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Research Article

Antidiabetic activity of ethanolic extract of *Rhynchosia suaveolens* (L.F.) DC. in Streptazotocin induced diabetic rats

Vinoth Kumar S*[1], Gopal V[2], Devanna N[3]

[1]Research Scholar, Jawaharlal Nehru Technological University Anantapur, Ananthpuramu, Andhra Pradesh, India
[2] Department of Pharmacognosy, Mother Therasa post graduate ad Research Institute of Health Sciences, Pondicherry, India
[3]Department of Chemistry, Jawaharlal Nehru Technological University, Ananthapuramu, Anantapur, Andhra Pradesh, India

ABSTRACT

To evaluate the antidiabetic potential of ethanolic extract of *Rhynchosia suaveolens* (L.F.) DC. (EERS) in Streptazotocin induced diabetic rats. The Preliminary Phytochemical analysis was done by standard laboratory methods and acute toxicity studies were performed by OECD test guide lines 423. The present study, the hypoglycaemic effect of ethanolic extract of *Rhynchosia suaveolens* (L.F.) DC. was evaluated by using streptazotocin (STZ) induced diabetic rats at doses of 100 and 200 mg/kg p.o. daily for 28 days. The effect of extracts on diabetic rats in body weight, blood glucose, cholesterol, triglycerides, serum protein, albumin, alkaline phosphates, SGOT, SGPT, serum creatinine and urea contents were analysed. EERS shown significant ($P < 0.01$) reduction in blood glucose. EERS treatment significantly increase the serum protein, albumin, HDL-C, liver glycogen. EERS also significantly reduced in SGOT, SGPT, ALP, serum creatinine, urea, cholesterol, triglycerides LDL-C and AIP. Histopathology of pancreas in EERS treated group showed regeneration of β- cells. The results of the study showed that EERS exerted Posses significant antidiabetic activity in STZ induced diabetic rats which justifying its traditional use.

Keywords: *Rhynchosia Suaveolens;* Streptozotocin; Antidiabetic; Hypoglycaemic effect.

INTRODUCTION

Traditional medicines (medicines derived mainly from plants) play major role in the management of chronic diseases like diabetes mellitus (Ahmed et al., 2004; Poonam Shokeen Patel and Srinivasan, 1997). A plenty of traditional herbal medicines practice has been adopted for the diagnosis, treatment and prevention of diabetes mellitus.

Diabetes mellitus is a common endocrine and metabolic disorder caused by absolute or relative lack of insulin or insulin reduced activity characterized by impaired homeostasis of lipid and carbohydrate metabolism which ultimately results in persistent hyperglycaemia. The severity of diabetes is increasing day by day. The traditional classification of diabetes mellitus includes two major types, type 1 Diabetes mellitus (T1DM) and type 2 Diabetes mellitus (T2DM). T1DM only accounts for 3–5% of Diabetes mellitus but more than 90% are of T2DM (Zimmet et al., 2001). There are number of factors responsible for the disease; among them ageing, urbanization, high fat diet, decreased physical activity (Tao Zheng). The typical characteristic feature of T2DM is insulin resistance (IR). High circulating lipids from high fat diet induces muscle and liver steatosis and is associated with the development of insulin resistance. This IR may further increases the severity of tissue steatosis and hyperlipidemia which contributes to the pathogenesis of cardiovascular diseases and mortality (Smith and Ravussin, 2002; Marchesini et al., 2001; Day and Saksena, 2002). Therefore it is essential not only to control hyperlipidemia but also hyperlipidemia and tissue steatosis for the ideal treatment of T2DM (Aissaoui et al., 2011).

Excess circulating lipids resulting from high-fat diet induce liver and muscle steatosis, which is tightly associated with the development of insulin resistant in these two tissues (Smith and Ravussin, 2002). In addition, IR may further increase the severity of tissue steatosis and hyperlipidemia and is contribute to the pathogenesis of cardiovascular disease and mortality (Eckel et al., 2004). Therefore, in addition to controlling hyperglycemia, dyslipidemia and tissue steatosis should be considered for ideal treatment of T2DM (Aissaoui et al., 2011). However, Hypolipidemic activity is not included in most of the antidiabetic medicines presently

* Corresponding Author
Email: vinogkcp@gmail.com
Contact: +91-9894756527
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in use. Searching for new reagents that are able to control both hyperglycemia and abnormal lipid profile is necessary to manage this disease.

World Health Organization (WHO) has recommended the use of medicinal plant for the treatments of diabetes as they are effective, non-toxic, with less or no side effects (Day, 1998). The genus *Rhynchosia* of twining or erect herbs found in the tropics of both hemispheres. About 22 species have been recorded in india; *Rhynchosia suaveolens* used for antinociceptive, anti-inflammatory, anti-diabetic, anti-fertility and anti-pyretic effects (The wealth of India, 1976). The present work was taken to explore the antidiabetic property of a plant *Rhynchosia suaveolens* (L) DL in streptozotocin induced diabetes rats.

MATERIAL AND METHODS

Plant collection and preparation of plant extract

The aerial parts of the plant were collected from the coastal areas of Tirunelveli, in the month of November and were identified and authenticated by Dr.S.JohnBritto, The director, The Rapinat herbarium centre for molecular systematic, Tiruchirapalli, Tamilnadu, The powdered aerial parts of *Rhynchosia suaveolens* was dried in shade for two weeks. After it was coarsely powdered sieved (40) and extracted with ethanol using soxhlation method. The extracts were evaporated using a rotary evaporator. The extract was preserved in refrigerator at 4^0 C until further use.

Animals

Healthy adult male Wistar rats weighing 150-200 gm were housed in stainless steel cages at a controlled room temperature of 24°C, under a 12 h light and 12 h dark cycle. After one week of acclimatization, the animals were used for experimentation. The experimental protocol was approved by the Institutional Animal Ethical Committee (1230/PO/E/S/08/CPCSEA).

Acute oral toxicity study

The acute oral toxicity study was accomplished as per the Organization for Economic and Cooperation Development (OECD) 423 guide lines. The animal received EERS starting at 2000mg/kg orally. The animals were observed continuously for 4hrs under following profiles i.e. mortality and medical signs of poisoning (general behaviour, respiratory patterns, cardiovascular signs, motor tasks, reflexes) (shirwaikar et.al., 2006).Finally the number of survivors were noted after 24 hours and then these animals were maintained for further 13 days with daily observations.

Induction of diabetes and experimental design

Diabetes was induced in overnight fasted rats by a single intraperitoneal (i.p.) of freshly prepared solution of STZ (50 mg/kg body weight) in 0.1 M citrate buffer (pH 4.5). After 72 hours of STZ administration blood was collected and serum glucose levels were observed. The animals confirmed as diabetic by the elevation blood glucose levels (more than 200 mg/dl) were used for the experiment.

Group- I - (Normal healthy control)given only vehicle (Tween 80, 1% v/v)
Group- II - Diabetic control (STZ 50 mg/kg body weight i.p)
Group -III- Diabetic rats treated with EERS (100 mg/kg b.wt) .
Group- IV- Diabetic rats treated with EERS (200 mg/kg b.wt)
Group -V- Diabetic rats treated with Metformin (10 mg/kg b.wt)

Choosing Group I as control and Group II as diabetic control, all the remaining groups (Group III-IV) had been considered as treated groups serving group V as positive control. For all the above stated groups, selected doses should be provided for duration of 28 days, continuously. The initial and final body weights were measured.

Biochemical analysis

Blood samples were collected on 28^{th} day and centrifuged (2000 rpm/10 min) to get the serum. The serum had been utilized for the estimation of various biochemical parameters such as glucose, Glycosylated HB, protein, cholesterol levels, creatinine, bilirubin, HDL, LDL, Albumin, Blood Urea, alkaline phosphatase (ALP), SGOT, SGPT, AIP, Liver & Kidney Glycogen as per reported methods (Dinesh kumar et.al) using ERBA diagnostic kits (Mumbai) using auto analyser (ERBA Chem-7).

Histopathology

Pancreas was instantly dissected out, excised and rinsed in ice-cold saline solution. A portion of pancreas was fixed in 10% neutral formalin solution. The sections were stained with haematoxylin-eosin and histological observations were made under a light microscope (Humason, 1979).

Statistical analysis

The statistical analysis were carried out by data were expresses as the mean ±SEM. Significance difference between groups were calculated according to one way ANNOVA followed by Dunnet's multiple comparison test for the control and treatment groups using Graph pad prism 5.0 P value ≤ 0.05 was considered as significance.

RESULTS

Phytochemical analysis

The presence of alkaloids, Glycosides, carbohydrate, flavonoids, terpenoids, phytosterols, proteins and

Table 1: Changes in blood glucose level of normal, diabetic rats after 28 days of treatment with EERS

Groups	0th	7th	14th	21th	28th
Normal	77.49±4.14	78.59±3.98	79.6±2.367	80.01±1.65	81.5±2.522
Diabetic control	260.81±8.87	265.97±6.45	266.91±8.14	268.03±7.71	268.61±6.78
Diabetic + EERS (100mg/kg)	247.66± 4.47**	184.05±4.25**	165.31±4.13**	146.84±4.22**	127.98±4.08**
Diabetic + EERS (200mg/kg)	254.54±4.19**	166.81±4.45**	136.21±3.06**	132.71±376**	105.85±2.55**
Diabetic + Metformin (10 mg/kg)	250.14±4.98**	156.73±4.17**	129.27±3.11**	121.1±4.38**	96.18±2.18**

Values are Mean ± SEM (n=6). *P < 0.05, **P < 0.01 and ***P < 0.001; (Metformin and EERS treated diabetic rats were compared with diabetic rats).

Table 2: Levels of body weight of normal, diabetic rats after 28 days of treatment with EERS

Experimental groups	Body weight (g)	
	Initial	Final
Normal	176±3.70	178.29±3.20
Diabetic control	178±3.07	128.29±2.87
Diabetic + EERS (100mg/kg)	182.12±2.18	173.12±2.25
Diabetic + EERS (200mg/kg)	177±1.69	176±3.96
Diabetic + Metformin (10 mg/kg)	180±3.82	188.14±3.24

Table 3: Activities of Serum lipid levels of normal, diabetic rats after 28 days of treatment with EERS

Group	Serum cholesterol (mg/dL)	HDL-C	LDL-C	Triglyceride (mg/dL)	AIP (mg/dL)
Normal	103.33±2.74	49.35±2.67	16.76±0.42	118.35±2.51	0.03075±0.021
Diabetic control	191.16±5.60	32.58±1.41	52.72±2.42	188.3±3.39	0.35425±0.04
Diabetic + EERS (100mg/kg)	142.66±3.64**	36.67±1.30 *	29.81±1.82**	151.32±3.02**	0.262±0.025^{ns}
Diabetic + EERS (200mg/kg)	130.83±2.18**	43.85±2.904**	23.99±1.63**	130.17±2.25**	0.113±0.028**
Diabetic + Metformin (10 mg/kg)	110.5±2.06**	48.25±2.634**	17.62±0.33**	118.81±3.02**	0.038±0.025**

Values are Mean ± SEM (n=6). *P < 0.05, **P < 0.01 and ***P < 0.001; (Metformin and EERS treated diabetic rats were compared with diabetic rats).

phenolic compounds were confirmed during preliminary phytochemical screening.

Acute toxicity study

The acute oral toxicity test showed the normal behaviour of the treated rats. No toxic effects were observed at a higher dose of 2000 mg/kg b.w. the body weight and food consumption was normal when compared to vehicle treated rats. Hence there were no lethal effects, which indicated that it may have a reasonable safety margin with regards to acute toxicity. For further studies the concentration was fixed as 100 and 200 mg/kg.

Effect of EERS on blood glucose level in diabetic rats

Serum glucose level was measured in normal and experimental rats on day 0, 7, 14, 21 and 28 of treatment. STZ- treated diabetic rats showed significant increase in the levels of blood glucose when compared to normal rats. After the treatment of EERS at 100 mg/kg and 200 mg/kg was significantly decreased (P<0.01) compared to the diabetic rats. The metformin treated rats also showed significant (P<0.01) reduction in plasma glucose level (Table 1).

Effect on body weight

STZ induced antidiabetic rats, with EERS showed significant antidiabetic activity at both doses i.e. 100 and 200 mg/kg b.w (P<0.01). The extracts significantly increased the body weight of diabetic rats at higher doses shown in (Table.2).

Biochemical parameters

Determination of serum lipid levels

Dyslipidemia in the form of elevated TC, TGL, AIP and LDL as well as decreased HDL were noticed in diabetic rats. When these diabetic rats were subjected to standard and EERS in 100, 200 mg/kg doses (Table. 3). These rats responded well in the form reversal of respective component of lipid profile back to normal

Table 4: Levels of serum glucose, Hb, albumin and total protein of normal, diabetic rats after 28 days of treatment with EERS

Group	Serum glucose (mg/dL)	Glycosylated Hb (%)	Serum Total Protein (g/dL)	Serum albumin (g/dL)
Normal	75.16±4.74	6.91±0.25	9.25±0.86	4.89±0.205
Diabetic control	230.16±6.74	15.87±0.40	5.06±0.69	2.19±0.104
Diabetic + EERS (100mg/kg)	151.92±3.32**	11.97±0.39**	7.45±0.53*	3.7±0.249**
Diabetic + EERS (200mg/kg)	92.52±4.89**	9.88±0.40**	8.36±0.64**	4.33±0.19**
Diabetic + Metformin (10 mg/kg)	80.09±4.30**	7.72±0.30**	7.75±0.88*	4.63±0.171**

Values are Mean ± SEM (n=6). *P < 0.05, **P < 0.01 and ***P < 0.001; (Metformin and EERS treated diabetic rats were compared with diabetic rats).

Table 5: Changes in renal parameters normal, diabetic rats after 28 days of treatment with EERS

Group	Serum Creatinine (mg/dL)	Serum Urea (mg/dL)	Liver glycogen mg/gm	Kidney glycogen mg/gm
Normal	0.505±0.029	46.35±3.10	23.96±0.97	0.1395±0.002
Diabetic control	1.458±0.030	85.75±3.52	14.35±0.51	1.63±0.13
Diabetic + EERS (100mg/kg)	0.77±0.04**	48.58±2.89**	16.52±0.53**	0.977±0.06**
Diabetic + EERS (200mg/kg)	0.55±0.02**	45.43±3.16**	18.33±0.59**	0.708±0.046**
Diabetic + Metformin (10 mg/kg)	0.465±0.029**	40.75±2.96**	19.50±0.51*	0.47±0.04**

Values are Mean ± SEM (n=6). *P < 0.05, **P < 0.01 and ***P < 0.001; (Metformin and EERS treated diabetic rats were compared with diabetic rats).

control to some extent or other. When the statistical analysis was done for intergroup the reversal was significant and it was dose dependent. Hence it is clear that the plant extract (EERS) have lipid regulating property.

Status of EERS on serum glucose, Hb, albumin and total protein in STZ induced diabetic rats

STZ has toxic effect on the serum Glucose, Glycosylated HB as well as decreased Serum total protein, albumin were noticed in diabetic rats. After the 28 days of treatment with EERS at 100 and 200 mg/kg, the serum glucose and Glycosylated HB level came down near normal level and also protein and albumin level increased and difference was statistically significant (P < 0.01) compared to diabetic control rats (Table. 4).

Determination of renal parameters and glycogen

Since STZ has toxic effect on the renal tissues and parameters such as Urea & creatinine and also enzymes involved in glycogen synthesis and prevents glycogenesis, it was assessed the status of decreased in liver glycogen and toxic effect kidney glycogen were estimated in diabetic rats found to be elevated in a significant manner, When compared to normal control. After the 28 days of treatment with EERS at 100 and 200 mg/kg, the urea and creatinine level and kidney glycogen came down near normal level and also Liver glycogen level increased and difference was statistically significant (P < 0.01) compared to diabetic control rats (Table. 5).

Status of EERS on SGOT, SGPT and alkaline phosphate in STZ induced diabetic rats

Since STZ has toxic effect on the SGOT, SGPT and alkaline phosphate were noticed in diabetic rats found to be elevated in a significant manner, when compared to normal control. After the 28 days of treatment with EERS at 100 and 200 mg/kg, the SGOT, SGPT and alkaline phosphate level came down near normal level difference was statistically significant (P < 0.01) compared to diabetic control rats (Table 6).

Histopathological study

Histopathology studies of pancreas of diabetic rats displayed reduction in size of islets, damaged islet population. EERS (100 and 200 mg/kg) and metformin treated rats restored and increased the size of islets shown in Figure 1.

Table 6: Effect of EERS on SGOT, SGPT and alkaline phosphate in STZ induced diabetic rats

Group	SGOT (IU/L)	SGPT (IU/L)	Alkaline Phosphate (IU/L)
Normal	15.38±1.45	13.58±1.33	47.83±1.81
Diabetic control	47.2±3.36	29.5±2.48	105.5±3.45
Diabetic + EERS (100mg/kg)	26.29±1.74**	21.5±2.00**	68.83±2.4**
Diabetic + EERS (200mg/kg)	19.48±1.29**	16.17±1.28**	60.23±2.34**
Diabetic + Metformin (10 mg/kg)	16.1±1.32**	14.16±1.35**	55.71±2.03**

Values are Mean ± SEM (n=6). *P < 0.05, **P < 0.01 and ***P < 0.001; (Metformin and EERS treated diabetic rats were compared with diabetic rats).

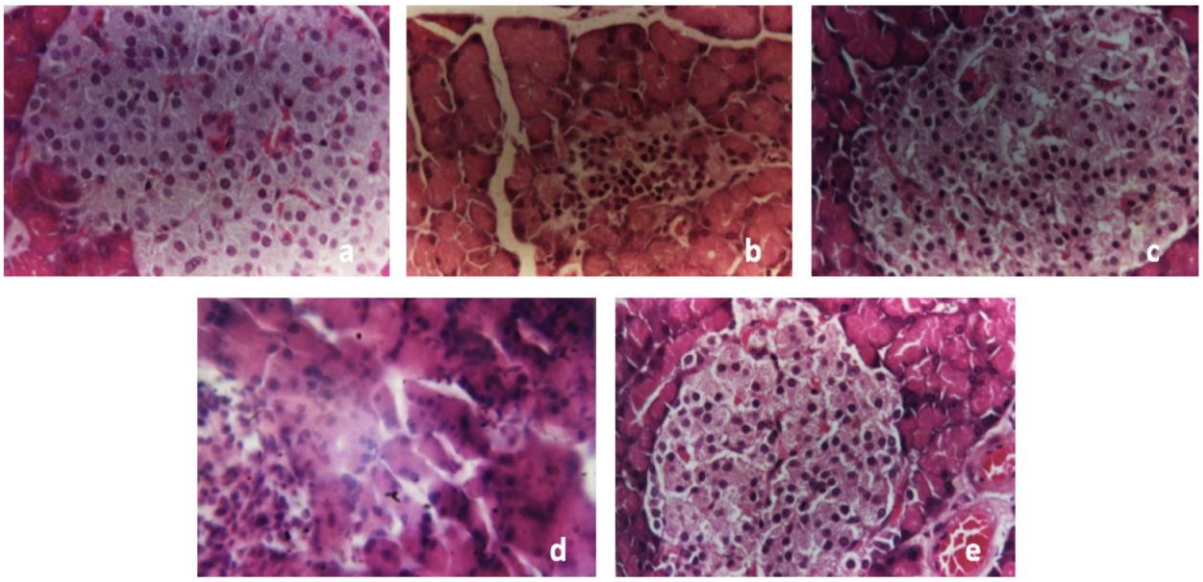

Figure 1: Histopathology studies a. Normal; b. Diabetic control; c. Diabetic+EERS (100mg/kg); d. Diabetic+EERS (200mg/kg); e. Diabetic+Metformin (10 mg/kg)

DISCUSSION AND CONCLUSION

The present study was conducted to evaluate the antidiabetic activity of the EERS on streptazotocin-induced diabetic rats. The results of toxicity study indicate that the lethal dose of EERS is higher than 2000mg/kg and there was no indication of toxicity after sub chronic administration.

The blood glucose level significantly decreased in streptozotocin-induced diabetic rats and the normal blood sugar level were achieved at 100 and 200 mg/kg of EERS (P<0.01) administration. Destruction of β-cells is the Molecular mechanism of induction of diabetes by Streptazotocin (Szkudelski and Szkudeska, 2002); thus in the current study, after the treatment of diabetic rats with EERS (100 and 200 mg/kg) there was a significant decrease in plasma glucose level and improve the insulin levels and it could also act by enhancing peripheral glucose uptake. It might be due to the presence of alkaloids, carbohydrate, flavonoids, proteins and phenolic compounds (Ojewole, 2005).

STZ-induced diabetes is characterized by a severe loss in body weight. The decrease in body weight is due to the increased muscle destruction or degradation of structural proteins. Thus the diabetic rats treated with EERS, showed improvement in body weight in comparison to diabetic control; it signifies the protective effect in controlling muscle wasting like reversal of gluconeogenesis (Salahuddin and Jalalpure, 2010).

STZ involves in elevating the levels of atherogenic index, triglycerides, LDL, total cholesterol and decrease HDL levels. Hypertriglyceridaemia and Hyper cholesterolaemia are foremost diabetic factors concerned in the advance secondary diabetic complications like CHD and atherosclerosis (Ananthan et al., 2003). The results were noticeable decreased in triglycerides, LDL, total cholesterol and raise in HDL levels showed by plant extract. It was concluded that the EERS helped to take care of long-term cardiovascular complications in diabetic conditions.

The role of STZ involves renal metabolism are altered, causes to protein synthesis, nitrogen balance and increases proteolysis (Tuvemo et al., 1997) and high serum levels of urea and creatinine leads to shown renal dysfunction. (Almadal and Vilstrup, 1988). In diabetic rats, elevated level of serum urea and creatinine were reduced by plant extract and it enhances the plasma protein level and preventing the progression of renal damage.

One of the primary storable form of glucose is glycogen and its level in different tissues reflects the activity of Insulin which promotes glycogen formation by stimulating the Enzyme Glycogen synthase. In diabetic animals there is a common decrease in liver glycogen which is due to Insulin deficiency (Chandramohan et al.,

2008). Treatment with EERS extract brought back liver glycogen to near normal which might be due to enhanced insulin levels.

SGOT, SGPT are reliable markers of liver function. In STZ induced diabetic rats, elevated level of SGOT, SGPT enzymes from liver indicate the hepatotoxicity. This was reversed by treating with EERS (Kasetti et al., 2010).

Aromatic plants with rich phenolic compounds has good medicinal values which helps to treat various diseases (Ramkumar et al., 2009). Plants with phenolic compounds are found to be effective anti-oxidants by scavenging free radicals and reduces the oxidative stress associated with diabetis mellitus (Kusirisinetal., 2009).

The results from present study also indicate that *Rynchosia suaveolens* extract may reduce the level of serum cholesterol, triglycerides, SGOT, SGPT, alkaline phosphatase and decrease level of total proteins. It might be due to presence of phenolic compounds vital tissue like pancreas there by reducing causation of diabetes in experimental animals.

The current study provides an evidence for the ethno-medicinal use of *Rynchosia suaveolens* and also indicates the potential for antidiabetic activity. Further research work is in progress to confirm the antidiabetic activity of this plant and to evaluate its potential in the treatment of diabetes.

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