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Research Article

Effect of Ethanolic Extract of Physalis angulata on Dyslipidemia in Diabetic Rats

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ABSTRACT

Type 2 diabetes and dyslipidemia is a chronic medical condition that requires regular monitoring and treatment throughout life. In India, natural compounds from plant sources have been extensively used as traditional medicines from centuries. *Physalis angulata* plant composites have been widely used for the traditional treatment of diabetic mellitus, treatment of chronic diseases. Therefore, the objective of this present study is to evaluate ethanolic extract of *P. angulata* (EEP) on dyslipidemia in diabetic rats. The collected fruits were dried and powdered and extracted with using ethanol solvent by soxhlet apparatus. Hyperglycemia was induced in rats by using streptozotosin and treated with different concentration of ethanol extracts. Blood glucose levels and lipid profiles were measured after the treatment period. Oral administration of EEP (100, 200, 300 mg/kg) showed a significant reduction of blood glucose level as compared with diabetic control group. EEP (300 mg/kg) exhibited maximum hypoglycemic effect with reduction of glucose concentration from 289 to 203 mg/dl as compared to other doses of EEP. Treatment with EEP (100, 200 and 300 mg/kg) exhibited improved body weight as compared with diabetic control group. Maximum improvement (5.31%) was observed in EEP (300 mg/kg) dose as compared to lower two dosages. The treatment with EEP (200 and 300 mg/kg) showed significant reduction in cholesterol level (155.5±4.45 and 150.13±2.13 mg/dl) as compared with diabetic control group after 7 days of treatment. This study concludes that, the fruits extracts of the selected plant has antidiabetic effects and possess beneficial effect on the hyperglycemia associated with hyperlipidemia/dyslipidemia.

1. Introduction

Diabetes is metabolic disorders and whole world is facing the problem of diabetes. Diabetes severely affect the normal routine life of human1,2. WHO stated that the occurrence of diabetes is enhanced by 35%. Presently 150 million people are effected by diabetes and it is assume to be increased by 300 million at the end of 20253. It is emerging as one of the leading causes of end stage renal disease, heart attack, non-traumatic amputation, and blindness, increasing the mortality and morbidity burden on the community.

Type 2 diabetes mellitus is a disorder that disrupts the way your body uses glucose (sugar). All the cells in your body need sugar to work normally. Sugar gets into the cells with the help of a hormone called insulin. If there is not enough insulin, or if the body stops responding to insulin, sugar builds up in the blood. This is what happens to people with diabetes mellitus. Dyslipidemia is characterized by abnormal level of lipid in blood, including lipoprotein overproduction or deficiency. Consequently, the total cholesterol, LDL, triglycerides, apo B or Lp(a) levels above the 90 percentile or HDL and Apo A levels below the 10 percentile of the general population in Dyslipidemia patient.

Physalis angulata, belongs to family Solanaceae commonly called as Mullaca, Wild gooseberry, annual ground cherry, bladderberry, bladder cherry, bush tomato, Chinese lantern, Chinese lanternplant, cutleaf ground cherry, goose berry, ground cherry, gooseberry,

husk tomato, wild tomato, Indian gooseberry weed, winter cherry, native gooseberry. In India, natural compounds from plant sources have been extensively used as traditional medicines from centuries. *Physalis angulata* plant composites have been widely used for the traditional treatment of diabetic mellitus, treatment of chronic diseases. The scientific studies on anti-diabetic activity of this plant ethanol extracts were not reported. Therefore this plant has been selected for this study and was planned to evaluate the antidiabetic activity of ethanolic crude extract

2. Material and Methods

2.1 Preperation of Crude Extracts

The fruits of *Physalis angulata* were collected from the local areas of Mahaboobnagar district, Telangana, India. The plant fruits were air dried under shade, powdered and extracted with ethanol (60^0-80^0C) with Soxhlet apparatus by successive solvent extraction method. Finally, the ethanolic extract of *P. angulata* (EEP) were evaporated by using rotary vacuum evaporator. The final yield was 13% and ethanol extract of *P. angulata* was used for further studies.

2.2 Animals

Healthy adult albino rats (125 – 150g) were used for the study and obtained from Animal House of University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana (protocol was approved by Institutional Animal Ethical Committee, KU).

Rats were housed in polypropylene cages in standard environmental conditions (temperature 25±50°C, relative humidity 55±10%). All the animals were acclimatized in laboratory condition for 7 days. The rats were fed on a standard pellet diet and had free access to water during acclimatization.

2.3 Induction of Diabetes

Hyperglycemia was induced in albino rats by the single dose of STZ (50 mg/kg, intraperitonially) reconstituted in normal saline after overnight fasting. On 5th day after STZ administration, the blood sample was collected through tail vein puncture and blood glucose level was measured using one touch select Glucometer strips. Rats with fasting blood glucose level 250 mg/dl were considered for hyperglycemic condition.

2.4 Experimental Study

Albino wistar rats were randomly divided into six groups (n=6). Group I served as normal control and received vehicle orally (N control) (0.25% carboxy methyl cellulose [CMC], 1 ml/kg body weight). Group II served as diabetic control, received 0.25% CMC (1 ml/kg body weight) (D control). Group III, IV, V and VI were given glibenclamide (G, 10 mg/kg), EEP (100 mg/kg), EEP (200 mg/kg) and EEP (300 mg/kg) orally, respectively. All these doses were administered after 5th day of STZ administration (except N control) and were given for seven days. Body weight and blood glucose were measured with strips on 1st, 3rd, 5th, and 7th day of treatment. On 8th day, blood was collected for further biochemical estimation.

2.5 Biochemical Evaluation:

Blood glucose level was measured by one touch select glucometer strips. Liver glycogen level was estimated by using anthrone method. Other estimations such as high density lipoprotein (HDL), total Triglycerides (TG) and total cholesterol (TC) in serum were also measured spectrophotometrically by using lipid profile kit to assess anti-lipidemic activity. Low density lipoprotein (LDL) and Very low density lipoprotein (VLDL) were calculated using Friendewald's Formula.

LDL (mg/dl) = TC – HDL – (TG/5)
VLDL (mg/dl) = TC – HDL – LDL

2.6 Statistical Analysis

The results are presented as mean § SEM using 1-way analysis of variance test (ANOVA) followed by Dunnett's *t* test. $P < 0.01$ was considered significant

3. Results and Discussion

3.1 Effect on Body Weight:

Effect of EEP on body weight in diabetic rats was assessed. Body weight of normal control group increased as compared with D control. D control group showed maximum percentage

Table-1: Effect of EEP on body weight (gm) on STZ induced rats.

Groups	1st day	3rd day	5th day	7th day	% Change in body weight
N Control	145.08±2.01	148.02±6.05	156.23±9.08	168.34±4.09	15.80
D Control	147.21±7.12	142.13±4.09	132.33±6.10	129.19±3.10	-12.20
D+G (10 mg/kg)	145.25±3.07	147.34±6.14	151.31±7.16[a]	157.18±2.00[a]	8.27
D+EEP (100 mg/kg)	144.15±7.03	145.41±4.15	145.32±6.03[b]	146.23±3.04[a]	1.38
D+EEP (200 mg/kg)	146.17±5.11	147.35±3.08	149.20±2.07[a]	151.09±3.18[a]	3.42
D+EEP (300 mg/kg)	145.27±7.22	148.25±6.10	149.19±3.07[a]	153.08±5.19[a]	5.51

Data represented as mean±SD. Statistically significant differences were between D control and G/EEP groups [one way-ANOVA followed by Bonferroni multiple comparison test; [a]p<0.001, [b]p<0.01]

Table 2: Effect of EEP on blood glucose level (mg/dl) on STZ induced diabetic rats.

Groups	1st day	3rd day	5th day	7th day
N Control	89.75±6.39	92.75±3.86	94.23±3.44	94.51±2.38
D Control	282.50±10.34	286.08±8.08	293.75±9.18	303.09±9.93
D+G (10 mg/kg)	275.75±8.77	254.5±9.38[a]	220.25±11.44[a]	178.75±6.02[a]
D+EEP (100 mg/kg)	290.06±5.54	288.11±4.65	281.37±5.11	278.33±2.54[a]
D+EEP (200 mg/kg)	295.5±7.74	281.27±7.50	260.75±2.87[a]	223.12±5.47[a]
D+EEP (300 mg/kg)	290.33±4.56	270.54±4.67[b]	240.38±5.52[a]	205.13±5.42[a]

Data represented as mean±SD. Statistically significant differences were observed between D control and G/EEP groups (100, 200 and 300 mg/kg) [one way-ANOVA followed by Bonferroni multiple comparison test; [a]p<0.001, [b]p<0.01]

Table-3: Effect of EEP on glycogen content in liver and lipid profile in serum (TG, TC, HDL and LDL) on STZ induced rats.

Groups	Glycogen (mg/gm)	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
N Control	39.46±2.62	78.75±5.12	59.5±6.55	38.75±3.30	28.1±1.36	11.9±0.29
D Control	17.03±1.78	193±12.05	160.5±6.75	26.75±3.5	134.15±2.19	32.1±1.08
D+G (10 mg/kg)	31.01±1.13[a]	142.5±4.20[a]	126.25±4.75[a]	35.75±2.21[a]	81.5±2.08[a]	25.25±1.96[a]
D+EEP (100 mg/kg)	22.45±2.23[a]	180±8.97	160±4.98	26.55±2.37	121.45±1.39[a]	32.09±1.73
D+EEP (200 mg/kg)	29.82±1.91[a]	157.5±6.45[a]	140±2.58[a]	28.5±3	101.45±1.98[a]	28.1±1.55[a]
D+EEP (300 mg/kg)	30.34±2.11[a]	150.33±2.43[a]	134.66±3.35[a]	32.11±2.55[c]	91.29±1.06[a]	26.6±1.18[a]

Data represented as mean±SD. Statistically significant differences were between D control and G/EEP groups [one way-ANOVA followed by Bonferroni multiple comparison test; [a]p<0.001, [c]p<0.05]

(-12.2%) of weight loss till the end of experiment. Treatment with EEP (100, 200 and 300 mg/kg) exhibited improved body weight as compared with D control group. Maximum improvement (5.31%) was observed in EEP (300 mg/kg) dose as compared to lower two dosages (Table-1).

3.2 Effect of Blood Glucose Levels

Changes in blood glucose level in all groups were assessed. Fasting blood glucose level of the normal control group were 87.65±5.39 mg/dl in 7 days of study, while there was the significant increase in blood glucose level of D control group (301±7.93mg/dl) in the similar experiment. G treated group caused significant reduction of blood glucose level from 273.55±6.57 to 176.55±4.02 mg/dl. Oral administration of EEP (100, 200, 300 mg/kg) showed a significant reduction of blood glucose level as compared with D control group. EEP (300 mg/kg) exhibited maximum hypoglycemic effect with reduction of glucose concentration from 289 to 203 mg/dl as compared to other doses of EEP (Table-2).

3.3 Effect on Lipid parameters and Glycogen in diabetic rats

The effect of EEP on glycogen content and lipid profile in diabetic rats was evaluated to assess dyslipidemia and anti-lipidemic activity. Glycogen content in liver is an important parameter to measure hypoglycemic effect of drugs. Oral administration of EEP at various doses showed statistically significant increase of glycogen content in liver with respect to D control group. The glycogen reduction effect of EEP at 300 mg/kg (29.24±1.91 mg/gm) was comparable to standard control (G group, 30.01±1.03 mg/gm).

In the present study, we observed that cholesterol level was significantly elevated in D control group (191±11.05 mg/dl) as compared to normal control group 76.55±3.12 mg/dl. The treatment with EEP (200 and 300 mg/kg) showed significant reduction in cholesterol level (155.5±4.45 and 150.13±2.13 mg/dl) as compared with D control group after 7 days of treatment. Similar trends were observed for TG, LDL and VLDL where we found that there was a significant reduction of all these parameters with respect to D control group. Treatment with EEP significantly reversed the TG level from 158 to 132 mg/dl where the effect was comparable to standard. Similarly, significant attenuation was observed in the case of LDL from 132 to 90 mg/dl in the dose dependent manner after EEP treatment. Moreover, EEP and G groups showed significant reduction in VLDL level as compared with D control group. Opposite trend was observed for HDL level where treatment

with EEP and G (glibenclamide) improved HDL level as compared to D control group.

Cardiovascular diseases constitute the main cause of morbidity and mortality in diabetes mellitus. Diabetic individuals have a 2- to 4-fold increased risk of clinical atherosclerotic disease [8,9]. Dyslipidemia has been proven to be the most important modifiable risk factor contributing to atherosclerosis in diabetes [10]. Furthermore, there is widespread acceptance of a possible role for reactive oxygen species, generated as a result of hyperglycemia, in causing many of the secondary complications of diabetes, such as nephropathy, retinopathy, and neuropathy [11].

4. Conclusions

In our study, EEP decreased blood glucose level and improved lipid profile. It also restored hepatotoxicity biomarkers, ALT and AST enzymes. These results suggested that EEP have antidiabetic and hypolipidemic activities in STZ induced diabetic rats and it could be good adjutants in pharmacotherapy of diabetes. Moreover, further work is required to explore the cellular and molecular mechanism of action of this extract. Finally, we observed that EEP had good antidiabetic activity and lesser toxicity potential which might be beneficial for future drug design perspective. Based on the overall results obtained from this study it concludes that the fruits extracts of the selected plant has antidiabetic effects and possess beneficial effect on the hyperglycemia associated with hyperlipidemia/dyslipidemia.

Competing Interests

The authors have declared that no competing interests exist.

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