Role of herbal plants on hepatoprotective activity

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ABSTRACT
Liver is a vital organ plays an important role in the regulation of physiological process. It involves in the metabolism, secretion, detoxification and digestion. Liver injury or liver dysfunction is a major health problem. Liver injury caused by various toxic chemicals like antibiotics and chemotherapeutic agents. Carbon tetrachloride CCl4, Paracetamol, thioacetamide, excessive alcohol consumption the available synthetic drugs to treat liver disorders in this condition also cause further damage to the liver. Now a day Herbal drugs have become more popular. Herbal medicines have been used in the treatment of liver disease for a long time. A number of herbal preparations are available in the market.

Keywords: Liver injury, paracetamol, CCl4, herbal plants, hepatotoxicity.

INTRODUCTION
The liver is key organ in the body. Liver plays major role in regulation of physiological process, detoxification, metabolism and secretion. And also shows important aspect in the digestion. It is located in the upper abdominal cavity. Liver Functions mainly includes Carbohydrate metabolism, protein metabolism, fat metabolism, immune function and vitamin storage.
Liver disorders

Liver disease is any disturbance of liver function that causes illness. Liver responsible for many functions in the body if it is diseased the loss of those functions may cause significant damage to the body. Liver disease also referred as hepatic disease. Common symptoms for liver disease includes,

- Nausea
- Vomiting
- Jaundice, yellow discoloration of skin [1].

HEPATITIS

Liver cells become inflamed because of infection. The liver inflammation caused by viruses like Hepatitis A, B, and C. Non-infectious also causes by heavy drinking, drugs, allergic reactions. Hepatitis A causes an acute inflammation of the liver. Hepatitis A vaccine can prevent this condition.

Hepatitis B spread by exposure to body fluids. It causes acute inflammation but also progress chronic inflammation it might be leads to cirrhosis, and liver cancer. The hepatitis B vaccine prevents this infection [7].

CIRRHOSIS

Cirrhosis is a complication of many liver diseases characterized by abnormal structure and function of the liver. It involves loss of liver cells and irreversible scaring of the liver. Alcohol, Viral hepatitis B & C are common causes for cirrhosis. The Complications of cirrhosis includes hepato renal syndrome, hepatopulmonary syndrome, and Hepatic encephalopathy.

Symptoms

- Fatigue
- Weakness
- Loss of appetite
- Itching

LIVER CANCER

Liver cancer, also known as hepatic cancer the leading cause of liver cancer is cirrhosis due to hepatitis B hepatitis C and alcohol. Other causes include aflotoxin, non-alcoholic fatty liver disease. The most common types are hepatocellular carcinoma and Cholangiocarcinoma [8-19].

Symptoms: cholangiocarcinoma includes

- Sweating
- Jaundice

Hepatocellular carcinoma includes

- Anemia
- Emesis
- Weight loss, abdominal pain
- jaundice

LIVER FAILURE

Liver failure is defined as the inability of liver to perform its normal synthetic metabolic functions
as physiology. Two forms of liver failure were recognized acute and chronic.

- Acute liver failure defined as the rapid development of hepatocellular dysfunction, mainly coagulopathy and encephalopathy in a patient without known prior liver disease.
- Chronic liver failure usually occurs in the perspective of cirrhosis. The result of many possible causes like excessive intake of alcohol, hepatitis B or C, hereditary and metabolic causes.
- Acute on chronic liver failure is assumed to occur when patient with chronic liver disease improves possibilities of liver failure.

**HAEMOCHROMATOSIS**

Extra buildup of iron in the body causes hemochromatosis. It is the most common form of iron overload disease. Without treatment it can damage organs such as liver, heart, endocrine glands, joints, and pancreas.

- Primary hemochromatosis
- Secondary hemochromatosis
- Neonatal hemochromatosis

**Complications**

- Cirrhosis or scarring of liver tissue
- Diabetes
- Arthritis
- Erectile dysfunction
- Increases the chance of developing liver cancer.

**WILSON DISEASE**

Wilson disease is a rare inherited disorder that prevents the extra accumulation of copper from the body. In large amounts copper is poisonous. Copper built-up in the liver and directly releases into blood stream it can cause damage to brain, kidney, and eyes.

Wilson disease existing at birth but symptoms generally started between ages 5-35. It first assaults liver or central nervous system or both.

**HEPATOTOXICITY**

Liver injury or damage can caused by the drug or chemical or any other agents. Symptoms of liver damage can depend on the exposure to toxic substances. Severe damage can ultimately result in the liver failure. Drug induced liver injury is responsible for 5% of all hospital cases and 50% of acute liver failure conditions.

**EVALUATION OF HEPATOPROTECTIVE ACTIVITY**

Most of the chemical substances or drug shows specific actions on liver. Which are known as hepatotoxins mostly used in experimental animals to simulate diseased conditions the protective effect measured by estimation of enzyme activities and the rate of endurance can be tested histologically. Available methods are in vivo, in vitro and ex vivo methods. All these methods are used to study the curative effect of any compound under test.

**In vivo methods**

This method used to study the mechanism of the toxicant. Hepatotoxicity produced in experimental animals by the administration of hepatotoxins like acetaminophen, thioacetamide, CCl₄, galactosamine, ethanol etc. which produce measurable effects, it can be measured by various liver function tests, Metabolic, biochemical and histological determinations.

**In vitro methods**

Hepatocytes are commonly isolated by using in-situ, two step recirculating collagenase perfusion technique. These are in small containers and exposed to samples and toxins after some time the rate of toxicity or protection assessed by viability tests and enzymatic levels such as SGOT, SGPT. Obtain By primary culture hepatocytes using hepatotoxins.

**Ex vivo methods**

In this method after the conclusion of preselected in vivo test protocol hepatocytes are isolated and the percentage of possible cells and biochemical parameters are determined as liver function tests. These models are well correlated to clinical models than in vitro or in vivo methods.

**EXPERIMENTAL MODELS OF HEPATOTOXICITY**

Several chemical substances which induce liposis, necrosis, cirrhosis, hepatobiliary...
Dysfunctions in experimental animals are classified as hepatotoxins. Some experimental models are explained by employing some of the important hepatotoxins.

**Paracetamol model**

Paracetamol induces acute hepatotoxicity. Paracetamol (800mg/kg) induces centrilobular necrosis without steatosis. Paracetamol at single dose of 3gms/kg p.o stimulates acute hepatic damage which induces toxicity within 48hrs.

**Thioacetamide model**

Thioacetamide (100mg/kg s.c) after 48hrs of administration induces hepatic damage. By the administration it causes sinusoidal congestion and hydropic swelling with increased mitosis.

**Chloroform model**

Chloroform inhalation or subcutaneous administration (0.4 - 1.5ml/kg) induces hepatotoxicity with extensive central necrosis, hepatic cell degeneration and necrosis fatty metamorphosis.

**Ethanol model**

A single dose of ethanol (1ml/kg) induces fatty degeneration. Administration of 40%v/v ethanol (2ml/100g/day p.o) for 21 days induces fatty liver. By the administration of country made liquor (3ml/100g/day) 21 days causes liposis.

**CCL4 model**

Administration of CCL4 (1ml/kg s.c) weekly twice for 8 weeks induce chronic, reversible liver damage weekly twice for 12 weeks causes chronic irreversible liver damage.

**D-galactosamine model**

D-galactosamine (800mg/kg i.p) after administration of 48hrs induces hepatotoxicity with diffused necrosis and steatosis.

**Role of herbal plants in hepatotoxicity**

Herbal drugs are safe and have potential to cure such diseases, so they developed most popular in recent years. In Ayurveda plant materials have been used to protect liver injury by various chemicals and dietary agents. Various plants and polyherbal formulations have hepatoprotective activity. So many medicinal plants, present in different parts of India have been mentioned as hepatoprotective drugs these are extensively used to treat the liver disorders. A large number of plants and formulations have hepatoprotective activity. In India more than 87 plants are used in 33 patented and proprietary multi ingredient plant formulations. The importance has been given globally to develop plant-based hepatoprotective drugs effective against a variety of liver disorders. The herbal drugs are believed to be harmless and free from serious adverse reactions obtained from nature and are easily available.

**HEPATOPROTECTIVE ACTIVITY OF MEDICINAL PLANTS**

Alcoholic extract of the fruits of coccinia grandis linn (Cucurbitaceae) was evaluated in CCL4 induced hepatotoxicity in rats. A dose level of alcoholic extract 250mg/kg. The levels of ALT, AST, ALP, total proteins, total and direct bilirubin was evaluated. The alcoholic extract significantly (p<0.05) decreased the activities of serum enzymes comparable to that the standard drug silymarin revealing its hepato-protective effect.

Protective effect of ethanol extract of sargassum polycystum was evaluated in D-galactosamine induced hepatitis in rats. Prior oral administration of S. polycystum extract (125mg/kg) body weight/day for 15 days. Significantly attenuated (p<0.05) the D-galactosamine induced increases in the levels of biochemical markers AST, ALT, and ALP in plasma of rats. It has also demonstrated antioxidant activity against D galactosamine-induced hepatitis by inhibiting the activation of lipid peroxidation. The ant hepatotoxic potential of S. polycystum might possibly due to its antioxidant property and membrane stabilizing action (Meena et al. 2008) the hepatoprotective activity of dushivishari agada in acute experimental liver injury induced by paracetamol in wistar albino rats. The hepatoprotective activity of dushivishariagada was also substained by significant decrease in levels of the biochemical parameters Evaluation of Dushivishari agada for inducing paracetamol 1g/kg. The extract human dose 1.08g/kg and 2.16 g/kg extract treatment on ponderal changes and biochemical parameters compared with the standard drug silymarin 50mg/kg. A level of (p<0.05) was considered as statistically significant & the value of (p<0.01) or (p<0.001) highly significant. Serum biochemical parameter indicated
reversal of important parameters like SGOT, SGPT, ALP, total and direct bilirubin in both test & reference standard. It shows presence of good anti-hepatotoxic effect. The trial drug dushivishariagada can be used as anti-hepatotoxic drug.

**Cyperus articulatus Linn**

The present study evaluated the hepatoprotective activity of the methanol extract of Cyperus articulatus Linn. (MECA) against paracetamol induced liver damage in rats. Hepatotoxicity was induced in Wister rats by oral administration of paracetamol (640mg/kg suspended in 1% Carboxy methyl cellulose), during 16 days treatment period. MECA was administered orally at the doses of 200 & 400 mg/kg for 16 days. Silymarin 25mg/kg was used as standard drug. Hepatoprotective activity was evaluated by the biochemical estimation of liver function parameters (SGPT, SGOT, ALP, total protein & total bilirubin) and histological study of liver tissue. P-Values of <0.001 were considered as statistically significant. The result show that Cyperus articulatus possesses hepatoprotective activity against paracetamol induced hepatotoxicity in rats.

**Curcumin**

Curcuma longa contains curcumin as major constituent. In this study a phytosome curcumin formulation and evaluated the hepatoprotective effect of phytosome curcumin on paracetamol induced liver damage in mice. Curcumin 100 and 200mg/kg were given gastrically and toxicity was induced by paracetamol 500mg/kg for 7 days. Animals were sacrificed on the final day and estimate the liver function markers. Hepatic antioxidants and lipid peroxidation in liver homogenates were estimated. P values p < 0.05 statistically significant. The hepatoprotective effect of phytosome curcumin may be explained by increasing levels of antioxidant enzymes and decreasing the lipid peroxidation and liver enzyme on paracetamol-induced damage in mice.

**Prunus armeniaca L. (Apricot) font color**

Evaluate the hepatoprotective effect of Prunus armeniaca L. (Apricot) font color leaf on paracetamol induced liver toxicity in rats. After induction of liver toxicity, the biochemical parameters such as serum glutamic pyruvic transaminase SGPT, SGOT, ALP, ALT, lactate dehydrogenase, total protein, albumin. The physical parameters including liver weight, body weight and histopathological changes in the liver were studied. Administration of paracetamol (3g/kg p.o) Methanol extract 200mg/kg, p.o the results of all the extracts including the standard drug are compared with the result produced by normal group, and it is considered as significant as p<0.05.

**Solanum nigrum Linn**

The present study of Solanum nigrum Linn ethanol extract investigated the hepatoprotective activity. Against carbon tetra chloride induced hepatic damage. CCl$_4$ 1.25ml/kg administered p.o, and ethanol extract 250mg/kg. The activity evaluated by using biochemical parameters such as ALP, ALT, AST. Histopathological observation demonstrates the protective role of the extract against liver damage. It proves the ethanol extract of dried fruits of S. nigrum has been remarkable activity effect in ccl4 induced liver damage.

**Cleome viscosa Linn**

Evaluate the hepatoprotective activity of ethanolic extract of Cleome viscosa Linn. Against carbon tetra chloride induced liver toxicity in experimental animals. Liver damage produced by inducing (2ml/kg b.w.) silymarin (50mg/kg b.w.) given orally which is used as standard drug. After administration of CCl$_4$ ethanolic extract used for the treatment 100mg/kg & 200mg/kg. Estimate the biochemical parameters. Treatment with ethanolic extract at dose of 100mg/kg decreased the SGOT, SGPT, ALP and Bilirubin. While using higher dose 200mg/kg it shows more effective. Results the ethanolic extract of Cleome viscosa has significant hepatoprotective activity.

**Pterocarpus Santalinus**

Evaluate the hepatoprotective activity of aqueous & ethanol stem bark extract of Pterocarpus santalinus using carbon tetrachloride induced liver damage in experimental animals. Aqueous 45mg/ml and ethanol 30mg/ml 1% gum tragacanth administered orally for 14days. Silymarin used as standard drug. The ethanol and aqueous extracts treated animals there was a decrease in serum levels of biomarkers and significant increase in total protein, indicating the recovery of hepatic cells. Ethanolic stem bark extract of Pterocarpus
Santalinus significant protection against CCl₄ induced hepatocellular injury.

**Trianthema decandra**

Present study designed the hepatoprotective of aqueous extract of Trianthema decandra roots against carbon tetrachloride induced liver damage. CCl₄ induced by intraperitoneal administration once daily for 7 days. Estimate the parameters. The aqueous extract 50mg/kg 100mg/kg and 200mg/kg orally administered to the animals and its effects on biochemical parameters were compared with silymarin 25mg/kg treated animals. Plant extract shows significant increase in the serum protein & albumin compared with CCl₄. Trianthema extract protects the liver when CCl₄ induced liver damage.

**Wedelia Calendulaceae L**

Hepatoprotective activity of ethanolic extract of Wedelia Calendulaceae L. studied against CCl₄ induced acute liver toxicity in rats. CCl₄ 0.2ml/100gms given orally which induce toxicity and treated with EEWC 25mg/g, 50mg/g daily dose for 10 days silymarin 2.5mg/100g used as standard drug. It possesses significant effect on CCl₄ induced toxicity. Decrease in the levels of AST, ALT and ALP with significant increase in protein after treatment with EEWC shows the effectiveness of the extract against CCl₄ induced hepatotoxicity.

**CONCLUSION**

Numerous formulations and traditional medicines are used to treat liver diseases. Plant drugs for liver diseases retain more efficacy to cure severe liver disorders caused by toxic chemicals, viruses, more intake of alcohol, and repeated administration of drugs like paracetamol, isoniazid. The hepatoprotective activity of plant possibly contains the presence of alkaloids, flavonoids, terpenoids, steroids and glycosides extracts of plants may demonstrates very active drugs. Herbal plants shows more protective effect maintains with proper pharmacological experiments and clinical trials. The extracts should be governed by standards of safety and efficacy.

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