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Beneficial effects of sodium selenite on some serum biochemical parameters in alloxan-induced diabetic rats

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ABSTRACT

The present study aimed to determine the possible protective effects of intraperitoneally administered sodium selenite for preventing diabetes in rats. Twenty-eight male albino rats were randomly divided into four equal groups of seven each: untreated control (G1), sodium selenite treated control (G2), untreated diabetic (G3), and sodium selenite-treated diabetic group (G4). Diabetes was induced by alloxan (150 mg/kg body weight) in groups G3 and G4 and rats were then treated with sodium selenite (5 μmol/kg body weight/day) for 4 weeks (G4). On day 28 after an overnight fasting, rats were killed and concentrations of serum glucose, total cholesterol, triglycerides, total lipid, urea, creatinine, uric acid, albumin and some enzymes activities: pancreatic lipase, glutamic oxalic transaminase (GOT), glutamic pyruvic transaminase (GPT), Alkaline phosphatase (ALP) were also estimated. The administration of alloxan significantly increased serum glucose, total cholesterol, triglycerides, total lipid, urea, uric acid levels, pancreatic lipase, GOT, GPT and ALP activities, body weight gain and albumin level were significantly decreased. This alteration was restored back to near normal in diabetic rats intraperitoneal treated with sodium selenite in comparison to non treated diabetic animals. Serum creatinine concentration was normal in all groups. The study concludes that alloxan diabetes mellitus induced severe biochemical alliterations in the glucose, lipid profile concentrations, liver and kidney function markers and sodium selenite has shown protective effects preventing at least partially diabetic complications.

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INTRODUCTION

Diabetes mellitus, characterized by a loss of glucose homeostasis, is a metabolic disease caused by insulin deficiency (Nazıroğlu *et al.*, 2012) and/or feeble tissue response to insulin. It affects the function of various organs as long-term complications. Rats treated with Streptozotozin (STZ) display many of the features seen in human subjects, including hyperglycemia, polyuria, polydipsia, and weight loss (Fein *et al.*, 1980; Regan *et al.*, 1977).

In experimental diabetic animals, some trace elements were found to have positive effects on some

parameters of glucose metabolism (Shechter, 1990; Mukherjee *et al.*, 1998). Selenium is a ubiquitous trace element in nature, which is essential for humans (Erbayraktar *et al.*, 2007).

Selenium is a mineral antioxidant which is an essential constituent of the enzyme glutathione peroxidase, which protects membrane lipids and other cell constituents from oxidative damage by free radicals (Al-Bideri, 2011). Previous studies have demonstrated a correlation between selenium supplementation and carbohydrate metabolism in rendered diabetic animals (Mcneill *et al.*, 1991). A lot of works have reported the efficacy of selenium either in diabetic animals or diabetic patients (Douillet *et al.*, 1998; Turan *et al.*, 2001).

The aim of this study was to evaluate the possible protective effects of intraperitoneally sodium selenite administration for prevention of the development of diabetic pathology in rats by evaluating body weight gain, biochemical parameters: glucose lipid profile tests, kidney and liver functional markers (total lipid, total cholesterol, triglycerides, urea, creatinine, uric acid, albumin) and the activities of some enzymes (pancreatic lipase, GOT: glutamic oxalic transaminase, GPT: glutamic pyruvic transaminase, ALP: Alkaline phosphatase) in serum of alloxan-induced diabetic rats.

MATERIALS AND METHODS

Animals

Twenty-eight male albino (Wistar) rats of 8 weeks of age, weighing between 250 -300 g, were purchased from Pasteur Institute (Algiers, Algeria). Rats were acclimated for two weeks at animal house, Badji Mokhtar University of Annaba. Animals were maintained in the same laboratory conditions of photoperiod (12 h light/12 h dark) with a relative air humidity of 40 – 60 % and room temperature of 22 $\pm$ 2°C. Standard rat food and water were available *ad-libitum*.

Induction of diabetes

In this study, diabetes was induced experimentally with monohydrate alloxan solution, which was intraperitoneally administered at a dose of 150 mg/kg body weight (Garg *et al.*, 2005). Glycemia was measured one week after alloxan administration to confirm the induction of diabetes on samples taken from the tail vein, using a glucose-meter (ACCU-CHEK).

Experimental procedure

In this study, 28 rats were used and were divided into four groups: (G1) untreated control, (G2) sodium selenite treated control, (G3) untreated diabetic, and (G4) sodium, selenite-treated diabetic groups. Diabetic animals were randomly divided into two groups. The second group received sodium selenite (Sodium selenite was administered at a dose of 5 μmol/kg body weight/day for 4 weeks) (Can *et al.*, 2005). Sodium selenite was dissolved in distilled water. Normal rats were divided into two groups the second group received sodium selenite (5 μmol/kg body weight/day for 4 weeks) (sodium selenite-treated control group).

Blood collection

At the end of the experimental period (28 days) after an overnight fast, rats were decapitated and blood samples were transferred into ice cold centrifuge tubes. The serum was prepared by centrifugation, for 10 min at 3000 rpm and utilized for serum analysis of biochemical parameters.

Measurement of biochemical parameters and activities of some enzymes in serum

Glucose, lipid profile tests (total lipid, total cholesterol, triglycerides, and pancreatic lipase), kidney functional markers (urea, creatinine, uric acid and albumin) and liver functional markers (GOT: glutamic oxalic transaminase, GPT: glutamic pyruvic transaminase, ALP: Alkaline phosphatase) were measured with commercial kits (Spinreact, Spain).

Statistical analysis

Results are expressed as means $\pm$ SEM. Analysis of variance (ANOVA) was used to compare multiple group means, followed by a student's *t*-test to determine statistical significance ($p \leq 0.05$) among the different groups. All statistical analysis was performed using MINITAB software (version 17).

RESULTS AND DISCUSSION

Effect of administration of sodium selenite on body weight gain

The results are presents in Table 1. In the present study, we observed after four weeks of treatment a significant decrease ($P \leq 0.01$) in body weight gain in untreated diabetic rats (G 3) compared to untreated control rats (G 1). Whereas diabetic rats intraperitoneally treated with 5 μmol/kg body, weight/day of sodium selenite resulted a significantly increase in body weight gain in sodium selenite-treated diabetic rats (G4) compared to untreated diabetic rats (G3) and a significantly decrease in body weight gain in sodium selenite treated control rats (G 2) compared with untreated control rats (G1).

Effect of administration of sodium selenite on

Table 1: Effect of administration of sodium selenite on body weight gain, serum biochemical parameters: Glucose, lipid profile tests (total cholesterol, triglycerides, total lipid and pancreatic lipase) of the studied groups

Parameters	Control		Diabetic	
	Untreated (G1)	Sodium selenite treated (G2)	Untreated (G3)	Sodium selenite treated (G4)
Initial body weight (g)	390.3 a ± 49.2	296.8 a ± 52.8	255.4 a ± 34.9	256.8 a ± 37.0
Bodyweight gain (g)	41.00 a ± 1.73	26.66 b ± 1.52	5.00 c ± 1.0	11.50 d ± 1.23
Glucose (mg/dl)	101.79 a ± 6.11	69.40 b ± 3.03	327.00 c ± 27.2	203.33 d ± 15.28
Total cholesterol (g/l)	0.81 a ± 1.73	0.77 a ± 0.11	1.11 b ± 0.08	0.87 a ± 0.05
Triglycerides (mg/dl)	58.18 a ± 5.43	63.19 a ± 9.49	90.89 b ± 9.96	65.66 ab ± 12.45
Total lipid (mg/dl)	152.03 a ± 7.24	147.80 a ± 24.1	232.90 b ± 32.1	180.4 ab ± 16.48
Pancreatic lipase (U/L)	20.50 ac ± 3.01	17.20 a ± 1.31	30.99 bc ± 4.00	27.50 bc ± 1.31

^{a,b,c} values within a horizontal line with different superscript letters were significantly different ($P \leq 0.05$)

Table 2: Effect of administration of sodium selenite on serum biochemical parameters of kidney function: urea, creatinine, uric acid and albumin concentrations of the studied groups

Parameters	Control		Diabetic	
	Untreated (G1)	Sodium selenite treated (G2)	Untreated (G3)	Sodium selenite treated (G4)
Urea (g/l)	0.45 a ± 0.02	0.48 a ± 0.05	0.97 bc ± 0.07	0.86 c ± 0.03
Creatinine (mg/l)	13.29 a ± 0.56	13.86 a ± 0.60	17.44 a ± 2.12	13.10 a ± 2.45
Uric acid (mg/dl)	1.88 a ± 0.22	1.80 a ± 0.76	3.77 b ± 0.19	2.30 a ± 0.12
Albumin (g/dl)	3.16 a ± 0.31	3.01 a ± 0.11	2.24 b ± 0.30	2.93 ab ± 0.34

^{a,b,c} values within a horizontal line with different superscript letters were significantly different ($P \leq 0.05$)

Table 3: Effect of administration of sodium selenite on serum biochemical parameters of liver function: GOT: glutamic oxalic transaminase, TGP: glutamic pyruvic transaminase, ALP: Alkaline phosphatase activities of the studied groups

Parameters	Control		Diabetic	
	Untreated (G1)	Sodium selenite treated (G2)	Untreated (G3)	Sodium selenite treated (G4)
GOT (U/L)	67.08 a ± 2.92	72.92 a ± 2.92	145.83 b ± 11.67	74.37 a ± 7.29
GPT (U/L)	50.56 a ± 6.74	46.67 a ± 5.83	72.92 bc ± 8.75	69.97 c ± 5.08
ALP (U/L)	67.65 a ± 8.25	74.72 a ± 13.20	133.92 bc ± 15.67	114.40 c ± 9.59

^{a,b,c} values within a horizontal line with different superscript letters were significantly different ($P \leq 0.05$)

serum biochemical parameters

Glucose and lipid profile tests

The results are presents in Table 1. The experimentally induced diabetes caused a significant increased the level of serum glucose ($P \leq 0.01$), total cholesterol ($P \leq 0.05$) triglycerides ($P \leq 0.05$), total lipids ($P \leq 0.05$) concentrations and pancreatic lipase activity ($P \leq 0.05$) in untreated diabetic rats (G 3) compared to untreated control rats (G 1).

The administration of sodium selenite resulted in a significant decrease in serum glucose ($P \leq 0.05$), cholesterol ($P \leq 0.05$) concentrations and no significant decrease in triglycerides, total lipid concentrations and pancreatic lipase activity ($P > 0.05$) in sodium selenite-treated diabetic rats (G4) compared to untreated diabetic rats (G3). Treatment with sodium selenite reversed these changes to near normalcy.

On the other hand, the administration of sodium selenite resulted a significantly decrease in serum glucose ($P \leq 0.01$) and no change ($P > 0.05$) in biochemical parameters (total cholesterol, triglycerides, total lipids and pancreatic lipase in sodium selenite treated control rats (G 2) compared with untreated control rats (G1).

Kidney function

The results are presents in Table 2. The experimentally induced diabetes caused a significant increased the level of serum urea ($P \leq 0.01$), uric acid ($P \leq 0.01$) concentrations. However, a significant decrease in serum albumin ($P \leq 0.05$) concentration in untreated diabetic rats (G 3) compared to untreated control rats (G 1).

The administration of sodium selenite resulted in a significant decrease in serum uric acid ($P \leq 0.01$) concentration and no significant decrease in urea concentration ($P > 0.05$). However, a no significant increase in serum albumin ($P > 0.05$) concentration in sodium selenite-treated diabetic rats (G4) compared to untreated diabetic rats (G3). These markers were maintained at close to normal levels in the sodium selenite treated diabetic rats.

The administration of sodium selenite resulted in no change ($P > 0.05$) in the biochemical parameters: (urea, creatinine, uric acid and albumin) in sodium selenite treated control rats (G 2) compared with untreated control rats (G1).

Serum creatinine concentration is normal in all groups.

Liver function

The results are presents in Table 3,which depicts the activities of GOT, GPT and ALP in the serum of experimental groups of rats. There was a significant increase in the activities of GOT ($P \leq 0.01$), GPT ($P \leq 0.05$) and ALP ($P \leq 0.01$) in the serum of untreated diabetic rats (G 3) compared to untreated control rats (G 1).

Daily intraperitoneal administration of 5 μmol/kg body weight/day of sodium selenite to diabetic rats for 28 days resulted in a significantly decrease in serum TGO activity ($P \leq 0.01$) and no significantly decrease in TGP, and ALP ($P > 0.05$) activities in sodium selenite-treated diabetic groups (G4) compared to untreated diabetic rats (G3).

This alteration was restored back to near normal in diabetic rats intraperitoneal treated with sodium selenite.

The administration of sodium selenite resulted no change in GOT, GPT, and ALP in the serum ($P > 0.05$) of sodium selenite treated rats (G 2) to near untreated control rats (G1).

This experiment was conducted to evaluate some protective effects of sodium selenite in rats rendered diabetic by alloxan administration.

Previous studies have presented conflicting results on the effects of selenium on diabetes mellitus. Some of these studies showed the protective effect of selenium against diabetes. In these studies, higher levels of selenium serum were observed in non-diabetes, while lower levels of selenium serum were observed in diabetic patients (Kornhauser *et al.*, 2008; Kilinc *et al.*, 2008; Park *et al.*, 2012).

The onset of diabetes mellitus is characterized by insulin resistance in tissues like liver, skeletal muscle and adipose tissue, leading to hyperglycemia, impaired lipid profiles and thus the potential risk of developing cardiovascular diseases (Kim *et al.*, 2009; Rezaei-Kelishadi, 2017). It is known that during the lack of insulin, the organism increase the protein catabolism activating the gluconeogenesis process which leads consecutively to weight loss (Kasetti *et al.*, 2010). Some authors have reported that sodium selenite administration may improve glycemic index and prevent weight loss (Moneim *et al.*, 2015).

An improvement of glycemia was observed, in our experiment, in rats treated with sodium selenite compared with the diabetic control. Selenium mediates insulin-like activities, including the stimulation of glucose absorption and the regulation of lipogenesis, gluconeogenesis, glycolysis, and the phosphogluconate pathway (S R Stapleton , 2000). Insulin-like and anti-diabetes effects of selenate and selenomethionine have been already observed in diabetes-induced in animals (Zeng *et al.*, 2009).

Other mechanisms of hypoglycemic activity of Selenium were documented as the intestinal glucose transport inhibition and the acceleration of renal glucose excretion in rats (Becker *et al.*, 1996).

Our findings have shown also an elevation of serum levels of total lipids, pancreatic lipase, triglycerides and cholesterol in diabetic animals; these disturbances may be attributed to the insulin deficiency. This later hormone may intervene in different ways in lipidic metabolism in normal conditions as reported elsewhere (Douaouya and Bouzerna, 2016; Shirwaikar *et al.*, 2004).

The results also demonstrated the beneficial effects of selenium in the restoration of lipidemic profile in diabetic treated rats which is in accordance with other findings (Ueki *et al.*, 1993; Ness *et al.*, 1994; Boussekine *et al.*, 2014). Sodium selenite has also ameliorated renal function in treated diabetic rats in comparison to diabetic non treated animals which have shown a renal dysfunction marked by high levels of urea and uric acid with low concentration of albumin.

Other studies showed that the treatment with selenium nanoparticles improves and reduces the levels of urea and creatinine in diabetic-induced rats (Moneim *et al.*, 2015), which is in according to our findings.

The results of this study showed that the serum albumin levels increased in the diabetic group receiving sodium selenite compared with diabetic controls.

A study of selenium effects on diabetic-induced rats has shown that the treatment with selenium leads to the restoration of endothelial dysfunction and vascular disorders through regulating antioxidant enzymes and releasing nitric oxide (Oztürk *et al.*, 2015).

Finally, the restoration of the enzyme activities of ALP, AST and ALT by the administration of sodium selenite may be attributed to the radical scavenging activity of this later (Messarah *et al.*, 2012).

CONCLUSIONS

The results obtained in the present study indicate that alloxan diabetes mellitus induced severe biochemical alterations in glucose, lipid profile concentrations, and liver and kidney functional markers. In addition, sodium selenite may exert some protective effects and reduces diabetic complications risk, which may be attributed to its scavenging activity.

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