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Evaluation of Antihyperglycemic and Lipid Lowering Activity of Caralluma Fimbriata in Diabetes Induced rats.

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ABSTRACT

This study evaluates antihyperglycemic and lipid lowering activity of *Caralluma fimbriata* in dexamethasone induced diabetic rats. Serum glucose and lipid lowering activity of *Caralluma fimbriata* was tested at dose of 50 mg/kg and 100 mg/kg per oral route against dexamethasone induced hyperlipidemia and hyperglycemia in Sprague-Dawley (SD) rats. On day 11, blood was collected for the estimation of serum glucose and lipids. *Caralluma fimbriata* in both the doses significantly decreased Serum glucose, total cholesterol, triglyceride and LDL as compared to dexamethasone only group ($P < 0.05$). *Caralluma fimbriata* has a significant antihyperglycaemic and lipid lowering activity in experimental rat models of diabetes.

Keywords: *Caralluma fimbriata*, glucose, lipid, dexamethasone, diabetes

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INTRODUCTION

The new millennium has witnessed the emergence of a modern epidemic, the metabolic syndrome, with frightful consequences to the health of humans worldwide. The metabolic syndrome, also referred to as "Diabesity" describes the increasing incidence of diabetes in combination with obesity as a result of changes in dietary pattern and the adoption of more sedentary lifestyles.¹ About 150 million people are suffering from diabetes worldwide and this may double by the year 2030. India leads the way with its largest number of diabetic patients in any given country. It has been estimated that number of diabetes in India is expected to reach 57.2 million by the year 2025.²

Diabetes mellitus is managed by insulin and oral hypoglycemic drugs such as sulfonylureas, biguanides, thiazolidenediones and α glucosidase inhibitors.³ Oral antidiabetic agents have not been much successful in maintaining euglycaemia and controlling long-term microvascular and macrovascular complications and they are also associated with number of side effects.⁴ Hence the search for safer and more effective hypoglycemic agent has continued to achieve better euglycemia and to prevent long term complications.

The use of herbal medicines for the treatment of diabetes mellitus has gained importance throughout the world. The World Health Organization also recommended and encouraged this practice especially in countries where access to the conventional treatment of diabetes is not adequate.⁵

Caralluma fimbriata is an edible cactus from the Asclepiadiceae family. The plant vary from thin, recumbent stems from ½ to 1½ inches thick to erect growing clumps up to 8 inches high. The star-shaped, fleshy flowers of these plants are some of the worst smelling of the succulent plants. Ordinarily borne in late summer, the foul-smelling blossoms are usually colored purple, black, yellow, tan, maroon, red or dark brown. In the wild, these blossoms are pollinated by flies which are greatly attracted to the plant. It is commonly used as a vegetable in several regions of India. It is eaten raw or cooked with spices. It is also used in pickles and chutneys.

A randomized placebo controlled clinical trial has shown that *Caralluma fimbriata* extract in a dose of 1 gm per day for 60 days has shown significant appetite suppressant and weight reduction activity as compared to placebo.⁶ The literature search showed no report of antihyperglycemic and lipid lowering activity of *Caralluma fimbriata*. It would be of great clinical significance in the treatment of diabesity if the same drug has weight reducing as well as blood glucose and lipid lowering activity.

MATERIALS AND METHODS:

Animals:

Sprague-Dawely rats of either sex weighing 150-200 gms were used in the present study. Animals were fed with commercially available 'Amrut rat pellet feed' manufactured by Pranav Agro Food, Pune. Rats were housed in groups of three, in a standard big polypropylene cages having wire mesh top with provision for drinking water and space for pellets. Husk was used as bedding material in each cage. The study was approved by the Institutional Animal Ethics Committee.

Dexamethasone induced diabetes

Rats were fasted overnight before administration of dexamethasone.

Rats selected at random were divided into following groups. (n = 10 each group)

Group I :Normal control – Rats were given distilled water 1 ml once daily subcutaneously for 11 days

Group II : Dexamethasone control – Rats were given dexamethasone 10 mg/kg once daily subcutaneously for 11 days.

Group III: Dexamethasone + Metformin - Rats were given Dexamethasone 10 mg/kg once daily subcutaneously and Metformin 45 mg/kg orally once a day for 11 days.

Group IV: Dexamethasone + 50 mg/kg *Caralluma fimbriata* - Dexamethasone 10 mg/kg once daily subcutaneously and 30% *Caralluma fimbriata* extract 50 mg/kg orally once a day for 11 days.

Group V: Dexamethasone + 100 mg/kg *Caralluma fimbriata* - Dexamethasone 10 mg/kg once daily subcutaneously and 30% *Caralluma fimbriata* extract 100 mg/kg orally once a day for 11 days.

On day 11, overnight fasted animals were anesthetized with ether and blood was collected by retro-orbital puncture for estimation of blood glucose and lipid profile. Fasting blood glucose was estimated by Optium Xceed glucometer and lipid profile (Total cholesterol, Triglyceride, LDL and HDL) was estimated manually on spectrophotometer. All the reagents for estimation of lipid profile were purchased from Erba Mannheim.

RESULTS AND DISCUSSION:

Results are expressed as mean \pm SEM and statistical significance between means was analyzed using one-way analysis of variance (ANOVA) followed by Tukey multiple comparison test. Value of $p < 0.05$ was considered as statistically significant.

Effect on serum glucose:

Dexamethasone administration resulted in significant increase in the serum glucose ($P < 0.05$). This rise in serum glucose with dexamethasone was prevented by 50 and 100 mg/kg of *Caralluma fimbriata*. Serum glucose of 100 mg/kg of *Caralluma fimbriata* group was comparable to 45 mg/kg of metformin group and control group. (Figure-1)

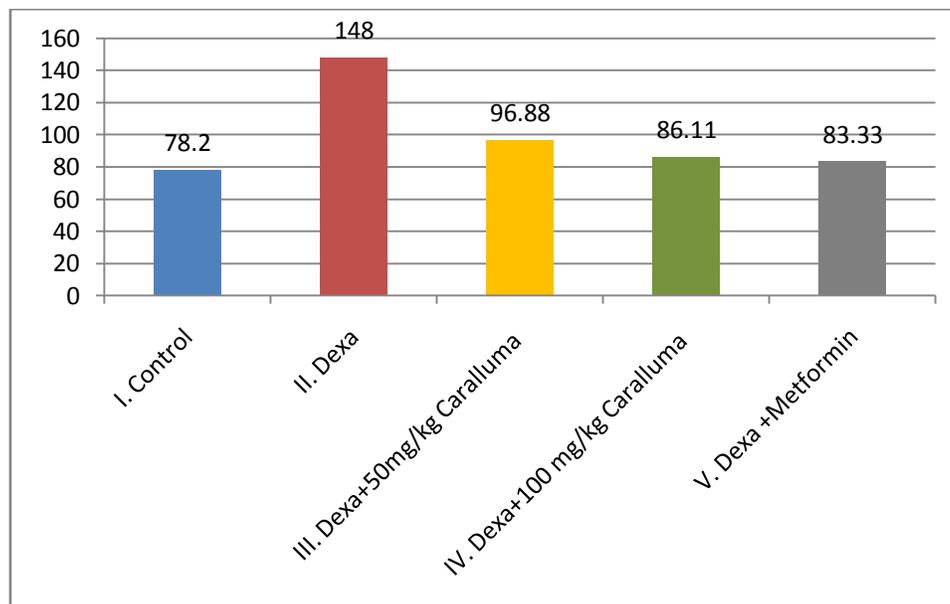


Figure - 1: Serum Glucose levels

$P < 0.05$, II vs I. $P < 0.05$, III vs II. $P < 0.05$, IV vs II. $P < 0.05$, V vs II ($F = 77.83$, $P < 0.001$, Highly significant difference is seen.)

Effect on lipid levels:

Dexamethasone administration resulted in significant increase in the total cholesterol, triglyceride and LDL ($P < 0.05$). *Caralluma fimbriata* in the dose of 50 and 100 mg/kg significantly lowered total cholesterol, triglyceride and LDL than dexamethasone group ($P < 0.05$). Metformin significantly lowered total cholesterol, triglyceride and LDL as compared to dexamethasone only group ($P < 0.05$). Total cholesterol, triglyceride and LDL level of 100 mg/kg of *Caralluma fimbriata* was comparable to metformin group and control group. There was no significant difference in the HDL level in all the groups. (Table-1)

Increase in the prevalence of metabolic syndrome put lots of burden to health care system especially in developing countries which are already straining under the burden of communicable diseases.⁷ In such a scenario use of alternative medicine such as herbal medicine can play an important role, as these drugs are comparatively safer and have low cost. Plant selected for the present study was *Caralluma fimbriata* locally known as Makadshingi.

Table-1: Serum Lipid levels

	Treatment	T Cholesterol (mg/dl)	Triglyceride (mg/dl)	LDL (mg/dl)	HDL mg/dl
I.	Control	89.1 ± 2.43	79.89 ± 1.78	37.44 ± 2.76	35.67 ± 1.33
II.	Dexamethasone (10 mg/kg)	131.9 ± 2.45*	112.2 ± 1.45*	74.98 ± 3.71*	34.43 ± 1.89
III.	Dexa + 50 mg/kg Caralluma fimbriata	106.6 ± 1.44 [#]	92.7 ± 1.65 [#]	53.1 ± 1.35 [#]	34.98 ± 1.08
IV.	Dexa + 100 mg/kg Caralluma fimbriata	93.77 ± 1.36 [†]	87.29 ± 1.25 [†]	40.71 ± 1.28 [†]	35.6 ± 1.07
V.	Dexa+ 45 mg/kg Metformin	91.66 ± 1.37 ^Δ	91.68 ± 1.78 ^Δ	38.55 ± 1.26 ^Δ	34.77 ± 0.81

* **P < 0.05, II vs I.** # **P < 0.05, III vs II.** † **P < 0.05, IV vs II.** Δ **P < 0.05, V vs II**

Subcutaneous administration of dexamethasone is a well established model of insulin resistance and hyperglycemia. Dexamethasone induces whole body insulin resistance by targeting mainly skeletal muscle, liver, adipose tissue and thereby decreases glucose utilization, increases glucose output and lipogenesis. In this study, daily subcutaneous administration of dexamethasone in a dose of 10 mg/kg for a period of 11 days was found to lead to insulin resistance, hyperglycemia and dyslipidemia characterized by increase in triglyceride, LDL and total cholesterol as reported in the previous studies.⁸⁻¹⁰

We have used 50 mg/kg and 100 mg/kg doses of Caralluma fimbriata extract. Oral administration of Caralluma fimbriata extract in both the doses was associated with significant lowering of blood sugar levels as compared to only dexamethasone administered rats ($P < 0.05$). Thus both the doses of Caralluma fimbriata were effective as antihyperglycemic, however 100 mg/kg dose of Caralluma fimbriata was found to be more effective.

Caralluma fimbriata significantly lowered total cholesterol, triglyceride and LDL than dexamethasone only group in a dose dependent manner ($P < 0.05$). This lipid lowering effect produced by 100 mg/kg Caralluma fimbriata was comparable to 45 mg/kg of metformin.

Caralluma fimbriata is safer to use. In addition to the long history of safe ingestion of the cactus as a food, further evidence of safety of its extract is evident through an acute oral toxicity study on rats which had shown that LD50 of Caralluma fimbriata for the rats exceeded 5g/kg.¹¹

Two clinical trials have been conducted so far for the evaluation of weight reduction activity of Caralluma fimbriata. Randomised placebo controlled clinical trial, conducted by Kurian et al, at Bangalore had shown that Caralluma fimbriata extract in a dose of 1 gm per day for 60 days causes significant appetite suppressant and weight reduction activity as compared to placebo. The adverse events were minor and limited to mild upset of the gastrointestinal tract.⁶

Proposed mechanisms for weight reduction of Caralluma fimbriata is that pregnane glycosides prevent fat accumulation via blocking citrate lyase. It also causes blockade of malonyl

Coenzyme A which could further lead to a decrease in fat formation in the metabolic pathway. *Caralluma fimbriata* is reported to suppress appetite hypothesized to be secondary to effects on the appetite control center of the brain.¹¹

Mechanism of hypoglycemic action of *Caralluma fimbriata* is not clearly understood. It has been reported to contain chemical constituents like pregnane glycosides, flavone glycosides, megastigmane glycosides, bitters principles, saponins etc. Several investigators have shown that flavonoids possess hypoglycemic effects in various experimental animal models.¹⁰ This hypoglycaemic action can be due to release of insulin, insulin sensitization or combination of both. Hence further studies need to be undertaken to determine the mechanism of action by measurement of either insulin or 'C' peptide levels.

CONCLUSION:

Oral administration of *Caralluma fimbriata* results in lowering of serum glucose and lipid levels in dose dependent manner. Antihyperglycemic and lipid lowering activity of *Caralluma fimbriata* is comparable to metformin.

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