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Research Article

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

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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 IIIreceived 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 nitrite-induced toxicity by improving several biochemical parameters in adult rats.

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

INTRODUCTION

Quercetin is a flavonoid (a type of flavonol) 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 (Yang*et 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 (Batiha *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 $NaNO_2$ (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

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 thyroidine 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 fromBDH 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 maleratsweighing 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

TheInstitutional 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 on18/8/2021 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 dispersedwith 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 detectedusing 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 (According to Equation cited inBcowe 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 Eq.1

T_3 (Triiodothyronine), T_4 (Thyroxine) and TSH (Thyroid stimulated hormone) determination

T_3, T_4, and TSH concentrations were measuredusing ELISA kit.

Lipid profile

With a Biolabo kit (France), lipid levels were measured enzymatically, as well as cholesterol and triglycerides (Burits et al., 2012) and HDL (Kostner,1976).

Statistical analysis

Using the P-value (which happens at P≤0.05), the ‘t’test was performed to compare the two variables and then identify a significant difference in values (Stell and Torrie, 1980).

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) whentreating ratswith 0.1mg\kg\ day. The potential of nitrite to boost gluconeogenesis (Gheibi*et 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 glycogenesis 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 queurcetin was used in different doses)- 5 240mg/kg/da. 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, glycogenolysis GLUT4 is a glucose transporter that hasa vital role in glucose absorption(Shi*et al*.,2019), limiting intestinal glucose absorption while stimulating glycogen 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 T_4 and TSH than the healthy controls (Table 2) at (p≤ 0.001). Itmatchesprior studies (Kostogrys*et al*., 2006_b; Zaki*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 (T_3 and T_4) into the blood, which leads to hypothyroidism and other health problems. (Kostogrys*et al*., 2006_a) 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(Dohan*et al*., 2003).

Serum T3 andT4 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 minimisedthe 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 $NaNO_2$ 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 $NaNO_2$ 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 andJornayvaz1,2021). Hypothyroidism is also linked to free.radical formation and a drop inthe 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 (Kuś *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.,*

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

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

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)**

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

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

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

Parameters	Control Group. I	Sodium nitrite Group. II	Quercetin + sodium nitrite Group. III
Cholesterol(mg/dl)	77.02 ±1.4	86**1.02 ± 37.	61.44 ±1.14**
Triglycerides(mg/dl)	82.6 ± 1.1	99**0.7± 05.	8*1.3 ± 9.75
HDL-C (mg/dl)	40.16 ± 1.5	23.19 ± 1.14***	30.12± 1.6**
LDL-C (mg/dl)	20.4 ± 1.7	4***3.4 ± 3.4	13***1.9 ± 3.
VLDL (mg/dl)	16.52 ±0.41	19.8**0.6 ±	17*0.3 ± 9.

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

2018;Muselin*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 affectscholesterol 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 animals'nd experimental medical studies through genetic control related to lipid metabolic activity (Huixing and Daoquan,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 treatmentlowering 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

1. Akhzari M, Shafiee S M ,Rashno S &Akmali M. (2019) Berberine Attenuated Oxidative Stress Induced by Sodium Nitrite in Rat Liver. *Jundishapur J Nat Pharm Prod*.,14(1)
2. Aljadaan, S.A.N.; Elias, R.S & Al-Anssari, R.A (2020) Investigation of the Antioxidant and Antibacterial Activity of Novel Quercetin Derivatives. BiointerfaceRes. *Appl. Chem*., 10, 7329–7336
3. Ansari P, Choudhury ST, Seidel V, Rahman AB, Aziz MA& Richi AE. (2022)Therapeutic potential of quercetin in the management of type-2 diabetes mellitus. *Life,*12(8),1146
4. Azeem. M., Hanif, M., Mahmood, K., Ameer, N., Chughtai, F & Abid, U. (2023) An insight into anticancer, antioxidant, antimicrobial, antidiabetic and anti-inflammatory effects of quercetin. *A review*. *Polymer Bulletin*., 80(1), 241-262
5. Batiha, G.S., Beshbishy ,A.M & Ikram, M. (2020) The pharmacological activity, biochemical properties,and pharmacokinetics of the major natural polyphenolic flavonoid: quercetin. *Foods*.9:374
6. Bowe, J.E.; Franklin, Z.J.; Hauge-Evans, A.C.; King, A.J.; Persaud, S.J.& Jones, P.M.(2014) Metabolic phenotyping guidelines: Assessing glucose homeostasis in rodent models. *J. Endocrinol.,* 222, G13–G25.
7. Burtis ,C.A, Ashwood, E.R.& Bruns, D.E. (2012). Tietz Textbook of clinical chemistry and molecular diagnostics. *By saunders, an imprint of Elsevier Inc*.USA.
8. Castillo, R.L., Herrera E.A., Gonzalez-Candia A., Reyes-Farias M., de la Jara N., Peña J.P. & Carrasco-Pozo ,C. (2018) Quercetin Prevents Diastolic Dysfunction Induced by a High-Cholesterol Diet: Role of Oxidative Stress and Bioenergetics in Hyperglycemic Rats. *Oxid. Med. Cell. Longev.* ;1–14,7239123
9. Dhanya, R & Kartha, C.C. (2021) Quercetin Improves Oxidative Stress-Induced Pancreatic Beta Cell Alterations via MTOR-Signaling. *Mol. Cell. Biochem.* 476,3879–3887.doi: 10.1007/s11010-021-04193-3.
10. Di Petrillo, A., Orrù, G., Fais, A. & Fantini, M.C. (2022) Quer-

cetin and its derivates as antiviral potentials: A comprehensive review. *Phytotherapy Res*. 36, 266–278
11. Dohan, O.& Carrasco N.(2003) Advances in Na+/I- symporter (NIS) research in the thyroid and beyond. *Mol. Cell Endocrin*., 213, 59–70
12. El-Nabarawy, N. A., Gouda, A. S., Khattab, M. A & Rashed, L. A.(2020). Effects of nitrite graded doses on hepatotoxicity and nephrotoxicity, histopathological alterations, and activation of apoptosis in adult rats. *Env.Sci Poll. Res*, 1–14.
13. El-Wakf A.M., Hassan, H.A, Mahmoud AZ.& Habza.,M.N. (2015) Fenugreek potent activity against nitrate-induced diabetes in young and adult male rats. *Cytotechnology*.;67 (3),437–47. 24615531. Available from.
14. Gheibi S, Bakhtiarzadeh F, Jeddi S, Farrokhfall K, Zardooz H.& Ghasemi A. (2018) Effects of long-term nitrate supplementation on carbohydrate metabolism, lipid profiles, oxidative stress, and inflammation in male obese type 2 diabetic rats .*Nitric Oxide.* 1,75,27-41
15. Helal,E G.., El-Sayed, R..A. & El-Gamal ,M. S.(2017) Assessment of the Physiological Changes Induced by Sodium Nitrite, Annatto or Mono Sodium Glutamate in Male Albino Rats.*EJHM*. 67(1) , 330- 335 .
16. Helal, E.G., Zahkouk, S.A. &. Mekawy, H.A.(2000). Effect of some food colours (synthetic and natural products) on liver and kidney functions of young albino rats. Egypt.*J.Hosp. Med*. 1, 103-113.
17. Hosseini, A.,Razavi B.M., Banach M. & Hosseinzadeh H. (2021) Quercetin and metabolic syndrome: A review. *Phytother. Res.* ;35,5352–5364.doi: 10.1002/ptr.7144
18. Huixing, L& Daoquan, P .(2022)Update on dyslipidemia in hypothyroidism: the mechanism of dyslipidemia in hypothyroidism .Euro sci *Endocrine:* 11(2)
19. Kahn, C.R.& Rosenthal, A.S. (1979)Immunologic reactions to insulin, insulin allergy, insulin resistance and autoimmune insulin syndrome. *J. Diabetes Care*.; 2: 283-295.
20. Karwowska,M&Kononiuk,A.(2020) Nitrates/Nitrites in Food—Risk for Nitrosative Stress and Benefits .*Antioxidants* . 9 (3), 241.
21. Kostner ,G.M. (1976) . Enzymatic determination of cholesterol in high density lipoprotein fraction prepered by polyanion precipitation. *Clinical. Chemistry*, 22(5): 698
22. Kostogrys RB., Pisulewski PM., PecioA.(2006)a Nitrates affect thyroid status and serum triacylglycerols in Wistar rats. *Pol. J. Food Nutr. Sci*. 15/56, 1, 71–76.
23. Kostogrys, R. B.; Pisulewski, P. M. and Pecio, A. (2006) $_b$Nitrites affect thyroid status and serum lipoproteins in wistar rats. *Pol. J. Food Nutr. Sci*; 15/56 (3):353–358.
24. Kuś A, Marouli E, Del Greco MF, Chaker L, Bednarczuk T. & Peeters R, (2021) Variation in normal range thyroid function affects serum cholesterol levels, blood pressure, and type 2 diabetes risk: a mendelian randomization study. *Thyroid;*31 721–731
25. Mavromati,M& Jornayvaz1,F (2021) Hypothyroidism-Associated Dyslipidemia:Potential Molecular Mechanisms Leading to NAFLD.*Int J Mol Sci* ; 22(23): 12797
26. Muselin F., Cristina R.T., Dumitrescu E., Doma A.O., Radulov I., Berbecea A.A., Horablaga A., Morariu F.E., Manea D.N. &Horablaga N.M. (2022) Quercetin Beneficial Role in the Homeostatic Variation of Certain Trace Elements in Dyslipidemic Mice. *Evid.-Based Complement. Altern. Med.* :3299505.doi: 10.1155/2022/3299505.
27. Papakyriakopoulou, P., Velidakis, N., Khattab, E .,Valsami, G., Korakianitis, &Kadoglou, N (2022) Potential Pharmaceutical Applications of Quercetin in Cardiovascular Diseases. *Pharmaceuticals*; 15(8), 1019
28. Shabbir U, Rubab M.&DaliriE.(2021) Curcumin, quercetin, catechins and metabolic diseases: the role of gut Microbiota. *Nutrients,*; 13, 206.
29. Shi, G.J., Li ,Y., Cao, Q.H., Wu ,H.X., Tang, X.Y. & Gao, X.H.(2019) In vitro and in vivo evidence that quercetin protects against diabetes and its complications: A systematic review of the literature. *Biomedicine & Pharmacotherapy*. 109,1085-1099.doi: 10.1016/j.biopha.2018.10.130.
30. Stell ,R .G and Torrie, J. H. (1980). Principles and produce of statistics. 2-nd ed. *Mc.Graw-Hill. Company. Inc*., London.
31. Tietz, N.W.(1990) Clinical Guide to laboratory tests. (2nd ed). *W.B. Saunders Company, Philadelphia*PP: 246-250.
32. Wai ,K. ,Yeung ,A., Choudhary, N & Tewari ,D (2021) Quercetin: total-scale literature landscape analysis of a valuable nutraceutical with numerous potential applications in the promotion of human and animal. *Anim Sci Paper Rep*., 39, 199–212.
33. Xie J., Song W., Liang X., Zhang Q., Shi Y., Liu W. & Shi X. (2020) Protective effect of quercetin on streptozotocin-induced diabetic peripheral neuropathy rats through modulating gut microbiota and reactive oxygen species level. *Biomed. Pharmacother.* ;127,110147.doi: 10.1016/j.biopha.2020.110147
34. Xie , Y., Geng,Y., Yao, J ., Chen, F., Xiao , J. & Hu, X (2023) N-nitrosamines in processed meats: Exposure, formation and mitigation strategies.*J.Agri.Food .Res*. 13,100645
35. Yang, D., Wang, T., Long, M & Li, P. (2020) Quercetin: Its main pharmacological activity and potential application in clinical medicine. *Oxid Med Cell Longev*.2020: 8825387.
36. Zaidi, Z.F. (2020) Sodium Nitrite-Induced Hypoxic Nephrotoxicity in Adult Rats*. Ann. Clin. Anat*. 3(1), 1009.
37. Zaki, A., Ait Chaoui, A., Talibi, A., Derouiche, A. F., Aboussaouira, T., Zarrouck, K., Chait, A., &Himmi, T. (2004). Impact of nitrate intake in drinking water on the thyroid gland activity in male rat. *Toxicol. Lett*. 147, 27–33.
38. Zhao, P., Hu ,Z., Ma ,W., Zang,L., Tian ,Z. &Hou,Q (2020) Quercetin alleviates hyperthyroidism-induced liver damage via Nrf2 Signaling pathway*. Biofactors,* 46(4),608-6