Compartments of Quercetin & *Allium cepa* (Onion) on Blood Glucose in Diabetic Rats

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Abstract

Background: The major concern in diabetes is increased oxidative stress. Maintaining a balance between reactive oxygen species (ROS) and antioxidants is a major mechanism in preventing damage from oxidative stress. Quercetin (QR) is a well-known flavonoid and a strong antioxidant derived from the onion, *Allium cepa*, and it has been shown to reduce oxidative stress in the long-term treatment of streptozotocin (STZ)-induced diabetes in animals.

Objective: We aimed to study on beneficial effects of QR & *Allium cepa* on regulation of blood glucose in diabetic model.

Methods: Seventy male 8-week-old Wistar albino rats weighing 250 ± 10 g were obtained, the rats were divided into seven groups comprising ten animals in each group. Diabetes induced with single intraperitoneal injection of STZ. Diabetic rats treated with quercetin (15mg/kg/day, started 48 hours after STZ injection) and *Allium cepa* juice (2cc/rat/day, started 48 hours after STZ injection). After 28 days treatment, analysis on blood glucose and insulin was done.

Results: The mean TAC showed a significant increase ($p < 0.05$) in the QR compared to the control, STZ and STZ + QR groups. Both QR and onion Juice had significant effect in lowering blood glucose (355.3 ± 104 mg/dl and 353.4 ± 103 mg/dl respectively) ($p<0.05$) in STZ induced diabetic animals. Both QR and onion juice had lowering effect in Serum insulin in healthy animals and significant increasing effect on serum insulin level in diabetic animals.

Conclusions: Both QR and onion juice had good effect in modifying diabetes related biochemical parameters and they are recommended to be studied more in order to being used in the therapy.

Keywords: Quercetin, Onion, Diabetes, Rat

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Introduction

The major concern in diabetes is increased oxidative stress. Thus, increased production of free radicals or reactive oxygen species (ROS) may induce oxidized low-density lipoproteins (Ox-LDL), which are key factors in the sequence of events leading to atherosclerosis. Thus, sustained hyperglycemia and increased oxidative stress are the major players in the development of secondary complications in diabetes. These abnormalities produce a variety of pathologies including vasculopathies, neuropathies, ophthalmopathies and nephropathies, among many other medical derangements [1]. Maintaining a balance between ROS and antioxidants is a major mechanism in preventing damage from oxidative stress. Therefore, dietary supplementation with antioxidants such as vitamins, and flavonoids has been used in attempts to prevent the occurrence of many chronic diseases [2]. Quercetin (QR) is a well-known flavonoid and a strong antioxidant derived from the onion, *Allium cepa*, and it has been shown to reduce oxidative stress in the long-term treatment of streptozotocin (STZ)-induced diabetes in animals [3]. Diabetes is associated with reproductive impairment in both men and women. We aimed to study on beneficial effects of QR & *Allium cepa* on regulation of blood glucose in diabetic model.

Materials and Methods

Animals

Seventy male 8-week-old Wistar albino rats weighing 250 ± 10 g were obtained from the animal facility of the Pasture Institute of Iran. Rats were housed in controlled rooms (temperature; 25°C ± 1°C, humidity 40% – 70% and a 12/12 h light/dark cycle) prior to use in experimental protocols. All animals were treated in accordance with the principles of laboratory animal care [NIH]. The experimental protocol was approved by the Animal Ethics Committee in accordance with the guide for the care and use of laboratory animals prepared by Tabriz University of Medical Sciences. All rats were fed a standard diet and water. The daily intake of animal water was monitored at least one week prior to start of treatments to determine the amount of water needed per experimental animal. Diabetes was induced by a single intraperitoneal (ip) injection of streptozotocin (STZ), (Sigma-Aldrich, St Louis, MO, USA) in 0.1 M citrate buffer (pH 4.0) at a dose of 55 mg/kg body weight [3]. Blood glucose concentration and changes in body weight was monitored regularly.

The rats were divided into seven groups comprising ten animals in each group as follows:

Group 1: Control rats given only 0.5 ml of citrate buffer (pH=4, STZ vehicle) daily.

Group 2: Control rats given only 0.5ml 20% glycerol in 0.9% normal saline (QR vehicle) daily

Group 3: Diabetic control (55mg/kg, single intraperitoneal injection of STZ)

Group 4: Normal rats given only quercetin (15mg/kg/day for 28 days)

Group 5: Normal rats given only *Allium cepa* (2cc/rat/day for 28 days)

Group 6: Diabetic rats treated with quercetin (15mg/kg/day, started 48 hours after STZ injection)

Group 7: Diabetic rats treated with *Allium cepa* (2cc/rat/day, started 48 hours after STZ injection)

At the end of the experiment, blood was collected into heparinised tubes, and serum

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were Separated by centrifugation and used for further analysis. All rats were euthanized.

Blood Glucose Determination

Blood samples were collected from the tail vein. Basal glucose levels were determined prior to STZ injection, using an automated blood glucose analyzer (Glucometer Elite XL, Bayer HealthCare, Basel, Switzerland). Samples were then taken 24 h after STZ injection and blood glucose concentrations were determined and compared between groups. Rats with blood glucose concentrations above 300 mg/dL were declared diabetic and were used in the experimental group. 48 hours after the induction of experimental diabetes, the experimental protocol was started.

Serum insulin level

Serum insulin concentrations were determined by using radioimmunoassay kit (Boehringer Mannheim, Germany).the insulin level in serum was expressed in µU/ml.

QR Preparation

QR was dissolved in 20% glycerol in 0.9% normal saline, mixed vigorously and stored in a dark bottle at 4 °C. The solution was prepared freshly each week.

Preparation of onion juice

The underground yellowish-white bulbs of *Allium cepa* (onion) was collected on August 2007 from Ilkhchi in the province of East Azerbaijan-Iran. The skin was removed and fresh juice of onions was prepared using Tefal-fruit juice supplying machine before experiments.

Analysis of onion juice

Onion juice was tested for the determination of flavonoids with Shinoda test [4]. Qualitative [thin-layer chromatography (TLC)] was employed for determination of the quercetin as a main flavonoid in onion. For TLC 10 ml fresh onion juice was dried under vacuum and resulted residue dissolved in 1ml methanol. 20 µl of methanolic solution was spotted on silica gel plate (10×20 cm, silica gel 60 GF254, Merck, Darmstadt, Germany) with a solvent system of EtOAc/MeOH (80:20). Quercetin, Sigma chemical Co. (St. Louis, MO, USA) was used as control. After developing and drying, TLC plate was sprayed with a 2% AlCl3 solution in methanol. Quercetin in onion sample appeared as yellow spot at RF=0.6. Separation of quercetin was performed with further purification by preparative TLC on silica gel and quantitative determination of quercetin carried out on a Model 2100 Spectrophotometer (Shimadzu, Japan) in 370 nm comparing to pure quercetin standard curve. The amount of quercetin in fresh onion was 12mg/100g.

Surgical Procedure

On the 28th day, (at the end of the treatment period), the rats were killed with diethyl ether and serum in control and experimental groups were removed immediately. The weight of testes was recorded.

Measurement of Serum Total Antioxidant Capacity (TAC)

TAC was measured in serum using a commercial kit (Randox Laboratories, Crumlin, UK). The assay is based on the incubation of 2, 2′-azino-di-(3-ethylbenzthiazoline sulfonate) (ABTS) with a peroxidase (methmyoglobin) and H2O2 to produce the radical cation ABTS+, which has a relatively stable blue-green color measured spectrophotometrically at 600 nm. The suppression of the color is compared with that

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of Trolox, which is widely used as a standard for TAC measurements and the assay results are expressed as Trolox equivalents (in nmol/mL) [5].

Statistical analysis

Statistical analysis was done using the ANOVA and test for comparison of data in the control group with the experimental groups. The results are expressed as the mean ± standard error of mean (SEM) and $p < 0.05$ was considered significant.

Results

Results of TAC, concentration of serum glucose and insulin in the experiment are given in brief in table 1.

TAC in Serum

The mean TAC showed a significant increase ($p < 0.05$) in the QR group (0.75 ± 0.03 nmol/mL) compared with the control (0.70 ± 0.03 nmol/mL), STZ (0.32 ± 0.04 nmol/mL) and STZ + QR (0.61 ± 0.05 nmol/mL) groups.

Blood glucose

Both QR and onion Juice had significant effect in lowering blood glucose (355.3± 104 mg/dl and 353.4 ± 103 mg/dl respectively) ($p<0.05$) in STZ induced diabetic animals. They also lowered blood glucose in non-diabetic animals significantly ($p<0.05$).

Blood insulin level

Both QR and onion juice had lowering effect in Serum insulin in healthy animals and these decrement were significant (both 20.3 ± 0.4 µU/ml) ($p<0.05$). At the other hand, they had significant increasing effect on serum insulin level in diabetic animals (both 20.3 ± 0.4 µU/ml)

Discussion

TAC levels showed marked decreases in the STZ-induced diabetic group compared with those seen in the control and other experimental groups and these results were in agreement with Tang et al. [6]. The Flavonoids are antioxidant agents widely distributed in dietary plants frequently consumed by humans such as fruits, vegetables, teas and wine [7]. The dietary intake of flavonoids in humans has been estimated to be 16 – 1000 mg/day. QR is

Table 1- Results of TAC, concentration of serum glucose and insulin in the experiment

	TAC nmol/ml	Glucose mg/dl	Insulin µU/ml
Group 1	0.7 ± 0.06	141.1 ± 0.8	27.2 ± 0.4
Group 2	0.68 ± 0.02	139.8 ± 0.8	27.5 ± 0.4
Group 3	0.3 ± 0.04	380.5 ± 0.7	11.1 ± 0.5
Group 4	0.7 ± 0.03	120.9 ± 1.1	20.3 ± 0.4
Group 5	0.7 ± 0.01	122.7 ± 1.1	20.3 ± 0.4
Group 6	0.6 ± 0.05	355.3 ± 1.4	17.2 ± 0.3
Group 6	0.5 ± 0.05	353.4 ± 1.3	17.2 ± 0.3

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regularly consumed by humans as it is the major flavonoid found in the human diet [8]. A number of beneficial effects of QR on human health have been known for some time [9, 10]. It is reported to decrease capillary fragility, to protect against diabetic cataracts, to possess antiviral and antiallergenic activities, to inhibit platelet aggregation and the oxidation of LDL and to act as an anti-inflammatory agent [11]. QR as an important dietary flavonoid possesses beneficial effects for human health because of its antioxidant function. One mechanism of the antioxidant action of QR is scavenging free radicals, such as the superoxide radicals generated by xanthine/xanthine oxidase [12]. Studies on the effects of QR on oxidative damage in cultured chicken spermatogonial cells showed that it had no deleterious effects at doses of 1 and 10 μg/mL. QR at 1 μg/mL increased the numbers of spermatogonial cells and reduced Aroclor-induced oxidative damage in the testes [13, 14]. In the present study, QR decreased the effect of STZ-induced diabetes on serum MDA and enhanced the serum TAC levels. Thus suggests that excessive ROS might have been involved in the damage. In our study QR treatment decreased the blood glucose levels showed significant decreased in STZ+ QR treated rats. These results are in agreement with these reported by Vessal etal ,who showed QR, a flavonoid with antioxidant properties brings about the regeneration of the pancreatic islets and probably increases insulin release in streptozocin-induced diabetic rats. This anti hyperglycemic effect consequently may alleviate testis cell damages associated with STZ-induced diabetic rats. The present study suggest beneficial effect of QR probably by its antioxidant and anti diabetic properties .As this antioxidant flavonoid is known to decrease the risk of degenerative diseases, we suggest that using dietary fruits, vegetables, onion, teas and red wine rich in flavonoids and QR could have beneficial effects on subjects with diabetes. Additional studies should be performed to better understand the mechanism of QR on spermatogenesis.

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References

1. Sexton WJ, Jarow JP. Effect of diabetes mellitus upon male reproductive function. *Urology*, 1997; 49: 508 – 13.

2. Peluso MR. Flavonoids attenuate cardiovascular disease, inhibit phosphodiesterase and modulate lipid homeostasis in adipose tissue and liver. *Exp Biol Med* (Maywood). 2006; 231 (8): 1287 – 99.

3. Mahesh T, Menon VP. Quercetin alleviates oxidative stress in streptozotocin-induced diabetic rats. *Phytother Res.* 2004; 18: 123 – 7.

4. Wagner H, Bladt S, Zgainski EM. Plant Drug Analysis. Springer – Verlag, Berlin: 1984, 298 – 334.

5. Quintanilha AT, Packer L, Davies JM, Racanelli TL, Davies KJ. 1982. Membrane

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[DOR: 20.1001.1.2717204.2010.9.33.31.7]

effects of vitamin E deficiency: bioenergetics and surface charge density studies of skeletal muscle and liver mitochondria. *Ann NY Acad Sci*. 1982; 393: 32 – 47.

6. Tang XY, Zhang Q, Dai DZ, Ying HJ, Wang QJ, Dai Y. Effects of strontium fructose 1,6-diphosphate on expression of apoptosis-related genes and oxidative stress in testes of diabetic rats. *Int. J. Urol*. 2008; 15 (3): 251 - 6.

7. Skibola C F, Smith M T. Potential health impacts of excessive flavonoid intake. *Free Radic. Biol. Med.* 2000; 29: 375 – 83.

8. Manach C,Morand C,Crespy V,Demigne C,Texier O,Regerat F,Remesy C. Quercetin is recovered in human plasma as conjugated derivatives which retain antioxidant properties. *FEBS Lett*. 1998; 426: 331 – 6.

9. Formica JV, Regelson W. Review of the biology of Quercetin and related bioflavonoids. *Food Chem. Toxicol.* 1995; 33: 1061 – 80.

10. Hertog MG,Hollman PC. Potential health effects of the dietary flavonol quercetin. *Eur. J. Clin. Nutr*. 1996; 50: 63 – 71.

11. Bors W,Michel C,Stettmaier K. Antioxidant effects of flavonoids. *Biofactors*. 1997; 6: 399 – 402.

12. Dok-Go H, Lee KH, Kim HJ, Lee EH, Lee J, Song YS, Lee YH, Jin C, Lee YS, Cho J. Neuroprotective effects of antioxidative flavonoids, quercetin, (1)-dihydroquercetin and quercetin 3-methyl ether, isolated from Opuntia ficus-indica var. saboten. *Brain Res*. 2003; 965: 130 – 6.

13. Mi Y, Zhang C. Protective Effect of Quercetin on Aroclor 1254–Induced Oxidative Damage in Cultured Chicken Spermatogonial Cells. *Toxicol. Sci.* 2005; 88 (2): 545 – 50.

14. Chandel A, Dhindsa S, Topiwala S, Chaudhuri A, Dandona P .2008.Testosterone concentration in young patients with diabetes. *Diabetes Care*. 2008; 31 (10): 2013 – 7.

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