A Review on the Herbal Approach of Hepatotoxicity

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ABSTRACT
Liver plays 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 such as certain anti-biotic, chemotherapeutic agents, carbon tetrachloride (CCL₄), thioacetamide, excessive alcohol consumption etc. The available synthetic drugs to treat liver disorders in this condition also cause further damage to the liver. Hence, Herbal drugs have become increasingly popular and their use is widespread. 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.

INTRODUCTION
Liver is the vital organ of metabolism and excretion. Hepatotoxicity is a damage or injury to liver which is caused by various drugs, chemicals and other agents. Extent of liver damage or injury depends on degree of exposure, mild liver damage cause dysfunction but severe liver damage result in liver failure. The liver is largest organ in a body weighing about 1.4-1.6 kg in the males and 1.2-1.4 kg in the females. The liver receives a dual blood supply with about 20% of blood coming from the hepatic artery and 80% from the portal circulation. The blood flow to the liver is around 20 to 25% of the total cardiac output. It serves various vital functions. The most important function of liver is to filter toxic substances from the body, including alcohol and various medications like chemotherapeutic drugs such as antibiotics, acetaminophen etc.

Damaged liver is unable to perform all these functions properly and it may not lead to secrete bile acid which is the primary way that liver dispose of waste products. Hepatic injury is associated with distortion of various metabolic functions. There are various mechanisms behind the toxicity of liver as well as various reasons or causative agents which are responsible for liver injury. Hepatic disorder is one of the major causes of death among the adult population globally. Evidence shows that cell death is involved in liver injury and liver diseases. Apoptosis and necrosis underlie many types of liver injury, including fibrosis, alcoholic liver diseases and hepatitis.

The unique property of liver to metabolize substances and its close relationship with the gastrointestinal tract, make it highly susceptible to injury from drugs and other substances. Approximately 75% of blood reaching the liver arrives directly from gastrointestinal organs and then spleen through portal veins which bring drugs and xenobiotics in concentrated form. Numerous mechanisms may be cited to be responsible for either inducing hepatic injury or worsening the damage process. Although the exact mechanism of hepatic injury remains largely unknown, it appears to involve 2 pathways—direct hepatotoxicity and adverse immune reactions. In most instances, hepatic injury is initiated by the bioactivation of drugs to chemically reactive metabolites, which have the ability to interact with cellular macromolecules such as proteins, lipids, and nucleic acids, leading to protein dysfunction, lipid peroxidation, DNA damage, and oxidative stress.

The liver has more functions than any other human organ. A person's entire blood supply passes through the liver several times a day. The liver has a pivotal role in human metabolism. Liver produces and secretes bile, it also produces prothrombin and fibrinogen, both blood clotting factors, and heparin, a mucopolysaccharide sulfuric acid ester that helps keep blood from clotting within the circulatory system. The liver converts sugar into glycogen.

Liver diseases have become one of the major causes of morbidity and mortality in man and
animals all over globe and hepatotoxicity due to drugs appears to be the most common contributing factor. Plant drugs are known to play a vital role in the management of liver diseases. There are numerous plants and polyherbal formulations claimed to have hepatoprotective activities. In India, more than 87 medicinal plants are used in different combinations in the preparation of 33 patented herbal formulations. Herbal drugs play a major role in the treatment of hepatic disorders. In Indian traditional systems of medicine there are number of medicinal plants and their formulations used to cure hepatic disorders. Some plants which have hepatoprotective activity are turmeric, garlic, solanum nigrum etc.

PRUNUS PERSICA

Biological name: Prunus persica
Common name: Peach
Family: Rosaceae

Prunus persica is growing naturally, it is a medium-sized tree, with spreading branches of quick growth and not long lived. The leaves are lance-shaped, about 4 inches long and 1.5 inch broad, tapering to a sharp point. The Peach is included by Hooker and other botanists in the genus Prunus, its resemblance to the plum being obvious. Others have classed it with the almond as a distinct genus, Amygdalus and others again have considered it sufficiently distinct to constitute it a separate genus, Persica. Prunus persica (Aaru) belongs to the family Rosaceae is a deciduous tree up to 10 metres high. Several constituents have been isolated from the plants of genus Prunus such as triterpenes, phenyl propanoid glucose esters, lignan xyllosides, flavans and proanthocyanidins, flavonols and anthocyanins, flavonoid-5-glucosides and phenolic glucosides. The ethanolic extract of Prunus persica was evaluated against paracetamol induced hepatotoxicity in albino rats. The extract when evaluated at the dose of 100 mg/kg was found to significantly reduced the elevated levels of serum lysosomal enzymes SGOT, SGPT, ALP and Bilirubin when compared with standard drug silymarin.

TURMERIC

Biological name: Curcuma longa
Common name: Haldi
Family: Zingiberaceae

Turmeric is the dried rhizome powder of Curcuma longa. It belongs to the Zingiberaceae family. It is cultivated extensively in Asia (India and China). 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 plant. 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).

GLYCHYRRHIZA GLABRA

Biological name: Glycyrrhiza glabra
Common name: Mulathi
Family:
**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 disease. 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 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 glycyrrhizin.

**ANDROGRAPHIS PANICULATA**

**Biological name:** Andrographis paniculata  
**Common name:** Kalmegh or Kalamegha  
**Family:** Acanthaceae

King of Bitters botanically known as *Andrographis paniculata* 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. It is known as Kalmegh and is used as a bitter ingredient in the Indian indigenous system of medicine. The leaves contain andrographolide, most active component of *Andrographis paniculata* is very bitter in taste. This compound have considerable dose dependent protective activity against paracetamol induced toxicity on isolated rat hepatocytes. Tryptan blue exclusion and oxygen uptake tests clearly indicate an augmented percent viability of the hepatocytes. 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.

**OCIMUM SANCTUM**

**Biological name:** Ocimum sanctum  
**Common name:** Tulsi  
**Family:** Labiatae

*Ocimum sanctum* commonly known as Tulsi in Hindi and Holy Basil in English a popular herb was used for various activities. This herb is found throughout the semitropical and tropical parts of India. It is an Antioxidant, Anticarcinogenic, Antiinflammatory, Antiulcerogenic, wound healing properties. The aqueous extract of *Ocimum sanctum* showed protection against carbon tetrachloride Induced hepatic toxicity in albino rats. The increased levels of Aspartate Transaminase (AST), Alanine Transaminase (ALT), Alkaline Phosphatase (ALP), Lactate Dehydrogenase (LDH) and bilirubin in the infected animals were marked reduced by different doses of *Ocimum sanctum*.

**SOLANUM NIGRUM**

**Biological name:** Solanum nigrum  
**Common name:** Night shade, Wonderberry  
**Family:** Solanaceae

*Fig. 4: Andrographis paniculata*

*Fig. 5: Ocimum sanctum*

*Fig. 6: Solanum nigrum*
The effects of *Solanum nigrum* extract (SNE) was evaluated on thioacetamide (TAA)-induced liver fibrosis in mice. Mice in the three TAA groups were treated daily with distilled water and SNE (0.2 or 1.0 g/kg) via gastrogavage throughout the experimental period. SNE reduced the hepatic hydroxyproline and α-smooth muscle actin protein levels in TAA-treated mice. SNE inhibited TAA-induced collagen (α1)(I), transforming growth factor-β1 (TGF-β1) and mRNA levels in the liver. Histological examination also confirmed that SNE reduced the degree of fibrosis caused by TAA treatment. Oral administration of SNE significantly reduces TAA-induced hepatic fibrosis in mice, probably through the reduction of TGF-β1 secretion.

REFERENCES