



CARALLUMA FIMBRIATA LEAVES: IN-VITRO ANTIOXIDANT AND IN-VIVO ANTI-DIABETIC ACTIVITY

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ABSTRACT

A comparison of antidiabetic activity was made between ethanolic and aqueous plant extracts and a known antidiabetic drug Glimpiride by alloxan induced diabetic rat model. The dried leaves of *Caralluma fimbriata* (CF) were subjected to extraction by continuous hot percolation using ethanol as solvent and by maceration using an aqueous solvent. Dose selection was made on the basis of acute oral toxicity study (500 mg/kg). Antioxidant activity was measured using DPPH assay. The ethanolic extract (IC₅₀ 170µg/mL) and aqueous extract (IC₅₀ 220µg/mL) showed significant antioxidant activity. The administration of both ethanolic and aqueous extract of CF (500mg/kg) for a period of 7 days resulted in a significant reduction of blood glucose level. The antidiabetic activity was found more for ethanolic extract (Et CF) in comparison with aqueous extract of *Caralluma fimbriata* (Aq CF). The blood glucose level on fourteenth day of the study were found to be 127± 2.5mg/dl with Et CF treated group and 139 ± 5.2 mg/dl with Aq CF treated group in comparison of diabetic control group (296.7 ± 2.6 mg/dl). The glucose loaded rats treated with Et CF exhibited glucose level of 120.6±1.00 mg/dl after 30 min and 87.2±1.36 mg/dl after 90 min, whereas the Aq CF treated animals exhibited glucose level of 122.8±1.34 mg/dl after 30 min and 93.2±3.13 mg/dl after 90 min. The obtained results indicate that both the extracts tested have the potential to reduce the blood sugar level and can be used as herbal anti-diabetic drug.

Key words: *Caralluma fimbriata*, Anti-oxidant activity, Anti-diabetic activity, Alloxan.

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INTRODUCTION

Diabetes mellitus recognized as hyperglycemia, resulting insulin secretion defects or less insulin stroke in blood streams or both. Type 1 diabetes is a metabolic defect arises due to the deficiency of insulin secretion from β-pancreatic cells. Type 2 diabetes characterized by obesity, unhealthy food habits resulting progressive insulin

resistance with time lapse. This causes reduction in peripheral glucose disposal; due to lack of ability of the pancreatic hormone resulting suppressed hepatic glucose output (Frode TS and Medeiros YS, 2008). The incidental rate of both type 1 and type 2 diabetes are rising at peak due to environmental factors specifically related to unbalanced diet. The other major factors elevating pandemic type 2 diseases are increased longevity, sedentary lifestyle and increasing urbanization. Various ageing scavenging process like oxygen free radical initiates lipid peroxidation processes, which in cascade stimulate non-enzymatic glycosylation of protein along with the inactivation of antioxidant enzymes implicating complications of diabetes (Patil AB, 2013; Baynes JW and Thorpe SR). Flavonoids play active role in

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suppressing these scavenging bodily process. These are the low molecular weight, bioactive polyphenol component having 2 – phenyl – benzo – gamma-pyrane nucleus as core. The major source of these are present in plants as phytochemicals compounds which act as antioxidants compound with redox and metal chelating properties. Many holistic plant materials such as eucalyptus, Lebanon cedar, peppers, cinnamon and curry leaves contains essential oils prominently showing α - amylase inhibitory and antioxidant activity. These α -amylase act as one of the main enzymes in human which catalyses 1, 4 - glucosidic linkage of complex carbohydrates into simple sugars. Inhibition of the α - amylase activity is one mechanisms that can be potentially used for controlling diabetes. Preventing the breakdown of the complex carbohydrates into simple drastically have impact on effective controlling of diabetes. Many inhibitory drugs such as carbose are available which inhibits α - amylase and α - glucosidase causing type 2 diabetic giving relief in diabetes patients but with undesirable side effects, especially flatulence and diarrhea. These side effects are nullified by introduction of natural products extracted from plants having ability in controlling hyperglycemia (Patil AB, 2013). India is now leading in terms of diabetic subject considered with the terminology “diabetes capital of the world”. World Health Organization, review shows prediction of doubling of diabetes globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. Further, International Diabetes Federation, published the number of people with diabetes in India currently is around 40.9 million and warned that it may rise to 69.9 million by 2025 unless preventive step are taken (Mohan V et al., 2007). *Caralluma fimbriata* [local names: KaraIlamu (Telegu), yugmaphallottatna (Sanskrit), makadshenguli, shindalamakadi (Marathi)] belonging to family Asclepiadaceae originated from India, Arabia, southern Europe, Ceylon, and Afghanistan. *Carallumafimbriata* are abundantly flourishing in large parts of interior India, especially Maharashtra. These plants are seen mostly in urban areas prominently as on roadside and as boundary marker in gardens. It is most commonly used as a vegetable in several regions of India. *Caralluma fimbriata* are explored as new dietary ingredient for appetite suppression leading to weight-loss and as best nutraceutical agent (Saboo B et al., 2011). The investigational aim of this study was to confirm the anti-diabetic activity of *Caralluma fimbriata* *In-vivo*. To carry out the study alloxan monohydrate induced animal models of diabetes mellitus was used, in order to comprehensively evaluate the impact of the ethanolic crude extract of *Caralluma fimbriata*.

Further studies were carried out by taking the aqueous extract of *Caralluma fimbriata* on several pathological states in relation to diabetes. Namely, Type 1 diabetes was induced by alloxan monohydrate, where alloxan was used as strong oxidizing agent latter formed hemiacetal with its reduced reaction giving the product of dialuric acid (in which a carbonyl group is reduced to a hydroxyl group) which is called alloxantin (Lenzen S et al., 1996). These radicals undergo dismutation to hydrogen peroxide with a simultaneous massive increase in cytosolic calcium concentrations, which causes rapid destruction of pancreatic β -cells (Federiuk IF et al., 2004), thus representing a typical model of insulin dependence. Secondly, the effects of extract of *Caralluma fimbriata* in a pre-diabetic insulin resistance model was studied which was induced in rats with a 10% glucose solution as drinking water (Rees DA and Alcolado JC, 2004).

MATERIALS AND METHODS

Animals

Healthy adult albino rats of Wister strain of either sex between the age of 2-3 months and weighing 150-200 grams were used for the present study. The animals were housed individually in polypropylene cages, maintained under standard conditions (12 hours light and 12 hours dark cycle, 25 \pm 5°C and 40-60% humidity). They were fed with standard rat pellet diet (National Institute for Nutrition, Hyderabad) and provided water ad libitum. All the animal experiments were conducted according to the ethical norms approved by CPCSEA, Ethical committee IAEC reg. no. (1090/PO/Ac/07/CPCSEA).

Chemicals

Alloxan monohydrate, Glimpiride, Dextrose, Tween-80, Auto analyzer (Analytical technological limited) and One-touch (Horizon). All the other chemicals and reagents used were of analytical grade.

Plant Material

Fresh leaves were collected from Sangli district, Maharashtra, India and authenticated by Dr. V. S. Jadhav (Rathod), Professor, Department of Botany Shivaji University, Kolhapur, Maharashtra, India.

Preparation of Plant Extraction

The collected leaves were shade dried and powdered in a grinder mixture to get coarse powder. The powdered leaves were extracted with ethanol and aqueous. The extract was evaporated to dryness, giving a residue of 42 % w/w and 28% w/w respectively.

Phytochemical Screening:

A preliminary phytochemical screening of ethanolic extracts of *Caralluma fimbriata* was carried by using the standard procedures (Roopashree TS *et al.*, 2008; Obasi NL *et al.*, 2010; Audu SA *et al.*, 2007)

In-Vitro Antioxidant study

DPPH Assay

1, 1-Diphenyl-2-picryl-hydrazyl (DPPH•) free radical scavenging activity:

The free radical scavenging activity of CF was measured by DPPH• assay, following the methodology described by Blois, 1958 wherein the bleaching rate of the stable free radical, DPPH• is monitored at a characteristic wavelength in the presence of the sample. In its radical form, DPPH• absorbs at 517 nm, but upon reduction by an antioxidant or a radical species its absorbance decreases. Briefly, 0.1 mM solution of DPPH• in ethanol was prepared and 1ml of this solution was added to 3 ml of CF solution in water at different concentration (50-300 µg/ml). Thirty minutes later, the absorbance was measured at 517 NM. Lower absorbance of the reaction mixture indicates higher free radical scavenging activity (Blois MS, 1958; Blois MS, 2011). IC50 value in the tested compound is the concentration required to scavenge 50% DPPH• free radicals. The DPPH• radical scavenging activity was calculated according to the following equation:

$$\text{DPPH radical scavenging activity (\%)} = \left[\frac{A_0 - A_1}{A_0} \right] \times 100.$$

Where,

A_0 is the absorbance of DPPH•

A_1 is the absorbance of DPPH• solution in presence of the extract.

H₂O₂ Free radical Scavenging Assay

Hydrogen peroxide (H₂O₂) scavenging capacity assay

The hydrogen peroxide scavenging ability of CF was determined according to the method of Ruch, 1989. A solution of H₂O₂ (40 mM) was prepared in phosphate buffer (pH 7.4). Different concentrations of CF (20-100 µg/ml) in phosphate buffer were added to an H₂O₂ solution (0.6 ml, 40 mM). The absorbance value of the reaction mixture was recorded at 230 nm (Ruch RJ *et al.*, 1989). Blank solution was containing phosphate buffer without H₂O₂. The percentage of H₂O₂ scavenging of CF and standard compound was calculated as-

$$\text{H}_2\text{O}_2 \text{ radical scavenging activity (\%)} = \left[\frac{A_0 - A_1}{A_0} \right] \times 100.$$

Where,

A_0 is the absorbance of H₂O₂

A_1 is the absorbance of H₂O₂ solution in the presence of extract

Acute Oral Toxicity Studies

Acute oral toxicity studies(OECD,2003) of the extracts were carried out as per the OECD guidelines, draft guidelines 423 adopted and received from Committee for the Purpose of Supervision and Control of Experiments on Animals (CPCSEA), Ministry of social justice and empowerment, Government of India. Administration of the stepwise doses of extracts of *Caralluma fimbriata* from 40 mg/kg body weight up to the dose 5000 mg/kg body weight caused no considerable signs of toxicity in the tested animals. One tenth of upper limit dose were selected as the level for examination of anti-diabetic activity.

Experimental model

Alloxan monohydrate was first weighed individually for each animal according to their weight and then solubilized with 0.2 ml saline just prior to injection. Diabetes was induced by injecting Alloxan at a dose of 120 mg/kg body weight intraperitoneally (Sellamuthu PS *et al.*, 2009). After 1 hour of Alloxan administration, the animals were given feed ad libitum, along with 5% dextrose solution in a feeding bottle for a day to overcome the early hypoglycemic phase. The animals were kept under observation and after 72 hours blood glucose was measured by One-touch glucometer. The diabetic rats (glucose level 200-300 mg/dl) were separated and divided into six different groups for experimental study, with each group containing six animals.

Experimental Design

Different groups of rats were used to study the effects of ethanolic and aqueous extract of *Caralluma fimbriata*. The rats were divided into five groups, each consisting of six rats.

Group-I: Normal/control animals received 1% tween80, 1ml per orally.

Group-II: Alloxan (120mg/kg body weight) induced diabetic animals received 1% tween80, 3ml/kg body weight per orally.

Group-III: Alloxan (120g/kg body weight) induced diabetic animals received Glimipiride 4mg/kg body weight per orally.

Group-IV: Alloxan (120mg/kg body weight) induced diabetic animals received ethanolic extract of *Caralluma fimbriata* 500mg/kg, body weight per orally.

Group-V: Alloxan (120mg/kg body weight) induced diabetic animals received aqueous extract of *Caralluma fimbriata* 500mg/kg, body weight per orally.

Significant hyperglycemia was achieved within 48 hrs after Alloxan (120mg/kg B.w.i.p.) injection induced diabetic rats with more than 200mg/dl of blood glucose were identified as to be diabetic and used for the study. In acute study all the surviving diabetic animals and normal animals were kept fasting overnight. Blood samples were collected from the fasted animals prior to the treatment with the above schedule and after administration, at each day up to 7 days.

Body Weight Measurement

Body weight was measured totally four times during the course of study period (Kannur DM et al., 2008) [i.e., before Alloxan induction (initial values), and on the first, fourth, and seventh days of the treatment period], using a weighing scale.

Statistical Analysis

The results of the study were subjected to one way analysis of variance (ANOVA) followed by Dunnett's t-test for multiple comparisons. Values with P 0.05 were considered significant.

RESULTS

Phytochemical Screening

Phytochemical screening of the extracts of *Caralluma fimbriata* showed the presence of various chemical constituents, mainly Alkaloids, Tannins, Flavonoids, Carbohydrates, Saponins, phenolics compounds. Flavonoids may be responsible for its anti-diabetic properties. The results obtained were comparable and satisfied by the standard literature.

In vitro antioxidant activity

DPPH assay

DPPH (1, 1-diphenyl-1-picrylhydrazyl) is a stable nitrogen free radical which accepts an electron or hydrogen radical to become stable diamagnetic radical. Here, DPPH radical itself acts as a color indicator which reacts with suitable reducing agent with number of electron present which is measured spectrophotometrically at 517 nm. Ethanolic extract of *Caralluma fimbriata* shows more potent anti-oxidant activity as compared to Aqueous extract of *Caralluma fimbriata*, shown in table no. 1 and figure 1.

H₂O₂ Assay

Ethanolic extract of *Caralluma fimbriata* shows more potent anti-oxidant activity as compared to the aqueous extract of *Caralluma fimbriata*, shown in table no. 2, figure 2.

Acute Oral Toxicity Studies

In acute oral toxicity studies, none of the

Studied ethanolic and aqueous extracts of leaves showed any significant toxicity sign when observed for the parameters during the first 4 hours followed by daily observations for 14 days also mortality was not observed. The drug was found to be safe at the tested dose level of 5000 mg/kg b. w. One-tenth of this dose level was taken as effective dose. All the extracts were experimented at the same dose of 500 mg/kg b. w. In order to ascertain a scientific base for the usefulness of this plant in the treatment of diabetes. It was decided to evaluate It was decided to evaluate experimental design of antidiabetic activity by Alloxan-induced model.

Oral glucose tolerance test:

The effect of different extracts on glucose tolerance test in normal rats is shown in Table No. 3 and figure 3. At 30 min. after glucose administration, the peak of blood glucose level increased rapidly from fasting value and then subsequently decreased. The ethanolic extracts of *Caralluma fimbriata* exhibited remarkable blood glucose lowering effect at 90 min. aqueous extracts of *Caralluma fimbriata* exhibited remarkable blood glucose lowering effect at 90 min.

Alloxan induced diabetic model:

As expected in the diabetic control, there was severe hyperglycemia as compared to the normal animals. Compared to the diabetic control, the *Caralluma fimbriata* lowered the elevated blood glucose levels only in subacute treatment, Table No. 4 and figure 4. It was observed that the standard drug Glimpiride lowered the blood glucose level significantly, bringing it nearly back to normal, where as ethanolic and aqueous extract of *Caralluma fimbriata* significantly decreased fasting blood serum glucose in diabetic rats on 3rd and 7th days as compared to initial (0 hr) blood serum glucose levels. When ethanolic and aqueous extract of *Caralluma fimbriata* were compared for their antidiabetic activity in comparison to active control, particularly Glimpiride, the results showed that their potential was lesser but significant than the standard drug at subacute level. Also in table no. 5 and figure no. 5 shows the significant effect of oral administration of the ethanolic and aqueous extracts *Caralluma fimbriata* on serum profile in experiment rats after 14 days.

Body Weight Measurement:

In the present study, diabetic rats had lower body weights and high blood glucose level as compared to normal rats. In spite of increased food consumption, loss of body weight due to defect in glucose metabolism and excessive breakdown of

tissue protein is a characteristic condition in diabetics. As shown in Table No.6 and figure 6, treatment with ethanolic and aqueous extracts *Caralluma fimbriata* improved the average body weights of rats, which indicates that control over polyphagia and muscle wasting resulted due to hyperglycemic condition.

Histopathology

Photomicrograph of Pancreas stained with

haematoxylin and Eosin (magnification x 400)

Figure no 7 shown as A) Group-I (Normal control) Normal islets with distension, B) Group-II (Diabetic control) islet cells with fatty access shows spoiled and atrophic islet with distension, C) Group-III (ethanolic extracts of CF) islets with normal round and elongated, D) Group-IV (aqueous extract of CF) islets with normal structural intactness with their nucleus, E) Group-V (Glimipiride) islet cells are small.

Table 1. In-vitro free radical scavenging activity of *Caralluma fimbriata* (CF) by DPPH reduction

| Concentration ($\mu\text{g/ml}$) | % inhibition (Aq CF) | %inhibition (Et CF) | % inhibition (Ascorbic acid) |
|------------------------------------|----------------------|---------------------|------------------------------|
| 10 | 28.44 \pm 0.22 | 37.51 \pm 0.29 | 48.51 \pm 0.23 |
| 20 | 43.21 \pm 0.15 | 56.69 \pm 0.17 | 62.40 \pm 0.16 |
| 30 | 58.74 \pm 0.27 | 68.55 \pm 0.14 | 78.46 \pm 0.22 |
| 40 | 62.64 \pm 0.05 | 76.55 \pm 0.22 | 82.8 \pm 0.13 |
| 50 | 70.90 \pm 0.17 | 83.44 \pm 0.13 | 87.26 \pm 0.20 |
| IC50 value | 24 | 16 | 11 |

Values are Mean \pm SEM of triplicate determination (n=3)

Table 2. In vitro free radical scavenging activity of *Caralluma fimbriata* (CF) by H2O2 Assay

| Concentration ($\mu\text{g/ml}$) | % inhibition (Aq CF) | %inhibition (Et CF) | % inhibition (Ascorbic acid) |
|------------------------------------|----------------------|---------------------|------------------------------|
| 10 | 28.44 \pm 0.22 | 37.51 \pm 0.29 | 48.51 \pm 0.23 |
| 20 | 43.21 \pm 0.15 | 56.69 \pm 0.17 | 62.40 \pm 0.16 |
| 30 | 58.74 \pm 0.27 | 68.55 \pm 0.14 | 78.46 \pm 0.22 |
| 40 | 62.64 \pm 0.05 | 76.55 \pm 0.22 | 82.8 \pm 0.13 |
| 50 | 70.90 \pm 0.17 | 83.44 \pm 0.13 | 87.26 \pm 0.20 |
| IC50 value | 24 | 16 | 11 |

Values are Mean \pm SEM of triplicate determination (n=3)

Table 3. Effect of ethanolic and aqueous extract of *Caralluma fimbriata* on blood glucose level in Oral glucose tolerance test in normal rats

| Sample | 0 min | 30 min | 90 min |
|---------------|-------------------------------|---------------------|--------------------|
| | Blood Glucose Levels (mg/ dl) | | |
| Vehicle | 85 \pm 1.065 | 120.3 \pm 1.33 | 82.4 \pm 0.912 |
| Et extract CF | 81.2 \pm 0.27*** | 120.6 \pm 1.00*** | 87.2 \pm 1.36*** |
| Aq extract CF | 84.3 \pm 2.43*** | 122.8 \pm 1.34*** | 93.2 \pm 3.13*** |
| Glimipiride | 80.6 \pm 0.66*** | 120.1 \pm 1.23*** | 86.3 \pm 1.65*** |

Values are expressed as Mean \pm SEM (n=6)

Table 4. Effect of treatment (21 days) of *Caralluma fimbriata* on Blood glucose level on Alloxan induced diabetic rats.

| Treatment and Dose (mg/kg) | 0 day | 7 th day | 14 th day | 21 th day |
|----------------------------|-------------------|---------------------|----------------------|----------------------|
| Vehicle | 84.93 \pm 1.367 | 84.87 \pm 1.3 | 84.9 \pm 1.3 | 84.36 \pm 1.3 |
| Inducer | 289.00 \pm 3.3 | 298 \pm 3.0 | 296.7 \pm 2.6 | 288.34 \pm 2.7 |
| Et extract CF | 283.39 \pm 2.8 | 265.21 \pm 4.1** | 127 \pm 2.5** | 86.15 \pm 1.2** |
| Aq extract CF | 285 \pm 2.3 | 264.01 \pm 3.8** | 139 \pm 5.2 ** | 83.62 \pm 1.6** |
| Glimipiride | 286.71 \pm 2.28 | 263.45 \pm 2.8** | 112 \pm 1.7** | 83.40 \pm 1.5** |

Values are expressed as Mean \pm SEM (n=6)

Table 5. Effect of Oral administration of the ethanolic and aqueous extracts *Caralluma fimbriata* on serum profile in experiment rats after 14 days.

| Treatment | TC | HDL | LDL | TG |
|------------------|----------------|--------------|----------------|-----------------|
| Vehicle | 74.31 ± 0.99 | 41.07 ± 1.1 | 61.78 ± 1.7** | 74.31 ± 1.74** |
| Diabetic Inducer | 183.6 ± 2.0 | 40.3 ± 1.2 | 146.86 ± 1.4 | 183.6 ± 2.0 |
| Et Extract CF | 172.5 ± 1.7** | 44.64 ± 1.1* | 84.69 ± 1.8** | 127.81 ± 2.03** |
| Aq Extract CF | 178.2 ± 2.2** | 48.75 ± 0.7* | 112.72 ± 2.3** | 140.58 ± 2.4** |
| Glimipiride | 170.17 ± 2.4** | 45.28 ± 1.8* | 80.74 ± 2.2** | 110.22 ± 3.5** |

Values are expressed as mean + SEM, n=6.

Statistical significance test for comparison was done by ANOVA, followed by Dunnett's t-test.

Values ***p<0.001, **p<0.01, *p<0.05.

Table 6. Effect of the ethanolic and aqueous extracts *Caralluma fimbriata* on body weight after treatment in diabetic rats.

| Group | Treatment | Average body weight (g) +SEM | |
|-------|------------------|------------------------------|----------------------|
| | | Initial | Day 14 th |
| I | Vehicle | 145±5.000 | 156±3.146 |
| II | Inducer | 185±4.146 | 167±2.032 |
| III | Et Extract of CF | 150±3.651 | 181±3.3 |
| IV | Aq Extract of CF | 151±3.076 | 163±3.0 |
| V | Glimipiride | 146±3.333 | 189±2.6 |

Values are expressed as mean + SEM, n=6.

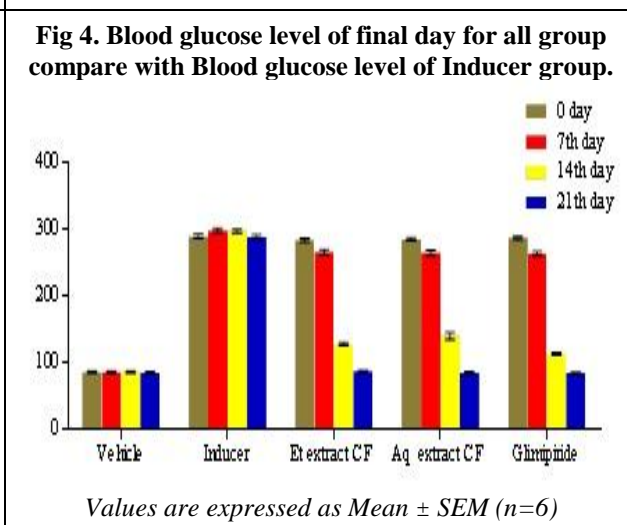
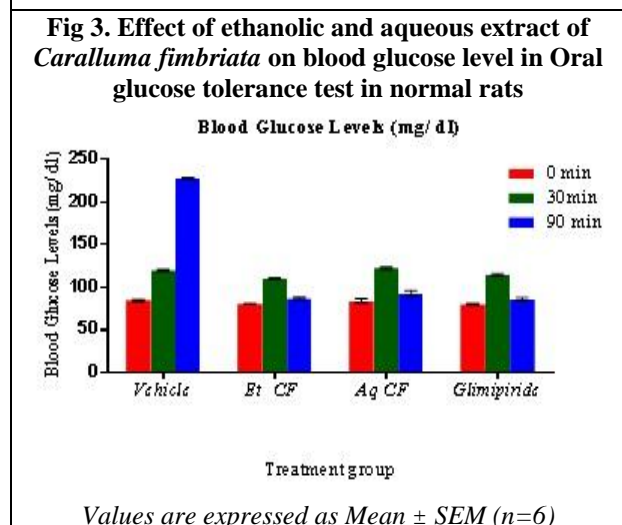
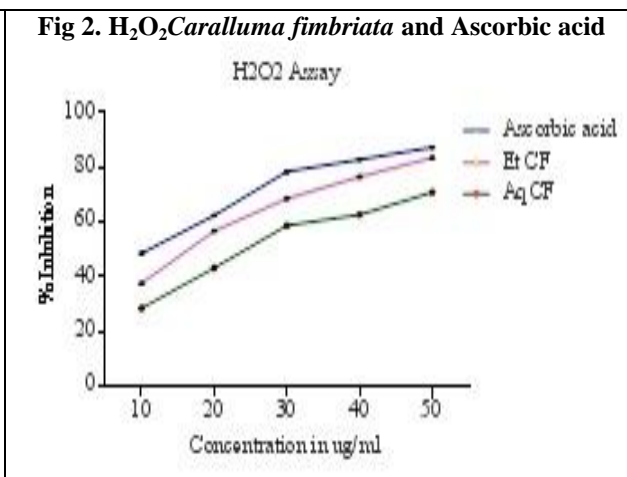
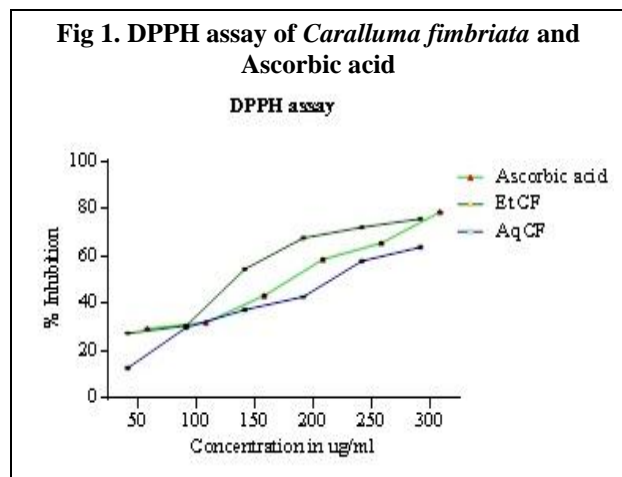
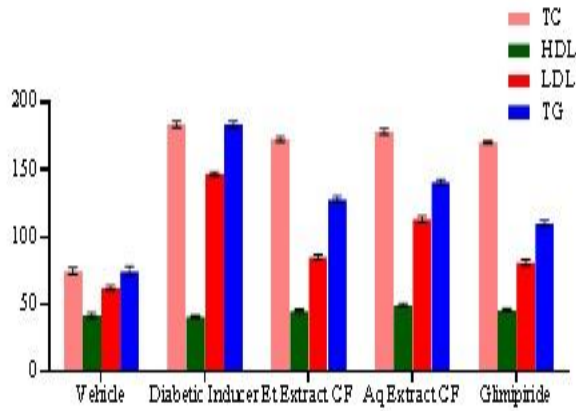
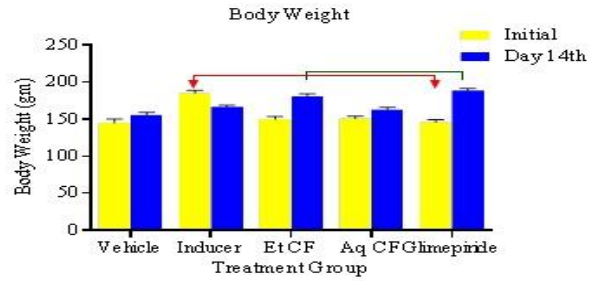


Fig 5. Effect of Oral administration of the ethanolic and aqueous extracts *Caralluma fimbriata* on serum profile in experiment rats after 14 days.



Values are expressed as Mean \pm SEM (n=6)

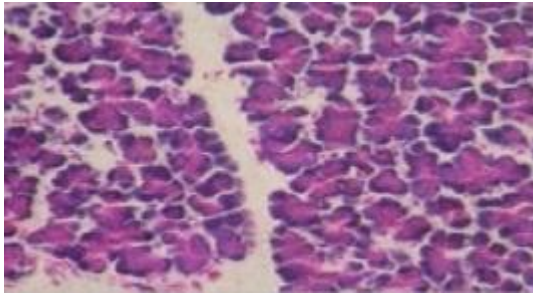
Fig 6. Effect of the ethanolic and aqueous extracts *Caralluma fimbriata* on body weight after treatment in diabetic rats



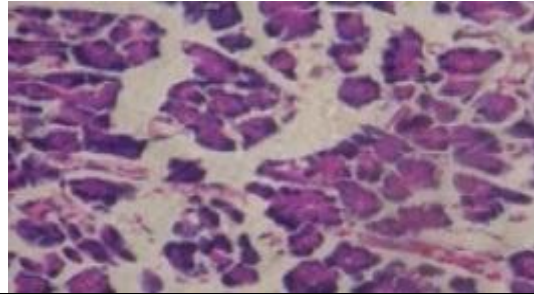
Values are expressed as mean + SEM (n=6)
 Statistical significant test for comparison was done by ANOVA, followed by Dunnett's *t*-test.
 The Average body weight values of groups are compared with normal control animals,
 Values *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

Fig 7. Photomicrograph of Pancreas stained with haemotoxylin and Eosin

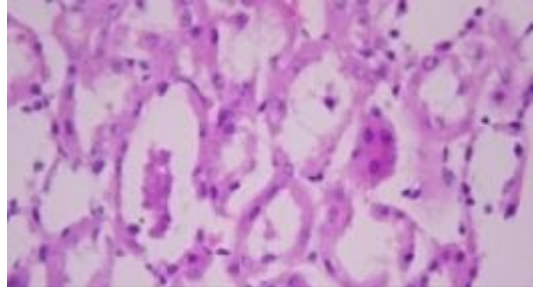
A. Group-I (Normal control) Normal islets with distension



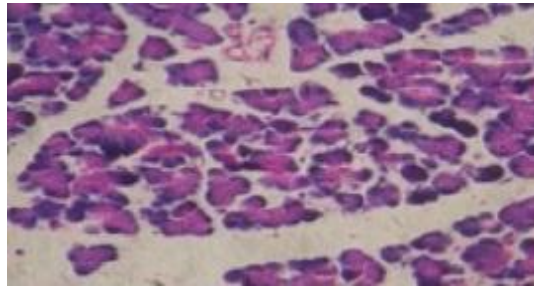
B) Group-II (Diabetic control) islet cells with fatty access shows spoiled and atrophic islet with distension.



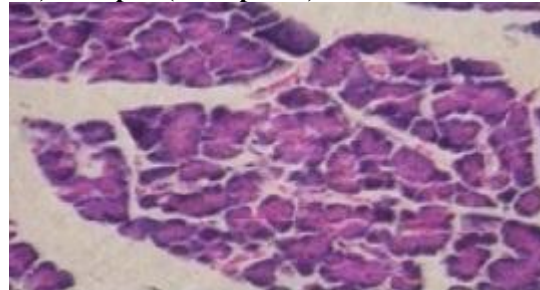
C) Group-III (ethanolic extracts of CF) islets with normal round and elongated



D) Group-IV (aqueous extract of CF) islets with normal structural intactness with their nucleus



E) Group-V (Glimipiride) islet cells are small



DISCUSSION

In the modern epoch many traditionally used medicinally important plants were tested for their hypoglycemic potential by various investigators in experimental animals. We have undertaken a study on *Caralluma fimbriata* for their antidiabetic activity.

The present research work was continuous post treatment for 7 days with the *Caralluma fimbriata* extract (Et/Aq) showed more potential hypoglycemic activity in normoglycemic rats and alloxan induced diabetogenic rats.

Preliminary phytochemical screening revealed that *Caralluma fimbriata* showed positive response to Alkaloids, Tannins, Flavonoids, Carbohydrates, saponins, phenolics compounds and quinine, the response was positive to Flavonoids. The increased level of glycosylated haemoglobin (HbA1c) is directly proportional to the decreased level of haemoglobin in diabetic control experimental rats. HbA1c is used as most reliable marker and standard diagnosis practices for estimating the degree of protein glycation during diabetes mellitus (Goldstein DE *et al.*, 1994). Proglycation is a non-enzymatic reaction between excess glucose present in the blood and free amino groups on the globin component of haemoglobin. Measurement of HbA1c level provides information of long term glycaemic status and to correlate with various complications related to Diabetes mellitus. On oral administration of TRME and KAME, the TRME, is more significantly decreased the Hb1c level possibly due to normoglycemic control mechanisms in experimental rats which also reflect the decreased protein glycation condensation reactions and the reports obtained is

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concordant with the previous result (Jain SK *et al.*, 2007).

A marked increase in serum concentration of TC, TG, LDL and decreased HDL was observed with diabetic rats than normal control group which is often linked with hyperlipidaemia. Hyperlipidaemia certainly contributes to major risk factor for cardiovascular diseases (Umesh CS *et al.*, 2011; Nikkila EA and Kekki M, 1993). During diabetic state, insulin deficiency contributes to derangements of various metabolic and regulatory mechanisms in body. At normal state insulin activates the lipolytic hormones action on the peripheral fat depots which hydrolyses triglycerides and prevents mobilization of free fatty acids (Briones ER *et al.*, 1984; Nikkila EA 1983). However, insulin deficiency inactivates the lipoprotein lipase which promotes liver conversion of free fatty acids into phospholipids and cholesterol and finally discharged into blood which resulted into elevated serum phospholipid level (Shirwaikar A *et al.*, 2004; Pushparaj PN *et al.*, 2007). The results of present study reveals that the administration of *Caralluma fimbriata* extract not only lowered TC, TG and LDL, but also enhanced the cardioprotective lipid HDL.

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