Antihyperlipidemic potential of Cucurbita maxima seeds in streptozotocin induced diabetic rats

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Aims: Cucurbita maxima seeds extract (CMSE) possess potent antidiabetic efficacy in vivo and in vitro which has already been published by our research group. The present study deals with antihyperlipidemic potential of CMSE in diabetic rats to validate our previous findings.

Keywords: Antihyperlipidemic Cucurbita maxima Seeds Streptozotocin

Original Article

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ABSTRACT

Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, hyperlipidemia, insulin resistance and insufficient insulin secretion [1]. It affects essential biochemical pathways of the body viz. carbohydrate, protein, and lipid metabolism [2]. It also causes various complications, including cardiovascular diseases, decreased renal function, atherosclerosis, blurred vision due to retinal bleeding, foot ulcers and peripheral neuropathies [3]. The level of serum lipids is usually elevated at diabetic state, which is a risk factor for type 2 diabetes associated cardiovascular diseases [4]. Although, it is difficult to cure diabetes completely but it can be managed well by keeping a control on blood glucose level. Thus, the treatment of diabetes should be focused on its prevention and not on cure. Treatment of diabetes using insulin or other oral hypoglycemic agents is limited and associated with economic load, side effects etc., thus the use of natural products are strongly recommended. A number of plants and plant derived products have been shown to possess antidiabetic activity on experimental models [5-8].

Cucurbita maxima Duch. (family: Cucurbitaceae) commonly known as pumpkin in English and Kadui in Hindi is an annual herb. It is used as a vegetable and its fruits are the most valuable part with high nutritional value [9]. Its seeds have been identified as an effective antimicrobial and antioxidant agent [10,11]. Its seeds have also been known for their antidiabetic effect in vitro and were found to be of high impact [12]. Preliminary phytochemical screening of the C. maxima seeds extract (CMSE) reveals the presence of alkaloids, tannins, saponins, proteins, carbohydrates and glycosides [10]. In our previous studies, we have reported the hypoglycemic and antidiabetic effects of CMSE in normal as well as streptozotocin (STZ) induced diabetic rats [13].

As an extension of our previous findings, the antihyperlipidemic efficacy of CMSE in STZ induced diabetic rats has been reported by our research group for the very first time in the present study.

MATERIAL AND METHODS

Plant material and preparation of CMSE

The seeds of C. maxima plant were procured from the local market of Allahabad, India and authenticated by Prof. Satya Narayan, Taxonomist, Department of Botany, University of Allahabad, Allahabad, India. A voucher specimen has been submitted to the University herbarium (No. MRL/CM/01). The seeds were washed well with water and dried in shade. The shade dried seeds were powdered and extracted with hot distilled water. Extract obtained was filtered, concentrated and lyophilized till constant weight. The dry powder so obtained of CMSE was stored at -40ºC for further use during experimental study.

Experimental animals

Albino Wistar rats of the same age group and body weight 150-200 g were selected for the experiments. Animals obtained from the National Institute of Communicable Diseases (NICD), New...
RESULTS

TC, TG, HDLc, LDLc and VLDLc studies of severely diabetic rats

Table 1 shows the impact of the most effective dose identified as 200 mg kg\(^{-1}\) of CMSE on serum lipid profile of severely diabetic rats after long term treatment of 28 days. The results showed that administration of CMSE decreased the levels of TC, TG, LDLc and VLDLc with a maximum fall of 53.0, 56.9, 75.6 and 56.9%, respectively. Whereas, in case of positive control, rats treated with 2.5 mg kg\(^{-1}\) of glipizide, a maximum fall of 27.0, 33.8, 39.8 and 33.7% in case of TC, TG, LDLc and VLDLc levels, respectively was observed. HDL cholesterol level was also significantly increased in severely diabetic rats after 28 days treatment. CMSE and glipizide showed a maximum rise of 36.4 and 31.5%, respectively in case of HDLc level. Moreover, the untreated diabetic rats continued to show enhanced levels of TC, TG, LDLc and VLDLc levels in addition to a slight percentage fall in HDL cholesterol level.

US, UP and BW studies of severely diabetic rats

Table 2 shows the effect of CMSE on urine sugar, urine protein and body weight of severely diabetic rats. CMSE considerably reduced urine sugar, urine protein and improved the body weight gain as compared with the diabetic control rats. Fall of 33.3 and 66.6% was observed in urine sugar and urine protein, respectively with CMSE. At the end of the experiment, the body weight of the diabetic rats was found to significantly increase with a rise of 7.1% on treatment with CMSE. However, glipizide treated rats showed a fall of 50% in case of urine sugar as well as urine protein and a slight increase of 8.1% in case of body weight. Whereas, elevated levels of urine sugar and body weight loss were observed in case of diabetic control group.

LD\(_50\) studies

LD\(_50\) experiment was carried out on healthy normal rats. The behaviour of the treated rats was found to appear normal. No toxic behaviour was reported at doses up to 10 and 15 times of the effective dose of CMSE and there was no death reported in any of these groups.

Table 1 Effect of long term treatment of CMSE on serum lipid profile of severely diabetic rats ± S.D.

Table 2 shows the effect of CMSE on serum lipid profile of severely diabetic rats ± S.D.
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Table 2 Effect of long term treatment of CMSE on US, UP and BW of severely diabetic rats.

<table>
<thead>
<tr>
<th>Treatment Groups</th>
<th>Dosage</th>
<th>0 Days</th>
<th>7 Days</th>
<th>14 Days</th>
<th>21 Days</th>
<th>28 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>D/W</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td>D/W</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>SD treated (C. maxima)</td>
<td>200 mg/kg</td>
<td>195</td>
<td>195</td>
<td>200</td>
<td>200</td>
<td>210</td>
</tr>
<tr>
<td>SD treated (G. pinnata)</td>
<td>2.5 mg/kg</td>
<td>185</td>
<td>185</td>
<td>190</td>
<td>195</td>
<td>210</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Some encouraging results of CMSE in controlling the surge of blood glucose level in normal as well as STZ induced diabetic rats motivated us to further validate the potential of the most effective dose of CMSE on lipid profile of STZ-induced diabetic rats during long term study. Thus, the present study was designed to explore the effect of CMSE on levels of different serum lipid cholesterol such as TC, TG, VLDLc, LDLC and HDLC in addition to other associated biochemical parameters viz. US, UP and BW.

Generally, it has been observed that hyperlipidemia is a complication associated with hyperglycemia and the most common lipid abnormality observed is hypertriglyceridemia which increases risk factor of strokes [19]. Therefore, ideal treatment of diabetes should have a favorable affect on lipid profiles. The present study reveals that CMSE evoked significant reductions in TC, TG, VLDLc and LDLc. It has been found that most of the drugs that decrease TC also decrease HDLC cholesterol [20]. But it is noteworthy to mention here, that in the present study the 200 mg kg$^{-1}$ dose of CMSE had an additional advantage over the existing drugs in the way that they not only decreased the TC, TG, LDLC and VLDLC but also increased the cardio protective HDLC cholesterol in severely diabetic rats significantly after 28 days of treatment. Thus, it is reasonable to inform that the CMSE could modulate blood lipid abnormalities associated with diabetes.

Other parameters such as US, UP and BW also get affected during diabetes. Administration of CMSE also decreased the elevated US and UP levels in severely diabetic rats thereby, causing a subsequent recovery towards normalization. Moreover, it was observed that the increase in body weight was almost at par in case of CMSE as well as standard drug, glipizide. While promoting herbal therapy with CMSE for alternative management of diabetes, toxicity study of CMSE was also carried out by using L$.D_{50}$ experiment. High value of L$.D_{50}$ for CMSE implies its great margin of safety. Moreover, phytochemical analysis of CMSE reveals the presence of a number of therapeutically significant phytocomstituents viz. alkaloids, tannins, saponins, proteins, carbohydrates and glycosides [10]. Hence, it could be presumed that the synergistic effect of these phytocomstituents may be responsible for the antihyperlipidemic activity of CMSE.

**CONCLUSION**

It can thus be concluded that CMSE has significant antihyperlipidemic potential in addition to antidiabetic and hence help in managing diabetes mellitus and its complications. It may act as valuable adjuncts in providing a new concept of healthcare and therefore it can be developed further as a novel therapeutic agent for managing not only diabetes but also its complications.

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**REFERENCES**


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