HEPATOPROTective EFFECT OF Ipomoea pes-caprae LEAVES EXTRACT IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Abstract
The aim of the present study was to investigate the hepatoprotective effect of Ipomoea pes-caprae leaves extract in streptozotocin induced diabetic rats. Diabetes was induced in male albino Wistar rats by a single intraperitoneal injection of streptozotocin (50 mg/kg body weight). Ethanol extract of Ipomoea pes-caprae was administered orally (300 mg/kg body weight) for 45 days. Glibenclamide was used as a standard drug. The levels of blood glucose, ALP, AST and ALT, were increased significantly in diabetic rats. The Ipomoea pes-caprae extract treated diabetic rats showed marked restoration in the activity of ALP, AST and ALT when compared with normal rats. Present results clearly indicate the Ip. pes-caprae has a potent efficacy for hepatoprotective effect in streptozotocin induced diabetic rats.

Keywords: Ipomoea pes-caprae, streptozotocin, ALT, AST, ALP.

Introduction
Diabetes mellitus (DM), is characterized by hyperglycemia and carbohydrate, protein and fat metabolism disturbances, is a wide spread metabolic disease (1). Diabetes mellitus is caused by inherited (or) acquired deficiency in insulin secretion and by decreased responsiveness of the organs to secrete insulin (2). The number of adults affected by diabetes in the world is expected to increase from 135 million in 1995 to 300 million in the year of 2025 (3). Elevated glucose causes oxidative stress as a result of increased production of mitochondrial reactive oxygen species (ROS), non-enzymic glycation of proteins and glucose autoxidation (4). In diabetes, glycosylation of hemoglobin and lipid peroxidation are important process in the development and progression of complications of diabetes (5). Liver has an important role in metabolism (6) and also maintains the glucose level in the body by store the glucose as glycogen. More oxidative stress affects the liver cells. Hence the activity of liver is impaired and therefore it is very important that the drug should have the protective effect on liver to maintain the normal metabolic activity.

Untreated diabetes mellitus leads to several complications like retinopathy neuropathy, hepatopathy, atherosclerosis, nephropathy and aging (7). Recent antihyperglycemic agents are having significant side effects (8) and many traditional plants reduce hyperglycemia and have no side effect (9). Hence recently appropriate hypoglycemic agents have been focused in traditional medicine, because some natural products in traditional medicine may be better treatments than currently used drugs (10). However, the compounds and precise antidiabetic mechanisms of most herbs remain to be indistinct.

Ipomoea pes-caprae, also known as beach morning glory or goat's foot, is a common pan-tropical creeping vine belonging to the family Convolvulaceae. It grows on the upper parts of beaches and endures salted air. This plant namely the subspecies brasiliensis is known as salsa-da-praia in Brazilian folk medicine and is used to treat inflammation and gastrointestinal disorders. It is used as a medicinal plant used in many countries for the treatment of several ailments, including inflammatory and analgesic processes (De Souza et al., 2007). Ipomoea pes-caprae is a traditional medicinal plant used in the treatment of headache and various types of inflammation including jellyfish sting dermatitis (Pongprayoon et al., 1991; Bandaranayake, 1998; 2002). Since there is no any innovative work has been initiated in such a plant against diabetic disorders. In view of above medicinal properties, the present study was designed to investigate the hepatoprotective activity of ethanol extract of Ipomoea pes-caprae in streptozotocin induced diabetic rats.

MATERIALS AND METHODS
Plant material
Ipomoea pes-caprae leaves were freshly collected from plants in Parangipettai, Tamil Nadu, India, and were botanically authenticated by Department of Botany,
Annamalai University.

**Preparation of Ipomoea pes-caprae leaf extract**

500 g of fresh *Ipomoea pes-caprae* leaves were powdered and then soaked in 1500 ml of 95% ethanol overnight. After filtration, the residue obtained was again suspended in equal volume of 95% ethanol for 48 hours and filtered again. The above two filtrates mixed and solvent was evaporated in a rotavapor at 40 – 50°C under the reduced pressure. The final concentrated extract obtained was stored at 0 – 4°C until used. A known volume of the ethanolic residual extract is suspended in distilled water and was orally administered to the animals by gastric intubation using a force feeding needle during the experimental period.

**Chemicals**

Streptozotocin was purchased from Sigma – Aldrich Chemicals Pvt. Ltd., Bangalore, India. All other chemicals and reagents used were of analytical grade.

**Experimental Animals**

Adult male albino rats of wistar strain weighing approximately 180 – 200 g were obtained from central animal house, department of experimental medicine, faculty of medicine, Rajah Muthiah Medical College, Annamalai University. The animals were housed in polycarbonate cages in a room with a 12h day – night cycle, temperature of 22 ± 2°C and humidity of 45 – 64%. During whole experimental period, animals were fed with a balanced commercial diet (Hindustan Lever Ltd, Mumbai, India) and water ad libitum. All animal experiments were approved by the Ethical committee No.1030, Annamalai University.

**Acute toxicity study**

Acute toxicity study of ethanol extract of *Ipomoea pes-caprae* leaves was determined as per the OECD guideline No: 423 (Acute toxic class method). It was observed that test extract was not lethal to the rats even at 2000 mg/kg dose. Hence; (300 mg/kg) of this dose were selected for further study.

**Induction of diabetes**

Diabetes mellitus was induced by a single intraperitoneal (i.p) injection of freshly prepared streptozotocin (50 mg/kg b.w) in 0.1 M citrate buffer (pH - 4.5) in a volume of 1 ml/kg b.w. The animals were allowed to drink 20% glucose solution over night to overcome the drug induced hypoglycemy. After 72 hours, plasma glucose was determined and those rats with fasting glucose levels greater than 250 mg/dl were used in the study.

**Experimental design**

All animals were randomly divided into four groups with six animals in each group.

- **Group I** – Normal rats (without any treatment)
- **Group II** – Diabetic control rats.
- **Group III** – Diabetic rats given ethanol extract of *Ipomoea pes-caprae* leaves (300 mg/kg b.w)
- **Group IV** – Diabetic rats given standard drug glibenclamide (600 µg/kg b.w)

**Biochemical analysis**

The animals were sacrificed at the end of experimental period by decapitation. Blood was collected, serum separated by centrifugation at 3000 g for 10 minutes. Serum hepatoprotective parameters are estimated by following the method of (11). Estimation of alkaline phosphatase (ALP) was carried out by following the method of (12). AST & ALT were estimated by (13). Bilirubin was estimated the method of (14).

**Statistical analysis**

Values are expressed as mean ± SD. The data were statistically analyzed using ANOVA followed by DMRT. The values were considered statistically significant if the p-value was less than 0.05.

**Results:**

In the present study the hepatoprotective markers of ALT, AST, ALP and serum bilirubin level and liver weight was consistently increased in diabetic groups. Whereas the *Lpes-caprae* plant and glibenclamide treated groups exhibited tremendous recovery level (Table.1).

**Discussion**

The currently available drug regimens for management of diabetes mellitus have certain drawbacks and therefore there is a need to find safer and more effective antidiabetic drugs (15). The present study was aimed to determine the efficacy of *Ipomoea pes-caprae* plant extract on hepatoprotective activity of normal and streptozotocin induced diabetic rats.

Streptozotocin (STZ) is commonly used for experimental induction of diabetes mellitus, which causes selective pancreatic islet β-cell cytotoxicity mediated through the release of nitric oxide. This results in rapid reduction in pancreatic islet pyridine nucleotide concentration and subsequent β-cell necrosis. The action of Streptozotocin on mitochondria generates SOD anion, which leads to diabetic complications (16 – 18). In the present investigation, streptozotocin is used to induce diabetic condition in male wistar rats. The glibenclamide is a standard antidiabetic drug, used to compare the antihyperglycemic property in experimental rats. Glibenclamide have been involved in stimulating insulin secretion from pancreatic β-cells principally inhibiting ATP sensitive k ATP channels in the plasma membrane (19). In the present study Streptozotocin - administered rats showed

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**Table.1.** Hepatoprotective markers in diabetic animals treated with *Lpes-caprae* plant extract

<table>
<thead>
<tr>
<th>Groups</th>
<th>Liver Weight (g)</th>
<th>Serum Bilirubin (mg/dl)</th>
<th>ALP (IU/L)</th>
<th>AST (IU/L)</th>
<th>ALT (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.80± 0.47</td>
<td>9.30±0.46</td>
<td>1.59±1.12</td>
<td>42.98±1.4</td>
<td>122.2±18.6</td>
</tr>
<tr>
<td>Diabetic</td>
<td>4.86±0.64</td>
<td>12.41±0.71</td>
<td>2.32±1.58</td>
<td>112.12±1.6</td>
<td>213.21±1.2</td>
</tr>
<tr>
<td>D+ <em>Lpes-caprae</em> (300 mg/kg)</td>
<td>6.24±0.28</td>
<td>10.22±0.44</td>
<td>1.90±0.42</td>
<td>69.21±1.5</td>
<td>153.20±0.4</td>
</tr>
<tr>
<td>D+Glibenclamide (600µg/kg)</td>
<td>6.67±0.63</td>
<td>10.9±0.42</td>
<td>1.62±1.71</td>
<td>55.21±1.1</td>
<td>132.43±1.2</td>
</tr>
</tbody>
</table>

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increased plasma glucose and decreased insulin levels. The administration of *Ipomoea pes-caprae* to diabetic rats showed the levels of plasma glucose and insulin towards near normalcy. When compared with diabetic groups, *Ipomoea pes-caprae* by its ability to scavenge reverted the hepatoprotective markers to normal level. Diabetes mellitus impairs the normal capacity of the liver to synthesize glycogen. Synthase phosphatase activates glycogen synthase resulting in glycogenesis and this activation appears to be defective in diabetes (20). The decrease in liver weight may be by necrosis due to decrease in cell mass (21). The diabetic rats treated with herbal extract maintained the liver weight near to normal levels. From our investigation, it is well clear that the extract prevents the glycation of proteins in the liver and serum. AST, ALT and ALP are reliable markers of liver function (22). An increase in the activities of AST, ALT, and ALP in plasma might be mainly due to the leakage of these enzymes from the liver cytosol into the blood stream which gives an indication of the hepatotoxic effect of streptozotocin (23). Treatment of the diabetic rats with *Ipomoea pes-caprae* reduced the activity of these enzymes in plasma compared to the diabetic untreated group and consequently alleviated liver damage caused by streptozotocin-induced diabetes. Significant reductions in the activities of these enzymes in *Ipomoea pes-caprae* treated diabetic rats indicated the hepatoprotective role in preventing diabetic complications.

**Conclusion**

In the present study, the hypoglycemic action of *Ipomoea pes-caprae* leaves has beneficial effects on blood glucose level. It also restored the altered serum enzymes (AST, ALT and ALP). The action of *Ipomoea pes-caprae* was comparable to the antidiabetic drug glibenclamide. Results of this experimental study indicated that *Ipomoea pes-caprae* possessed hepatoprotective activities. Further pharmacological and biochemical investigations are under way to elucidate the mechanism of the antidiabetic effect of *Ipomoea pes-caprae*.

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**Reference**


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