EFFECT OF *CARALLUMA FIMBRIATA* EXTRACT IN ALLOXAN INDUCED DIABETIC RATS

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ABSTRACT

Abstract: There is a need to search for newer antidiabetic agents that retain therapeutic efficacy and reduce the side effects and also risk factor like hyperlipidemia, hypertension. **Method:** Wistar rats of either sex weighing 150-200 grams were divided into 5 groups (n=6 in each group). Rats in Group 3, Group 4 and Group 5 were made diabetic by single i.p., injection of 150 mg kg bw of alloxan monohydrate and group 4,5 treated with *Caralluma fimbriata* (n=8), Glibenclamide (600mcg/kg b.w) + *Caralluma fimbriata respectively.* Liver function tests, Kidney function tests, Glucose and insulin were studied initially and end of the study. **Result:** Rats in Diabetic control lost body weight significantly ($p<0.001$) compared to normal control group. Reduction in body weight was prevented (insignificantly) by CFE and test drug treatment. Diabetic groups (Group 3, 4 and 5) blood glucose and serum insulin levels were significantly ($p<0.001$) high at the beginning of the study. From day 10 onwards, rats in standard drug (Glibenclamide) treatment group (Group 5) blood glucose and serum insulin values were reduced significantly ($p<0.001$) compared to Diabetic control group (Group 3). Rats treated with CFE were also shown significant reduction ($p<0.05$) in blood glucose and serum insulin levels from day 30 compared to Diabetic Control group and were comparable to standard treatment group. Increased levels of SGOT, SGPT and ALP were came back to normal after standard drug and CFE treatment. Kidney function test were normal and no significant differences were observed. **Conclusion:** The dry extract of *Caralluma fimbriata* significantly controlled the diabetic condition including oxidative stress in liver.

KEYWORDS: *Caralluma fimbriata*, Alloxan induced diabetic, Glibenclamide, Rat

INTRODUCTION

Diabetes mellitus is a global health problem throughout the world [1]. Which is characterized by derangement in carbohydrate, fat and protein metabolism, affecting nearly 10% of the population [2]. In the year 2000, 150 million people world-wide had diabetes, and this is expected to double by 2010 This global pandemic principally involves type 2 diabetes, and is associated with several contributory factors such as increased longevity, obesity, unsatisfactory diet, sedentary lifestyle[3]. Globally, type 1 DM affects considerable percentage of population and it leads to morbidity and mortality of the diabetic patients. The plasma lipids usually raised in Diabetic which causes risk factor for Coronary Heart disease [4]. The treatment of Diabetic mellitus is based on oral hypoglycaemic agents and insulin [5]. Lack of insulin affects the metabolism of carbohydrate, protein and fat, and causes a significant disturbance of water and electrolyte homeostasis, the actions of insulin are also impaired by insensitivity of target tissues [3]. The oral hypoglycaemic agents currently used in clinical practice have characteristic some serious side effects. In both type 1 and type 2 diabetes, the actions of insulin are also impaired by insensitivity of target tissues. While this is a fundamental defect in type 2 diabetes, hyperglycaemia can also reduce insulin secretion by the effect of glucose toxicity on beta cell function.

Hence, there is a need to search for newer antidiabetic agents that retain therapeutic efficacy and reduce the side effects and also risk factor like hyperlipidemia, hypertension and so on [6]. There is an increased demand by patients to use natural products with antidiabetic activity. Hence, today there is need for finding the alternatives which will minimize the side effects and the cost of drug. Therefore it become necessary to make use of vast reserves of plant origins for medical purposes which will help to search effective as well as safer drug remedy for diabetes mellitus.

Caralluma fimbriata plant having synuonym *caralluma ascendens* which belongs to family Asclepiadaceae. It is wisdly found in Africa, the Canary Islands, India, Arabia, southern Europe,

Afaganisthan. *Caralluma fimbriata* is a dry herb growing in the dry parts of the india. *Caralluma fimbriata,* a traditional Indian "famine food" with no history of adverse effects[7].The key phytochemical constituents of the herb are pregnane glycosides, flavone glycosides, megastigmane glycosides, and saponins. Some of the active components present in this plant are Caratuberside A, Caratuberside B, Bouceroside IX, Tomenkogenin, Sitosterol etc [8].

The plant is found to have anti-oxidant activity hence it can be used in the treatment of diabetes mellitus. Fresh leaf extract of *Caralluma fimbriata* has been reported to reduce blood glucose in normal and alloxan diabetic rabbits.

In this study the prolonged effect (up to 50 days) of the dry extract of whole plant of *Caralluma fimbriata* on blood glucose, and biochemical parameters such as serum insulin, liver function tests (SGOT, SGPT, ALP) and kidney function tests (serum creatinine, blood urea and uric acid) levels were studied in alloxan induced diabetic rats. This study was designed to examine the hypoglycemic effects of *Caralluma fimbriata* on alloxan induced Diabetes Mellitus based on the local uses of the plant for the treatment of diabetes mellitus.

MATERIALS AND METHODS

Animals: Wistar rats of either sex weighing 150-200 gms obtained from Central animal house, BLDEU's Shri BM Patil Medical College, Hospital & Research Center were used in the present study. Animals were fed with commercially available 'Rat pellet feed' manufactured by VRK Nutritional Solutions, Sangli, Maharashtra. 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. They were maintained at a temperature of 25 ± 50C and relative humidity of 50% to 55%. The study was approved by the Institutional Animal Ethics Committee.

GROUPING OF ANIMALS:

Rats selected at random were divided into following groups. (n=8 each group)

Group 1: Control (n=8), **Group 2:** Animals receiving *Caralluma fimbriata* (n=8), **Group 3:** Alloxan induced diabetic rats (n=8), **Group 4:** Alloxan induced diabetic rats + *Caralluma fimbriata* (n=8), **Group 5:** Alloxan induced diabetic rats + Glibenclamide (600mcg/kg b.w) + *Caralluma fimbriata* (n=8)

Caralluma fimbriata dry extract is given in the dose of 100mg/kg/day orally in boiled milk as vehicle

Alloxan-induced hyperglycemia:

Rats in Group 3, Group 4 and Group 5 were made diabetic by single i.p., injection of 150 mg kg bw of alloxan monohydrate (AVRA Synthesis Private Limited, Hyderabad, Telangana) by method of Nagappa et al. (2003).[9] Since, alloxan is capable of producing fatal hypoglycemia as a result of massive pancreatic insulin release, rats were kept for next 24 h on 5% w/v glucose solution to prevent hypoglycaemia as per Gupta et al. (1984).[10] 10 days later blood samples were drawn and glucose levels were determined to confirm development of diabetes (>250 mg dl). Those rats showing Blood glucose levels more than 250mg/dl were included in the study.

Assessment: Blood samples from the experimental rats were collected from retro orbital vein. The collected blood samples were analyzed for

- Liver function tests (toxicity markers): Initially and at the end of the study
  - SGOT, SGPT, ALP.
- Kidney function tests (toxicity markers): Initially and at the end of the study
  - Creatinine, urea and uric acid.
- For every 10 days
  - Glucose and insulin.

Body weight and food consumption was measures for every 10 days.

RESULTS

Table 1: Showing values of Liver Function Tests

Group	SGOT		SGPT		ALP	
	Day 0	Day 50	Day 0	Day 50	Day 0	Day 50
Normal Control	22±1.4	52.66±2.2	18.38±1	52.75±2.8	216.75±14	304.13±3.3
NC+CFE	23.13±1.6	53±3.7	18.38±0.8	50.13±1.9	221.38±14	316.25±6.7
Diabetic Control	47.38±5.7	73.38±4.7*	37.25±6.5	45.13±5.9*	312.25±15	385.25±15*
Diabetic + CFE	43.63±3.2	47.66±2.2#	43.63±2.3	49.25±3.4#	302.38±11	285.75±11#
Diab + Glib+ CFE	42.25±3.9	46±3#	40.88±3.3	49.25±1.4#	309.25±13	265.63±7#

**p<0.001 compared to normal control, #p<0.05 compared to diabetic control,* data presented as mean±SEM

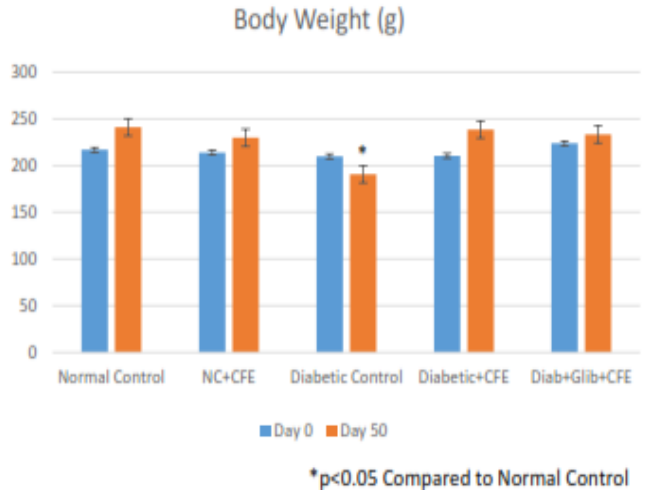

Fig 1: Showing Body weight in various groups

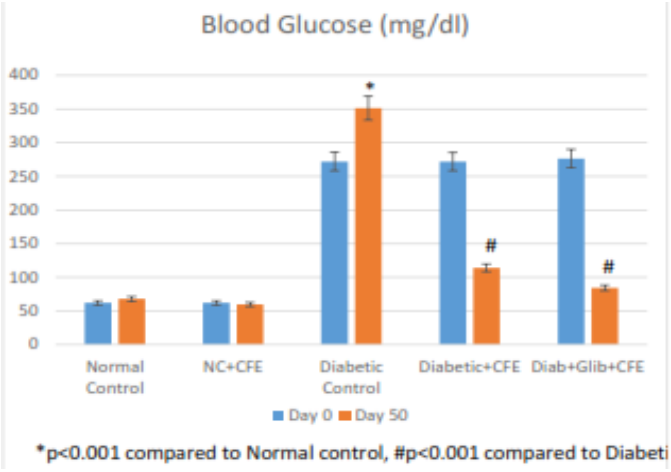

Fig 1: Showing Blood Glucose levels in various groups

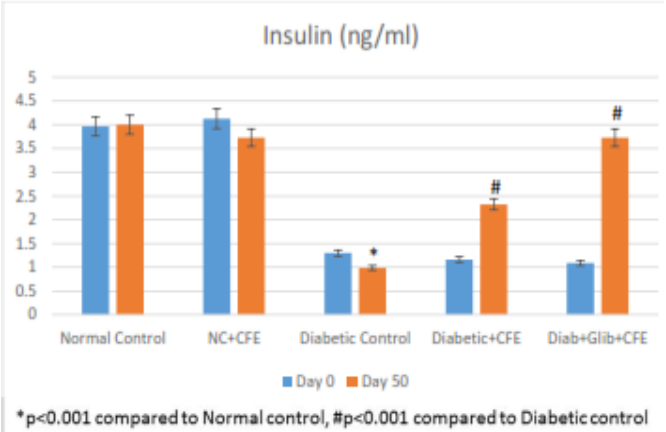

Fig 2: Showing Serum Insulin levels in various groups

Body weight, insulin and blood glucose values were shown in (Fig 1-3). The 0 day values of Normal Control (Group 1) and Normal Control+CFE (Group 2) were comparable. Body weight in all the groups except Diabetic control group were comparable throughout the study period. Rats in Diabetic control lost body weight significantly (p<0.001) compared to normal control group. Reduction in body weight was prevented (but not significantly) by CFE and test drug treatment. Diabetic groups (Group 3, 4 and 5) blood glucose and serum insulin levels were significantly (p<0.001) high at the beginning of the study. From day 10 onwards, rats in standard drug (Glibenclamide) treatment group (Group 5) blood glucose and serum insulin values were reduced significantly (p<0.001) compared to Diabetic control group (Group 3). Rats treated with CFE were also shown significant reduction (p<0.05) in blood glucose and serum insulin levels from day 30 compared to Diabetic Control group and were comparable to standard treatment group. Increased levels of SGOT, SGPT and ALP were came back to normal after standard drug and CFE treatment (Table 1). Kidney function test were normal and no significant differences were observed.

DISCUSSION

Diabetes Mellitus is a metabolic disorder characterized by a loss of glucose homeostatis with the disturbance of carbohydrates, fat, protein metabolism resulting from defects in insulin [11]. In our

study, diabetes was induced in rats by single intraperitoneal injection of alloxan 150mg/kg b.w [9] and the hepatoprotective, antidiabetic activity of CFE was determined. Treatment of Diabetes mellitus with oral hypoglycemic agents like sulphonylurea and biguanide is associated with severe adverse effects [12]. Therefore, herbal drugs are gaining importance in the treatment of various diseases. The administration of alloxan to the

normal rats results in the destruction of beta cells of Islets of Langerhans and malfunctioning of the pancreas. This results in the diabetic condition leading to the increase in the blood glucose levels and decreased body weight in the untreated diabetic rats. Due to the action of alloxan, the beta cells undergo destruction of necrosis [13]. The elevation of blood glucose in alloxan induced diabetic rats may be due to lower levels of plasma insulin [14]. We observed a significant reduction of blood glucose in CFE and Glibenclamide treated diabetic rats was compared to diabetic control. This is due to the pancreatic secretion of insulin from beta cells of the Islets of Langerhans. Increased insulin levels in CFE treated rats showed the possible mechanism of glucose uptake. The obtained result is similar to *Caralluma edulis* [15], *Calocybe indicia* [16], *Helianthus annuus* [17], *Swertia chirayita, Andrographis paniculata* [18] and *Xanthosoma sagittifolium* [19] treated diabetic rats.

The blood glucose level was estimated in both normal and alloxan induced diabetic rats. After treatment with alloxan, the fasting blood glucose level was significantly increased and it was significantly ($p< 0.05$) reduced by 50 days treatment with CFE. On the progression of treatment with CFE, blood glucose reduced from 30th day. In alloxan induced diabetic rats, CEF treatment increased the body weight and reduced plasma glucose levels. The results showed that the decreased postprandial glucose in animals may be correlated with decreased gluconeogenic activity [20]. So, this may be the reason for the increased body weight in CEF treated rats [21]. Serum transaminases are responsible for producing ketone bodies from amino acids and produce increased concentration of glucose levels [22]. Increase in SGOT and SGPT results in increased glucose levels. After the treatment with *Caralluma fimbriata*, SGPT, SGOT levels was brought back to normal suggesting the regeneration process. Similar results found in Xanthosoma sagittifolium treated diabetic rats [19]. Reduction in ALP shows its stability of biliary function against the damage caused by alloxan.

CONCLUSION

The dry extract of *Caralluma fimbriata* significantly controlled the diabetic condition including oxidative stress in liver. Further investigations regarding the synergistic activity of the extract and phytochemical isolation are to be done.

Conflict of interest: Nil

REFERENCES

1. A.H. Morkadad, E.S. Ford, B.A. Bowman, D. E. Nelson, M.M. Engelgau, F. Vincor, J. S. Marks.(2000), Diabetes trends in the U.S: 1990-1998. Diabetes Care 23, 1278-1283.
2. Kirithikar, K.R., Basu, B.D., An, I.C.S., 1995. Indian Medicinal Plants. Vol.1, International book distributors, Dehradun, India, 371 – 372.
3. DEVIDSONS PRINCIPLES AND PRACTICE OF MEDICINE 19 TH EDITION. PG NO.641.
4. B.-K. Yang, S.-C. Jeong, H.-J. Lee, D.-H. Sohn, C.-H. Song. "Antidiabetic and hypolipidemic effects of Collybia confluens mycelia produced by submerged culture in streptozotocin-diabetic rats," Archives of Pharmacal Research, 2006; 29(1):73–79.
5. Chattopadhyay et al. , 1993; Ponnachan and Panikkhar, 1993; Subramonium et al. 1996) . The oral hypoglycaemic agents currently used in clinical practice have characteristic profiles of serious side effects (Prout, 1974; Holm an and Tuener, 1991).
6. Kumar et al. 249 Prout TE Malaisse WJ, Pirart J (1974) Proceedings VIII Congress of International Diabetes Federation, Excerpta Medica, Amsterdam, pp. 162. (2005).
7. Bansi Saboo, Dia care, Hemant Zaveri, Recent update in management of obesity and Overweight Patients: Standardized extract of *Caralluma fimbriata* safe and effective Therapy. International Journal of Clinical Cases and Investigations 2011. Volume 2 (Issue 1), 5:9, 6th February 2011.
8. Scientific Opinion on the substantiation of a health claim related to ethanol-water extract of *Caralluma fimbriata* (Slimaluma and helps to reduce body weight pursuant to Article 13(5) of Regulation (EC) No 1924/20061 EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA).
9. Nagappa, AN., PA Thakurdesai, NV Rao and J. Singh, 2003. Antidiabetic acitivity of Termaninalia catappa Linn Fruits. I. Ethnopharmacol., 88: 45-50.
10. Gupta, M.P., N.G. Solis, M. Esposito and S. Sanchez, 1984. Hypoglycemic activity of NeuroZaena Zobata (L.). J. Ethnopharmacol., 10: 323-327.
11. Barcelo A, Rajpathak S. Incidence and prevalence of diabetes mellitus in the Americas. Am J Public Health 2001; 10:300-308.

12. Weidmann P, Boehlen LM, De-courten M. Pathogenesis and treatment of hypertension associated with diabetes mellitus. Am Heart J 1993; 125:1498-1513.
13. Szkudelski T. The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. Physiol Res 2001; 50(6):537-546.
14. Maiti R, Jana D, Das UK, Ghosh D. Antidiabetic effect of aqueous extract of seed of Tamarindus indica in streptozotocin induced diabetic rats. J Ethnopharmacol 2004; 92: 85-91.
15. Sayantan R, Abhishek S. Antidiabetic activity of Caralluma edulis bark and leaf extract against streptozotocin induced diabetic rats. NSHM J Pharm Healthcare Management 2012; 03:76-81.
16. Paramasivam R, Shanmugasundaram K. Potent antihyperglycaemic activity of Calocybe indica in streptozotocin induced diabetic rats antihyperglycemic activity of Calocybe indica. Int J Pharm Pharm Sci 2013; 5(2):512-515.
17. Shivani S, Sunil S. Antidiabetic effect of Helianthus Annuus L., seeds ethanolic etract in streptozotocin-nicotinamide induced type 2 diabetes mellitus. Int J Pharm Pharm Sci 2013; 5(2):382387.
18. Vinod KV, Khomedndra KS, Kamaruz ZMD. Antihyperglycemic activity of Swertia chirayita and Andrographis paniculata plant extracts in streptozotocin induced diabetic rats. Int J Pharm Pharm Sci 2013; 5(3):305-311.
19. Shajeela PS, Kalpanadevi V, Mohan VR, Potential antidiabetic, hypolipidaemic and antioxidant effects of Xanthosoma sagittifolium extract in alloxan induced diabetic rats. Int J Pharm Pharm Sci 2013; 5(1):27-31.
20. Oliveira HC, Dos SMP, Grigulom R, Lima LL, Martins DTO, Lima JCS, Stoppiglia LF, Lopes CF, Kawashita NF, Antidiabetic activity of Vatairea macrocarpa extract in rats. J Ethnopharmacol 2008; 115:515-519.
21. Pandikumar P, Prakash BN, Ignaciumuthu S. Hypoglycemic and antihyperglycemic effect of Begonia malabarica Lam. In normal and streptozotocin induced diabetic rats. J Ethnopharmacol 2009; 124:111-115.
22. Lemieux J, Pichette C, Vinay P, Gougoux A. Cellular Mechanism of antiammoniagenic effect of ketone bodies in the dog. Am J Physiol-Renal 1980; 239(5):420-426.