ALP, Total bilirubin and LPO	Krishna Mohan *et al.*, 2007
20	*Cymbropogon citratus*	Paracetamol	Malondialdehyde, Vitamin C, Catalase, Cholesterol and Phospholipids	Ojo *et al.,* 2006
21	*Moringa oleifera Lam*	CCl_4	Total and Direct Bilirubin , AST, ALT	Selvakumar and Natarajan, 2008
22	*Oldenlandia Umbellata*	CCl_4	AST, ALT, ALP, LPO and GSH	Gupta *et al.,* 2007
23	*Teucrium polium* L.	CCl_4	LPO, GSH, SOD and Catalase	Panovska *et al.*, 2007
24	*Amburana cearensis*	CCl_4	AST, ALT, LPO and catalase	Leal *et al.,* 2005
25	*Eclipta alba and Piper longum*	CCl_4	SGOT, SGPT, ALP, LDH, ACP, GGT and 5' Nucleotidase,	Samudram *et al.,* 2008

26	*Thespesia lampas*	CCl_4	SGOT, SGPT, ALP, bilirubin and Protein	Sangameswaran *et al.,* 2008
27	*Berchemia floribunda.*	D-galactosamine	MTT assay, IR spectrum and NMR	Wei *et al.*, 2008
28	*Cajanus indicus*	D-galactosamine	Creatinine and Blood urea nitrogen, SOD, GR CAT, , GST, GSH, total thiols, GSSG & LPO	Sinha *et al.,* 2007
29	*Phyllanthus rheedii*	D-galactosamine	ALT, AST, LDH, GGT, ALP and total bilirubin, cytokines (TNF-a, and TGF-β), RT-PCR. Histology	Suresh and Asha, 2008
30	*Trianthema decandra*	CCl_4	SGOT, SGPT, ALP, total protein and albumin	Sengottuvelu *et al.,* 2008
31	*Commiphora berryi (Arn)*	CCl_4	SGOT, SGPT, ALP, bilirubin, SOD, GPx and CAT	Gowri Shankar *et al.,* 2008
32	*Trianthema decandra Linn.*	CCl_4	AST, ALT, ALP, TP, albumin, GPx, GR, SOD, CAT and Histology	Balamurugan and Muthusamy, 2008
33	*Platycodon grandiflorum*	CCl_4	GPx and SOD	Lee *et al.,* 2008
34	*Gongronema latifolium*	CCl_4	ALT, AST and ALP	Etim *et al.,* 2008
35	*Euphorbia antiquorum Linn.*	CCl_4	Bilirubin, cholesterol, TG, LPO and GSH	Jyothi *et al.,* 2008
36	*Aegle Marmelos*	Alcohol	LPO, GSH, SOD, GPx, CAT, Vitamin A and C	Singanan *et al.,* 2007
37	*Picrorrhiza Rhizoma*	CCl_4	ALT, AST, LPO and hydroxyproline contents	Lee *et al.,* 2007

Diarylhepatonoids including curcumin is the active constituent of the plant (Jain *et al.,* 2007).

Tamarindus indica (Linn.)**:** It grows as a large tree and is found all over India. *T. indica* was found to be used in jaundice and other liver complaints in folk medicine Tamarind fruit contains the high amount of ascorbic acid and β-carotene. Pharmacological studies on the plant revealed that tamarind possess antibacterial, antidiabetic, antifungal, antiinflammatory, antimalarial and antioxidant activities (Abukar *et al.*, 2008; Pimple *et al.,* 2007).

Tephrosia purpurea (Linn.)**:** Oral administration of *Tephrosia purpurea* at 500 mg/kg and *Tecomella undulata* at 1000mg/kg resulted in a significant reduction in serum AST, ALT, ALP, γ-GT, total bilirubin, liver LPO and significant improvement in liver GSH when compared with TAA damaged rats (Khatri *et al*., 2009; Pavana *et al.*, 2007; Deshpande *et al.,* 2003).

Andrographis paniculata (Burm.f.)**:** For centuries Andrographis has been an important herb in the Asian healing systems of Ayurveda, Unani and Traditional Chinese Medicine. Traditionally, this herb has been used to potentiate immune system response to inflammation and infections, and as an anti-inflammatory, antipyretic and a hepatoprotective. The active constituent *Andrographolide* showed a significant dose dependent protective activity. It completely antagonized the toxic effects of APAP in serum as well as in isolated hepatic cells. Andrographolide was found to be more potent than silymarin (Visen *et al.,* 1993).

Boerhavia diffusa (Linn.)**:** An alcoholic extract of whole plant *Boerhavia diffusa* given orally exhibited hepatoprotective activity against experimentally induced CCl_4 hepatotoxicity in rats and mice. The extract also produced an increase in normal bile flow in rats suggesting a strong choleretic activity. The extract does not show any signs of toxicity up to an oral dose of 2g/kg in mice (Muthulingam, 2008; Ujowundu *et al*., 2008).

Eclipta alba (Linn.)**:** The hepatoprotective effect on the ethanol/water (1:1) extract of *Eclipta alba* was studied at subcellular levels in rats against CCl_4 induced hepatotoxicity. The study shows that hepatoprotective activity of *Eclipta alba* is by regulating the levels of hepatic microsomal drug metabolizing enzymes (Sagar *et al.*, 2006; Tabassum *et al.,* 2004).

Terminalia belerica (Roxb.)**:** Compound I isolated from fraction TB_5 of *Terminalia belerica* and finally identified as 3,4,5-trihydroxy benzoic acid (gallic acid) led to significant reversal of a majority of the altered parameters. Our results confirm the presence of hepatoprotective activity in altered parameters. Our results confirm the presence of hepatoprotective activity in compound, I (Jain *et al.,* 2008; Jadon *et al.,* 2007; Rasool *et al.,* 2007).

Tinospora cordifolia (Willd.)**:** Outstanding results in people suffering from jaundice have been obtained using an herb called *Tinospora Cordifolia*: Rege *et al.,* (1994) used the herb in malignant obstructive jaundice, half of the group received conventional treatment-drugs and drainage - the other half was treated with

drainage plus *T. Cordifolia*. After the conclusion of treatment, 50% of the drug-treated groups were found to have blood poisoning while none of the herbs treated group developed this problem. After surgery, only 40% of the drug-treated group survived, whereas an amazing 92.4% 0f, those treated with the herb lived. It proved effective for the prevention of fibrosis, and in stimulating regeneration of hepatic tissue.

According to Latha *et al.,* (2005) some plants as *Ixora coccinea*, *Lawsonia inermis*, *Nyctanthes arbor-tristis*, *Phyllanthus myrtifolius*, *Spilanthes ciliata* and *Wedelia calendulacea* were discussed along with their hepatoprotective properties that had been confirmed pharmacologically (Panchabhai *et al.*, 2008; Adhvaryu *et al.,* 2008).

DISCUSSION

Our current investigation verifies for the first time, the hepatoprotective effects of *Various herbal plants* against hepatotoxicants. The hepatoprotective action is likely related to its potent antioxidative and anti-inflammatory activity. Neutralizing reactive oxygen species by non enzymatic mechanism and enhancing the activity of original natural hepatic antioxidants enzymes may be the main mechanisms against injury. These data provide a scientific explanation for the folkloric uses of in the treatments of hepatic disorders. The findings provide a rationale for further studies on pharmacological evaluation.

REFERENCES

Abukar MG, Ukwuani AN, Shehu RA. Phytochemical screening and antibacterial activity of Tamarindus indica Pulp extract. Asian J Boichem 2008, 3: 134-138.

Adhvaryu MR, Reddy N, Parabia MH. Anti-Tumor Activity Of Four Ayurvedic Herbs In Dalton Lymphoma Ascites Bearing Mice And Their Short-Term In Vitro Cytotoxicity On Dla- Cell-Line. Afr J Trad 2008, 5: 409-418.

Balamurugan G, Muthusamy P. Observation of the hepatoprotective and antioxidant activities of Trianthema decandra Linn. (Vallai sharunnai) roots on carbon tetrachloride-treated rats. Bangladesh J Pharmacol 2008, 3: 83-89.

Balderas-Renteria I, Camacho-Corona MR, Carranza-Rosales P, Lozano-Garza HG, Castillo-Nava D, Alvarez-Mendoza. Hepatoprotective effect of Leucophyllum frutescens on Wistar albino rats intoxicated with carbon tetrachloride. Ann Hepatol 2007, 6: 251-254.

Bhadauria M, Nirala SK, Shukla S. Duration-dependent hepatoprotective effects of propolis extract against carbon tetrachloride-induced acute liver damage in rats. Adv Ther 2007, 24: 1136-1145.

Chrubasik S, Enderlein W, Bauer R, Grabner W. Evidence for antirheumatic effectiveness of Herba Urticae dioicae in acute arthritis: A pilot study. Phytomedicine 1997, 4: 105-108.

Dahiru D, Obi OJ, Umaru H. Effect of Hibiscus sabdariffa calyx extract on carbon tetrachloride induced liver damage. Biokemistri 2003, 15: 27-33.

Dash DK, Veerendra C, Yeligar, Nayak Siva S, Ghosh T, Rajalingam D, Sengupta P, Bhim CM, Maity TK. Evaluation of hepatoprotective and antioxidant activity of Ichnocarpus frutescens (Linn.) R.Br. on paracetamol-induced hepatotoxicity in rats. Tropical J Pharm Res 2007, 6: 755-765.

Datta S, Sinha S, Bhattacharyya P. Hepatoprotective activity of a herbal protein CI-1, purified from Cajanus indicus against beta-galactosamine HCl toxicity in isolated rat hepatocytes. India Phytother Res 1999, 13: 508-512.

Deshpande SS, Shah GB, Parmar NS. Antiulcer activity of Tephrosia purpurea in rats. Indian J Pharmacol 2003, 35: 168-172.

Dhanabal SP, Syamala G, Satish Kumar MN, Suresh B. Hepatoprotective activity of the Indian medicinal plant Polygala arvensis on D-galactosamine-induced hepatic injury in rats. Fitoterapia 2006, 77: 472-474.

Dubey NK, Kumar R, Tripathi P. Global promotion of herbal medicine: India's opportunity. Current Science 2004, 86: 1-10.

Duwiejua M, Zeitlin IJ, Waterman PG and Gray AI. Anti-inflammatory activity of Polygonum bistorta, Guaiacum officinale and Hamamelis virginiana in rats. J Pharm Pharmacol 1994, 46: 286-290.

Etim OE, Akpan EJ, Usoh IF. Hepatotoxicity of Carbon Tetrachloride: Protective Effect of Gongronema Latifolium Pak J Pharm 2008, Sci 21: 268-274.

Galisteo M, Suarez A, Montilla MP, Fernandez MI, Gil A, Navarro MC. Protective effects of Rosmarinus tomentosus ethanol extract on thioacetamide-induced liver cirrhosis in rats. Phytomedicine 2006, 13: 101-108.

Gowri Shankara NL, Manavalanb R, Venkappayyac D, Rajd CD. Hepatoprotective and antioxidant effects of Commiphora berryi (Arn) Engl bark extract against CCl4-induced oxidative damage in rats. Food Chem Toxicol 2008, 46: 3182-3185.

Gupta AK, Misra N. Hepatoprotective Activity of Aqueous Ethanolic Extract of Chamomile capitula in Paracetamol Intoxicated Albino Rats. Am J Pharm Toxicol 2006 (a), 1: 17-20.

Gupta M, Mazumder UK, Kumar RS, Kumar TS. Antitumor activity and antioxident role of Bauhinia racemosa against Ehrlich ascites carcinoma in Swiss albino mice. Acta Pharmacol 2004, 25: 1070-1076.

Gupta M, Mazumder UK, Thamilselvan V, Manikandan L, Senthilkumar GP, Suresh R, Kakott BK. Potential

Hepatoprotective Effect and Antioxidant Role of Methanol Extract of Oldenlandia umbellata in Carbon Tetrachloride Induced Hepatotoxicity in Wistar Rats. IJPT 2007, 6: 5-9.

Hamza AA. Curcuma longa, Glycyrrhiza glabra and Moringa oleifera Ameliorate Diclofenac-induced Hepatoxicity in Rats. Am J Pharm Toxicol 2007, 2: 80-88.

He SX, Luo JY, Wang YP, Wang Y, Fu H, Xu JL, Zhao G, Liu EQ. Effects of extract from Ginkgo biloba on carbon tetrachloride- induced liver injury in rats. World J Gastroenterol 2006, 24: 28-39.

Iqbal MJ, Dewan ZF, Choudhury SAR, Mamun MIR, Mashiuzzaman M, Begum M. Pre-treatment by hexane extract of Phyllanthus niruri can alleviate paracetamol -induced damage of the rat liver. Bangladesh J Pharmacol 2007, 2: 43-48.

Jadon A, Bhadauria M, Shukla S. Protective effect of Terminalia belerica Roxb and gallic acid against carbon tetrachloride induced damage in albino rats. J Ethnopharmacol 2007, 109: 214-218.

Jain BB, Rathi BS, Thakurdesai PA, Bodhankar SL. Antipyretic activity of aqueous extract of leaves of Cocculus hirsutus. Indian J Nat Prod 2007, 23: 26-29.

Jyothi TM, Prabhu K, Jayachandran E, Lakshminarasu S, Setty RS. Hepatoprotective and antioxidant activity of Euphorbia antiquorum. Phcog Mag 2008, 4: 127-133.

Kamble MB, Dumbre RK, Rangari VD. Hepatoprotective activity studies of herbal formulations. Int J Green Pharm 2008, 2: 147-151.

Khatri A, Garg A, Agrawal SS. Evaluation of hepatoprotective activity of aerial parts of Tephrosia purpurea L. and stem bark of Tecomella undulata. J Ethnopharmacol 2009, 122: 1-5,.

Koneri R, Balaraman R, Firdous, Kumar VM. Hepatoprotective Effects of Momordica Cymbalaria Fenzl against Carbon Tetrachloride Induced Hepatic Injury in Rats. Pharmacologyonline 2008, 1: 365-374.

Kumar SS, Kumar RB, Mohan GK, Antihepatotoxic Activity Of Trichosanthes Cucumerina On Carbon Tetrachloride Induced Liver Damage In Rats. Pharmacologyonline 2007, 3: 461-469.

Kuppuswamy R, Govindaraju A, Velusamy G, Balasubramanian R, Balasundarm J, Sellamuthu M. Effect of Dried Fruits of Solanum nigrum LINN against CCl4-Induced Hepatic Damage in Rats. Biol Pharm Bul 2003, 26: 1618-1619.

Latha PG, Suja SR, Shyamal S, Rajasekharan S. Some hepatoprotective garden plants. Natural Product Radiance 2005, 4: 278-279.

Leal, Nobre JHV, Cunha GMA, Moraes MO, Pessoa C, Oliveira RA, Silveira ER, Canuto KM, Viana GSB. Amburoside A, a glucoside from Amburana cearensis, protects mesencephalic cells against 6-hydroxydopamine-induced neurotoxicity. Neuroscience Letters 2005, 388: 86-90.

Lee KJ, Choi JH, Kim HG, Han EH, Hwang YP, Lee YC, Chung YC, Jeong HG. Protective effect of saponins derived from the roots of Platycodon grandiflorum against carbon tetrachloride induced hepatotoxicity in mice Food Chem Toxicol 2008, 46: 1778-1785.

Lin HM, Tseng HC, Wang CJ, Lin JJ, Lo CW, Chou FP. Hepatoprotective effects of Solanum nigrum Linn extract against CCl4-iduced oxidative damage in rats. Chemico-Biological Interactions 2008, 3: 283-293.

Manjunatha BK. Hepatoprotective activity of Pterocarpus santalinus L.f., an endangered medicinal plant. Indian J Pharmacol 2006, 38: 25-28.

Manoharan KP, Yang D, Hsu A, Huat BT. Evaluation of Polygonum bistorta for anticancer potential using selected cancer cell lines. Med Chem 2007, 3: 121-126.

Mogre K, Vora KK, Sheth UK. Effect of Picrorhiza kurroa and Eclipta alba on Na+ K+T Pase in hepatic injury by hepatotoxic agents. Ind J Pharmac 1981, 13: 252-259.

Muthulingam M. Antihepatotoxic Effects of Boerhaavia diffusa L. on Antituberculosis Drug, Rifampicin Induced Liver Injury in Rats. J Pharmacol Toxicol 2008, 3: 75-83.

Naus P, Henson R, Bleeker G, Wehbe H, Meng F, Patel T. Tannic acid synergizes the cytotoxicity of chemotherapeutic drugs in human cholangiocarcinoma by modulating drug efflux pathways. J Hepatol 2007, 46: 222-229.

Ojo OO, Nadro MS, Tella IO. Protection of rats by extracts of some common Nigerian trees against acetaminophen-induced hepatotoxicity. African J of Biotech 2006, 5: 755-760.

Olaleye MT, Adegboye OO, Akindahunsi AA. Alchornea cordifolia extract protects wistar albino rats against acetaminophen-induced liver damage. African J of Biotech 2006, 5: 2439-2445.

Oshima Y, Namao K, Kamijou A, Matsuoka S, Nakano M, Terao K, Ohizumi Y. 1995. Powerful hepatoprotective and hepatotoxic plant oligostilbenes, isolated from the Oriental medicinal plant Vitis coignetiae (Vitaceae). CMLS 1995, 51: 63-66.

Ozbek H, Ugras S, Bayram I, Uygan I, Erdogan E, Öztürk A, Huyut Z. Hepatoprotective effect of Foeniculum vulgare essential oil: A carbon-tetrachloride induced liver fibrosis model in rats. Scand. J. Lab. Anim. Sci 2004, 31: 9-17.

Palanivel MG, Rajkapoor B, Kumar RS, Einstein JW, Kumar EP, Mani RK, Kunchu K, Mohanraj PK, Balasundaram J. Hepatoprotective and Antioxidant Effect of Pisonia aculeata L. against CCl4- Induced

Hepatic Damage in Rats. Sci Pharm 2008, 76: 203-215.

Panchabhai TS, Ambarkhane SV, Joshi AS, Samant BD, Rege NN. Protective effect of Tinospora cordifolia, Phyllanthus emblica and their combination against antitubercular drugs induced hepatic damage: an experimental study. Phytother Res 2008, 22: 646-650.

Panovska TK, Kulevanova S, Gjorgoski I, Bogdanova M, Petrushevska G. Hepatoprotective effect of the ethyl acetate extract of Teucrium polium L. against carbontetrachloride-induced hepatic injury in rats. Acta Pharm 2007, 57: 241-248.

Pavana P, Sethupathy S, Manoharan S. Antihyperglycemic and antilipidperoxidative effects of Tephrosia purpurea seed extract in streptozotocin induced diabetic rats. IJCB 2007, 22: 77-83.

Pilankar PD. A study of hepatoprotective effects of some indigenous plants in experimental animals. Ph.D. Thesis. University of Bombay 1981.

Pimple BP, Kadam PV, Badgujar NS, Bafna AR, Patil MJ. Protective effect of Tamarindus indica linn against paracetamol-induced hepatotoxicity in rats. Indian J Pharm Sci 2007, 69: 827-831.

Rajesh MG, Latha MS. Protective activity of Glycyrrhiza glabra Linn. on carbon tetrachloride-induced peroxidative damage. Indian J Pharmacol 2004 (a), 36 (5): 284-287.

Rajshekharan PE. Herbal medicine. In World of Science 2002, 3.

Rao CV, Verma AR, Gupta PK, Vijayakumar M. Anti-inflammatory and anti-nociceptive activities of Fumaria indica whole plant extract in experimental animals. Acta Pharm 2007, 57: 491-498.

Rasool MK, Sabina EP, Lavanya K, Nithya P. Therapeutic effect of Indian ayurvedic herbal formulation Triphala on acetaminophen induced hepatotoxicity in Mice. J Pharmacol and Toxicol 2007, 2: 725-731.

Rathi A, Srivastava AK, Shirwaikar A, Rawat AKS, Mehrotra S. Hepatoprotective potential of Fumaria indica Pugsley whole plant extracts, fractions and an isolated alkaloid protopine. Phytomedicine 2008, 15: 470-477.

Rege N, Dhanukar S, Karandikar SM. Hepatoprotective Effect of Tinospora cordifolia against CCl4 induced liver damage. Ind Drugs 1994, 21: 544-555.

Saber AS, Hawazen A. Lamfon, Sabah F. El-Abd. Ameliorative Effect of Lupinus Seeds on Histopathological and Biochemical Changes Induced by Aflatoxin-Bl in Rat Liver. J Appl Sce Res 2006, 2: 290-295.

Sagar BPS, Rajiv Panwar, Goswami A, Kadian K, Tyagi K, Chugh M, Dalal S, Zafar R. Pharmacokinetic Interactions of Antihepatotoxic Wedelolactone with Paracetamol in Wistar Albino Rats. Pharmaceutical Biology 2006, 44: 554-561.

Samudram P, Hari R, Vasuki R, Geetha A, Sathiya moorthi P. Hepatoprotective activity of Bi - herbal ethanolic extract on CCl4 induced hepatic damage in rats. Afr J Biochem Res 2008, 2: 061-065.

Sangameswaran B, Deshraj C, Balakrishnan BR, Jayakar B. Hepatoprotective Effects of Thespesia lampas Dalz & Gibs in CCl4 Induced Liver Injury in Rats. J Pharm Sci 2008, 7: 11-13.

Selvakumar D, Natarajan P. Hepatoprotective activity of Moringa oleifera Lam leaves in carbon tetrachloride induced hepatotoxicity in albino rats. Phcog Mag 2008, 4: 97-98.

Selvam R, Subramanian L, Gayathri R. The anti-oxidant activity of turmeric (Curcuma longa). J Ethnopharmacol 1995, 47: 59-67.

Sen A, Sahin B, Agus HH, Bayav M, Sevim H, Semiz A, Prevention of Carbon Tetrachloride-Induced Hepatotoxicity by Urtica urens in Rats. JABS 2007, 1: 29-32.

Sengottuvelu, S, Srinivasan, D, Duraisami, R, Nandhakumar, J, Vasudevan, M, Sivakumar, T. Hepatoprotective activity of Trianthema decandra on carbon tetrachloride-induced hepatotoxicity in rats. Phcog Mag 2008, 3: 120-123.

Sethuraman MG, Lalitha KG, Rajkapoor B. Hepatoprotective activity of Sarcostemma brevistigma against carbon tetrachloride induced hepatic damage in rats. Curr Sci 2003, 84: 1186-1187.

Singanan V, Singanan M, Begum H. The Hepatoprotective Effect of Bael Leaves (Aegle Marmelos) in Alcohol Induced Liver Injury in Albino Rats. International Journal of Science & Technology 2007, 2: 83-92.

Singh N, Misra N, Singh SP, Kohli RP, Bhargava KP. Protective effect of Picrorhiza kurroa against cutaneous vaccinial (viral) infection in guinea pigs. J Res Ay Sid 1982, 33: 162-171.

Sinha M, Manna P, Sil PC. Amelioration of galactosamine-induced nephrotoxicity by a protein isolated from the leaves of the herb, Cajanus indicus L. BMC Compl Alt Med 2007, 7: 1-18.

Smolarz HD, Bogucka-kocka A, Kocki J, Olearnik M. Induction of apoptosis in human leukemic Jurkat cells by the extracts from Polygonum amphibium and Polygonum lapathifolium – a pilot study. Annals Universitatis Mariae Curie Sklodowska 2007, 20: 59-63.

Sumanth M, Ahmed R. Antihepatotoxic and Antioxidant Activity of Roots of Taraxacum officinale in CCl4-Intoxicated Rats. Phcog Mag 2008, 4 (16): 188-194.

Suresh V, Asha VV. Preventive effect of ethanol extract of Phyllanthus rheedii Wight. on D-galactosamine in-

duced hepatic damage in Wistar rats. J Ethnopharmacol 2008, 16: 447-453.

Tabassum N, Shyam S, Agrawal. Hepatoprotective activity of eclipta alba hassk. against paracetamol induced hepatocellular damage in mice. JK-Practitioner 2004, 11: 278-280.

Tang X, Gao J, Chen J, Xu L, Tang Y, Dou H, Yu W, Zhao X. Expression of VDAC Regulated by Extracts of Limonium sinense Ktze root Against CCl4-induced Liver Damage. Int J Mol Sci 2007, 8: 204-213.

Thyagarajan SP, Jayaram, S, Gopalakrishnan V, Hari R, Jeyakumar P, Sripathi, MS. Herbal medicines for liver diseases in India. Journal of Gastroenterology & Hepatology 2002, 17: 370-376.

Ujowundu CO, Lgwe CU, Enemor VHA, Nwaogu LA, Okafor OE. Nutritional and Anti-Nutritive properties of Boerhavia diffusa and Commelina nudiflora Leaves. Pak J Nutr 2008, 7: 90-92.

Usha K, Kasturi GM, Hemalatha P. Hepatoprotective Effect Of Hygrophila Spinosa And Cassia Occidentalis On Carbon Tetrachloride Induced Liver Damage In Experimental Rats. Indian J Clin Biochem 2007, 22: 132-135.

Visen PK, Shukla B, Patnaik GK, Dhawan BN. Andrographolide protects rat hepatocytes against paracetamol-induced damage. J Ethnopharmacol 1993, 40: 131-136.

Wei X, Jiang JS, Feng M, Zhang PC. Anthraquinone-benzisochromanquinon dimers from the roots of Berchemia floribunda. Chem Pharmaceut Bull 2008, 56: 1248-1252.

World Health Organization (WHO) Traditional Medicine Strategy 2002–2005. WHO/EDM/TRM/2002.1. Geneva, Switzerland: World Health Organization 2002.