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## ANTI-HYPERGLYCEMIC EFFECT OF *CARALLUMA LASIANTHA* EXTRACT ON HYPERGLYCEMIA INDUCED BY CAFETERIA-DIET IN EXPERIMENTAL MODEL

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**ABSTRACT:** *Caralluma lasiantha* is a succulent plant belongs to Ascalpedaceae family. The objective of this study was to evaluate and to compare the anti-hyperglycemic effect of *Caralluma lasiantha* with Chromium Picolinate on hyperglycemia induced by Cafeteria-Diet in Wistar albino rats. Hyperglycemia was induced in experimental rats by feeding Cafeteria-Diet for a study period of 90 days. *Caralluma lasiantha* (10, 20, and 40 mg/kg b.w.) & Chromium Picolinate (10 mg/kg b.w.) were administered orally once every day throughout the study and serum glucose levels were determined in different experimental days. Treatment with *Caralluma lasiantha* significantly reduced the serum glucose level in dose dependant manner. Data reveal an appreciated beneficial effect of *Caralluma lasiantha* on hyperglycemic rats. *Caralluma lasiantha* possesses anti-hyperglycemic effect, which promisingly support the use of *Caralluma lasiantha* as a food supplement or an adjunct treatment for hyperglycemia

**INTRODUCTION:** Diabetes is increasing at an alarming rate worldwide, which can mainly be attributed to the sedentary life style and calorie-rich diet. Diabetes is often linked with abnormal lipid metabolism and is considered as a major factor for the development of atherosclerosis and cardiovascular complication.<sup>1</sup> Diabetes is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbance of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both.<sup>2</sup> Hyperglycemia is a common end point for all types of DM and it is an important parameter which can be assessed to evaluate the effectiveness of anti-diabetic drugs.

The goals of therapy for diabetes are to alleviate the symptoms which are related to hyperglycemia and to prevent or reduce the acute and chronic complications of diabetes.<sup>3</sup>

Many oral anti-hyperglycemic agents, such as sulfonylurea and biguanides, are available along with insulin for the treatment of diabetes, but these agents have significant side effects, and some are ineffective in chronic diabetes patients.<sup>4</sup> Thus, there is an increasing demand for new natural anti-hyperglycemic agents with fewer side effects and high anti-hyperglycemic potential. WHO Expert Committee recommended the importance to investigate and explore hypoglycemic agents from plant origin because plants used in the traditional medicine have fewer side effects than synthetic drugs.<sup>5</sup>

Hyperglycemia can be induced in experimental animals like rats by offering them diet that is high in sugar, fat or both. The most pronounced effects

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are obtained when the animals are offered an assortment of tasty fat and sugar-rich foods marketed for human consumption, which is referred to as cafeteria diet (CD). Hence cafeteria diet fed rat model was used to emulate hyperglycemia - like condition in humans, in order to evaluate and to compare the effects of *Caralluma lasiantha* (CL) with Chromium Picolinate (Cr.Pic) in hyperglycemia.

Chromium is an essential trace mineral that occurs naturally in small amounts in some foods, including brewer's yeast, lean meat, cheese, pork kidney and whole grain bread and cereals. It is poorly absorbed by the human body but is known to play an important role in the metabolism of carbohydrate, fat and protein.<sup>6</sup> Inadequate amounts of Chromium may result in improper functioning of the metabolic process and lead to a number of physiological disorders that increase risk for diabetes and cardiovascular diseases.<sup>7</sup>

Oral Chromium Picolinate (Cr.Pic) Improves Carbohydrate and Lipid Metabolism in Obese, Hyper-insulinemic Rats and Human studies suggest that Cr.Pic decreases insulin levels and improves glucose disposal in obese and type 2 diabetic populations.<sup>8</sup> Chromium Picolinate is a stable compound for better absorption and it contains trivalent chromium which is chelated to three picolinic acid molecules.<sup>9</sup> With this background, Chromium Picolinate (Cr.Pic) has been used in this study to evaluate and to compare anti-hyperglycemic effect of *Caralluma lasiantha* (CL) by animal model.

*Caralluma* species has been used for centuries in semi-arid areas of India. *Caralluma edulis* & *Caralluma sinaica* are known for their anti-diabetic properties,<sup>10, 11</sup> *Caralluma* is a genus in the *Asclepiadaceous* family. There are approximately 100 variable species in the genus.<sup>12</sup> *Caralluma lasiantha* belongs to the same family and genus of *Caralluma edulis* & *Caralluma sinaica* after literature survey it was found that no scientific investigation has so far been conducted on the anti-hyperglycemic / hypoglycemic effect of *Caralluma lasiantha* thus the present study was carried out to evaluate the effect of methanolic extract of *Caralluma lasiantha* (CL) on hyperglycemia

induced by Cafeteria-Diet in experimental rats. In view of the reported anti-diabetic activity of other *Caralluma* species and traditional claim, *Caralluma lasiantha* was screened for anti-hyperglycemic activity with the aim of developing a natural anti-hyperglycemic drug.

## MATERIALS AND METHODS:

**Alcohol extract preparation:** The shade dried aerial part of the plant material was coarsely powdered. The powdered plant material was taken in a round bottomed flask to which the Soxhlet apparatus was attached. Extraction was made with Methanol for 14 Cycles at boiling point of (65°C) temperature. The Methanol extract was concentrated in a rotary evaporator and stored at 4°C.

**Clearance from the Institutional Animal Ethical Committee (IAEC):** All procedures were conducted in accordance with national guidelines and protocols, approved by the institutional ethical committee (IAEC No: SSIMS & RC / IAEC/021/12). The study was performed after obtaining clearance from IAEC.

**Chromium Picolinate** (Batch no- CP/OL/12/01) Oceanic Laboratories (P) LTD.,

**Other requirements:** Ether, Heparinized Micro capillary tubes, Centrifuge, Auto analyzer, etc.,

**Animals:** Inbred strains of *Wistar albino rats* (n=36) weighing 180-200g of either sex were taken from the Central animal house, S.S. Institute of Medical Sciences & Research Center, Davangere. Rats were housed in polypropylene cages and maintained under standard conditions (12 h light and 12 h dark cycle, at 23±4° C and 40-60% humidity) and provided with standard rat pellet chow feed and water *ad libitum*. The animals were acclimatized to the Central animal house conditions before experimentation.

**Grouping of the animals for treatment (*Wistar albino rats*):** The rats were divided into six groups of six animals each for 90 days study and they were placed individually in different cages, one rat each in one cage. After 1 week of adaptation period, treatment is started.

**Group 1:** Rats were fed Normal-Diet (ND) and treated with distilled water (DW).

**Group 2:** Rats were fed Cafeteria-Diet (CD) + ND and treated with DW.

**Group 3:** Rats were fed the CD + ND and treated with Cr.Pic 10 mg/kg/day.

**Group 4:** Rats were fed the CD + ND and treated with CL 10 mg/kg/day.

**Group 5:** Rats were fed the CD + ND and treated with CL 20 mg/kg/day.

**Group 6:** Rats were fed the CD + ND and treated with CL 40 mg/kg/day.

Test solutions were prepared fresh daily and the dose volume was adjusted to 1 ml/day.

All the rats were treated orally once daily with their respective drugs (Group 3 to 6) and they received fixed quantity of Cafeteria-diet as mentioned below and table-1 and pellet-chow (ND) & water *ad libitum* for 90 consecutive days except Group 1, which was fed only with pellet-chow & water *ad libitum*.

#### Composition of Cafeteria-Diet (CD):

The Cafeteria-Diet consisted of 3 diets: (a) Condensed Milk (8g) + Bread (8g); (b) Chocolate (3g) + Biscuit (6g) + Dried coconut (6g); (c) Cheese (8g) + Boiled Potato (10g). The three diets were presented to the individual rats on day one, two and three, respectively, and then repeated in the same succession. The caloric value of CD is given in **Table 1**.<sup>13</sup>

**TABLE 1: CALORIC VALUE OF CAFETERIA DIET**

Ingredients	Caloric Value (kcal/100g)
Condensed Milk	335
Bread	230
Chocolate	550
Biscuit	360
Dried Coconut	660
Cheese	320
Boiled potato	80

#### Sample Collection:

During the treatment period, the animals were observed daily for toxic manifestations. Blood serum glucose parameter was assessed on 0<sup>th</sup>, 30<sup>th</sup>, 60<sup>th</sup> and 90<sup>th</sup> day of treatment. Blood samples were collected from the retro-orbital plexus of each rat after induction of mild anesthesia with ether using micro capillary tubes<sup>14</sup> for serum glucose estimation.

#### Statistical Analysis:

The results obtained were expressed as mean  $\pm$  S.D and subjected to Analysis of Variance (ANOVA) and Multiple Comparison Test using SPSS statistical package (Version: 17.5). The difference between the means with p values < 0.05 were considered statistically significant.

Within the group comparison was made between initial (Day '0') reading and readings recorded at different intervals (durations) of their respective groups to overcome the disparity in initial values between the different groups. Percent change was

calculated by keeping the initial reading as 100% to assess the trend of change occurring during specific treatment period. In between group comparison was made, group 2 was compared with group 1 to assess the CD induced hyperglycemia and all the groups were compared with group 2 & 3.

#### RESULTS:

##### Within group comparison (Table. 2, 2a & Fig. 1):

**Group 1:** There was no significant change in serum glucose after 30, 60 & 90 days compared to day 0. Percent change varied from 0.92% after 30 days and 8.35% after 90 days.

**Group 2:** Compared to day 0 the serum glucose was increased to significant (p < 0.001) extent after 30, 60 & 90 days. Variation in percent change was from 41.08 % on 30<sup>th</sup> day to 102.65% on 90<sup>th</sup> day.

**Group 3:** Significant (p < 0.001) increase in glucose level after 30, 60 & 90 days compared to

day 0. The percent change was 22.23 % after 30 days and 46.53% after 90 days respectively.

**Group 4:** Serum glucose was increased significantly ( $p < 0.001$ ) after 30, 60 & 90 days compared to initial level. The percent change was 17.64% after 30 days and 39.85% after 90 days.

**Group 5:** Compared to day 0 there was significant increase in serum glucose after 30 days ( $p < 0.01$ ), 60 & 90 days ( $p < 0.001$ ). The level fluctuated between 10.80% to 26.96% after 30 & 90 days respectively.

**Group 6:** Serum glucose level was significantly increased after 30 ( $p < 0.05$ ), 60 & 90 days ( $p < 0.001$ ). The variation in the percent change was

from 7.48 % (after 30 days) to 17.00% (after 90 days).

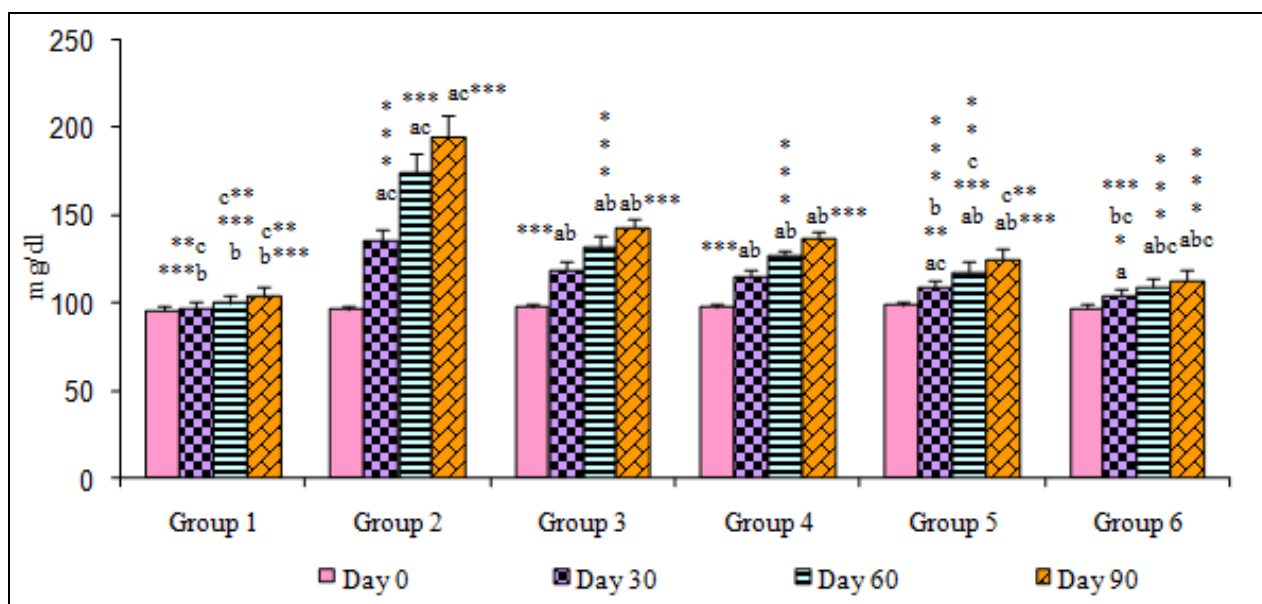
**Between groups comparison (Table 2 and Fig. 1)**  
 Compared to group 1, there was significant increase in serum glucose level in group 2 on all the experimental days ( $p < 0.001$ ). The serum glucose level was significantly ( $p < 0.001$ ) decreased in all the groups of the experimental days throughout the study, compared to group 2.

Serum glucose level was less in group 1 on day 30, 60 & 90 ( $p < 0.01$ ) compared to group 3. Significant decrease in the serum glucose level was seen in group 5 on day 60 & 90 ( $p < 0.01$ ) & group 6 on day 30, 60, 90 ( $p < 0.001$ ) compared to group 3.

**TABLE 2: EFFECT OF CL ON SERUM GLUCOSE (MG/DL) IN WISTAR ALBINO RATS FED WITH CD**

Duration	Group 1 Normal Diet (ND)	Group 2 Cafeteria Diet (CD) + ND	Group 3 CD + ND + CrPic. 10mg/Kg	Group 4 CD + ND + CL 10mg/Kg	Group 5 CD + ND + CL 20mg/Kg	Group 6 CD + ND + CL 40mg/Kg
Day '0'	95.76 ± 2.99	96.49 ± 2.28	97.65 ± 1.58	97.63 ± 1.94	98.62 ± 1.80	96.93 ± 2.29
Day '30'	96.64 ± 4.74 b***c**	136.13 ± 6.04 ac***	119.36 ± 4.88 ab***	114.86 ± 4.03 ab***	109.28 ± 3.48 ac** b***	104.18 ± 3.61 a*bc***
Day '60'	100.24 ± 3.79 b***c**	174.53 ± 10.69 ac***	131.76 ± 6.44 ab***	127.04 ± 3.21 ab***	117.97 ± 6.42 ab***c**	109.09 ± 4.87 abc***
Day '90'	103.76 ± 5.60 b***c**	195.54 ± 11.34 ac***	143.08 ± 4.98 ab***	136.55 ± 4.67 ab***	125.21 ± 5.96 ab***c**	113.41 ± 5.08 abc***

n=6. Mean ± S.D. a - compared with day '0', b - compared with group '2', c - compared with group '3'. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ .



**FIG. 1: EFFECT OF CL ON SERUM GLUCOSE (mg/dl) IN WISTAR ALBINO RATS FED WITH CD**



TABLE 2A: EFFECT OF CL ON SERUM GLUCOSE IN WISTAR ALBINO RATS FED WITH CD (PERCENT CHANGE)

Duration	Group 1 Normal Diet (ND)	Group 2 Cafeteria Diet (CD) + ND	Group 3 CD + ND + Cr.Pic 10mg/Kg	Group 4 CD + ND + CL 10mg/Kg	Group 5 CD + ND + CL 20mg/Kg	Group 6 CD + ND + CL 40mg/Kg
Day '0'	-	-	-	-	-	-
Day '30'	0.92	41.08	22.23	17.64	10.80	7.48
Day '60'	4.68	80.88	34.93	30.12	19.62	12.55
Day '90'	8.35	102.65	46.53	39.85	26.96	17.00

Percent change calculated by keeping the '0' day value as 100%

**DISSCUSSION:** In the present study, group 1 rats were fed with pellet chow (normal diet) and water *ad libitum*. Group 2, 3, 4, 5 and 6 rats were fed with fixed quantity of Cafeteria-diet and pellet-chow (ND) and water *ad libitum* for 90 consecutive days, which produced significant increase in the serum glucose level in group 2, 3, 4, 5 and 6 on day 30, 60 and 90 respectively compared to their initial (day 0) serum glucose level.

Serum glucose level was in the normal limits throughout the study period without any significant fluctuation in control animals (group 1). In Cafeteria Diet group (CD) there was increase in glucose level and it seems to be duration dependent since there was a steady increase during the course of the experimental period. Though there was a duration dependent increase in glucose level in Cr.Pic group 3 the increase was less than that seen with CD group 2 indicating a suppressive impact on CD induced hyperglycemia.

Treatment with *Caralluma lasiantha* extract in the dose range of 10 - 40 mg/kg/day significantly reduced the increase in serum glucose level compared to group 2 rats. Decrease in serum glucose was in a dose-dependent manner, during treatment with *Caralluma lasiantha*.

Serum glucose levels of *Caralluma lasiantha* treated rats at a dose of 10 mg/kg/day were comparable to group 3 rats treated with Cr.Pic 10 mg/kg/day. *Caralluma lasiantha* at a higher dose of 20 and 40 mg/kg/day decreased serum glucose levels significantly on 30<sup>th</sup>, 60<sup>th</sup> and 90<sup>th</sup> day when compared to group 3 rats treated with Cr. Pic 10 mg/kg/day. In the highest dose studied a trend towards normal level was seen indicating that *Caralluma lasiantha* is most effective in decreasing the CD induced hyperglycemia than Cr.Pic (10 mg/kg/day).

The results observed in present study shows that the *Caralluma lasiantha* extract has anti-hyperglycemic effect. Such an effect has been reported earlier with other *Caralluma* species. *Caralluma sinaica* extract was reported for its antidiabetic activity and was found to contain chemical constituents like phenolic alkaloids, glycosides, flavonoids, coumarins, steroids and tannins.<sup>11</sup> *Caralluma attenuata* claimed to be a cure for diabetes, has been reported to have luteolin-4'-*O*-neohesperidoside.

Similarly *Caralluma tuberculata* claimed to be a cure for diabetes and stated to have luteolin-4'-*O*-neohesperidoside<sup>15</sup> has been shown to possess hypoglycemic activity. Since *Caralluma lasiantha* has been reported to contain pregnane glycosides, flavonoid glycosides, and luteolin neohesperidoside compounds,<sup>16</sup> the anti-hyperglycemic activity of the plant extract observed in the present study could be attributed to the presence of these chemical constituents.

The anti-hyperglycemic activity of *Caralluma lasiantha* (10, 20 and 40 mg/kg/day) on cafeteria diet induced hyperglycemia showed significant effect when compared to untreated *Caralluma lasiantha* group in a dose dependant manner.

**CONCLUSION:** Experimental results obtained in the present *in vivo* animal study indicates that the oral administration of Methanolic extract of *Caralluma lasiantha* possess anti-hyperglycemic effect in Cafeteria-Diet induced hyperglycemia in *wistar albino* rats. It has to confirm by further extensive studies for clinical usefulness of *Caralluma lasiantha* on hyperglycemia.

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