

# Taurine Modulates Hyperglycemia-Mediated Oxidative Stress and Protects Hepatocytes in Experimental Diabetes

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**Abstract:** *The present study was conducted to investigate the beneficial effects of taurine (TAU) on glucose and lipid metabolism and its positive roles in the correction of oxidative stress diabetes-related complications in STZ diabetic rats. Diabetic rats showed significant ( $P < 0.05$ ) increase in the levels of glucose, HbA1c, AST, ALT, LDH, liver and kidney weights, urea, uric acid, creatinine and significant decrease in the levels of body and pancreas weights, insulin, pancreatic amylase, hexokinase, liver and muscle glycogen, total protein, albumin, antioxidant enzymes and HDL-C. Also, higher levels of cholesterol, TG, total lipids, LDL-C and MDA were noticed in diabetic rats. The taurine administration (50 mg/kg) showed antihyperglycemic effect as indicated by reduced glucose levels, HbA1c and improved insulin level and carbohydrate hydrolyzing enzymes. In addition, taurine supplementation normalized liver function and inhibited lipid profile alterations while, kidney weight, urea, creatinine, uric acid, total protein and albumin levels were partially improved. The obtained results revealed that taurine exhibited an inhibitory effect on oxidative stress indices (MDA) and partially improved antioxidant levels. Taurine could have potential as a pharmaceutical drug for diabetes mellitus (DM). Additional study is needed to investigate whether taurine has the same beneficial effects in human diabetic patients.*

**Keywords:** Diabetes, taurine, glycosylated hemoglobin, insulin, rats.

## 1. Introduction

Diabetes is a complex, chronic illness that requires consistent medical care and treatment to help control blood sugar levels and prevent acute or long-term complications of the disease, such as kidney failure and amputations [1]. It is growing with a fast rate and is likely to affect 340 million people, which is expected to reach 552 million in 2030 [2], consequently, diabetes presents a major challenge to healthcare systems around the world.

Concerning the terrible increase in the worldwide diabetic population, there is a need for new therapies that are more effective with minimum adverse effects [3]. Many oral antihyperglycemic agents have significant side effects and some are ineffective in chronic diabetic patients [4]. In spite of the introduction of hypoglycemic drugs, diabetes and related complications continue to be a major medical problem [5]. Thus, there is an increasing need of new natural antihyperglycemic products especially nutraceuticals with less side effects, safe, and high antihyperglycemic potential.

Taurine (2-aminoethylsulphonic acid, TAU) is a non-protein amino acid present in nearly all animal tissues and the most plentiful free intracellular amino acid in human cells [6]. The main source of taurine *in vivo* is dietary intake and biosynthesis. Endogenous production of taurine is insufficient, so that it needs to be provided through the diet. Taurine, the end product of L-cysteine metabolism has shown capacity in protecting from various free radicals associated with pathological conditions. It exerts anti-inflammatory, neuromodulator [7], immunomodulator [8] and it has been used as a treatment for alcoholism [9]. In addition, this conditionally essential amino acid is also

an authenticated potent scavenger of the hydroxyl radical, a membrane stabilizing agent and as a detoxifying agent [10]. Taurine is now thought to play a more important role in human nutrition, and dietary intake of taurine has been linked to several beneficial health outcomes in various diseases and medical conditions [11].

In the present study, we have evaluated taurine antidiabetic activity and its positive roles in the correction of oxidative stress diabetes-related complications in STZ diabetic rats.

## 2. Materials and Methods

### 2.1. Animals

Male *Wistar* rats (200-250 g), were obtained from the Faculty of Medicine, Alexandria University, Egypt. The animals were held in an air conditioned room ( $22 \pm 3^\circ\text{C}$ ) with  $55 \pm 5\%$  humidity and a 12-hour light/dark cycle. They were fed with a standard diet and had free access to water. The local committee approved the design of the experiments and the protocols were carried out according to the guidelines of the National Institutes of Health (NIH).

### 2.2. Chemicals

Streptozotocin (STZ) and taurine (TAU) were purchased from Sigma-Aldrich Chemical Company (St. Louis, MO, USA). All other chemicals and reagents used were of analytical grade.

### 2.3. Induction of Diabetes:

Diabetes was induced by administration of a single intraperitoneal injection of 40 mg/kg body weight STZ which was prepared freshly. Three days after administration of STZ,

serum glucose levels were determined. Only rats with fasting blood glucose over 250 mg/dl [13] were considered diabetic and included in the experiments.

#### 2.4. Experimental Design

40 male rats were randomly divided into four groups (10 rats/group) as follows:

- Group 1:** Animals of this group were injected with 0.1ml of citrate buffer (pH: 4.5).
- Group 2:** Animals of this group were injected intraperitoneally with TAU at dose 50 mg/kg body weight for 15 days [14].
- Group 3:** Animals of this group were injected intraperitoneally with STZ at single dose 40 mg/kg body weight [15].
- Group 4:** Animals of this group were injected intraperitoneally with STZ at a single dose (40 mg/kg body weight) and after 3 days they were injected with TAU at a dose (50 mg/kg body weight) for 15 days.

At the end of experiment body, liver, kidney and pancreas weights were recorded.

#### 2.5. Preparation of Plasma

The heparinized blood samples were centrifuged at 3000 g for 15 min. Plasma was separated and then stored at -20 °C until biochemical analysis.

#### 2.6. Preparation of Liver and Pancreas Homogenates:

Whole tissues of the liver and pancreas were obtained by dissection, cleaned from adhering matters, washed with physiological saline. Then a portion of the liver and pancreas tissues from each rat was minced and homogenized in 5-10 ml cold buffer (i.e. 50 mM potassium phosphate, pH 7.4, 1mM ethylene diamine tetracetic acid, EDTA). Homogenates were centrifuged at 10,000×g for - 20 minutes at 4 °C and the clear supernatants were separated for antioxidant determination and lipid peroxidation.

#### 2.7. Biochemical Studies

Glucose level was measured as reported by Trinder [16] method. Glycosylated hemoglobin (HbA1c) was estimated by fast ion – exchange resin separation method [17]. Insulin, pancreatic amylase and hexokinase were determined according to the methods of Finlay and Dillard [18], Pulse and Schmidt [19] and Gubern et al. [20], respectively. Liver and muscle glycogen contents were determined by the method of Huijing [21]. Enzymatic activities of aspartate transaminase (AST), alanine transaminase (ALT) and lactate dehydrogenase (LDH) were determined according to Tietz [22] and Henry (1974) [23] methods. Total protein was determined by Gornall et al. [24] method. Determination of total cholesterol, low density lipoprotein (LDL) and high density lipoprotein (HDL) were estimated by the methods of Allain et al. [25] and Burstein et al. [26]. Triglycerides and total lipids were determined according to Wahlefeld and Bergmeyer [27] and Frings et al. (28) methods, respectively. Urea,

creatinine and uric acid were estimated by using the method of Newman and Price [29]. Pancreas and liver lipid peroxidation end products, MDA, were measured according to Ohkawa et al. [30] method. Also, the levels of glutathione (GSH) [31] and the activities of the antioxidant enzymes, including superoxide dismutase (SOD) [32], the catalase enzyme (CAT) [323] and glutathione peroxidase (GPx) [34] were assayed in liver and pancreas homogenates.

#### 2.8. Data and Statistical Analysis

Data were expressed as mean ± standard error. The data were analyzed using SPSS Statistical Package Version 19 (Chicago, IL, USA). Statistical comparisons between all groups were performed by using ANOVA-1. The significant differences were considered at P<0.05.

### 3. Results

#### 3.1. Effect of taurine on the body, liver, kidney and pancreas weights in STZ induced diabetic rats:

The body weight of diabetic rats was significantly decreased from basal value of the control group. With respect to the liver and kidney weight changes, significant increase was observed in STZ treated rats in comparison with the control one. On the other hand, pancreas weight was decreased in the STZ group as compared with the control group. The TAU supplementation ameliorated these changes as compared to the STZ group (Table 1).

**Table 1:** Effect of taurine supplementation on body, liver, kidney and pancreas weights in STZ induced diabetic rats.

Parameters	Experimental groups			
	Control	TAU	STZ	TAU+STZ
Body weight (g)	203.00±15.556	210.00±5.944	172.60±22.130 <sup>a</sup>	200.25±10.210 <sup>b</sup>
Liver weight (g)	6.110±0.735	6.042±0.695	7.630±1.506 <sup>a</sup>	6.01±1.712 <sup>b</sup>
Kidney weight (g)	0.619±0.127	0.614±0.175	0.868±0.173 <sup>a</sup>	0.703±0.124 <sup>ab</sup>
Pancreas weight (g)	0.422±0.064	0.423±0.061	0.319±0.097 <sup>a</sup>	0.425±0.067 <sup>b</sup>

-Values represent the mean ± SE of 10 individual rats.  
 -a-means significantly different from the control group.  
 -b-means significantly different from the streptozotocin treated group.  
 -P>0.05.

#### 3.2. Effect of taurine on serum glucose, insulin, HbA1c, α-amylase, hexokinase and glycogen in STZ-diabetic rats

Injection of male rats with STZ induced a significant increase in glucose and HbA1c levels. The administration of TAU resulted in a significant reduction of glucose and HbA1c levels as compared to STZ treated group. STZ administration was associated with a highly significant decrease in insulin, α-amylase and hexokinase levels as compared to the control group. Administration of TAU improved the insulin, α-amylase and hexokinase levels in comparison with the STZ group (Table 2). Also, supplementation of TAU improved the decreased liver and kidney glycogen in STZ group.

**Table 2:** Effect of taurine supplementation on serum glucose, insulin, HbA1c,  $\alpha$ -amylase, hexokinase and glycogen in STZ-diabetic rats

Parameters	Experimental groups			
	Control	TAU	STZ	TAU+STZ
Glucose (mg/dl)	89.200 ± 9.935	90.000 ± 4.546	321.500 ± 6.520 <sup>a</sup>	94.600 ± 5.588 <sup>b</sup>
Insulin (mIU/ml)	2.920 ± 0.879	2.680 ± 0.936	1.25 ± 0.918 <sup>a</sup>	1.860 ± 0.783 <sup>b</sup>
HbA1c (%)	5.180 ± 0.766	5.140 ± 1.197	9.125 ± 0.793 <sup>a</sup>	7.260 ± 1.443 <sup>b</sup>
Amylase (U/L)	8.280 ± 2.184	8.940 ± 2.721	4.100 ± 2.974 <sup>a</sup>	6.880 ± 2.660 <sup>b</sup>
Hexokinase (U/L)	11.880 ± 2.875	10.60 ± 3.52	4.375 ± 1.621 <sup>a</sup>	9.180 ± 1.911 <sup>b</sup>
Liver glycogen (mg/g tissue)	215.80 ± 6.1757	200.00 ± 6.4884	68.60 ± 7.0894 <sup>a</sup>	144.40 ± 11.6086 <sup>b</sup>
Kidney glycogen (mg/g tissue)	156.20 ± 10.7256	152.00 ± 4.7497	73.60 ± 7.3864 <sup>a</sup>	122.00 ± 7.1861 <sup>b</sup>

-Values represent the mean ± SE of 10 individual rats.  
 -a-means significantly different from the control group.  
 -b-means significantly different from the streptozotocin treated group.  
 -P>0.05

**3.3. Effect of taurine on AST, ALT, LDH, total protein and albumin levels in STZ-diabetic rats**

AST, ALT and LDH levels were significantly increased in STZ treated rats as compared to the control value. The co-administration of TAU with STZ resulted in significant reduction in liver function enzymes as compared to STZ treated group. Concentrations of total protein and albumin were significantly decreased after STZ injection compared to the control. Administration of TAU followed STZ injection for 15 days improved the total protein and albumin levels (Table 3).

**Table 3:** Effect of taurine supplementation on AST, ALT, LDH, total protein and albumin levels in STZ-diabetic rats.

Parameters	Experimental groups			
	Control	TAU	STZ	TAU+STZ
AST (U/dl)	61.600 ± 9.072	66.200 ± 19.854	156.750 ± 17.233 <sup>a</sup>	96.600 ± 16.003 <sup>b</sup>
ALT (U/dl)	32.800 ± 8.643	31.200 ± 15.595	88.250 ± 9.811 <sup>a</sup>	55.800 ± 15.287 <sup>b</sup>
LDH (U/dl)	116.400 ± 28.059	113.000 ± 29.155	255.500 ± 18.141 <sup>a</sup>	191.800 ± 17.167 <sup>b</sup>
Total protein (g/dl)	6.900 ± 0.778	6.720 ± 0.581	4.925 ± 0.222 <sup>a</sup>	6.660 ± 0.647 <sup>b</sup>
Albumin (g/dl)	3.660 ± 0.541	3.400 ± 0.539	2.225 ± 0.602 <sup>a</sup>	3.120 ± 0.952 <sup>b</sup>

-Values represent the mean ± SE of 10 individual rats.  
 -a-means significantly different from the control group.  
 -b-means significantly different from the streptozotocin treated group.  
 -P>0.05

**3.4 Effect of taurine on serum lipid profile in STZ-diabetic rats**

STZ administration was associated with a significant increase in lipid profile [Total cholesterol (TC), total lipid (TL), triglycerides (TG), low density lipoproteins (LDL-C)] in the plasma except high density lipoprotein (HDL-C) as shown in table 5. TAU treatment in combination with STZ improved the hyperlipidemia of diabetic rats. Also, TAU treatment in combination with STZ improved the decrease in HDL (Table 4).

**Table 4:** Effect of taurine supplementation on serum lipid profile in STZ-diabetic rats.

Parameters	Experimental groups			
	Control	TAU	STZ	TAU+STZ
Total Cholesterol (mg/dl)	133.60 ± 23.298	129.60 ± 32.921	266.00 ± 58.839 <sup>a</sup>	174.40 ± 19.715 <sup>b</sup>
Total lipid (mg/dl)	457.00 ± 54.240	464.20 ± 86.459	1045.00 ± 224.767 <sup>a</sup>	631.40 ± 74.36 <sup>b</sup>
Triglyceride (mg/dl)	82.40 ± 15.678	84.00 ± 14.000	234.00 ± 67.735 <sup>a</sup>	124.00 ± 25.49 <sup>b</sup>
HDL-C (mg/dl)	50.80 ± 8.349	49.80 ± 4.382	31.25 ± 7.932 <sup>a</sup>	44.40 ± 10.286 <sup>b</sup>
LDL-C (mg/dl)	66.32 ± 21.180	63.00 ± 31.664	187.95 ± 48.638 <sup>a</sup>	106.00 ± 12.033 <sup>b</sup>

-Values represent the mean ± SE of 10 individual rats.  
 -a-means significantly different from the control group.  
 -b-means significantly different from the streptozotocin treated groups.  
 -P>0.05

**3.5 Effect of taurine on urea, creatinine and uric acid levels in STZ-diabetic rats**

STZ administration was associated with a highly significant increase in urea, creatinine and uric acid levels as shown in table 6. Injection of TAU following STZ administration partially improved these elevations since there was a significant difference between values of this group and the control group (Table 5).

**Table 5:** Effect of taurine supplementation on urea, creatinine and uric acid levels in STZ-diabetic rats.

Parameters	Experimental groups			
	Control	TAU	STZ	TAU+STZ
Urea (mg/dl)	28.000 ± 6.892	28.400 ± 7.569	38.250 ± 8.921 <sup>a</sup>	33.200 ± 6.791 <sup>ab</sup>
Creatinine (mg/dl)	0.498 ± 0.151	0.444 ± 0.129	1.300 ± 0.392 <sup>a</sup>	0.704 ± 0.142 <sup>ab</sup>
Uric acid (mg/dl)	1.500 ± 0.604	1.400 ± 0.604	4.000 ± 2.309 <sup>a</sup>	2.340 ± 0.627 <sup>ab</sup>

-Values represent the mean ± SE of 10 individual rats.  
 -a-means significantly different from the control group.  
 -b-means significantly different from the streptozotocin treated group.  
 -P>0.05

**3.6 Effect of taurine on malondialdehyde (MDA) in streptozotocin-diabetic rats**

Administration of TAU together with STZ partially improved the increased levels of MDA in liver and pancreas as compared to the untreated group (Table 6).

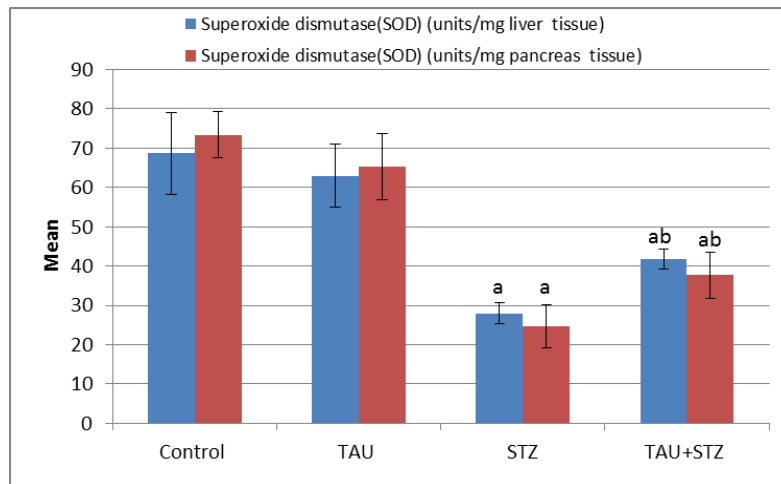
**Table 6:** Effect of taurine supplementation on malondialdehyde (MDA) in streptozotocin-diabetic rats.

Parameters	Experimental groups			
	Control	TAU	STZ	TAU+STZ
MDA liver (nmol/mg)	15.000 ±3.606	16.000 ±6.000	47.000 ±11.136 <sup>a</sup>	32.333 ±7.506 <sup>ab</sup>
MDA pancreas (nmol/mg)	15.333 ±5.132	15.333 ±2.887	67.000 ±9.165 <sup>a</sup>	39.333 ±8.505 <sup>ab</sup>

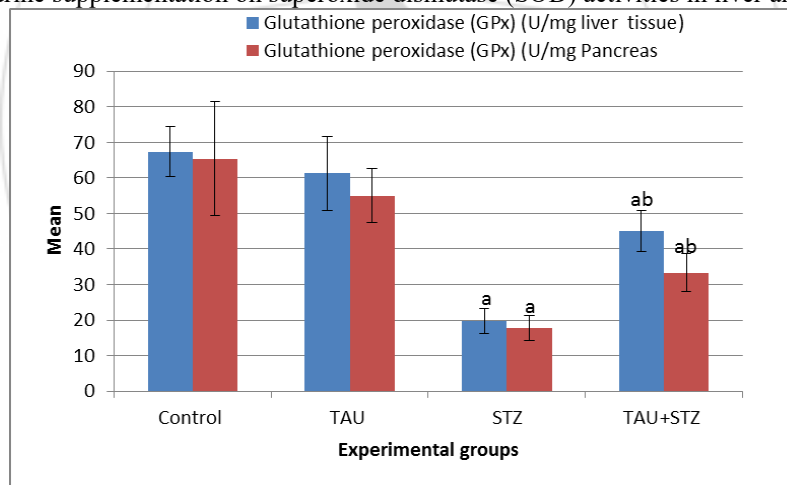
-Values represent the mean ± SE of 10 individual rats.  
 -a-means significantly different from the control group.  
 -b-means significantly different from the streptozotocin treated groups.  
 -P>0.05

### 3.7 Effect of taurine on some antioxidant enzymes activities in liver and pancreas homogenates

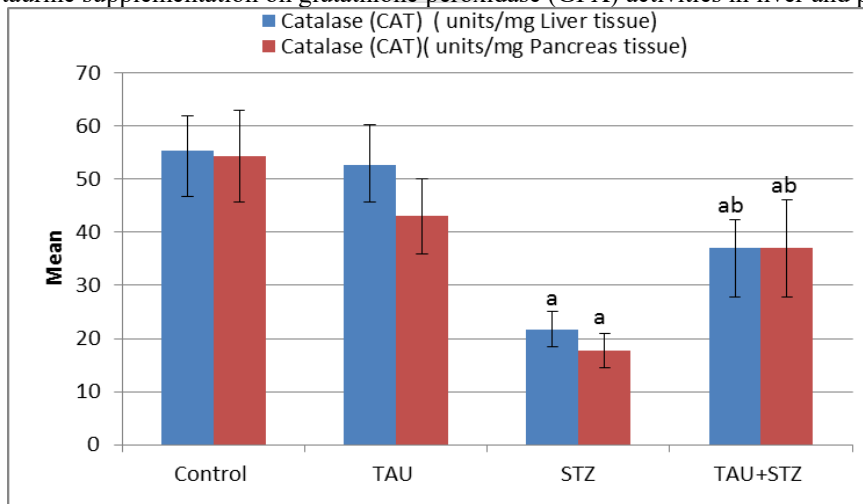
A significant decrease was observed in liver and pancreas antioxidant enzyme levels (SOD, GPX and CAT) in rats treated with STZ comparing with the control group. TAU treatment in combination with STZ partially improved these decreased levels as compared with untreated diabetic rats (Figures 1, 2 and 3).



**Figure 1:** Effect of taurine supplementation on superoxide dismutase (SOD) activities in liver and pancreas homogenates



**Figure 2:** Effect of taurine supplementation on glutathione peroxidase (GPX) activities in liver and pancreas homogenates



**Figure 3:** Effect of taurine supplementation on Catalase (CAT) activities in liver and pancreas homogenates

### 3.8 Effect of taurine supplementation on non enzymatic antioxidant in liver and pancreas:

GSH of liver and pancreas in STZ treated group were decreased as compared with the control group. Administration of TAU together with STZ partially improved these decreased levels as compared to STZ group (Figure 4).

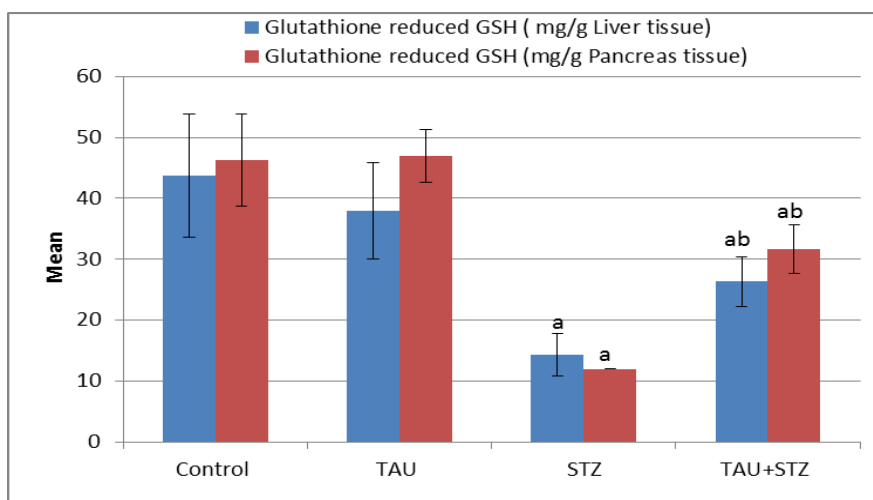


Figure 4: Effect of taurine supplementation on glutathione reduced (GSH) in liver and pancreas homogenates

## 4. Discussion

The reduction in the body weight of the diabetic animals has been linked to degradation of structural proteins and muscle wasting due to unavailability of carbohydrate for utilization as an energy source. The body weight loss came accordance with the finding of Oyedemi et al. [35]. Lee et al. [36] found that the animal treated with STZ appeared ill-looking with the loss of their body weights.

The increase in the kidney weight may be due the cellular autophagy in the cells of proximal and distal convoluted tubules that due to the hypertrophic growth of kidney cortex [37] or may be due to tubulointerstitial fibrosis and fibronectin in diabetic rats [38]. The increment of liver weight may be due to increase triglyceride accumulation leading to enlarged liver which could be due to the increased influx of fatty acids into the liver induced by hypoinsulinemia and the low capacity of excretion of lipoprotein secretion from the liver [37]. The decrease in the pancreas weight agrees with the results of Heidari et al. [39] who stated that the loss of pancreas weight may be due to destruction of pancreatic islets and insulin-producing cells. The amelioration effect of taurine on body, liver, kidney and pancreas weights suggesting that TAU exhibits a protective effect against cellular- stress as reported by Ito et al. [12].

The mechanism by which STZ brings about its diabetic state included selective destruction of pancreatic insulin secreting  $\beta$ -cells, which make cells less active, leading to poor glucose utilization by tissues. The present hyperglycemia was found consistent with the results obtained by Anusuya et al. [40]. Glycosylated hemoglobin (HbA1c) is useful in the demonstration of glycemic control in patients with DM [41]. HbA1c level was found to be increased in the untreated diabetic rats [42]. It is produced by non-enzymatic condensation of glucose molecules with free amino acid on the globin component of hemoglobin [43].

It seemed that the initial drop in the  $\alpha$ -amylase activity may be interpreted by the impaired pancreatic exocrine secretion due to a decrease in the insulin stimulatory action [44]. The present finding came accordance with Burski et al. [45] who stated that  $\alpha$ -amylase activity in the rabbit serum, within the first three weeks of diabetes, was dropped to the levels below the half of the values noted in healthy controls. Hexokinase plays a central role in the maintenance of glucose homeostasis. The hexokinase activity was found to be decreased in diabetic rats which may be due to insulin deficiency [46]. The observed decrease in hepatic and muscle glycogen may be due to insufficient insulin and inactivation of the glycogen synthetase system in the diabetic state [47].

Taurine exerts hypoglycemic effects by regulating the expression of genes required for the glucose-stimulated insulin secretion and enhancing insulin action [48], as well as by facilitating the interaction of insulin with its receptor [9]. On the other hand, TAU enhances glycogenesis, glycolysis and glucose oxidation [49]. Taurine has also demonstrated to have hypoglycemic effects producing a decrease in the concentrations of glucose and fructosamine as well as an increase in the contents of insulin, C-peptide, and glycogen in the liver [50]. Kim et al. [51] reported that taurine ameliorated hyperglycemia by improving insulin sensitivity in OLETF rats with long-term diabetes. Decreased HbA1c levels in the TAU treated diabetic rats could be due to an improvement in insulin secretion from the remnant pancreatic  $\beta$ -cells in diabetic rats, consequently, resulting in improvement in glycemic control [47].

The present elevations of AST, ALT and LDH observed in diabetic rats agree with Kumarappan et al. [52]. The increase in AST and ALT may be due to leakage of these enzymes from the liver cytosol into the blood stream and/or change in the permeability of liver cell membranes take place [53]. Ahn et al. [54] suggested that serum ALT concentrations were independently associated with type 2 diabetes in both sexes. They stated that increased AST, ALT, and GGT levels reflect

an excess deposit of fat in the liver, a condition known as non-alcoholic fatty liver disease (NAFLD).

The present study disclosed a significant decrease in total protein concentration as a result of insulin deficiency which leads to increased catabolism of protein. The increased rate of proteolysis leads to elevated concentration of amino acids in plasma that serve as precursors for hepatic and renal glyconeogenesis, which further contributes to the hyperglycemia seen in DM [55]. Also, this decrease in total protein might be due to microproteinuria which was an important clinical marker of diabetic nephropathy. The present result coincided with the findings of Daisy et al. [56].

The reversal of ALT and AST activities in TAU treated diabetic rats towards near normalcy indicate the liver protective nature. These results were in agreement with Turner and Wass [57] who reported marked reductions in proteinuria in STZ-induced diabetic rats with decreased renal lipid peroxidation after oral supplementation of taurine. Zhang et al. [58] reported that TAU improved hepatic enzymes in hepatotoxicity.

Hyperlipidemia is a relatively common problem in patients with poorly controlled diabetes mellitus [59] and coexists with hyperglycemia and is characterized by increased levels of cholesterol, triglycerides and phospholipids, and also changes in lipoproteins. The diabetic hyperlipidemia was attributed to the disturbance of hormonal regulation of glucose metabolism. The present hyperlipidemia was in line way with a previous investigation of Bagri et al. [60].

The hypolipidemic effect of TAU was partly due to the inhibition of cholesterol absorption in the intestine or increasing the conversion of cholesterol to bile acid. Furthermore, it has been suggested that TAU may be responsible for the increase of HDL or end balance of the serum lipoprotein fractions containing cholesterol [61]. Moreover, it is likely possible that drinking TAU increases serum cholesterol clearance and decreases hepatic TC level in high-fat/cholesterol dietary hamsters, which may be up due to regulations of the LDL receptor, thus increasing fecal TC and bile acids output [62]. Yang et al. [63] stated that TAU could alleviate blood lipids and hepatic damage induced by a high-fat/cholesterol-dietary diet. The data of Saleh [43] indicated that the treatment of diabetic rats with TAU induced decrease in lipid profile except HDL-cholesterol.

The increase in urea and creatinine levels, recorded in STZ-diabetic rats, may be due to increase protein catabolism, glomerular injury and renal dysfunction. This finding was found in agreement with the results of Prangthip et al. [64]. Taurine administration prevented the occurrence and development of diabetic nephropathy by decreasing blood glucose, improving lipid metabolism and glomerular basement membrane metabolism [65]. Taurine in the drinking water of diabetic rats helped them recover from kidney damage [60]. The effects of taurine on diabetic nephropathy showed the results of improvements in oxidative stress [66].

The present study revealed that the elevation in MDA level might be a reflection of a decrease in enzymatic and non-enzymatic antioxidants of defense systems. Previous studies have reported that there was an increase in lipid peroxidation in liver, kidney, brain, heart [67], pancreas [60], and erythrocytes [68] of diabetic rats. Patel et al. [69] suggested this elevation in hepatic MDA level might be due to high concentration of lipid, which was found in liver of diabetic rats, and resulted in the activation of NADPH dependent microsomal lipid peroxidation in liver.

The effects of long-term diabetes on the antioxidant enzymes in the rat liver have been reported. Selvan et al. [70] stated that hepatic SOD and CAT activities were decreased significantly in STZ-induced diabetic rats. Also, Chandramohan et al. [68] suggested that the decrease in the activities of hepatic SOD and CAT in diabetic rats may result in a number of deleterious effects due to the accumulation of superoxide anion radical and hydrogen peroxide. Furthermore, the decrease in the activity of CAT could result from inactivation by superoxide radical and glycation of the enzyme [60].

In the present work, the decreased activity of GPx in liver during diabetes mellitus may be attributed to the production of reactive oxygen species (ROS) such as superoxide ( $O_2^-$ ), hydrogen peroxide ( $H_2O_2$ ), and hydroxyl radical ( $OH$ ) [71]. Similarly, previous investigator indicated that the hepatic GSH-Px activity of STZ-induced diabetic rats decreased significantly as compared to the normal control group [72].

The reduction in GSH was consistent with El-Shenawy and Abdel-Nabi [73] who reported that the hepatic and pancreas GSH decreased significantly in alloxan-diabetic mice. Chakraborty and Das [74] and Veerapur et al. [75] mentioned that the concentration of GSH significantly decreased in the liver of STZ-diabetic rats, and this decrease represented an increase in the utilization due to the oxidative stress. Also, the decrease in GSH levels could probably be due to decreased synthesis or increased degradation of GSH by oxidative stress as reported by Saravanan and Ponmurugan [76]. A decrease in the level of GSH in the liver [77], plasma [78], cardiomyocyte [79] and pancreas [80] have been reported in diabetic rats.

The prevention of oxidative stress by taurine was also reported in alloxan-induced type 1 diabetic [81]. Interestingly, taurine supplementation for 2 days later of STZ injection, prolonged survival in diabetic rats [82]. This observation indicates that taurine may confer resistance against some stresses induced by hyperglycemia, which may associate with the beneficial role against the complications. Administration of taurine protected the tissue damage produced by the acute sublethal dose of  $\gamma$ -irradiation in rats by decreasing oxidative stress [83].

The benefits of the taurine amino acid appears to be due to its various actions on cellular functions while toxicity seems relatively low, further studies are important to fill the gaps between animals and humans.

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