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Antidiabetic activity of ethanol extract of leaves of flax plant (*Linum usitatissimum* L.)

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Abstract

The aim of the present study was to evaluate antidiabetic activity of ethanol extract of leaves of Flax plant (*Linum usitatissimum*) in streptozotocin (STZ) induced diabetic rats. Ethanol extract of leaves of *Linum usitatissimum* (EELL) or glibenclamide was administered to the rats orally daily for 28 days. Blood glucose levels at weekly interval and on 29th day, serum biochemical parameters were carried out to evaluate its antidiabetic effect in diabetic rats. Blood glucose, creatinine, BUN, AST and ALT levels were significantly increased in STZ induced diabetic rats as compared to vehicle control rats. After 28 days administration of EELL showed the significant decrease in above levels as compared to diabetic control rats. The study results suggest that the ethanol extract of leaves of *Linum usitatissimum* clearly demonstrated the antidiabetic activity in an experimental model of rats.

Keywords: *Linum usitatissimum*; Glibenclamide; Streptozotocin; Diabetic rats

1. Introduction

Diabetesis a complex multisystemic disorder characterized by a relative or absolute insufficiency of insulin secretion and disturbances in carbohydrate, protein and lipid metabolism [1]. The worldwide prevalence of diabetes has continued to increase dramatically. According to International Diabetes Federation 7th edition, the number of individuals with diabetes in 2015 crossed 415 million and by 2040, this will rise up to 642 million [2]. Therapies currently available for diabetes include oral hypoglycemic agents like glibenclamide, glipizide, gliclazide, repaglinide, acarbose, miglitol, dipeptidylpeptidase, sitagliptin, linagliptin, alogliptin, gemiglaptin and injectable insulin but they have their ownlimitations due to selective mechanism of action [3]. Drawbacks of insulin therapy are like local pain, inconvenience of multiple injections, insulin edema, lipohypertropy, allergy and resistance. Therefore, searching for effective, low cost and less side effect containing herbalhypoglycemic agents is important. In recent findings, extracts of various plant materials arecapable of decreasing blood sugar level in experimental animal models and are considered to be less toxic than synthetic ones.

Linum usitatissimum plant is a blue or purple flowering crop and a member of family Linaceae commonly called Flax seed or linseed in english, and it is distributed in tropical India [4]. Flax seed playing a major role in the field of diet and disease research due to its health benefits associated with high content of α-linolenic acid and major lignin namely secoisolariciresinol diglucoside (SDG). Based on previous study reports, medicinal activities of flax seed include antioxidant, anticancer, antiviral, bactericidal, anti-inflammatory and antiatherosclerotic [4], decreases the blood glucose and cholesterol levels [5] and decrease the risk of obesity, dyslipidemia and resistance to insulin [6]. Hence in

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the present study research was done to evaluate the antidiabetic activity of ethanol extract of leaves of *Linum usitatissimum* in streptozotocin (STZ) induced diabetic rats.

2. Material and methods

2.1. Experimental Animals

The study was conducted on 30 healthy male Sprague-Dawley rats of 8-12 weeks of age. Rats were purchased from Srinivasa enterprises, Bengaluru India. The experimental protocol was approved by Institutional Animal Ethics Committee (Project No. SCIP/IAEC/01/2021-22) and protocols were followed according to the guidelines of committee for the purpose of control and supervision of experiments on animals (CPCSEA). The animals were housed in standard polypropylene cages and maintained under controlled room temperature (22 ± 2^0C) and humidity (55 ± 5%) with 12 h light and 12 h dark cycle. All the rats were fed normal pellet diet and deionized water was provided *adlibitum* throughout the course of the experiment. All the rats were kept under acclimatization for 5days prior to grouping and initiation of experiment. Rats were kept under constant observation during entire period of study.All necessary managemental procedures were adopted to keep the rats free from stress.

2.2. Drugs and Chemicals

Streptozotocin was purchased from Hi-Media Laboratory Pvt. Ltd., India and glibenclamide was received as gift sample from Sigma-Aldrich. Serum biochemical kits for estimation of serum biochemical parameters were purchased from Coral Clinical System (Goa, India).

2.3. Preparation of the plant extract

Leaves of *L. usitatissimum* were taken and dried under shade, then powdered by mechanical grinder and stored in air tight containers. The dried powder of leaves of *L. usitatissimum* was used for the preparation of ethanol extract. The extract obtained was concentrated in rotary evaporator at 50-60°C under reduced pressure. Ethanol extract of *L. usitatissimum* obtained was transferred to a petri dish and kept over water bath (50°C) until the solvent gets completely evaporated. It was stored in airtight glass containers in refrigerator at 2-8°C for further use in experiments.

2.4. Acute toxicity study

The acute oral toxicity study was carried out as per Organization for Economic Cooperation and Development (OECD) guideline No. 423 [7]. Sprague Dawley rats were taken for the study and dosed once with 2000 mg/kg, orally. The treated rats were monitored for 24 hours and up to 14 days for general clinical signs and symptoms as well as mortality. It was observed that the ethanol extract of *L. usitatissimum* showed no mortality in rats even at 2000 mg/kg dose. Hence 200 and 400 mg/kg dose of extract were selected and considered safe for further study.

2.5. Induction of diabetes in rats

Experimentally induction of diabetes in rats was done by administering single intraperitoneal (i.p.) injection of Streptozotocin at a dose of 60 mg/kg in overnight fasted rats [8].

2.6. Experimental design

The present study was conducted on thirty (30) rats dividing them into various groups, having six rats in each group (n=6).

- Group I-Vehicle control(received normal saline)
- Group II-Diabetic control(received60mg/kg of STZ)
- Group III-Diabetic rats treated with Glibenclamide (5mg/kg)
- Group IV- Diabetic rats treated with EELL (200 mg/kg)
- Group V-Diabetic rats treated with EELL (400mg/kg)

2.7. Body weight and feed consumption

Body weight and feed consumption of all rats were measured weekly interval for 28 days.

2.8. Estimation of blood glucose

Blood was collected from the dorsal vein of the tail and blood glucose was estimated by Dr. Morepen Gluco One (Model: BG-03, Morepen Laboratories Ltd., Delhi, India) on day 0 of treatment and weekly for 28 days [9].

2.9. Biochemical estimation

On termination of experiment, blood samples were collected from retro-orbital plexuses under light anesthesia with the help of capillary tube. Serum biochemical parameters like serum creatinine blood urea nitrogen (BUN), serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT)were estimated by using auto serum chemistry analyser (MindrayBS-120,Mumbai, India) [10].

2.10. Statistical analysis

All the data have been presented as mean ± SE. Statistical comparisons of the results were made using one way analysis of variance (ANOVA) by using software SPSS (Version 20). Significant differences (p<0.05) between different experimental groups were analyzed by Duncan's test [11].

3. Results and discussion

3.1. Effect on body weight and feed consumption

There was significant reduction in body weight gain from 7th to28th day of study and increase feed consumption from 1st, 3rd and 4th week of study in diabetic rats compared to vehicle control rats. Following 28 days oral administration of ethanol extract of leaves of *L. usitatissimum* at the dose 200 and 400 mg/kg showed significant increase body weight gain at 21 and 28 days and decrease feed consumption in diabetic treated rats.

3.2. Effect on blood glucose

There was significant increase in blood glucose Evelin diabetic control rats as compared to vehicle control rats from 0 to 28th day of study, whereas administration of EELL at a dose of 200 and 400 mg/kg and glibenclamide in diabetic rats for 28 days showed significant reduction of the elevated level of blood glucose at 21st and 28th days of study (Table 1). EELL showed its effectiveness in dose dependent manner.

3.3. Effect on biochemical parameters

There was significant increased serum concentration of creatinine, BUN, AST and ALT levels (1.02 ±0.03mg/dl, 32.29±0.34mg/dl, 161.52±9.67U/l, 84.98±2.59 U/l respectively) in diabetic control rats as compared to vehicle control rats (0.34 ± 0.02mg/dl, 18.34 ± 0.20 mg/dl, 103.78 ± 1.64 U/l, 41.54 ± 3.67U/l respectively). While daily oral administration of EELL at the dose 200 and 400 mg/kg in diabetic rat for 28 days produced significant reduction in the serum creatinine, BUN, AST and ALT level as compared to diabetic control rats as depicted in Table 2.

Table 1 The effect of oral administration of EELL on blood glucose of rats for 28 days

Group	Blood glucose (mg/dl) (Mean±S.E.) (n=6)				
	0day	7day	14day	21day	28day
I	108.73 ±5.14^{a}	116.17 ±3.84^{a}	102.17±3.67^{a}	106.01 ±6.20^{a}	115.17 ±3.22^{a}
II	367.00±26.56^{b}	371.33±27.58^{b}	375.50±27.50^{c}	376.33±24.74^{c}	375.83±25.98^{e}
III	391.17±27.18^{b}	347.17±21.92^{b}	297.17±20.80^{bc}	226.50±17.20^{b}	142.00 ±7.57^{ab}
IV	365.33±51.88^{b}	361.67±53.78^{b}	316.50±43.78^{bc}	250.67±38.13^{b}	205.83±27.85^{cd}
V	329.00±32.32^{b}	325.00±31.78^{b}	280.33±29.24^{b}	205.00±16.31^{b}	155.50±12.19^{abc}

Mean value with dissimilar superscript in a column vary significantly at$p$<0.05.VC:VehicleControl,DC=DiabeticControl,TC:TreatmentControl

Table 2 The effect of oral administration of EELL on Creatinine, BUN, AST and ALT of rats for 28 days

Group	Mean±SE values of creatinine (mg/dl) and BUN (mg/dl) in rats of all groups (n=6)			
	Creatinine (mg/dl)	BUN (mg/dl)	AST (U/l)	ALT (U/l)
I	0.34±0.02^{a}	18.34±0.20^{a}	103.78 ±1.64^{a}	41.54±3.67^{a}
II	1.02±0.03^{b}	32.29±0.34^{f}	161.52 ±9.67^{d}	84.98±2.59^{d}
III	0.34±0.03^{a}	19.53±0.38^{b}	116.06 ±5.71^{ab}	46.84±3.31^{ab}
IV	0.38±0.02^{a}	23.48±0.25^{d}	125.63±4.14^{bc}	55.65±4.54^{abc}
V	0.34±0.02^{a}	20.63±0.36^{c}	115.80 ±3.41^{ab}	50.70 ±9.57^{abc}

Mean value with dissimilar superscript in a column vary significantly at $p<0.05$

4. Conclusion

At present, therapeutic options for diabetes are diet, exercise, oral hypoglycemic drugs and insulin therapy [12]. The management of diabetes with the agents devoid of any side effects is still a challenge to the medical system [13]. This concern has led to an increased demand for safe and natural herbal derived treatment of diabetes [14]. Hence the present study was aimed to evaluate the antidiabetic effect of ethanol extract of leaves of *L. usitatissimum* in comparison with Glibenclamide in STZ induced diabetic rat model.

In the present study, the significant increase in blood glucose was observed in STZ induced diabetic rats from 0 to 28th day of study and when diabetic rats administered orally with ethanol extract of leaves of *L. usitatissimum* (200and400mg/kg) and standard drug glibenclamide, a reduction in glucose levels at 21st and 28th days in dose dependent manner were observed. Similar observations were reported for the ethanolic extract of leaves of *L.usitatissimum* administered at dose of 200 and 400 mg/kg.

The results of present study showed significant reduction in the serum creatinine, BUN, AST and ALT levels in ethanol extract of leaves of *L. usitatissimum* at 200and 400mg/kg treated diabetic rats.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflicts of interest.

Statement of ethical approval

Ethical approval for this study was obtained from Institutional Animal Ethics Committee.

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