Beneficial Role of Taurine on Biochemical Parameters of Diabetic Female Rats

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ABSTRACT
For studying the positive effects of taurine (TAU) on lipid and glucose metabolism. Moreover, the present paper examines the positive roles of glucose and lipid on the correction of oxidative stress diabetes-related complications in alloxan diabetic rats. To achieve the objective of study, 24 of female rats (Rattus norvegicus) have been used. The division of animals was done in 4 groups (6 each). Diabetes was enhanced by injected intraperitoneally with alloxan at a single dose in body weight; 125 mg/kg. Diabetic rats go through a specific rise (p ≤ 0.05) in the glucose levels, triglyceride, total cholesterol, very-low-density lipoprotein, low-density lipoprotein, and malondialdehyde and an important noticeable decrease in high-density lipoprotein, glutathione, and albumin. In addition, taurine supplementation caused a significant reduction in the glucose, total cholesterol, triglycerides, low-density lipoprotein, and very low-density lipoprotein levels. The obtained results revealed that taurine exhibited an inhibitory effect on oxidative stress indices (MDA) and improved antioxidant levels. Taurine could have potential as a pharmaceutical drug for diabetes mellitus (DM), and this invites further studies in this field.

Keywords: Antioxidants, Diabetes, Lipid profile, Malondialdehyde, Taurine.

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INTRODUCTION
Diabetes can be defined as a complex, chronic illness that needs consistent medical care and treatment to control blood sugar levels and prevent hard and unexpected or long-term complications of the disease.1 There is a rapid growth of this disease and can harm 340 million population; it is expected that the number of diabetes patients could reach 552 million in 2030.2 Therefore, diabetes indicates a real challenge to healthcare systems globally. An absolute reduction of the secretion of insulin is seen in type-1 diabetes, associated to the destruction of pancreatic β-cells. It is majorly inherited from the previous generations.3 Furthermore, a combination of resistance of insulin action and impaired secretion of insulin causes type 2 diabetes, and more than 90% of cases fall under this category.

As there is a rapid increase in the global diabetic population, new therapies are required for impactful yet less adverse effects. There are various oral antihyperglycemic agents that have beneficial side effects and some do not possess an effect on chronic diabetes.5 Despite introducing hypoglycemic drugs, diabetes and associated complications continue to be a complicated medical problem.6 So, there is an increasing need for new natural antihyperglycemic products, especially nutraceuticals with less side effects, safe, and high antihyperglycemic potential.

Taurine or 2-aminoethylsulfonic acid is a non-protein and non-essential amino acid. Its presence is important in the cases of diet, disease, and aging.7-8 Taurine is a vital acid in insulin immunity and sensitivity.9-10 Because of its benefits, it is considered as wonder molecule,11 the control on diabetes and its consequences. The results studies in animals concluded that having suitable taurine levels helps the control of diabetes. This can be by the reduction of blood glucose and restoring insulin sensitivity.12

In this paper, the anti-diabetic activity of taurine was evaluated. Moreover, a role in the correction of oxidative stress diabetes-related complications in alloxan diabetic rats was also assessed.

Materials and Methods
Animals
Female rats (190-200 g), were collected from the department of biology (animal house unit), college of Science, University of Thi-Qar, Iraq. An air-conditioned room was used by the animals (22 ± 3°C) with 12 hours light/dark cycle and 55 ± 5% humidity. The diet had free access to water and was standard.

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The local committee gave permission for the design of the experiments, and the protocols were conducted based on the guidelines of the National Institutes of Health (NIH).

**Chemicals**

Alloxan, taurine, trichloroacetic acid (TCA), thiobarbituric acid (TBA), paraphenylenediamine (PPD), azide sodium, and sodium carbonate anhydrate was purchased from BDH, England. Sodium phosphate acidic NaH₂PO₄, Sodium phosphate basic Na₂HPO₄ were purchased from FlukaGarnatie Switzerland).

**Diabetic Increase**

A single intraperitoneal injection of 125 mg/kg body weight alloxan-induced diabetes, which went through advanced preparation, seven days later, determination of serum glucose levels was done. The experiments included rats with fasting blood glucose over 250 mg/dL, and they were deemed.

**Experimental Design**

Four groups (6 rats/group) were used to divide twenty-four female rats as follows:

1. **Group 1**: Treatment was given to animals with distilled water for 15 days.
2. **Group 2**: Animals were injected intraperitoneally with alloxan at a single dose 125 mg/kg body weight.
3. **Group 3**: Intrapitoneal injections of taurine were given to animals at a dose of 100 mg/kg bodyweight for 15 days.
4. **Group 4**: Intraperitoneal injections were given to animals with alloxan at a single dose (125 mg/kg body weight) and taurine was injected at a dose (100 mg/kg body weight) after 7 days for 15 days.

**Biochemical Parameters**

The measurement of glucose was done by using serum. The method of Barham et al. (1972) was used to measure it (Randox, UK) supplied the required reagents. Total cholesterol (TC) was measured according to the method of Allan and Dawson (1979), the utilized reagents were supplied by (Biolabo, France). Triglycerides levels were observed by applying the method of Tietz et al.(1999), the used reagents were supplied by (Biolab, France), high-density lipoprotein (HDL) was determined according to the method of Lopes-Virella (1977), the utilized reagents were supplied by (Biolabo, France), very low-density lipoprotein (VLDL), and low-density lipoprotein (LDL) were measured by the use of method of Friedwald et al. (1972), malondialdehyde (MDA) was measured based on the method of Fong et al. (1973). Albumin was also measured, and it is performed by the method of (Doumas et al. (1971)), the used reagents was supplied by (Biolabo, France), decreased glutathione was measured based on the method of Ellman’s (1959).

**Statistical Analysis**

The software SPSS version 15.0 was used to obtain the statistical analysis; mean ± standard deviations (mean ± SD) and LSD were used to express the results. One-way ANOVA test was examined for the comparison parameters of the various groups that have been studied. p-values (p ≤ 0.05) were statistically important for the study.

**RESULTS**

**Effect of Taurine on Serum Glucose and Lipid Profile in Alloxan- Diabetic Rats**

The results showed a specific increase (p ≤ 0.05) in the concentration of serum glucose, triglycerides (TG), TC, very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) in group 2 compared with group 1. A nonspecific difference in the serum glucose concentration, TG, TC, VLDL and LDL in group 3 in comparing with group 1. Also, there was a specific reduction of (p ≤ 0.05) in the concentration of serum glucose, TG, TC, LDL and VLDL in group 4 compared with group 2. While there was a specific reduction of (p ≤ 0.05) in the concentration of serum high-density lipoprotein (HDL) in group 2 in comparison with group 1. Furthermore, there was no specific variation in the serum HDL concentration in group 3 in comparing with group 1. Furthermore, there was a specific enhancement of (p ≤ 0.05) in the concentration of serum HDL in group 4 in comparison with group 2. (Table 1).

**Table 1**: Effect of taurine on serum glucose and lipid profile in diabetic rats.

<table>
<thead>
<tr>
<th>Parameters/groups</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>LSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose(mg/dL)</td>
<td>96.20 ±</td>
<td>270.70 ±</td>
<td>95.96 ±</td>
<td>116.49 ±</td>
<td>19.44</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>131.34 ±</td>
<td>279.25 ±</td>
<td>120.92 ±</td>
<td>174.75 ±</td>
<td>21.70</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>87.52 ±</td>
<td>248.30 ±</td>
<td>82.46 ±</td>
<td>131.28 ±</td>
<td>13.26</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>46.79 ±</td>
<td>31.61 ±</td>
<td>48.91 ±</td>
<td>55.12 ±</td>
<td>4.23</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>67.04 ±</td>
<td>197.48 ±</td>
<td>55.53 ±</td>
<td>93.38 ±</td>
<td>21.83</td>
</tr>
<tr>
<td>VLDL (mg/dL)</td>
<td>17.51 ±</td>
<td>49.55 ±</td>
<td>16.49 ±</td>
<td>26.26 ±</td>
<td>2.65</td>
</tr>
</tbody>
</table>

- The mean ± standard deviation value of 6 rats was presented.
- Different letters refer to a significant difference at (p ≤ 0.05).
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Table 2- Effect of taurine on oxidant-antioxidant markers in diabetic rats.

<table>
<thead>
<tr>
<th>Parameters/Groups</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>LSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (µmol/L)</td>
<td>1.67 ±  c</td>
<td>3.05 ±  c</td>
<td>1.52 ±  c</td>
<td>1.87 ±  c</td>
<td>0.48</td>
</tr>
<tr>
<td>Glutathione (µmol/L)</td>
<td>327.60 ± 3.36 ±</td>
<td>320.32 ± 3.36 ±</td>
<td>292.85 ± 3.05 ±</td>
<td>275.31 ± 3.05 ±</td>
<td>24.89</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.41 ±  a</td>
<td>3.36 ±  b</td>
<td>4.04 ±  a</td>
<td>4.31 ±  a</td>
<td>0.51</td>
</tr>
<tr>
<td>Glutathione (µmol/L)</td>
<td>4.24 ±  a</td>
<td>0.41 ±  b</td>
<td>0.38 ±  a</td>
<td>0.39 ±  a</td>
<td>0.51</td>
</tr>
</tbody>
</table>

- The mean± standard division value of 6 rats was represented.
- Different letter refers to a significant difference at (p ≤ 0.05).

Effect of Taurine on Serum Malondialdehyde (MDA) and Antioxidants in Alloxan- Diabetic Rats.

The results showed a noticeable increase (p ≤ 0.05) in the serum MDA concentration in group 2 by comparing with group 1. No specific difference in the serum MDA concentration in group 3 was noticed by comparing with group 1. Additionally, there was a specific reduction of (p ≤ 0.05) in the serum malondialdehyde (MDA) concentration in group 4 by comparing it with group 2. While there was a specific reduction of (p ≤ 0.05 ) in the serum albumin and glutathione (GSH) concentration in group 2 by comparing with group 1. Furthermore, no specific difference in the serum albumin concentration in group 3 by comparing with group 1. Also, there was a specific reduction of (p ≤ 0.05) in the serum albumin and glutathione (GSH) concentration in group 4 by comparing with group 2 (Table 2).

DISCUSSION

The mechanism through which alloxan brings about its diabetic state included selective destruction of pancreatic β-cells that secrete insulin, which reduces the activity of cells, leading a weakness in the utilization of glucose by tissues. Taurine exerts hypoglycemic effects by regulation of gene expression needed for the insulin secretion of stimulated glucose and development of insulin action, as well as by facilitating the insulin interaction with its receptor. On the other hand, taurine increases glycolysis, glucose oxidation, and glycogenesis. It has hypoglycemic effects, and this forms a reduction in the fructose amine and glucose levels along with an enhancement in the glycogen, C-protein and insulin level, and glycogen in the liver.

Hyperlipidemia is a relatively common challenge in patients with poorly controlled diabetes mellitus and coexists with hyperglycemia, which is attributed by enhanced triglycerides, cholesterol, and phospholipids levels, and also lipoprotein modification. The diabetic hyperlipidemia was characterized to the imbalance of regulation of hormone of metabolism of glucose. The hypolipidemic impact of TAU could be partial because of the inhibition of the absorption of cholesterol in intestine or the enhancement of cholesterol conversion to bile acid. Moreover, it might be because that TAU is responsible for the HDL increase or ending the serum lipoprotein balance that contains cholesterol. Moreover, it is likely possible that drinking TAU can enhance clearance of serum cholesterol and reduce TC level in liver in high-fat/cholesterol dietary hamsters, which may be because of LDL receptor regulations, thus increases fecal TC and bile acids output. Yang et al. (2010) stated that TAU could alleviate blood lipids and hepatic damage induced by a high-fat/cholesterol-dietary diet. The data of Saleh (2012) indicated that the treatment of diabetic rats with TAU induced a decrease in lipid profile except for HDL-cholesterol.

The present study revealed that the elevation in MDA level might be a reflection of a decrease in the 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, pancreas, and erythrocytes of diabetic rats. Patel et al. (2009) suggested this elevation in hepatic MDA level might be due to high concentration of lipid, which was found in the liver of diabetic rats, and resulted in the activation of nicotinamide adenine dinucleotide phosphate (NADPH) dependent microsomal lipid peroxidation in the liver. The decreasing in albumin level is due to the increase of the synthesis of lipid peroxide and increase the formation of free radicals, which result in increasing of membranes permeability and leaking the proteins outside the vascular system. Hyperglycemia causes an increase in reactive oxygen metabolites and their derivatives. Since GSH is an important antioxidant, GSH deficiency causes increase in oxidative stress. Hyperglycemia induced oxidative stress and reduction in the levels of GSH in the vascular straight muscles. The prevention of oxidative stress by taurine was also reported in alloxan-induced type 1 diabetic. Interestingly, taurine supplementation for 2 days later of STZ injection, prolonged survival in diabetic rats. 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 γ- irradiation in rats by decreasing oxidative stress.

CONCLUSION

The benefits of the taurine amino acid appear to be due to its various actions on cellular functions, while toxicity seems relatively low. The possible taurine impact in improving diabetic complications is showed generally post-treatment supplementation for diabetes induced by alloxan.
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REFERENCES


