

(Review Article)



Received on 05 /01/2012;

Revised on 18/01/2012;

Accepted on 29/01/2012.

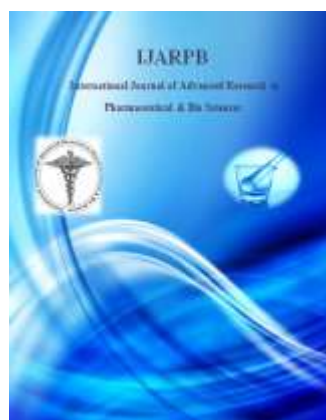
A Review on Hepatoprotective Activity of Medicinal Plants

S. Vipin Kumar*¹, T. Sanjeev¹, S. Ajay¹, S. Pravesh Kumar², S. Anil³

¹Seth G. L. Bihani S. D. College of Technical Education, Sri Ganganagar, Rajasthan, India

²Sanjeevan College of Pharmacy, Dausa, Rajasthan, India

³B. R. Nahata College of Pharmacy, Mandsaur, M.P., India



Corresponding Author:

S. Vipin Kumar*¹

Seth G. L. Bihani S. D. College of Technical Education¹, Sri Ganganagar, Rajasthan, India

Email:Vipinmpharma@gmail.com

ABSTRACT

Liver is a vital organ play a major role in metabolism and excretion of xenobiotics from the body. Liver injury or liver dysfunction is a major health problem that challenges not only health care professionals but also the pharmaceutical industry and drug regulatory agencies. Liver cell injury caused by various toxic chemicals (certain anti-biotic, chemotherapeutic agents, carbon tetrachloride (CCL₄), thioacetamide (TAA) etc.), excessive alcohol consumption and microbes is well-studied. Herbal medicines have been used in the treatment of liver diseases for a long time. A number of herbal preparations are available in the market. The present review is aimed at compiling data on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models using modern scientific system.

KEY WORDS: Herbal drugs, Liver Injury, Carbon tetrachloride (CCL₄), Hepatotoxicity.

(Review Article)**INTRODUCTION**

The liver plays an astonishing array of vital functions in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction. And it functions as a centre of metabolism of nutrients such as carbohydrates, proteins and lipids and excretion of waste metabolites. The bile secreted by the liver has, among other things, plays an important role in digestion. Therefore, maintenance of a healthy liver is essential for the overall well being of an individual¹. Liver cell injury caused by various toxicants such as certain chemotherapeutic agents, carbon tetrachloride, thioacetamide, chronic alcohol consumption and microbes are common. Enhanced lipid peroxidation during metabolism of ethanol may result in development of hepatitis leading to cirrhosis³.

Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. The Indian Traditional Medicine like Ayurveda, Siddha and Unani are predominantly based on the use of plant materials. The association of medical plants with other plants in their habitat also influences their medicinal values in some cases. One of the important and well documented uses of plant-products is their use as hepatoprotective agents. Hence, there is an ever increasing need for safe hepatoprotective agent². In spite of tremendous strides in modern medicine, there are hardly any drugs that stimulate liver function, offer protection to the liver from damage or help regeneration of hepatic cell. Many formulations containing herbal

extracts are sold in the Indian market for liver disorders⁴.

But management of liver disorders by a simple and precise herbal drug is still an intriguing problem. Several Indian medicinal plants have been extensively used in the Indian traditional system of medicine for the management of liver disorder. Some of these plants have already been reported to possess strong antioxidant activity^{5,6}.

Liver Diseases and Medicinal Plants:

Liver has a pivotal role in regulation of physiological processes. It is involved in several vital functions such as metabolism, secretion and storage. Furthermore, detoxification of a variety of drugs and xenobiotics occurs in liver. The bile secreted by the liver has, among other things, an important role in digestion. Liver diseases are among the most serious ailments⁷. They may be classified as acute or chronic hepatitis (inflammatory liver diseases), hepatosis (non-inflammatory diseases) and cirrhosis (degenerative disorder resulting in fibrosis of the liver). Liver diseases are mainly caused by toxic chemicals (certain antibiotics, chemotherapeutics, peroxidised oil, aflatoxin, carbon-tetrachloride, chlorinated hydrocarbons, etc.), excess consumption of alcohol, infections and autoimmune/disorder¹¹. Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages in liver. Enhanced lipid peroxidation produced during the liver microsomal metabolism of ethanol may result in hepatitis and cirrhosis^{9,10}.

(Review Article)

Medicinal herbs are significant source of pharmaceutical drugs. Latest trends have shown increasing demand of phytodrugs²⁷ and some medicinal herbs have proven hepatoprotective potential. Silymarin, a flavonolignan mixture extracted from the milk thistle (*Silybum marianum*) is a popular remedy for hepatic diseases⁸. Today every herbal company is marketing formulations for liver disorders but the actual scene is that only selected medicinal herbs have been tested for hepatoprotective activity¹⁵. Some herbal formulations claiming to be hepatoprotective may actually contain chemical constituents having hepatotoxic potential. Andrographolide (*Andrographis paniculata*), Glycyrrhizin (*Glycyrrhiza glabra*), Picrorrhizin (*Picrorrhiza kurroa*) and Hypo-phyllanthin (*Phyllanthus niruri*) are potential candidates with hepatoprotective activity. The article reviews latest trends in testing of isolated constituents with hepatoprotective activity^{12, 13}.

Taraxacum officinale

Traditionally *Taraxacum 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. Generally, the roots of the plant have the most activity regarding the liver and gallbladder¹⁴. Oral administration of extracts from the roots of *Taraxacum officinale* has been shown to act as a cholagogue, increasing the flow of bile. Bitter constituents like taraxecerin and taraxcin are active constituents of the medicinal herb.

Cichorium intybus

Cichorium intybus is a popular Ayurvedic remedy for the treatment of liver diseases. It is commonly known as *kasni* and is part of polyherbal formulations used in the treatment of liver diseases. In mice, liver protection was observed at various doses of *Cichorium intybus* but optimum protection was seen with a dose of 75 mg/kg given 30 minutes after CCl₄ intoxication. In preclinical studies an alcoholic extract of the *Cichorium intybus* was found to be effective against chlorpromazine-induced hepatic damage in adult albino rats.

Solanum nigrum

In Ayurveda, the drug is known as *kakamachi*. Aromatic water extracted from the drug is widely prescribed by herbal vendors for liver disorders. Although clinical documentation is scarce as far as hepatoprotective activity is concerned, but some traditional practitioners have reported favorable results with powdered extract of the plant²¹.

Glycyrrhiza glabra

Glycyrrhiza 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 potential for therapeutic use in liver disease¹³.

Experimental hepatitis and cirrhosis studies on rats found that it can promote the regeneration of

(Review Article)

liver cells and at the same time inhibit fibrosis. Glycyrrhizin can alleviate histological disorder due to inflammation and restore the liver structure and function from the damage due to carbon tetrachloride²⁹. The effects including: lowering the SGPT, reducing the degeneration and necrosis and recovering the glycogen and RNA of liver cells.¹⁶ Effects of glycyrrhizin have been studied on free radical generation and lipid peroxidation in primary cultured rat hepatocytes. Favorable results have been reported in children suffering from cytomegalovirus after treating with glycyrrhizin⁸.

Wilkstroemia indica

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 activator of protein kinase C¹⁴.

Curcuma longa

Like silymarin, turmeric has been found to protect animal livers from a variety of hepatotoxic substances, including carbon tetrachloride, galactosamine, pentobarbitol, 1-chloro-2, 4-dinitrobenzene, 7 4-hydroxy-nonenal, and paracetamol. Diarylhepatonoids including Curcumin is the active constituent of the plant²². The active constituent of *Curcuma longa* is Curcumin, which is the yellow pigment of turmeric. At the dose of 600 mg/kg, paracetamol induced liver damage in rats as manifested by statistically significant increase in serum alanine aminotransferase (ALT) and Aspartate

aminotransferase (AST) and alkaline phosphatase (ALP)²³.

Tephroia purpurea

In Ayurveda, the plant is known as *sharpunkha*. Alkali preparation of the drug is commonly used in treatment of liver and spleen diseases. In animal models, it offered protective action against carbon tetrachloride and D-galactosamine poisoning¹¹. The roots, leaves and seeds contain tephrosin, deguelin and quercetin. The hepatoprotective constituent of the drug is still to be proved.

Picrorhiza kurroa

Administration of picroliv, a standardized fraction of alcoholic extract of *Picrorhiza kurroa* (Scrophulariaceae) (3-12 mg/kg/day for two weeks) simultaneously with P.

Bergheim infection showed significant protection against hepatic damage in *Mastomys natalensis*²⁵. The increased levels of serum glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase, lipoprotein-X (LP-X) and bilirubin in the infected animals were markedly reduced by different doses of picroliv. In the liver, picroliv decreased the levels of lipid peroxides and hydroperoxides and facilitated the recovery of superoxide dismutase and glycogen²⁴.

Aegle marmelos

Aegle marmelos leaves (Bael, family of Rutaceae) which is also called as *Bilva* in ancient Sanskrit, was used as herbal drug in the Indian System of medicine. The hepatoprotective effect

(Review Article)

of *Aegle marmelos* in alcohol induced liver injury was evaluated rats using essential marker biochemical parameters. The results indicated that, the Bael leaves have excellent hepatoprotective effect. Similar findings were also reported by other workers²⁶.

Andrographis paniculata

Antihepatotoxic activity of the *Andrographis paniculata* (acanthaceae) methanolic extract (equivalent to 100 mg/kg of andrographolide) and 761.33 mg/kg ip, of the andrographolide free methanolic extract (equivalent to 861.33 mg/kg of the methanolic extract) of the plant, using CCl₄-intoxicated rats. Biochemical parameters like serum transaminases--GOT and GPT, serum alkaline phosphatase, serum bilirubin and hepatic triglycerides were estimated to assess the liver function. The results suggest that andrographolide is the major active antihepatotoxic principle present in *A. paniculata*²⁸.

CONCLUSION

It has been encouraging to witness the recent discoveries in HBV infection with insights into the existence of genotype subgroups, mutant variants, knowledge regarding host, viral and

environmental factors on the disease course, as well as advances in new treatment modalities. However, despite the much progress in understanding the natural history of HBV infection, we still have a long way to go before we can conquer hepatitis B infection. For instance, more studies are needed to clarify whether there is an association between genotype, mutant variants and the development of hepatocellular carcinoma. In the HBeAg-positive subgroup, there still lacks a consensus on how to manage these patients when they present with signs of mild liver disease activity with alanine aminotransferase less than two fold increase; future studies with longer follow-up may help us gain knowledge about the HBV behavior in these individuals. There is much more to be understood about mutations and their impacts on the clinical course and long-term outcome of hepatitis B infection. For instance, it has been suggested that mutations can arise from vaccine-induced antibodies and this renders the immune response generated by the vaccination ineffective. Therefore, mutations may play a key role in the difficulties of managing hepatitis B infection. Hence, further research and understanding in this sector may bring exciting new information and better understanding of the natural history of HBV and supplement our existing armamentarium to combat this persistent worldwide prevalent disease.

(Review Article)**Table: Review of Plant Used In the Treatment of Liver Disease.**

Drug	Plant Part	Biological Source (Family)	Active Constituent	Use
GARLIC ⁸ (ALLIUM)	Bulb	Allium sativum (Liliaceae)	Allicin, propyl disulphide, Allin	Carminative, Expectorant, Anthelmintic
TURMERIC ^{13,14} (CURCUMA)	Fresh Rhizomes	Curcuma longa (Zingiberaceae)	Curcuminoides Volatile oils	Anti-inflammatory Condiment
LIQUORICE ¹⁶ (MULETHI)	Dried Roots and Stolon	Glycyrrhiza glabra (Leguminosae)	Glycyrrhizin, 18-B-Glycyrrhetic acid	Peptic ulcer, Expectorant
PICRORRHIZA (KUTKI) ¹⁷	Dried Rhizomes	Picrorrhiza kurroa (Scrophulariaceae)	Picroside-1, Kutkoside, Amarogentin	Hepatoprotective bitter, bitter tonic
BOLDO ¹¹	Dried leaf	Peumus boldus mol. (Monimiaceae)	Limonene, Linalol, Rhamnetin, B-pinene	Dyspepsia, Heart burn
FUMITORY ^{11,12}	Flower	Fumaria officinalis (Fumariaceae)	Protopine, Fumaritrine, Fumaricine	Enhance urinary and digestive elimination function
TEA (THEA) ¹⁶	Leaf buds	Thea sinensis (Theaceae)	Caffeine, Theobromine, Theophylline	CNS stimulant, Diuretic
GOLDEN SEAL ^{13,14}	Dried rhizome and roots	Hydrastis Canadensis (Ranunculaceae)	Hydrastine, Berberine	Conjunctival hyperthermia of allergic or seasonal origin
KALMEGH ^{8,14,16}	Leaves or entire aerial	Adrographis paniculata (Acanthaceae)	Adrographolide, Kalmeghin, Flavonoids, Phenols	Stomachic, cholagogue, Liver protective, Dyspepsia
GADUCHI ^{12,13,14}	Dried stem	Tinospora cardifolia (Monispermeceae)	Clerodone, Tinosporal, Tinosporon, Berberine	Antipyretic, Analgesic
PUNARNAVA ⁸	Dried whole plant	Boerhavia diffusa (Nictagenaceae)	Punarnavine, Punarnavoside	Hepatoprotective, Diuretic

(Review Article)**REFERENCES**

1. Smuckler EA, Alcoholic Drink: Its Production and Effects. Fed Proe 1975, 34, 2038-44.
2. Ward FM, and Daly MJ, Hepatic Disease, Clinical Pharmacy and Therapeutics, Churchill Livingstone, New York, 1999, 195-212.
3. Agarwal SS, Development of hepatoprotective formulations from plant sources, Pharmacology and Therapeutics in the New Millennium, New Delhi, 2001, 357-358.
4. Achuthan CR, et.al. Antioxidant and Hepatoprotective effects of Rosa damascene, Pharmaceut. Biol., 41, 2003, 357-361.
5. Aniya Y, et.al. Free radical scavenging action of the medicinal herb Limonium wrightii from the Okinawa islands, Phytomedicine, 9, 2002, 239-244.
6. Gupta AK, Antioxidant activity of Chamomile recutita capitula methanolic extracts against CCl4-induced liver injury in rats Journal of Pharmacology and Toxicology, 1, 2006, 101- 107.
7. Samir S, Hepatoprotective Natural Products, 2001, 2(5), 110-111
8. PDR for herbal medicines. First edition. Montvale, New Jersey 1998, 1177-1178.
9. Ross and Wilson Anatomy and Physiology in Health and illness, Ninth Edition, 2005, published by Elsevier Ltd., 307-310, 333-336.
10. Tortora and Grabowski, Principle of Anatomy and Physiology, 2003(10), 875-879.
11. Malhotra S, Hepatoprotective Natural Products, 2001, vol.2 (5); 110-111.
12. Qadry JS, Pharmacognosy, 10, 2007-08, B.S. Prakashan, Ahmedabad, 156,195.
13. Trease and Evans, Pharmacognosy, 10, 2007, Elsevier Publishers, New Delhi, 414-418.
14. Kokate CK, and Gokhle SB, Pharmacognosy, 39, 2007, Nirali Prakashan, Pune, 156-157, 249-250.
15. Bruneton J, Pharmacognosy Phytochemistry Medicinal Plants, IInd 1999, Lavoisier Publishing, 207-209.
16. Handa SS, Text Book of Pharmacognosy, IInd 2003, Vallabh Prakashan, Delhi, 202-211.
17. Vaidya AB, et. Al. Picrorhiza kurroa (Kutki) Royle ex Benth as a hepatoprotective agent-experimental & clinical studies, 1996, Vol. 42(4), 105-108
18. Vogel G, New Natural Products and Plant Drugs with pharmacological, biological or therapeutical Activity. New York: Springer, 1977, 249-262.
19. Pandey GP, Hepatogenic effect of some indigenous drugs on experimental liver damage .PhD Thesis, Jabalpur, MP, 1990.

(Review Article)

20. Luper S, A Review of plants used in the treatment of liver disease; Part I *Altem Med Rev* 2009, 3(5), 116-24.
21. Chang-Chi H, Hsun-Lang F, Wen-Chuan L. Inhibitory effect of *Solanum nigrum* on thioacetamide-induced liver fibrosis in mice. *J Ethnopharmacol* 2008, 117–121.
22. Kapoor LD, *CRC Handbook of Ayurvedic Medicinal Plants*, Boca Raton, CRC Press, 1990, 149-150.
23. Somchit MN, Hepatoprotective effects of *Curcuma longa* rhizomes in paracetamol-induced liver damage in rats, *Proceedings of the Regional Symposium on Environment and Natural Resources*, 1, 2002, 698-702.
24. Chander R, Evaluation of hepatoprotective activity of picroliv from *Picrorhiza kurroa* in *Mastomys natalensis* infected with *Plasmodium berghei*, *J Medicinal Res.*, 92, 1990, 34-7.
25. Ansari RA, Antihepatotoxic properties of picroliv: an active fraction from rhizomes of *Picrorhiza kurroa*, *J Ethnopharmacol.*, 34(1), 1991, 61-8.
26. Vinodhini S, Hepatoprotective effect of bael leaves (*aegle marmelos*) in alcohol induced liver injury in albino rats, *international journal of science & technology*, 2, 2007,83-92.
27. Agrawal SS, *Drug Technology*, 1st, 2007, Universities Press (India) Pvt. Ltd., Hyderabad, 578-582.
28. Handa SS, Hepatoprotective activity of andrographolide from *Andrographis paniculata* against carbontetrachloride, *Indian J Med Res.*, 92, 1990, 276-83.
29. Stickel F, Schuppan, D. Herbal medicine in the treatment of liver diseases, *Digestive and Liver Disease*, 39, 2007, 293–304.