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ANTIDIABETIC AND HYPERINSULINEMIC EFFECTS OF FENUGREEK AND TERMIS SEEDS AQUEOUS EXTRACTS IN EXPERIMENTAL RATS

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Abstract:-

To investigate antidiabetic efficacy of Fenugreek (F) and Termis (T) seeds aqueous extracts in streptozotocine induced diabetes in rats. Experimental diabetes was induced by intraperitoneal injection of a single dosage of STZ (50 mg/kg, i.p.). Adult male rats were divided into five groups; ***(1)*** *normal control,* ***(2)*** *diabetic control,* ***(3)*** *diabetic-F supplement (1 g/kg b. wt.),* ***(4)*** *diabetic-T supplement (1 g/kg b. wt.) and* ***(5)*** *diabetic- mixture (M) supplement (1 g/kg b. wt.) of each seed extracts concurrently for 30 days. The decreased insulin, plasma GSH, GST, CAT, as well as liver and muscle glycogen content and increased serum glucose, total lipids, triglycerides, total cholesterol, creatinine, urea, uric acid, AST, ALT, and ALP were the salient features recorded in diabetic control rats. This study showed that the regular intake of the T. foenum graecum, L. albus seeds water extract and their mixture can improve antioxidant status and considered as an effective agent in modulating the alterations due to diabetes.*

Keywords:-*Fenugreek, Termis, Streptozotocin, Diabetic rats, insulin.*

INTRODUCTION

Diabetes mellitus is the most common serious metabolic disorder, and it is considered to be one of the five leading causes of death in the world [1]. Throughout the world, many traditional plant treatments for diabetes exist, and therein lies a hidden wealth of potentially useful natural products for the control of diabetes [2]**.** Herbal medicines have been long used for the treatment of diabetic patients and they are currently accepted as an alternative therapy for diabetic treatment. Induction of diabetes in laboratory animals is convenient and useful strategy in the understanding and treatment of the disease. Streptozotocin-induced diabetic rats are one of the animal models of human insulindependent diabetes mellitus [3]. According to the previous investigations there are some medicinal plants and herbs which exert hypoglycemic effect such as *Trigonella foenum graecum* (Hulba Seeds) [4]**,** and *Lupinus albus* (Termis) seeds **[5].** They added that the components responsible and the mechanism by which *Trigonella* exerts these effects are not clearly understood. However, several studies have shown the presence of steroid saponins in *Trigonella* seeds [6]**.** Saponin compounds diasgenin, alkaloids and trigonelline inhibit intestinal glucose uptake *in vitro* [7]**.** *Lupinus albus* (Termis) exerted hypoglycemic effect and an increase in the level of serum insulin in normal and diabetic subjects as well as in normal and alloxan-diabetic animals [5]**.** Previous studies have shown that termis as hypoglycemic herbs contained saponins, alkaloids, tannins and quinovic acid [8]**.** It is well established that some saponins have hypoglycemic activity through the inhibition of liver gluconegenesis and/or glycogenolysis [9].

MATERIALS AND METHODS

Animals:

A total of 35 Adult male albino *Rattus norvegicus* rats (100-120 g) purchased from the National Research Centre, Cairo, Egypt, were used in the study. The animals were grouped and housed in polyacrylic cages at the animal's house of the Zoology department, Faculty of Science, Cairo University. The photoperiod was regulated at 12 hours light/12 hours dark cycle and temperature was adjusted at 25±1˚C. The rats were fed on commercial standard pellet and offered drink water *ad libitum*. The animals were acclimatized to laboratory conditions for one week before commencement of the experiment.

Plant material:

The dry seeds of Fenugreek (*Trigonella foenum graecum*) and Termis (*Lupinus albus*) were obtained from local herbal market.The seeds were identified and authenticated by the Herbarium of Botany Department, Faculty of Science, Cairo University.

Seeds aqueous extract preparation:

The seeds were cleaned and powdered using commercial blender. One kilogramme from both Fenugreek and Termis seeds powder were used for extract each with ten liters of distilled water for 24 hours. The aqueous extract of each plant seeds was filtered and the filtrates were lyophilized with a freeze dryer (LABCONCO lyophilizer, shell freeze system, U.S.A). The yield weight (of one kg each) of the Fenugreek and Termis seed extracts was 102.5 g and 70.5 g, respectively. The appropriate weight of the lyophilized extracts powder were dissolved in distilled water for oral administration to the experimental animals.

Induction of experimental diabetes:

After the rats were fasted for 12 h they allowed access to the water before induction of diabetes. intraperitoneal injection of a freshly prepared solution of streptozotocin (STZ) in 0.1M sodium citrate buffer (pH 4.5) at a dose of 50 mg/kg b. wt [10]. Blood glucose concentration was checked after 48 h. Rats with blood glucose level exceeding 200 mg/100 ml were considered diabetic and included in the diabetic experiments. Treatment with seeds was started 48 h. after streptozotocin injection.

Experimental design:

The rats were divided randomly and equally (7 rats) in to 5 groups. **Group 1,** Normal control (NC) given distilled water orally. **Group 2,** diabetic control (DC) injected intraperitoneally by a single dose of STZ (50 mg/kg b. wt.), and given dist. water. **Group 3,** diabetic + Fenugreek (DF) orally received 1g/kg b. wt. of Fenugreek aqueous extract dissolved in one ml. dist. Water. **Group 4** diabetic + Termis (DT) orally administered 1g/kg b. wt. of Termis aqueous extract dissolved in one ml. dist. Water. **Group 5** diabetic+ Mixture (DM) orally administered with 1g/kg b. wt. Of each of both two seeds aqueous extract dissolved in one ml. dist. Water. The duration of experiment for each group was 30 days.

Collection of blood:

At the end of the experimental period (30 days), overnight fasting rats were deprived of food but allowed for free access of drinking water. Rats were sacrificed by decapitation and the shed blood was collected in two cleaned vials, one (with EDTA) for blood reduced glutathione (GSH) estimation and plasma separation for determination of glutathione-STransferase (GST) and Catalase (CAT) activities. The second vails without anticoagulant for serum separation. Both plasma and sera were obtained by centrifugation at 3000 rpm for 10 min at 4°C... The serum was analyzed to determine insulin by using Insulin Mouse ELISA kit **(**American Diagnostica Inc., South San Francisco, CA, USA**)** The micro plate reader used was Hy-prep system Plus, Hyperion (Hyperion Inc., Miami, FL, USA**)** [11], glucose, the Aspartare amino transferase (AST), Alanine amino transferase (ALT), and Alkaline Phosphatase (ALP) activiyies. In addition total lipids, triglycerides, total cholesterol, creatinine, urea and uric acid concentrations were also determined in serum.

Liver and right gastrocnemius skeletal muscle were dissected out rapidly and washed. Parts of liver (100 mg) and of muscle (200 mg) were immediately digested in 2 ml of 30 % KOH solution and were used for determination of glycogen content by anthrone method [12].

Statistical analysis:
The results were analyzed using SPSS. All values were recorded as Mean+ standards error of the mean, whereas, the statistical differences between the means were determined by ANOVA, and the P< 0.05 was accepted as significant level.

RESULTS
Table 1 shows serum insulin, glucose concentrations and glycogen content of liver and muscle. Serum insulin concentrations was significantly decreased in STZ-diabetic rats compared with normal and the percentage decrease was 26.55% Fenugreek and Termis seeds and their mixture aqueous extract supplementation significantly increased STZinduced the hypoinsulinemic and the percentage elevation was 36.14%, 22.04%, and 31.14%, respectively in comparison with the diabetic control. Accordingly, there was a significant increase in serum glucose concentrations in diabetic rats, compared with normal control (127.78%), and administration of F, T, and M tended to decrease the glucose levels, and the percentage reduction was 62.40%, 60.16% and 71.05%, respectively as compared to the diabetic control. It seems that the administration of seeds mixture is more effective on decreasing the serum glucose of the diabetic rats than the administration of both seeds powder singly. As shown in Table 1, STZ-induced diabetes in rats caused a reduction in the liver and muscle glycogen content as compared with the normal control group (35.14% and 65.53%, respectively). Oral administration of F, T, and M aqueous extract to diabetic rats for 30 days succeeded to significantly elevate liver and muscle glycogen contents. Concerning liver glycogen, the percentage of increase was 60.42%, 80.99% and 81.77%, respectively, whereas for muscle glycogen it was 63.38%, 97.18% and 91.55%, respectively. It seems that the administration of the mixture is more prominent than that of both seeds extract singly on increasing the liver glycogen content of the diabetic rats.

A significant increas in creatinine (46.67 %), urea (27.93%) and uric acid (38.06%) serum levels in rats with STZ- induced diabetes was recorded compared to that of normal control rats (Table 2). Administration of F, T and M, for 30 days, caused a significant reduction in the levels of creatinine (31.82%, 27.27 %and 45.45%), urea (33.12%, 33.29% and 31.10%) and uric acid (19.94 %, 24.63% and 25.81 %), respectively when compared to diabetic control.
Serum total lipids, triglycerides and total cholesterol concentrations were increased in STZ-diabetic rats and the percentage of increase was 40.79 %, 25.57% and 44.48%, respectively when compared with the normal control rats. On the other hand, treatment of the STZ-diabetic rats with the aqueous extract of fenugreek, termis or their mixture caused a significant decrease in their concentrations significantly, Concerning total lipids, the percentage of reduction was 35.51, 49.53 and 57.94, respectively, for triglycerides it was 49.45, 40.52and 47.71, respectively, and for cholesterol it was 36.16, 53.62 and 45.92, respectively, when compared to the untreated diabetic rats (Table3).
As shown in Table 4, the activities of liver function markers (AST, ALT, and ALP) were significantly elevated in STZ-diabetic rats by 25%, 29.31% and 237.68%, respectively when compared with the normal controls rats. Rats administrated F, T and M for 30 days showed significant reduction in these marker enzyme activities to almost normal levels. The percentage of decrease, was 21.18%, 25.47% and 26.32% for AST; 31.57%, 37.25% and 39.24% for ALT and 11.67%, 13.23% and 39.96% for ALP, respectively, when compared to diabetic control rats. Streptozotocin at a dose of (50 mg/kg body weight) significantly increased the levels of plasma marker enzymes (GSH), (GST) and (CAT). The calculated percentage of increase were 47.08%, 57.83% and 57.25% respectively, as compared with the normal controls rats. Conversely a signifcant decrease in the activities of these maker enzymes was recorded in diabetic rats after administration of F, T and M for 30 days, the percentage of reduction was 109.47%, 108.98% and 112.19% for GSH; 232.86%, 282.86% and 258.57% for GST and 147.20%, 171.68% and 123.89% for CAT respectively, as compared with normal rats (Table 5).

Table 1: Effect of 30 days treatment with seeds aqueous extract of Fenugreek, Termisand their mixture on glucose, insulin and liver and muscle glycogen concentrations of rats

Groups / Parameters	N.C	D.C	F	T	M
Insulin (mg/ml) % of Change from N.C % of Change from D.C	34.28±0.58	25.18±2.36[a] -26.55	34.28±0.57[b] 36.14	30.73±0.43[b] 22.04	33.02±0.17[b] 31.14
Glucose (mg/dl) % of Change from N.C % of Change from D.C	96.46±4.32	219.72±8.21[a] 127.78	82.62±2.18[b] -62.40	87.53±4.12[b] -60.16	63.60±3.83[b] -71.05
Liver glycogen (mg/g tissue) % of Change from N.C % of Change from D.C	11.84±0.89	7.68±0.04[a] - 35.14	12.32±0.22[b] 60.42	13.90±0.90[b] 80.99	13.96±0.47[b] 81.77
Muscle glycogen (mg/ g tissue) % of Change from N.C % of Change from D.C	2.06± 0.58	0.71±0.06[a] - 65.53	2.16 ±0.07[b] 63.38	1.40 ±0.12[b] 97.18	1.36±0.22[b] 91.55

Values are given as mean ± SE for 7 rats in each group.
[a] significant (P< 0.05) as compared with normal (N.C).
[b] significant (P< 0.05) as compared with the diabetic control (D.C)

Table 2: Effect of 30 days treatment with seeds aqueous extract of Fenugreek, Termis and their mixture on creatinine, urea, and uric acid concentrations of rats.

Parameters \ Groups	N.C	D.C	F	T	M
Creatinine (mg/dl)	0.15±0.008	0.22±0.02[a]	0.15±0.02[b]	0.16±0.01[b]	0.12±0.008[b]
% of Change from N.C		46.67	-31.82	-27.27	-45.45
% of Change from D.C					
Urea (mg/dl)	32.9±0.52	42.09±3.10[a]	28.15±1.88[b]	28.08±1.10[b]	29.00±0.95[b]
% of Change from N.C		27.93	-33.12	-33.29	-31.10
% of Change from D.C					
Uric acid (mg/dl)	2.47±0.09	3.41±0.10[a]	2.73±0.10[b]	2.57±0.10[b]	2.53±0.08[b]
% of Change from N.C		38.06	-19.94	-24.63	-25.81
% of Change from D.C					

Values are given as mean ± SE for 7 rats in each group.
[a] Significant (P< 0.05) as compared with normal (N.C).
[b] significant (P< 0.05) as compared with the diabetic control (D.C).

Table 3: Effect of 30 days treatment with seeds aqueous extract of Fenugreek, Termis and their mixture on total lipids, triglycerides, and total cholesterol concentrations of rats.

Parameters \ Groups	N.C	D.C	F	T	M
Total lipids (g/dl)	0.76±0.04	1.07±0.10[a]	0.69±0.04[b]	0.54±0.04[b]	0.45±0.02[b]
% of Change from N.C		40.79	-35.51	-49.53	-57.94
% of Change from D.C					
Triglycerides (mg/dl)	138.28±1.84	137.64±1.34[a]	87.78±5.82[b]	103.28±1.10[b]	90.8±6016[b]
% of Change from N.C		25.57	-49.45	-40.52	-47.71
% of Change from D.C					
Total cholesterol (mg/dl)	108.27±2.69	156.43±3.59[a]	99.86±4.87[b]	72.56±4.11[b]	84.60±2.71[b]
% of Change from N.C		44.48	-36.16	-53.62	-45.92
% of Change from D.C					

Values are given as mean ± SE for 7 rats in each group.
[a] Significant (P< 0.05) as compared with normal (N.C).
[b] significant (P< 0.05) as compared with the diabetic control (D.C).

Table 4: Effect of 30 days treatment with seeds aqueous extract of Fenugreek, Termis and their mixture on aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase acivities of rats.

Parameters \ Groups	N.C	D.C	F	T	M
AST (U/L)	41.4±0.28	51.75±2.58[a]	40.79±0.61[b]	38.57±1.22[b]	38.13±1.26[b]
% of Change from N.C		25.00	-21.18	-25.47	-26.32
% of Change from D.C					
ALT (U/L)	35.79±1.25	46.28±2.12[a]	31.67±1.19[b]	29.04±0.70[b]	28.12±1.10[b]
% of Change from N.C		29.31	-31.57	-37.25	-39.24
% of Change from D.C					
ALP (U/L)	83.47±1.64	281.86±7.66[a]	248.98±8.68[b]	244.56±10.31[b]	169.22±11.23[b]
% of Change from N.C		237.68	-11.67	-13.23	-39.96
% of Change from D.					

Values are given as mean ± SE for 7 rats in each group.
[a] Significant (P< 0.05) as compared with normal (N.C).
[b] significant (P< 0.05) as compared with the diabetic control (D.C).

Table 5: Effect of 30 days treatment with seeds aqueous extract of Fenugreek, Termis and their mixture on glutathione reduced, glutathione - s- transferase, and catalase activities of rats.

Parameters \ Groups	N.C	D.C	F	T	M
GSH (mg/dl)	34.73±1.16	18.38±0.49[a]	38.50±1.15[b]	38.41±0.75[b]	39.00±0.62[b]
% of Change from N.C		-47.08	109.47	108.98	112.19
% of Change from D.C					
GST (U/g protein)	1.66±0.06	0.7±0.09[a]	2.33±0.13[b]	2.68±0.23[b]	2.51±0.04[b]
% of Change from N.C		-57.83	232.86	282.86	258.57
% of Change from D.C					
Catalase (U/g protein)	7.93±0.55	3.39±0.31[a]	8.38±0.98[b]	9.21±0.74[b]	7.59±0.36[b]
% of Change from N.C		- 57.25	147.20	171.68	123.89
% of Change from D.C					

Values are given as mean ± SE for 7 rats in each group.
[a] Significant (P< 0.05) as compared with normal (N.C).
[b] significant (P< 0.05) as compared with the diabetic control (D.C).

DISCUSSION

The present study demonstrated that the seeds aqueous extract of *T. foenum graecum* and *L. albus* singly seeds (or mixture of *T. foenum graecum* and *L. albus*) only a significant hypoglycemic effect to STZ-diabetic rats. Similarly, administration of *T. foenum* seed powder to diabetic animals has been shown to lower blood glucose levels and partially restore the activities of key enzymes of carbohydrate and lipid metabolism close to normal values in various animal model systems [13]. Mohammad *et al*. (2006) [14] reported that *T. foenum graecum* treatment of diabetic rats increases the insulin level due to stimulation of residual beta cells. *Lupinus albus* (Termis) exerted hypoglycemic effect and an increase in the level of serum insulin in normal and diabetic subjects as well as in normal and alloxandiabetic animals [5]. The present data demonstrated that blood glucose level was significantly increased and serum insulin was significantly decreased after STZ injection in rats. Jakus (2000) [15] reported that hyperglycemia is accompanied by reduced insulin action and high oxidative stress. In the present study, aqueous extract of *T. foenum graecum* and *L. albus* singly or both of them simultaneously produced a significant decrease in blood glucose of the STZ-diabetic rats. The presence of hypoglycemic activity in aqueous extract indicates that the active compounds are polar in nature [16]. The hypoglycemic effect of plants may be due to the presence of insulin-like substances in plant [17]. In addition stimulation of □-cells to produced more insulin [18]. Chemical analysis showed that the major constituent of the Soluble Dietary Fiber (SDF) fraction of *T. foenum graecum* is a galactomannan, confirm the involvement of SDF in the hypoglycemic effect of *Trigonella foenum graecum* seeds. However, compound(s) other than SDF is (are) also involved in the hypoglycemic activity [4]. The present data demonstrated that liver and muscle glycogen content were significantly decreased in STZ-induced diabetic rats. These findings were found in agreement with Ferronnini *et al*. (1990) [19] who indicated that after 5 weeks of STZ administration, glycogen content in liver and muscle was reduced by approximately 75 and 68%, respectively, in comparison to the non-diabetic controls. Diabetes mellitus is characterized by partial or total deficiency of insulin resulting in derangement of carbohydrate metabolism and a decrease in enzymatic activity of glucokinase, hexokinase and phosphofructokinase resulting in depletion of liver and muscle glycogen [20]. These findings support the current results which revealed an enormous depletion in hepatic and muscle glycogen content of diabetic rats.

The diabetic hyperglycemia induced elevation of the serum levels of urea and creatinine which may be considered as a significant marker of renal dysfunction [21]. These effects might be due to increase of the transaminase activities (ALT and AST) that increase the catabolism of amino acids. Again, the present study goes in harmony with the previous work of Mansour *et al*. (2002) [22] who illustrated that the levels of billrubin, urea and creatinine were significantly increased in plasma of alloxan-diabetic rats as compared with control group. The current results revealed that treatment of diabetic rats with *T. foenum graecum* or *L. albus* seeds extract ameliorated the recorded increase in their serum urea and creatinine levels. These results are in agreement with Mansour *et al*. (2002) [22] who indicated that the administration of the Termis, Halfa barr and Kammun quaramany suspension to the diabetic rats could restore the change in the level of creatinine after 4 weeks of treatment to their normal level. The current study demonstrated that serum uric acid concentration was significantly increased in the streptozotocin diabetic rats and decreased after the treatment with each of *T. foenum graecum* or *L. albus* seeds extract or suspension. It was demonstrated that STZ inhibits substantially decrease oxygen consumption by mitochondria [23]. And inhibits the krebs cycle [24]. These effects strongly limit mitochondrial ATP production and cause depletion of this nucleotide in β-cells [23]. The increments in uric acid concentrations might be due to degradation of purines or to an increase of uric acid level by either overproduction or inability of excretion [25]. The present study demonstrated that serum total lipid, triglycerides, and total cholesterol levels were decreased in both of normal and diabetic rats subsequent to the administration of both *T. foenum graecum* and *L. albus* seeds extract**.** The hypolipidemic action could also be the result of retardation of carbohydrate and fat absorption due to the presence of bioactive fiber in the agent [26]. Similarly to the present study Yadav *et al*. (2004) [27] indicated that administration of Fenugreek seeds powder to diabetic animals prevented the development of hyperglycemia and alteration in lipid profile in plasma and tissues and maintained it near normal. Sharma (1986) [28] demonstrated that fenugreek administration increased excretion of bile acids and neutral sterols in feces, thus depleting the cholesterol stores in the body in experimental rats. Sirtori *et al*. (2004) [29] suggested that the protein isolated from white lupine (*L. albus*) has been shown to have a similar hypocholesterolemic effect in rats like that of Soy protein.

The present study illustrated a significant increase in serum AST, ALT and ALP activities in streptozotocin-induced diabetic rats. These results agree with the findings recorded by [30]. They reported that the rise in activity of AST, ALT and ALP is mainly due to leakage of these enzymes from the liver into the blood stream as a result of streptozotocin toxicity which leads to the hepatocellular damage. Meanwhile, the present study revealed that treatment of streptozotocin diabetic rats with the two seeds powder extract restore the activities of the aforementioned enzymes to near their normal level. These decreases might be ascribed to the improved liver function with return of gluconeogenesis toward its normal levels [31].

Abnormally high level of free radicals and the simultaneous decline of antioxidant defense mechanisms can lead to damage of cellular organelles and enzymes, increased lipid peroxidation, and development of insulin resistance [32]. Besides the enzymatic antioxidants such as GST and CAT, reduced GSH is also an important antioxidant [33]. The present data demonstrated that diabetic rats exhibit a marked decrease in plasma GSH concentration, as compared to normal one. Similarly**,** veerapur *et al*. (2010) [34] demonstrated a marked decrease in GSH level in liver after streptozotocin treatment, as compared to the control animals. Seven *et al*. (2004) [35] suggested that the decreased hepatic GSH concentration in diabetic rats could be the result of decreased synthesis, increased consumption or increased loss through efflux.

Administration of each of F, T seeds singly and their mixture as aqueous aqueous extract, caused an increase in the level of the antioxidant enzymes of the normal and diabetic rats. These findings suggested that F and T seeds might be involved in the restoration of the antioxidant defense system by regulating the activities of antioxidant enzymes (GST and CAT) and non-enzymatic one (GSH) in STZ-induced diabetic rats. Reduced GSH could protect the cells from the toxic effects of ROS [36] and GST and CAT play a prominent role in scavenging free radical [37].

CONCLUSIONS

The use of Fenugreek and Termis seeds aqueous extracts in streptozotocine induced diabetes in rats at dose (1 g/kg b. wt.) improve antioxidant status and considered as an effective agent in modulating the alterations due to diabetes.

REFERENCES

[1].Gipsen, W.H. and Biessels, G.J. (2000). Cognition and synaptic plasticity in diabetes mellitus. Trends Neurosci., 23: 542-549.

[2].Gray, A.M. and Flatt, P.R. (1997). Nature's own pharmacy: The diabetes perspective. Proc. Nutr. Soc., 56: 507-517.

[3].Bach, J.F. (1994). Insulin-dependent diabetes mellitus as an autoimmune disease. Endocrine Reviews, 15: 516-542.

[4].Ali, L.; Azad, K.A.K.; Hassan, Z.; Mosihuzzaman, M.; Nahar, N.; Nasreen, T.; Nur-eAlam, M. (1995). Characterization of the hypoglycemic effect of Trigonella foenum graecum seed. Planta Med., 61(4): 358-360.

[5].Eskander, E.F. and Won Jun, H. (1995). Hypoglycemic and hyperinsulinemic effects of some Egyptian herbs used for the treatment of diabetes mellitus (type II) in rats. Egypt. J. Pharm. Sci., 36(1-6): 331-342.

[6].Vats, V.; Yadav, S.P. and Grover, J.K. (2003). Effect of T. foenum graecum on glycogen content of tisues and the key enzymes of carbohydrate metabolism. J. Ethnopharmacol., 85(2-3): 237-242.

[7].Yoshikawa, M.; Murakami, T.; Komatsu, H.; Murakami, N.; Yamahara, J. and Matsuda, H. (1997). Medicinal foods stuffs: IV. Fenugreek seed. (1): Structures of trigoneosides Ia, Ib, IIa, IIb, IIIa and IIIb, new furostanol saponins from the seeds of Indian Trigonella foenum graecum L. Chemical and Pharmaceutical Bulletin, 45(1): 81-87.

[8].Al-Habori, M.; Raman, A.; Lawrence, M.J. and Skett, P. (2001). In vitro effect of fenugreek extracts on intestinal sodium-dependent glucose uptake and hepatic glycogen phosphorylase A. International Journal of Experimental Diabetes Research, 2(2): 91-99.

[9].El-Gamal, H.M.; Shaker, H.K.; Pöllmann, K. and Seifert, K. (1995). Triterpenoid saponins from Zygophyllum species. Phytochemistry, 40(4): 1233-1236.

[10]. Sheweita, S.A.; Newairy, A.A.; Mansour, H.A. and Yousef, M.I. (2002). Effect of some hypoglycemic herbs on the activity of phase I and II drug-metabolizing enzymes in alloxan-induced diabetic rats. Toxicology, 174: 131-139.

[11]. Kanter,M.; Meral, I.; Yener, Z.; Ozbek, H. and Demir, H. (2003). Partial Regeneration / Proliferation of the □-cells in the islets of langerhans by Nigella sativa L. in streptozotocin-induced diabetic rats. Tohoku J. Exp. Med., 201(4): 213-219.

[12]. Byersdorfer, C.A.; Schweitzer, G.G. and Unanne, E.R. (2005). Diabetes is predicted by the beta cell level of autoantigen. J. Immunol., 175(7): 4347-4354.

[13]. Trevelyan, W.E. and Harrison, J.S. (1952). Fractionation and microdetermination of cell carbohydrates. Biochem. J., 50: 298-303.

[14]. Mohammad, S.; Taha, A.; Bawezai, R.N.K. and Baquer, N.Z. (2006). Modulation of glucose transporter (GLUT4) by vanadate and Trigonella in alloxan-diabetic rats. Life Sciences, 78(8): 820-824.

[15]. Jakus, V. (2000). The role of free radicals, oxidative stress and antioxidant systems in diabetic vascular disease. Bratist Lek. Listy., 101(10): 541-551.

[16]. Zia, T.; Hasnain, S.N. and Hasan, S.K. (2001). Evaluation of the oral hypoglycemic effect of Trigonella foenum graecum L. (methi) in normal mice. J. Ethnopharmacol., 75: 191-195.

[17]. Collier, E.; Walkinson, A.; Cleland, C.F. and Roth, J. (1987). Partial purification and characterization of an insulin-like material from spinach and Lemna gibba G3. J. Biol. Chem., 262: 6238-6247.

[18]. Chang, M.W. and Johnson, M.A. (1980). Effect of garlic on carbohydrate metabolism and lipid synthesis in rats. J. Nutr., 110: 931-936.

[19]. Ferronnini, E.; Lanfranchi, A.; Rohner-Jeanrenaud, F. and Van de Werve, G. (1990). Influence of longterm diabetes on liver glycogen metabolism in the rat. Metabolism, 39: 1082-1088.

[20]. Murphy, E.D. and Anderson, J.W. (1974). Tissue glycolytic and gluconeogenic enzyme activities in mildly and moderately diabetic rats. Influence of tolbultamide administration. Endocrinology, 94: 27-34.

[21]. Almdal, T.P. and Vilstrup, H. (1988). Strict insulin treatment normalizes the organic nitrogen contents and the capacity of urea-N synthesis in experimental diabetes in rats. Diabetologica, 31: 114-118.

[22]. Mansour, H.A.; Newairy, A.A.; Yousef, M.I. and Sheweita, S.A. (2002). Biochemical study on the effects of some Egyptian herbs in alloxan-induced diabetic rats. Toxicology, 170: 221-228.

[23]. Nukatsuka, M.; Yoshimura, Y.; Nishida, M. and Kawada, J. (1990b). Allopurinol protects pancreatic beta cells from the cytotoxic effect of streptozotocin: in vitro study. J. Pharmcoloiodyn, 13: 259-262.

[24]. Turk, J.; Corbett, J.A.; Ramanadham, S.; Bohrer, A. and McDaniel, M.L. (1993). Biochemical evidence for nitric oxide formation from streptozotocin in isolated pancreatic islets. Biochem. Biophys. Res. Commun., 197: 1458-1464.

[25]. Wolf, P.I. (1972). Methods and techniques in clinical chemistry. Wiley Interscience a division of John Wiley and Sons, New York, pp. 348.

[26]. Hannan, J.M.A.; Rokeya, B. and Faruque, O. (2003). Effect of soluble dietary fiber fraction of Trigonella foenum graecum on glycemic, insulinemic, lipidemic and platelet aggregation status of Type 2 diabetic model rats. J. Ethnopharmacol., 88: 7377.
[27]. Yadav, U.C.; Moorthy, K. and Baquer, N.Z. (2004). Effects of sodium-orthovanadate and Trigonella foenum graecum seeds on hepatic and renal lipogenic enzymes and lipid profile during alloxan diabetes. J. Biosci., 29(1): 81-91.
[28]. Sharma, R.D. (1986). Effects of fenugreek seeds and leaves on blood glucose and serum insulin responses in human subjects. Nutr. Res., 6: 1353-1364.
[29]. Sirtori, C.R.; Lovati, M.R.; Manzoni, C.; Castiglioni, S.; Duranti, M. and Magni, C. (2004). Proteins of white lupine seed, a naturally isoflavone-poor legume, reduce cholesterolemia in rats and increase LDL receptor activity in HepG2 cells. J. Nutr., 134: 18-23.
[30]. Jung, C.H.; Zhou, S.; Ding, G.X.; Kim, J.H.; Hong, M.H.; Shin, Y.C.; Kim, G.J. and Ko, S.G. (2006). Antihyperglycemic activity of herb extracts on streptozotocin-induced diabetic rats. Biosci. Biotechnol. Biochem., 70(10): 2556-2559.
[31]. Abdel-Moneim, A.; El-Zayat, E. and Mahmoud, S. (2002). Effect of some antioxidants on streptozotocin diabetic rats. J. Egypt. Ger. Soc. Zool., 38(A): 213-245.
[32]. Maritim, A.C.; Sanders, R.A. and Watkins, J.B. (2003). Diabetes, oxidative stress, and antioxidants: A Review. J. Biochem. Mol. Toxicol., 17(1): 24-38.
[33]. Zhang W, Zhao J, Wang J, Pang X, Zhuang X, Zhu X, Qu W.(2010). Hypoglycemic effect of aqueous extract of seabuckthorn (Hippophaer hamnoides L.) seed residues in streptozotocin-induced diabetic rats. Phytother Res; 24: 228-232.
[34]. Veerapur, V.P.; Prabhakar, K.R.; Parihar, V.K.; Bansal, P.; Srinivasan, K.K.; Priyadarsini, K.I. and Unnikrishnan, M.K. (2010). Antidiabetic, hypolipidamic and antioxidant activity of Dodonaea viscosa aerial parts in streptozotocin – induced diabetic rats. International Journal of phytomedicine, 2 : 59-70.
[35]. Seven, A.; Guzel, S.; Seymen, O.; Civelek, S.; Bolayirli, M.; Uncu, M. and Burcak, G. (2004). Effects of vitamin E supplementation on oxidative stress in stretptozotocin induced diabetic rats: Investigation of liver and plasma. Yonsei Medical Journal, 45(4): 703-710.
[36]. Akbas SH, Yegin A, Ozben T. Effect of pentylenetetrazol-induced epileptic seizure on the antioxidant enzyme activities, glutathione and lipid peroxidation levels in rat erythrocytes and liver tissues. Clin Biochem 2005; 38: 1009-1014.
[37]. Rahimi R, Nikfar S, Larijan B, Abdollahi M.(2005). A review on the role of antioxidant in the management of diabetes and its complications. Biomed Pharmacother; 59: 365-373.