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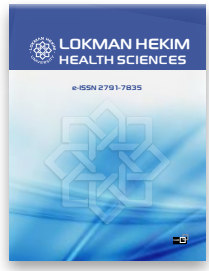

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ORIGINAL ARTICLE

Renoprotective Influence of Quercetin Administration on Na^+/K^+-ATPase Levels and Indicators of Oxidative Stress in Rats with High Sucrose Intake

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Abstract

Introduction: This study aimed to examine the consequences of high sucrose intake (935 mM sucrose) on the kidney, concentrating on indicators of oxidative stress and renal Na^+/K^+-ATPase (NKA) protein level. Antioxidants that act as reducing agents, especially those that can capture reactive oxygen species, are protective effects against metabolic syndrome-induced renal deterioration.

Methods: In this study, we looked into the consequences of quercetin (15 mg/kg/day) administration for 2 weeks following high sucrose intake on plasma blood urea nitrogen, albumin, creatinine, urea, and uric acid levels and oxidative stress status in kidney tissue. We also investigated the possible changes in renal NKA protein levels due to kidney damage induced by high sucrose intake.

Results: High sucrose intake caused increased body weight, hyperinsulinemia, hypertriglyceridemia, insulin resistance, and deterioration of renal properties in rats. It also resulted in increased oxidative stress. However, quercetin administration improved glycemic control, renal function parameters, renal NKA protein levels, and oxidative stress in the kidney.

Discussion and Conclusion: Application of quercetin was found to have a beneficial impact on oxidative stress damage in the kidneys of rats given a diet high in sucrose.

Keywords: Kidney; Metabolic syndrome; Na^+/K^+-ATPase; Oxidative stress; Quercetin

Metabolic syndrome (MS), commonly known as insulin resistance syndrome, is characterized by hypertension, hyperglycemia, dyslipidemia, and abdominal obesity, affecting multiple organs, particularly within the cardiorenal system.[1] Renal dysfunction in MS is believed to result from a combination of atherogenic dyslipidemia, obesity, endothelial dysfunction, hyperglycemia, and activation of vasoconstrictive pathways, mediated in part by systemic release of glycosylated compounds, reactive oxygen species (ROS), and pro-inflammatory agents such as uric acid.[2]

MS-induced oxidative stress is a key contributor to kidney injury, primarily through ROS generated from elevated blood glucose and free fatty acids. Impairments in renal function and redox regulation suggest involvement of the myeloperoxidase/hydrogen peroxide axis, likely mediated by lipid peroxidation, with increased plasma levels of malondialdehyde (MDA),

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hydrogen peroxide, and myeloperoxidase serving as interrelated markers of oxidative damage.[3]

Na^+/K^+-ATPase (NKA) is essential for maintaining renal ion homeostasis and is implicated in both renal and cardiovascular pathophysiology. Diabetes adversely affects renal recovery after ischemia-reperfusion injury, with altered NKA activity linked to tubular proliferation, capillary density, T cell infiltration, and inflammation.[4] Angiotensin II has been shown to rapidly stimulate NKA activity via Ser938 phosphorylation, promoting its trafficking to the plasma membrane in proximal tubule cells, underscoring its role in renal function and blood pressure regulation.[5] Moreover, targeting the DR region of NKA ameliorated cardiac hypertrophy and fibrosis in a 5/6 nephrectomy model, suggesting the therapeutic potential of NKA modulation in renal disease-associated cardiac complications.[6]

Quercetin (3,3,4,5,7-pentahydroxyflavone) is a potent antioxidant flavonoid with recognized benefits for kidney health. In experimental diabetic nephropathy, quercetin protects renal cells from oxidative stress and apoptosis, while its antioxidant, anti-inflammatory, and cytoprotective actions reduce renal inflammation and fibrosis, highlighting its potential as a therapeutic agent in kidney diseases.[7,8]

Considering that MS-induced oxidative stress impairs renal function and alters NKA expression, we hypothesize that quercetin supplementation may attenuate oxidative stress and restore NKA protein levels in the kidneys of high-sucrose-fed rats. By scavenging ROS, modulating adipokine signaling, and improving renal functional markers, quercetin is expected to exert renoprotective effects, offering insight into its potential to preserve renal homeostasis in MS.[1,10]

Materials and Methods

Ethical Statement

This study was approved by the Ankara University Faculty of Medicine Animal Experiments Local Ethics Committee (2015-2-37). The study was conducted in accordance with the Declaration of Helsinki.

Study Design and Study Groups

The rats were randomly assigned to four experimental groups, as described below:

1. Control group (C, n=8): Rats received standard chow and water throughout the 20-week study period and were administered corn oil through gavage during the final 2 weeks to serve as a vehicle control for the quercetin-treated groups
2. High-sucrose-fed group (HSF, n=8): Rats were given 935 mM (≈32% w/v)[11] sucrose in drinking water for 20 weeks to induce metabolic stress and received corn oil via gavage during the final 2 weeks as a vehicle control.
3. Control group treated with quercetin (Q, n=8): Rats received standard chow and water, and were administered quercetin dissolved in corn oil at 15 mg/kg/day via gavage during the final 2 weeks (Sigma-Aldrich, Missouri, USA).
4. Quercetin-treated high-sucrose-fed group (HS-Q, n=8): Rats received 935 mM (≈32% w/v) sucrose in drinking water for 20 weeks and were administered quercetin (15 mg/kg/day in corn oil) through gavage during the final 2 weeks.

The quercetin administration period was determined based on durations commonly used in the literature[12] and on considering the potential effects of extended treatment on animal aging and the measured parameters. Both the C and HSF groups received corn oil through gavage to serve as appropriate procedural controls. Randomization was performed using numbers generated in Microsoft Excel.

Laboratory Animals and Care

Male Wistar Albino rats, 3 months old and weighing between 200 and 250 g, were utilized in the study. They were maintained under controlled conditions, including a 12-h light/dark cycle, a temperature of 24°C±2°C, and 35–60% humidity. The rats were provided with standard laboratory feed and had ad libitum access to water.

Laboratory Investigations

Measurement of Biochemical Parameters

The body weights of the rats were recorded weekly to monitor any changes. Following an overnight fast, fasting blood glucose (FBG) levels were measured in each experimental group every week throughout the study period. FBG was determined by collecting blood samples from the tail vein using a standard glucometer (ACCU-CHEK Performa Nano). At the end of the experimental period, insulin and triglyceride levels were measured in blood samples collected from the experimental groups using commercial kits (Cayman). The homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using the formula: HOMA-IR = (FBG [mmol/L]×fasting insulin [mU/L])/22.5. The HOMA-β index was determined using the formula: HOMA-β=(×20 fasting insulin [mU/L])/(fasting glucose [mmol/L] - 3.5).

Measurement of Renal Function Markers in Serum

Serum levels of renal function markers, including uric acid, urea, and creatinine, were determined using the Berthelot reagent method described by Akpotaire and Seriki,[13] the enzyme colorimetric method by Ran et al.,[14] and the method of Qin et al.,[15] respectively. Serum albumin and blood urea nitrogen (BUN) levels were measured using quantitative diagnostic kits (Abcam, Cambridge, MA, USA).

Preparation of Renal Tissue Homogenates

Kidney tissues were homogenized in ice-cold Tris-HCl buffer (20 mM, pH 7.4) containing 150 mM NaCl, 2 mM KCl, 2 mM EDTA, 0.5 mM DTT, ×100 protease inhibitor cocktail, 0.4 mM PMSF, and 2% NP-40 using a Teflon homogenizer. Protein concentrations were quantified by the Bradford method (Bio-Rad), with bovine serum albumin used as the calibration standard.

Assessment of Oxidative Stress Markers in Kidney Tissue

The amount of reduced glutathione (GSH) in kidney tissue homogenates was determined according to the method described by Ellis.[16] Superoxide dismutase (SOD) activity was measured using an enzymatic assay based on its ability to inhibit the reduction of nitroblue tetrazolium (NBT) by the xanthine–xanthine oxidase system, which generates superoxide radicals. One unit of SOD activity corresponded to 50% inhibition of NBT reduction. MDA levels were determined using the thiobarbituric acid reaction, and the intensity of the resulting pink coloration was measured spectrophotometrically at 532 nm. Total antioxidant status (TAS) and total oxidant status (TOS) were measured using commercial kits (Rel Assay Diagnostics).

Determination of NKA Protein Levels in Renal Tissue Homogenate

NKA protein expression was assessed by Western blotting. Kidney samples containing 20 µg of protein were separated on a 10% sodium dodecyl sulfate-polyacrylamide gel electrophoresis gel and subsequently transferred onto a nitrocellulose membrane. The membranes were incubated with specific primary antibodies against NKA (1:300, Santa Cruz Biotechnology) and β-actin (1:2000, Santa Cruz Biotechnology). After thorough washing, the blots were treated with a goat anti-mouse secondary antibody (1:12,000, Santa Cruz Biotechnology). Immunoreactive protein bands were visualized using an enhanced chemiluminescence (ECL) detection system (ECL; GE Healthcare Life Sciences, Budapest, Hungary). β-actin was used as an internal reference (loading control) to normalize protein levels. Band intensities were analyzed using ImageJ software (IJ 1.46r).

Table 1. Body weights of experimental groups measured at the beginning and end of the experimental period

Parameters/ groups	Body weight (0 day) (g)	Body weight (after 20 weeks) (g)
C (n=8)	224.9±17.0	323.8±20.1
HSF (n=8)	225.8±19.1	422.0±20.1[a]
Q (n=8)	225.3±13.3	328.4±25.1[b]
HS-Q (n=8)	224.8±10.6	417.5±19.8[a,c]

Different superscript letters indicate significant pairwise differences ($p<0.05$): a: Versus C; b: Versus HSF; c: Versus Q. C: Control group, HSF: High sucrose-fed group, Q: Quercetin-treated group, HS-Q: Quercetin-treated high sucrose-fed group. All parameters are expressed as mean±standard deviation. n: Number of animals.

Statistical Analysis

Statistical analyses were performed using GraphPad Prism version 5.0 (GraphPad Software, Boston, MA, USA). Data are presented as mean±standard deviation. Normality and homogeneity of variances were assessed using the Shapiro–Wilk and Levene's tests, respectively, and all datasets met these assumptions. Comparisons among groups were performed using one-way analysis of variance followed by Bonferroni's post hoc test. Detailed results of these analyses are provided in the Supplementary Material.

Results

Influence of Quercetin on Metabolic Parameters

At the end of the twenty-week experimental period, the HSF group showed weight gain and central obesity compared with controls ($p<0.001$), while quercetin supplementation partially attenuated weight gain ($p>0.05$) (Table 1). Adiposity in the HSF group was associated with increased food and water intake. Metabolic parameters, including FBG, insulin, HOMA-IR, and triglycerides, were elevated in the HSF group compared with controls (FBG, insulin, HOMA-IR, TG; all $p<0.001$). Quercetin administration reduced these elevations, although only TG levels were significantly lower in the HS-Q group compared with HSF ($p<0.001$). No significant differences were observed between the control and quercetin-only groups (all $p>0.05$) (Table 2).

Quercetin Ameliorated Renal Parameters in HSF Rats

Renal function parameters are presented in Table 2. The HSF group showed elevated serum urea, uric acid, creatinine, and

Table 2. Biochemical parameters of the experimental groups

Parameters/groups	C (n=8)	HSF (n=8)	Q (n=8)	HS-Q (n=8)
Urea (mg/dL)	20.1±5.14	49.7±5.26[a]	21.0±3.82[b]	32.5±6.07[a,b,c]
Uric acid (mg/dL)	1.44±0.42	4.35±0.48[a]	1.36±0.40[b]	1.96±0.26[b,c]
Creatinine (mg/dL)	0.65±0.24	1.54±0.35[a]	0.59±0.29[b]	1.05±0.24[b,c]
Albumin (g/dL)	4.5±0.5	2.2±0.4[a]	4.0±0.5[b]	3.8±0.7[b]
BUN (mg/dL)	32.2±6.1	54.1±5.5[a]	30.7±4.5[b]	49.7±6.9[a,c]
Blood glucose (mg/dL)	302.3±53.8	435.8±34.1[a]	3245.0±29.39[b]	413.3±31.6[a,c]
Insulin (ng/mL)	1.1±0.2	2.9±0.3[a]	1.0±0.5[b]	2.2±0.6[a,c]
Triglyceride (mg/dL)	31.8±5.8	65.1±6.9[a]	33.4±6.2[b]	45.5±5.4[a,b,c]
HOMA-IR	10.1±3.4	17.7±4.0[a]	10.7±1.8[b]	15.0±3.4
HOMA-β	0.52±0.04	0.46±0.03[a]	0.49±0.04	0.47±0.04

Different superscript letters indicate significant pairwise differences (p<0.05): a: Versus C; b: Versus HSF; c: Versus Q. C: Control group; HSF: High sucrose-fed group; Q: Quercetin-treated group; HS-Q: Quercetin-treated high sucrose-fed group; BUN: Blood urea nitrogen; HOMA-IR: Homeostatic model assessment of insulin resistance. All parameters are expressed as mean±standard deviation. n: Number of animals.

BUN levels (all p<0.001), while serum albumin was decreased (p<0.001) compared with controls. Quercetin treatment attenuated these changes, restoring urea, uric acid, and albumin levels close to control values (all p<0.001). Creatinine and BUN showed decreasing trends after quercetin treatment, although differences with controls were not statistically significant (creatinine, BUN; p>0.05). Quercetin alone did not affect basal renal parameters (all p>0.05).

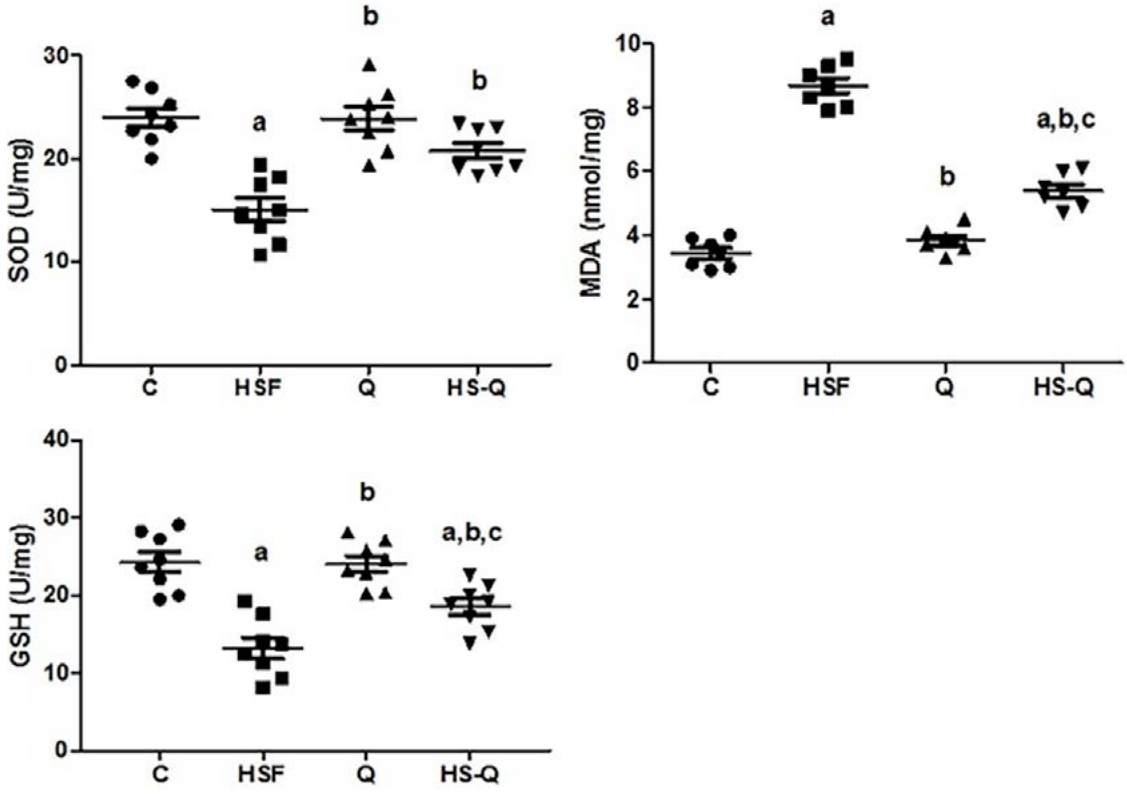

Figure 1. Oxidative stress parameters measured in the kidney tissues of experimental groups.

The annotation "a" indicates a significant difference compared with the C group at p<0.05. The annotation "b" indicates a significant difference compared with the HSF group at p<0.05. The annotation "c" indicates a significant difference compared with the Q group at p<0.05. SOD: Superoxide dismutase; MDA: Malondialdehyde; GSH: Reduced glutathione; C: Control group; HSF: High sucrose-fed group, which received 935 mM sucrose in drinking water for 20 weeks; Q: Quercetin-treated group, administered 15 mg/kg/day by gavage during the last 2 weeks (Sigma-Aldrich, Missouri, USA); HS-Q: Quercetin-treated high sucrose-fed group, which received 15 mg/kg/day quercetin by gavage during the past 2 weeks.

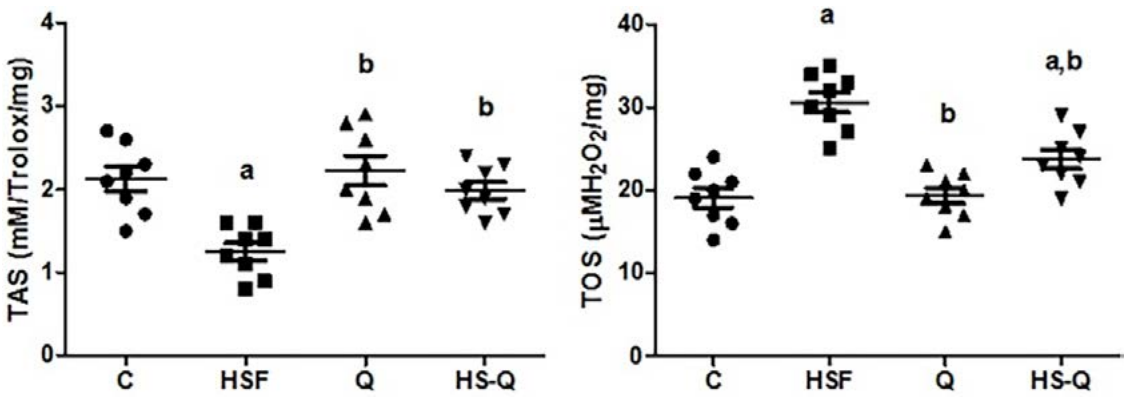

Figure 2. Total antioxidant status level and total oxidant status level measured in kidney tissues of experimental groups.

The annotation "a" indicates a significant difference compared with the C group at p<0.05. The annotation "b" indicates a significant difference compared with the HSF group at p<0.05. The annotation "c" indicates a significant difference compared with the Q group at p<0.05. C: Control group; HSF: High sucrose-fed group, which received 935 mM sucrose in drinking water for 20 weeks; Q: Quercetin-treated group, administered 15 mg/kg/day by gavage during the past 2 weeks (Sigma-Aldrich, Missouri, USA); HS-Q: Quercetin-treated high sucrose-fed group, which received 15 mg/kg/day quercetin by gavage during the past 2 weeks.

Effects of Quercetin on Oxidative Stress Parameters in Renal Tissue

As shown in Figure 1, high-sucrose treatment increased oxidative stress, as indicated by decreased SOD activity and GSH levels (p<0.001), and increased MDA concentrations (p<0.001) compared with controls. Quercetin supplementation partially restored SOD (p>0.05) and GSH (p>0.05) levels and reduced MDA (p<0.001). No significant differences were observed between the control and quercetin-only groups (all p>0.05).

Influence of Quercetin on TAS and TOS Levels in Kidney Tissue

As shown in Figure 2, high-sucrose treatment impaired renal antioxidant defense, as indicated by decreased TAS activity (p<0.001) and increased TOS levels (p<0.001) compared with controls. Quercetin administration partially restored TAS (p>0.05) and reduced TOS (p<0.001). No significant differences were observed between the control and quercetin-only groups (all p>0.05).

High Sucrose Intake Raised Levels of NKA Protein in the Tubules

As shown in Figure 3, high-sucrose treatment increased renal NKA protein levels compared with controls (p<0.001). Quercetin administration partially reduced this elevation (p>0.05), although the difference was not statistically significant. No significant differences were observed between the control and quercetin-only groups (p>0.05).

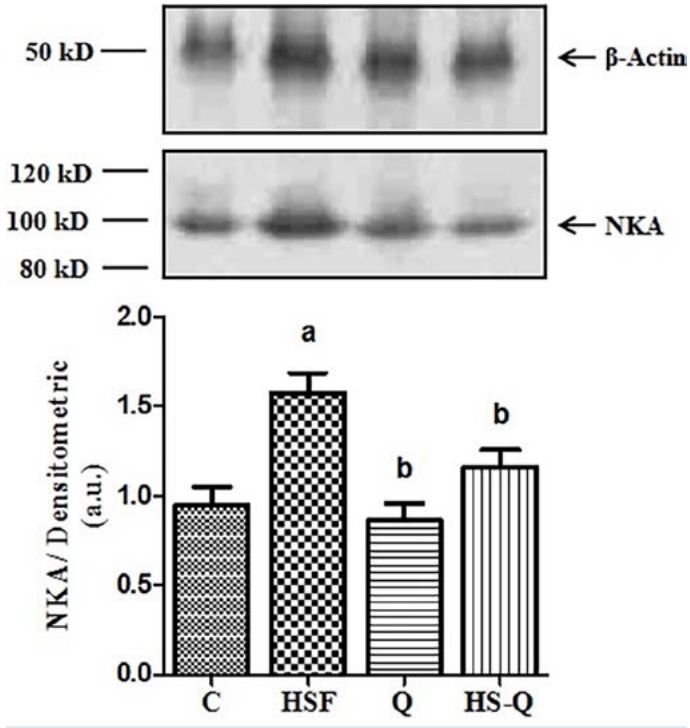

Figure 3. Tubular Na+/K+ ATPase (NKA) protein levels measured in kidney tissues of experimental groups. Upper figure: Representative examples of western blot analysis. Lower figure: Densitometric analysis of NKA protein levels in kidney homogenates.

The annotation "a" indicates a significant difference compared with the C group at p<0.05. The annotation "b" indicates a significant difference compared with the HSF group at p<0.05. The annotation "c" indicates a significant difference compared with the Q group at p<0.05. Data are presented as mean±standard deviation. n: number of animals=8. C: Control group; HSF: High sucrose-fed group, which received 935 mM sucrose in drinking water for 20 weeks; Q: quercetin-treated group, administered 15 mg/kg/day by gavage during the last 2 weeks (Sigma-Aldrich, Missouri, USA); HS-Q: Quercetin-treated high sucrose-fed group, which received 15 mg/kg/day quercetin by gavage during the past 2 weeks.

Discussion

Hyperglycemia, a defining feature of MS as outlined by the National Cholesterol Education Program Adult Treatment Panel III (ATP III), is a key driver of ROS production and oxidative stress.[17] Elevated ROS disrupts insulin signaling and promotes insulin resistance,[18] thereby contributing to the pathogenesis and progression of MS and its related complications.[19] In this context, the present study investigated whether oral quercetin administration could attenuate renal oxidative damage, assessed through oxidative stress markers and NKA protein expression, as well as systemic metabolic parameters, including glucose, insulin, and HOMA-IR levels, in a high-sucrose-induced MS rat model. Furthermore, we examined whether quercetin's potential renoprotective effects are mediated through improvements in local renal parameters, systemic metabolic regulation, or both.

At the end of the experiment, rats receiving the high-sucrose diet exhibited increased body weight, abdominal obesity, insulin resistance, hyperglycemia, and elevated HOMA indices, confirming successful induction of MS. The absence of significant improvement in fasting glucose, insulin, and HOMA-IR following quercetin treatment suggests that the compound exerts limited influence on systemic glycemic control under the present conditions. This lack of systemic effect may relate to the relatively short treatment duration, as extending the quercetin exposure could have introduced confounding, age-related physiological changes in the animals.

Serum urea, uric acid, and creatinine are reliable systemic markers of renal function, with elevated levels reflecting impaired filtration and excretion. Consistent with previous findings that obesity and hyperglycemia cause renal dysfunction,[20] high sucrose intake in our model increased these parameters. Quercetin supplementation effectively reversed these alterations, indicating a protective effect on renal excretory function. These observations are consistent with prior reports of antioxidant interventions in diabetic nephropathy models. For instance, curcumin treatment in streptozotocin-induced diabetic rats significantly reduced elevated serum urea, uric acid, creatinine, and BUN levels, indicating improved renal excretory function and mitigation of oxidative damage.[21] Taken together, these results suggest that quercetin can restore kidney function parameters, likely by attenuating hyperglycemia-induced oxidative stress and preserving renal tissue integrity.

MS promotes lipid peroxidation of polyunsaturated fatty acids, leading to the formation of MDA, a key marker of local oxidative stress. In this study, MDA concentrations were significantly elevated in the kidneys of high-sucrose-fed rats, while quercetin treatment markedly lowered them, indicating effective attenuation of oxidative stress. Similar reductions in renal MDA have been observed with other antioxidant interventions, such as Hibiscus sabdariffa supplementation in MS rats.[22] The antioxidant effect of quercetin observed here likely reflects its ROS-scavenging ability and capacity to strengthen endogenous antioxidant defenses, thereby preventing lipid peroxidation-mediated injury.

Clinical studies in MS patients have reported diminished antioxidant defenses, reflected by decreased SOD activity and increased protein and lipid oxidation.[23] Consistent with these findings, we observed that sucrose feeding significantly reduced renal SOD and GSH levels, which serve as local antioxidant parameters, reflecting impaired oxidative balance. Previous studies have also shown that oxidative alterations in diabetes vary depending on the disease stage and cellular compartment. For instance, transient increases in mitochondrial GSH and glutathione peroxidase activity occur during early experimental diabetes as compensatory responses to oxidative stress, before antioxidant systems become depleted.[24] In contrast, the decline in total renal SOD and GSH observed in our model likely reflects exhaustion of these adaptive mechanisms under prolonged metabolic stress. Notably, the antioxidant effect of quercetin involves reinforcement of endogenous defense pathways and attenuation of oxidative injury in renal tissues.

While clinical interventions, such as SGLT2 inhibitors, have been shown to increase TAS levels without significantly altering TOS, indicating enhanced systemic antioxidant capacity rather than a reduction in oxidant load[25] our high-sucrose feeding model decreased renal TAS and increased TOS, reflecting a disruption of redox homeostasis and an elevated local oxidative burden. Quercetin supplementation counteracted these changes, further supporting its renoprotective and antioxidant effects against metabolic-stress-induced oxidative injury.

A recently identified mechanism of ROS-mediated tubular injury involves the myo-inositol oxidizing enzyme, expressed in renal tubules and regulated by oxidative stress and hyperglycemia. Its overactivation contributes to tubulointerstitial damage, particularly under obese or diabetic conditions.[26] Consistent with this mechanism, insulin resistance, abdominal obesity, and hyperglycemia in our model likely contributed to renal oxidative stress and subsequent tubular dysfunction.

In diabetic nephropathy, NKA upregulation has been associated with its mislocalization from the basolateral to apical membranes or into cytoplasmic regions, impairing physiological function despite higher expression.[27] Thus, the increase observed in sucrose-fed rats may represent a maladaptive, functionally compromised state. Conversely, other studies have reported decreased NKA activity and mRNA expression in diabetic kidneys, both of which were partially restored by quercetin through its antioxidant action.[28] In fructose-fed rats, quercetin improved ATP-binding affinity but did not fully restore catalytic activity (Vmax), underscoring oxidative stress-induced structural and kinetic disruption of the enzyme.[29] Therefore, quercetin's ability to normalize NKA levels in our model may reflect the prevention of pathological overexpression and mislocalization rather than simple downregulation. By mitigating oxidative stress and stabilizing NKA subunits, quercetin may help maintain appropriate enzyme localization and activity, thereby preserving sodium-driven glucose reabsorption and tubular homeostasis under metabolic stress. These findings are consistent with broader evidence of quercetin's renoprotective effects across diverse models of diabetic nephropathy.

Notably, quercetin administration in healthy rats did not significantly alter renal or oxidative parameters, indicating that its beneficial effects are more pronounced under metabolic or oxidative stress conditions.

Our findings indicate that administering 15 mg/kg/day of quercetin via gavage during the final two weeks of a 20-week MS induction in rats represents a short-term therapeutic intervention rather than a chronic treatment. Using body surface area normalization (Km=6 for rats, Km=37 for humans), this corresponds to a human equivalent dose of approximately 2.4 mg/kg, which falls within the lower range of doses reported as safe and biologically active in human clinical studies. The short duration was intentionally selected to avoid age-related physiological changes in the rats, which could confound metabolic, oxidative, and inflammatory parameters. While this regimen captures the acute corrective or antioxidant effects of quercetin, translating these findings to human metabolic disorders, such as obesity, insulin resistance, or dyslipidemia, would likely require longer treatment periods, formulations with enhanced bioavailability, or higher daily doses to achieve meaningful clinical outcomes. Furthermore, potential side effects in humans, including gastrointestinal discomfort, headache, or mild interactions with certain medications, should be carefully considered when designing clinical interventions. These considerations highlight the importance of careful dose selection, treatment duration, and safety monitoring when extrapolating preclinical quercetin data to human applications.

Limitations

The current study has the following limitations: First, urine collection from the experimental groups was not performed, preventing measurement of proteinuria and albuminuria levels; and second, histological examination was not conducted.

Conclusion

Quercetin may enhance antioxidant capacity and provide a protective effect on renal function in rats exposed to high-sucrose diets. This protective effect appears to result from a direct local antioxidant action rather than indirect effects via systemic glycemic control. Rats fed a high-sucrose diet exhibited MS features, including abnormal fat accumulation, reduced insulin sensitivity, elevated triglycerides, and hyperglycemia, all of which were partially ameliorated by quercetin treatment, as reflected in improved renal function tests. By demonstrating renoprotective actions, including reduced oxidative stress and regulation of NKA expression, quercetin shows potential for kidney protection in conditions associated with MS or diet-induced renal stress. From a clinical perspective, these findings provide supportive evidence for exploring quercetin as a therapeutic adjunct; however, further human studies are needed to confirm its efficacy, optimal dosing, and safety profile before any clinical recommendations can be made.

Ethics Committee Approval: The Ankara University Faculty of Medicine Animal Experiments Local Ethics Committee granted approval for this study (date: 11.02.2015, number: 2015-2-37).

Informed Consent: An experimental study, not applicable.

Conflict of Interest: None declared.

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References

1. Lin L, Tan W, Pan X, Tian E, Wu Z, Yang J. metabolic syndrome-related kidney ınjury: a review and update. Front Endocrinol (Lausanne) 2022;13:904001. [CrossRef]
2. Xiao H, Shao X, Gao P, Zou H, Zhang X. Metabolic syndrome components and chronic kidney disease in a community population aged 40 years and older in southern china: a cross-sectional study. Diabetes Metab Syndr Obes 2022;15:839-48. [CrossRef]
3. Siraki AG. The many roles of myeloperoxidase: From inflammation and immunity to biomarkers, drug metabolism and drug discovery. Redox Biol 2021;46:102109. [CrossRef]
4. Kim TM, Lee KW, Kim HD, Hong SO, Cho HJ, Yang JH, et al. Evaluation of selected markers in kidneys of cynomolgus monkey (Macaca fascicularis) with induced diabetes during renal ischemia-reperfusion injury. Comp Med 2023;73(5):357-72. [CrossRef]
5. Massey KJ, Li Q, Rossi NF, Keezer SM, Mattingly RR, Yingst DR. Phosphorylation of rat kidney Na-K pump at Ser938 is required for rapid angiotensin II-dependent stimulation of activity and trafficking in proximal tubule cells. Am J Physiol Cell Physiol 2016;310(3):C227-32. [CrossRef]
6. Zheng J, Lan P, Meng X, Kang MC, Huang X, Yan X. Na+/K+-ATPase DR region antibody ameliorated cardiac hypertrophy and fibrosis in rats with 5/6 nephrectomy. Exp Biol Med (Maywood). 2022;247(19):1785-94. [CrossRef]
7. Tunçdemir M, Mirzataş EB, Uzun H. Renoprotective potential of quercetin in experimental diabetic nephropathy: assesing antiapoptotic and antioxidant effects. Arch Clin Exp Med 2018;3(3):179-85. [CrossRef]
8. Chen YQ, Chen HY, Tang QQ, Li YF, Liu XS, Lu FH, et al. Protective effect of quercetin on kidney diseases: From chemistry to herbal medicines. Front Pharmacol 2022;13:968226. [CrossRef]
9. Zeng YF, Li JY, Wei XY, Ma SQ, Wang QG, Qi Z, et al. Preclinical evidence of reno-protective effect of quercetin on acute kidney injury: a meta-analysis of animal studies. Front Pharmacol 2023;14:1310023. [CrossRef]
10. Kılıç Toprak E, Tunç Ata M. Yüksek fruktozlu diyet ile metabolik sendrom oluşturulmuş sıçanlarda quercetinin perirenal yağ dokusu, adiponektin ve resistin düzeyleri üzerine etkisi. Pam Tıp Derg 2024;17:347-57.
11. Dubljević O, Ković V, Pavković Ž, Mitić M, Pešić V. The influence of unlimited sucrose intake on body weight and behavior-findings from a mouse model. Brain Sci 2022;12(10):1332. [CrossRef]
12. Silvestro S, Bramanti P, Mazzon E. Role of quercetin in depressive-like behaviors: findings from animal models. Appl Sci 2021;11(15):7116. [CrossRef]
13. Akpotaire PA, Seriki SA. Assessment and correlation of serum urea and creatinine levels in normal, hypertensive, and diabetic persons in Auchi, Nigeria. Arch Pathol Clin Res 2023;7:007-16. [CrossRef]
14. Ran Z, Wang X, Zhang L, Yang Y, Shang Z, Chen Q, et al. Enzymatic colorimetric method for turn-on determination of l-lactic acid through indicator displacement assay. J Biosci Bioeng 2023;136:159-65. [CrossRef]
15. Qin X, Yuan C, Geng G, Shi R, Cheng S, Wang Y. Enzyme-free colorimetric determination of uric acid based on inhibition of gold nanorods etching. Sens Actuators B Chem 2021;333:129638. [CrossRef]
16. Ellis HR. On 'Tissue sulfhydryl groups' by George L.Ellman. Arch Biochem Biophys 2022;726:109174. [CrossRef]
17. Sharma L, Sharma D. Role of antioxidants as immunity booster in obesity and diabetes: a systematic review on neuro-gliopathies perspective. Explor Neurosci 2024;3:103-29. [CrossRef]
18. McKeegan K, Mason SA, Trewin AJ, Keske MA, Wadley GD, Della Gatta PA, et al. Reactive oxygen species in exercise and insulin resistance: Working towards personalized antioxidant treatment. Redox Biol 2021;44:102005. [CrossRef]
19. Bigagli E, Lodovici M. Circulating oxidative stress biomarkers in clinical studies on type 2 diabetes and its complications. Oxid Med Cell Longev 2019;2019:5953685. [CrossRef]
20. Amin KA, Nagy MA. Effect of Carnitine and herbal mixture extract on obesity induced by high fat diet in rats. Diabetol Metab Syndr 2009;1(1):17. [CrossRef]
21. ALTamimi JZ, AlFaris NA, Al-Farga AM, Alshammari GM, BinMowyna MN, Yahya MA. Curcumin reverses diabetic nephropathy in streptozotocin-induced diabetes in rats by inhibition of PKCβ/p66Shc axis and activation of FOXO-3a. J Nutr Biochem 2021;87:108515. [CrossRef]
22. Rodríguez-Fierros FL, Guarner-Lans V, Soto ME, Manzano-Pech L, Díaz-Díaz E, Soria-Castro E, et al. Modulation of renal function in a metabolic syndrome rat model by antioxidants in Hibiscus sabdariffa L. Molecules 2021;26(7):2074. [CrossRef]
23. Martemucci G, Fracchiolla G, Muraglia M, Tardugno R, Dibenedetto RS, D'Alessandro AG. Metabolic syndrome: a narrative review from the oxidative stress to the management of related diseases. Antioxidants (Basel) 2023 8;12(12):2091. [CrossRef]
24. Kiraz ZK, Kar E, Kar F, Kocatürk E, Kebapçı MN, Alataş İÖ, et al. Oxidative status and thiol/disulfide homeostasis are changed during 75 g oral glucose tolerance test over a five-hour period. J Invest Surg 2022;35(8):1626-34. [CrossRef]
25. Buyukaydin B, Ozer OF, Ozder A, Yildiz C. The changes of oxidative stress markers and vitamin E in patients with diabetes using SGLT2 inhibitors. Int J Med Biochem 2023;6(3):185-90. [CrossRef]
26. Gronda E, Jessup M, Iacoviello M, Palazzuoli A, Napoli C. Glucose metabolism in the kidney: neurohormonal activation and heart failure development. J Am Heart Assoc 2020;9(23):e018889. [CrossRef]
27. Banki NF, Ver A, Wagner LJ, Vannay A, Degrell P, Prokai A, et al. Aldosterone antagonists in monotherapy are protective against streptozotocin-induced diabetic nephropathy in rats. PloS one 2012;7(6):e39938. [CrossRef]

28. Bashir SO, Morsy MD, Sakr HF, El Refaey HM, Eid RA, Alkhateeb MA, et al. Quercetin ameliorates diabetic nephropathy in rats via modulation of renal Na+, K+-ATPase expression and oxidative stress. Am J Pharmacol Toxicol 2014;9(1):84-95. [CrossRef]

29. Vrbjar N, Vlkovicova J, Snurikova D, Kalocayova B, Zorad S, Culafic T, et al. Alterations in oxidative stress markers and Na,K-ATPase enzyme properties in kidney after fructose intake and Quercetin intervention in rats. Life 2023;13(4):931. [CrossRef]