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The Impressive Evaluation of Selenium Yeast Role Against Diabetes Mellitus and its Comorbidities by Streptozotocin-Induced Diabetes in Rats

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ABSTRACT

Current anti-diabetic drugs exhibit many side-effects and alternative strategies with minimal side effects and low cost are greatly needed. This study aimed to evaluate selenium yeast (SY) role against diabetes mellitus (DM) in Streptozotocin (STZ)-induced DM. STZ was intraperitoneal injected daily to Sprague-dawley rats to induce DM. SY (0.2 mg/kg) anti-diabetic effect on DM complications was evaluated after 8 weeks of treatment. Biochemical analyses were performed to evaluate SY effectiveness on glucose level, insulin sensitivity, lipid disturbances, oxidative mediators and inflammatory markers. STZ induced DM with toxic effect accompanied with toxic hepatic tissues, lipid disturbances, remarkable oxidative damage and hyper-inflammation. Although there was no significant difference, SY anti-diabetic effect illustrated by decreases in fasting blood glucose, insulin, HbA1c and HOMA-IR levels. SY significantly attenuated ($P<0.05$) lipid disturbances and their associated elevated atherogenic biomarkers. Moreover, SY treatments exhibited an anti-inflammatory effect as it ameliorated the increase in inflammatory parameters (CRP, TNF-α, IL-6). Also, it restored total antioxidant capacity and peroxisome proliferator-activated receptor (PPARϒ) levels that decreased by STZ-DM induction. This study highlighted SY promising therapeutic role in DM. SY ameliorated lipid accumulation, alleviated pro-inflammatory cytokines expression and restoring the antioxidant capacity. Further studies needed to evaluate SY combination with other standard anti-diabetic drugs to improve its efficacy.

Keywords: *Selenium yeast; Anti-diabetic; Antioxidant; Anti-inflammatory; Diabetes mellitus*

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1.INTRODUCTION

Diabetes mellitus (DM) is multifactorial chronic progressive metabolic disease that related to varied pathological alterations including macro-vascular and microvascular complications that affect almost every body part [1]. These associate with increased mortality, poor quality of life and high medical costs [2]. Due to hypoinsulinism or insulin resistance (IR), DM is characterized by abnormal protein, lipid, and carbohydrate catabolism and anabolism [3]. The global prevalence of impaired glucose tolerance and type 2 DM (T2DM) is estimated to be 7.5% (374 million) and 9.3% (463 million individuals) which may be projected to 8.0% (454 million) and 10.2% (578 million), respectively by 2030 [2].

Nowadays, the use of many drugs for T2DM management has been increased, such as agonists of peroxisome proliferator activated receptor-γ (PPARγ), which maintains glucose homeostasis and metformin, which inhibits hepatic gluconeogenesis. Sulfonylureas stimulate insulin secretion from pancreatic β-cells and α-glucosidases interfere with intestinal glucose absorption. Insulin augments glucose utilization and stimulates hepatic glucose suppression [2, 4-6]. However, these drugs are related to varied adverse side effects including renal failure, hypoglycaemia, vomiting, diarrhea, etc. [7]. So, alternative antidiabetic strategies with minimal or no hazardous side effects are required [8].

In 1957, selenium (Se) was first identified as essential to mammals, when it was reported to inhibit necrotic hepatic degeneration [9]. Owing to sialoproteins anti-inflammatory and antioxidant effects, it was expected that Se would be beneficial for DM management, given that T2DM is related to oxidative stress [9]. Indeed even at high supra-nutritional doses, Se has insulin-mimetic and anti-diabetic effects [10]. Se yeast (SY) is enriched recognized organic selenium source that naturally present in various food types [10]. Limited studies reported the impact of SY administrations on attenuation DM and its related complications [10].

This study aimed to evaluate SY anti-diabetic effects including attenuation of glucose related parameters (blood glucose, glycosylated haemoglobin (HbA1c), insulin, homeostatic model assessment of insulin resistance (HOMA-IR)), lipid profile, anti-inflammatory and antioxidant activities.

2. MATERIAL AND METHODS

The study animals and experiments were based on the National Research Council's suggested criteria for animal care and use [11]. The design was approved by the Animal Ethics Committee of School of Graduate Studies, Jordan University.

2.1. Reagents and materials

SY was purchased from ISURA Co., USA. STZ (>95%; bioXTra, UK, Lot # 18883-66-4) and Deionized water (B#1207702; Thermo Fisher Scientific, USA) were purchased. All enzyme immune assay kits (including interleukin (IL)-6 and tumor necrosis factor-α (TNF-α)) were purchased from MyBioSource, USA. The following instruments were used: Multiskan Go Spectrophotometer, Model 1510, Thermo Fisher, UK-Bath, Sonicator Crest model-175T (UltraSonics CORP), Sartorius analytical balance, and Centrifuge (Eppendorf 5417C).

2.2. Animals, diabetic induction and study design

Sprague-Dawley male rats (220-300 g; n=27) were included from Animal house, School of Graduate Studies, Jordan University, Jordan. Under nutritional necessities and standardized environmental, all animals were housed with free access to food and water. Rats classified into 3 main groups (9/each group). G0 (Negative control) received just regular baseline animal. All other groups were subsequently intraperitoneal daily given a low amount of STZ (40 mg/kg of freshly prepared STZ solution (32.25 mg/ml in 0.05 M sodium citrate buffer, pH 4.5)). T2DM was obtained in animals when fasting blood glucose (FBG) was ≥120 mg/dL and non-FBG was ≥250 mg/dL. G1 was baseline DM animals and G2 was SY (0.2 mg/kg) group.

2.3. Evaluation of diabetic related, lipid profile, anti-inflammatory and antioxidant parameters

Before, during and after the treatment stage (about 6 weeks), cardiac puncture and blood were collected into plain tubes. Using fresh blood, FBG (SPINREACT, Spain) and HbA1c (Automatic protein analyzer, GenruiPA120) were analyzed. To obtain serum, remaining blood is left to clot and then centrifuged. Serum samples were preserved frozen for biochemical testing. Selenium, leptin, PPAR-γ, insulin, TNF-α IL-6, C-reactive protein (CRP) and total antioxidant capacity (TAC) (all from My BioSource, Rat, ELISA Kits) and lipid profile including cholesterol, triglycerides, LDL-C, and HDL-C (all from SPINREACT, Spain) were analyzed using specialized kits and following the manufactures′ detailed instructions. HOMA-IR was calculated from the following equation [fasting insulin (μ/ml) × fasting glucose (mmol/l) / 22.5] [12].

2.4. Statistical analysis

Results are expressed as mean ± standard error of the mean. P<0.05 was considered to be statistically significant. For statistical analysis of the data obtained from various groups, one-way analysis of variance (ANOVA) was performed followed by Tukey–Kramer as post hoc test. Pearson's correlation test was used to assess the interrelationships between biomarkers. Statistical analysis software (SAS version 9, USA) was used to analyse the data.

3. RESULTS

3.1. Weight change, food and water intake between untreated and treated rats

The pancreas damage by STZ injection resulted in DM onset. During the study course, body weight varied significantly (*P*<0.05) as a function of diets. Also, feed intake increased significantly (P<0.05) in the diabetic groups. Water intake increased significantly with the passage of study compared to non-diabetic rats. With DM induction, liver weights significantly increased (G1) and this effect was attenuated in SY treated group (G2) (Table 1).

3.2. Effect of selenium yeast on diabetic markers

In comparison with normal non-diabetic rats (G0), STZ-induced DM exhibited hyperglycaemia that associated with significantly (P<0.05) increased FBG, serum insulin, HbA1c and HOMA-IR levels. Although there was no significant difference, SY treated group (G2) showed decrease in FBG, HbA1c, serum insulin and HOMA-IR levels compared to diabetic control group (G1) (Figure 1).

3.3. Selenium yeast improve lipid profile and atherogenic biomarkers

As shown in Table 2 and compared to normal non-diabetic group, DM control group shown significant increase in cholesterol, triglyceride and LDL-C and significant decrease in HDL-C (P< 0.05). Consequently, rats with DM were also associated with significantly (P<0.05) increased lipid-related atherogenic biomarkers including atherogenic index of plasma (AIP), atherogenic coefficient (AC) and cardiac risk ratio (CRR) (Figure 2). Treatment with SY attenuated these lipid alterations and increased atherogenic biomarkers (P<0.05 for most of parameters compared to DM untreated rats) (Table 2 and Figure 2).

3.4. Effect on inflammatory and antioxidant statuses

Compared to non-diabetic rats, DM inducing elevated (P<0.05) levels of anti-inflammatory parameters including CRP, TNF-α and IL-6. Also, diabetic rats were associated with increased (P<0.05) leptin serum levels. In contrast, DM induction causes significantly (P<0.05) reduction in TAC and PPARϒ expression (Table 3). After treatments with SY these issues were ameliorated (Table 3).

4. DISCUSSION

Due to their anti-inflammatory and antioxidant effects, selenoproteins was expected to be beneficial for patients with T2DM [9, 13]. Although Se (as selenate) has insulin-mimetic and anti-diabetic effects [14], the Se role in DM

is still a matter of discussion with respect dietary Se supply and requirements [9]. Therefore, this study aimed to evaluate SY, as enriched selenoproteins source [15], anti-diabetic effects including attenuation of blood glucose, HbA1c, insulin, HOMA-IR, lipid profile, anti-inflammatory and antioxidant activities.

In this study as accepted DM model, we used STZ-induced DM in Sprague-Dawley male rats. It is known that STZ caused pancreas β-cell damage, the main event in DM development [16]. Here, we demonstrated that STZ-induced DM and IR, resulting in hyperinsulinemia, hyperglycaemia and increased HbA1c levels. Although there was no significant difference, DM rats treated with SY resulted in improved insulin levels and glycemic control with values closed to control rats.

In line with our results, limited studies evaluated the anti-diabetic effect of SY as dietary form [17] and they reported that SY possess hypoglycaemic property as rats treated with SY had lower FBG compared to diabetic rats and rats treated with DM standard drug Glibenclamide. Other studies reported that SY in a nanoparticles form improve these antidiabetic activity [16, 18]. Se antidiabetic activity may be due to its ability to renew β-cells activity, insulin release stimulation and, thus, lowering serum glucose level [16]. Also, its hypoglycemic effect may be due to other mechanisms including intestinal glucose transport inhibition and accelerate renal glucose excretion [19]. By activation of insulin signaling cascade Akt and other kinases, Se is capable of possess insulin-mimetic effects [20]. In isolated rat adipocytes, some studies found that selenate salts stimulated glucose uptake by activating serine/threonine kinases and translocating glucose transporters to the plasma membrane [21, 22]. Moreover, selenate salts reported to improve glucose homeostasis and this effect have been related to partial reversal of abnormal gluconeogenic and glycolytic liver enzymes activity [19].

From another hand, we reported in this study that SY had important role in attenuation of lipid dysfunction and its related inhibition of atherosclerosis formation [23]. SY effecting beneficial changes in cholesterol, triglycerides, LDL and HDL levels. It also improved related atherogenic biomarkers including AIP, AC and CRR. Similar association between adequate Se levels and reduced atherogenic risk was previously reported [24].

In both human and animal models, several studies elucidate oxidative stress implication in DM as common factor that causes increasing tissues-specific IR [16]. Also, hyperglycemia can significantly enhance the oxidative stress and the imbalance between the reactive oxygen species (ROS) production and the anti-oxidative protective system [25]. In the DM development, inflammation have important role and hyperglycemia was reported to elevate serum inflammatory markers [25]. Also during DM development, recent studies exhibit that inflammation and IR are directly related to each other [16].

Elevated Se levels in aqueous solutions caused an increase in antioxidant enzymes activity including catalase, glutathione peroxidase, superoxide dismutase and glutathione reductase [26]. Experimental studies suggest Se antioxidant supplements could delay DM development by decreasing oxidative and inflammatory stress [10]. Se exhibited an anti-inflammatory and antioxidant effects by cytokine expression mitigation and increase TAC [16]. Similar to previous studies, treatments with SY in this study ameliorated increasing inflammatory parameters (CRP, TNF-α and IL-6) and decreasing TAC and PPARɣ levels that caused by STZ-DM induction.

5. CONCLUSIONS

This study highlighted the anti-diabetic potential of SY supplementation. Although SY may delay DM onset and subsequently minimizes the risk of its related complications, some evaluated parameters did not show significant difference. Thus, further studies are recommended to evaluate SY synergistic effect with other established anti-diabetic drugs to improve their efficiency.

Ethics Approval

All experiments and animals involved in this study were carried out according to the National Research Council's suggested criteria for animal care and use. The study protocol was approved by the Animal Ethics Committee of School of Graduate Studies, Jordan University.

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The authors declare they have no financial interests.

Conflict of Interest

Authors have no conflicts of interest to declare.

Author Contributions

Conceptualization, L.N.T.; methodology, L.N.T AND Z.Z. and T.Y.A; software, M.J.S, and W.A.B.; validation, R.H.A.; formal analysis, M.J.S.; investigation, W.A.B.; resources and data curation, All Authors; writing— original draft preparation, All Authors; writing—review and editing, All authors; visualization, All Authors; supervision and project administration: W.A.B. and, L.N.T.; All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. Hassan, R.M., et al., Mitigating effect of single or combined administration of nanoparticles of zinc oxide, chromium oxide, and selenium on genotoxicity and metabolic insult in fructose/streptozotocin diabetic rat model. Environ Sci Pollut Res Int, 2021. 28(35): p. 48517-48534.
2. Singh, P., et al., Assessment of antidiabetic effect of 4-HIL in type 2 diabetic and healthy Sprague Dawley rats. Hum Exp Toxicol, 2022. 41: p. 9603271211061873.
3. Nasir, A., et al., Anti-diabetic potential of 'Safūf-i-Dhayābītus' as standalone and as an adjuvant with glibenclamide in streptozotocin-induced diabetic rats. Phytomedicine Plus, 2022. 2(1): p. 100218.
4. Hailat, M.; Zakaraya, Z.;Al-Ani, I.; Meanazel, O.A.;Al-Shdefat, R.; Anwer, M.K.; Saadh,M.J.; Abu Dayyih,W. Pharmacokinetics and Bioequivalence of Two Empagliflozin,with Evaluation in Healthy Jordanian Subjects under Fasting and Fed Conditions. Pharmaceuticals 2022, 15,193. https://doi.org/10.3390/ph15020193
5. Amawi, Kawther Faisal, et al., Diabetes upregulates the expression of HSP90 and downregulates HSP70 in the liver of diabetic rats. Comparative Clinical Pathology, 2019. 28: p. 473-478.
6. Kim, Y.D., et al., Metformin inhibits hepatic gluconeogenesis through AMP-activated protein kinase-dependent regulation of the orphan nuclear receptor SHP. Diabetes, 2008. 57(2): p. 306-14.
7. Aziz, T.A., et al., The efficacy and safety of Ginkgo biloba extract as an adjuvant in type 2 diabetes mellitus patients ineffectively managed with metformin: a double-blind, randomized, placebo-controlled trial. Drug Des Devel Ther, 2018. 12: p. 735-742.
8. L.N. Tamimi, Z. Zakaraya, M. Hailat, W. Abu Dayyih, E. Daoud, A. Abed, M.J. Saadh, et al. Anti-diabetic effect of cotreatment with resveratrol and pioglitazone in diabetic rats. European Review for Medical and Pharmacological Sciences, 2023; 27: 325-332
9. Steinbrenner, H., L.H. Duntas, and M.P. Rayman, The role of selenium in type-2 diabetes mellitus and its metabolic comorbidities. Redox Biol, 2022. 50: p. 102236.
10. Tanko, Y., et al., Effects of Selenium Yeast on Blood Glucose and Antioxidant Biomarkers in Cholesterol Fed Diet Induced Type 2 Diabetes Mellitus in Wistar Rats. Nig J Physiol Sci, 2017. 31: p. 147-152.
11. National Research Council, Guide for the Care and Use of Laboratory Animals. 8th edition ed. 2011: Washington (DC): National Academies Press (US).
12. Wareham, N.J., et al., The 30 minute insulin incremental response in an oral glucose tolerance test as a measure of insulin secretion. Diabet Med, 1995. 12(10): p. 931.
13. Alkather, Zainab; Hailat, Mohammad; Al-Shdefat, Ramadan; Abu Dayyih, Wael. Development and Validation of HPLC Method for Five Gliptins in Pharmaceutical Dosage Forms in Finished Marketed Products. Current Pharmaceutical Analysis, 2021, 17(10), pp. 1263-1271(9
14. Steinbrenner, H., Interference of selenium and selenoproteins with the insulin-regulated carbohydrate and lipid metabolism. Free Radic Biol Med, 2013. 65: p. 1538-1547.

15. Hariharan, S. and S. Dharmaraj, Selenium and selenoproteins: it's role in regulation of inflammation. Inflammopharmacology, 2020. 28(3): p. 667-695.
16. Abdulmalek, S.A. and M. Balbaa, Synergistic effect of nano-selenium and metformin on type 2 diabetic rat model: Diabetic complications alleviation through insulin sensitivity, oxidative mediators and inflammatory markers. PLoS One, 2019. 14(8): p. e0220779.
17. Ahmed, M.K., et al., Ameliorative Effect of Selenium Yeast on Blood Glucose Level in Streptozotocin Induced Diabetes in Wistar Rats. Cell Biology, 2015. 3(1): p. 14-18.
18. Abd El-Hakim, Y.M., et al., Chitosan-Stabilized Selenium Nanoparticles and Metformin Synergistically Rescue Testicular Oxidative Damage and Steroidogenesis-Related Genes Dysregulation in High-Fat Diet/Streptozotocin-Induced Diabetic Rats. Antioxidants (Basel), 2020. 10(1).
19. Zainab ZZ et al. Ameliorative effect of selenium yeast in combination with pioglitazone on diabetes outcomes in streptozotocin-induced J Popul Ther Clin Pharmacol, December 2022.Vol 29(4):e202–e210; 24
20. Steinbrenner, H., et al., High selenium intake and increased diabetes risk: experimental evidence for interplay between selenium and carbohydrate metabolism. J Clin Biochem Nutr, 2011. 48(1): p. 40-5.
21. Hei, Y.J., et al., Stimulation of MAP kinase and S6 kinase by vanadium and selenium in rat adipocytes. Mol Cell Biochem, 1998. 178(1-2): p. 367-75.
22. Ezaki, O., The insulin-like effects of selenate in rat adipocytes. J Biol Chem, 1990. 265(2): p. 1124-8.
23. Agbor, G.A., et al., Effect of selenium- and glutathione-enriched yeast supplementation on a combined atherosclerosis and diabetes hamster model. J Agric Food Chem, 2007. 55(21): p. 8731-6.
24. AL-Auqbi, T.F.R., A.M.R. Al-Mussawi, and A.-S.A.K.Y. J., Evaluation of the Potential Role of Serum Selenium in Diabetic Patients. AL-Kindy College Medical Journal, 2008. 4(2): p. 45-49.
25. Matough, F.A., et al., The role of oxidative stress and antioxidants in diabetic complications. Sultan Qaboos Univ Med J, 2012. 12(1): p. 5-18.
26. Talbi, W., et al., Effects of selenium on oxidative damage and antioxidant enzymes of eukaryotic cells: wine Saccharomyces cerevisiae. J Appl Microbiol, 2019. 126(2): p. 555-566.

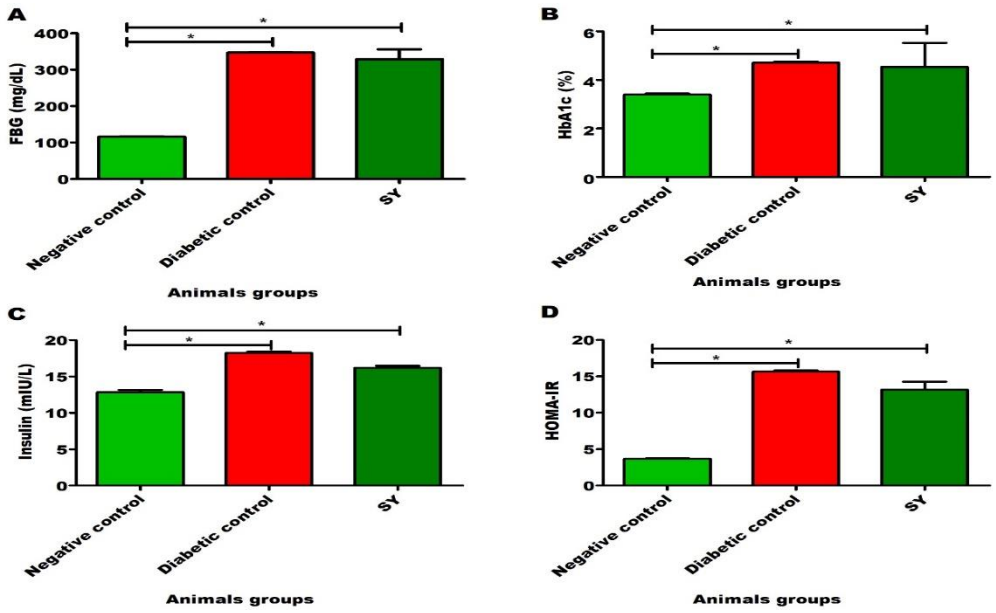

FIGURE 1: Diabetic markers between SY treated and untreated rats. Although there was no significant difference, SY treatment significantly attenuated increased (A) FBG, (B) HbA1c, (C) insulin and (D) HOMA-IR levels. Values are the means±SEM. Abbreviations: SY: selenium yeast; FBG: fasting blood glucose; HbA1C: glycosylated hemoglobin; HOMA-IR: homeostatic model assessment of insulin resistance. * means that values are significantly different at $P<0.05$.

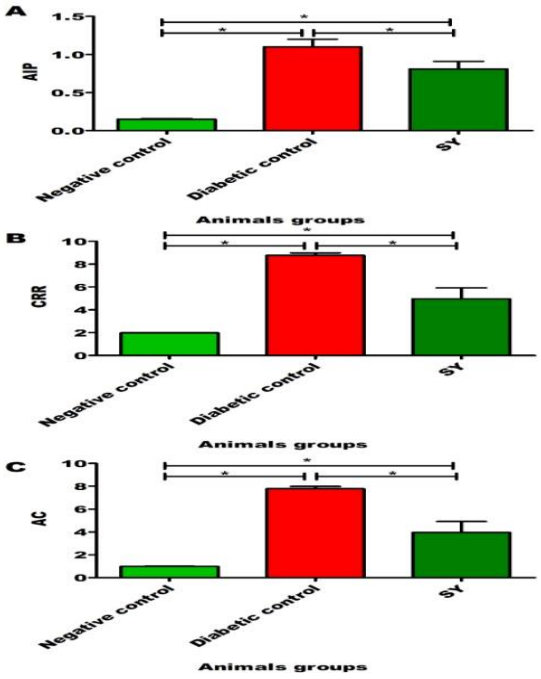

FIGURE 2: Atherogenic biomarkers between SY treated and untreated rats. Compared to diabetic controls, SY treatment significantly improve (A) AIP, (B) CRR and (C) AC atherogenic indices. Abbreviations: SY: selenium yeast; AIP: atherogenic index of plasma [log (Triglyceride/HDL-C)]; AC: atherogenic coefficient [TC-HDL-C/HDL-C]; CRR: cardiac risk ratio (TC/HDL-C). * means that values are significantly different at P<0.05.

TABLE 1: Food and water intakes and body and liver weight of the study groups

Variables	**Non-Diabetic Control**	**Streptozotocin-Induced Diabetic Groups**	
		Control	**SY**
	(n=9)	(n=9)	(n=9)
Initial weight (g)	249±14	231.6±1.5	274.0±15.9
Final weight (g)	253.1±14.2	221.0±2.2	248.4±13.2
Δ Weight (g/day)	0.09±0.01	-0.25±0.03	-0.61±0.26a
Food intake (g/day)	0.32±0.01	0.50±0.0	0.71±0.01a
FER	27.58±3.14	-0.5±6.99a	-85.6±35.7a
Water intake (ml/day)	0.93±0.01	1.85±0.0a	2.60±0.01a,b
Liver weight (g)	7.52±0.24	8.77±0.27a	6.9±0.13b
Liver index	3.05±0.20	3.97±0.13a	2.84±0.15b

Values are the means±SEM. Abbreviations: SY: selenium-yeast; FER: food efficiency ratio (bodyweight change/100g food intake); liver index: liver weight (g)/100g final body weight. Values are significantly different at P<0.05. a significantly different from non-diabetic control, b significantly different from diabetic control.

TABLE 2: Lipid profile between untreated and treated rats

Variables	Non-Diabetic Group	Streptozotocin-induced diabetic groups	
		Control	SY
	(n=9)	(n=9)	(n=9)
Cholesterol (mg/dl)	54.9±0.3	106.2±1.0a	89.3±14.3a,b
LDL-C (mg/dl)	20.88±0.49	67.12±0.8a	45.7±5.4 a,b
HDL-C (mg/dl)	27.62±0.13	12.13±0.3a	19.4±1.56a,b
Triglycerides (mg/dl)	39.5±1.1	134.8±1.1a	131.9±16.4a
LDL-C/HDL-C	0.76±0.02	5.56±0.15a	2.6±0.44a,b
Cholesterol/Triglycerides	1.40±0.04	0.79±0.01a	0.80±0.16a

Values are the means±SEM. Abbreviations: SY: selenium-yeast; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol. Values are significantly different at $P<0.05$. a significantly different from non-diabetic control, b significantly different from diabetic control.

TABLE 3: Anti-inflammatory and anti-oxidant parameters between untreated and treated rats

Variables	Non-Diabetic Group	Streptozotocin-induced diabetic groups	
		Control	SY
	(n=9)	(n=9)	(n=9)
CRP (ng/ml)	2952±856	12188±316a	2786±730b
TNFα (pg/ml)	241.8±1.5	542.1±3.5a	491.9±89.8a
IL-6 (pg/ml)	20.89±0.03	92.71±1.33a	85.27±2.30a
TAC (U/ml)	0.23±0.01	0.15±0.01a	0.16±0.01a
PPARɣ (pg/ml)	305.9±4.6	125.4±1.1a	170.2±57.3b
Leptin (ng/ml)	8.37±0.12	18.04±0.18a	14.02±0.59a
Selenium (µmol/ml)	0.34±0.12	0.31±0.14	0.13±0.04

Values are the means±SEM. Abbreviations: SY: selenium-yeast; CRP: C-reactive protein; TNFα: tumor necrosis α; IL-6: interleukin 6; TAC: total antioxidant capacity; PPAR ɣ: Peroxisome proliferator-activated receptor-gamma. Values are significantly different at $P<0.05$. a significantly different from non-diabetic control, b significantly different from diabetic control.