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Antidiabetic effect of *Cleome aspera* in type 2 diabetic rats

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ABSTRACT

The antidiabetic effect of methanolic extract of whole plant of *Cleome aspera* was investigated in Streptozotocin induced type 2 diabetic rats. The *C. aspera* showed a dose dependent hypoglycemic effect and prevented rise in blood glucose levels in diabetic rats. The blood glucose levels were measured at 0, 2, 4, 6 and 8 h after the treatment. The methanolic extract of *C. aspera* at a doses of 100, 200 and 400 mg/kg body weight (b.w.) reduced the blood glucose levels of the normal rat from 75.29±6.4 to 68.18±6.59 mg/dl, 87.19±5.1 to 71.28±7.45 mg/dl and 85.45±7.6 to 68.16±7.45 respectively at 6 h after oral administration of the extract ($P<0.05$) and also significantly lowered blood glucose levels in Streptozotocin induced diabetic rats from 238.62±9.60 to 176.96± 6.40 mg/dl at 4 h after oral administration of the 400 mg/kg b.w. extract ($P<0.05$). In glucose tolerance test, extract markedly reduced the external glucose load. The antihyperglycemic activity of *C. aspera* was compared with glibenclamide (10 mg/kg), an oral hypoglycemic agent. The above results suggest that *C. aspera* is a potent antidiabetic agent.

Keywords: *Cleome aspera*; Streptozotocin; Glibenclamide; type 2 diabetic; Neonatal rats

1.Introduction

Diabetes mellitus is an endocrine disorder, which characterized with hyperglycemia and effecting nearly 10% of the population all over the world [1] . In modern medicine no satisfactory effective therapy is still available to cure diabetes mellitus [2]. There is increasing demand by patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents [3,4,5]. The world health organization has also recommended the evaluation of the effectiveness of plants in condition where we lack safe mode drugs .

Cleome aspera J. Koeing ex DC a small decumbent prickly herb belonging to the family of Cleomaceae is grown as weed in most tropical countries. It is locally called as "*Karumpoondu*". Native Ethnic tribes in Tamil Nadu use the leaf paste to cure eczema[6]. Most of the Cleome species show antidiabetic activity. The present study focused to evaluate alcoholic extract of *C. aspera* roots at various doses in normal and Streptozotocin induced diabetic rats

2. Experimental

2.1. Plant material

Cleome aspera plants were collected freshly in and around Kakatiya university campus, Warangal, Southern India. The plant was identified at Plant Systematics Laboratory, Department of Botany, Kakatiya University, Warangal.

2.2. Methanolic extraction

The dried whole plant macerated in methanol and evaporated to dryness gave an extract. The extract was evaporated to dryness under vacuum and dried in vacuum desiccator (12.5%w/w).

2.3. Animals

Laboratory bred Sprague Dawley rats of either sex weighing 150-200 g were selected. The rats were maintained under standard laboratory conditions at 25 ± 2°C, relative humidity 50 ± 15% and normal photo period (12 h dark / 12 h light) were used for the experiment. Commercial pellet diet (Ratan Brothers, India) and water were provided *ad libitum.* The experimental protocol has been approved by the Institutional Animal Ethics committee (CPCSEA Reg. No 169/1999)and by the regulatory body of the government of India.

2.4. Induction of diabetes

Type 2 diabetes (non-insulin-dependent diabetes mellitus) was induced in 1-day-old male Wistar rats (neonatal rats)by treating them with a single intraperitoneal injection of 95 mg/kg body weight streptozotocin[7]. After weaning, rats were individually housed withwater and food available *ad libitum.* When rats were 9-week old they were used to evaluate the effect of drugs under investigation. Control animals received only the vehicle.

2.5. Experimental protocol

In the experiment a total of 42 rats (12 diabetic surviving rats, 30 normal rats) were used. The rats were divided into eight groups after the induction of streptozotocin diabetes. In the experiment six rats were used in each group. Group 1 treated with vehicle (5%gum acacia) and served as normal untreated group, and Group 2, Group 3 and Group 4 treated with alcoholic extract of *C. aspera* at a doses of 100, 200 and 400 mg/kg respectively, Group 5 Diabetic rats treated with vehicle (5%gum acacia) served as diabetic control, Group 6 diabetic rats treated with alcoholic extract of *C. aspera* at a dose of 400 mg / kg respectively, Group 7 diabetic rats treated with 10 mg/kg dose of glibenclamide.

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Table 1: Hypoglycemic effect of the extracts in normal rats (Mean ± SD)

Group	Dose (mg/kg)	Blood Glucose levels (mg/dl) Pretreatment (h)	Post treatment (h)			
		0	2	4	6	8
Control	-	85.91±7.4	84.62±9.6	83.22±6.1	82.94±8.4	84.19±10.96
(5% gum acacia in water)			(1.50±0.09)	(3.13±0.10)	(3.47±0.37)	(2.04±0.27)
Glibenclamide	10	82.23±4.18	63.21±6.17*	56.12±5.72*	58.53±5.9*	72.81±6.04
			(23.13±2.9)	(31.75±4.10)	(28.82±2.09)	11.45±1.4
C.aspera	100	75.29±6.4	70.45±5.1	64.38±6.49	68.18±6.59	71.46±4.94
			(6.42±1.57)	(14.49±3.48)	(9.44±1.85)	(5.08±0.59)
C.aspera	200	87.19±5.1	82.6±6.41	68.92±7.2*	71.28±7.45*	79.26±6.06
			(10.24±1.3)	(20.95±3.9)	(18.24±2.95)	(9.09±1.60)
C.aspera	400	85.45±7.6	74.12±4.41	66.32±8.92*	68.16±7.45*	75.51±2.76
			(13.25±1.4)	(22.38±2.1)	(20.23±2.95)	(11.63±1.60)

*Values are mean±SD, n = 6 in each group.*P < 0.05 when compared with vehicle-treated group (Dunnett's test).*

Table 2: Antihyperglycemic effect of the extracts in Streptozotocin induced diabetic rats (Mean ±S.D)

Group	Dose (mg/kg)	Blood Glucose levels (mg/dl) Pretreatment (h)	Post treatment (h)			
		0	2	4	6	8
Diabetic Control	-	217.19±11.86	213.26± 13.86	207.82±11.22	205.19±10.50	212.31±10.91
			(1.8±1.06)	(4.31±2.08)	(5.52±1.61)	(2.24±3.76)
Glibenclamide	10	235.45±15.86	214.12 ± 15.29	171.31 ± 11.27*	198.16± 14.88*	209.29 ± 4.91*
			(9.05 ± 4.89)	(27.23 ± 11.27)	(15.83 ± 4.49)	(11.11 ± 4.73)
C.aspera	200	238.62±9.60	209.03±16.55	176.96± 6.40*	189.57± 9.00*	205.36± 8.02*
			(12.40±2.72)	(25.84±1.14)	(20.55±2.28)	(13.96±3.40)

*Values are mean±SD, n = 6 in each group. *P < 0.05 when compared with vehicle-treated group (Dunnett's test).*

Table 3 Oral glucose tolerance test in Normal and Streptozotocin induced diabetes rats (Mean ± S.D)

Group	Dose(mg/kg)	Blood Glucose levels (mg/dl) Pretreatment (min)	Post treatment (min)			
		0	30	60	90	120
Control(5% gum acacia)	-	75.04±7.31	127.01±8.33	135.31±10.74	94.36±8.15	80.72±7.83
Diabetic control	-	217.84 ± 11.3	324.74 ± 12.07	387.01 ± 10.59	354.68 ± 13.77	316.66 ± 13.57
Glibenclamide	10	74.17±6.73	101.82±8.03	115.48±7.2*	86.37±5.18*	71.35±4.09
C.aspera	200	76.19±6.03	109.45±9.72	123.92±7.03*	89.37±6.38*	76.04±5.93
Diabetic +*C.aspera*	200	224.72 ± 13.05	207.02 ± 11.39	173.3 ± 13.46*	119.37 ± 9.11*	97.16 ± 8.74
Diabetic + Glibenclamide	10	233.02 ± 13.68	217.1 ± 11.72	187.34 ± 14.73*	113.62 ± 11.35*	83.68 ± 9.59

*Values are mean±SD, n = 6 in each group. *P < 0.05 when compared with vehicle-treated group (Dunnett's test).*

After an overnight fast, the plant extract suspended in 5% gum acacia was fed by gastric intubations with a syringe. Blood samples were collected for the measurement of blood glucose by puncture of retro-orbital plexus at 0, 1, 2, 4, 6 and 8 h after feeding the plant extracts. The samples were collected into glass vials containing of a small quantity of a mixture of potassium oxalate and sodium fluoride as anticoagulant. The blood glucose levels were determined by using GOD—POD method [8]

2.6. Oral glucose tolerance test

Effect of methanolic extract of C. aspera on oral glucose tolerance test (OGTT) in normal rats and diabetic rats were divided into six groups (n=6), viz, group I only glucose (normal rats, 2 g/kg, p.o.), II only glucose (Diab2 g/kg, p.o.), group III glibenclamide (10 mg/kg, p.o.), group IV glibenclamide (diabetic rats,10 mg/kg, p.o.), group V methanolic extract of C. aspera (normal rats , 200 mg/kg, p.o.) and group VI—methanolic extract of C. aspera (diabetic rats, 200 mg/kg, p.o.). The animals were fasted overnight before commencing the experiment. All rats were loaded with 2 g/kg, p.o., d-glucose solution (S.D. Fine-Chem. Ltd, Mumbai) after 0.5 h of drug administration. Blood samples were collected by the retro orbital sinus puncture (ROP) [9] method just prior to drug administration and 30, 60, and 120 min after glucose loading. Serum glucose level was measured immediately [10].

2.7. Statistical analysis

The results are expressed as mean± SD. Comparison between the groups was made by analysis of variance (ANOVA), followed by Dunnett's test as per suitability. $P < 0.05$ was considered significant.

3. Results

3.1. Effect on normal rats

The effect of different doses of methanolic extract of *C. aspera* on fasting blood sugar level was assessed in normal rats at various time intervals (Table 1). It produce significant ($P<0.05$) maximum reduction in blood glucose level 14.49±3.48 %, 20.95±3.9 % and 22.38±2.1 % of normal rats treated with alcoholic extract of *C. aspera* at a doses of 100, 200 and 400 mg/kg respectively, after 4 h of the treatment.

3.2. Effect on Streptozotocin induced diabetic rats

The antihyperglycemic effect of the extract on the fasting blood glucose levels on diabetic rats is shown in Table 2. The alcoholic extract of *C. aspera* at a dose of 200 mg/kg produced the significant ($P<0.05$) maximum fall of 25.84±1.14 % on the blood glucose levels of diabetic rats after 6 h of the treatment.

Table 3 shows the changes in the levels of blood glucose in normal, diabetic control and experimental groups after oral administration of glucose (2 g/kg). The diabetic rats showed that significant

increase in the blood glucose at 60 min and 90 min. In *C. aspera* treated animals blood glucose concentration was significantly ($P<0.05$) decreased after 60 min and 90 min. *C. aspera* treated animals tend to bring the values to near normal. C. aspera (200mg/kg) were more effective then glibenclamide.

4. Discussion

In this study the methanolic extract of whole plant of *C. aspera* at different doses produce a significant fall in the blood glucose level in both normal and diabetic rats in a dose dependent manner and this was evident 1 h after the administration of the extract. On the other hand glibenclamide caused significantly more hypoglycemia in comparison with the plant extract (200 mg/kg). As emphasize is laid on glucose homeostasis as a severe hypoglycemia can result in life threatening situation. Therefore, lesser hypoglycemia with plant extract in comparison with glibenclamide is a desirable feature. *C. aspera* might enhance glucose utilization because it significantly decreased the blood glucose level in glucose loaded rats. It seems to suggest that *C. aspera* may have a mechanism of action similar to that of glibenclamide. This may be due to restoration of delayed insulin response or due to inhibition of intestinal absorption of glucose. The mechanism of this hypoglycemic effect of the extract is not elucidated in this study. Further studies will be focused on the determination of the mechanism(s) of action, as well as on the isolation of bioactive principles.

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