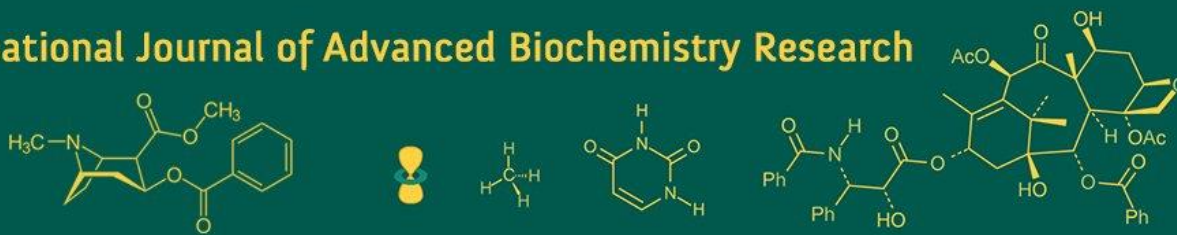


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Antidiabetic activity of alcoholic extract of *Linum usitatissimum* in streptozotocin induced diabetic rats

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Abstract

The aim of the present study is to evaluate antidiabetic activity of alcoholic extract of *Linum usitatissimum* (LU) seeds in streptozotocin (STZ) induced diabetic rats. The LU seeds extract was administered to the rats orally daily for 28 days. Blood glucose measured at weekly interval and various hematological parameters (Hb, RBC, PCV, TLC, MCV, MCH and MCHC), serum biochemical parameters (creatinine, BUN, AST, ALT and total cholesterol) as well as histopathology were carried out at the end of treatment to evaluate its antidiabetic effects in diabetic rats. After 28 days administration of alcoholic extract of LU showed the significant reduction in the elevated blood glucose, creatinine, BUN, AST, ALT and total cholesterol levels along with restoration of the pathological lesions in histoarchitecture of pancreas as compared to diabetic control rats. Our results suggest that the alcoholic extract of LU seeds clearly demonstrated the antidiabetic activity in an experimental model of rats.

Keywords: *Linum usitatissimum*, streptozotocin, glibenclamide, diabetic rats

1. Introduction

Diabetes is a complex multisystemic disorder characterized by a relative or absolute insufficiency of insulin secretion and disturbances in carbohydrate, protein and lipid metabolism (Barik *et al.*, 2008) [6]. 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 (IDF, 2015) [13]. Therapies currently available for diabetes include oral hypoglycemic agents like glibenclamide, glipizide, gliclazide, nateglinide, repaglinide, acarbose, miglitol, dipeptidylpeptidase, sitagliptin, linagliptin, alogliptin, dutogliptin, gemigliptin and injectable insulin but they have their own limitations due to selective mechanism of action (Mangesh *et al.*, 2014) [19]. Drawbacks of insulin therapy are like local pain, inconvenience of multiple injections, insulin edema, lipohypertrophy, allergy and resistance. Therefore, searching for effective, low cost and less side effect containing herbal hypoglycemic agents is important. In recent findings, extracts of various plant materials are capable 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, Alsi or Tisi in hindi, Alsi in gujarati and Atasi in sanskrit and it is distributed in tropical India (Anjaria *et al.*, 2002) [3]. 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 lignan namely secoisolariciresinol diglucoside (SDG). Based on previous study reports, medicinal activities of flaxseed include antioxidant, anticancer, antiviral, bactericidal, anti-inflammatory and antiatherosclerotic (Halligudi, 2012) [11], decreases the blood glucose and cholesterol levels (Kristensen *et al.*, 2012) [14] and decrease the risk of obesity, dyslipidemia and resistance to insulin (Saxena and Katare, 2014) [21]. Hence in the present study research was done to evaluate the antidiabetic activity of alcoholic extract of *Linum usitatissimum* seeds in Streptozotocin (STZ) induced diabetic rats.

2. Materials and Methods

2.1 Experimental animals

The study was conducted on 36 healthy male Sprague-Dawley rats of 8-12 weeks of age. Rats were procured from Zydus Research Centre (ZRC), Ahmedabad, India. The experimental protocol was approved by Institutional Animal Ethics Committee (Project No. 258/VPT/2017) at College of Veterinary Science and Animal Husbandry, Anand, Gujarat 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 °C) and humidity ($55 \pm 5\%$) with 12h light and 12h dark cycle. All the rats were fed normal pellet diet and deionized water was provided *ad libitum* throughout the course of the experiment. All the rats were kept under acclimatization for 5 days 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 purchased from Sigma-Aldrich (Spruce Street, St. Louis, MO, U.S.A.). Serum biochemical kits for estimation of serum biochemical parameters were purchased from Coral Clinical System (Goa, India).

2.3 Collection and authentication of plant materials

Seeds of *L. usitatissimum* were purchased from local market of Anand district (Gujarat) and identified and authenticated by Botanist of Department of Genetics and Plant Breeding, B. A. College of Agriculture, Anand Agricultural University, Anand.

2.4 Preparation of the plant extract

Seeds of *L. usitatissimum* were taken and dried under shade, then powdered by mechanical grinder and stored in air tight containers. The dried powder of *L. usitatissimum* was used for the preparation of alcoholic extract. Exactly 100g of coarse powdered of *L. usitatissimum* seeds was successfully extracted in soxhlet extractor with alcohol. The extract obtained were concentrated in rotary evaporator at 50-60 °C under reduced pressure leaving a brown residue. Alcoholic 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 air tight glass containers in refrigerator at 2-8 °C for further use in experiments. Respective doses for the study were prepared by reconstituting the extract in distilled water.

2.5 Acute toxicity testing of plant extract

The acute oral toxicity study was carried out as per Organization for Economic Cooperation and Development (OECD) guideline No. 423. 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 alcoholic extract of *L. usitatissimum* showed no mortality in rats even at 2000 mg/kg dose. Hence, 100, 200 and 400 mg/kg dose of this plant extract were selected and considered safe for further study.

2.6 Induction of diabetes in rats

Experimentally induction of diabetes in rats by administered single intraperitoneal (i.p.) injection of STZ at dose level of 60 mg/kg in overnight fasted rats. STZ formulation was prepared by using 0.1 M citrate buffer (pH 4.5) solution. Citrate buffer solution was prepared by dissolving 1.47 g of sodium citrate in 50 ml of distilled water and adjust the pH to 4.5 by citric acid solution and kept it in ice cold. STZ was dissolved in freshly prepared citrate buffer solution and used immediately because STZ is pH sensitive compound.

2.7 Experimental design

The present study was conducted on thirty six (36) rats dividing them in various groups, having six rats in each group (n = 6).

Group I-Vehicle control (received normal saline)

Group II-Diabetic control (given STZ 60 mg/kg)

Group III-Treatment control treated with glibenclamide (5 mg/kg)

Group IV-Diabetic rats treated with LU extract (100 mg/kg)

Group V-Diabetic rats treated with LU extract (200 mg/kg)

Group VI-Diabetic rats treated with LU extract (400 mg/kg)

2.8 Body weight and feed consumption

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

2.9 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 day.

2.10 Hematological and biochemical estimation

On 29th day of experiment, blood samples were collected from retro-orbital plexuses under light anesthesia with the help of capillary tube. Blood samples collected in test tubes with K₃EDTA were utilized for estimation of various hematological parameters (Hb, RBC, PCV, TLC, MCV, MCH and MCHC) by hematology auto analyzer (Mindray, BC-2800 Vet, Garnerville, New York). Serum biochemical parameters like serum creatinine, blood urea nitrogen (BUN), serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT) and total cholesterol (TC) were estimated by using auto serum chemistry analyser (Mindray BS-120, Mumbai, India).

2.11 Histopathology

After opening the carcass, gross lesions were recorded and collected tissues like pancreas, kidney, liver, spleen and heart were fixed in 10% formalin. The formalin fixed tissues were processed by paraffin wax embedding method of tissue sectioning. Sections from the tissues were cut at 5-6 microns thickness with automatic section cutting machine (Leica, Automatic Microtome Machine, Germany) and were stained with Haematoxylin and Eosin (H & E) stains.

2.12 Statistical analysis

All the data have been presented as mean \pm 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.

3. Results

3.1 Effect on body weight and feed consumption

There was significant reduction in body weight gain from 7th to 28th 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 alcoholic extract of *L. usitatissimum* at the dose levels of 200 and 400 mg/kg showed significant increase body weight gain at 21 and 28 days and decrease feed consumption in diabetic treated rats. The result of body weight depicted in Table 1.

3.2 Effect on blood glucose

There was significant increase in blood glucose level in diabetic control rats as compared to vehicle control rats from 0 to 28th day of study. Whereas administration of alcoholic extract of *L. usitatissimum* at the dose levels of 100, 200 and 400 mg/kg and glibenclamide in diabetic rats for 28 days showed significant reduction in the elevated level of blood glucose at 21st and 28th days of study as depicted in Table 2. Alcoholic extract of *L. usitatissimum* showed their effectiveness in dose dependent manner.

3.3 Effect on hematological parameters

Diabetic control rats showed significant decrease in Hb, RBC and PCV as compared to vehicle control rats whereas significant increase in TLC as compared to vehicle control rats. While daily oral administration of alcoholic extract of *L. usitatissimum* at the dose of 100, 200 and 400 mg/kg body weight for 28 days showed significant increase in the Hb, PCV and also significant increase in RBC count at the dose levels of 200 mg/kg and 400 mg/kg body weight extract treated rats, whereas significant decrease in TLC within normal physiological range in at higher dose (400 mg/kg) extract treated rats as compared to diabetic control rats as depicted in Table 3.

3.4 Effect on biochemical parameters

There was significant increased serum concentration of creatinine, BUN, AST, ALT and total cholesterol level in diabetic control rats as compared to vehicle control rats. While daily oral administration of alcoholic extract of *L. usitatissimum* at the dose levels of 100, 200 and 400 mg/kg in diabetic rat for 28 days produced significant reduction in the serum creatinine, BUN, AST, ALT and TC level as compared to diabetic control rats as depicted in Table 4.

3.5 Histopathology

In the present study, histopathological examination of section of pancreas from vehicle control rats showed normal architecture of β cells of islets of Langerhans and acinar cells as depicted in Figure 1. Pancreas of diabetic control rats revealed destruction and decrease in number, derangement, diminished size and shape of β cells and damaged acinar cells with abnormal architecture of islets of Langerhans (Figure 2), while pancreas of glibenclamide and alcoholic extract treated rats at dose level of 400 mg/kg daily for 28 days showed no defined pathological lesions in histoarchitecture of islets of Langerhans and acinar cells (Figure 3). Whereas other organs like kidney, liver, spleen and heart from diabetic control, treatment control and alcoholic extract treated rats did not showed any marked gross and microscopic alterations.

4. Discussion

At presently, therapeutic options for diabetes are diet, exercise, oral hypoglycemic drugs and insulin therapy. The management of diabetes with the agents devoid of any side effects is still a challenge to the medical system. This concern has led to an increased demand for safe and natural herbal derived treatment of diabetes [Sharma *et al.*, 2011 & Are *et al.*, 2011] [26, 4]. Hence the present study aimed to evaluate the antidiabetic effect of alcoholic extract of *L. usitatissimum* seeds in comparison with Glibenclamide in STZ induced diabetic rat model.

In our 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 alcoholic extract of *L. usitatissimum* (100, 200 and 400 mg/kg) and standard drug glibenclamide, a reduction in glucose levels at 21st and 28th days in dose dependent manner were observed. Similar study were also reported for the ethanolic extract of *L. usitatissimum* administered at dose levels of 200 and 400 mg/kg for 28 days showed significant reduction in serum glucose level on day 7, 14, 21 and 28 respectively as compared to diabetic control group. Likewise, linseed oil administered at the dose levels of 500 and 1000 mg/kg/day for 28 days showed significant decreased glucose level in diabetic rats (Kumar *et al.* 2013). Similar results were also founded for 10% and 20% flax seed treated group showed significant reduction in fasting blood sugar at 14th day compare to standard drug metformin (Venkatachalam *et al.* 2015) [24]. Flaxseed was given at 0.714 g/kg/day orally in 0.1% carboxymethyl cellulose for 12 weeks showed significant decreased blood glucose level compare to diabetic control rats (Gok *et al.* 2015) [10]. Oral administration of herbal formulation of flaxseed, fenugreek and jamun seeds (1:1:1) at dose of 200 mg/kg and their individual compounds for 28 days showed significant ($P < 0.05$) reduction in blood glucose level compare to diabetic control rats (Latha *et al.*, 2016) [17]. Additionally in agreement to our study, decreased glucose level in rats after administration of flaxseed extract orally at dose of 400 mg/kg for 4 weeks as compare to diabetic control group were also reported (Al-Ania *et al.* 2017) [1].

In the present study, finding showed significant increased Hb, PCV and RBC count in alcoholic extract treated diabetic rats. Similar result was also reported as feeding of 10% flaxseed for 56 days showed significantly increase in total RBC and PCV count in diabetic rats (Babu *et al.* 2000) [5]. Likewise, oral administration of herbal formulation of flaxseed, fenugreek and jamun seeds (1:1:1) at dose of 200 mg/kg and their individual drug for 28 days showed significant increased Hb level in diabetic rats (Latha *et al.* 2016) [17].

The results of present study showed significant reduction in the serum creatinine, BUN, AST, ALT and TC levels in alcoholic extract of *L. usitatissimum* at the dose levels of 100, 200 and 400 mg/kg treated diabetic rats. Similarly, feeding of flaxseed oil for eight weeks showed significant reduced serum creatinine and urea levels diabetic rats (Soltan, 2012) [23]. Likewise another report on flaxseed supplemented (10% w/w) for 8 weeks showed significant decreased serum creatinine, BUN, AST and ALT level in rats (Al-Bishri, 2013) [2]. Additionally, administration of flaxseed oil at dose of 500 mg/kg daily for 8 weeks showed significant ($P < 0.01$) decreases in the elevated creatinine, BUN, AST and ALT levels in rats (Wahba and Ibrahim,

2013) [25]. In another report showed significant decreased serum creatinine and BUN level in different levels of flaxseed oil (20, 30 and 40 g/kg) given rats (Sayeda *et al.*, 2014) [22]. Similarly, administration of (33%) flax and pumpkin seed mixture for 30 days leads to significant decreased plasma and liver AST, ALT and TC level in alloxan induce diabetic rats (Makni *et al.* 2011) [18]. In another report, administration of linseed oil at dose of 500 and 1000 mg/kg/day for 28 days showed significant decreased total cholesterol level in diabetic rats (Kumar *et al.*, 2013) [16], also administration of 4% flaxseed oil in diabetic rats showed significantly decrease in TC level. Flaxseed given (0.714 g/kg/day, orally) for 12 weeks showed significant decreased in AST and ALT level in diabetic rats (Gok *et al.*, 2015) [10]. The flaxseed extract given orally at dose of 20 mg/kg body weight for 14 days showed significant decreased total cholesterol in rats (Haran

et al., 2017). Similarly, flaxseed oil administered at the dose 1.8 mg/kg for 8 week showed significant decreased total cholesterol level in rats. (Elimam and Ramadan, 2018) [9]. The findings of the present study showed no defined pathological lesions in histoarchitecture of pancreas of alcoholic extract treated diabetic rats. In agreement to our report, administration of (33%) flax and pumpkin seed mixture supplemented for 30 days showed normal β cell architecture in pancreas (Makni *et al.* 2011) [18]. Similarly, 8 weeks feeding of flaxseed oil showed protection of the pancreatic β -cells and preserving pancreatic normal structure with no histopathological changes in diabetic rats (Soltan, 2012) [23]. In another report, treatment of mice orally at dose of 100 μ g/200 μ L of *Linum usitatissimum* fraction suspended in distilled water with 0.5% DMSO for 21 days showed potential for the formation of new islets *in vitro* as well as *in vivo* in the pancreas (Dusane and Joshi, 2013) [8].

Table 1: The effect of 28 days oral administration of alcoholic extract of *L. usitatissimum* on body weight of rats

Group	Treatment	Body weight (g) (Mean \pm S.E.) (n = 6)				
		0 day	7 day	14 day	21 day	28 day
I	VC	242.00 \pm 3.44	272.00 \pm 7.22 ^b	303.67 \pm 3.51 ^e	326.17 \pm 3.83 ^e	336.67 \pm 5.59 ^e
II	DC	230.67 \pm 4.96	234.33 \pm 5.17 ^a	229.17 \pm 5.37 ^a	225.33 \pm 4.56 ^a	226.83 \pm 5.25 ^a
III	TC	243.17 \pm 5.88	267.83 \pm 4.36 ^b	278.83 \pm 10.62 ^d	300.50 \pm 2.46 ^{cd}	312.83 \pm 2.12 ^f
IV	LU AI-100	244.50 \pm 3.61	246.00 \pm 3.79 ^a	243.67 \pm 3.62 ^{abc}	243.17 \pm 3.89 ^b	243.67 \pm 5.47 ^b
V	LU AI-200	244.67 \pm 2.64	248.50 \pm 3.25 ^a	252.00 \pm 4.46 ^{bc}	256.67 \pm 5.77 ^{bc}	261.83 \pm 5.78 ^{cde}
VI	LU AI-400	246.17 \pm 3.16	250.00 \pm 3.93 ^a	257.33 \pm 4.92 ^c	265.67 \pm 3.04 ^c	277.00 \pm 3.02 ^e

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

Table 2: The effect of 28 days oral administration of alcoholic extract of *L. usitatissimum* on blood glucose of rats.

Group	Treatment	Blood glucose (mg/dl) (Mean \pm S.E.) (n = 6)				
		0 day	7 day	14 day	21 day	28 day
I	VC	107.83 \pm 5.54 ^a	118.17 \pm 3.94 ^a	103.17 \pm 3.77 ^a	107.00 \pm 6.10 ^a	118.17 \pm 3.32 ^a
II	DC	368.00 \pm 26.66 ^b	370.33 \pm 27.48 ^b	374.50 \pm 27.70 ^c	375.33 \pm 27.74 ^c	376.83 \pm 26.98 ^e
III	TC	390.17 \pm 27.08 ^b	346.17 \pm 20.92 ^b	298.17 \pm 20.90 ^{bc}	227.50 \pm 17.10 ^b	143.00 \pm 7.97 ^{ab}
IV	LU AI-100	319.00 \pm 34.15 ^b	316.50 \pm 34.64 ^b	306.00 \pm 34.42 ^{bc}	281.50 \pm 27.55 ^b	264.67 \pm 27.50 ^d
V	LU AI-200	360.33 \pm 29.79 ^b	353.67 \pm 27.66 ^b	320.67 \pm 26.77 ^{bc}	280.67 \pm 23.74 ^b	248.17 \pm 18.95 ^d
VI	LU AI-400	333.17 \pm 28.07 ^b	331.00 \pm 27.12 ^b	284.50 \pm 17.28 ^{bc}	242.00 \pm 14.29 ^b	180.83 \pm 11.69 ^{bc}

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

Table 3: The effect of 28 days oral administration of alcoholic extract of *L. usitatissimum* on Hb, RBC, PCV, TLC MCV, MCH and MCHC of rats.

Group	Treatment	Mean \pm SE values of Hb (g/dl), RBCs ($10^6/\mu$ L), PCV (%) and TLC ($10^3/\mu$ L) in rats (n = 6)						
		Hb (g/dl)	RBC ($10^6/\mu$ L)	PCV (%)	TLC ($10^3/\mu$ L)	MCV (fl)	MCH (pg)	MCHC (g/dl)
I	VC	16.52 \pm 0.66 ^b	8.14 \pm 0.35 ^{bcd}	42.25 \pm 1.57 ^c	8.95 \pm 0.29 ^{ab}	52.46 \pm 3.37	20.64 \pm 1.68 ^{ab}	39.41 \pm 2.29 ^a
II	DC	14.85 \pm 0.39 ^a	6.67 \pm 0.20 ^a	31.85 \pm 2.21 ^a	12.03 \pm 0.39 ^c	48.27 \pm 4.41	22.40 \pm 0.98 ^{bc}	47.60 \pm 2.99 ^{bc}
III	TC	17.13 \pm 0.21 ^b	8.09 \pm 0.35 ^{bcd}	41.05 \pm 1.64 ^{bc}	9.89 \pm 0.28 ^{ab}	50.98 \pm 2.05	21.39 \pm 1.02 ^{ab}	42.14 \pm 2.04 ^{ab}
IV	LU AI-100	16.65 \pm 0.59 ^b	7.27 \pm 0.17 ^{ab}	37.00 \pm 0.78 ^b	10.43 \pm 0.28 ^{abc}	51.08 \pm 1.76 ^a	23.03 \pm 1.23 ^{bc}	45.07 \pm 1.70 ^{abc}
V	LU AI-200	17.30 \pm 0.29 ^b	7.76 \pm 0.35 ^{bc}	40.49 \pm 0.85 ^{bc}	10.29 \pm 0.31 ^a	52.94 \pm 3.39 ^a	22.49 \pm 0.82 ^{bc}	42.87 \pm 1.45 ^{abc}
VI	LU AI-400	16.80 \pm 0.64 ^b	8.95 \pm 0.35 ^d	40.67 \pm 1.45 ^{bc}	9.63 \pm 0.32 ^{ab}	45.70 \pm 2.10 ^a	18.80 \pm 0.48 ^a	41.44 \pm 1.61 ^a

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

Table 4: The effect of 28 days oral administration of alcoholic extract of *L. usitatissimum* on creatinine and BUN, AST, ALT and TC of rats.

Group	Treatment	Mean \pm 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)	TC (mg/dl)
I	VC	0.36 \pm 0.02 ^a	18.44 \pm 0.30 ^a	103.98 \pm 1.54 ^a	41.58 \pm 3.77 ^a	82.95 \pm 4.84 ^a
II	DC	1.03 \pm 0.02 ^b	32.19 \pm 0.44 ^f	161.51 \pm 9.87 ^d	83.98 \pm 2.69 ^d	149.48 \pm 5.07 ^e
III	TC	0.36 \pm 0.02 ^a	19.52 \pm 0.39 ^b	117.07 \pm 5.70 ^{ab}	46.88 \pm 3.41 ^{ab}	97.95 \pm 1.63 ^{bc}
IV	LU AI-100	0.44 \pm 0.03 ^a	26.19 \pm 0.35 ^e	135.58 \pm 12.11 ^{bc}	67.90 \pm 8.36 ^c	119.42 \pm 2.37 ^d
V	LU AI-200	0.41 \pm 0.02 ^a	24.33 \pm 0.39 ^d	120.95 \pm 3.66 ^{abc}	63.53 \pm 5.17 ^{bc}	106.18 \pm 2.73 ^{cd}
VI	LU AI-400	0.38 \pm 0.03 ^a	21.58 \pm 0.32 ^c	117.70 \pm 1.66 ^{ab}	54.29 \pm 1.46 ^{abc}	94.74 \pm 8.84 ^{abc}

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

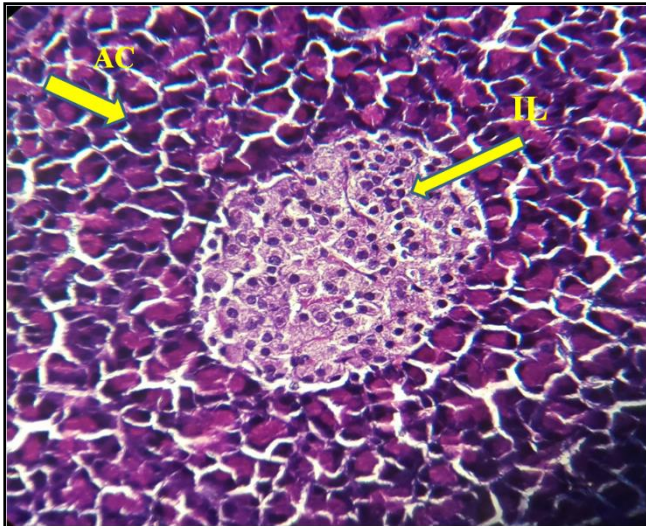


Fig 1: Section of pancreas from vehicle control rats (group I) showing normal architecture of β cells of islets of Langerhans (IL) and acinar cells (AC) (H & E stain X 120)

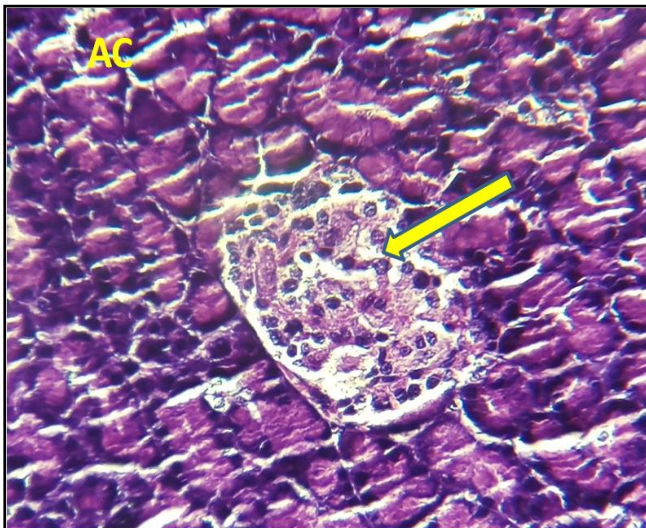


Fig 2: Section of pancreas from diabetic control rats (group II) showing destruction and decrease number of β cells (H & E stain X 240).

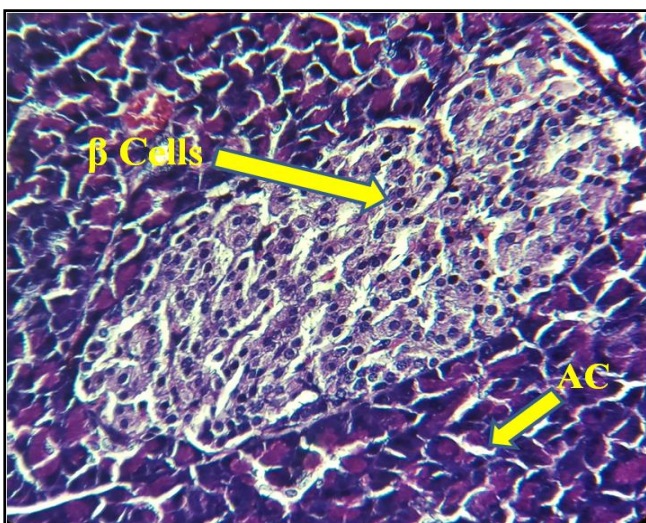


Fig 3: Section of pancreas from diabetic rats treated with alcoholic extract of *L. usitatissimum* at dose level of 400 mg/kg daily for 28 days (group VI) showing no defined pathological lesions in histoarchitecture structure of islets of langerhans (IL) and acinar cells (AC) (H & E stain X 120).

5. Conclusion

The present study revealed that alcoholic extract of *L. usitatissimum* is having dose dependent antidiabetic effect in an experimental model of rats. The extract at higher dosage tested was found safe following repeated oral administration at dose level of 400 mg/kg for 28 days in rats. Further investigation to define efficacy of *L. usitatissimum* seeds in clinical cases of diabetes mellitus would be highly desirable.

6. Acknowledgements

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7. Conflict of Interest

The authors declare that they have no conflict of interest.

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