

HEPATOPROTECTIVE ACTIVITY OF *ELETTARIA CARDAMOMUM* AGAINST PARACETAMOL INDUCED HEPATOTOXICITY

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ABSTRACT

Aim of study: To evaluate the hepatoprotective activity of fruits of *Elettaria cardamomum* extract against Paracetamol induced hepatotoxicity.

Materials and methods: Methanolic extract at doses of 100, 200 and 400 mg/kg were administered orally once daily for 7 days. The hepatoprotective activity was assessed using various biochemical parameters like alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and total bilirubin, along with histopathological studies of liver.

Result: *Elettaria cardamomum* exhibited significant hepatoprotective activity by reversing bio-chemical changes induced by paracetamol. Histology of the liver sections of the animals treated with the extracts showed the presence of almost normal hepatocytes, absence of necrosis and fatty infiltration, which further evidenced the hepatoprotective activity.

Conclusion: Methanolic extract of fruits of *Elettaria cardamomum* has liver protective effect against paracetamol induced hepatotoxicity. Further studies are needed to isolate and characterize the active principles and to find out the mechanism responsible for its hepatoprotective activity.

Keywords: Antihepatotoxic, Paracetamol, *Elettaria cardamomum*, Liver injury.

INTRODUCTION

Liver is one of the largest organs in human body and the chief site for intense metabolism and excretion. So it has a surprising role in the maintenance, performance and regulating homeostasis of the body¹. The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamins. Thus, to maintain a healthy liver is a crucial factor for overall health and well being. But it is continuously and variedly exposed to environmental toxins, prescribed and over-the-counter drugs which can eventually lead to various liver ailments like hepatitis, cirrhosis and alcoholic liver disease². Thus liver diseases are some of the fatal disease in the world today. They pose a serious challenge to international public health. Modern medicines have little to offer for alleviation of hepatic diseases and it is chiefly the plant based preparations which are employed for the treatment of liver disorders. But there is not much drug available for the treatment of liver disorders³. In absence of a reliable liver protective drug in the modern system of medicine, a number of medicinal preparations in Ayurveda, the Indian system of medicine, are recommended for the treatment of liver disorders. Natural remedies from medicinal plants are considered to be effective and safe alternative treatments for hepatotoxicity⁴. In view of this, the present study is undertaken to investigate the hepatoprotective activity of *Elettaria cardamomum* fruits against paracetamol induced hepatotoxicity in rats.

MATERIALS AND METHODS

Plant material and extraction

The dried fruits of *Elettaria cardamomum* were purchased from the local markets of Kerala in the month of June 2010. The fruits were identified and authenticated by Dr. Jomy Augustine, Head of the Department of Botany, St. Thomas College, Pala, Kerala. After cleaning of adulterant material, the fruits were ground with an electric grinder into a coarse powder. About 500 g of ground material was soaked in methanol (70%) at room temperature (23–25 °C) for 3 days with occasional shaking. It was filtered through a muslin cloth and then through a Whatman qualitative grade 1 filter paper. This procedure

was repeated twice and the combined filtrates were evaporated on rotary evaporator under reduced pressure (–760 mmHg) to a thick, semi-solid pasty mass of dark brown color; i.e. the crude extract yielding approximately 4.9%.

Experimental animals

Albino Wistar rats of either sex (150-200 g) were obtained from the laboratory of NGSIM Institute of Pharmaceutical Sciences, Deralakatte, Mangalore. Four animals were housed in a cage in a climate-controlled room under standard conditions with 12:12 hour's light/dark cycles and free access to water and food. Animals were brought in to the laboratory for at least a week before experimental testing commenced. Each experimental group of rats were randomly chosen and used only once. All the experiments were performed within the guidelines of the institutional animal ethical committee of KSHEMA, Deralakatte, Mangalore (KSHEMA/AEC/40/2010).

Hepatoprotective Activity

Animals were divided into six groups of 6 animals each. The first group received saline 1 ml/kg for one week (control). The group II received saline 1 ml/kg for one week (positive control). The group III received silymarin (25 mg/kg p.o.). The group IV, V and VI received 100, 200 and 400 mg/kg of extract respectively once a day for seven days. On the fifth day, after the administration of the respective treatments, all the animals of groups II, III, IV, V and VI were administered with paracetamol 2 g/kg orally. On the seventh day after 2 h of respective treatments, the blood samples were collected from all groups of rats by puncturing the retro-orbital plexus. Serum was separated by centrifugation at 2500 rpm at 37°C for 15 min and analyzed for various biochemical parameters. Liver was dissected out and used for histopathological studies⁵.

Assessment of liver functions

Biochemical parameters, such as Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP) and Total bilirubin (TBIL) were estimated using the assay kit (AGAPPE Diagnostics Ltd, Ernakulam, Kerala).

Histopathology

The liver tissue was dissected out and fixed in 10% formalin solution, dehydrated in ethanol (50–100%) cleared in xylene and embedded in paraffin wax. 5–6mm thick sections were prepared and then stained with hematoxylin and eosin dye for photomicroscopic observation.

Statistical Analysis

The data were expressed as mean ± S.E.M. Statistical differences at P < 0.05 between the groups were analyzed by one-way ANOVA followed by Dunnett's multiple comparison test using SPSS 15.0 software.

RESULTS

The methanolic extract of fruits of *Elettaria cardamomum* was found to be nontoxic when administered orally to rats and its LD₅₀ value was found to be safe up to 2 g/kg body wt.

Serum parameters determination

Administration of paracetamol to rats caused significant liver damage, as evidenced by the altered serum biochemical parameters. Pretreatment of rats with methanolic extract of *Elettaria cardamomum* exhibited marked protection against paracetamol induced hepatotoxicity, (shown in Table 1). The effects produced by methanolic extract of *Elettaria cardamomum* were comparable with that produced by the standard, silymarin.

Table 1: Effect of methanolic extracts of fruits of *Elettaria cardamomum* on paracetamol induced hepatotoxicity in rats.

Group No.	Groups (n=6)	ALT (IU/L)	AST (IU/L)	ALP (IU/L)	Total Bilirubin (mg/dL)
I	Control	89.0±1.15	110.2±1.35	142.0±2.01	0.74±0.02
II	Pcml Treated	288.3±1.47 ^a	383.8±3.38 ^a	389.7±2.49 ^a	2.23±0.02 ^a
III	Pcml + Silymarin (25 mg/kg body wt.)	97.83±1.66 ^b	123.8±2.71 ^b	152.3±2.12 ^b	0.85±0.02 ^b
IV	Pcml + MEC (100 mg/kg body wt.)	195.2±1.13	285.2±1.30	294.8±1.27	1.74±0.01
V	Pcml + MEC (200 mg/kg body wt.)	134.5±1.12 ^b	182.5±0.76 ^b	194.0±1.18 ^b	1.15±0.01 ^b
VI	Pcml + MEC (400 mg/kg body wt.)	112.8±2.97 ^b	162.0±1.15 ^b	169.0±1.75 ^b	0.88±0.01 ^b

Values are expressed as mean ± SEM, n=6 rats in each group

a - significant (p<0.05) compared to control, b - significant (p<0.05) compared to Pcml

Histopathological studies under light microscopy

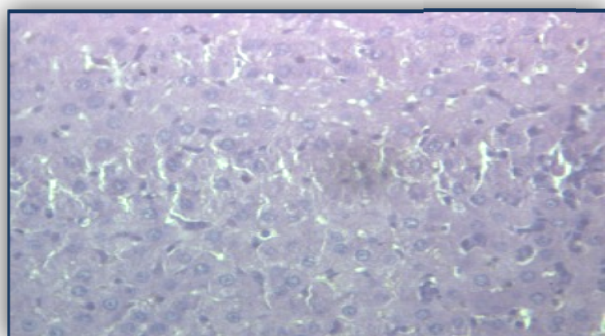


Fig. 1: Liver tissue: Control Group

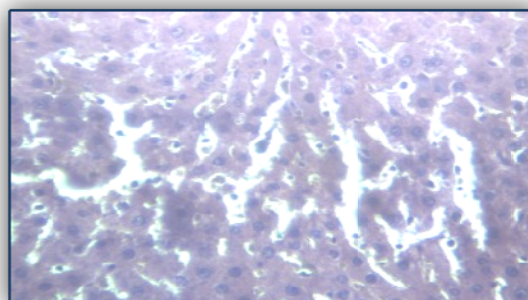


Fig. 2: Liver tissue: Paracetamol Treated Group

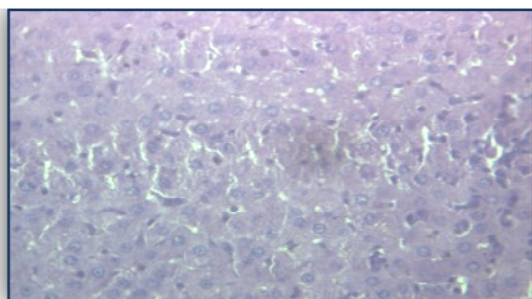


Fig. 3: Liver tissue: Silymarin Treated

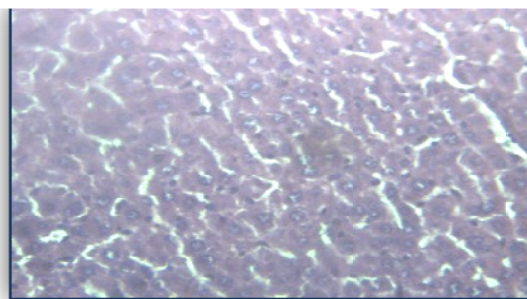


Fig. 4: Liver tissue: (100mg/kg extract) Group Treated Group

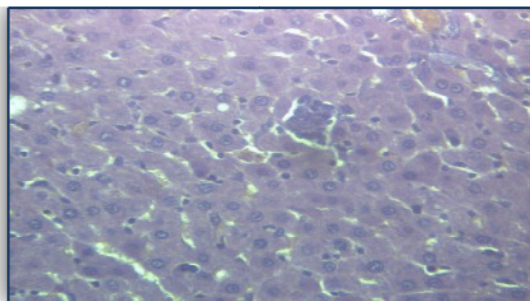


Fig. 5: Liver tissue: (200mg/kg extract) Treated Group

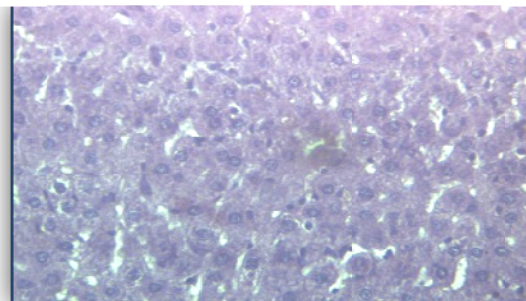


Fig. 6: Liver tissue: (400mg/kg extract) Treated Group

DISCUSSION AND CONCLUSION

The present study was undertaken to determine the hepatoprotective activity of methanolic extract of fruits of *Elettaria cardamomum*. The methanolic extract did not show any sign and symptoms of toxicity and mortality up to 2000 mg/kg dose.

Administration of paracetamol elevated the serum levels of ALT, AST, ALP and Total Bilirubin significantly. This is due to its bioactivation to a toxic electrophile, N-acetyl-p-benzoquinone-imine. Pretreatment with methanolic extract of fruits of *Elettaria cardamomum* was able to prevent the elevation of ALT, AST, ALP and Total Bilirubin by paracetamol. These biochemical effects may be due to the inhibitory effects on cytochrome P450 and/or promotion of its glucuronidation^{6,7}. These biochemical findings were further substantiated by histopathological studies.

Paracetamol is normally eliminated mainly as sulfate and glucuronide. Only 5% of the paracetamol is converted into N-acetyl-p-benzoquinoneimine. However, upon administration of toxic doses of paracetamol, the sulfation and glucuronidation routes become saturated and hence, higher percentage of paracetamol molecules are oxidized to highly reactive N-acetyl-p-benzoquinoneimine (NAPQI) by cytochrome-450 enzymes. A semiquinone radical, obtained by one electron reduction of NAPQI, can covalently binds to macromolecules of cellular membrane and increases the lipid peroxidation resulting in the tissue damage⁸.

With aid of enzyme levels and histopathological studies of rat liver we can conclude that methanolic extract of fruits of *Elettaria cardamomum* have hepatoprotective activity against Paracetamol induced liver damage. Further studies are needed to isolate and characterize the active principles and to find out the mechanism responsible for its hepatoprotective activity.

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