

Hepatoprotective Natural Products

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Abstract

Medicinal herbs are significant source of pharmaceutical drugs. Latest trends have shown increasing demand of phytodrugs and some medicinal herbs have proven hepatoprotective potential. Silymarin, a flavonolignan mixture extracted from the *Silybum marianum* (milk thistle) is a popular remedy for hepatic diseases. 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 activity. 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.

(Keywords: Natural products/ Medicinal herbs/ Hepatoprotective/.)

Alternative systems of medicine viz. Ayurveda, Siddha, and Traditional Chinese Medicine have become more popular in recent years.¹ Medicinal herbs and extracts prepared from them are widely used in the treatment of liver diseases like hepatitis, cirrhosis, and loss of appetite.² Medicinal herb is a biosynthetic laboratory, for chemical compounds like glycosides, alkaloids, resins, oleoresins, etc. These exert physiological and therapeutic effect.³ The compounds that are responsible for medicinal property of the drug are usually secondary metabolites.

A number of recent reviews have focused on the adverse effects of herbal products.⁴ In the current review, we will highlight on herbs known to be hepatoprotective, mechanisms of hepatoprotectivity, and clinical documentation.⁵

In fact some herbal products claiming to be hepatoprotective may actually be having some components with hepatotoxic potential.

Silybum marianum, *Picrorrhiza kurroa*, *Andrographis paniculata*, *Phyllanthus niruri*, and *Eclipta alba* are proven hepatoprotective medicinal herbs, which have shown genuine utility in liver disorders.⁶ These plants are used widely in hepatoprotective preparations and extensive studies have been done on them. Their discussion is beyond the scope of the article.

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 gallbladder. Oral administration of extracts from the roots of *Taraxacum officinale* has been shown to act as a cholagogue, increasing the flow of bile.⁷ Bitter constituents like taraxecerin and taraxcin are active constituents of the medicinal herb.⁸

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.⁹ In preclinical studies an alcoholic extract of the *Cichorium intybus* was found to be effective against chlorpromazine-induced hepatic damage in adult albino rats. A bitter glucoside, Cichorin (C₃₂H₃₄O₁₉) has been reported to be the active constituent of the herb.

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 plant.

Glycyrrhiza glabra

Glycyrrhiza glabra, commonly known as licorice contains triterpene saponin, known as glycyrrhizin, which

has potential hepatotprotective 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 disease. ¹⁰

Experimental hepatitis and cirrhosis studies on rats found that it can promote the regeneration of 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 tetrachloride. The effects including: lowering the SGPT, reducing the degeneration and necrosis and recovering the glycogen and RNA of liver cells. Effects of glycyrrhizin has been studied on free radical generation and lipid peroxidation in primary cultured rat hepatocytes. ¹¹

Favorable results have been reported in children suffering from cytomegalovirus after treating with glycyrrhizin. ¹²

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 C. ¹³

Curcuma longa

Like silymarin, turmeric has been found to protect animal livers from a variety of hepatotoxic substances, including carbon tetrachloride, ¹⁵ galactosamine, pentobarbitol, 1-chloro-2,4-dinitrobenzene, ⁷ 4-hydroxy-nonenal, ¹⁶ and paracetamol. Diarylhepatonoids including Curcumin is the active constituent of the plant.

Tephrosia 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 poisoning. ¹⁷ The roots, leaves and seeds contain tephrosin, deguelin and quercetin. The hepatotprotective constituent of the drug is still to be proved.

References

1. Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States – Prevalence, costs and patterns of use. *NEJM* 1993;328-246-252.
2. Cupp MJ. Herbal remedies: adverse effects and drug interactions. *Am Fam Physician* 1999; 59: 1239 – 44.
3. PDR for herbal medicines. First edition. Montvale, New Jersey .1998: 1177-1178.
4. De Smet PAGM, Keller K, Hansel R, Chandler RF, eds Adverse effects of herbal drugs. Berlin, Germany: Springer – Verlag, 1997.
5. Samir Malhotra, Amritpal Singh, G.Munjal. Hepatotoxic potential of commonly used herbal products. *Gastroenterology Today* 2001; 5: 110-111.Vol.V No.2.ISSN 0971-8222.
6. Bisset NG, ed. Herbal drugs and phytopharmaceuticals. A handbook for practice on a specific basis. Stuttgart: Medpharm Scientific, 1994: 326-8.
7. Vogel G. Natural substances with effects on the liver. In: Wagner H, Wolff P, eds. *New Natural Products and Plant Drugs with Pharmacological, Biological or Therapeutic Activity*. Heidelberg: Springer-Verlag; 1977.
8. Cordatos E. *Taraxacum officinale*. In: Murray M, Pizzorno J, eds. *A Textbook of Natural Medicine*. Seattle: Bastyr University Press; 1992.
9. H. Kalantari PhD, M. Rastmanesh Pharm D. Protective Property of *Cichorium Intybus* in CCL4 Induced Liver Damage in mice. School of Pharmacy, Ahwaz University of Medical Sciences, Ahwaz, Iran.
10. Sanwa Kagaku Kenkyusha Co. Ltd.: Marmen Pharmaceutical Co. Ltd. - Japanese patent. *Chem Abst.* 102: 32261 b (1985).
11. Zhao, M. Q. et al.: *Acta Pharm. Sin.* IS: 325 (1983).
12. Numazaki, K., et al. Effect of glycyrrhizin in children with liver dysfunction associated with cytomegalovirus infection. *Tohoku J Exp Med.* 1994 Feb; 172(2): 147-53.
13. Chen HC, Chou CK, Kuo YH, Yeh SF. Identification of a protein kinase C (PKC) activator, dephnoretin, that suppresses hepatitis B virus gene expression in human hepatoma cells. *Biochem Pharmacol* 1996; 52:1025-1032.
14. Duke JA (1985) Die amphocholeretische Wirkung der *Fumaria officinalis* .*Z Allg Med* 34:1819.
15. Srinivas L, Shalini VK. DNA damage by smoke: Protection by turmeric and other inhibitors of ROS. *Free Radical Biol Med* 1991; 11:277-283.
16. Selvam R, Subramanian L, Gayathri R, et al. The anti-oxidant activity of turmeric (*Curcuma longa*). *J Ethnopharmacol* 1995; 47:59-67.

17. M.Sree Rama Murthy, M.Srinivasan, R&D Department, TTK Pharma Limited. Hepatoprotective Effect of *Tephrosia pupurea* in experimental animals. Indian Journal of Pharmacology 1993; 25:34-36.
18. Adzet T, Camarasa J, Laguna JC. Hepatoprotective activity of polyphenolic compounds from *Cynara scolymus* against CCl₄ toxicity in isolated rat hepatocytes. Departamento de Farmacognosia y Farmacodinamia, Facultad de Farmacia, Nucleo Universitario de Pedralbes, Barcelona, Spain. J Nat Prod 1987 Jul-Aug; 50(4): 612-7.
19. 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. Department of Chemistry, Bose Institute, 93/1, A.P.C. Road, Calcutta 700009, India. Phytother Res 1999 Sep; 13(6): 508-12.