Journal of Ayurveda and Integrative Medicine 11 (2020) 426–431

Contents lists available at ScienceDirect

Journal of Ayurveda and Integrative Medicine

journal homepage: http://elsevier.com/locate/jaim

Original Research Article (Experimental)

Protective role of *Convolvulus pluricaulis* on lipid abnormalities in high-fat diet with low dose streptozotocin-induced experimental rat model

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ARTICLE INFO

Article history:
Received 22 January 2019
Received in revised form
18 July 2019
Accepted 11 June 2020
Available online 17 August 2020

Keywords:
Convolvulus pluricaulis
Streptozotocin
Hypolipidemia
High fat diet

ABSTRACT

Background: The methanolic extract of *Convolvulus pluricaulis* had earlier shown lipid lowering activity in Triton induced reversible hyperlipidemia model, but, the hypolipidemic activity in irreversible models and hypoglycaemic activity are not investigated so far.
Objective: This study was designed to validate the lipid and glucose-lowering actions of *C. pluricaulis* methanolic extract (CPME) by using ingredients from the Indian diet for induction of hyperlipidemia and diabetes on experimental rats.
Materials and methods: Experimental animals were divided into four groups having six animals in each group ($n = 6$). Animals of Group I II, III and IV received - no treatment, 0.9% NaCl, Glipizide (GPZ) 5 mg/kg and CPME 400 mg/kg once daily for two weeks respectively. Animals of all groups except group I were fed a high fat-based Indian diet for 21 days followed by a single STZ (35 mg/kg) i.p. administration in model induction phase. Afterwards, animals were sacrificed, and the pancreas was dissected for histological changes, and blood was collected for measuring lipid parameters, FBS, insulin levels, and HOMA scores.
Results: CPME significantly ameliorate the lipid abnormalities in HFD-STZ-treated experimental model ($p < 0.001$) but fails to reverse the hyperglycaemia developed in diabetic rats with no protective effect on islet architecture ($p > 0.05$) as compared to experimental group while, GPZ showed protective effect on both lipid abnormalities and hyperglycemia by modulating the levels of lipid parameters and insulin respectively.
Conclusion: In conclusion, the study confirm that CPME possesses significant hypolipidemic activity but fails to reverse the hyperglycaemia developed in diabetic rats.

1. Introduction

Macrovascular angiopathies involving coronary or cerebral vasculature are the prime causes of deaths in patients with diabetes mellitus [1]. Type 2 diabetes (T2D) is associated with specific lipid abnormalities and high blood pressure which ultimately expose the diabetic patients to cardiovascular complications such as angina, coronary vasculopathies, and cerebral infarcts [2]. Therefore, diabetic patients are at two to three times more at risk to develop cardiac problems than those without diabetes [3]. Targeting low-density lipoprotein cholesterol (LDL-c), total cholesterol (TC) by statins, or aiming at triglycerides and high-density lipoprotein cholesterol (HDL-c) by fibrates is an indispensable need in diabetic patients to avoid macrovascular angiopathies [4,5].

Currently, statins and fibrates are the primarily used drugs for the treatment of hyperlipidemia. However, long-term usage of these drugs leads to inevitable side-effects [6,7]. Besides, the overlapping nature of side-effects makes the combination a hard choice for the prescribers in resistant hyperlipidemia cases [8]. Therefore, safe lipid-lowering drugs that are an alternative to

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Peer review under responsibility of Transdisciplinary University, Bangalore.

https://doi.org/10.1016/j.jaim.2020.06.011

statins and fibrates are sought. On a similar note, there are different treatment options available for diabetes including oral and parenteral drugs which are being used since many years. However, the usage of these drugs is restricted to some extent because of considerable side-effects such as hypoglycaemia, weight gain, and so on. These agents also fail to stop the disease progression and its complication [9]. Hence, the hunt for new molecules has been moving towards herbal medicines, as these are natural, plant-based, and therapeutically beneficial. These medicines are also considered to be safe with no apparent harmful effects compared to contemporary synthetic medications.

India is home to a plethora of medicinally important herbs which are traditionally used as therapeutic agents. *Convolvulus pluricaulis* (Shankhpushpi) is a common plant in India and is widely mentioned in Ayurveda for its therapeutic uses [10]. *C. pluricaulis* extract is known to possess neuroprotective, anxiolytics and antidepressant activity [10–12]. In acute toxicity studies, a single dose of 2000 mg/kg showed no morbidity and mortality for 14 days observatory period with no macroscopic and morphologic alteration. Therefore, single dose of *C. pluricaulis* i.e. 2000 mg/kg seems to be safe in experimental animals [10]. The LCMS characterisation of *C. pluricaulis*, showed the presence of pharmacologically active phytochemicals including convolidine, scopoletin, kaempferol, and convolamine. But, in particular, scopoletin is reported to possess strong antioxidant activity in various in-vivo and in-vitro studies [13]. Furthermore, Scopoletin is a coumarin which is well known for their antidiabetic actions [14]. The methanolic extract of *C. pluricaulis* ameliorated the lipid levels in triton-induced hyperlipidemia in rats. Triton is a reversible and temporary induction agent of hyperlipidemia in experimental animals [15]. Hence, scientific validity needs to be confirmed in animals with chronic and permanent hyperlipidemia for establishing possible clinical utility in trials. Thus, the present study planned to validate the lipid-lowering action and assess the antihyperglycemic action of methanolic extract of *C. pluricaulis* in experimental rats. The scope of present research was extended further to corroborate usefulness of common Indian dietary ingredients for induction of hyperlipidemia and diabetes in rats.

2. Materials and methods

2.1. Preparation of plant extract

The plant was collected from the Panjab University Botanical Garden, Chandigarh, India. The plant was identified and authenticated by Dr. Vandita Kakkar, Pharmacognosist and Phytochemist at Panjab University, Chandigarh, India. A specimen was submitted to the Department of Pharmacology, PGIMER, with a voucher specimen (AP/PGI/Pharma/CP001/17) for future reference. The cold maceration technique was used for the preparation of extract which involves macerating the coarse powder with methyl alcohol (100%) for 72 h. Cotton wool was used as a filter to separate the particulate matter after every 24 h. Finally, rotafil apparatus was used to evaporate the liquid by-product for obtaining the resinous extract. A dark-green resinous extract was obtained with yield value 9.60% (w/w).

2.2. Chemicals

Streptozotocin (STZ) was purchased from Sigma–Aldrich, USA; Biochemical Kits for measuring TC, TG, LDL-c and HDL-c were obtained from Roche Co., Ltd; a sample of glipizide was accepted from Zydus Research Centre, Ahmedabad, India. Accu-chek glucometer (Roche) was already available from previous experiments. Rat insulin ELISA Kit was purchased from GenX biotech and other reagents were procured from Himalayan Scientific House, Chandigarh, India. High Fat diet was prepared in house from coconut oil (Parachute brand) and Vanaspati ghee (Dalda brand), the common dietary ingredients of the Indian diet.

2.3. Animals

All the experiments on the animals were carried out as per the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines. Wistar rats weighing 200–300 g. were used for the study. The rats were acclimatised to the house conditions for seven days before the commencement of the experimental procedures and had free access to food and water. All the protocols were approved by the Institutional Animal Ethics Committee (86/IAEC/570 held on 09/02/2017) of the Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh.

2.4. Preparation of high-fat diet

Coconut oil and Vanaspati ghee were used for preparation of high-fat diet. They were mixed in a 3:1 (v/v) ratio and this emulsion was given to the rats at a dose of 3 ml/kg by oral gavage daily [16].

2.5. Experimental design

Four groups (in each group, n = 6 rats) were segregated for this study. Overnight fasting with free water access was maintained prior to the commencement of the experiment. On day one, zero-time Fasting blood sugar (FBS) and insulin levels were measured. Thereafter, group I served as the normal control group receiving no treatment, group II received HFD plus STZ (35 mg/kg; i.p.) [17] and served as the Experimental Control (EC) group, group III received HFD plus STZ (35 mg/kg; i.p.) with glipizide (5 mg/kg) and served as the GPZ5 group, and group IV received HFD plus STZ (35 mg/kg; i.p.) with CPME dose of 400 mg/kg and served as the CP400 group. Glipizide and CPME was dissolved in 0.9% saline and given by oral gavage (p.o) at a dose of 5 mg/kg and 400 mg/kg respectively for two weeks after model development. The animals were weighed at the beginning of the experiment and then every week thereafter. The blood collection was done through retro-orbital puncture on day 0, 28, and 42 for estimation of insulin levels, lipid profiles, and FBS under ketamine (50 mg/kg) and xylazine (10 mg/kg) anesthesia. On completion of biochemical assessment, the experimental rats were sacrificed. Pancreas were dissected and fixed into 10% formalin solution for histological examination.

2.6. Induction of diabetes with lipid abnormalities

Animals were separated into control and experimental groups after a one-week acclimatisation period. Control group rats were fed regular chow diet while experimental group rats were fed a high-fat diet (3 mL/day by oral gavage) for three weeks before STZ administration. After a three-week period, a single streptozotocin dose i.p (35 mg/kg; dissolved in the citrate buffer, 4.3 pH) was given to the rats for induction of diabetes in the experimental group and a week-long period was given for stabilisation of hyperglycaemia. Animals of the control group were administered with vehicle citrate buffer. Glucose levels were measured one week post streptozotocin administration. Rats were considered as diabetic when they had crossed the fasting blood glucose target of 300 mg/dl and considered for further experimentation. At day 28, treatment was started with standard and test drugs for two weeks. Throughout the experiment, a high-fat diet was maintained for the rats.

2.7. Blood biochemistry analysis

A digital glucometer was used for measuring fasting sugar level. Serum was separated after centrifugation (3000 g, 10 min, 4 °C) and stocked up at −20 °C until further assessment. A semi auto analyser with Roche biochemical test kits were used for estimation of serum low-density lipoprotein cholesterol (LDL-c), total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-c) levels by colorimetric methods. Serum insulin assessment was done with enzyme-linked immunosorbent assay (ELISA) kit.

2.8. Assessment of β-cell homeostasis model (HOMA-β)

HOMA of β-cell function (HOMA-B) is a mathematical model describing the functioning of the β-cell which is calculated as the multiplication of baseline insulin with 20, divided by the baseline glucose level minus 3.5 [18]. The value obtained is HOMA-β.

2.9. Histopathology

The animals were sacrificed on day 42 and pancreatic tissue was cautiously removed and fixed into 10% formalin. This was subjected to histological studies using hematoxylin and eosin (H&E) stain.

2.10. Statistical analysis

Data were expressed as mean plus/minus standard error of mean (SEM) and statistical analysis was done by SPSS 22.0 version. One-way ANOVA followed by Tukey's test was used for various lipid parameters, FBS, insulin level, and HOMA-β.

3. Results

3.1. Effect of CP on lipid profile

Lipid profile parameters, namely TG, TC, LDL-c, and HDL-c, had no statistically significant difference in intergroup comparison at baseline. HFD with low dose STZ (35 mg/kg) induced hyperlipidemia model and this was evident by the significant rise of serum TG (148.16 ± 7.78 in EC versus 84.88 ± 5.09 in NC; $p < 0.001$), TC (136.28 ± 5.17 in EC versus 60.25 ± 2.69 in NC; $p < 0.001$), and LDL-c levels (30.59 ± 1.36 in EC versus 8.81 ± 0.95 in NC; $p < 0.001$) on day 28. In contrast, serum HDL-c levels were significantly reduced (34.07 ± 3.05 in EC versus 56.10 ± 3.77 in NC; $p < 0.001$) on day 28. Glipizide-treated group had significant effect on three parameters of lipid profile namely TG (121.56 ± 4.31 versus 158.83 ± 5.16 in EC group; $p < 0.001$), TC (62.50 ± 7.57 versus 122.78 ± 12.06 in EC group; $p < 0.001$), and LDL-c (11.37 ± 1.44 versus 24.76 ± 2.23 in EC group; $p < 0.001$) with non-significant effects on HDL-c (35.55 ± 3.17 versus 32.62 ± 3.17 in EC group) on day 42. CPME significantly reduced serum TG (91.35 ± 3.66 versus 158.83 ± 5.16 in EC group; $p < 0.001$), TC (57.71 ± 3.57 versus 122.78 ± 12.06 in EC group; $p < 0.001$), and LDL-c levels (13.11 ± 0.44 versus 24.76 ± 2.23 in EC group; $p < 0.001$) with significant rise in HDL-c levels (51.52 ± 2.66 versus 32.62 ± 1.83 in EC group; $p < 0.001$) on day 42 as shown in Table 1.

3.2. Effect of CP on fasting blood sugar and insulin levels

In intergroup comparison, there was no statistically significant difference in FBS and insulin levels among all groups at baseline. HFD with STZ low dose (35 mg/kg) induced hyperglycemia and it was marked by a significant rise in FBS level (341.33 ± 11.48 in EC group versus 71.67 ± 1.84 in NC group; $p < 0.001$) and significant decrease in insulin levels (6.23 ± 1.72 in EC group versus 41.42 ± 7.78 in NC group; $p < 0.001$) on day28. Glipizide-treated group had significant effect on FBS levels (98.33 ± 4.86 in GPZ5 group versus 459.67 ± 12.36 in EC group; $p < 0.001$) and insulin levels (20.49 ± 2.15 in GPZ5 group versus 7.03 ± 1.57 in EC group; $p < 0.01$) on day 42. CPME had no significant effect on FBS levels (427.67 ± 4.86 in CP400 group versus 459.67 ± 12.36 in EC group) and insulin levels (6.02 ± 1.72 in CP400 group versus 7.03 ± 1.57 in EC group) on day 42 (Tables 2 and 3).

3.3. HOMA model for functional assessment of β-cell and insulin resistance

Animals of EC group showed significant decline in function of β-cell with HOMA-β scoring (in EC group 0.31 ± 0.72 versus 8.02 ± 0.76 in NC group; $p < 0.001$). Glipizide treatment significantly improves the HOMA-β index (In GPZ5 group 4.29 ± 0.31 versus 0.31 ± 0.72 in EC group; $p < 0.001$) while CPME had no effect on HOMA-β index (0.28 ± 0.77). Significant statistical difference could not be observed in HOMA-IR scoring in all groups (121.23 ± 17.18 in NC group, 143.95 ± 31.49 in EC group, 91.26 ± 13.38 in GPZ5 group, 116.02 ± 3 4.88 in CP400 group) (Fig. 1).

3.4. Histopathological analysis

A qualitative histological analysis was done to determine the relative dimension and number of islets of pancreas in different experimental groups by using H&E stains in 20× light microscope. Histopathological examination of the pancreas discovered a

Table 1
Effect of various treatment on Lipid profile in HFD with low dose STZ (35 mg/kg) induced diabetic dyslipidemia in rats.

		Groups			
		NC	EC	GPZ5	CP400
TC (mg/dL)	Day 0	53.98 ± 1.56	56.82 ± 3.27	55.77 ± 2.41	60.02 ± 1.78
	Day 28	60.25 ± 2.69	136.28 ± 5.17#	138.77 ± 7.92#	136.91 ± 5.73#
	Day 42	56.77 ± 1.98	122.78 ± 12.06#	62.50 ± 7.57*	57.71 ± 3.57*
TG (mg/dL)	Day 0	81.57 ± 5.79	84.75 ± 3.33	83.23 ± 3.57	86.63 ± 2.59
	Day 28	84.88 ± 5.09	148.16 ± 7.78#	136.56 ± 3.68#	149.71 ± 5.78#
	Day 42	75.65 ± 7.25	158.83 ± 5.16#	121.56 ± 4.31*	91.35 ± 3.66*
HDL (mg/dL)	Day 0	54.85 ± 3.67	55.93 ± 2.86	53.50 ± 3.84	57.50 ± 3.41
	Day 28	56.10 ± 3.77	34.07 ± 3.05#	26.41 ± 2.88#	29.71 ± 2.37#
	Day 42	56.52 ± 2.68	32.62 ± 1.83#	35.55 ± 3.17	51.52 ± 2.66*
LDL (mg/dL)	Day 0	7.13 ± 0.72	9.02 ± 0.96	8.93 ± 1.26	7.67 ± 0.98
	Day 28	8.81 ± 0.95	30.59 ± 1.36#	31.71 ± 2.43#	29.04 ± 2.33#
	Day 42	7.97 ± 0.84	24.76 ± 2.23#	11.37 ± 1.44*	13.11 ± 0.44*

Data was expressed as mean ± SEM. #P < 0.001 vs NC, *P < 0.001 vs EC.

Table 2
Effect of various treatment on Fasting blood sugar (FBS) level in HFD with low dose STZ (35 mg/kg) induced diabetic dyslipidemia hyperlipidemia in rats.

Groups	FBS (mg/dL)		
	Day 0	Day 28	Day 42
NC	69.33 ± 1.48	71.67 ± 1.84	83.67 ± 4.21
EC	71.50 ± 3.7	341.33 ± 11.48#	459.67 ± 12.36#
GPZ5	66.67 ± 2.23	428.17 ± 11.86	98.33 ± 4.86*
CP400	65.56 ± 5.55	438.67 ± 17.89	427.50 ± 11.74

Data was expressed as mean ± SEM. #P < 0.001 vs NC, *P < 0.001 vs EC.

Table 3
Effect of various treatment on Insulin level in HFD with low dose STZ (35 mg/kg) induced diabetic dyslipidemia in rats.

Groups	Insulin (μIU/mL)		
	Day 0	Day 28	Day 42
NC	37.99 ± 8.18	41.42 ± 7.78	32.16 ± 3.52
EC	44.08 ± 4.02	6.23 ± 1.72#	7.03 ± 1.57#
GPZ5	35.02 ± 3.69	6.5 ± 1.05	20.49 ± 2.15*
CP400	46.44 ± 3.87	9.58 ± 1.42	6.02 ± 1.72

Data was expressed as mean ± SEM. #P < 0.001 vs NC, *P < 0.01 vs EC.

significant reduction in the size and number of pancreatic islets in the EC group as compared to the NC group. Whereas, GPZ5 group showed an islet size close to normal. CPME 400 mg/kg group showed islet size equal to EC group (Fig. 2).

3.5. Body weight

In intergroup comparison, insignificant statistical difference in body weight was observed among all groups at baseline. Animals of EC, GPZ5, and CP400 groups were observed to have significant increase in body weight after feeding of HFD for 21 days (245.67 ± 1.48 g. in EC group; $p < 0.01$, 278.00 ± 6.92 g. in GPZ5 group; $p < 0.001$, 240.50 ± 1.65 g. in CP400 group; $p < 0.05$ versus 220.67 ± 6.39 g. in NC group). However, after one week of STZ administration (Day 28), there was significant decrease in body weight of these three groups as compared to their own respective body weights on day 21. Glipizide treatment significantly reduced the fall in body weight (226.33 ± 7.94 g. versus 202.00 ± 3.183 g. in EC group; $p < 0.05$), while CP400 group had no effect on fall in body weight (185.33 ± 3.04 g. versus 202.00 ± 3.183 g. in EC group) (Table 4).

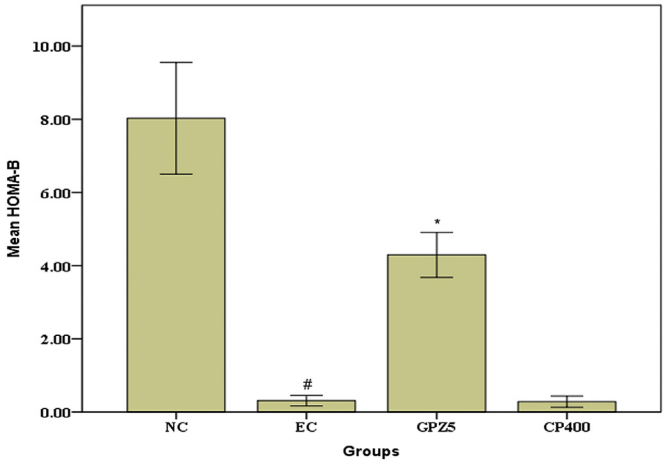

Fig. 1. Effect of various treatments on Homeostasis Model Assessment (HOMA)-β in HFD with low dose STZ (35 mg/kg) induced diabetic dyslipidemia in rats. Data was expressed as mean ± SEM. #P < 0.001 vs NC, *P < 0.001 vs EC.

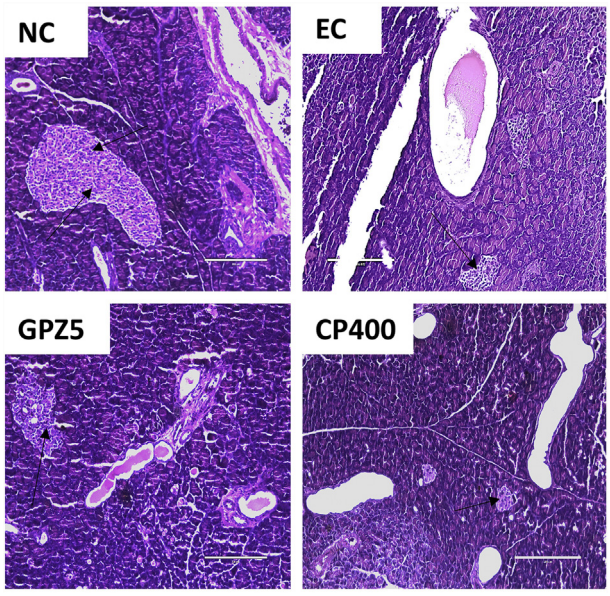

Fig. 2. Effect of various treatments on morphology of endocrine pancreas in HFD with low dose STZ (35 mg/kg) induced diabetic dyslipidemia in rats (Magnification 20×).

4. Discussion

The present study was designed to validate the lipid-lowering action of C. Pluricaulis and hyperlipidemia plus diabetes induction in rats by using Indian dietary ingredients. In literature there exists a single report of the hypolipidemic action of CPME in triton-induced hyperlipidemia in rats. Thus the clinical utility of this plant extract can only be considered once it is validated in a more robust and permanent hyperlipidemia animal model which is induced with a high-fat diet. For the present study, authors selected dosage of 400 mg/kg of the plant extract, which had previously produced significant hypolipidemic action in triton-induced hyperlipidemia [15]. Glipizide fits as an ideal comparison for simultaneous evaluation of antihyperglycemic and hypolipidemic action of any plant. In the present study, the treatment with glipizide exhibited a significant decrease in TC, TG, and LDL-c with a non-significant increase in HDL-c. These results were parallel to previous studies which showed the hypolipidemic activity of glipizide and glibenclamide respectively. The hypolipidemic action of these sulfonylureas is attributed to insulin secretagogues action [17,19–21]. Extract of *C. pluricaulis* also showed a similar statistically significant reduction in TG, TC, LDL-c, with an increase in HDL-c, as compared to the EC group. The antihyperlipidemic effect of CPME was apparently better for serum TG and TC as compared to LDL-c and HDL-c levels. This partly can be elucidated by the well-known lipid metabolism rule that VLDL have a significant amount of triglyceride in its composition than cholesterol. The findings of present research lead to one probable proposition that the plant extract may have a capacity to restore, at least to some extent, lipoproteins breakdown. The investigation in mechanism is not carried out in the present study; nevertheless, increased stimulation of the catabolic action of lipoprotein lipase could be the reason for restoring VLDL catabolism by the plant extract [22]. Therefore, the study confirms the previous hypolipidemic activity report of *C. pluricaulis* in a more valid, robust, and chronic model of hyperlipidemia. This lipid-lowering

Table 4
Effect of various treatment on Body weight in HFD with low dose STZ (35 mg/kg) induced diabetic dyslipidemia in rats.

Groups	Body Weight (g)				
	Baseline	Day 21	Day 28	Day 35	Day 42
NC	217.33 ± 4.26	220.67 ± 6.39	232.67 ± 7.11	239.00 ± 7.67	242.67 ± 5.32
EC	210.00 ± 1.83	245.67 ± 1.48$^{\#\#}$	220.50 ± 2.04[a]	211.00 ± 1.32	202.00 ± 3.18
GPZ5	222.67 ± 4.78	278.00 ± 6.92$^{\#\#\#}$	248.83 ± 8.86[b]	235.67 ± 7.78*	226.33 ± 7.94*
CP400	210.33 ± 3.06	240.50 ± 1.65$^{\#}$	215.67 ± 1.87[c]	193.33 ± 1.73	185.33 ± 3.04

Data was expressed as mean ± SEM. $^{\#}P < 0.05$ vs. NC, $^{\#\#}P < 0.01$ vs. NC, $^{\#\#\#}P < 0.001$ vs. NC, *P < 0.05 vs. EC.
[a] P <0.05 vs. EC group body weight on day 21.
[b] P < 0.01 vs. GPZ5 group body weight on day 21.
[c] P < 0.05 vs. CP400 group body weight on day 21.

activity may be attributed to the potent antioxidant properties of *C. pluricaulis* [23–25].

In Asian countries like India, people regularly consume food that is prepared in oil or ghee which consist of a high amount of saturated fats with a meagre amount of polyunsaturated fatty acids (PUFAs). Increased consumption of fast food rich in fat content in the form of pizza, burger, French fries is correlating with the rising trend of diabetes. Faulty dietary habits and a sedentary lifestyle together have contributed to the development of several other disorders like a variety of hyperlipidemias which further leads to the development of CHD [26]. In the literature, it was well established that vegetable oils can be used in the development of experimental models like hyperlipidemia, diabetes, and metabolic syndrome [16]. Hence, in the present study, an effort was made to develop a cost-effective, easy-to-prepare, and rapid onset experimental model using a high-fat diet which is made of vegetable oils with a low dose STZ for evaluation of hypolipidemic and antihyperglycemic activity of *C. pluricaulis*. Low dose STZ with HFD is a well-established model for the development of diabetes. However, the high cost of HFD is always a concern for researchers, especially from developing nations [27]. In the present study, the low levels of insulin in the experimental group rats suggested incomplete destruction but the preservation of some functional β-cell mass which was later confirmed by histological assessment, showing the presence of pancreatic islets. Moreover, an increase in levels of insulin and HOMA- β with glipizide treatment supported the presence of viable and functionally intact B-cell mass. HOMA-β is an index for the measurement of functional β-cell mass presence which is calculated using fasting blood sugar and insulin values. *C. pluricaulis* fails to decrease the fasting blood sugar level, indicating that the plant extract does not have the antihyperglycemic effect. Altogether, this cost-effective alternative model can be used for further studies of compounds screening for antihyperglycemic and antihyperlipidemic activity [16].

Controversial findings exist in literature pertaining to a low dose of STZ and effect on body weight. According to certain studies, there is increase in the body weight with a low dose of STZ [17,28] while others report no change or the reduction in body weight [29,30]. In the present study, the body weight of rats was decreased significantly in HFD-STZ fed group. This decrease in body weight can be attributed to the development of hypoinsulinemia. However, *C. pluricaulis* did not ameliorate the reduction in body weight. In histological analysis, it was observed that there was a significant reduction in the number and dimensions of islets of the pancreas in STZ-diabetic rats. Particularly, STZ leads to increased production and accumulation of reactive oxygen species (ROS), and superoxide and hydroxyl radicals which are cytotoxic. A significant number of reactive oxygen species molecules produced by STZ led to mitochondrial leakage, ensuing in pancreatic β-cell death. Hence, unbalancing the release of insulin [31]. Animals treated with glipizide were found to have the same islet architecture in some places as in normal rats. However, *C. pluricaulis* did not produce any beneficial effect on islet architecture. It is noteworthy that hypolipidemic action, so far tested in both acute and chronic animal models, leads the path for consideration of plant extract to be tested as an add-on to statins or fibrates in resistant hyperlipidemia patients.

5. Conclusion

In conclusion, we validated a cost-effective diabetic hyperlipidemia model that mimics an abundance of metabolic features of diabetes and hyperlipidemia in humans. The plant possesses potential usefulness as a natural hypolipidemic agent and paves the path towards testing in controlled clinical studies. The absence of antidiabetic action with 400 mg/kg of CP extract suggests that the therapeutic dose may be different for these two indications or there can be a sheer absence of the action.

Source(s) of funding

The study received funding support from PGIMER Intramural grant Vide Letter No. 71/2-eDU-6/1172.

Conflict of interest

None.

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