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Hepatoprotective Activity of Ethanolic Extract of Leaves of Piper Cubeba

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Abstract

Liver being vulnerable to exogenous substances makes disease associated with it a matter of worldwide concern. Several research thus focus on hepatoprotection, Preventive and therapeutic activity of plants as a hepatoprotective agent is a topic of interest for researchers. Hepatotoxic agents like carbon tetrachloride, paracetamol, isoniazid etc. increase the serum biomarkers of liver where ALT is more specific than AST in detecting liver injury. Drug-induced liver injury (DILI) wherein more than 900 drugs have been implicated in causing liver injury. Plant phenolics include simple phenols, phenolic acids, coumarins, lignans, flavonoids, diaryl-alkanoids, stilbenoids, proanthocyanins, tannins, and anthocyanins some alkaloids. The greater the content of alkaloids, flavonoids, and saponins in an extract, the higher the hepatoprotective activity possessed by the extract. This paper reveals hepatoprotective activity of ethanolic extract of leaves of Piper cubeba.

Keywords: Piper cubeba, liver toxins, hepatoprotective, ethanolc extract, phtyoconstituents.

Introduction:

Liver is the major site of xenobiotic metabolism in any vertebrate living system. Therefore, injury to liver caused by toxic chemicals, drugs and virus infiltration from ingestion or infection may be harmful and can lead to various complications. Alcoholic liver disease (ALD) is one of the most serious consequences of chronic alcohol abuse. Liver cirrhosis, the culmination of the illness, is one of the leading causes of death in western countries. The present study was aimed to investigate the hepatoprotective activity of leaves of Piper cubeba in CCl4 induced hepatic model in rats.**1-2**

Materials and Method

Plant materials

Piper cubeba was obtained from rural areas of Alwar, Rajasthan. The plants were previously identified and authenticated by experts in the

Animals

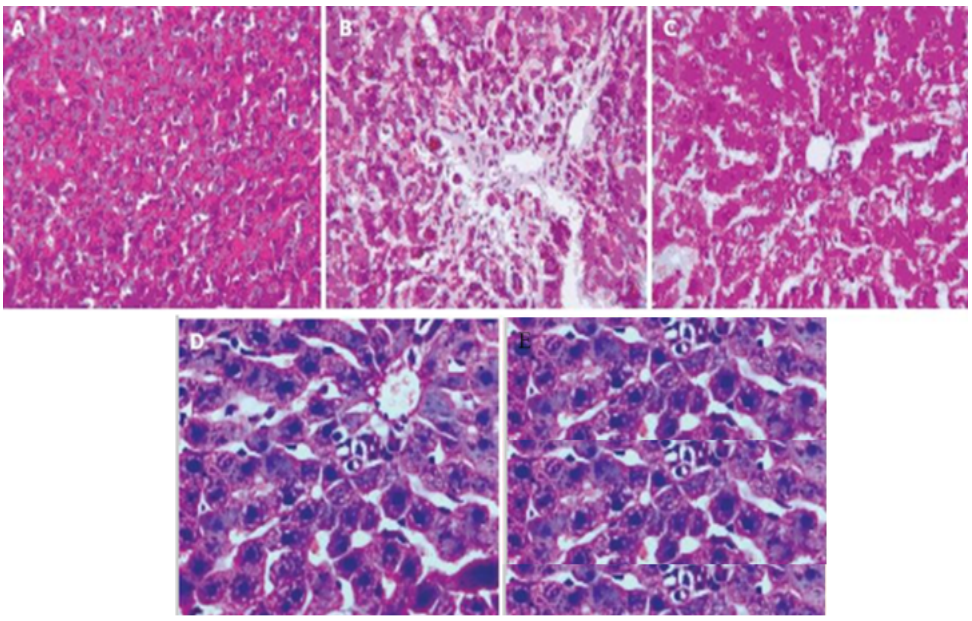
Male Wister rats weighing 175-200 g were obtained from the animal house of Lords International College of Pharmacy and housed in polycarbonate cages. The rats had free access to standard pellet chow and water *ad libitum* throughout the experiment with the exception of some experiments in which the animals were deprived of food, but not water, for 18-24 h before the experiments were performed. After procurement, all the animals were divided into different groups and were left for one week for acclimatization to experimentation room and were maintained on standard conditions (23°C, 60%-70% relative humidity and 12 h photo period). There were six animals in each group for observational screening and acute toxicity studies. All experimental protocols described below were approved by the ethical board.

CCl4 is one of the most powerful hepatotoxin in terms of severity of injury. It causes toxic necrosis leading to biochemical changes having clinical features similar to those of acute viral hepatitis. Liver injury was produced by administration of CCl4 mixed with liquid paraffin. Animals were given single doses of CCl4 100 µL/kg p.o. per day through out the experimental setup. Control animals received an equal volume of liquid paraffin.**3-4**

In vivo:

Detailed evaluation of extracts of *P.cubeba*for hepatoprotective activity was carried out against CCl_4. The animals were divided into five groups of six animals each. Group 1 served as vehicle control and was administered with normal saline. Group 2 rats were given CCl_4 1.0 mL/kg, *p.o* checking the biochemical parameters periodically for hepatotoxicity. Group 3 rats were given CCl_4 + extracts of *P.cubeba* 250mg/kg, *p.o*. Group 4 rats were given CCl_4 + *P.cubeba* extracts of 500mg/kg, *p.o*. Group 5 rats were given CCl_4 + Silymarin 50 g/kg, *p.o*. Blood was collected from the orbital sinus in all animals 2 h after last treatment and serum separated for different estimations. The rats were anesthetized and sacrificed after the experimental period by cervical decapitation. The liver tissue was examined histopathologically.

Liver section of control rat showed normal hepatocytes and normal architecture. Liver sections from CCl4 treated rats demonstrated the destruction of architectural pattern, nodule formation in the lobular zone, inflamed periportal zone, and moderate inflammation of portal area. Liver sections from Silymarin treated rats showed regeneration of normal hepatocytes. *P. cubeba*treated rat showed normal lobular architecture, and no necrosis or fatty changes or inflammatory reaction were seen. These histopathological findings demonstrate a hepatoprotective effect of the extracts against CCl4-mediated liver damage.



Photograph of rat liver shows.

A: Liver of a control rat showing normal hepatocytes and normal architecture;

B: Liver section from a CCl4 treated rat demonstrating the destruction of architectural pattern, nodule formation in the lobular zone, inflamed periportal zone, moderate inflammation of portal area;

C: Liver section from a Silymarin treated rat showing regeneration of normal hepatocytes;

D: Liver section from a *P. cubeba*250mg/ kgtreated rat showing normal lobular architecture;

E: Liver section from a *P. cubeba*500mg/kgtreated rat showing normal lobular architecture no necrosis or fatty changes or any inflammatory reaction can be seen.

Results and Discussion

The purpose of this study was to explore the hepato-protective effect of *P. cubeba*extracts in the hepatic damage caused by CCl4. Administration of CCl4 to normal rats increased serum levels of AST, ALT, ALP, and bilirubin. The enzymes leaking out from damaged liver cells into circulating blood represent the damage to hepatic cells.

It is well established that the toxic metabolite of CCl4, a free radical CCl3 is responsible for damage to liver cells. *P. cubeba*extract caused statistically significant decrease in all the above parameters at the dose of 250mg/kg and 500mg/kg given orally to CCl4 treated rats. Histopathological examination of the liver sections of rats treated with CCl4 showed destruction of architectural pattern, nodule formation in the lobular zone, inflamed periportal zone, moderate inflammation of portal area.The group of rats treated with an extract of *P. cubeba*showed normal lobular architecture.

The group of rats treated with *P. cubeba*showed normal lobular architecture and no necrosis or fatty changes or inflammatory reaction. This suggests the reparative quality and maintenance of structural integrity of hepatocytic cell membrane of damaged liver cells by the extracts. The group of rats treated with Silymarin showing regeneration of normal hepatocytes was taken as standard.

The ability of *P. cubeba*to reduce the injurious effect or to preserve normal hepatic function disturbed by the hepatotoxin CCl4 is the index of its hepatoprotective effect.

These findings show the prophylactic and curative efficacy of *P. cubeba*in maintaining the integrity and functional status of hepatocytes.

In conclusion, the data presented here indicate that the extracts of *P. cubeba*are hepatoprotective both in CCl4 treated male rats and in CCl4 treated cultured primary rat hepatocytes. In addition, the in vivo studies carried out using the extracts also proved to be highly efficient in terms of dosage, tolerability, and restoring the liver. We now intend to look at the mechanism by which these extracts maintain the integrity of the liver.

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