The Effects of Quercetin on Antioxidant System and Some Blood Parameters in Experimental Diabetic Rats

Gökmen Kılıçarslan¹, Nurcan DÖNMEZ²*
¹University of Giresun, Faculty of Sport Sciences, Giresun, TURKEY.
²University of Selcuk, Faculty of Veterinary 42075, Konya, TURKEY
Corresponding Address: nurcandonmez@selcuk.edu.tr

ABSTRACT
The aim of this study was to evaluate the effects of quercetin on antioxidant system and some blood parameters at streptozotocin (STZ)-induced diabetic rats. 32 adult male Wistar albino rats, whose weights were similar to each other, were used in this study. Experimental animals were divided into four equal groups as Control (C), Diabetes (D), Quercetin (Q) and Diabetes+Quercetin (DQ). In blood samples SOD, MDA, GSH, insulin, glucose, ALT and AST were determined at the end of the study. MDA level was increased significantly (p<0.05) in diabetic rats when compared with other three groups. MDA level was significantly lower in DQ group than D group and it was very close to the levels of K and Q group (p<0.05). The serum glucose, ALT and AST levels in D group were significantly higher than other groups but insulin level was considerably low (p<0.05). As a result, it was found that in experimental diabetic rats with STZ, diabetes had negative effects on observed parameters. Also quercetin treatment which was an effective antioxidant did not have a negative effect on healthy rats, but it was shown remarkable in terms of mitigating the negative effects on diabetic rats.

Key Words: Antioxidants; Diabetes Mellitus; quercetin, biochemical parameters.

INTRODUCTION
Diabetes Mellitus, defined as chronic hyperglycemia, is a metabolic disease which affects protein, fat and carbohydrate metabolism because of the lack of insulin secretion in pancreas or disruption of tissue response to insulin. Today it becomes an important health problem because it reduces the quality of life due to its lifelong acute and chronic complications [1-5]. Oxidative stress plays an important role in the etiology of diabetes [6]. Diabetics and experimental animal models exhibit high oxidative stress markers and reactive oxygen species (ROS) in pancreatic islets due to persistent and chronic hyperglycemia, thereby deplete the activity of the antioxidative defense system and thus promote free radical generation [7,8]. It leads to structural and functional abnormalities in liver by affecting the diabetes, glycogen and lipid metabolism [9]. Flavonoids occur commonly, and its widespread in the plant kingdom. They function as plant pigments, and are responsible for the colors in flowers and fruits [10]. They are often closely associated with vitamin C, to which they offer synergistic effects. One of the main group of polyphenolic substances of natural flavonoid, quercetin is a compound with antioxidant and anti-inflammatory activity. It is reported that as a member of the flavonoids' family quercetin (3,5,7,3 ', 4'-pentahydroxyflavo’s) which is taken 50-500 mg in a normal daily diet has many functions such as antioxidant for metabolism, anticarcinogenic, antiviral, anti-thrombotic, anti-ischemic, anti-inflammatory and antiallergenic feature [10,11]. The aim of the study was to evaluate the beneficial and preventive effects of quercetin on oxidative stress, and some blood parameters in streptozotocin (STZ)-induced diabetic rats.

MATERIALS AND METHODS
Experimental design and laboratory animals
32 adult male Wistar albino, whose weights were close to each other, were used in the study. The animals were divided into 4 equal groups as control (C), diabetes (D), quercetin (Q) and Diabetes + Quercetin (DQ). The rats were hosted in the experimental animal unit, in plastic rat cages, at 23 ± 2 °C room temperature, 50% ± 10 relative damp environments, in 12/12 at night / daylight period. The animals
were given standard rat pellets and tap water ad-libitum. The research project and animal housing conditions were approved by the Ethical Committee for Animal Studies (No. 2014-042). 60 mg/kg of STZ (Sigma S0130-1G) dissolved in 0.1 M citrate buffer (pH: 4.5) was injected intraperitoneal as a single dose to the (D) and (DQ) groups. After 72 hours STZ administration from the tail end of the capillary fasting blood glucose meters (plusMED), blood glucose levels was controlled by measuring and whether or not diabetes. The animals whose blood glucose levels of 250 mg/dl or above were considered diabetic. Quercetin (15 mg/kg, live weight/day) were intraperitoneally injected to the Q and DQ groups (after diabetes had happened) daily for 4 weeks.

Blood analyzes
At the end of the 4 week trial period, through cardiac puncture, blood samples were collected to containing anticoagulant and without anticoagulant blood tubes under general anesthesia. Plasma SOD, MDA, GSH, insulin, glucose, ALT and AST levels were determined were determined by commercial kits (Siemens, Oxis, Cayman) using ELISA (Biotek 800 ELX).

Statistical analysis
Statistical differences among the groups were tested by analysis of variance (ANOVA) which is followed by Duncan’s test using SPSS for windows version 17.0.

RESULTS AND DISCUSSION
Results obtained from all groups were given in table 1 and 2.

Table 1: The impact of quercetin application on the levels of MDA, SOD and GSH in experimental diabetic rats. (X ± SEM, n=8)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>K</th>
<th>Q</th>
<th>D</th>
<th>DQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (nmol/ml)</td>
<td>0.90 ± 0.09^{c}</td>
<td>1.10 ±1.14^{c}</td>
<td>2.61 ± 0.36^{a}</td>
<td>1.75 ±1.12^{b}</td>
</tr>
<tr>
<td>SOD (U/ml)</td>
<td>0.45 ± 0.01^{a}</td>
<td>0.44 ± 0.01^{a}</td>
<td>0.37 ± 0.01^{b}</td>
<td>0.43 ± 0.01^{a}</td>
</tr>
<tr>
<td>GSH (µM)</td>
<td>4.25 ± 0.71^{a}</td>
<td>3.81 ± 0.72^{a}</td>
<td>1.01 ± 0.29^{b}</td>
<td>2.85 ± 0.85^{ab}</td>
</tr>
</tbody>
</table>

a,b,c: The differences between average values indicated by different letters in the same row of the same parameters are important (p<0.05).

Table 2. The effects of the application of quercetin on plasma insulin, glucose, ALT and AST levels in experimental rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>K</th>
<th>Q</th>
<th>D</th>
<th>DQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (uU/ml)</td>
<td>0.69 ± 0.09^{a}</td>
<td>0.65 ± 0.11^{a}</td>
<td>0.25 ± 0.03^{b}</td>
<td>0.49 ±0.12^{ab}</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>134,50±14,59^{b}</td>
<td>163,33±15,62^{b}</td>
<td>435,00±9,75^{a}</td>
<td>252,66±57,29^{b}</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>56,50 ± 2,56^{b}</td>
<td>70,00 ± 6,11^{b}</td>
<td>98,00 ± 12,86^{a}</td>
<td>72,16 ± 9,47^{b}</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>92,00 ± 3,80^{a}</td>
<td>97,33 ± 4,07^{b}</td>
<td>142,50±17,98^{a}</td>
<td>104,16 ± 9,92^{b}</td>
</tr>
</tbody>
</table>

a,b,c: The differences between average values indicated by different letters in the same row of the same parameters are important (p<0.05).

The main problem associated with diabetes mellitus (DM) are the elevation of blood glucose levels due to impaired metabolism, and the generation of harmful free radicals as a result of the use of lipids for energy production. In cases of diabetes, the auto-oxidation of glucose increases and during the conversion of oxidized glucose into glucose acid, free radicals are generated [12, 13, 14]. In a study on the oxidant-antioxidant status before and after the development of diabetes in rats, Akkaya and Çelik [15] determined that the level of malondialdehyde (MDA), which is an end-product of lipid peroxidation, significantly increased in diabetic animals, and suggested that increased lipid peroxidation could be used as an indicator of diabetes and diabetes-induced complications. In a previous study on the effects of quercetin on organ damage caused by DM-induced oxidative stress, and on antioxidant capacity, in rats with STZ-induced DM, according to the results of hepatic MDA, SOD, CAT, GPx, ALT, AST and fasting blood glucose concentration measurements, it was ascertained that, while MDA, GPx, ALT and AST and glucose levels were significantly higher in the diabetic group, the same parameters had drawn closer to the values of the control animals in the diabetic group administered with quercetin [16]. In research conducted by Molina et al. [17] and Adewole et al. [18] on the effects of quercetin against oxidative stress, it was demonstrated that, ALT and AST levels and GSH, SOD, CAT and GPx activities were significantly decreased, and MDA levels increased as a result of oxidative stress, and it was reported that

Kılıçarslan and Donmez
This study was financed under a project supported by the Selcuk University Scientific Research investigations.

The results obtained in the present study are consistent with these reports. Thus, it is considered that the restoration of the efficiency of the antioxidant system is of particular significance in the treatment of diabetes. The results of the present study suggest that, quercetin, which was specifically used for this purpose in this study, may play an active role in the regulation of increased oxidative stress, protein glycation and glucose metabolism in cases of diabetes.

In conclusion, in the present study it was determined that, quercetin, which is a natural flavonoid that has found common use owing to its strong antioxidant effect, restored MDA, insulin and glucose levels, and SOD, GSH, ALT and AST activities in STZ-induced diabetic rats, and did not cause any adverse effect in rats administered with quercetin alone. Therefore, quercetin was considered worthy of further extensive investigations.

ACKNOWLEDGMENTS
This study was financed under a project supported by the Selcuk University Scientific Research Coordinatorship.
REFERENCES


CITATION OF THIS ARTICLE