STUDIES OF HYPOGLYCEMIC EFFECTS OF *Stevia rebaudiana* Bertoni LEAVES, THEIR AQUEOUS EXTRACT AND STEVIOSIDE ON DIABETIC RATS

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ABSTRACT

The present study was carried out to determine whether *Stevia rebaudiana* Bertoni leaves, their aqueous extract and Stevioside improves blood glucose, triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol and plasma transaminases activities in Streptozotocin diabetic rats.

Chemical composition of Stevia leaves powder was determined, experimental Ablino rats were injected with Streptozotocin (65 mg/kg body weight) to induce diabetes, Stevia leaves powder was administrated to diabetic rats at three levels 1, 2 and 3% and Stevioside was administrated at two levels 0.5 and 1%, the aqueous extract of the Stevia leaves was prepared and used instead of water in one group of the treated rats.

Throughout the experimental period, the level of blood glucose were measured weekly. At the end of the experiment, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides and plasma transaminases (GPT and GOT) activities were performed in the serum of the rats.

Results showed a decrease in weight gain of diabetic rats compared with the normal ones. The serum glucose in the diabetic rats fed on different doses of sweeteners decreased. Also, the results indicated that, plasma triglycerides, total cholesterol, LDL-C concentration, GPT and GOT were decreased, while HDL-C was increased after administration of Stevia leaves powder, their aqueous extract and stevioside as compared to the control diabetic rats.

INTRODUCTION

Stevia rabaudiana Bertoni is a small perennial shrub of the compositaé family whose leaves contain different diterpene glycosides. All those compounds are non caloric sweeteners

(Shaffert and Chebotar, 1994 and Chalapalhi *et al.*, 1997). The leaves of this plant contain stevioside (Stevia sweetener), diterpene glycosdie, which is the major sweetener in the leaves, it has the property of being 300 times sweeter than sucrose (Das *et al.*, 1992; Hanson and DeOliveria, 1993 and Richard, 1996).

The Stevia leaves are delicious food, enhancing their natural flavour and no calorie sweetener. Then leaves contain a mixture of at least eight different glycosides derived from tetracycilic diterpene steriol (Steviolbioside, stevioside rebaudiosides A, B, C, D, E and dulcosides). This natural products taste intensity sweet 250-300 times as sweet as sucrose (Richman *et al.*, 1999). Stevia is rich nutrient, containing substantial amount of protein, calcium, phosphorus and other important nutrient (Kinghorn and Soejarto, 1985 and Tsanava *et al.*, 1989).

Stevia sweetener has particular advantage for persons suffering from obesity, diabetics, heart disease and dental caries (Melis, 1995).

Stevia would regulate effectively blood sugar and brings it towards a normal balance (Kinghorn and Soejiarto, 1985 and Jeppensen *et al.*, 2000). In addition to being a sweetener, Stevia is considered (in Brazilian herbal-medicine) to be hypoglycemic, hypotensive, diuretic, cardiotonic and tonic. The leaf is used for diabetes, obesity, cavities, hypertension, fatigue, depression, sweet cravings and infections (Ferreira *et al.*, 2006).

Gretersen *et al.* (2004) mentioned that Stevia leaf (at dosages higher than used for sweetening purposes) has been documented to have a hypoglycemic effect. Those with diabetes should use high amounts of Stevia with caution and monitor their blood sugar levels as medications may need adjusting. They also reported that Stevioside and Steviol are able to stimulate insulin secretion via a direct action on beta cells. This means that these compounds may have a potential role as antihyperglycemic agents in the treatment of type 2 diabetes mellitus".

Gardana *et al.* (2003) reported that, water extracts of Stevia leaves had a hypoglycemic effect and increased glucose tolerance in humans, reporting that, blood glucose was reduced by 35% after 6-8 hours oral ingestion of a hot water extract of the leaf. Chen *et al.* (2005) reported that Stevia is considered to be a great help in weight loss programs because it is very low in calories and its sweetness is so concentrated. It is supportive to the pancreas and has been used in treatment of diabetes, hypertension and infections.

Diabetes mellitus is one of the most serious rampant diseases in modern days. In fact, it is one of the common causes of death in Egypt. The number of diabetics has been increasing at a rate of around 6% per year. At this rate the incidence of diabetes can be expected to double every 15 years (Jansen *et al.*, 1990).

As reported by WHO (2000), in Egypt there are about 5 million diabetics. The prevalence of diabetes mellitus in Egypt and all over the world caused many problems. One of them is the complications on the body organs besides the potential side effects of insulin injection or oral hypoglycemic agents. The other one is the high cost of drugs.

Today, Stevia leaves and leaf extracts are commonly found in most health food stores, however; they may only be sold in the United States as dietary/herbal supplements, not as food additives or sweeteners (Grefersen *et al.*, 2004).

Consequently, this study was designed to investigate the hypoglycemic effect of *Stevia rebaudiana* Bertoni leaves, their aqueous extract and stevioside on diabetic rats.

MATERIALS AND METHODS

Materials:

Stevia rebaudiana Bertoni leaves were obtained from El-Sabahia Station, Agricultural Research Center, Alexandria, Egypt. Stevia leaves were dried in an air oven at 45 ± 2°C until reaching stable moisture content (9.11%), then grinded and passed through 60 mesh sieve and kept in polyethylene bags at -18 ± 2°C until use.

Stevioside (300 times as sucrose) was purchased from L.M.G. international trade corporation, Egypt.

Streptozotocine was used in this work to induce-diabetic rats, is a product of Sigma, Sigma, USA.

Male albino rats of body weight 140-150 gm. were purchased from Faculty of Science, Tanta University, Egypt.

Methods:

Preparation of the aqueous extract of Stevia leaves:

Dried Stevia leaves (50 gm) were extracted by the addition of 1000 ml distilled water, then boiled for 30 min., and allowed to infuse for 15 min. The suspension was filtered and the filtrate was evaporated to dryness using a rotary evaporator. The dried product was dissolved in distilled water before administration to diabetic rats and the volume was adjusted to 1000 ml with distilled water. 50

ml of the aqueous extract were put in polyethylene bags, and stored at -18 ± 2°C till the day of use (Gallagher *et al.*, 2003).

Chemical analysis:

Moisture, protein, ether extract, ash and crude fiber were determined according to A.O.A.C. (1990). Total carbohydrates content was calculated by difference. Minerals were determined using atomic absorption spectrophotometer Perken Elmer Model 2180 as describe by A.O.A.C. (1990).

Biological evaluation:

Stevia rebaudiana Bertoni leaves, their aqueous extract and Stevioside were evaluated nutritionally to study their effect in lowering the level of blood glucose as well as different lipid parameters in diabetic cases, through animal feeding study.

Experimental diets:

Diet composition was prepared and mixed according to Kim and Shin (1998) as shown in Table (1).

Table (1): Composition of experimental diets (g/kg diet).

Constituents*	G_1	G_2	G_3	G_4	G_5	G_6	G_7	G_8
Starch	498	498	698	698	698	698	648	698
Sucrose	200	200	0	0	0	0	50*	0
Casein	200	200	200	200	200	200	200	200
Corn oil	50	50	50	50	50	50	50	50
Mineral	35	35	35	35	35	35	35	35
Vitamin Mix	10	10	10	10	10	10	10	10
DL-Methionin	3	3	3	3	3	3	3	3
Cholin biotart	2	2	2	2	2	2	2	2
Cholesterol	2	2	2	2	2	2	2	2

G_1 Normal control (control -) fed on diet free from Stevia leaves or stevioside.
G_2 Diabetic control (control +) fed on diet free from Stevia leaves or stevioside.
G_3 Diabetic group fed on diet contains 1% Stevia leaves powder.
G_4 Diabetic group fed on diet contains 2% Stevia leaves powder.
G_5 Diabetic group fed on diet contains 3% Stevia leaves powder.
G_6 Diabetic group fed on diet free of Stevia leaves or stevioside and drink about 15-20 ml of previous prepared aqueous extract of Stevia leaves powder.
G_7 Diabetic group fed on diet contains 0.5% stevioside.
G_8 Diabetic group fed on diet contains 1% stevioside.
* Replacement of sucrose depending on stevioside sweetness (300 times of sugar).

Experimental animals:

Male albino rats (40 rats) of weight ranging between 140 and 150 gm were obtained from the Faculty of Science, Tanta University, Egypt. Each animal was individually housed in a wire bottomed, stainless steel cage, under normal healthy laboratory conditions. The experimental animals fed on basal diet for one week

to acclimate them to our facility and basal diet. Rats were given free access to food and water throughout the experimental period of 6 weeks.

Design and induction of diabetes:

After acclimation, rats were randomly divided into two main groups. The first one (5 rats) was fed on diet free from Stevia leaves powder or stevioside that was considered as the normal control group (G_1). Diabetes was induced by injection of Strptozotocin (STZ) in a single dose of 65 mg/kg body weight after 12 hour fasting. STZ was dissolved in a freshly prepared 0.01 M citrate buffer (pH 4.5). So the second main group (35 rats) were injected with a single dose of STZ solution (65 mg/kg body wt) after 12 hour, fasting, to induce hyperglyemia (Bolkent *et al.*, 2000).

Animals having blood glucose level over 248.4 mg/dL were considered diabetes as reported by Esmerino (1998).

After four days of the injection with STZ the second main group (35 diabetic rats) were divided into seven subgroups (5 rats each) and fed on different diets as shown and given in Table (1).

All rats were weighted weekly and food intake, faces of each group were collected, dried in an air oven at 50°C, then weighted and recorded.

Blood sampling:

From all the previously mentioned groups, blood samples were taken at the end of the experiment. The blood samples were collected after 12 hours fasting from vein plexus eye into dry clean centrifuge tubes and left to colt. The blood was centrifuged for 15 minutes at 3000 r.p.m. to separate the serum, which was carefully aspirated and transferred into clean quite plastic tubes and kept frozen at -18 $\pm$ 2°C until biochemical analysis (El-Khamissy, 2005).

Determination of blood glucose:

Blood glucose was measured according to the method described by Alles *et al.* (1999) using blood glucose meter (free style TM). A drop of blood was taken from tail of the rats, placed on a test strip and blood glucose was measured immediately by the blood glucose meter.

Serum analysis:

The concentration of total cholesterol, high-density lipoprotein cholesterol (HDL-C) and triglyceride in the serum were determined by using enzymatic colorimetric methods with

commercially available kits (Cholesterol , kit # 276-64909; high-density lipopreotein, kit # 278-67409 and triglyceride, kit #274-26807; wake chemicals, Osaka, Japan) as described Kim and Shin (1998). Low-density lipoprotein cholesterol (LDL-C) concentration was calculated as the difference between total and HDL-cholesterol according to the method of Freiedwald *et al.* (1972). Serum transaminases (GPT and GOT) activities were estimated according to the method described by Reitman and Frankel (1957).

Statistical analysis:

Most of the received data were analyzed statistically using the analysis of variance and the means were further tested using the least significant difference test (LSD) as outlined by Steel and Torrie (1980).

RESULTS AND DISCUSSION

Chemical composition of *Stevia rebaudiana* Bertoni leaves:

Chemical composition of Stevia leaves presented in Table (2) show that, Stevia leaves contained high levels of total carbohydrates, ash, crude protein, crude fiber and ether extract. The presented results were in agreement with those of Hassan *et al.* (2002), who reported that *Stevia rebaudiana* Bertoni leaves contained 79.71% moisture, 12.46% protein, 4.98% crude fat, 13.45% ash, 10.94% crude fiber and 58.17% carbohydrates, respectively.

From the results in the same table, it could be concluded that potassium content was the highest. On the other hand the leaves contained small amounts of iron, sodium and zinc comparing with potassium and calcium. Such minerals are essential for regulator of osmotic pressure and acid base balance (Gabr, 1998).

Table (2): Chemical and minerals composition of *Stevia rebaudiana* Bertoni leaves (on dry weight basis)

Components	%	Elements	%
Moisture	74.95	Zinc (Zn)	0.004
Crude protein	13.10	Manganese (Mn)	1.78
Ether extract	4.71	Iron (Fe)	0.178
Total ash	14.21	Calcium (Ca)	2.14
Crude fiber	11.18	Sodium (Na)	0.164
Total carbohydrates*	56.80	Potassium (k)	3.31

* Total carbohydrates calculated by difference

Biological effect of diets contain different levels of Stevia leaves, their aqueous extract and stevioside on experimental rats:

1. Effect on body weight:

The data in Table (3) represented body weight changes in normal and diabetic rats receiving either sucrose at a ratio of 200 g/kg or as replaced by different proportions of Stevia leaves, their aqueous extract and stevioside sweetener based on the degree of sweetness and compensated by starch to keep all diets iso-caloric. Sucrose was completely replaced by Stevia leaves, their aqueous extract and stevioside in all groups with the one exception, sucrose was replaced by 75% of its content by stevioside in group No. 7 replacement of sucrose depending on stevioside sweetness 300 times of sucrose.

Table (3): Effect of *Stevia rebaudiana* Bertoni leaves, their aqueous extract and Stevioside on daily food intake, body weight and fecal output of normal and diabetic rats.

Dietary groups	Daily food intake (g)	Initial body weight (g)	Final body weight after 6 weeks	Changes in body weight (g)	Fecal output (g)
G_1	17.63 d ± 0.92	143.71 a ± 1.21	169.61 c ± 2.37	+25.9	12.33 a ± 0.53
G_2	9.12 a ± 0.46	149.66 b ± 0.87	122.81 b ± 2.60	-26.85	16.82 cd ± 0.76
G_3	10.33 abc ± 0.69	146.87 ab ± 1.33	128.68 b ± 2.95	-18.19	14.10 ab ± 0.88
G_4	11.95 bc ± 0.52	148.36 ab ± 1.79	125.51 b ± 0.07	-22.85	17.58cd ± 1.11
G_5	11.53 bc ± 0.58	150.91 b ± 2.37	124.87 b ± 2.08	-26.04	20.73 e ± 0.81
G_6	10.27 ab ± 0.40	147.68 ab ± 1.10	127.19 b ± 1.44	-20.49	16.96 cd ± 0.70
G_7	12.44 c ± 0.64	150.11 b ± 2.14	116.12 a ± 1.60	-33.99	15.29 bc ± 0.99
G_8	12.24 bc ± 0.81	149.43 ab ± 1.91	110.27 a ± 2.25	-39.16	19.07 de ± 0.81

Each value is an average of five determinations

Values followed by the same letter in column are not significantly different $P \leq 0.05$

G_1, G_2, G_3, ... etc. were as given in Table (1).

G_1 was not injected with streptozotocin

So, it can be observed that normal rats (G_1) receiving 200 gm sucrose/kg diet have manifested body weight increases, while the diabetic group receiving the same diet showed relative reduction in body weight. Also, diabetic groups receiving diets containing 1, 2 and 3% Stevia leaves, aqueous extract and 0.5 and 1% stevioside (e.g. G_3, G_4, G_5, G_6, G_7 and G_8, respectively) showed body weight reduction after 6 weeks of feeding. Appeared also from the same table that, the maximum decrease in body weight was -39.16 gm when rats feeding on diet containing 1% stevioside. These results were in agreement with those findings of Grefersen *et al.* (2004), who reported that body weight loss in case of stevioside treatments

may be due to further increased lypolysics or the absence of quick glucose releasing source. The body weight decrease in diabetic rats is generally due to insulin deficiency and increased lypolysis (Jeppesen *et al.*, 2000), hence increase the amount of fecal output of these groups. Ferreira *et al.* (2006) reported that, faecal output of total bile acids or salt neutral sterols were found to be enhanced in the experimental animals fed on Stevia and Stevioside compared to the positive (diabetic) group (G_2).

2. Effect on blood glucose:

Table (4) illustrated the mean blood glucose levels of normal control and diabetic groups through the experimental period. Blood glucose levels of diabetic groups (after 4 days induce diabetes with Streptozotocin) were markedly higher than the normal control (G_1). Administration of diets containing Stevia leaves powder at levels 1%, 2% and 3% as well as the aqueous extract and stevioside at levels 0.5% and 1% led to decrease in blood glucose levels of the diabetic groups (G_3, G_4, G_5, G_6, G_7 and G_8), respectively compared with the diabetic group fed on control diet (G_2). Such reduction was observed after one week of feeding till the end of the experimental period, also the reduction was increased with prolonging the feeding time. Apparent also from the Table (4) that, stevioioside at level 1% had more effect on reduction of blood glucose levels comparing with the other treatments.

Serum glucose content in the last group (G_8) was quite similar with the level observed with normal rats.

Alternatively, stevioside dose dependently decreased protein levels of phosphoenol pyruvate a carboxykinase, (PEPCK) and PEPCK mRNA after 15 days of treatment (Chen *et al.*, 2005). They also found that, steviosdie also reduced insulin resistance in the diabetic animals as shown by the glucose lowering effects of tolbutamide. In conclusions, stevioside was able to regulate blood glucose levels by enhancing not only insulin secretion, but also insulin utilization in insulin-deficient rats; the latter was due to decreased PEPCK gene expression in rat liver by Stevioside's action of slowing down gluconeogenesis. Also, Toskulkao *et al.* (1997) suggested that steviol, which is stevioside metabolite, was concluded to exert its action through the inhibition of glucose absorption.

Table (4): Effect of *Stevia rebaudiana* Bertoni leaves, their aqueous extract and Stevioside on blood glucose levels of normal and diabetic rats.

Dietary groups	Before treatment (after 24 hr. fasting)	After injected with streptozotocin (after 4 days)	Blood glucose level mg/dl (weeks)					
			1st	2nd	3rd	4th	5th	6th
G_1	79.51 a±1.17	81.7a±2.95	98.7 a±4.97	101.30 a±5.44	97.13 a±2.25	99.20 a±4.57	100.60 a±3.64	102.10 a±2.94
G_2	81.63 ab±1.80	357.55 d±3.59	373.38e±4.29	367.10 d±4.97	381.35 f±2.60	364.54 e±4.75	3689 f±10.9	375.29 f±8.52
G_3	82.41 ab±2.49	339.49 bc±3.49	315.5c±3.53	294.11 c±3.41	268.3 e±3.70	243.60 d±3.70	217.9 e±5.20	193.05 e±3.29
G_4	90.13 cd±2.25	354.73 d3.29	329.15 ±4.68	297.20 c±4.80	270.31 e±4.62	237.45 d±3.24	205.28 de±4.69	175.38 d±3.99
G_5	84.22 ab±0.79	335.70 b±1.24	305.91 ±1.07	276.10 b±0.9	252.29 d±1.21	220.48 c±1.13	189.67 cd±1.41	156.86 c±1.3
G_6	82.15 ab±2.08	348.70 cd±2.85	314.67bc±4.51	279.72 b±3.53	246.87 cd±4.12	216.90 c±5.29	179.10 c±4.59	145.15 bc±5.32
G_7	93.56 d±1.79	343.10 cd±3.19	307.99 ±3.26	272.9 b±4.23	237.79 bc±3.48	202.70 b±4.24	167.60 c±3.15	132.49 b±4.91
G_8	87.13 bc±1.56	356.0 d±5.38	322.58cd±2.37	278.45 b±2.96	230.32 b±2.96	197.11 b±2.85	144.78 b±13.97	100.22 a±4.51

Each value is an average of five determinations

Values followed by the same letter in column are not significantly different $P \leq 0.05$

G_1, G_2, G_3, … etc. were as given in Table (1).

G_7 was not injected with streptozotocin.

3. Effect on serum lipid:

Although the relationship between lipids pattern abnormalities and diabetes is complex, there is usually a specific lipid abnormality found in diabetes (Rosalyn and Bauman, 1983). It was reported that hypertriglyceridemia, hyperchoelsterolemia, and reduced HDL-C levels are commonly observed in diabetes. Normal values in humans should be in the range of: Total triglycerides (50 to 250 mg/dL), LDL-C (< 160 mg/dL), TC (below 200 mg/dL), and HDL-C (above 45 mg/dL) (Baur, 1995).

Table (5): Effect of *Stevia rebaudiana* Bertoni leaves, their aqueous extract and Stevioside on serum lipid concentration in normal and diabetic rats.

Dietary groups	TC (Total cholesterol) mg/dl	HDL cholesterol mg/dl	LDL cholesterol mg/dL	TC/HDL-C ratio	TC/LDL-C ratio	LDL-C/HDL-C ratio	Total triglyceride mg/dl
G_1	108.35b±0.14	79.47h±0.01	28.88a±0.03	1.36a±0.0	3.75h±0.0	0.363a±0.0	182.1g±0.01
G_2	198.58h±0.22	37.81a±0.03	160.47h±0.03	5.24h±0.0	1.24a±0.0	4.244h±0.0	186.30h±0.02
G_3	146.53g±0.29	49.35b±0.02	97.18g±0.02	2.97g±0.01	1.51b±0.0	1.969g±0.0	131.35f±0.02
G_4	131.97f±0.07	52.75c±0.02	79.22f±0.01	2.50f±0.0	1.67c±0.0	1.50f±0.0	125.55e±0.02
G_5	119.14e±0.18	58.23d±0.02	60.91e±0.03	2.05e±0.0	1.96d±0.0	1.046e±0.0	117.62c±0.03
G_6	116.0d±0.09	62.98e±0.03	53.02d±0.02	1.84d±0.0	2.19e±0.0	0.842d±0.0	121.89d±0.02
G_7	110.86c±0.16	67.43f±0.01	43.43c±0.02	1.64c±0.0	2.55f±0.0	0.644c±0.0	112.40b±0.02
G_8	102.70a±0.11	73.15g±0.02	29.55b±0.04	1.40b±0.0	3.47g±0.01	0.403b±0.0	109.68a±0.03

Each value is an average of five determinations

Values followed by the same letter in column are not significantly different $P \leq 0.05$

G_1, G_2, G_3, ... etc. were as given in Table (1).

G_1 was not injected with streptozotocin.

According to the results given in Table (5), it could be concluded that, diabetic rats fed on diets containing Stevia leaves powder, aqueous extract and Stevioside (G_3-G_8) had a lower serum total cholesterol (TC), low density lipoprotein (LDL), total triglycerides and higher level of high density lipoprotein (HDL) compared with those of diabetic control. Therefore, the ratio of TC/HDL-C was higher in case of diabetic rats (control, G_2) and lower in groups fed on diet containing of Stevia leaves and stevioside. These results are in agreement with those of Melis (1995), who found that, after treatment with Stevioside and aqueous extract of Stevia, a clear gradually reduced plasma total cholesterol to a level almost the same of control. It was also observed a decrement in HDL-C level and an increment in the total cholesterol/HDL-C ratio in the diabetic rats. It was stated that the ratio of TC to HDL-C to be desirable should be between 4.0; border line 4.0-6.0 and high risk of heart disease above 6.0 (Baur, 1995).

So, it seems to be that the TC/HDL-C ratio is important as indicator of the coronary altery disease.

Escander *et al.* (1995) reported that, the plasma triglycerides levels of diabetic rats were significantly elevated as compared with those of non-diabetic controls, suggested that either the removal of triglyceride from the circulation or its entry into the circulation or both was impaired in the midley insulin-deficient rats.

4. Effect on plasma transaminases activities:

The assay of enzyme levels in the extracellular body fluid, such as blood serum, is important aid to the clinical diagnosis and management of the disease. Measurements of the changes in enzyme levels offer a greater degree of injury, than is possible using the other clinicochemical parameters. Most significant for the development of diagnostic enzymology were the studies on the transaminases, particularly glutamic-pyruvic transaminase (GPT) or alanine-aminotransferase (ALT) and glutamic oxaloacetic transamianse (GOT) or aspartate-amino transferase (AST). In all liver dysfunctions, the (GPT) and (GOT) levels are increased in serum, the extents giving a useful differential index of the type of dysfunction. The activity of (GOT) was found to be elevated in serum after myocardial infraction and liver disease (Foster, 1980).

Table (6): Effect of *Stevia rebaudiana* Bertoni leaves, their aqueous extract and Stevioside on plasma transaminases GPT and GOT (IU/L) activities of normal and diabetic rats.

Dietary groups	GPT (ALT) (IU/L)	GOT (AST) (IU/L)	GOT/GPT ratio
G_1	22.7 ab ± 0.06	44.7 a ± 1.15	1.97 a ± 0.01
G_2	29.30 e ± 0.64	70.40 f ± 0.64	2.40 cd ± 0.03
G_3	26.71 de ± 1.15	67.28 e ± 0.81	2.52 d ± 0.08
G_4	25.11 cd ± 0.75	61.30 d ± 1.10	2.44 cd ± 0.03
G_5	23.66 bc ± 0.98	54.5 c ± 0.92	2.30 bc ± 0.06
G_6	22.51 abc ± 1.10	52.00 bc ± 0.60	2.31 bc ± 0.09
G_7	22.0 ab ± 0.92	50.20 b ± 0.87	2.28 bc ± 0.06
G_8	20.35 a ± 0.64	45.03 a ± 1.21	2.21 b ± 0.01

Each value is an average of five determinations

Values followed by the same letter in column are not significantly different $P \leq 0.05$

G_1, G_2, G_3, ... etc. as in Table (1).

G_1 was not injected with streptozotocin.

From Table (6), it was observed that, both plasma glutamic-pyruvic transamianse (GPT) and glutamic oxalo-acetic-transaminase (GOT) activities were enhanced in diabetic rats, and shortage of insulin caused stimulation of gluconeugenesis i.e. protein breakdown and this action increased the level of GPT and

GOT in plasma in diabetic rats, such symptoms agreed with Williams, (1995). The results also showed that, the diets containing Stevia leaves, aqueous extract and stevioside led to gradual reduction in plasma GPT (ALT) and GOT (AST) levels. All ratios of substitution have reduced their levels to normal levels.

CONCLUSION

From the obtained results, it could be concluded that, Stevia leaves powder, aqueous extract and Stevioside seems to posses a promising therapeutical role in diabetic rats and potential source of a new orally active agents for diabetic therapy and they show also a hypolipoidemic effects.

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الملخص العربى

دراسات على استخدام أوراق نبات الاستيفيا ومستخلصها المائى والأستيفوسيد كمواد خافضة للسكر فى الفئران المصابة بالبول السكرى

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أجريت هذه الدراسة بهدف توضيح الأثر الفعال لأوراق نبات الأستيفيا ومستخلصها المائى وكذلك الأستيفوسيد فى خفض مستويات السكر فى الدم والجلسريدات الثلاثية والكوليسترول والإنزيمات الناقلة لمجموعة الأمين فى الفئران المصابة بمرض السكر نتيجة حقنها بمادة الأستربيتوزيتوسين بمعدل 65مجم/كجم/وزن الجسم. تم تقدير التركيب الكيماوى لمسحوق أوراق نبات الأستيفيا وكذلك تم إعداد المستخلص المائى لها ثم استخدم مسحوق الأوراق بثلاث نسب وهى: 1 ، 2 ، 3%. وقد تم استخدام المحلى الطبيعى الأستيفوسيد بنسب 0.5 ، 1.0% وكذلك استخدام المستخلص المائى بدلا من الماء فى إحدى المجموعات المستخدمة و تم قياس معدل الجلوكوز أسبوعيا على مدار فترة التجربة فى نهاية التجربة تم تقدير مستويات الجليسريدات الثلاثية والكوليسترول والإنزيمات الناقلة لمجموعة الأمين.

وقد أظهرت النتائج أن هناك انخفاضا فى وزن الفئران المصابة بالسكر بالمقارنة بالفئران السليمة أما بالنسبة لمكونات سيرم الدم (جلوكوز الدم ، الكوليسترول ، الجليسريدات الثلاثية والإنزيمات الناقلة لمجموعة الأمين) فإنها أظهرت انخفاضا فى مستواها فى الفئران المصابة بالسكر والمغذاة على النسب المختلفة من مسحوق أوراق الأستيفيا ومستخلصها المائى وكذلك المحلى الطبيعى الأستيفوسيد مقارنة بمجموعة الفئران المصابة بالسكر والمغذاة على الوجبة القياسية.