International Journal of Anatomy and Research,
Int J Anat Res 2022, Vol 10(4):8496-04. ISSN 2321-4287
DOI: https://dx.doi.org/10.16965/ijar.2022.238

Original Research Article

Protective Role of Quercetin on Thioacetamide-Induced Renal Injury in Adult Male Albino Rats

Sally Mahmoud Mohamed Hussein omar *[1], Marwa Mohamed Abd El Aziz Ahmed [2], Marwa Mahmoud Mady [3].

*[1] Lecturer, Department of Anatomy and Embryology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.

[2] Lecturer, Pathology Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt.

[3] Lecturer, Department of Anatomy and Embryology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.

ABSTRACT

Background: Thioacetamide (TAA) is a recognized industrial poisonous agent drastically used in animal studies for induction of hepatic necrosis, fibrosis and cirrhosis. It is additionally reported to be nephrotoxic through induction of oxidative stress. Quercetin (QE) has a high antioxidant capacity via free radical scavenging, transition metal ion binding, and lipid peroxidation inhibition.

Aim of the work: The goal of this research was to see if QE may help reduce the negative effects of thioacetamide on renal tissue by histological examination of the kidney.

Material and methods: Twenty four adult male Albino rats 7–9 weeks old around 180–200g body weight were allocated into 3 groups; Group I (n=8) receiving distilled water, Group II (n=8); rats receiving TAA and Group III (n=8); receiving TAA and QE.

Results: Renal tissues were examined under a light microscope stained by Harris Hematoxylin & Eosin (H&E stain), Periodic acid Schiff (PAS) and Masson's Trichrome for TAA-treated groups revealed severe histopathological changes, whereas specimens obtained from QE-treated groups showed only mild changes. Immunohistochemical results corroborated these findings.

Conclusion: This study demonstrated the ameliorative consequences of QE in opposition to TAA-induced renal injury in rats. The result of this study might contribute in the development of a novel complementary alternative medication in combating and therapeutic intervention of TAA-induced renal injury.

KEY WORDS: Thioacetamide, renal, quercetin, albino rat and histopathology.

Corresponding Author: Dr. Sally Mahmoud Mohamed Hussein Omar, Department of Anatomy and Embryology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.
E-Mail: saliy.hessen@alexmed.edu.eg

Access this Article online	Journal Information
Quick Response code	**International Journal of Anatomy and Research** ISSN (E) 2321-4287 | ISSN (P) 2321-8967 **https://www.ijmhr.org/ijar.htm** **DOI-Prefix:** https://dx.doi.org/10.16965/ijar
DOI: 10.16965/ijar.2022.238	**Article Information** Received: 07 Aug 2022 Peer Review: 09 Aug 2022 Accepted: 20 Sep 2022 Published (O): 05 Dec 2022 Published (P): 05 Dec 2022

INTRODUCTION

In the majority of individuals with acute liver failure who are in the advanced stages of their disease, kidney dysfunction is a common concern[1].

Hepatotoxic supplies such as acetaminophen, carbon tetrachloride, lipopolysaccharides, TAA, D-galactosamine, and tumour necrosis factor alpha have all been implicated in experimentally induced hepatic damage [2-4].

Furthermore, it is now understood that TAA's damaging effects are not limited to the liver,

but may also cause morphological damage in organs such as the kidney and brain[5]. TAA was also said to be genotoxic and carcinogenic[6].

TAA is a widely used sulfur containing compound in the laboratory and in a number technical functions as fungicides, rubber chemicals, curing agents, cross linking agents, insecticides, and pharmaceuticals are just a few of the products available[7]. TAA toxicity is caused by its rapid conversion to reactive metabolites by cytochrome P450 and flavin-containing monooxygenases (thioacetamide-S- oxide and reactive oxygen species; ROS) [8].

The kidney's reaction to toxins differs with the aid that it manifests itself in a variety of morphological forms, starting with tubular or interstitial alterations and progressing to nephropathy [9]. The nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, as a major source of reactive oxygen species (ROS) in the kidney, has been significantly linked to the development of renal oxidative injury[10]. Therefore, a fantastic interest has been paid to antioxidants or free radical scavengers for the prevention and cure of kidney damage.

Quercetin (QE) is a flavonoid (of the flavonols subclass) that is extensively distributed in plants[11]. It's abundant in red wine, onions, green tea, apples, broccoli, berries, ginkgo biloba, and buck wheat tea, among other plants, plant products, and meals. [12]

In various studies, QE has been shown to be a powerful antioxidant with a high free radical scavenging activity [13]. It also has a number of pharmacological properties, including anti-diabetic, anti-inflammatory, and immuno-stimulatory properties, as well as the ability to protect low-density lipoprotein from oxidation[14].

Furthermore, studies have shown that quercetin can effectively reduce drug-induced toxicity and oxidative stress in vivo [15-17].

The goal of this study was to investigate if quercetin cotreatment might protects rats against Thioacetamide-induced kidney damage in rat models.

Aim: Present study was to investigate if Quercetin might protect against TAA-induced kidney injury.

MATERIALS AND METHODS

Animals: Twenty four adult male Albino rats 7–9 weeks old; 180–200 g body weight were obtained from the animal house, Alexandria University, Egypt. The animals were kept in the lab for a week under controlled settings.

Chemicals: Both TAA and QE were obtained from Sigma-Aldrich Corp., St. Louis, MO, USA

Experiment design: Rats were allocated into 3 groups; Group I (Control, n=8): Rats in this group received distilled water by gavage and intraperitoneal injection of normal saline (NaCl 0.9%), 5 days/week for 28 days. Group II (Thioacetamide (TAA) group, n=8); rats received TAA dissolved in NaCl 0.9% given intraperitoneally in a dose of 50mg/kg/day, 5 days/week for 28 days, this dose and duration causes low grade injury as described by Murad et al. [18] Group III (TAA-quercetin treated group, n=8); rats in this group received TAA as in group 2 and quercetin that was dissolved in distilled water and given daily. Rats will be sacrificed under anesthesia using 50 mg/kg of sodium pentobarbital.

Methods

The kidneys were harvested and 10% neutral buffered formalin used for fixation. Sections were then dehydrated by ascending grades of ethanol (70%, 90% and 100%). Xylene was used as a clearing agent then both soft and hard paraffin were consecutively used for embedding. Five–micron-thick slices were obtained and dewaxed in xylene before being rehydrated with ethanol in declining grades. (100%, 90% & 70%). Sections from the kidneys were stained by Harris Hematoxylin & Eosin (H&E), Periodic – acid Schiff (PAS) and Masson Trichrome stain. Sections were subjected to immunohistochemical staining for CD10 (Clone 56C6, ready to use, mouse monoclonal antibody, DAKO, USA), and myeloperoxidase (clone IR511, ready to use, rabbit, polyclonal antibody, DAKO, USA) performed by DAKO Autostainer. All sections were examined under light microscope (Olympus CX23). The sections were examined for signs of injury in tubules (acute tubular

injury/ necrosis), interstitial inflammation, pattern of CD10 expression (luminal / cytoplasmic) and compartmental expression of myeloperoxidase (MPO) (tubular/cytoplasmic).

RESULTS

Mortality rate: Calculated mortality rate was 50% in the TAA group throughout the period of the study (4 out of 8). No mortalities were found in the TAA-quercetin treated group or the control group. (Table 1)

Group I (Control, n=8): Sections obtained from renal tissue showed normal cortex with normal glomeruli, normal blood vessels, normal proximal and distal convoluted tubules with intact brush borders (Highlighted by PAS and CD10), intact tubular basement membrane (Highlighted by PAS and trichrome). Neither interstitial inflammation nor fibrosis was seen. Myeloperoxidase staining was completely negative both in tubules and glomerular tuft. CD10 staining was restricted to the luminal brush border with no cytoplasmic staining in the tubules. (**Fig. 1.A, Fig. 2.A & B, Fig.3.A & B**)

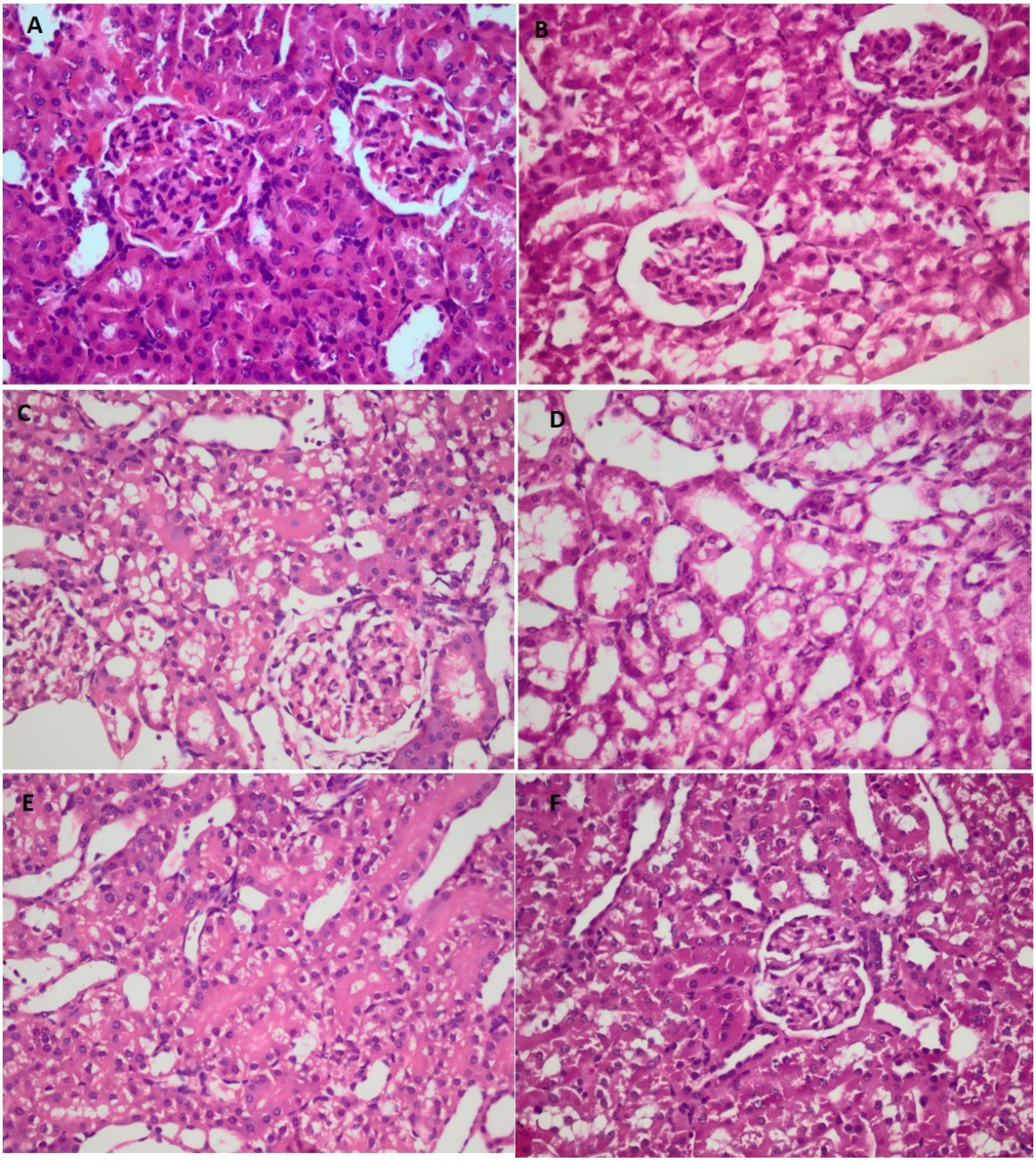

Fig. 1: A: Normal kidney in group I. B: Moderate injury in group II. C: Severe injury in group II. D: severe tubular injury in group II. E: Moderate tubular injury in group II. F: Mild injury in group III.

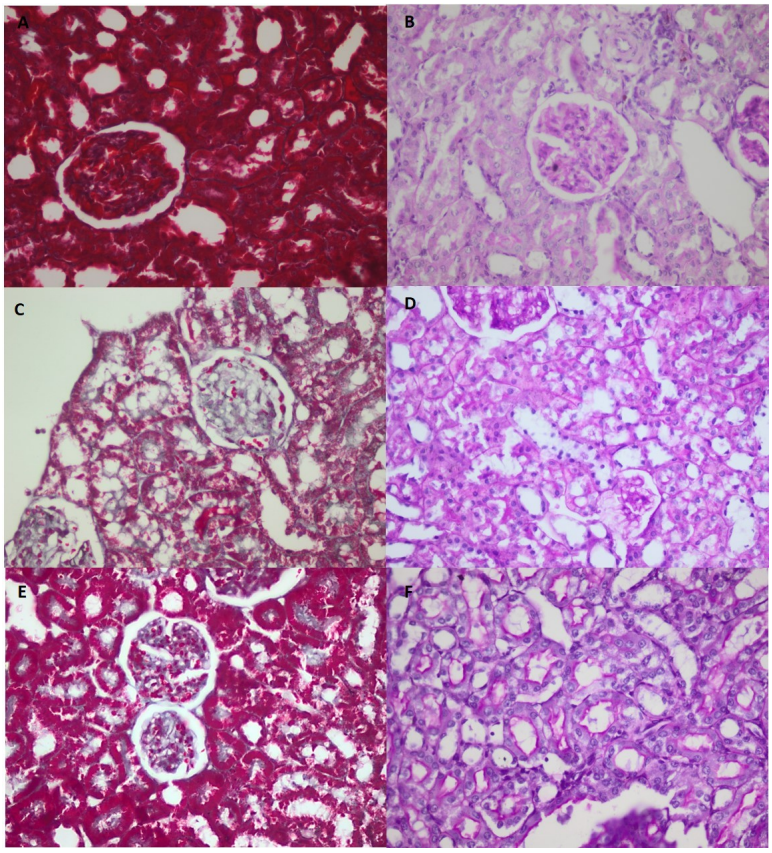

Fig. 2: A &B: Normal kidney in group I. C&D: Severe injury in group II. E&F: Mild injury in group III.

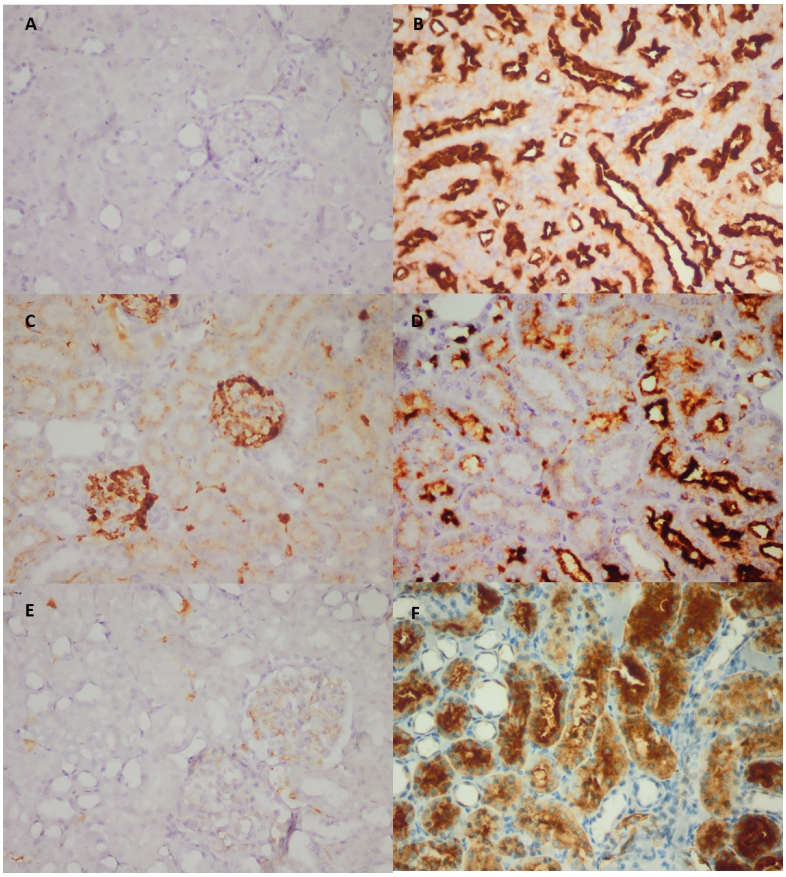

Fig. 3: Immunostaining for MPO and CD10. A: Negative MPO staining both in tubules and glomeruli in group I. B: Strong luminal CD10 staining in group I. C: Strong cytoplasmic MPO staining in glomeruli and moderate diffuse granular staining in tubular epithelium in group II. D: Weak to moderate cytoplasmic CD10 staining with focal strong cytoplasmic staining in group II. E: Weak focal MPO staining in the glomeruli with negative staining in the tubules in group III. F: Moderate to strong cytoplasmic CD10 staining in the tubules with luminal accentuation in group III. (x400).

Table 1: Comparison between the three studied groups according to mortality.

Mortality	Group I (n=8)	Group II (n=8)	Group III (n=8)	$\chi 2$	^{MC}p
No	8 (100%)	4 (50%)	8 (100%)	7.257*	0.019*
Yes	**0 (0%)**	**4 (50%)**	**0 (0%)**		

χ^2: **Chi square test** MC: **Monte Carlo**
p: p value for comparing between **the three studied groups**
*: Statistically significant at $p \leq 0.05$

Table 2: Comparison between the three studied groups according to different parameters

	Group I (n=8)	Group II (n=4)	Group III (n=8)	Test of sig.	P
Acute tubular necrosis %					
Median (Min. – Max.)	0 (0 – 0)	30 (20 – 40)	0 (0 – 0)	F=	<0.001*
Mean ± SD.	0 ± 0	30 ± 8.2	0 ± 0	122.40*	
Sig. bet. groups		p_1<0.001*, p_2=1.000, p_3<0.001*			
Acute tubular injury%					
Median (Min. – Max.)	0 (0 – 0)	42.5 (30 – 50)	10 (10–10)	F=	<0.001*
Mean ± SD.	0 ± 0	41.3 ± 8.5	10 ± 0.0	178.937*	
Sig. bet. groups		p_1<0.001*, p_2<0.001*, p_3<0.001*			
MPO tubular					
Negative	8 (100%)	0 (0%)	8 (100%)	χ^2=	^{MC}p
Positive	0 (0%)	4 (100%)	0 (0%)	14.411*	<0.001*
CD10 cytoplasmic					
Negative	8 (100%)	0 (0%)	0 (0%)	χ^2=	^{MC}p
Positive	0 (0%)	4 (100%)	8 (100%)	20.117*	<0.001*
Interstitial inflammation					
Negative	8 (100%)	0 (0%)	8 (100%)	χ^2=	^{MC}p
Positive	0 (0%)	4 (100%)	0 (0%)	14.411*	<0.001*
CD10 luminal					
Negative	0 (0%)	4 (100%)	5 (62.5%)	χ^2=	^{MC}p=
Positive	8 (100%)	0 (0%)	3 (37.5%)	12.580*	0.002*
MPO Glomerular					
Negative	8 (100%)	0 (0%)	5 (62.5%)	χ^2=	0.002*
Positive	0 (0%)	4 (100%)	3 (37.5%)	11.202*	

χ^2 : **Chi square test** MC: **Monte Carlo**
F: **F for One way ANOVA test**, Pairwise comparison between each 2 groups was done using **Post Hoc Test (Tukey)**
p: p value for comparing between **the three studied groups**
p_1: p value for comparing between **group I** and **group II**
p_2: p value for comparing between **group I** and **group III**
p_3: p value for comparing between **group II** and **group III**
*: Statistically significant at $p \leq 0.05$

Group II (Thioacetamide (TAA) group, n=8): H & E stained sections of TAA treated rats (group II) showed signs of acute tubular necrosis (enlarged tubules, disrupted tubular basement membrane, vacuolated cytoplasm, sloughed brush border, luminal casts, nuclear pyknosis and karyolysis) ranging from 20-40% of the tubules of surviving rats. Acute tubular injury was found in 30-50% of the tubules of the surviving rats. The glomeruli showed glomerular basement membranes of average thickness. The interstitium showed mild focal lymphocytic infiltrate in all surviving rats not exceeding 10% in each. (Table 2) No interstitial fibrosis was detected. The blood vessels were normal. Myelo-peroxidase staining showed moderate to intense granular cytoplasmic staining in the tubules with strong staining in the glomeruli of all surviving rats.

CD10 showed only cytoplasmic staining but no luminal staining was observed in the tubules, denoting loss of the brush border staining. No significant fibrosis was seen in the interstitium. (Trichrome). (**Fig.1. B & C & D & E, Fig. 2.C & D, Fig.3. C & D)**

Group III (TAA-quercetin treated group, n=8): H&E stained sections depict acute tubular injury (tubular vacuolization in with intact brush borders and intact tubular basement membrane) in 10% of the tubules in 8⁄8 rats. No acute tubular necrosis was detected. The glomeruli, blood vessels and intersitium were normal. CD10 showed cytoplasmic staining of the tubules in 8⁄8 rats with luminal accentuation in 3⁄8 rats. Myeloperoxidase staining was negative in all tubules with faint positive staining in the glomerular tuft in 3⁄8 rats. (Table 2) (**Fig. 1.F, Fig. 2.E & F, Fig. 3.E & F**). Comparison between the three studied groups according to different parameters and statistical analysis was performed. Results are shown in table 2.

DISCUSSION

Various beneficial medications, such as acetaminophen and gentamicin, as well as several environmental and industrial toxins, can cause severe kidney damage by activating highly reactive free radicals[19]. TAA is one among the most well-studied compounds and industrial toxins. TAA has been linked to centrilobular hepatic necrosis, liver cirrhosis, hepatocellular cancer, and bile duct proliferation, as well as damage to the proximal renal tubule's terminal region [20-23]. TAA undergoes a large metabolism after injection, generating sulfine (sulfoxide) and sulfene (sulfone). Both are circulated throughout the body, passing through various vital organs before being converted to acetate and eliminatedein urine within 24 hours [21].

The 50% mortality rate in TAA treated rat group for the duration of the 28days study length explained by renal dysfunction precipitated by TAA. Absence of mortalities in the TAA-quercetin treated crew denotes instantaneous amelioration of renal dysfunction.

The existing study confirmed that rats exposed to TAA suffer from renal damage, as evidenced by histological alterations. As depend of fact, signs of acute tubular necrosis, acute tubular injury had been found. The glomeruli showed glomerular basement membranes of average thickness. The interstitium showed mild focal lymphocytic infiltrate Furthermore, various investigations have looked into the harmful effects of TAA on the kidneys of experimental animals. Light microscopic examinations of renal tissues revealed severe histopathological changes, including glomeruli congestion and focal mesengial cell proliferation, expanded deposition of collagen in the renal medulla and fibrin in the cortex, disrupted and swollen cells of convoluted tubules and lobulated atrophied glomeruli, tubular epithelial cell necrosis associated with diffuse tubular swelling, and inflammatory cell infiltrate [24-26] .

Atef et al. [27] found that In contrast to control findings, there were some changes in kidney structures, including necrosis and high glomerular degeneration, and Bowman capsules in mice were only exposed to thioacetamide. Similarly, Kadir et al.[26] emphasized that histological examination of sections from rat kidneys treated with TAA, renal shape is damaged by severe and wide spread tubular epithelium.

TAA caused toxicity and organ dysfunction could be attributed to the generations of Reactive Oxygen Species (ROS), secondary to its metabolism into TAA-S-dioxide, which binds to cellular macromolecules leading to alternate in cell permeability and calcium uptake. This interruption of calcium stores inhibits mitochondrial activity[28]. A number of preceding researches proved the occurrence of oxidative stress in hepatic tissues following TAA administration[29]. Etoh et al., [30] mentioned that Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase, as a major source of reactive oxygen species (ROS) in the kidney, has been linked to the development of renal oxidative injury. Peroxidation of lipids is thought to be visible in the renal brush border, as well as changing the characteristics of biological membranes, culminating in severe cell damage and lyses [31-33].

Moreover, examination of PAS stained sections of TAA group in the current study revealed enlargement of the tubular epithelial cells and evident signs of injury in the shape of disrupted tubular basement membrane, vacuolated cytoplasm and luminal debris. Some of the nuclei exhipit pyknosis and karyolysis. This was in settlement with some authors who stated that this may be due to up-regulation of integrins, laminin and fibronectin with subsequent disruption in basement membrane [34].

In addition, there was slough of the brush border, this was in settlement with EZZ-DIN D., et al [35] who observed the loss of the brush boundary, cell polarity, and cell-cell adhesion to the basement membrane, and explained their results by the fact that necrosis and apoptosis may all cause tubular cells to detach from the basement membrane, leaving patches of denuded basement membrane behind.

MPO activity was measured as a neutrophil-specific marker of immune system activation in this work and notably showed moderate to intense granular staining of the tubular cytoplasm in response to TAA intoxication. This associated inflammation is explained by Amer et al., [36] who proven an elevation of inflammatory cytokines; Interleukinj(IL)-6, tIL-1B and Tumor Necrosis Factor (TNF)-a in blood samples of TAA-treated group.

Vokalova et al., [37] have shown that liver and kidney damage precipitated through TAA is associated with release of DNA that activates innate immunity and causes sterile inflammation, causing tissue damage to worsen. A study on liver via Selders et al.,[38] proven that TAA administration led to degenerative changes such as necrosis and neutrophilic infiltrates. Hepatocytes that have been damaged have been replaced by aggregates including a mix of macrophages and neutrophils, which can cause persistent inflammation and fibrosis.

Quercetin is a necessary member flavonoid family member, is a potent antioxidant found in a variety of vegetables and fruits, most notably grape and red wine [39]. It has been shown that residents of southern France had a lower incidence of coronary heart disease, which has been linked to frequent intake of a Mediterranean diet rich in quercetin and other antioxidant flavonoids [40]. Suzuki *et al.* [41] have mentioned that Oral quercetin has been shown to have stomach cytoprotective and ulcer-restorative properties, at least in part, by scavenging free radicals produced in the wounded or ulcerated region.

Furthermore, due to its antioxidant and cytoprotective properties, quercetin has been shown to protect cardiac tissue against global ischemia and reperfusion damage[39].

In addition, Duarte *et al.*[42] have pronounced that quercetin reduces the elevated blood pressure, the cardiac and renal hypertrophy in spontaneously hypertensive rats and have attributed these consequenceseto the reduced oxidants status due to the antioxidant properties of the drug. From the above data, the workable protective effect of quercetin against TAA-induced nephrotoxicity deserves study.

In TAA-quercetin group, marked amelioration of the congestion; noted both in peritubular capillaries and in the glomerular tuft. Few tubules showed vacuolated cytoplasm, with intact brush borders and intact tubular basement membrane. According to the pathological findings, quercetin may be protective against degenerative damage produced by TAA therapy.

The capacity of flavonoids, along with quercetin, to change peroxidation kinetics by modifying lipid packing order and reducing membrane fluidity, is the mechanism underlying their antioxidative activities. These changes should prevent free radicals from spreading and limiting their peroxidative responses [43].

CONCLUSION

The overall findings of this study showed that TAA caused kidney damage based on histological and immunohistochemical studies. Concurrent treatment with QE gave a significant level of protection against TAA's harmful renal side effects. Finally, QE may operate as a natural antioxidant in the kidney, presumably by scavenging free radicals, to prevent continued TAA-induced nephrotoxicity and oxidative stress.

Author Contributions:

Sally Mahmoud Mohamed Hussein omar, Marwa Mohamed Abd El Aziz Ahmed, and Marwa Mahmoud Mady wrote the main manuscript text and prepared the figures and tables. All authors reviewed the manuscript. The authors read and approved the final manuscript.

ORCiD

Sally Mahmoud Mohamed Hussein omar: 0000-0001-6601-4243
Marwa Mohamed Abd El Aziz Ahmed: 0000-0003-4230-7775
Marwa Mahmoud Mady: 0000-0003-2318-7368

Funding This study has no special funding from any organization.

Declarations

Ethics approval and consent to participate the present study was approved by the Ethical guidelines of Alexandria University on laboratory animals and the national institute for the care and use of laboratory animals. Further the Alexandria Faculty of Medicine ethical committee approval was obtained.

Conflicts of Interests:

Sally Mahmoud Mohamed Hussein omar, Marwa Mohamed Abd El Aziz Ahmed, and Marwa Mahmoud Mady declare that we have no conflict of interest.

REFERENCES

[1]. Ring-Larsen H and Palazzo U. Renal failure in fulminant hepatic failure and terminal cirrhosis: a comparison between incidence, types and prognosis. Gut, 1981;22:585-591.

[2]. Bourdi M, Masubuchi Y, Reilly TP, Amouzadeh HR, Martin JL, George JW, Shah AG and Pohl LR. Protection against acetaminophen induced liver injury and lethality by interleukin 10: Role of inducible nitric oxide synthase. Hepatology, 2002;35: 289-298.

[3]. Morio LA, Chiu H, Sprowless KA, Zhou P, Heck DE, Gordon MK and Laskin DL. Distinct roles of tumour necrosis factor-alpha and nitric oxide in acute liver injury induced by carbon tetrachloride in mice. Toxicol. Appl. Pharm., 2001;172: 44-51.

[4]. Cengiz M, Kutlu HM, Burukoglu DD and Ayhanci A. A comparative study on the therapeutic effects of Silymarin and Silymarin-Loaded Solid Lipid Nanoparticles on D-GaIN/TNF-á-induced Liver Damage in Balb/c Mice. Food and Chemical Toxicology, 2015;77: 93-100.

[5]. Liu L, Han D and Ren D. Effect of intestinal endotoxemia induced by thioacetamide. Chung-HuaKan Tsang Ping Tsa. Chin., 2000;8:174-179.

[6]. Caballero ME, Berlanga J, Ramirez D, Lopez-Saura P, Gozalez R, Floyd DN, Marchbank T and Playford RJ. Epidermal growth factor reduces multiorgan failure induced by thioacetamide. Gut., 2001;48: 34-40.

[7]. ICHIMURA R., MIZUKAMI S., TAKAHASHI M., TANI-AI E., KEMMOCHI S., MITSUMORI K. and SHIBUTA-NI M. Disruption of Smad-dependent signaling for growth of GST-P-positive lesions from the early stage in a rat two-stage hepatocarcinogenesis model. Toxicology and Applied Pharmacology, 2010;246: 128-40.

[8]. KADIR F.A., OTHMAN F., ABDULLA M.A., HUSSAN F. and HASSANDARVISH P. Effect of Tinospora crispa on thioacetamide-induced liver cirrhosis in rats. Indian J. Pharmacol., 2011;43(1):64-8.

[9]. Begum Q, Noori S, Mahboob T. Antioxidant effect of sodium selenite on thioacetamide-induced renal toxicity. Pakistan Journal of Biochemistry and Molecular Biology, 2011;44(1):21–26.

[10]. Silva FG: Chemical-induced nephropathy. A review of the renal tubulointerstitial lesions in humans. Toxicol Pathol, 2004;32(2):71–84.

[11]. Etoh T, Inoguchi T, Kakimoto M, Sonoda N, Kobayashi K, Kuroda J, Sumimoto H, Nawata H. Increased expression of NAD (P) H oxidase subunits, NOX4 and p22phox, in the kidney of streptozotocin-induced diabetic rats and its reversibity by interventive insulin treatment. Diabetologia, 2003;46(10):1428–1437.

[12]. C. A. Rice-Evans, N. J. Miller, and G. Paganga, (1996)"Structure-antioxidant activity relationships of flavonoids and phenolic acids," Free Radical Biology and Medicine, 1996;20(7):933–956.

[13]. K. Murota and J. Terao. Antioxidative flavonoid quercetin: implication of its intestinal absorption and metabolism," Archives of Biochemistry and Biophysics, 2003;417(1):12–17.

[14]. H. Liu, L. Zhang, and S. Lu. Evaluation of antioxidant and immunity activities of quercetin in isoproterenol-treated rats. Molecules, 2012; 17(4):4281–4291.

[15]. E. Atef and A. El-Baky. Quercetin protective action on oxidative stress, sorbitol, insulin risistance and cells function in expermintal diabetic rats. International Journal of Pharmaceutical Studies and Research, 2011;2(2):11–18.

[16]. S. K. Mishra, P. Singh, and S. K. Rath. Protective effect of quercetin on chloroquine-induced oxidative stress and hepatotoxicity in mice. Malaria Research and Treatment, 2013;aricle ID 141734, 10 pages.

[17]. Y. S. Dong, J. L. Wang, D. Y. Feng et al. Protective effect of quercetin against oxidative stress and brain edema in an experimental rat model of subarachnoid hemorrhage. International Journal of Medical Sciences, 2014;11(3):228–290.

[18]. MURAD H.A.S., RAFEEQ M.M. and MALATANI N.N. Effects of Candesartan and Losartan on Thioaceta-mide Induced Low Grade Renal Dysfunction in Rats. International Journal of Pharmacology, 2018;14: 1046-50.

[19]. Olagunju J, Adeneye A, Fagbohunka B, Bisuga N, Ketiku A, Benebo A, Olufowobi O, Adeoye A, Alimi M, Adeleke A. Nephroprotective activities of the aqueous seed extract of Carica papaya Linn. in carbon tetrachloride induced renal injured Wistar rats: a dose-and time-dependent study. Biol Med, 2009;1(1):11–19.

[20]. Kadir FA, Othman F, Abdulla MA, Hussan F, Hassandarvish P. Effect of Tinospora crispa on thioacetamide-induced liver cirrhosis in rats. Indian J Pharmacol, 2011;43(1):64–68.

[21]. Kadir FA, Kassim NM, Abdulla MA, Yehye WA. Hepatoprotective Role of Ethanolic Extract of Vitex negundo in Thioacetamide-Induced Liver Fibrosis in Male Rats. Evidence-Based Complementary and Alternative Medicine 2013.

[22]. Stankova P, Kucera O, Lotkova H, Rousar T, Endlicher R, Cervinkova Z. The toxic effect of thioacetamide on rat liver in vitro. Toxicol In Vitro, 2010; 24(8):2097–2103.

[23]. Madani H, Talebolhosseini M, Asgary S, Naderi G. Hepatoprotective activity of Silybum marianum and Cichorium intybus against thioacetamide in rat. Pakistan J Nutr, 2008;7(1):172–176.

[24]. Ring-Larsen H and Palazzo U. Renal failure in fulminant hepatic failure and terminal cirrhosis: a comparison between incidence, types and prognosis. Gut, 1981; 22: 585-591.

[25]. Mahmoud, N.H. Protective effect Of Panax ginseng against thioacetamide cytotoxicity in liver and kidney of albino rat. J. Egypt. Soc. Toxicol. 2006;34: 43–54.

[26]. Kadir, F.A., Kassim, N.M., Abdulla, M.A., Yehye, W.A. Effect of oral administration of ethanolic extract of Vitex negundo on thioacetamide induced nephrotoxicity in rats. BMC Complement. Altern. Med 2013;13:294.

[27]. Atef M, Ali A and Daklallah A. Protective effect of olive and juniper leaves extracts on nephrotoxicity induced by thioacetamide in male mice. *Saudi J. Biol. Sci., 2017;* 24(1):15-22.

[28]. HAJOVSKY H., HU G., KOEN Y., SARMA D., CUI W., MOORE D.S., STAUDINGER J.L. and HANZLIK R.P. Metabolism and toxicity of thioacetamide and thioaceta-mide S-oxide in rat hepatocytes. Chem. Res. Toxicol., 2012;25(9): 1955-63.

[29]. SANZ N., DIEZ-FERNANDEZ C., ANDRES D. and CASCALES M. Hepatotoxicity and aging: Endogenous antioxidant systems in hepatocytes from 2-, 6-, 12-, 18- and 30-month-old rats following a necrogenic dose of thioacetamide. Exp. Toxico. Patho., 2002;64: 287-93.

[30]. ETOH T., INOGUCHI T., KAKIMOTO M., SONODA N., KOBAYASHI K., KURODA J., SUMIMOTO H. and NAWATA H. Increased expression of NAD (P) H oxidase subunits, NOX4 and p22phox, in the kidney of streptozo-tocin-induced diabetic rats and its reversibity by interven-tive insulin treatment. Diabetologia, 2003;46(10):1428-37.

[31]. HAMED M.A., ALI S.A. and EL-RIGAL N.S. Therapeutic potential of ginger against renal injury induced by carbon tetrachloride in rats. Scientific World Journal, 2012;840421.

[32]. AL-YAHYA M., MOTHANA R., AL-SAID M., AL-DOSARI M., AL-MUSAYEIB N., AL-SOHAIBANI M., PARVEZ M.K. and RAFATULLAH S. Attenuation of CCl4-Induced Oxidative Stress and Hepatonephrotoxicity by Saudi Sidr Honey in Rats. Evid. Based Complement. Alternat. Med.,2013;569037.

[33]. HESAMI Z., JAMSHIDZADEH A., AYATOLLAHI M., GERAMIZADEH B., FARSHAD O. and VAHDATI A. Effect of Platelet-Rich Plasma on CCl4- Induced Chronic Liver Injury in Male Rats. Int. J. Hepatol., 2014;932930.

[34]. GHALY E.N., GERGIS S.W., AZIZ J.N., YASSA H.D. and HASSAN H.A. Role of mesenchymal stem cell therapy in cisplatin induced nephrotoxicity in adult albino rats: Ultrastructural and biochemical study. Acta Medica International, 2014;32 (1):57-66.

[35]. EZZ-DIN D., GABRY M.S., FARRAG A.R. and ABDEL-MONEIM A.E. Physiological and histological impact of Azadirachta indica (neem) leaves extract in a rat model of cisplatin-induced hepato and nephrotoxicity. J. Med. Plants. Res., 2011;5(23): 5499-506.

[36]. AMER M.G., MAZEN N.F. and MOHAMED A.M. Caffeine intake decreases oxidative stress and inflammatory biomarkers in experimental liver diseases induced by thioacetamide: Biochemical and histological study. Inter-national Journal of Immunopathology and Pharmacology, 2017;30 (1):13-24.

[37]. VOKÁLOVÁ L., LAUKOVÁ L., CONKA J., MELIļSKOVÁ V., BORBÉLYOVÁ V., BÁBÍ_KOVÁ J., TÓTHOVÁ L., HODOSY J., VLKOVÁ B. and CELEC P. Deoxyribonuclease partially ameliorates thioacetamide-induced hepatorenal injury. Am. J. Physiol. Gastrointest. Liver Physiol., 2017;312: G457-G463.

[38]. SELDERS G.S., FETZ A.E., RADIC M.Z. and BOWLIN G.L. An overview of the role of neutrophils in innate immunity, inflammation and host-biomaterial integration. Regen. Biomater., 2017;4(1):55-689.

[39]. Ikizler M., Erkasap N., Dernek S., Kural T., Kaygisiz Z., Anadolu Kardiyol. Derg 2007;**7:**404—410.

[40]. Formica J. V., Regelson W. Food Chem. Toxicol., 1995;33:1061—1080.

[41]. Suzuki Y., Ishihara M., Segami T., Ito M., Jpn. J. Pharmacol., 1998;78, 435—441.

[42]. Duarte J., Pérez-Palencia R., Vargas F., Ocete M. A., Pérez-Vizcaino F., Zarzuelo A., Tamargo J., Br. J. Pharmacol., 2011;133:117—124.

[43]. Arora A., Byrem T. M., Nair M. G., Strasburg G. M.,Arch. Biochem. Biophys., 2000;373:102—109.

How to cite this article: Sally Mahmoud Mohamed Hussein omar, Marwa Mohamed Abd El Aziz Ahmed, Marwa Mahmoud Mady. Protective Role of Quercetin on Thioacetamide-Induced Renal Injury in Adult Male Albino Rats. Int J Anat Res 2022;10(4):8496-8504. **DOI:** 10.16965/ijar.2022.238