Official Journal Issued by Faculty of Veterinary Medicine

Benha Veterinary Medical Journal

Journal homepage: https://bvmj.journals.ekb.eg/

Since 1990

Original Paper

Ameliorative effect of coenzyme Q10 against deltamethrin-induced renal toxicity in broiler chickens

Ali Allam1, Alshaimaa Mohamed Said2, Samar Saber Ibrahim3, Gehan Youssef3, Mohamed Aboubakr1*

[1]*Department of Pharmacology, Faculty of Veterinary Medicine, Benha University, 13736 Moshtohor, Toukh, Qaliobiya, Egypt .*

[2]*Biochemistry Department, Faculty of Veterinary Medicine, Benha University, 13736 Moshtohor, Toukh, Qaliobiya, Egypt.*

[3]*Department of Forensic Medicine and Toxicology, Faculty of Veterinary Medicine, Benha University, 13736 Moshtohor, Toukh, Qaliobiya, Egypt*

ARTICLE INFO

Keywords

Deltamethrin
CoQ10
Oxidative stress
Caspase-3
BCl2
Renal
Apoptosis
Broilers

Received 18/01/2022
Accepted 24/02/2022
Available On-Line 01/04/2022

ABSTRACT

The ameliorating effect of Coenzyme Q10 (CoQ10) supplementation was evaluated on broiler chickens intoxicated with deltamethrin (DM) through serum biochemical analysis, antioxidant capacity, and pathological examination. Cobb broiler chicks (60) aged 1 day were allocated into 4 experimental equal groups. For each group, three replicates of 5 chicks were used. The first group (control) received only the basal diet, the second group received CoQ10 (40 mg/kg diet), the third group received DM (300 mg/kg diet), and the fourth group received both DM (300 mg/kg diet) and CoQ10 (40 mg/kg diet). The experimental period was 35 days has been given to the last 3 groups. DM intoxication was associated with significant increases in creatinine, urea, malondialdehyde (MDA), and a drop in levels of reduced glutathione (GSH) and superoxide dismutase (SOD). In addition, DM increased blood cholesterol, triacylglycerols, and low-density lipoprotein (LDL), while lowered high-density lipoprotein (HDL). *Caspase-3 and B cell lymphoma 2* (*BCl2*) were substantially unregulated by DM in the kidney tissues. The microscopic examination of the kidneys revealed congestion of the renal blood vessels with necrosis of the lining epithelium of the renal tubules. Concurrent supplementation of CoQ10 with DM resulted in a notable improvement in estimated parameters compared to the DM group. Dietary CoQ10 is therefore advised because of its preventive properties against DM-induced renal toxicity in broilers.

1. INTRODUCTION

Pesticides containing organophosphorus have played a crucial role in enhancing agricultural production for many years, however, they will soon be replaced with safer ones (Kumar et al. 2016). Several agricultural countries now prefer pyrethroid pesticides due to their rapid environmental breakdown and low mammalian toxicity, as well as their greatest insecticidal efficacy (Ogaly et al. 2015). As a type-II pyrethroid, DM controls pests in agriculture, cattle, and poultry production as well as human houses (Siwicki et al. 2010). DM was mainly used to protect crops. Birds, living in the same ecosystem are at risk of exposure to DM (Allam et al. 2022; Chandra et al. 2013; Ibrahim et al. 2021). The human body is highly exposed to DM residues via polluted crops, water, and animal feedstocks, as well as from occupational exposure to DM residues in the workplace (Swarnam and Velmurugan 2013). The kidneys, which responsible for excreting metabolic and waste products, are also damaged by DM exposure (Gündüz et al. 2015; Liu et al. 2015). The harmful effects of DM on many organs can be explained by the accumulation of ROS (Kumar et al. 2016). As a result, enhancing the antioxidant system is essential to prevent the harmful effects of oxidative stress caused by DM exposure. The antioxidant system of poultry can be enhanced using many feed additives such as probiotics, phytogenic feed additives (Abdel-Latif et al. 2018; Saeed et al. 2020).

CoQ10 is a lipophilic vitamin-like quinine derivative containing 10 isoprenyls units (Nepal et al. 2010). The mitochondrial respiratory chain requires it for electron transport and stability (Shukla and Dubey 2018). DNA, cellular proteins, and membrane lipids are protected from free radical damage by CoQ10, especially in organs with high energy demand, such as the heart, liver, and kidney (Gueven et al. 2015). CoQ10 has a protective effect on hepato-renal toxicity (Geng and Guo 2005; Mwaeni et al. 2021). Also, CoQ10 is documented to have a potent free radical scavenging activity that helps to maintain the mitochondrial membrane potential and to decline protein oxidation, and DNA damage; so, it can restore cell function when subjected to oxidative stress (Abdeen et al. 2020) .

In broiler chickens, DM caused renal toxicity (Ibrahim et al. 2021), however, there are no data on the preventive

* Corresponding author: mohamed.aboubakr@fvtm.bu.edu.eg

effects of CoQ10. Therefore, this study set out to evaluate the protective impact of CoQ10 on DM-induced renal toxicity in broiler chickens.

2. MATERIAL AND METHODS

2.1. Chemicals

DM (Butox® 50 mg/ml; Intervet Co., France). CoQ10 was kindly supplied as (Coenzyme Q10®, 30 mg) from MEPACO, Cairo, Egypt. The commercial kits used for biochemical and antioxidant biomarkers were obtained from Biodiagnostic Co., Egypt.

2.2. Experimental Animals

Sixty Cobb broiler chicks (one day) were obtained From El-Wataniya Poultry Company, Egypt. These chicks were housed under hygienic measures in separate units. The temperature starts at 32°C, they declined to 2°C each week. Feed and water were supplied *ad-libitum* and continuous lightning was used.

2.3. Experimental design

The chicks were divided into 4 groups, each was subdivided into 3 replicates (5 chicks each). The 1st group (control group) received basal diet only; 2nd group (CoQ10 group) supplemented with CoQ10 40 mg/kg diet (Gopi et al. 2015), 3rd group (DM group) received a DM at 300 mg/kg diet (Ibrahim et al. 2021) and 4th group (DM; 300 mg/kg diet +CoQ10; 40 mg/kg diet) and all treatments performed for 35 days. Ethical Committee (Faculty of Veterinary Medicine, Benha University) approved the design of this experimental study (Approval number: BUFVTM 03-01-22).

2.4. Sampling

2.4.1. Blood sampling

At the end of the study, blood was obtained from all chickens in different groups from wing veins in dry, clean tubes. Blood was left at room temperature in a slope position to clot. Serum was gathered by centrifugation (10 min at 2000 *g*), transferred to dry, clean vials, and frozen at –20 °C until used for biochemical analyses.

2.4.2. Tissue sampling

Chickens were dissected and the kidneys were collected, washed with physiological saline, and divided into three portions. One part was homogenized within potassium phosphate buffer and centrifuged (20 min at 1600 *g* at 4°C). The supernatant was stored at -20°C for the determination of oxidative stress markers. Another part was kept in -80°C till analysis of gene expression. The last portion was fixed in a 10% formalin solution for histopathological examination.

2.5. Biochemical analysis

Urea (Cat. No. UR 2110) and creatinine (Cat. No. CR 1250) were assessed in the serum by Coulombe and Favreau (1963); Larsen 1972), respectively. Serum total cholesterol (Cat. No. CH 1220), triglycerides (Cat. No. TR 2030), and HDL-C concentrations (Cat. No. CH 1230) were determined according to Burstein et al. (1970); Stein and Myers (1995); Young et al. (1975), respectively and serum LDL-C concentration was calculated (Friedewald et al. 1972).

The oxidative stress markers were assessed in kidney tissues. MDA as an indicator of lipid peroxidation was determined (Ohkawa et al. 1979). The activity of SOD (Nishikimi et al. 1972), and GSH level were assessed (Beutler 1963). All Kits were obtained from Biodiagnostic CO, Giza, Egypt.

2.6. Quantitative real-time PCR (qRT-PCR) and gene expression

Total RNA was extracted from kidney tissue using RNeasy Mini Kit (Qiagen, USA, Cat. No. 74104) and determined for purity at 260/280 nm. Then, cDNA was synthesized using a High Capacity cDNA Reverse Transcription kit (Qiagen, USA, Cat. No. 205311). The primer sequence was: sense (5'-TGGCCCTCTTGAACTGAAAG-3') and antisense (5'- TCCACTGTCTGCTTCAATACC -3') for *caspase-3* and since (5'-ATCGTCGCCTTCTTCGAGTT-3') and antisense (5'- ATCCCATCCTCCGTTGTTCT-3') for *BCl2*. Chicken *β-actin* was used as a housekeeping gene. The *β-actin* primer used was: sense (5'-CCACCGCAAATGCTTCTAAAC-3') and antisense (5'-AAGACTGCTGCTGACACCTTC-3'). The cycling condition of SYBR Green real-time PCR was: 94°C for 5 minutes (primary denaturation), 40 cycles at 94°C for 15 seconds (secondary denaturation), 60°C for 30 seconds (annealing), and 72°C for 30 seconds (extension stage). Cycle threshold (CT) values were determined using Stratagene MX3005P software. Data were analyzed using the $2^{-\Delta\Delta ct}$ method.

2.7. Histopathology

Small tissue specimens were collected from the sacrificed chickens and immediately fixed at least 24 hrs in 10% formalin solution. The fixed tissues were washed, dehydrated in ascending series of ethanol, then tissue paraffin sections sliced into sections (4 µm thick). All slices cleared in xylene and stained with hematoxylin and eosin (H&E) then examined using a Leica DM3000 microscope.

2.8. Statistical analysis

All analysis was conducted with the program SPSS 25. (SPSS Inc., Chicago, USA). Data were mean ± SE, a one-way variance analysis (ANOVA) followed by Duncan's post-hoc test was used to compare group means. *P* values of less than 0.05 were considered significant.

3. RESULTS

3.1. DM and/or CoQ10 effect on kidney serum biomarkers

The DM group showed an observable increase in creatinine and urea concentrations (Figure 1 A, B) compared to the control. In addition, DM and CoQ10 showed a remarkable reduction in these parameters compared with the DM group.

3.2. Effect of DM and/or CoQ10 on lipid profile

DM induced significantly higher levels of serum cholesterol, triglycerides, and LDL-C (Figure 1 C, D, E) as well as a markedly lower level of HDL-C (Figure 1 F) compared to the control. However, concurrent supplementation of CoQ10 with DM resulted in an enhancement in cholesterol, triacylglycerols, LDL and HDL serum concentrations compared to the DM group.

3.3. DM and/or CoQ10 effect on renal oxidative stress markers

As illustrated in Figure (2), DM toxicity was accompanied with a marked increases the MDA level (Figure 2A), decreased SOD activity (Figure 2B), and reduced GSH

level (Figure 2C) in kidney tissues when compared to control. However, the DM+CoQ10 group showed a substantial amelioration in renal antioxidant status compared to the DM group. Interestingly, SOD activity and GSH level were almost restored to the control values.

3.4. Effect of DM and/or CoQ10 on Caspase-3 and BCl2 gene expression

DM exhibited marked upregulation of *Caspase-3* and a significant downregulation in *BCl2* in the kidney. However, a diet supplemented with CoQ10 induced dramatic deregulation of *Caspase-3* (Figure 2D) and a notable up-regulation of *BCl2* (Figure 2E) in the kidney. When DM+CoQ10 was compared to the DM group, an observable downregulation of renal *Caspase-3* expression and remarkable upregulation of renal *BCl2* expression were recorded. Of note, CoQ10 supplementation to DM intoxicated broiler chickens restored renal *BCl2* gene expression to control values.

3.5. Histopathological examination

The examined kidneys of the control and CoQ10 groups (Figure 3A, B) showed well-organized renal tubules which consisted of the proximal convoluted tubule (PCT), distal convoluted tubule (DCT), collecting ducts, and renal corpuscles. However, the DM group (Figure 3C) revealed congestion of the renal tubular epithelium with necrosis of the lining epithelium of the renal tubules. In contrast, the DM+ CoQ10 group (Figure 3D) showed cloudy swelling of some renal tubules and detachment of some epithelium lining few renal tubules and swelling of the DCT.

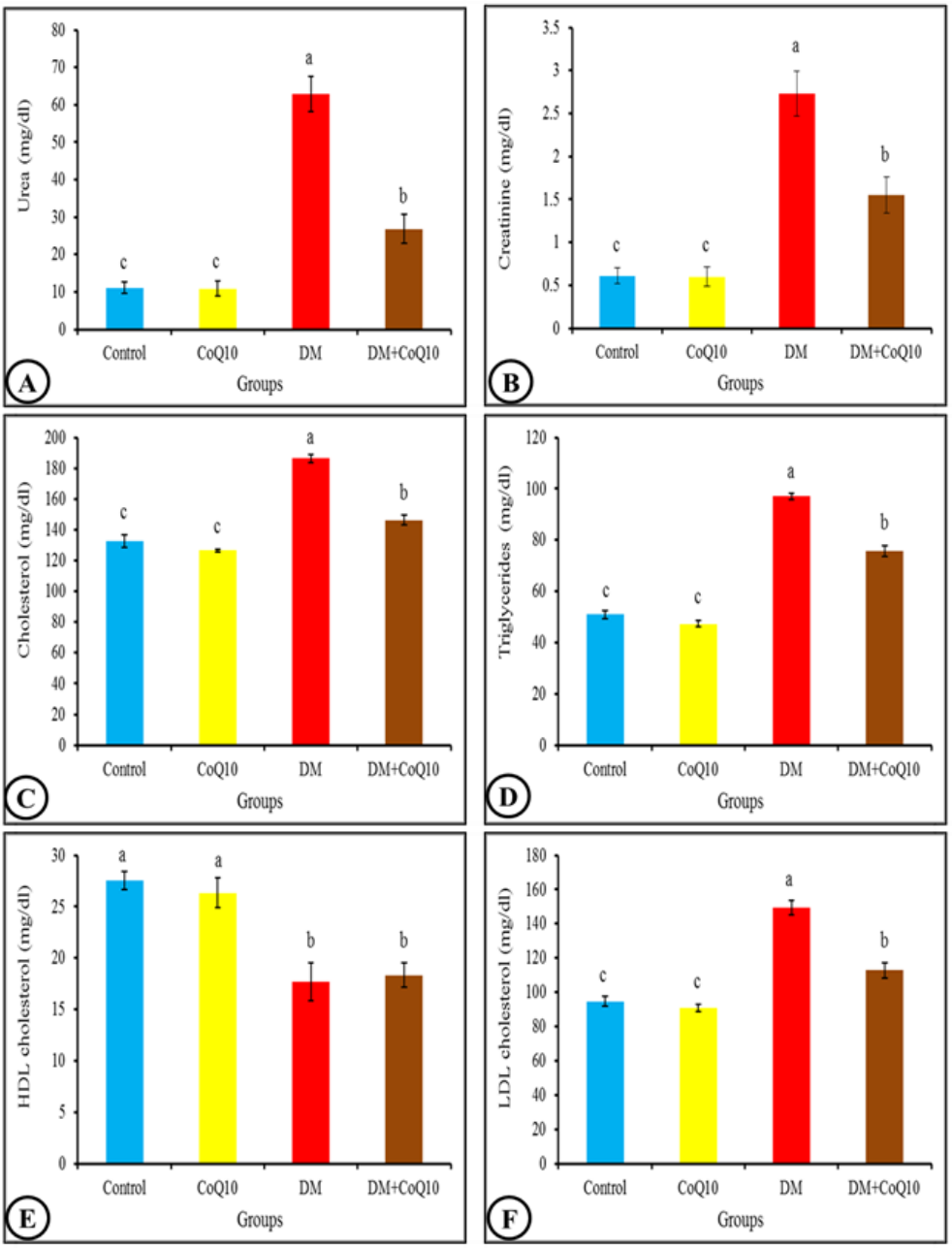

Figure 1: Effect of DM (300 mg/kg diet) and/or CoQ10 (40 mg/kg diet) on urea (A), creatinine (B), cholesterol (C), triglycerides (D), HDL-C (E), and LDL-C (F) in broiler chickens.

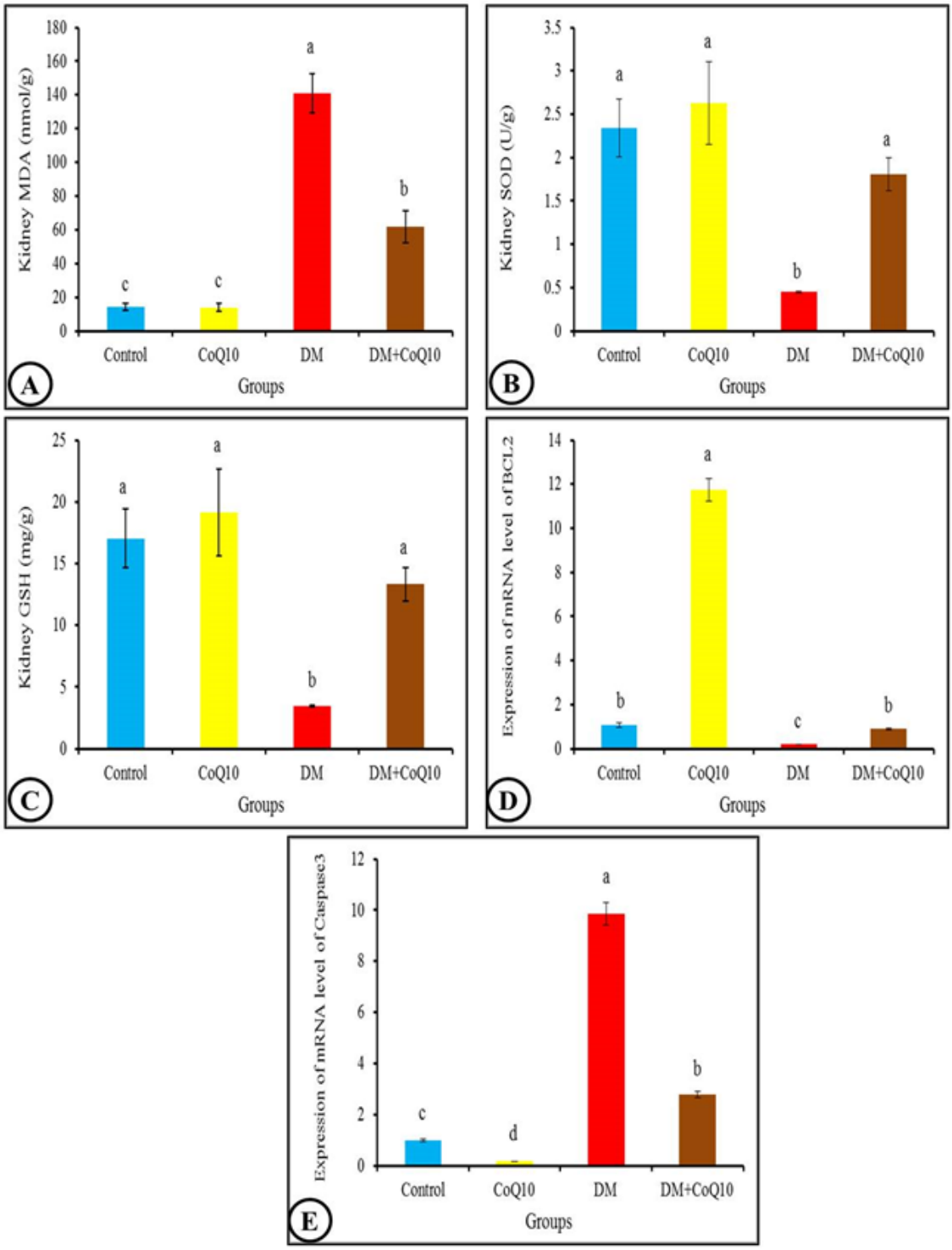

Figure 2: Effect of DM (300 mg/kg diet) and/or CoQ10 (40 mg/kg diet) on renal oxidative stress markers; MDA level (A), SOD activity (B) GSH level (C) and on renal gene expression of *Caspase-3* (D) and *BCl2* (E) in broiler chickens.

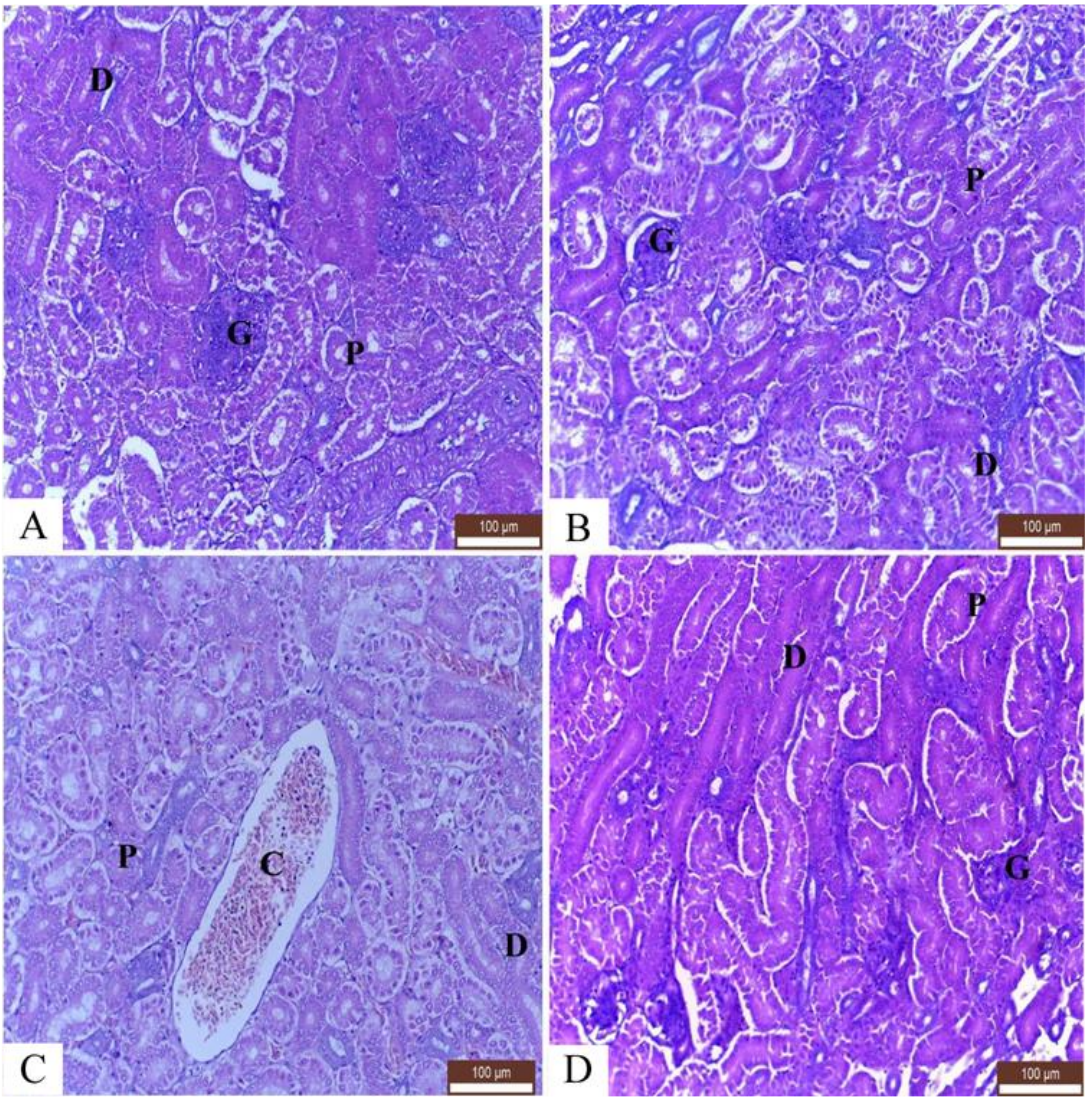

Figure 3: Photomicrographs of the kidneys chickens treated with DM (300 mg/kg diet) and/or CoQ10 (40 mg/kg diet). A; control, B; CoQ10, C: DM and D; DM+ CoQ10 groups. H& E stain.

4. DISCUSSION

In the present study DM toxicity was associated with severe alterations in kidney function which confirmed by biochemical analysis and histopathological examination which consistent with the previously recorded nephrotoxicity in mice (Tewari et al. 2018) and humans (Valcke et al. 2017). The metabolic product of DM is mainly excreted through the urinary tract (Lin et al. 2011) that could be accused of the recorded nephrotoxic changes in the DM group.

DM intoxicated broiler chickens exhibited an elevation in serum cholesterol and triglycerides. These results concur, well with Han et al. (2020); Tewari et al. (2018), which may be explained by the fact that DM affects cellular permeability and lipid metabolism (El-Sayed and Saad 2008).

The overproduction of free radicals was the most prominent mechanism of DM toxicity (Narra et al. 2017; Hattab et al. 2015). This study indicated that DM induced a remarkable state of oxidative stress in the kidney. During oxidative phosphorylation, mitochondria produce a considerable amount of ROS (Lv et al. 2020) which were able to induce massive cellular oxidative damage if they are not scavenged by endogenous antioxidants (Yang et al. 2016). Chronic exposure to pesticides resulted in excessive lipid peroxidation in various organs and exhaustion of cellular antioxidant defensive mechanisms (Abdel-Daim et al. 2020; Abdou et al. 2020; Soliman et al. 2020 a, b; Zhang et al. 2017), as seen in the DM group.

Also. In the present investigation, DM exposure significantly altered the gene expression of apoptotic and anti-apoptotic markers, which provides additional support for apoptosis as a possible mechanism by which DM may induce kidney damage. The expression of *caspase-3* as apoptotic protein was increased in our study. Moreover, Maalej et al. (2017) reported that DM administration induced apoptosis through up-regulation of p53 and Cyclo-

oxygenase 2 in the kidney tissues. In the current study, the downregulation of *BCl2* expression, an anti-apoptotic protein, confirmed their results since it is inversely related to p53.

The most remarkable result to emerge from the data is that feeding a diet supplemented with CoQ10 to DM intoxicated broiler chickens exhibited a significant amelioration of the damaging effects on kidney tissues induced by DM. Serum biochemical and histopathological findings demonstrated the potential effects of CoQ10 in renal protection. This finding was in complete agreement with Albadrany and Naser (2020). A possible theory for CoQ10's protection from DM toxicity may be the impact of its antioxidant action. The ability of CoQ10 to maintain an antioxidant/pro-oxidant balance (Sohal and Forster 2007; Ghule et al. 2009) counteracts the production of ROS during DM metabolism and excretion.

The current study showed that CoQ10 supplemented diet remarkably attenuated the alteration in lipid profile resulting from DM exposure. This fits well with the previous study of Albadrany and Naser (2020). The decline in serum cholesterol level reported could be due to HMGCoA reductase inhibition, the key enzyme in cholesterol synthesis (Honda et al. 2009). Consequently, LDL production decreased. There may be another possible explanation, the antioxidant behavior of CoQ10 protects LDL oxidation by harmful ROS (Singh et al. 2007). In the same line, CoQ10 attenuates tissue damage, which prevents disturbances in fatty acid metabolism. This could explain the decrease in serum triacylglycerols.

As expected, concurrent supplementation of CoQ10 to DM intoxicated broiler chickens significantly improved both enzymatic (SOD) and non-enzymatic (GSH) antioxidants and diminished MDA production in kidney tissues. Our results were confirmed by previous studies (Gopi et al. 2014; Huang et al. 2011; Maalej et al. 2017). Many possible explanations might explain our findings such as CoQ10 suppresses ROS overproduction, ROS quenching, and endogenous antioxidant maintenance (Ratliff et al. 2016).

Also, the results of this experiment reveal CoQ10 to be anti-apoptotic. The current study demonstrated that co-administration of CoQ10 with DM was accompanied with downregulation in *caspase 3* and up-regulation in *BCL2* expression of renal tissues. These results were in agreement with Abdeen et al. (2020). Kidneys observed a downregulation of *caspase-3*. The anti-apoptotic activity of CoQ10 could be attributed to its capability to regulate the perturbation electrochemical gradients on the mitochondrial level (Formigli et al. 2003).

Consequently, the presence of congestion of the renal tubular epithelium with necrosis of the lining epithelium of the renal tubules in DM treated group. In contrast, the DM+CoQ10 group showed cloudy swelling of some renal tubules and detachment of some epithelium lining few renal tubules. It is strongly reported that the inflammatory response is associated with oxidative stress; herein, the inflammatory cell infiltrations were seen in the kidney tissue after DLM exposure (Allam et al. 2022; Ibrahim et al. 2021). All of the detected pathological lesions improved with CoQ10 treatment.

CoQ10 acts as a potent antioxidant free radical scavenger, thus limiting damage associated with oxidative stress (Abdeen et al. 2020). CoQ10 in the diet improved reproductive performance (Rafieian-Naeini et al. 2021).

Conclusions

DM induced disturbance in renal function, lipid peroxidation, glutathione function, and antioxidant enzymes. CoQ10 acts as a potent antioxidant free radical scavenger, thus limiting damage associated with oxidative stress and so antagonize this harmful effect of DM on the kidney of chickens.

6. REFERENCES

1. Abdeen A, Abdelkader A, Elgazzar D, Aboubakr M, Abdulah OA, Shoghy K, Abdel-Daim M, El-Serehy HA, Najda A, El-Mleeh A. (2020) Coenzyme Q10 supplementation mitigates piroxicam-induced oxidative injury and apoptotic pathways in the stomach, liver, and kidney. Biomed & Pharmacother 130:110627
2. Abdel-Daim MM, Abd Eldaim MA, Mahmoud MM. (2014) Trigonella foenum-graecum protection against deltamethrin-induced toxic effects on haematological, biochemical, and oxidative stress parameters in rats. Can J Physiol Pharmacol. 92(8):679-85 .
3. Abdel-Daim MM, Abuzead SM, Halawa SM. (2013) Protective role of Spirulina platensis against acute deltamethrin-induced toxicity in rats. PLoS One. 8(9):e72991 .
4. Abdel-Daim MM, Dawood MAO, Elbadawy M, Aleya L, Alkahtani S. (2020) *Spirulina platensis* Reduced Oxidative Damage Induced by Chlorpyrifos Toxicity in Nile Tilapia (*Oreochromis niloticus*). Animals. 2020; 10(3):473. https://doi.org/10.3390/ani10030473
5. Abdou RH, Elbadawy M, Khalil WF, Usui T, Sasaki K, Shimoda M. (2020) Effects of several organophosphates on hepatic cytochrome P450 activities in rats. J Vet Med Sci. 82(5):598-606. https://doi.org/10.1292/jvms.19-0452
6. Albadrany Y, Naser A (2020) Coenzyme Q10 coadministration with diclofenac augmented impaired renal function in broiler chickens (Gallus gallus domesticus). Vet world 13:642
7. Ali AA, Khalil MG, Abd El-Latif DM, Okda T, Abdelaziz AI, Abu-Elfotuh K, Kamal MM, Wahid A. (2022) The influence of vinpocetine alone or in combination with Epigallocatechin-3-gallate, Coenzyme COQ10, Vitamin E and Selenium as a potential neuroprotective combination against aluminium-induced Alzheimer's disease in Wistar Albino Rats. Arch Gerontol Geriatr. 98:104557 .
8. Allam A, Abdeen A, Devkota HP, Ibrahim SS, Youssef G, Soliman A, Abdel-Daim MM, Alzahrani KJ, Shoghy K, Ibrahim SF, Aboubakr M. (2022) N-Acetylcysteine Alleviated the Deltamethrin-Induced Oxidative Cascade and Apoptosis in Liver and Kidney Tissues. Int J Environ Res Public Health. 19(2):638 .
9. Beutler E (1963) Improved method for the determination of blood glutathione. J lab clin Med 61:882–888

10. Burstein M, Scholnick HR, Morfin R (1970) Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. J Lipid Res 11:583–595
11. Chandra N, Jain NK, Sondhia S, Srivastava AB (2013) Deltamethrin induced toxicity and ameliorative effect of alpha-tocopherol in broilers. Bull Environ Contam Toxicol 90:673–678
12. Chargui I, Grissa I, Bensassi F, Hrira MY, Haouem S, Haouas Z, Bencheikh H. (2012) Oxidative stress, biochemical and histopathological alterations in the liver and kidney of female rats exposed to low doses of deltamethrin (DM): a molecular assessment. Biomed Environ Sci 25:672–683
13. Dahamna S, Belguet A, Bouamra D, Guendouz A, Mergham M, Harzallah D. (2011) Evaluation of the toxicity of cypermethrin pesticide on organs weight loss and some biochemical and histological parameters. Commun Agric Appl Biol Sci 76:915–921
14. El Golli-Bennour E, Timoumi R, Annaibi E, Mokni M, Omezzine A, Bacha H, Abid-Essefi S. (2019) Protective effects of kefir against deltamethrin-induced hepatotoxicity in rats. Environ Sci Pollut Res Int. 26(18):18856-18865 .
15. Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 18:499–502
16. Geng AL, Guo YM (2005) Effects of dietary coenzyme Q10 supplementation on hepatic mitochondrial function and the activities of respiratory chain-related enzymes in ascitic broiler chickens. Br Poult Sci 46:626–634
17. Ghule AE, Kulkarni CP, Bodhankar SL, Pandit VA (2009) Effect of pretreatment with coenzyme Q10 on isoproterenol-induced cardiotoxicity and cardiac hypertrophy in rats. Curr Ther Res 70:460–471
18. Gopi M, Purushothaman MR, Chandrasekaran D (2014) Effect of dietary coenzyme Q10 supplementation on the growth rate, carcass characters and cost effectiveness of broiler fed with three energy levels. Springerplus 3:1–7
19. Gueven N, Woolley K, Smith J (2015) Border between natural product and drug: comparison of the related benzoquinones idebenone and coenzyme Q10. Redox Biol 4:289–295
20. Gündüz E, Ülger BV, İbiloğlu İ, Ekinci A, Dursun R, Zengin Y, İçer M, Uslukaya Ö, Ekinci C, Güloğlu C. (2015) Glutamine provides effective protection against deltamethrin-induced acute hepatotoxicity in rats but not against nephrotoxicity. Med Sci Monit. 21:1107-14 .
21. Huang B, Guo Y, Hu X, Song Y (2011) Effects of coenzyme Q10 on growth performance and heart mitochondrial function of broilers under high altitude induced hypoxia. J Poult Sci 48:40–46
22. Hussein RM, Sawy DM, Kandeil MA, Farghaly HS. (2021) Chlorogenic acid, quercetin, coenzyme Q10 and silymarin modulate Keap1-Nrf2/heme oxygenase-1 signaling in thioacetamide-induced acute liver toxicity. Life Sci. 277:119460 .
23. Ibrahim SS, Elsabagh R, Allam A, Youssef G, Fadl SE, Abdelhiee EY, Alkafafy M, Soliman A, Aboubakr M. (2021) Bioremediation role of Spirulina platensis against deltamethrin-mediated toxicity and its chemical residues in chicken meat. Environ Sci Pollut Res 28(40):56188-56198
24. Li S, Zheng X, Zhang X, Yu H, Han B, Lv Y, Liu Y, Wang X, Zhang Z. (2021) Exploring the liver fibrosis induced by deltamethrin exposure in quails and elucidating the protective mechanism of resveratrol. Ecotoxicol Environ Saf 207:111501
25. Lv Y, Bing Q, Lv Z, Xue J, Li S, Han B, Yang Q, Wang X, Zhang Z. (2020) Imidacloprid-induced liver fibrosis in quails via activation of the TGF-β1/Smad pathway. Sci Total Environ 705:135915
26. Maalej A, Mahmoudi A, Bouallagui Z, Fki I, Marrekchi R, Sayadi S. (2017) Olive phenolic compounds attenuate deltamethrin-induced liver and kidney toxicity through regulating oxidative stress, inflammation and apoptosis. Food Chem Toxicol 106:455–465
27. Mazandaran AA, Khodarahmi P. (2021) The protective role of Coenzyme Q10 in metallothionein-3 expression in liver and kidney upon rats' exposure to lead acetate. Mol Biol Rep. 48(4):3107-3115 .
28. Mongi S, Mahfoud M, Amel B, Kamel J, Abdelfattah el F. (2011) Protective effects of vitamin C against haematological and biochemical toxicity induced by deltamethrin in male Wistar rats. Ecotoxicol Environ Saf. 74(6):1765-9 .
29. Narra MR, Rajender K, Reddy RR, Murty US, Begum G. (2017) Insecticides induced stress response and recuperation in fish: biomarkers in blood and tissues related to oxidative damage. Chemosphere 168:350–357
30. Nemati MH, Shahir MH, Harakinezhad MT, Lotfalhian H (2017) Cold-induced ascites in broilers: effects of vitamin C and coenzyme Q10. Brazilian J Poult Sci 19:537–544
31. Nishikimi M, Rao NA, Yagi K (1972) The occurrence of superoxide anion in the reaction of reduced phenazine methosulfate and molecular oxygen. Biochem Biophys Res Commun 46:849–854
32. Ohkawa H, Ohishi N, Yagi K (1979) Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem 95:351–358
33. Okudan N, Belviranlı M, Sezer T. (2022) Potential Protective Effect of Coenzyme Q10 on Doxorubicin-Induced Neurotoxicity and Behavioral Disturbances in Rats. Neurochem Res. doi: 10.1007/s11064-021-03522-8 .
34. Rafieian-Naeini HR, Zhandi M, Sadeghi M, Yousefi AR, Benson AP. (2021) Effects of coenzyme Q10 on reproductive performance of laying Japanese quail (Coturnix japonica) under cadmium challenge. Poult Sci 100(11):101418
35. Ratliff BB, Abdulmahdi W, Pawar R, Wolin MS. (2016) Oxidant mechanisms in renal injury and disease. Antioxid Redox Signal 25:119–146
36. Rjeibi I, Ben Saad A, Hfaiedh N. (2016) Oxidative damage and hepatotoxicity associated with deltamethrin in rats: The protective effects of Amaranthus spinosus seed extract. Biomed Pharmacother. 84:853-860 .
37. Sohal RS, Forster MJ (2007) Coenzyme Q, oxidative stress and aging. Mitochondrion 7 Suppl(Suppl):S103-11.
38. Soliman MM, Aldhahrani A, Gaber A, Alsanie WF, Mohamed WA, Metwally MM, Elbadawy M, Shukry M. (2022a) Ameliorative impacts of chrysin against gibberellic acid-induced liver and kidney damage through the regulation of antioxidants, oxidative stress, inflammatory cytokines, and apoptosis biomarkers. Toxicol Res. 11(1): 235–244, https://doi.org/10.1093/toxres/tfac003
39. Soliman MM, Gaber A, Alsanie WF, Mohamed WA, Metwally MMM, Abdelhadi AA, Elbadawy M, Shukry M. (2022b) Gibberellic acid-induced hepatorenal dysfunction and oxidative stress: Mitigation by quercetin through modulation of antioxidant, anti-inflammatory, and antiapoptotic activities. J Food Biochem. 46(2): e14069. https://doi.org/10.1111/jfbc.14069
40. Stein EA, Myers GL 1995) National Cholesterol Education Program recommendations for triglyceride measurement: executive summary. The National Cholesterol Education

Program Working Group on Lipoprotein Measurement. Clin Chem 141:1421-1426

41. Swarnam TP, Velmurugan A (2013) Pesticide residues in vegetable samples from the Andaman Islands, India. Environ Monit Assess 185:6119–6127
42. Tekeli MY, Eraslan G, Çakır Bayram L, Soyer Sarıca Z. (2021) Effect of diosmin on lipid peoxidation and organ damage against subacute deltamethrin exposure in rats. Environ Sci Pollut Res Int. 28(13):15890-15908 .
43. Xu MY, Wang P, Sun YJ, Wang HP, Liang YJ, Zhu L, Wu YJ. (2015) Redox status in liver of rats following subchronic exposure to the combination of low dose dichlorvos and deltamethrin. Pestic Biochem Physiol 124:60–65
44. Yang D, Tan X, Lv Z, Liu B, Baiyun R, Lu J, Zhang Z. (2016) Regulation of Sirt1/Nrf2/TNF-α signaling pathway by luteolin is critical to attenuate acute mercuric chloride exposure induced hepatotoxicity. Sci Rep 6:1–12
45. Yang JS, Park Y (2018) Insecticide exposure and development of nonalcoholic fatty liver disease. J Agric Food Chem 66:10132–10138
46. Young DS, Pestaner LC, Gibberman VAL (1975) Effects of drugs on clinical laboratory tests. Clin Chem 21:1D--432D
47. Yousef MI, Awad TI, Mohamed EH. (2006) Deltamethrin-induced oxidative damage and biochemical alterations in rat and its attenuation by Vitamin E. Toxicology. 227(3):240-7.
48. Zhang Z, Li S, Jiang H, Liu B, Lv Z, Guo C, Zhang H. (2017) Effects of selenium on apoptosis and abnormal amino acid metabolism induced by excess fatty acid in isolated rat hepatocytes. Mol Nutr & food Res 61:1700016.