PHYTOMEDICINES FOR LIVER DISEASES

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Introduction

Medicinal plants play a key role in human health care. About 80 per cent of the world's population relies on the use of traditional medicines, which is predominantly of plant origin. Although herbal medicines are effective in the treatment of various ailments, very often these drugs are unscientifically exploited or improperly used. Therefore these plant drugs reserve detailed studies in the light of modern medicine. There are more than hundred drugs of known structure that are extracted from higher plants and are used in allopathic medicine.

Liver plays a pivotal role in maintenance of many physiological processes. It is actively involved in many vital functions such as metabolism, secretion and storage. Further more detoxification of a variety of drugs and xenobiotics occurs in liver. Bile secreted by the liver has an important role in digestion. Liver diseases are among the most serious ailments. They may be classified as acute or chronic hepatitis (inflammatory liver diseases), hepatosis (non inflammatory liver diseases) and cirrhosis (degenerative liver disorder resulting in fibrosis of liver).

Liver diseases are mainly caused by toxic chemicals like certain antibiotics (erythromycin, chloramphenicol), chemotherapeutics (paracetamol, anti tubercular drugs), peroxidised oil, aflatoxin, carbon tetrachloride, chlorinated hydrocarbons and excess of alcohol, infections and autoimmune disorders. Most of the hepatotoxic chemicals damage liver mostly by inducing lipid peroxidation and other oxidative damages in liver. In this article the plants that are commonly found in our country and those possess scientifically proven hepatoprotective effect is discussed.

Medicinal plants

Plant drugs are known to play a vital role in the management of liver diseases. There are numerous polyherbal formulations claimed to have hepatoprotective activity. In India more than eighty-seven medicinal plants are used in different combinations in the preparation of thirty-three patented herbal formulations. Most commonly used plants and herbal formulations in liver disorders are given below:

Phyllanthus niruri : Phyllanthus is a herb common to central and southern India. All parts of the plant are employed therapeutically. Phyllanthus primarily contains lignans (e.g., phyllanthine and hypophyllanthine), alkaloids, and bioflavonoids (e.g., quercetin). While it remains unknown as to which of these ingredients has an antiviral effect, research shows that this herb acts primarily on the liver. This action in the liver confirms its historical use as a remedy for jaundice. The plant inhibits the endogenous DNA Polymerase of hepatitis B virus and bind to the surface antigen of the virus.

Emblica officinalis : Traditionally used for enlarged liver and for liver revitalizing. Emblica act as antioxidants and help to support the liver enzymes.

Azadirachta indica: Popularly known as neem. Aqueous extract of the plant contains six flavonol o- glycosides responsible for hepatoprotective activity. The leaf extract prevent inflammatory hepatic damage. The drug could act as a free radical scavenger and reduced the elevated levels of serum enzymes by its membrane stabilizing action in liver diseases.

Curcuma longa: Turmeric is a very important herb in Indian Ayurvedic medicine. The active constituent is known as curcumin. It has been shown to have a wide range of therapeutic effects. It affords protection against free radical damage, as it is a strong antioxidant. Also it reduces

inflammation of hepatocytes by virtue of its ability to reduce histamine levels and possibly by increasing production of natural steroidal hormones by the adrenal glands. Again, it

protects the liver from the degeneration of hepatic cells by a number of toxic compounds. Curcumin has a protective effect on liver tissue exposed to hepatotoxic drugs. It had been traditionally used for the treatment of liver ailments. Consuming alcohol regularly or using the pain killer acetaminophen tends to increase the risk for liver damage; but turmeric may help in minimizing this damage to some extent.

Tinospora cordifolia: Tinospora is a large climbing shrub, used in Ayurvedic medicine. Modern research suggests that this herb may help to modulate the antioxidant and immune system activities. Tinospora may be considered to be a "detoxifying herb" because of its ability to scavenge free radicals and heavy metals and alleviate symptoms of liver toxicity, hepatitis, and liver fibrosis. Its active ingredients include alkaloids and terpene glycosides, such as tinosporine, tinosporide, cordifolide, clerodane furanoditerpene, and diterpenoid furanolactone tinosporidine. The plant has been shown decrease fibrosis of liver and significantly improved hepatic kupffer cell function in chronic liver damage. It increases the phagocytic and intracellular killing capacities of poly morphonuclear cells.

Andrographis paniculata: The diterppenes, andrographolide, andrographoside and neo andrographolide isolated from the plant have anti oxidant effect. Administration of aqueous extract of *A. paniculata* in liver disorders lowered the raised serum enzyme levels and raised the lowered protein concentration. It also plays a role in reducing hepatic tumorogenic condition.

Aegle marmelos: Commonly called Indian bael, the plant is grown throughout the sub continent. The plant contains aegelin, alloimperatorin, imperatorin, marmelide, marmeline, marmelosine and psoralen. In liver damage *A.marmelos* leaf extract induces antioxidant defense system and reduces lipid peroxidation and elevated serum enzyme levels.

Nigella sativa: The plant is commonly known as black cumin. The plant is commonly used in Ayurveda as one of the ingredients of liver tonic formulations and used in the treatment of jaundice.

Holostema adakodien: Commonly called adkodien, is a climbing shrub distributed mainly in tropical Himalaya, Deccan and Kerala. The root is the main medicinal part of the plant. The medicinal properties are attributed to the aminosugars present in the root like amyrin, lupeol and a-sitosterol. It also cantain six amino acids like alanine, aspartic acid, valine, glycine, serine and threonine. The drug prevented the free radical mediated membrane peroxidation. *H. adakodien* has potent antioxidant activity, which may be responsible for hepatoprotective activity also.

Picrorrhiza curroa: Used traditionally in Ayurveda for centuries as a general liver tonic and for liver cleansing, hepatitis, biliousness, fevers and poisoning. In a randomized, double-blind, placebo-controlled trial in patients with acute viral hepatitis, the drug led to rapid fall in serum bilirubin levels toward normal range and quicker clinical recovery with no side effects. Current evidence also indicates Picrorrhiza root protects against

Silybum marianum: Silymarin, derived from the milk thistle plant, *Silybum marianum*, has been used for centuries as a natural remedy for diseases of the liver and biliary tract. . Silymarin and its active constituent, silybin, have been reported to work as antioxidants scavenging free radicals and inhibiting lipid peroxidation. Studies also suggest that they protect against genomic injury, increase hepatocyte protein synthesis and decrease the activity of tumor promoters,

Piper longum: *Piper longum* is a slender aromatic climber with perennial woody roots. The fruits are used for treatment of diseases. Piperine, an active alkaloid constituent, has been shown to exert a significant protection against liver toxicity induced by tert-butyl hydro peroxide and carbon tetrachloride by reducing in both vitro and vivo lipid peroxidation by decreasing the reduction of GSH.

Eclipta alba: Traditionally used as a cholagogue (aids bile secretion) and deobstruent (removes functional obstructions in the body) in hepatic enlargement, for jaundice, and other ailments of the liver and gall bladder. Two coumestans, wedelolactone and demethyl-wedelolactone, were isolated as the main active principles present in trailing Eclipta. Both constituents showed anti-hepatotoxic activity in assays using liver enzyme-induced cytotoxicity in cultured rat hepatocytes. These constituents also showed a significant stimulatory effect on liver cell regeneration. Evidence suggests that trailing

Eclipta exerts its protective action through a reduction in GSH depletion.

***Cichorium intybus*:** Popularly known as Chicory, *Cichorium intybus* possesses liver protective properties. Traditionally used for hepatic conditions and liver rejuvenation and has shown protective effects in mice with high levels of liver damaging enzymes. It stimulates the production of bile and empties the gall bladder, and thus acts as a cholagogue. These actions make it an herb of choice in cases of biliary insufficiency.

Boerhavia diffusa: Traditionally used for hepatic disorders and for internal inflammation.

Conclusion

In spite of immense advances made in the field of allopathic medicine, there is no effective hepatoprotective medicine available for Veterinary use. The above-discussed plants are readily available in our country, have time tested efficacy and margin of safety and is clinically used in various dosage forms for thousands of years. But for acceptance for the use in modern medicine, they need more detailed scientific investigations and clinical trials in optimized situations, regarding their active ingredients, mechanism of action and toxicological profile. Promising works in this regard are occurring in various laboratories in this regard, which will be helpful for the practicing clinicians. Isolation of active phytomoiety will be advantageous for chemical synthesis of active ingredient in its pure form and more active semi-synthetic derivatives. Also since so many farmers are still relying upon the indigenous drugs for treatment of their livestock, it is the need of practicing clinician also, to have a general awareness and knowledge about such plants.

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leaves was also reported to have significant antineoplastic activity. Essential oil as well as butanolic extract were shown to increase the activity of glutathione-S-transferase in hepatic and extrahepatic tissue.

Radio protective activity

Leaf extract of *O. sanctum* protects chromosomes from radiation induced damage. Orientin and Vicenine- two flavonoids obtained from *O. sanctum* leaves also have considerable radioprotective effect and they have a high margin of safety which increases its usefulness as a drug. Free radical scavenging was suggested to be the likely mechanism of protection against the radiation induced cytogenetic damage

Conclusion

The field of medicinal plant research is gaining momentum throughout the world. This area of research in India got a boost when patents were granted to U.S. researchers for our traditional remedies like neem and turmeric. After a prolonged legal battle India forced the U.S. patent trademark office to revoke the patent granted on the use of turmeric for wound healing, but patent granted for neem was upheld.

The use of medicinal plants in the modern medicine suffers from the fact that scientific evidence is lacking in most cases Crude plant extracts have been used in many of these studies and the mechanisms of action have not been investigated thoroughly. Future emphasis should be given to identify and isolate the active principle(s) present in this plant with particular therapeutic action. The molecular mechanism of that action if understood will pave a long way for the rational use of the natural drug(s) present in this plant.

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