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Antidiabetic Activity of Methanol Extract of *Asteracantha Longifolia* Induced By Streptozocin in Rats

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ABSTRACT

The present investigation was carried out to study the antidiabetic effects of the methanol (70:30) extract of *Asteracantha longifolia,* In normal and streptozocin induced diabetic model. *Asteracantha longifolia,* are reported to have medicinal values including antidiabetic properties. Decreased blood glucose level of the test animals shows that the extract exhibit significant anti-diabetic activity when compared to diabetic control group. Effect of various doses (100, 200mg/kg p.o) extract was studied on streptozotocin induced both diabetic and non diabetic rats. The results also indicated the dose dependent effect. The antidiabetic activity produced by the extract may be due to increased uptake of glucose at the tissue level or by an increase in pancreatic beta cell function or due to inhibition of intestinal absorption of glucose. The present study supports the use of this herbal drug as anti-diabetic. The reduction in the glucose level in induced diabetic rats proved that *Asteracantha longifolia* having the antidiabetic activity.

Key words: *Asteracantha longifolia,* Anti Diabetic and Streptozocin.

1. INTRODUCTION

Diabetics have significantly accelerated levels of oxidative stress and this contributes massively to most neurological, cardiovascular, retinal, renal diabetic complications [1]. Diabetes mellitus is a metabolic disorder characterized by fasting hyperglycemia and alterations in carbohydrate, fat and protein metabolism, associated with absolute or relative deficiencies in insulin secretion and/or insulin action [2]. Experimentally, streptozotocin (STZ) or alloxan are used to induce diabetes in rodents. STZ is effective in triggering islet cell death by acute oxidative stress. STZ-induced diabetic rats are one of the animal models of insulin dependent diabetes mellitus characterized by high fasting blood glucose levels and drastic reduction in plasma insulin concentration [3]. Although different types of oral hypoglycemic agents are available along with insulin for the management of diabetes mellitus, there is a growing interest in herbal remedies due to the side effects associated with these therapeutic agents [4]. Thus plants have played a major role in the discovery of new therapeutic agents. The present study was undertaken to investigate the anti-hyperglycemia effect of the methanol of *Asteracantha longifolia* on the diabetes induced by a multiple dose of STZ in diabetic rats.

2. MATERIAL AND METHODS

2.1. Plant Material

The leaves of *Asteracantha longifolia* used in the present study was collected and authenticated.

2.2. Experimental Animals

Albino Wistar rats of either sex, weighing 150–200 g, were used in the study. They were kept in standard laboratory conditions under natural light and dark cycle, and are housed at ambient temperature (22±1°C), relative humidity (55±5%). Animals had access to standard pellet diet and water given *ad libitum*.

2.3. Induction of Diabetes

2.3.1. Streptozotocin-induced diabetes

Streptozocin was obtained from Himedia Laboratories, Mumbai. All other chemicals used for this study were of analytical grade. Streptozotocin (55 mg/kg) was dissolved in 0.1M citrate buffer (pH 4.5). Six rats per group were administered by subcutaneous injection. After 48 hrs, fasting blood glucose levels as well as glycosuria were assessed to confirm the diabetic state. Only rats with a fasting blood glucose level of at least 250 mg/dL and positive urine glucose

were considered diabetic and were used in the experiment.

2.4. Experimental Design

Male Wistar albino rats weighing 150–200 g (90 to 110 days old) were used. The animals were randomly divided into five groups of six animals each.

Group 1: Normal control (non-diabetic, untreated) rats.

Group 2: Diabetic control (diabetic, untreated) rats.

Group 3: Diabetic test rats given *Asteracantha longifolia* extracts at the dose of 100 mg/kg.

Group 4: Diabetic test rats given *Asteracantha longifolia* extracts at the dose of 200 mg/kg.

Treatment of experimental animals with plant extracts was initiated 2 days post streptozotocin injection and was carried out once daily, by orally, for 14 days. Food and water were made freely available.

2.5. Measurement of body weight gain, food, water intake and blood glucose

Body weight gain, food and water intakes were monitored daily during the 14 days experimental period. Blood samples for glucose determination were obtained from the tail tip of 12 hrs fasted rats on day 0 (before streptozotocin administration), days 2 (48 h post streptozotocin injection), 5, 8, 11 and 14th day of the experiments. Blood glucose level was determined using a glucometer. Urine glucose was also assessed in fresh urine using glucose indicator sticks before and 48 hrs after streptozotocin administration, for the confirmation of the diabetic state of animals.

2.6. Statistical Analysis

Mean values were obtained by one-way analysis of variance (ANOVA) followed by Dunnet's't' test, using the computer software, Graph pad Prism 5. The significance of difference between and within various groups was determined. The results are expressed as mean ± S.E.M. Values of $p < 0.05$ were taken to imply as statistically significant.

3. RESULTS AND DISCUSSION

The effects of the *Asteracantha longifolia* extract on the body weight of diabetic rats are shown in the following;

3.1. Effects of *HAAL* on the body weight of STZ-induced diabetic rats.

During the 2 weeks of observation of the extract treated diabetic rats at doses of 200 mg/kg, there were very significant ($p < 0.01$) weight gains relative to day 2 showed a very significant ($p < 0.01$) weight increase in the body compared to untreated diabetic rats.

Table -1: Effects of *HAAL* on the body weight of STZ-induced diabetic rats.

Group (n=6)	Body weight (g)	
	2days after STZ injection	14 days after administration of plant extract
Normal control rats	198.0 ± 3.821*	218.5±3.227**
Diabetic control rats	180.2 ± 3.541	164.5±3.227
Test I (*HAAL* 100mg/kg)	193.6 ± 1.631*	176.0±4.708*
Test II (*HAAL* 200mg/kg)	195.6 ± 1.631*	180.5±5.204**

Results are expressed as mean ± SEM, n=6

3.2. Food and fluid intakes of rats treated with *HAAL* for **2** weeks

When compared to the untreated diabetic rats, untreated diabetic rats had severe polyphagia and polydipsia at the end of the second week of the experiment with respective increase in food and fluid intakes. However, in the presence of *Asteracantha longifolia* extracts extract (100mg/kg and 200 mg/kg), food intake was reduced when compared with diabetic control rats but its not statistically significant (p>0.05). Fluid intakes showed decrease in *Asteracantha longifolia* extracts treated diabetic rats at doses of both 100 mg/kg and 200 mg/kg when compared with diabetic control rats.

Table -2: Food and fluid intakes of rats treated with *HAAL* for **2** weeks

Group (n=6)	Food in-take (g/rat/week)		Fluid in-take (ml/rat/week)	
	Week **1**	Week **2**	Week **3**	Week **4**
Normal control rats	59.20 ±1.683	61.00± 1.291	22.50± 3.227*	21.25± 1.493
Diabetic control rats	69.50± 2.630	69.50± 2.533	22.50± 3.227*	21.25± 1.493
Test I (*HAAL* 100mg/kg)	59.00± 1.683	54.50± 1.041	32.25± 2.175	42.25± 3.326
Test II (*HAAL* 200mg/kg)	58.00± 1.472	50.25± 1.250	38.00± 2.483	39.50± 1.708

Results are expressed as mean ± SEM, n=6

Following a 48 h post streptozotocin injection, all diabetic rats exhibited hyperglycemia, which ranged between 330 and 400 mg/dL while normal control rats showed a normal blood sugar level of 110 mg/dL. After 2 weeks of treatment with the extracts, the glycemic level of 100 mg/kg *Asteracantha longifolia* extract treated diabetic rats dropped significantly from

369.8±4.090 on day 2 to 120.3 ±4.442 mg/dL (p < 0.01) on day 14 and from 362.3±5.977 to 116.8±4.854mg/dL (p < 0.01) for 400 mg/kg dose respectively.

3.3. Blood glucose level (mg/dL) of rats **2** days post STZ administered and after 14 days

In diabetes, oxidative stress is due to both an increased production of plasma free radical concentration and a sharp reduction of antioxidant defenses. GSH, being the most important bio-molecule against chemically induced toxicity can participate in the elimination of reactive intermediates by reduction of hydro peroxides in the presence of Glutathione peroxidase. Glutathione (GSH) also functions as free radical scavenger and in the repair of free radical caused biological damage [5]. The important mechanism implicated in the diabetes-genic action of STZ is by increased generation of oxygen free radicals, which causes a decrease in plasma GSH concentration, and plasma GSH/GSSG ratio [6].

Table -3: Blood glucose level (mg/dL) of rats **2** days post STZ administered and after 14 days

Group (n=6)	Glycemia (mg/dL)		
	Before STZ	**2** Days after STZ	After 14 days treatment
Normal control rats	105.0 ±6.455	110.0±4 .564**	105.5±2.72 3**
Diabetic control rats	108.8±4. 270	387.8±7 .375	373.5±6.88 6
Test I (*HAAL* 100mg/kg)	111.3±4. 270	369.8±4 .090	120.3 ±4.442**
Test II (*HAAL* 200mg/kg)	103.8±8. 985	362.3±5 .977*	116.8±4.85 4**

Our results suggest that the methanol *Asteracantha longifolia* extracts have dose-dependent anti-diabetic activities on streptozotocin-induced diabetes. The metabolic disturbances were corrected after the plant extracts were administered for 2 weeks, as shown by the normalization of fasting blood glucose levels, reduction in polyphagia and polydipsia and weight gain by diabetic-treated rats but reduction in polyphagia and polydipsia are not statistically significant [7]. The mechanisms by which streptozotocin brings about its diabetic state include selective destruction of pancreatic insulin secreting beta cells, which make cells less active [8] and lead to poor glucose utilization by tissues [9]. *Asteracantha longifolia* significantly reduced the high fasting glucose levels in streptozotocin-induced diabetic rats. This suggests that the extracts may possess an insulin like effect on peripheral tissues by either promoting glucose uptake and metabolism, by inhibiting hepatic gluconeogenesis [10] or absorption of glucose into the muscles and adipose tissues [11] by the stimulation of a regeneration process and revitalization of the remaining beta cells [12,13].

4. CONCLUSION

In conclusion the present investigation showed that *Asteracantha longifolia* extract possess anti-diabetic activity.

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