

A REVIEW ON HEPATO-PROTECTIVE HERBS USED IN AYURVEDA

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ABSTRACT

Liver is considered to be one of the vital organs which helps in maintaining the health of body. *Yakrit* (liver) is being described right from the vedic period. Modern lifestyles can overstress the liver and make it malfunctioning. No significant and safe hepato-protective drugs are available in modern therapeutics. The nature has bestowed some plants with the property to prevent, treat and cure hepatic disturbances with interception of fewer side effects. The focus of this review is to elucidate the importance of liver and aimed at compiling data based on reported works on medicinal plants that have been tested in hepato-toxicity models and proved as hepato-protective. Also the probable mode of action of a few herbs has been discussed in Ayurvedic and modern aspect.

KEY WORDS: Liver, *Yakrit*, Hepato-protective, Medicinal plants.

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INTRODUCTION

"Is your life worth living"? It depends on the liver as it is the largest glandular organ in the body which works all the time to keep the body healthy. The liver is important because a person's nutritional level is not only determined by what he or she eats, but by what the liver processes. The incredible complexity of liver chemistry and its fundamental role in human physiology is so daunting to researchers that the thought that simple plant remedies might have something to offer is astonishing and incredible!

Liver is considered to be one of the most vital organs that functions as a centre of metabolism of nutrients such as carbohydrates, proteins and lipids and excretion of waste metabolites. Additionally, it is also handling the metabolism and excretion of drugs and other xenobiotics from the body thereby providing protection against foreign substances by detoxifying and eliminating them.

In Ayurvedic literature, *yakrit* (liver) is considered as an important *anga* (organ) of the human body right from the vedic period. Bhavamisra (16th Century) has described that it is situated right and below to the *hridaya* (heart) and is the *sthana* (seat) of *pitta* and *sonitha* (blood) (Srikantha Murthy, 2002). Susrutha (500 BC) mentioned *yakrit* (liver) as

the abode of *ranjaka pitta* (Srikantha Murthy, 2004).

Susrutha (500 BC) describes *yakrit* (liver) as the *sthana* (seat) of *rakta* (blood) (Srikantha Murthy, 2005). Charaka (1000 BC) while describing the *srotas* (body channels), mentioned *yakrit* (liver) and *pleeha* (spleen) as the *moola* (root) of *raktavaha Srotas* (blood carrying channels) (Sharma and Dash, 2007). But it is Bhavamisra who for the first time introduced the term '*yakrit vikara*' (liver disorders). Madhavanidana, in *parishista prakarana*, explains *yakrit roga* (liver disease) as a separate entity (Yadunandan Upadhyaya, 2000). The etio-pathogenesis of *Yakrit roga* has been described in Figure 1.

In dealing with problems of the liver, the primary goal is to enhance liver detoxification processes and to help protect against further liver damage. Significant and safe hepato-protective agents are unavailable in modern therapeutics. Therefore, due importance has been given globally to develop plant-based hepato-protective drugs effective against a variety of liver disorders.

The present review is aimed at compiling data based on reported works on promising phytochemicals from medicinal plants that have been tested on hepato-toxicity models.

Figure 1: Etio-pathogenesis of *yakrit roga* (liver disease)

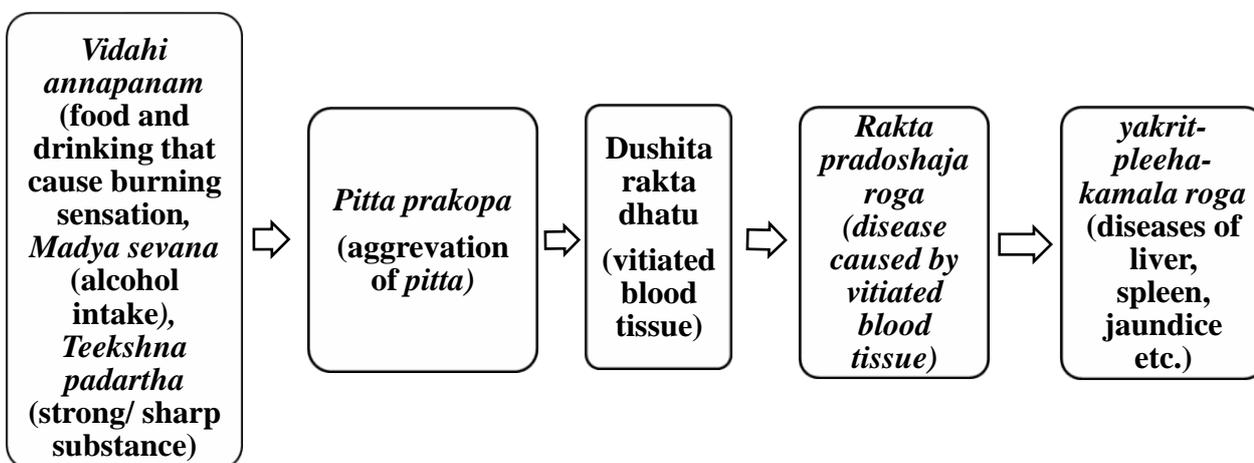


Table 1. showing some hepato-protective herbs with their pharmacological properties (Sharma P.V, 2009)

S.N	Plant	Rasa	Guna	Virya	Vipaka	Dosakarma
1.	<i>Guduchi</i> (<i>Tinospora cordifolia</i> (Willd.) Miers.)	Tikta, Kashaya	Guru, Snigdha	Ushna	Madhura	Tridosahara
2.	<i>Pippali</i> (<i>Piper longum</i> Linn.)	Katu	Laghu, Snigdha, Teekshna	Ushna	Madhura	Tridosahara
3.	<i>Punarnava</i> (<i>Boerhavia diffusa</i> Linn.)	Madhura, Tikta, Kashaya	Laghu, Ruksha	Ushna	Madhura	Tridosahara
4.	<i>Kalamegha</i> (<i>Andrographis paniculata</i> Nees.)	Tikta	Laghu, Ruksha	Ushna	Katu	Kaphapittahara
5.	<i>Bhumyamalaki</i> (<i>Phyllanthus niruri</i> Linn.)	Tikta, Kashaya, Madhura	Laghu, Ruksha	Seeta	Madhura	Kaphapittahara
6.	<i>Daruharidra</i> (<i>Berberis aristata</i> DC.)	Tikta, Kashaya	Laghu, Ruksha	Ushna	Katu	Kaphapittahara
7.	<i>Katuki</i> (<i>Picrorhiza kurroa</i> Royle ex Benth.)	Tikta	Laghu, Ruksha	Seeta	Katu	Kaphapittahara
8.	<i>Rohitaka</i> (<i>Techoma undulata</i> G. Don.)	Katu, Tikta, Kashaya	Laghu, Ruksha	Seeta	Katu	Kaphapittahara
9.	<i>Bhringaraja</i> (<i>Eclipta alba</i> Hassk.)	Tikta, Kashaya	Laghu, Ruksha	Ushna	Katu	Kaphavatahara
10.	<i>Sharapunkha</i> (<i>Tephrosia purpurea</i> Pers.)	Tikta, Kashaya	Laghu, Ruksha, Teekshna	Ushna	Katu	Kaphavatahara

[Rasa (taste) – *Katu* (pungent), *Tikta* (bitter), *Kashaya* (astringent)

Guna (quality) – *Guru* (difficult to digest), *Snigdha* (unctuous) *Laghu* (easily digestible), *Ruksha* (dry), *Teeksha* (sharp)

Virya (potency) – *Seeta* (cold), *Ushna* (hot)

Vipaka (post metabolic effect)

Dosa karma (action on functional entities of the body), *hara* (pacifies)]

Hepatoprotective Drugs

The important herbs used in Ayurveda to treat Liver diseases have been described in Table 1.

Tinospora cordifolia (Willd.) Miers. (*Guduchi*)

Tinospora cordifolia (Willd.) Miers., known as *Guduchi*, *Amrita* is one of the most valuable medicinal herbs of Ayurveda. The

term '*Amrita*' is attributed to this herb in recognition of its ability to impart youthfulness, vitality and longevity to its patron. In modern medicine, it is well known for its hepatoprotective, adaptogenic, immunomodulatory activities and anti-fibrotic activity. The active principle *Tinosporin* corrects immunosuppression associated with deranged hepatic function (Varsha *et al.*, 2011).

Kupffer cells are major determinants of outcome of liver injury. The effect of *Tinospora cordifolia* (Willd.) Miers. was evaluated on Kupffer cell function, using carbon clearance test as a parameter. Antihepatotoxic activity of *Tinospora cordifolia* (Willd.) Miers. was studied in albino rats intoxicated with Carbon tetrachloride (CCl₄). Liver function was assessed based on morphological, biochemical (SGPT, SGOT, Serum alkaline phosphatase, Serum bilirubin) and functional (Pentobarbitone sleep time) tests. A study conducted by Nagarkatti *et al.*, (1994) on *Tinospora cordifolia* (Willd.) Miers. indicates that it had decreased fibrosis in rats, induced by CCl₄ and significantly improved the suppressed Kupffer cell function in another rat model of chronic liver damage induced by heterologous serum. This raises the possibility that anti-fibrotic effect of *Tinospora cordifolia* is mediated through activation of kupffer cells.

***Piper longum* Linn. (Pippali)**

Piper longum Linn. belongs to the family Piperaceae, is a common Indian dietary spice which has been shown to possess a wide range of therapeutic utilities. It has been reported to possess antiasthmatic, antiinflammatory, hepatoprotective, hypocholesteremic and immunomodulatory activities. It contains various alkaloids like piperine, piperlongumine, piperlonguminine, etc. which helps in the regeneration of hepatocytes (Gupta AK, 2003).

A study conducted by Jagruti and Urvi (2009) showed a significant hepatoprotective effect on *Piper longum* Linn. milk extract treatment in CCl₄ induced hepatic damage. An evident decrease in level of serum enzymes, total bilirubin and direct bilirubin was observed. Histo-pathological findings indicated that administration of *Piper longum* Linn. milk extract offered protection to the hepatocytes from damage induced by CCl₄, with mild fatty changes in the hepatic parenchymal cells, which corroborated the changes observed in the hepatic enzymes. It also showed regenerating liver cells around the necrotic area.

***Boerhavia diffusa* Linn. (Punarnava)**

The roots of *Boerhavia diffusa* Linn., commonly known as 'Punarnava', are used by a large number of tribes in India for the treatment of various hepatic disorders and for internal inflammation. Clinical data has also reported effectiveness of *Boerhavia diffusa* Linn. in cases of oedema and ascites resulting from early cirrhosis of the liver and chronic peritonitis (Varsha *et al.*, 2011). The effect of ethanolic extract of roots of *Boerhavia diffusa* Linn. on country made liquor induced hepatotoxicity was studied in albino rats by Agarwal *et al.*(1991). Histo-pathological studies showed marked reduction in fat deposits in animals receiving *Boerhavia diffusa* Linn. along with country made liquor. The plant protected the rats from hepatotoxic action by decreasing the serum alanine amino transferase (ALT), triglycerides, cholesterol and total lipid levels in both serum and tissues.

Punarnava contains alkaloids named as punarnavine and punarnavoside which shows anti-fibrinolytic activity but the hepatoprotective activity has been attributed to ursolic acid. Keppler and co-workers demonstrated that ursolic acid isolated from the leaves showed a dose dependent (5–20 mg/kg) hepatoprotective activity (21–100%) in rats against thioacetamide, galactosamine and carbon tetrachloride induced hepatotoxicity in rats. These hepatotoxins decreased the viability of hepatocytes as assessed by trypan blue exclusion and rate of oxygen uptake tests and decreased the volume of bile as well as the level of its contents. Pretreatment with ursolic acid increased the viability of rat hepatocytes significantly (Keppler *et al.*, 1968).

***Andrographis paniculata* Nees. (Kalamegha)**

Andrographis paniculata Nees. is an ancient Indian medicinal herb, which has been used for centuries in Asia for its effects on various bodily functions and ailments, ranging from degenerative diseases to the common cold. The plant is known as King of Bitters. Andrographolide is an active constituent

extracted and isolated from *Andrographis paniculata* Nees which is very bitter in taste (Anil Kumar *et al.*, 2012).

A study conducted by Visen *et al.* (1993) on andrographolide showed a significant dose dependent protective activity against paracetamol-induced toxicity on *ex vivo* preparation of isolated rat hepatocytes. It significantly increased the percent viability of the hepatocytes as tested by trypan blue exclusion and oxygen uptake tests. It blocked the toxic effects of paracetamol on certain enzymes (GOT, GPT and alkaline phosphatase) in serum as well as in isolated hepatic cells. The bioactive constituent also antagonizes toxic effects of CCl₄ and acetaminophen on certain enzymes (GOT, GPT and alkaline phosphates) in serum as well as in isolated hepatic cells. The results clearly depicted the plant extract to exert a choleric effect that reduces the cholestasis and diminishes retention as well as increase the excretion of toxic xenobiotics from liver. Further, it also stimulated immune system to fight against inflammation, is mediated from the release of cytokinin from immunomodulators (Varsha *et al.*, 2011).

***Phyllanthus niruri* Linn. (Bhumyamalaki)**

Phyllanthus niruri Linn. is a medicinal herb used in connection with secondary hepatitis and other ailments, in ayurvedic medicine for over 2000 years.

It is a proved antiviral drug in Hepatitis-B in human subjects. In the preliminary study, carriers of Hepatitis-B virus were treated with a preparation of the plant 200 mg for 30 days. 22 of the 37(59%) treated patients had lost Hepatitis-B surface antigen, when tested 15–20days after the end of the treatment, compared with only 1 out of 23 (4%) placebo treated controls. It has exhibited an inhibition of DNA polymerase on Hepatitis–B virus which is responsible for the replication of virus (Mehrotra *et al.*, 1991).

In a study, phyllanthin, hypophyllanthin and tricotanol were isolated from petroleum ether extract of *Phyllanthus niruri* Linn. shows

significant results on rat hepatocytes. Preclinical studies demonstrate that an extract of the *Phyllanthus niruri* Linn. plant inhibits endogenous DNA polymerase of hepatitis B virus and binds to the surface antigen of Hepatitis B virus. Extracts of *Phyllanthus niruri* Linn. have been shown to exert hepatoprotective effect against CCl₄ induced HepG2 cell damage in rabbits. Pre-treatment with extract of *Phyllanthus niruri* Linn., reduced paracetamol-induced acute liver damage in rats as monitored by estimating the SGOT. In the *in vitro*-study, it decreased the release of AST and ALT in rat primary cultured hepatocytes being treated with ethanol (Tabassum *et al.*, 2005).

***Berberis aristata* DC. (Daruharidra)**

Berberis asiatica DC. being an important medicinal plant is used extensively for treating variety of ailments like infection of eyes, skin diseases, jaundice and rheumatism (Kirtikar and Basu, 1933). The major alkaloid of this plant is reported to be berberin which possess anti-oxidant property (Brijesh and Khosa, 2010).

The roots of *Berberis aristata* DC. possess more effective hepatoprotective activity against CCl₄ intoxication in rats because of its antioxidant bearing capacity. Acute CCl₄ administration increased serum and liver lipid peroxides significantly. Berberine treatment could reduce these elevated levels. Pathological analysis showed degeneration and necrosis after CCl₄ administration. Berberine treatment could minimize these effects to a certain extent. (Brijesh and Khosa, 2010)

***Picrorhiza kurroa* Royle ex. Benth (Katuki)**

Picrorhiza kurroa Royle ex Benth. is a renowned herb in the Ayurvedic system of medicine and has traditionally been used to treat disorders of the liver, upper respiratory tract, reduce fevers, treat dyspepsia, chronic diarrhoea, and scorpion sting. Kutkin, the active principal of *Picrorhiza kurroa* Royle ex. Benth is comprised of kutkoside and iridoid

glycosides like picosides I, II, and III (Chaturvedi and Singh, 1996).

The hepato-protective action of *Picrorhiza kurroa* Royle ex Benth. may be attributed to its ability to inhibit the generation of oxygen anions and to scavenge free radicals. *Picrorhiza's* antioxidant effect has been shown to be similar to that of superoxide dismutase, metal-ion chelators and xanthine oxidase inhibitors. Animal studies indicate that *Picrorhiza's* constituents exhibit a strong anti-cholestatic activity against a variety of liver-toxic substances, appearing to be even more potent than silymarin (Chander *et al.*, 1992).

Picrorhiza also exhibits a dose-dependent choleric activity, evidenced by an increase in bile salts and acids, and bile flow (Shukla *et al.*, 1991).

***Techoma undulata* G. Don (Rohitaka)**

Techoma undulata G. Don is a tropical coastal shrub that grows up to 1 m in height. It occurs throughout the Indian subcontinent. *Techoma undulata* G. Don leaves were tested against liver damage of albino rats. Loss of membrane structure and integrity because of lipid peroxidation was accompanied with the elevated levels of marker enzymes like SGOT, SGPT and total bilirubin. This shows that the plant has got membrane stabilizing function. *Techoma undulata* G. Don was potentially effective in blunting lipid peroxidation, suggesting that the extract possibly has antioxidant property to reduce ethanol-induced membrane lipid peroxidation and thereby to preserve membrane structure and might be due to the presence of glycosides, flavonoids, proteins, amino acids, tannins, saponins and triterpenoids (Singh D. *et al.*, 2011).

***Eclipta alba* Hassk. (Bhrngaraja)**

Eclipta alba Hassk. known as *Bhringraja*, is a plant belonging to the family Asteraceae. In ayurvedic medicine, the leaf extract is considered a powerful liver tonic. It possesses a wide range of biological activities and is used for the treatment of hepatitis and cirrhosis

(Wagner, H. 1986). A study conducted by Murugaian P *et al.*, 2008 on the whole plant extract of *Eclipta alba* Hassk. exhibited the protective activity against CCl₄ induced liver injury. The plant contains an alkaloid Ecliptine which has got choleric action. The extract augmented the bile flow in rats suggesting a stimulation of liver secretory capacity.

***Tephrosia purpurea* Pers. (Sharapunkha)**

Tephrosia purpurea Pers. known as *Sharapunkha*, forms one of the most effective ingredients of formulations available in Indian market for liver ailments. In the traditional Indian medicine it is famous for its effectiveness in bilious febrile attacks, obstruction of liver and spleen apart. Especially, it has shown good results in cirrhosis and viral hepatitis in clinical trials (human studies). Dried ethanolic extract of *Tephrosia purpurea* Pers. was studied for its efficacy using both acute and chronic models CCl₄ of experimentally induced hepatotoxicity. *In vitro* studies exploiting trypan blue exclusion assay revealed that the alcoholic extract exerted a significant hydroxyl radical scavenging activity (Sree Rama Murthy and Srinivasan, 1993).

Hepato-protective effect of aerial parts was evaluated against CCl₄ induced hepatotoxicity in rats. An oral dose of powdered aerial parts to rats prevented the elevation of SGOT, SGPT, Bilirubin levels caused by CCl₄. The mechanism of hepato-protection by *Tephrosia purpurea* Pers. mainly involves membrane stabilization of liver cells as indicated by decrease in levels of SGOT, SGPT and bilirubin levels, wherein it prevents cellular leakage and loss of functional integrity of the liver cell membranes caused by various hepatotoxic agents. *Tephrosia purpurea* Pers. also leads to increase in hepatic regeneration, which again contributes to its hepatoprotective efficacy (Jain, A. *et al.*, 2006).

DISCUSSION

Yakrit (liver) is the *sthana* (seat) of *pitta dosha* (functional entity of the body), *rakta*

dhatu (blood tissue) and *agni* (power of digestion). Treatment of all liver diseases in Ayurveda concentrates mainly on *pitta dosha* rather than the organ itself. Most of the hepato-protective drugs are *kapha pitta samaka* (pacifies *pitta* & *kapha* entities). The medicines and diets that normalise *pitta* are commonly used for all types of liver diseases.

Most of the hepato-protective herbs are having predominantly *Tikta- Katu rasa* (bitter and pungent taste) and *deepana- pachana karma* (digestive stimulant and carminative). These herbs are mainly *agni vardhaka* (increases fire entity in the body) and act on *jatharagni* (digestive fire) as well as *dhatwagni* (fire residing in tissues). These *rasas* (taste) have the property of increasing metabolism (mainly enhancing catabolism), thereby these herbs help in digestion of nitrogenous waste products collected in body, due to disturbed metabolism. Most of the hepato-protective herbs possess *laghu* (easy to digest) and *ruksha* (dry) *gunas* (quality). *Laghu guna* (easy to digest quality) helps in increasing *jatharagni* (digestive fire) as they are easily digestible and they form less nitrogenous waste products. *Ushna virya* (hot potency) help in enhancing the *Jatharagni* (digestive fire) as well *dhatwagni* because *ushna virya* (hot potency) increases metabolism (catabolism).

According to modern pharmacology, the main mechanism involved in the protection of liver could be associated with the strong capability of hepato-protective drugs to reduce the intracellular levels of reactive oxygen species by enhancing the level of both enzymatic and non-enzymatic antioxidants. These drugs protect liver tissues against oxidative damage and somehow help in stimulating the repair mechanism of liver.

The mode of action of hepato-protective herbs varies from herb to herb. Hepatocyte membrane stabilizing capacity is shown by *Techoma undulata* G. Don., thereby preventing toxins from entering the cell through entero-hepatic recirculation. *Berberis aristata* DC., *Tephrosia purpurea* Pers. and *Piper longum*

Linn. help in regeneration of liver cells by stimulating nuclear polymerase A and increasing ribosomal protein synthesis. *Tinospora cordifolia* (Willd.) Miers. enhance the activity of Kuffer cells which is involved in the production of substances like interleukins and tumour necrosis factors which activate the immune system of the body and act as immuno-modulatory. *Phyllanthus niruri* Linn. possess antiviral property and help in microsomal induction or inhibition. *Boerhavia diffusa* Linn possess antifibrinolytic activity. *Eclipta alba* Hassk., *Andrographis paniculata* Nees. and *Picrorhiza kurroa* Royle ex Benth. increase the choleric activity.

Different single herbs are very much useful in liver disorders as shown by research studies. A few Ayurvedic compound formulations such as *Phalatrikadi kwatha*, *Vasa guduchyadi kashaya*, *Patola katurohinyadi kashaya*, *Guda pippali*, *Arogyavardhini vati*, *Rohitakarista* mentioned in Sharangadhara Samhitha (13th Century) are also found to be promising in hepatopathy.

CONCLUSION

The challenge that modern medical system face with liver disorders is that such drugs would have to be metabolized in the liver. Since the liver itself is in disorder, the problem is how to ensure effective metabolism of the drugs that have been prescribed. In this context, Ayurveda sages have used their genius, to formulate such herbal formulations that can be metabolized even by a sluggish liver. The logic on which such formulations work is that they first heal and reinvigorate the liver and thus contribute to the restoration of its normal functions. Preserving health of the liver means adding healthier years to one's life. Be polite to your liver & Keep it Living and Lively!!

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