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ORIGINAL ARTICLE **OPEN ACCESS**

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

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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.*

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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)

Parameters	K	Q	D	DQ
MDA (nmol/ml)	0,90 ± 0,09^{c}	1,10 ±1,14^{c}	2,61 ± 0,36^{a}	1,75 ±1,12^{b}
SOD (U/ml)	0,45 ± 0,01^{a}	0,44 ± 0,01^{a}	0,37 ± 0,01^{b}	0,43 ± 0,01^{a}
GSH (µM)	4,25 ± 0,71^{a}	3,81 ± 0,72^{a}	1,01± 0,29^{b}	2,85 ±0,85^{ab}

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.

Parameters	K	Q	D	DQ
Insulin (uU/ml)	0,69 ± 0,09^{a}	0,65 ± 0,11^{a}	0,25 ± 0,03^{b}	0,49 ±0,12^{ab}
Glucose (mg/dl)	134,50±14,59^{b}	163,33±15,62^{b}	435,00±49,75^{a}	252,66±57,29^{b}
ALT (U/L)	56,50 ± 2,56^{b}	70,00 ± 6,11^{b}	98,00 ± 12,86^{a}	72,16 ± 9,47^{b}
AST (U/L)	92,00 ± 3,80^{b}	97,33 ± 4,07^{b}	142,50±17,98^{a}	104,16 ± 9,92^{b}

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

quercetin administration normalized all values and preserved the integrity of pancreatic β-cells. In further research on the antioxidant activity of quercetin, it was determined that the administration of this substance increased SOD, CAT and GPx activities and decreased MDA levels [19-24].

In the present study, the significant increase detected in the serum MDA levels of the diabetic rats by the end of the trial, which was in fact an indicator of lipid peroxidation, agreed with literature reports pointing out to oxidative stress development as a result of diabetes [25-27]. Furthermore, in addition to the increased serum MDA levels, the significant decrease detected in the activities of SOD and GSH, which are antioxidants that play an important role in the prevention of oxidative stress, in the diabetic rats, was also consistent with the results of previous research. Furthermore, in the present study, the MDA, SOD and GSH activities having been found to be similar in the control group and Group Q, as well as in Group DQ and the groups other than Group D, whereas having been observed to significantly differ between Groups DQ and D (Table 1) was attributed to the strong antioxidant effect of quercetin.

In diabetic patients, the liver, skeletal muscles and adipose tissue are the major sites of insulin resistance. Nonetheless, the liver plays a greater role than the extrahepatic tissues in insulin resistance [28]. Diabetic patients frequently present with increased levels of serum aminotransferases, and this increase is generally attributed to lipid infiltration in the liver [29]. It has been reported that serum glucose concentrations, AST and ALT activities significantly increased in diabetes cases [30]. In fact, it is suggested that elevated levels of transaminases (ALT/AST) and gamma glutamyl transferases (GGT) are associated with diabetes-induced complications, namely, retinopathy and neuropathy [31].

In a study, in which quercetin was used as an antioxidant against oxidative stress-induced damage to the hepatic, renal, cerebral and cardiac tissues in STZ-induced diabetic rats, it was ascertained that hepatic ALT and AST activities and serum glucose concentrations had significantly increased in the group suffering from DM. On the other hand, these parameters were observed to be similar in the control group and the group administered with quercetin, and to be higher in the diabetic group administered with quercetin. The researchers attributed these results to the subacute effects of quercetin [32].

In another study on the effects of quercetin on oxidative stress-induced functional and morphological changes in STZ-induced diabetic rats, it was demonstrated that while the ALP and ALT activities had significantly increased in the diabetic animals, in comparison to the control group, the same parameters had drawn closer to the values of the control animals in the diabetic group administered with quercetin [26].

In the present study, the decreased insulin levels and the increased ALT and AST activities and blood glucose concentrations determined in the diabetes group (Group D), in comparison to the other groups, were expected results confirming those reported in previous research (Table 2). Furthermore, when compared to Group D, the administration of quercetin having been determined to decrease glucose concentrations, and ALT and AST activities in the diabetic rats, and no significant alteration having been determined in Group Q, which presented with values similar to those of the control group, were also in agreement with the results of previous research [26, 32-35]. Researchers have attributed such results to the decrease of oxidative stress as a result of the antioxidant effect of quercetin.

In previous research on the association of oxidative stress with diabetes and diabetes-induced complications, it has been suggested that damage to the pancreatic β-cells, which are highly sensitive to oxidative stress, could result from the toxic effects of hyperglycaemia [8, 26, 34, 35, 37]. Literature reports also indicate that alterations in the energy metabolism as well as tissue damage induced by metabolic stress, hypoxia and ischemia-reperfusion injury increase the generation of free radicals and inhibit the antioxidant system. 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.

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REFERENCES

1. Akçay, G., Akçay, M.N., Akarsu, E. (2000) Endocrine and metabolic diseases. 1st edition, Erzurum, Active publishing. 191-235.
2. Saredi, S., Patte-Mensah, C., Melcangi, R.C., Mensah-Nyagan, A.G. (2005) Effect of streptozotocin-induced diabetes on the gene expression and biological activity of 3beta-hydroxysteroid dehydrogenase in the rat spinal cord. Neurosci. 135(3): 869-77.
3. Onat, T., Emerk, K., Sözmen, E.Y. (2006) Human biochemistry. 12th edition, Ankara, Palme publishing. 80-6:526-31, 749-57.
4. Öntürk, H., Özbek, H. (2007) Carried out of experimental diabetes and the measurement of glycemic activity. General Medical J. 17(4): 231-6.
5. Yeğin, S.Ç., Mert, N. (2013) Investigation on the HbA1c, MDA, GSH-Px and SOD Levels in Experimentally Diabetic Rats. Yüzüncü Yıl Univ. Vet Med J. 24(2): 51-4.
6. Vural, H., Sabuncu, T., Arslan, S.O., et al. (2001) Melatonin inhibitis lipid peroxidation and stimulates the antioxidant status of diabetic rats. J. Pineal Res. 31: 93-8.
7. Vincent, A.M., Russell, J.W., Low, P., Feldman, E.L. (2004) Oxidative stress in the pathogenesis of diabetic neuropathy. Endocrine Reviews. 25: 612-28.
8. Altan, N., Dinçel, A.S., Koca, C. (2006) Diabetes mellitus and oxidative stress. Turkish J Biochem. 31(2): 51-6.
9. Sanchez, S.S., Abregü, A.V., Aybar, M.J., Riera, A.N.S. (2000) Changes in liver gangliosides in streptozotocin-ınduced diabetic rats. Cell Biol Int. 24(12): 897-904.
10. Aguirre, L., Arias, N., Macarulla, M.T., Gracia, A., Portillo, M.P. (2011) Beneficial effects of quercetin on obesity and diabetes. The Open Nutraceuticals J. 4: 189-98.
11. Elik, M., Serdaroğlu, G., Özkan, R. (2007)The investigation of antioxidant activities of myricetin and quercetin with dft methods. Cumhuriyet Univ. Sci J 28(2): 53-65.
12. [12] Giugliano, D., Ceriello, A., Paolisso, G. (1995)Diabetes mellitus, hypertension, and cardiovascular disease: which role for oxidative stress? Metabolism. 44(3): 363-8.
13. Alam, M., Meerza, D., Naseem, I. (2014) Protective effect of quercetin on hyperglycemia, oxidative stress and DNA damage in alloxan induced type 2 diabetic mice. Life Sci. 109 (1): 8-14.
14. Cho, S.Y., Park, J.Y., Park, E.M., et al. (2002) Alternation of hepatic antioxidant enzyme activities and lipid profile in streptozotocin-induced diabetic rats by supplementation of dandelion water extract. Clinica Chimica Acta. 317: 109–17.
15. Akkaya, H., Çelik, S. (2010) Oxidant and antioxidant situation before and after diabetes in rat. Fırat Unv. Health Sci Vet J. 24(1): 5-10.
16. Edremitlioğlu, M., Antiç, M.F., Sayın, D.B., et al. (2011) Quercetin, a powerful antioksidant bioflavonoid, attenuates renal dysfunction in long-term experimental diabetes mellitus. Marmara Med. J. 24(2): 88-99.
17. Molina, M.F., Sanchez-Reus, I., Iglesias, I., Benedi, J. (2003) Quercetin, a flavonoid antioxidant, prevents and protects against ethanol-ınduced oxidative stress in mouse liver. Biol. Pharm. Bull. 26(10): 1398-1402.
18. Adewole, S.O., Caxton-Martins, E.A., Ojewole, J.A.O. (2007) Projective effect of quercetin on the morphology of pancreatic β-cells of streptozotocin-treated diabetic rats. Afr. J Trad. CAM. 4(1): 64-74.
19. M. Alia, S. Ramos, R. Mateos, et al. Quercetin protects human hepatoma hepg2 against oxidative stress ınduced by tert-butyl hydroperoxide. Toxicology and Applied Pharmacol. 212: 110-8.
20. Phachonpai, W., Wattanathorn, J., Muchimapura, S. et al. (2010) Neuroprotective effect of quercetin encapsulated liposomes: a novel therapeutic strategy against alzheimer's disease. Am J Applied Sci. 7(4): 480-5.
21. Çiftçi, R., Yüce, A. (2013) Effect of Quercetin on Homocysteine Level and Coronary Vascular Damage in Rats with Liver Fibrosis. Fırat Unv. Health Sci. Vet J. 27 (3): 159-67.
22. Ben Abdallah, F., Zribi, N., Ammar-Keskes, L. (2011) Antioxidative potential of quercetin against hydrogen peroxide ınduced oxidative stress in spermatozoa in vitro. Andrologia. 43: 261-5.
23. El-Baky, A.E. (2011) Quercetin protective action on oxidative stress, sorbitol, ınsulin resistance and β-cells function in experimental diabetic rats. IJPSR. 2(2): 11-8.
24. Sriraksa, N., Wattanathorn, J., Muchimapura, S., et al. (2012) Cognitive-Enhancing effect of quercetin in a ratmodel of parkinson's disease ınduced by 6-hydroxydopamine. Evidence-Based Complementary and Alternative Med. 823206: 1-9.
25. Braga, C.P., Momentti, A.C., Peixoto, F.B.,et al.(2013) Influence of treatment with quercetin on lipid parameters and oxidative stress of pregnant diabetic rats. Can. J. Physiol. Pharmacol. 91:171–7.
26. Maciel, R.M., Costa, M.M., Martins, D.B., et al. (2013) Antioxidant and anti-ınflammatory effects of quercetin in functional and morphological alterations in streptozotocin-ınduced diabetic rats. Res Vet Sci. 95: 389-97.
27. Antu, K.A., Riya, M.P., Mishra, A., et al. (2014) Symplocos cochinchinensis attenuates streptozotocin-diabetes ınduced pathophysiological alterations of liver, kidney, pancreas and eye lens in rats. Exp and Toxicologic Pathol. 66: 281-91.
28. Çambay, Z. (2011) Investigation of the effects of pomegranata flower (punica granatum)on serum aspartate amınotransferase and alanine amınotransferaselevels in diabetic rats. Ecological Life Sci. 6(4): 124-33.
29. Miyake, Y., Eguchi, H., Shinchi, K., et al. (2003)Glucose ıntolerance and serum aminotransferase activities in japanese men. J Hepatology. 38: 18-23.
30. Maritim, A.C., Sanders, R.A., Watkins, J.B. (2003) Diabetes, oxidative stress, and antioxidants: a review. Inc. J Biochem Mol Toxicol. 17: 24-38.

31. Jamieson, A. (2003) Deranged liver function tests in type 1 diabetes mellitus: an unusual presentation of treponema pallidum ınfection. European J Internal Med. 14: 113-5.
32. Sanders, R.A., Rauscher, F.M., Watkins, J.B. (2001) Effects of quercetin on antioxidant defense in streptozotocin-ınduced diabetic rats. Inc. J Biochem Mol Toxicol. 15:143-9.
33. Vessal, M., Mina Hemati, M., Vasei, M. (2003) Antidiabetic effects of quercetin in streptozocin-induced diabetic rats. Comparative Biochem and Phy Part C . 135: 357-64.
34. Coşkun, Ö., Kanter, M., Korkmaz, A., Öter, Ş. (2005) Quercetin, a flavonoid antioxidant, prevents and protects streptozotocin-induced oxidative stress and ß cell damage in rat pancreas. Pharmacological Res. 51: 117-23.
35. Abdelmoaty, M.A., Ibrahim, M.A., Ahmed, N.S., Abdelaziz, M.A. (2010) Confirmatory studies on the antioxidant and antidiabetic effect of quercetin in rats. Indian J Clin Biochem. 25 (2): 188-92.
36. Altan, N., Yiğit, Ş., Elmalı, E. et al. (1997) Effects of the sulfonylurea glyburide on superoxide dismutase in streptozotocine-ınduced diabetic rat muscle. General Pharm. 28(5): 795-6.
37. Erukainure, O.L., Ebuehi, O.A.T., Adeboyejo, F.O., et al. (2013) Hematological and biochemical changes in diabetic rats fed with fiber-enriched cake. J Acute Med. 3: 39-44.

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