

# Effect of Coenzyme Q10 Supplementation on Markers of Oxidative Stress in Streptozotocin Induced Diabetic Rats

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## ABSTRACT

Increasing evidences link free radicals and oxidative stress to the pathogenesis of diabetes and related complications. The aim of this study was to investigate the effects of exogenous coenzyme Q10 supplementation on streptozotocin induced experimental diabetes in rats. Experimental diabetes was induced by single subcutaneous injection of streptozotocin ( 50 mg/kg/ body weight) . Forty male albino rats were used in this study, they were divided into 4 groups: control group, coenzyme Q10 treated group, diabetic group and coenzyme Q10 treated diabetic group. At the end of the experiment (8 weeks) urine samples were collected, rats were sacrificed and blood samples were collected for biochemical analysis. Significant high levels of blood sugar, glycated Hb, total cholesterol, triglyceride, LDL cholesterol, advanced oxidative protein products , 8-hydroxy-2-deoxyguanosine and percent of DNA damage as well as significant low levels of nitric oxide and HDL cholesterol were observed in diabetic group. Significant low levels of blood sugar, glycated Hb, cholesterol, triglyceride, LDL cholesterol, advanced oxidative protein products, 8-hydroxy-2-deoxyguanosine and percent of DNA damage as well as significant high levels of nitric oxide and HDL cholesterol were observed in coenzyme Q10 treated diabetic group. The data confirmed the property of coenzyme Q10 as an antioxidant that ameliorates oxidative stress and that it may be used as an additional therapeutic agent for prophylaxis and slowing down the progression diabetic complications.

## INTRODUCTION

In the recent decades, oxidative stress has become focus of interest in most biomedical disciplines and many types of clinical research. Clinical trials have revealed that oxidative stress may increase reactive oxygen species (ROS) formation and reduce antioxidant defenses (Stocker and Kearney 2004) ,these cause a complex dysregulation of cell metabolism and cell-cell homeostasis through which risk factors of several diseases as diabetes, obesity, inflammation and hypertension, can exert their deleterious effects (Pitocco *et al.*, 2010). There is evidence that hyperglycemia in diabetes results in oxidative stress through an increase in ROS production and a decrease in ROS scavenging (Ceriello,2006). Mitochondria can contribute to the development of this disease because they generate high levels of ROS (Rolo and Palmeira 2006), which could promote oxidative

stress. It was found also that there was a significant correlation between the increased blood sugar levels and the depletion of the antioxidants ,this depletion was a major risk factor for the development of the complications (Baburao and Anand 2012).In many tissues, antioxidant therapy has been shown to reduce or retard the damaging effect of ROS in diabetes and diabetes-related complications (Singh, 2007). Coenzyme Q10 (CoQ10 or Ubiquinone) is a naturally occurring quinone that is found in most aerobic organisms from bacteria to mammals. The level of CoQ10 is the highest in organs with high rates of metabolism such as the heart, kidney, and liver (114, 66.5, and 54.9g/g tissue, respectively), where it functions as an energy transfer molecule. It is a lipid-soluble benzoquinone with 10 isoprenyl units in the side chain and is a key component of the mitochondrial respiratory chain for adenosine triphosphate (ATP) synthesis (Bhagavan and Chopra 2006). As most cellular functions are dependent on an adequate supply of ATP, CoQ10 is essential for the health of virtually all human tissues and organs. CoQ10 is a well-known antioxidant and has bioenergetic and anti-inflammatory effects.

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It exerts some impact on the generation and half-life of  $O_2^{\cdot-}$ . There are two potential ways in which CoQ10 might suppress  $O_2^{\cdot-}$  production. One possibility is that CoQ10 decreases cytoplasmic NADH concentration by enhancing electron shuttle mechanisms that transfer electrons and  $H^+$  from cytoplasmic NADH to the mitochondrial respiratory chain. Another possibility is that CoQ10 collects electrons in all cells' plasma membranes which otherwise could be used for generation of  $O_2^{\cdot-}$ , so it is an important inhibitor of oxidative damage (Kędziora-Kornatowska 2010). In many disease conditions connected with increased generation and the action of reactive oxygen species the concentration of coenzyme Q10 in the human body decreases (Rosenfeldt *et al.*, 2003; Beal, 2004).

Quantitative or functional deficiency in CoQ10 may potentially occur in diabetic patients as a consequence of increase in the cytosolic redox potential that over delivers electrons into the mitochondrial transportation system and uncouples the production of ATP. An absolute or relative deficiency in CoQ10 could result in a dysfunctional increase in transfer of electrons to molecular oxygen. The mitochondria then become a source of superoxide radical overproduction. CoQ10 deficiency may be involved in the pathogenesis diabetes by depressing b-cell function and mitochondrial dysfunction has also been linked with the development of insulin resistance (Chew and Watts 2004).

This study aimed to evaluate the beneficial effects of the antioxidant coenzyme Q10 supplementation in improving the adverse changes associated with the oxidative stress in streptozotocin induced diabetic rats.

## MATERIALS AND METHODS

### Chemicals

Streptozotocin (STZ) were purchased from Sigma Aldrich Chemicals Company St.Louis USA. CoQ10 capsules were purchased from Arab Company for Pharm. & Medicinal Plants (MEPACO-MEDIFOOD) Enshas-Sharkeya-Egypt

### Experimental Animals

Forty male Albino rats (weighing about 170-200 g) were used in this study, they were obtained from the animal house of National Research Centre, Cairo, Egypt. The animals were kept under good ventilation and daily received a standard commercial diet and water ad libitum throughout the experimental period (8Weeks).The experiment was carried-out in accordance with the regulations of Ethical Committee, National Research Center.

### Induction of diabetes

Diabetes was induced in the overnight fasted rats by a single subcutaneous injection of streptozotocin (50 mg/kg body weight) dissolved in citrate buffer (pH=4.5). Normal control rats received 50 mg/kg body weight citrate buffer only as vehicle. Fasting blood sugar was estimated after 72 hours to confirm the development of diabetes (Uchiyama and Yamaguchi, 2003).

### Experimental design

Forty male albino rats were divided into four groups (ten rats in each group) as follow:

#### Control group

Healthy rats received intragastric corn oil (10 mg / kg body weight /day)

#### CoQ10 treated group

Healthy rats received intragastric CoQ10 (10 mg / kg body weight /day).

#### Diabetic group

Diabetic rats received intragastric corn oil (10 mg / kg body weight /day).

#### CoQ10 treated diabetic group

Diabetic rats received intragastric CoQ10 (10 mg /Kg body weight /day).

### Urine and Blood Samples collection

Eight weeks after streptozotocin injection, rats were individually housed in metabolic cages and allowed to adapt for 48 hours. Following this, 24-hour urine collections were obtained. Urine was centrifuged and then the samples were frozen at  $-20^{\circ}C$  until used. Then the animals were kept fasting for 12 h and anesthetized by diethyl ether, the blood was withdrawn from the retro-orbital venous plexus using capillary tubes. One mL of blood was collected in tube containing EDTA for estimation of glycated hemoglobin, one mL was collected in tubes contain sodium fluoride for blood glucose estimation and the rest of the sample was collected in clean polypropylene tube, which was left to clot at  $37^{\circ}C$  for 10 min, then centrifuged and serum was separated. All sera were frozen at  $-20^{\circ}C$  until used.

### Biochemical assays

#### Blood glucose determination

Fasting blood glucose was determined according to the method described previously by Trinder (1969).

#### Glycated hemoglobin (HbA1c)

HbA1c was determined spectrophotometrically using commercially kit supplied by Stanbio, USA according to the method described by Trivelli *et al.* (1971).

### Lipid Profile

Cholesterol and triglyceride were determined using commercially kits supplied by Biocon Diagnostic, Germany, according to methods previously described by Allain *et al.* (1974) and Glick *et al.* (1986) respectively. HDL-cholesterol ( Lopez-Virella *et al.*, 1977) was determined using commercially kits supplied by Biocon Diagnostic, Germany. LDL-cholesterol was calculated according to equation developed by Friedewald (1972).  $LDL = \text{total cholesterol} - (\text{HDL-cholesterol} + \text{triglycerides})$

### Evaluation of urinary 8-hydroxy-2-deoxyguanosine (8-OHdG)

Protocol for urinary 8-OHdG analysis was modified from the method described by Shigenaga *et al.* (1989). Briefly; 8-OHdG was extracted from 1 ml urine. The eluents were dried under ultra-pure N<sub>2</sub> stream and reconstituted in 5 ml deionized water for injection in high performance liquid chromatography (HPLC) system, Agilent technologies 1100 series, equipped with a quaternary pump (Quat. pump, G131A model).

#### HPLC condition

HPLC column for 8-OHdG was C18 (250 ×4.6 mm, particle size 5µm). The mobile phase consists of acetonitrile / methanol/ phosphate buffer (25/10/965). Phosphate buffer was prepared by dissolving 8.8 of potassium dihydrogen phosphate in 1000 ml deionized water and PH was adjusted at 3.5, the buffer then filtered 2 times before using flowrate 1ml/min and using electrochemical detector with cell potential 600 mv.

### Quantitative determination of advanced oxidation protein products (AOPP)

This was performed according to the method of Witko-Sarsat *et al.* (1996). The kit was supplied from immunodiagnostic AG, Germany. The assay is based on the spectroscopic analysis of modified proteins at 340nm. Samples assayed for AOPP were placed in each well of a 96- well microtiter plate. The chloramines-T (CT) absorbance at 340 nm being linear within the range of 0-100 µmol/L. AOPP concentrations were expressed as CT equivalents.

### Determination of serum nitrite/nitrate (NOx) as index of Nitric oxide

NOx was measured by the modified Griess method according to Tatsch *et al.* (2011)

### Determination of serum CO Q10

Co Q<sub>10</sub> measurement was performed using high performance liquid chromatography (HPLC) assay described by Mosca *et al.* (2002).

### Measurement of coenzyme Q10 in pancreatic tissue

#### Preparation of tissue homogenate

The frozen Pancreatic tissues were cut into small pieces and homogenized in 5 ml cold buffer (0.5 g of Na<sub>2</sub>HPO<sub>4</sub> and 0.7 g of NaH<sub>2</sub>PO<sub>4</sub> per 500 ml deionized water (pH 7.4) per gram tissue, then centrifuged at 4000 rpm for 15 minutes at 4°C and the supernatant was removed for chemical parameters estimation (Manna *et al.*, 2005).

#### Estimation of Pancreatic CoQ10 by HPLC

Determination of Pancreatic CoQ10 was carried out using HPLC system, Agilent technologies 1100 series, equipped with a quaternary pump (Quat. pump, G131A model). Homogenate samples were treated with 2ml ethanol and CoQ10 was extracted with 5ml hexane ,after vigorous shaking, 4ml of

hexane layer were separated and dried under nitrogen gas.The residue was dissolved in 400 µl ethanol and 20 µl. were injected in HPLC system.

#### HPLC condition

Separation was achieved on ODS-reversed phase column (C18, 25 9 0.46 cm i.d. 5 µm). The mobile phase consisted of ethanol/methanol 70/30 (v/v) and was delivered at a flow rate of 2 ml/min. UV detection was performed at 275 nm. The concentration CoQ10 was determined by external standard method using peak areas. Serial dilutions of standards were injected, and their peak areas were determined. A linear standard curve was constructed by plotting peak areas versus the corresponding concentrations. Samples concentrations were obtained from the curve.

### Determination of tissue MDA

The samples were first homogenized by a homogenizer in cooled phosphate buffer saline. Next, 200µL of the homogenized sample was poured into test tubes. Then, a mixture of certain amounts of 20% acetic acid, 8% thiobarbituric acid, and 8.1% sodium dodecyl sulphate was added to all of the tubes. The tubes containing this suspension were heated in a water bath at 95°C for 60 minutes and after being cooled in ice water, 4mL of n-butanol was added to each of them. The tubes were centrifuged at 4000 rpm for 10 minutes and the light absorption of the upper layer was measured at 532 nm by a spectrophotometer . Tetraethoxypropane was used as the external standard(Ohkawa *et al.*,1979)

### Comet Assay

Comet Assay was performed according to Singh and colleagues (Singh *et al.*, 1988) with modifications according to Blasiak *et al.* (2003).

Lymphocytes were isolated by Ficoll–Hypaque density gradient (Pharmacia LKB Biotechnology, Piscataway, NJ, USA) and washed by phosphate-buffered saline (PBS) at pH 7.4. Ten µl of the cells were suspended in 75 µl of 0.5% low melting agarose for pipetted on microscopic slides with a layer of 1% agarose, spread using a coverslip and maintained on an ice-cold flat tray for 5min to solidify. After removal of the coverslip, the slides were immersed in cold lysis solution at 4 °C for 1 h, followed by electrophoresis at 25 V, 300 mA, for 40 min at steady temperature. After electrophoresis, the slides were gently removed from the tank and washed three times with neutralising buffer 0.4 M Trisma base at pH 7.5 for 10 min. Twenty µl ethidium bromide (10 µg/ml) was added to each slide.

#### Visualization and analysis of Comet Slides

The slides were examined at 40× magnification using an inverted fluorescence microscope (IX70; Olympus, Tokyo, Japan) equipped with an excitation filter of 549 nm and a barrier filter of 590 nm, attached to digital camera (Olympus). Damaged cells were visualized by the “comet appearance”, with a brightly

fluorescent head and a tail to one side formed by the DNA containing strand breaks that were drawn away during electrophoresis. Samples were analyzed by counting the damaged cell out of 100 cells per slide to calculate the percent of damage.

### Statistical analysis

Data entry and analysis were done using the statistical package for the social sciences (SPSS) program, version 16 and Microsoft Excel 2007. Data are presented means  $\pm$  standard deviation (SD). The significance difference between values was estimated using student's t-test. A p value less than 0.05 was considered to indicate a statistically significant difference. One way ANOVA test was used.

### RESULTS

Rats fed on standard diet and treated with Q10 did not show any significant changes in the parameters examined except serum and tissue Q10 levels which were high significantly compared to the other groups.

The mean values of plasma glucose and glycated Hb in diabetic rats were significantly high compared to control group, after CoQ10 supplementation this values were low significantly compared to diabetic group, but they were still significantly high compared to control group. The mean values of total cholesterol and triglyceride were significantly high in diabetic rats compared to control group, after CoQ10 supplementation these values were low significantly compared to diabetic rats, but they were still significantly high compared to control and CoQ10 treated groups. In CoQ10 treated diabetic group, the mean value of tissue MDA was significantly high compared to control and CoQ10 treated groups, significant low value was observed in diabetic rats CoQ10 treated group compared with diabetic group indicating the reduction of oxidative stress.

As regard AOPP, 8 OH guanosin and percent of DNA damage, their mean values were high significantly in diabetic rats compared to control and CoQ10 treated groups, significant low values were observed in CoQ10 treated diabetic group compared with diabetic group. Significant low plasma and tissue CoQ10 mean levels were observed in diabetic rats compared to control and CoQ10 treated groups, significant high levels of them in Q10 treated diabetic group compared to diabetic group.

The recorded values of NOx in control and CoQ10 treated groups were significantly high compared to diabetic group. Also it was significantly in CoQ10 treated diabetic group compared to diabetic group. (**Table 1**).

The comet analysis showed that the control group had the most compact DNA and maintained the circular form of a normal nucleus, with no evidence of comet formation (**Fig. 1**). In contrast, cells from diabetic group exhibited different degrees of a distorted appearance (**Fig. 2**), CoQ10 treated diabetic group showed distorted cells less than diabetic group (**Fig. 3**).

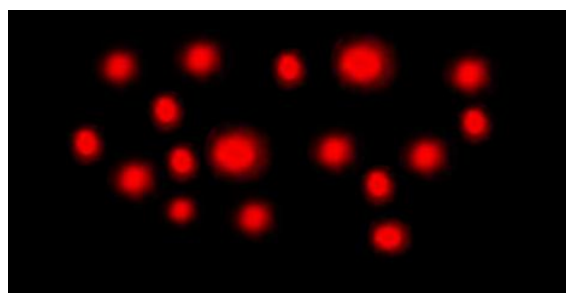


Fig. 1: Percent of DNA damage in control group.

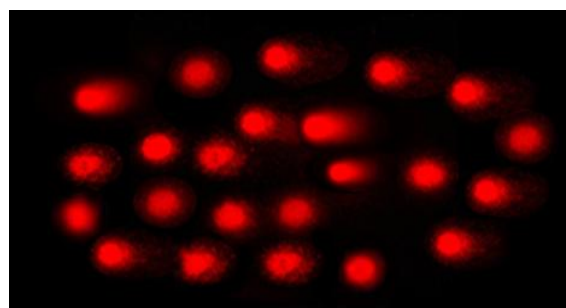


Fig. 2: Percent of DNA damage in diabetic group.

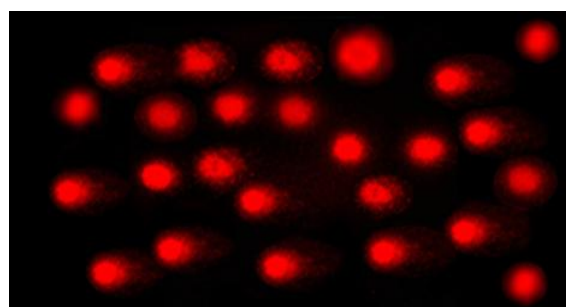


Fig. 3: Percent of DNA damage in CoQ10 treated diabetic group.

**Table. 1:** Mean  $\pm$  SD of the investigated parameters in the different studied groups.

Parameter	Control group	Q10 treated group	Diabetic group	Q10 treated diabetic group
FBS mg/dl	90 $\pm$ 11.24	95.5 $\pm$ 8.99 <sup>b</sup>	341 $\pm$ 67.52 <sup>a</sup>	171 $\pm$ 23.77 <sup>a, b, c</sup>
HbA1c (%)	5.4 $\pm$ 0.350	5.26 $\pm$ 0.38 <sup>b</sup>	9.27 $\pm$ 1.26 <sup>a</sup>	7.06 $\pm$ 0.40 <sup>a, b, c</sup>
T-Cholesterol (mg/dl)	91.7 $\pm$ 18.31	103 $\pm$ 19.09 <sup>b</sup>	190.6 $\pm$ 7.93 <sup>a</sup>	97.16 $\pm$ 22.56 <sup>b</sup>
Triglyceride (mg/dl)	92.2 $\pm$ 13.24	97 $\pm$ 29.81 <sup>b</sup>	193 $\pm$ 11.37 <sup>a</sup>	78.5 $\pm$ 30.25 <sup>b</sup>
Serum HDL-C (mg/dl)	49.8 $\pm$ 1.3	47.8 $\pm$ 1.5 <sup>b</sup>	37.4 $\pm$ 0.90 <sup>a</sup>	45.3 $\pm$ 0.5 <sup>b</sup>
Serum LDL-C (mg/dl)	56.5 $\pm$ 0.81	55.7 $\pm$ 0.51 <sup>b</sup>	121.3 $\pm$ 0.84 <sup>a</sup>	77.5 $\pm$ 0.54 <sup>b</sup>
serum Q10 ( $\mu$ g/ $\mu$ L)	0.634 $\pm$ 0.035	1.887 $\pm$ 0.06 <sup>a, b</sup>	0.312 $\pm$ 0.023 <sup>a</sup>	0.695 $\pm$ 0.148 <sup>b, c</sup>
Tissue Q10 ( $\mu$ g/g tissue)	0.0454 $\pm$ 0.008	0.0882 $\pm$ 0.014 <sup>a, b</sup>	0.019 $\pm$ 0.004 <sup>a</sup>	0.050 $\pm$ 0.008 <sup>b, c</sup>
Tissue MDA (nm/ml)	189.4 $\pm$ 42.09	186.6 $\pm$ 36.59 <sup>b</sup>	413.5 $\pm$ 90.51 <sup>a</sup>	290.7 $\pm$ 32.2 <sup>b</sup>
AOPP ( $\mu$ mol/l)	12.09 $\pm$ 1.61	11.48 $\pm$ 0.62 <sup>b</sup>	14.11 $\pm$ 1.16 <sup>a</sup>	12.17 $\pm$ 0.95 <sup>b</sup>
8 OHG (nmol/ml)	16.24 $\pm$ 16.77	15.97 $\pm$ 1.66 <sup>b</sup>	31.94 $\pm$ 8.42 <sup>a</sup>	16.29 $\pm$ 2.02 <sup>b</sup>
DNA damage (%)	17.66 $\pm$ 3.65	17.93 $\pm$ 7.75 <sup>b</sup>	37 $\pm$ 5.09 <sup>a</sup>	28.66 $\pm$ 3.88 <sup>a, b, c</sup>
Nitric oxide ( $\mu$ mol/ml)	155.59 $\pm$ 34.70	146.62 $\pm$ 33.47 <sup>b</sup>	80.34 $\pm$ 35.74 <sup>a</sup>	113.23 $\pm$ 19.28 <sup>a, b, c</sup>

Data are expressed as mean  $\pm$  SD. p < or = 0.05: significant

a: significance from control group

b: significance from diabetic group

c: significance from Q10

## DISCUSSION

The observation that oxidative stress is increased in diabetes has generated the notion that antioxidants and other regulators of oxidative stress may protect against diabetic complications. The present study was undertaken to assess the possible protective role of exogenous supplementation of CoQ10 by examining different biochemical parameters of oxidative damage in diabetic rats. In the current study fasting blood sugar as well as glycaemic control monitored by measurement of HbA1c was significantly low in CoQ10 treated diabetic group compared to diabetic group, this may be due to improvement of insulin secretion (Mezawa *et al.*, 2012). Quiles *et al.*, 2005 reported improvement of glycemic control in diabetic rats after a low dosage of coenzyme Q10 due to a decrease in oxidative stress. Similar results were previously shown by Shargorodsky *et al.*, (2010) who reported improved glycemic control with a modest decrement in glycated hemoglobin levels after Co Q10 supplementation in diabetic patients. As regard lipid profile the results revealed significant low levels of cholesterol, triglyceride, LDL-cholesterol and significantly increase HDL-cholesterol in Co Q10 treated diabetic group, this may be due to increased levels of ubiquinol-10 (reduced form of CoQ10) within circulating lipoproteins and increased resistance of human low-density lipoproteins to the initiation of lipid peroxidation, moreover, to its direct anti-atherogenic effect (Littarru and Tiano 2007). Similar results were previously shown by Al-Thakafy *et al.* (2004) who reported that daily supplementation with CoQ10 (10 mg/kg body weight, one month) to streptozotocin-induced diabetic rats resulted in significant decrease in triglyceride and cholesterol. Also Özdoğan *et al.*, 2012 reported that Q10 supplementation corrected the dyslipidemia in fructose fed rats as a model of dietary-induced insulin resistance. Lipid peroxidation, which is mediated by free radicals, is considered to be the major mechanism of cell membrane destruction and cell damage. Recent studies showed that MDA is an important marker of lipid peroxidation and is correlated with oxidative stress (Mogadam *et al.*, 2008). In agreement with the study by Sena *et al.* (2008), we observed significant low value of tissue MDA Co Q10 treated diabetic group, suggesting that this compound may diminish ROS concentration. Moreover low MDA levels in the plasma after administration of CoQ10 were also noted by Naudi *et al.* (2012), they reported that CoQ10 may recycles and regenerates of other antioxidants like vitamin E which prevents lipid peroxidation. Oxidative DNA damage is usually evaluated by measuring the oxidized base 8-hydroxy-2-deoxy-guanosine (8-OHdG) in white blood cells or urine (Hinokio *et al.*, 1999) or by using a comet assay in white blood cells (King and Loeken 2004). 8-OHdG, a result of DNA base modification produced by the oxidation of deoxyguanosine, is considered as the most sensitive and useful marker of oxidative DNA damage (Tuzgen *et al.*, 2007). It is also considered to be a measurable risk factor for co-morbid illnesses like atherosclerosis and diabetes (Wu *et al.*, 2004). It can be generated by several different ROS, including hydroxyl radicals,

singlet oxygen, peroxy radicals and peroxyxynitrite, which are able to produce other modifications to the DNA bases as well as strand breaks and various other DNA damage (Whiteman *et al.*, 2002)

In the present study, a significant high level of 8-OHdG was recorded in diabetic group compared with control group suggesting the involvement of hyperglycemia in oxidative DNA damage (Simone *et al.*, 2008), in Co Q10 treated diabetic group level of 8-OHdG was significantly low compared with diabetic group due to improvement of hyperglycemic state.

As regard our results from the comet assay, high percent of DNA damage in diabetic group was observed that may be due to oxidative stress, our results are in agreement with those showing the increased extent of DNA damage in the blood cells from diabetic patients (Blasiak *et al.*, 2004). This percent was significantly low in Co Q10 treated diabetic group, which may be due to a direct effect of Co Q10 on DNA protection and/or to improvement of mitochondrial function, thus leading to decreased free radical insult on DNA (Tiano *et al.*, 2011) or due to improvement of insulin secretion by Co Q10 supplementation which regulates the synthesis of the DNA repair enzyme xeroderma pigmentosum complementation group D (XPD) which playing a pivotal role in nucleotide excision repair (Merkel *et al.*, 2003). Advanced oxidation protein products were described by Witko-Sarsat *et al.* (1996) for the first time. They are formed during oxidative stress by the action of chlorinated oxidants, mainly hypochlorous acid and chloramines (produced by myeloperoxidase in activated neutrophils). Concentration of AOPP is significantly higher in diabetic rats comparing to control group. Changes in AOPP level are connected with poor glycemic control, dyslipidemia, and diabetic complications (Piwowar, 2010), significant low level of AOPP level in Co Q10 treated diabetic group perhaps due to the antioxidant properties of Co Q10 in scavenging free radicals leading to modulating the oxidative stress and detoxifying enzyme system (Niklowitz *et al.*, 2007) According to our results serum NOx concentration was significantly low in diabetic group compared to control and Co Q10 treated groups. These results are in agreement with finding of Suresh and Undurti (2006) who reported that diabetes mellitus is associated with decreased nitric oxide production from endothelial cells, as high glucose level exacerbates aldose reductase activity leading to depletion of the NADPH required for the generation of nitric oxide from L-arginine by nitric oxide synthase. Also Kasznick *et al.* (2012) reported that oxidative stress due to chronic high glucose concentration induced the decrease of NO level and impaired its bioavailability in diabetic patients. In Co Q10 treated diabetic group NOx concentration was significantly high compared to diabetic group as CoQ10 may recoupling endothelial nitric oxide synthase and modulating NO-related signaling (Tsai *et al.*, 2012).

## CONCLUSION

Coenzyme Q 10 seems to be a beneficial compound in protecting the diabetic rats against oxidative stress, so it may be

prudent to suggest that this compound should be further investigated as a potential adjuvant therapy for diabetic patients.

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## DISCLOSURE STATEMENT

All authors confirm that no competing financial, personal, political, or academic interests exist in connection with this article.

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