Effect of quercetin on some biochemical parameters in adult rats treated with sodium nitrite

Eman Salem Mahmoud*
Department of Basic Sciences, Dentistry College, Mosul University, Iraq
Mutaa Abdulmtaleb Al-Hayali
Department of Physiology, Biochemistry and Pharmacology, Veterinary College, Mosul University, Iraq
Sana abdulilahabdulmawjood
Chemistry Department, Science College, Mosul University, Iraq

*Corresponding author. E-mail: Eman_salim@uomosul.edu.iq

Research Article

INTRODUCTION

Quercetin is a flavonoid (a type of flavanol) that can be found in tea, spices, nuts, vegetables, fruits (Shabbir et al., 2021 .(There are numerous health benefits to this flavonoid, including its ability to reduce inflammation, inhibit the growth of bacteria and viruses; and prevent blood clots formation (Aljadaan et al., 2020; Di Petrillo et al., 2022). It is a metal chelator with a high concentration of phenolic hydroxyl groups (Yanget al., 2020) Quercetin has been revealed in animal studies to protect against drug-induced genotoxicity lung damage, and oxidative stress (Wai et al., 2020). The anti-diabetic properties of quercetin can be used to treat atherosclerosis, heart disease, kidney damage, and liver fibrosis. Finally, current research suggests that flavonoids may be anti-diabetic (Ansari et al., 2022 ). Quercetin has anticarcinogenic, cataract-prevention, anti-ulcer, anti-allergic and anti-diabetic properties and cardio-vascular protection (Bahiya et al., 2020; Azeem et al., 2023).

Sodium nitrite stops bacteria from growing and makes meat and fish taste better, which makes them last longer. (Karwowska et al., 2020) The nitrosamines and the reactivity of additives with amines in food explain the harmful effects of NaNO2 (Xie et al., 2023) Nitrosamines produced by this process can cause lipid peroxidation, membrane fluidity degradation, and cell membrane damage (Karwowska et al., 2020). Due to nitrite exposure, the production of ROS (reactive oxygen species) , RNS (reactive nitrogen species) goes up. This can cause hepatotoxicity, nephrotoxicity, inflammatory

Abstract

Sodium nitrite and quercetin are frequently employed as protective agents on glucose levels, levels of thyroid hormones, and lipid profile. The present study aimed to see the quercetin effect on some biochemical parameters in adult rats treated with sodium nitrite. A total of twenty-one laboratory animals (Wistar albino rats) were used in this experiment, separated into three groups of seven animals each. During the trial, Group I was given water only to drink and Group II received sodium nitrite directly by oral feeding needle. The study used 80 mg.kg-1/body weight (BW) of sodium nitrite, while Group III received drinking water containing sodium nitrite orally in doses of up to 80 mg.kg-1 BW and quercetin with a (50 mg/kg ). After blood was drawn and serum extracted, the parameters determined were thyroid hormones, lipids, Homeostasis Model Evaluation for Insulin Resistance (HOMA-IR) and glucose level. The study observed that compared to the controls, the insulin (HOMA-IR) and sugar levels and lipid profile of the sodium-nitrite treated group were much higher. The sodium nitrite-treated group also had a substantial drop in thyroid hormone concentrations and a rise in Thyroid Stimulated Hormone (TSH), whereas the quercetin alleviated the harmful effects of sodium nitrate by lowering blood sugar, insulin, HOMA-IR, and improved the lipid profile. There was an improvement in glucose, insulin resistance, lipidemia, and TSH hormone levels, which increased as a result of exposure to nitrite. Thus, the present study demonstrated how quercetin protected against sodium nitrate-induced toxicity by improving several biochemical parameters in adult rats.

Keywords: Glucose, Insulin, Lipid profile, Quercetin, Sodium nitrite, Thyroid hormones

How to Cite


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process dysregulation, cell damage (Zaidi et al., 2020), problems with glucose metabolism, lipid metabolism, and changes in thyroid hormone metabolic activity by reducing thyroid hormone iodine absorption (El-Nabarawy et al., 2020). The study focused on evaluating the efficiency of quercetin in reducing hyperglycemia, hyperlipidemia and thyroid hormone disorder due to exposure to sodium nitrite.

**MATERIALS AND METHODS**

**Chemicals**

The compounds employed in this investigation were sodium nitrite (NaNO2), which was procured from BDH Laboratory reagent Chemicals Ltd, Poole, England, and quercetin (3,3,4,5,7-pentahydroxyflavone), which was acquired in powder form from Sigma - Aldrich (USA).

**Experimental design**

The Veterinary College of Mosul University provided 24 Wistar albino male rats weighing 200-220 grams. Standard ventilation, 25°C temperature, 60–70% humidity, and a light/dark ratio of 12/12 were used to house the animals in this study. The animals were split into three subgroups of eight, which each received the treatment described below for 30 days.

- **Group I (Control):** The animals were given drinking water only.
- **Group II (Sodium nitrite treatment group):** The animals were given sodium nitrite-tainted water to drink during the study. The sodium nitrite was given orally through a gavage needle at a dose body weight of (80 mg.kg-1).
- **Group III (An infected group treated with quercetin):** Throughout the trial, the animals were given drinking water containing (80 mg/kg BW) sodium nitrite and quercetin (50 mg/kg) of animal weight.

**Animal ethical approval**

The Institutional Animal Care Commission in the Veterinary Medicine College at the Mosul University aligned with the ethics of international principles in dealing with animals, reviewed the application submitted to it by us on 18/8/2021 with the code UM.VET.2021.079 and gave approval for the present study.

**Animal blood sample collection**

A pre- and post-treatment samples of the animals’ blood were collected directly from the orbital sinus puncture (intraocularly) and deposited into plain tubes after therapy; the clot was dispersed with a glass rod. Within two days of being centrifuged for 15 minutes at 3000 x, the levels of biochemical markers were measured.

**Biochemical analysis**

The level of glucose (mg/dl) was detected using a test reagent kit (Tietz, 1990). Insulin levels (U/ml) were evaluated using the sandwich principle-based (Elisa) to estimate insulin levels and determine insulin resistance (Kahn and Rosenthal, 1979).

**Insulin Resistance Evaluation Making Use of a Homeostasis Model (HOMA-IR)**

Calculation of insulin sensitivity was done with the help of the HOMA-IR (Accoding to Equation cited in Bcowe et al., 2014). HOMA-IR was determined using glucose levels and plasma insulin concentrations.

Glucose fasting mg/dl x Insulin u/L/405 = HOMA – IR

**RESULTS AND DISCUSSION**

During a 30-day treatment period, the results of sodium nitrite (80 mg/kg) and quercetin (50 mg/kg) treated animals’ body biochemical parameters were compared to those of animals who did not get any treatment.

**Sodium nitrite and quercetin’s impact on glucose and insulin hormone**

When compared to controls (HOMA-IR) (Group I) glucose, insulin, and insulin sensitivity were all elevated in the sodium nitrite group (p ≤ 0.001) (Table 1). These results align with a prior study (Helal et al., 2017) when treating rats with 0.1mg/kg day. The potential of nitrite to boost gluconeogenesis (Gheibiet al., 2018) and enhance hepatic glycogenolysis is responsible for the elevated amount of glucose in the blood. Because of the increased activity of amylase and phosphorylase that is caused by sodium nitrite, glucose is released from glycogen, which in turn causes an increase in blood sugar levels. This rise in glucose levels can also be caused by a decrease in hepatic glycogen synthesis or a reduction in glucose mobilisation (Helal et al., 2017). In addition, nitroso-compounds can potentially damage the antioxidant state, which can lead to metabolic disruption and hyperglycemia which can lead to metabolic disruption and hyperglycemia (Akhzari et al., 2019). As...
a direct consequence of these findings, patients’ insulin resistance increased (HOMA-IR). According to the calculation, the Group II treated with sodium nitrite had significantly higher insulin and glucose levels at (p ≤ 0.001). The effectiveness of the homeostasis model depends on the body’s glucose and insulin levels. The therapy with quercetin (Group III) led to a significant drop in blood sugar levels at (p ≤ 0.01). The results match those found in the previous study (Hosseini et al., 2021), where quercetin was used in different doses—5-240mg/kg/day. This improvement may be attributed to quercetin effectively mitigating the adverse effects of sodium nitrite and smoothing out glucose abnormalities. (Xie et al., 2020; Dhanya et al., 2021) Quercetin helps to increase insulin sensitivity by stimulating the proliferation of pancreatic -cells, rebuilding pancreatic islets, and protecting -cells from the oxidative damage caused by sodium nitrite. Quercetin also increases the amount of glucose transporter (GLUT4) in tissue, which makes them take in more glucose. Glycolysis GLUT4 is a glucose transporter that has vital role in glucose absorption(Shie et al., 2019), limiting intestinal glucose absorption while stimulating glucose synthesis (Ansari et al., 2022). Increasing sensitivity of insulin (Xie et al., 2020).

Quercetin and sodium nitrite altering thyroid hormones

The sodium nitrite group (Group II) had relatively lower rates of T4 and TSH than the healthy controls (Table 2) at (p = 0.001). Its matches prior studies (Kostogryz et al., 2006; Zakiet et al., 2004). To stop thyroid hormone production, nitrate blocks the sodium iodide symporter, which helps to absorb iodine into the thyroid and suppresses thyroidal iodide uptake. This disrupts the hypothalamic-thyroid hormonal axis, which results in altered thyroid hormone metabolism and decreased thyroid hormone release (T3 and T4) into the blood, which leads to hypothyroidism and other health problems. (Kostogryz et al., 2006) In response to reduced thyroid hormone synthesis, the anterior pituitary releases TSH. Nitrate can interfere with iodine binding by blocking the Na+/K+ ATP-ase complex and the sodium-iodide symporter Na+/I−. When blood hormone levels are low, TSH production goes up, the thyroid can not work as well because of oxidative stress and peroxidation of cell membrane lipids, and thyroid hormone-binding proteins are lost through urine(Dohanet al., 2003).

Serum T3 and T4 levels did not vary significantly among rats given (80 mg.kg^{-1}) sodium nitrite and (50mg.kg^{-1}) quercetin, as shown in Table 2. According to these results, quercetin efficiently minimized the negative effects of nitrite exposure while also healing the damage (Wai et al., 2021). In rats, quercetin has been demonstrated to be an effective therapy for hypothyroidism caused by NaNO2 medication. The findings of the present study confirm those of previous studies that reached similar conclusions (Zhao et al., 2020).

Serum lipid profiles using sodium nitrite and quercetin

In Table 3, when compared to the control group, rats given sodium nitrite had vastly greater concentrations of cholesterol (TC), and triacylglycerols (TG, LDL, VLDL) but substantially lower levels of high-density lipoproteins (HDL). These findings support those obtained by El-Wakf et al., 2015; Helal et al., 2017) when treating rats with sodium nitrite.

The rise in serum TC concentrations in the NaNO2 treated group could be attributed to membrane lipid peroxidation, Unsaturated fatty acid mobilization from fatty tissue into blood, and a rise in acetyl CoA levels, which causes an increase in cholesterol synthesis (Helal et al., 2000). Alternatively, the increase in serum TC concentrations could have been caused by a blockage in bile ducts in the liver, which stops or slows bile flow into the duodenum (Helal et al., 2000). Reduced thyroid secretion causes an increase in plasma levels, lipids, and TG, which almost always increases in the amount of fat being stored in the liver. This directly results from reduced thyroid secretion (Mavromati and Jornayvaz 1, 2021). Hypothyroidism is also linked to free radical formation and a drop in the body's antioxidative defenses (Huixing and Daoquan, 2022). Hyperlipidemia and oxidative stress are both caused by hypothyroidism. Both of these factors speed up the process of lipid peroxidation, which usually results in more severe atherosclerotic disease. Inflammatory responses are also caused by oxidative processes, which is a well-known harmful process in all stages of atherosclerosis (Kuš et al., 2021).

Quercetin proved effective in treating dyslipidemia brought on by sodium nitrite; when given at a daily dose of 80 mg.kg^{-1} of quercetin a day The cholesterol levels were lowered along with total fat and LDL cholesterol, while HDL-C levels were increased (Castillo et al., 2022).

Table 1. Showing biochemical parameters in rats of different Groups (n=7)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Group I</th>
<th>Sodium nitrite Group II</th>
<th>Quercetin + Sodium nitrite Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl)</td>
<td>90.02 ± 1.4</td>
<td>120.37 ± 1.02**</td>
<td>101.44 ± 1.14**</td>
</tr>
<tr>
<td>Insulin (ng/dl)</td>
<td>7.6 ± 1.1</td>
<td>10.5***0.7±</td>
<td>8.05 ± 1.3</td>
</tr>
<tr>
<td>HOMA-IR (ng/dl)</td>
<td>1.68 ± 1.5</td>
<td>3.1 ± 1.14*</td>
<td>1.9± 1.6</td>
</tr>
</tbody>
</table>

Values are expressed (average ± SD); *: p ≤ 0.05, **: p ≤ 0.01, ***: p ≤ 0.001
Table 2. Impact of sodium nitrite and quercetin on hormone and TSH levels in the blood (n=7)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Group. I</th>
<th>Sodium nitrite Group. II</th>
<th>Quercetin + Sodium nitrite Group. III</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3 hormone (ng/dl)</td>
<td>3.02 ± 1.4</td>
<td>2.72 ± 1.02</td>
<td>2.74 ± 1.14</td>
</tr>
<tr>
<td>T4 hormone (ng/dl)</td>
<td>73.6 ± 1.1</td>
<td>59.05 ±0.7***</td>
<td>70.75 ± 1.3</td>
</tr>
<tr>
<td>TSH hormone (ng/dl)</td>
<td>2.16 ± 1.5</td>
<td>4.49 ± 1.14**</td>
<td>3.12 ± 1.6*</td>
</tr>
</tbody>
</table>

Values are expressed (average ± SD); * p˂0.05, ** p˂0.01, ***p˂0.001

Table 3. Showing a changes in blood cholesterol levels using sodium nitrite and quercetin (n=7)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Group. I</th>
<th>Sodium nitrite Group. II</th>
<th>Quercetin + Sodium nitrite Group. III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>77.02 ± 1.4</td>
<td>86** ± 1.02 ± 37</td>
<td>61.44 ± 1.14**</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>82.6 ± 1.1</td>
<td>99** ± 0.7* ± 05</td>
<td>81.3 ± 9.75</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>40.16 ± 1.5</td>
<td>23.19 ± 1.14***</td>
<td>30.12 ± 1.6**</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>20.4 ± 1.7</td>
<td>4*** ± 3.4 ± 3.4</td>
<td>13*** ± 1.9 ± 3.2</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>16.52 ± 0.41</td>
<td>19.8** ± 0.6 ±</td>
<td>17* ± 0.3 ± 9.</td>
</tr>
</tbody>
</table>

Values are expressed (average ± SD); * p˂0.05, ** p˂0.01, ***p˂0.001.

2018; Muselinet et al., 2022). Most of these beneficial effects on health can be attributed to quercetin's antioxidant capabilities (Papakyriakopoulou et al., 2022; Zhang et al., 2023). One method of polyphenol impact has been associated with antioxidant activity, which lowers LDL oxidation. These substances also alter the hepatic level of cholesterol and the synthesis and generation of triglycerides. In addition, quercetin affects cholesterol absorption in the liver, the formation and release of triglycerides, and the activity of phosphodiesterases in both fatty tissue and the liver (Papakyriakopoulou et al., 2022).

The ability of thyroid hormone to lower saturated fat and triglycerides levels in animal's nd experimental medical studies through genetic control related to lipid metabolic activity (Huixing and Diaoquan, 2022) and quercetin's role in reducing overall hepatic lipogenesis (Shabbir et al., 2021) are both other hypotheses that could explain quercetin’s role in lowering atherogenic indicators.

Conclusion

The present study concluded that quercetin not only helped reduce the negative side effects of sodium nitrite therapy but also helped boost the beneficial effects of the treatment lowering glucose levels and insulin resistance, reducing hyperlipidemia and improving thyroid hormone levels in Wistar albino rats exposed to sodium nitrite.

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Conflict of interest

The author declare that they have no conflict of interest.

REFERENCES

cetin and its derivatives as antiviral potentials: A comprehensive review. Phytotherapy Res. 36, 266–278


