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Ameliorative impact of coenzyme Q10 supplementation on deltamethrin-induced hepatic damage in broiler chickens

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ABSTRACT

Deltamethrin (DM) is a synthetic insecticide that is commonly used in agriculture and veterinary medicine. Furthermore, animal and human studies have shown that DM has a negative impact on the liver. This study was carried out to evaluate the protective effect of Coenzyme Q10 (CoQ10) supplementation against DM hepatotoxicity in broiler chickens. Sixty chicks were divided into 4 groups. First group (basal diet), second group (40 mg CoQ10 /kg diet), third group (300 mg DM/kg diet), and the fourth group (300 mg DM /kg diet) and (40 CoQ10mg/kg diet). The treatment was administered to the final three groups for 35 days. DM declined body weight (BW), body weight gain (BWG), and increased feed conversion rate (FCR). Significant increases in aspartate aminotransferase (AST), alanine aminotransferase (ALT), malondialdehyde (MDA), with a significant drop in levels of reduced glutathione (GSH) and superoxide dismutase (SOD) were also recorded in this group. *Caspase-3* and *B cell lymphoma 2* (*BCl2*) were substantially upregulated by DM in liver tissues. In addition, alterations in histopathology as severe congestion and mononuclear inflammatory cellular infiltration of the hepatic parenchyma with vacuolation of the hepatic cells were recorded in the examined liver of chickens intoxicated with DM. Concurrent CoQ10 supplementation with DM resulted in a significant improvement in estimated parameters when compared to the DM group. Because of its protective effects against DM-induced hepatotoxicity in broilers, dietary CoQ10 is recommended.

1. INTRODUCTION

Humans are highly exposed to DM residues through polluted crops, water, and animal feedstocks, as well as occupational exposure to DM residues in the workplace (Swarnam and Velmurugan 2013). Numerous investigations have shown that DM has negative effects on the liver (Yang and Park 2018) because of its role in metabolism and detoxification of pesticides (El Golli-Bennour et al. 2019: Xu et al. 2015). DM induced hepatotoxicity (Abdel-Daim et al. 2013; El Golli-Bennour et al. 2019; Gündüz et al. 2015; Mongi et al. 2011; Rjeibi et al. 2016; Tekeli et al. 2021). The overproduction of free radicals was the most prominent mechanism of DM toxicity (Abdel-Daim et al. 2014; Narra et al. 2017; Tekeli et al. 2021).

Coenzyme Q10 (CoQ10) is a lipophilic vitamin-like quinine derivative with ten isoprenyl units has antioxidant, anti-hyperlipidemic, anti-inflammatory, and anti-hyperglycemic properties. (Ali et al. 2022; Okudan et al. 2022). 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 liver toxicity (Hussein et al. 2021; Mazandaran and Khodarahmi 2021). Furthermore, CoQ10 has been shown to have potent free radical scavenging action, which aids in the maintenance of mitochondrial membrane potential and the reduction of protein oxidation and DNA damage; hence, it can restore cell function when subjected to oxidative stress (Abdeen et al. 2020) .

DM causes liver damage in broilers (Ibrahim et al. 2021), but there are no data on the preventative effects of CoQ10. As a result, the purpose of this study was to assess the protective effect of CoQ10 on DM-induced liver toxicity in broiler chickens to better understand the many mechanisms of action.

2. MATERIAL AND METHODS

2.1. Chemicals

CoQ10 was kindly supplied as (Coenzyme Q10®, 30 mg) from MEPACO, Cairo, Egypt. DM (Butox® 50 mg/ml;

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Intervet Co., France). All used Kits for serum biochemical analysis were obtained from Biodiagnostic CO, Giza, Egypt.

2.2. Experimental Animals

Sixty-one-day Cobb broiler chicks were purchased from El-Wataniya poultry company, Egypt. The chicks were housed in separate units under sanitary conditions. The temperature begins at 32°C and drops by 2°C each week. Ad libitum food and water were provided, and continual lighting was used. Ethical Committee of the Fac. Vet. Med. Benha University approved the study (BUFVTM 02-01-22).

2.3. Experimental design

The chicks were separated into 4 groups, each was subdivided into 3 replicates (5 chicks each). The 1st group (control group) received basal diet only; 2nd group was supplemented with 40 mg CoQ10/kg diet (Gopi et al. 2015), 3rd group received 300 mg DM /kg diet (Ibrahim et al. 2021) and 4th group (300 mg DM /kg diet + 40 mg CoQ10/kg diet) and All treatments performed for 35 days.

2.4. Growth parameters

The feed intake (FI), body weight gain (BWG), and feed conversion rate (FCR) were estimated. FCR= feed consumption/ weight gain. BWG was calculated by subtracting the initial weight (at 35 days) from the initial weight (at 7 days).

2.5. Sampling

2.5.1. Blood sampling

At the end of the trial, blood was drawn from wing veins in dry, clean tubes from all chickens in separate groups. To allow the blood to coagulate, it was left at room temperature in a sloping position. Serum was collected by centrifugation (10 minutes at 2000 *g*), transferred to dry, clean vials, and stored at –20°C until employed in biochemical tests.

2.5.2. Biochemical analysis

Serum ALT (Cat. No. AL 1031(45)) and AST (Cat. No. AS 1061(45)) activities were measured. The oxidative stress markers were assessed in liver tissues. MDA (Cat. No. MD 2529) as an indicator of lipid peroxidation was determined (Ohkawa et al. 1979). The activity of SOD (Cat. No. SD 2521; Nishikimi et al. 1972), and GSH level (Cat. No. GR 2511) were assessed (Beutler 1963).

2.5.3. Tissue sampling

Liver was quickly collected, washed with physiological saline, and divided into small 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. The second part was kept at -80°C till analysis of gene expression. The third portion was fixed in a 10% formalin solution for histopathological examination.

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

Gene expression of *caspase-3* and *BCl2* was performed according to Allam et al. (2022).

2.7. Histopathology

The liver of chickens in all groups were grossly examined and small specimens were collected and quickly fixed at least 24 h in 10% formalin solution. The fixed tissues were dehydrated in graded dilutions of ethyl alcohol and cleared in xylol, then embedded in paraffin, and then sliced into sections (4 µm thick). These sections were stained with hematoxylin and eosin (H&E) and examined using a Leica DM3000 microscope.

2.8. Statistical analysis

All analysis was conducted with the program SPSS 25. (SPSS Inc., Chicago, USA). One-way variance analysis (ANOVA) followed by Duncan's post-hoc test was used to compare group means and data were represented as mean ± SE. Significant *p* values were assessed <0.05.

3. RESULTS

3.1. DM and/or CoQ10 effect on growth performance

The effect of DM and/or CoQ10 on growth performance (BW, BWG, FC, and FCR) was demonstrated in figure (1). Compared to the control group, the group of coQ10 showed an increase in BW, BWG, and reduction in FCR. While broiler chickens intoxicated with DM revealed a drastic decline in BW, WG, and a rise in FCR compared to the control group. Meanwhile DM intoxicated chickens fed on a diet supplemented with CoQ10 exhibited an alleviation in growth performance parameters compared to DM-treated group.

3.2. DM and/or CoQ10 effect on liver serum biomarkers

DM intoxicated group induced a notable increase in liver enzyme activities comparing with control group (Figure 2A, B). While chicken intoxicated with in addition of DM and cotreated with CoQ10 showed a remarkable reduction in all parameters compared with the DM group.

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

As seen in Figure (2), when DM is administered to chickens, it significantly raises MDA levels (Figure 2C), decreases SOD activity (Figure 2D), and decreases GSH levels (Figure 2E). In addition, when compared to the DM group, the DM+CoQ10 group exhibited a significant improvement in both hepatic antioxidant status. Remarkably, SOD activity and GSH levels were nearly recovered to control levels.

3.4. Effect of DM and/or CoQ10 on Caspase-3 and BCl_2 gene expression

A diet supplemented with CoQ10 induced dramatic downregulation of *Caspase-3* (Figure 2F) and a notable up-regulation of BCl_2 (Figure 2G) in the liver. However, DM exhibited marked upregulation of *Caspase-3* and a significant downregulation in BCl_2 in the liver. When DM+CoQ10 was compared to the DM group, significant downregulation of hepatic *Caspase-3* expression was recorded. Also, remarkable upregulation of hepatic BCl_2 expression was observed. Of note, CoQ10 supplementation to DM intoxicated broiler chickens restored hepatic BCl_2 gene expression to control values.

3.5. Histopathological examination

A liver tissue section of the control and CoQ10 groups (Figure 3A, B) showed well-arranged hepatic cords around blood sinusoids. In contrast, the liver of DM intoxicated broiler chickens revealed vacuolation of the hepatocytes with congestion of hepatic blood vessels and diffuse mononuclear inflammatory cellular infiltration mainly lymphocytes in-between the cords and around the

congested blood vessels (Fig 3C). In the DM+CoQ10 group (Figure 3D), congestion of the blood vessels with perivascular edema were the only detectable microscopic findings.

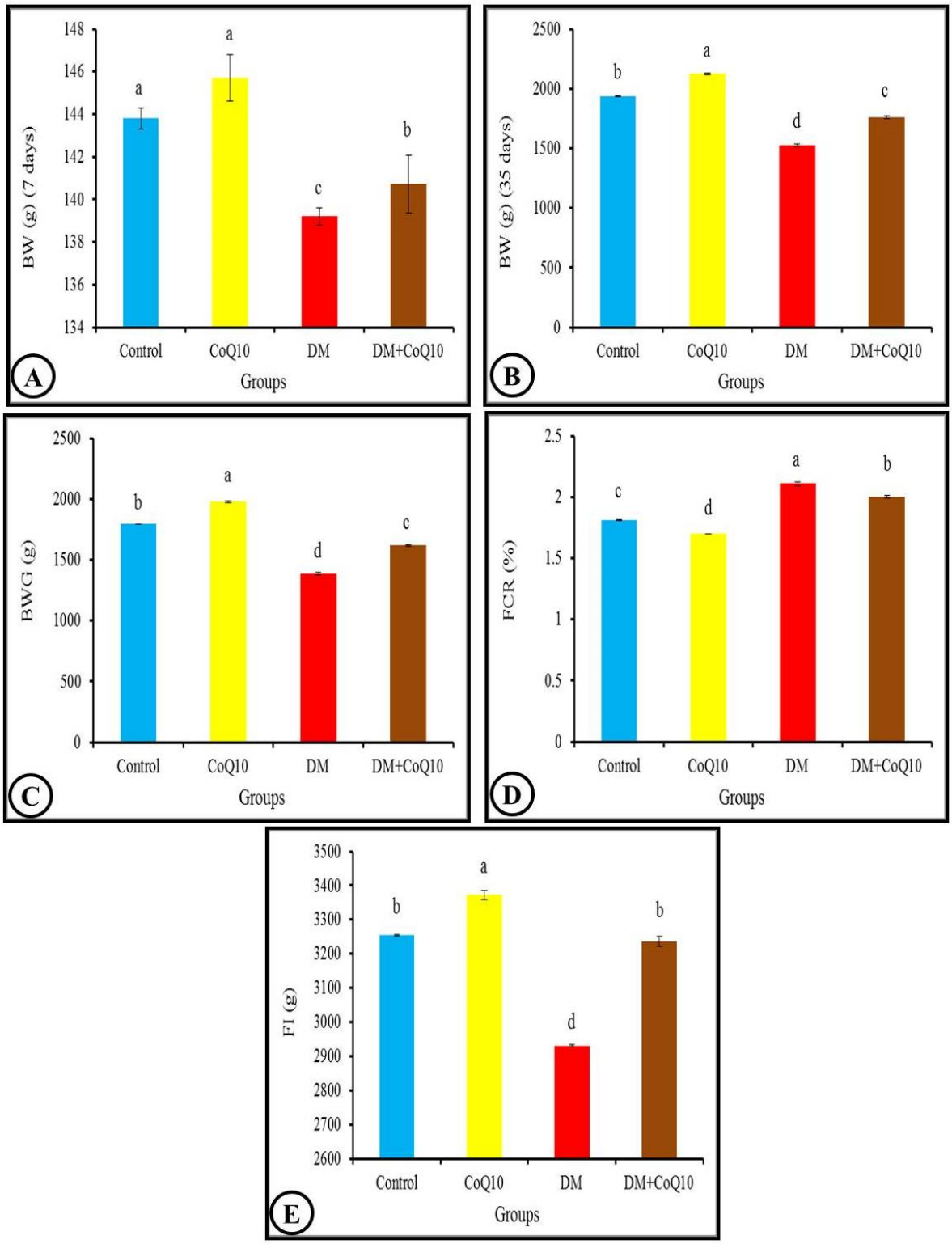

Figure 1: Effect of DM (300 mg/kg diet) and/or CoQ10 (40 mg/kg diet) on growth performance parameters in broiler chickens (n=15). Coenzyme Q10 (CoQ10); deltamethrin (DM); Body weight (BW); Body weight gain (BWG); Feed intake (FI); Feed conversion rate (FCR).

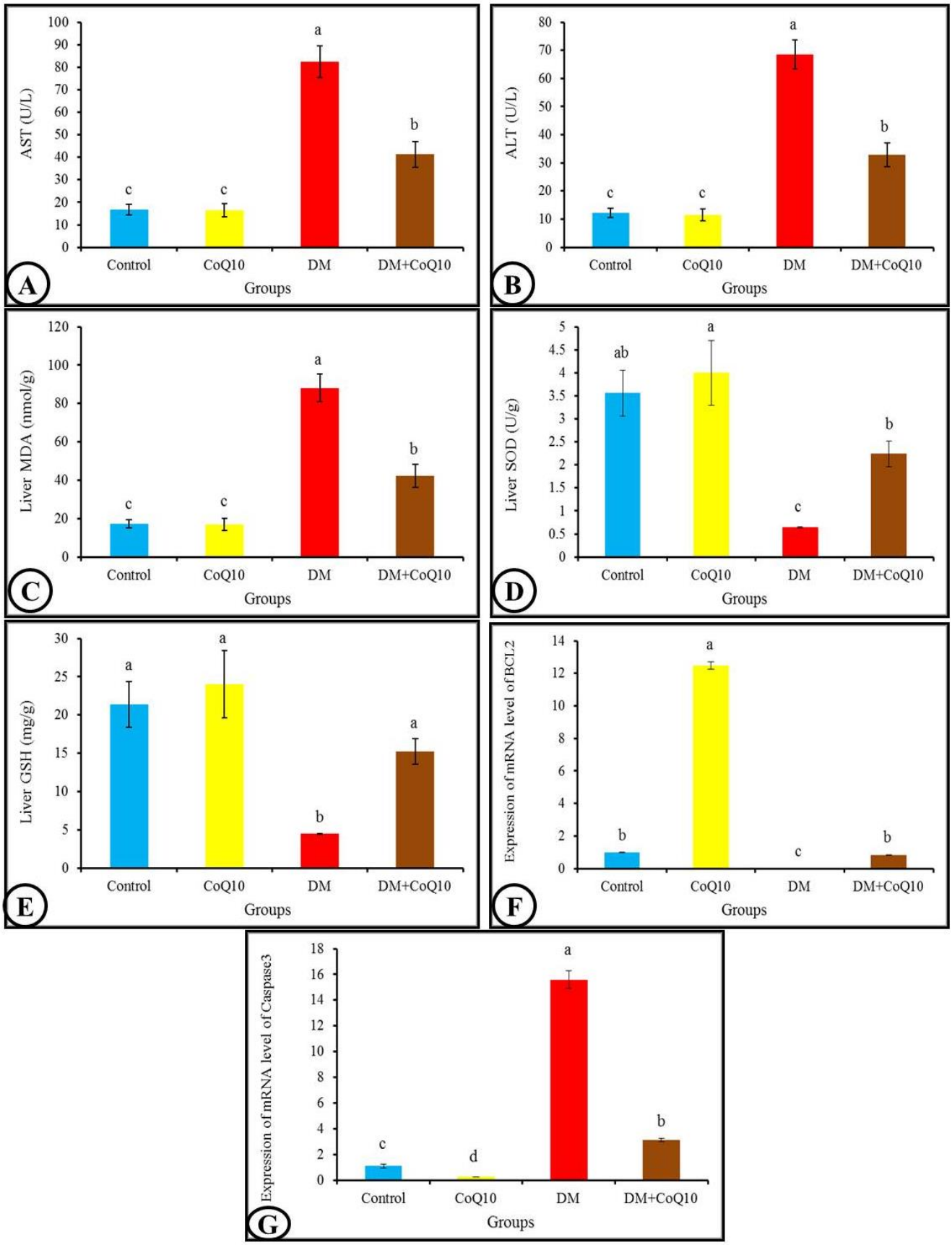

Figure 2: Effect of DM and/or CoQ10 on AST (A), ALT (B), hepatic oxidative stress markers; MDA level (C), SOD activity (D), GSH level (E), hepatic gene expression; *caspase-3* (F) and *BCl2* (G) in broiler chickens.

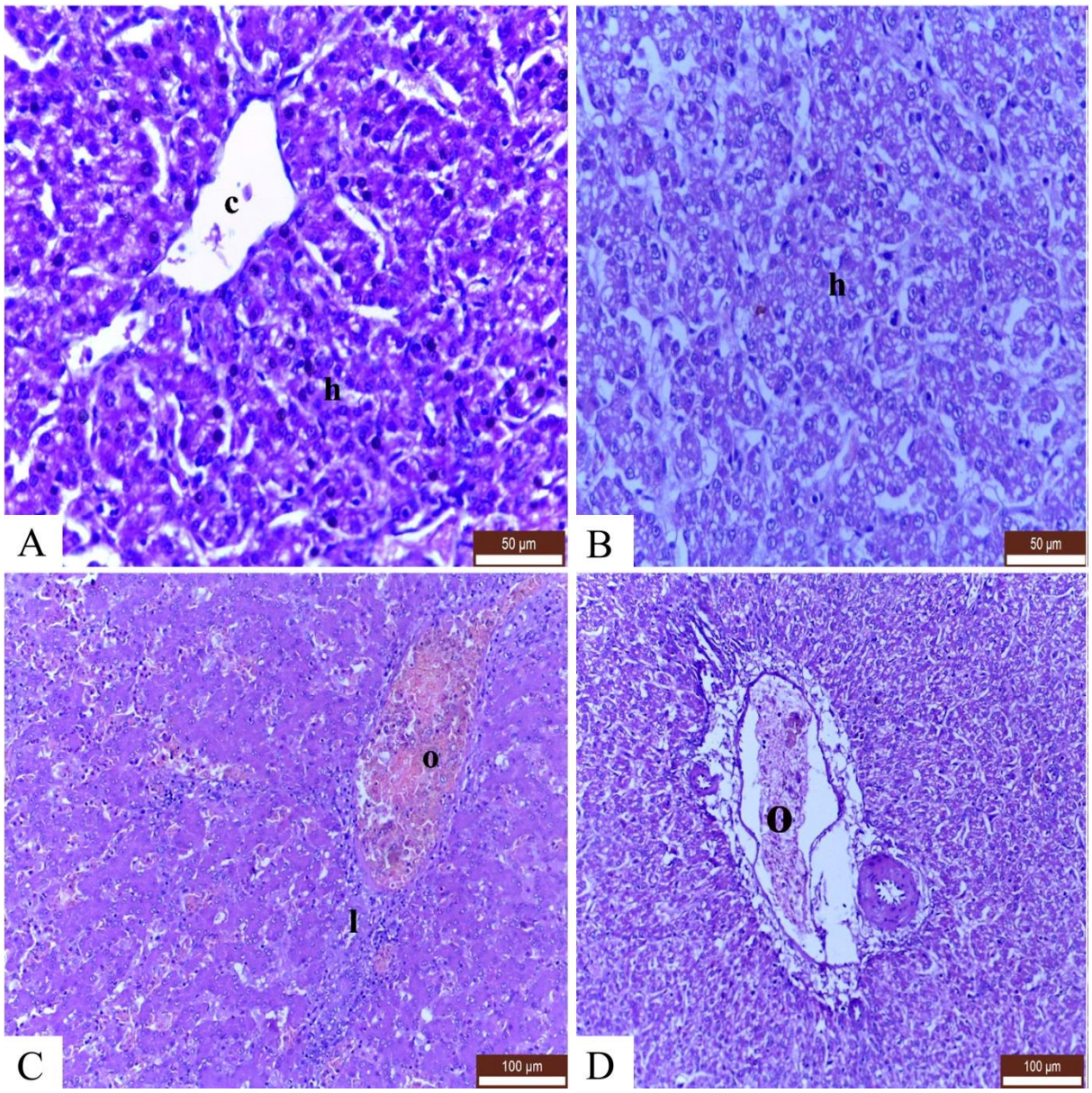

Figure 3: Photomicrographs of the liver of chickens treated with DM and/or CoQ10. A; control, B; CoQ10, C: DM and D; DM+ CoQ10. H&E stain.

4. DISCUSSION

According to the results of the present work, broiler chicken, which supplements CoQ10 diets, has the best growth performance. Previous studies have proven that supplementing CoQ10 diet has a beneficial impact on the performance of poultry (Nemati et al. 2017). These favorable effects of CoQ10 are believed to be generated by alleviating mitochondrial function and a decrease in assets because of its direct antioxidant capability (Geng and Guo 2005). The decline of the BW of DM group could be mainly due to poor feed conversion effectiveness. DM-CoQ10 group demonstrated an improvement in the BWG, which revealed that CoQ10 had a positive influence on the BWG. The excessive increase in saprophytic bacteria in chicken feed leads to a release of many compounds that increased DM's toxicity and decrease rate of growth (Chandra et al. 2013). The addition to CoQ10 boosted the BW increase. The BW of broilers reduced considerably in DM intoxicated group.

DM caused hepatotoxicity, evidenced by higher ALT and AST values. Changes in the histological examination of the DM group were conformable with the biochemical results. These findings were attributed to cytochrome P450 detoxifying in the liver for over-production of ROS (Dahamna et al. 2011; Chargui et al. 2012). The previous studies of Yousef et al. (2006) suggested that hepatotoxicity associated with DM exposure is related to oxidative stress and subsequent tissue damage. Inflammation and steatosis induced these changes (Li et al. 2021) .

The most significant mechanism of DM toxicity was free radical overproduction (Abdel-Daim et al. 2013, 2014; Narra et al. 2017). According to the findings of this study, DM causes a significant rise in oxidative stress in the liver. DM is detoxified in the liver by cytochrome P450, which results in the formation of free radicals (Dahamna et al. 2011). During oxidative phosphorylation, mitochondria generate a significant amount of ROS (Lv et al. 2020), which can cause substantial cellular oxidative damage if 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 .

Another significant finding was that DM exposure significantly changes the gene expression of apoptotic and anti-apoptotic markers, lending credence to apoptosis as a plausible mechanism by which DM may cause liver damage. In our research, the expression of *caspase-3*, an apoptotic protein, was elevated. Furthermore, Maalej et al. (2017) found that DM treatment caused apoptosis in liver tissues via up-regulating p53 and cyclo-oxygenase 2. Downregulation of *BCl2* expression, an anti-apoptotic protein, confirmed their findings in the current study because it is adversely connected to p53.

The most important observation from the data is that feeding a feed supplemented with CoQ10 to DM-intoxicated broiler chickens significantly reduced the adverse effects of DM on liver tissues. All of the findings from biochemistry and histopathology that we observed show the impact of CoQ10 on hepatic protection. This is in complete agreement with Albadrany and Naser (2020). The influence of CoQ10's antioxidant function could be one explanation for its protection against DM toxicity. CoQ10's ability 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 .

As expected, concurrent supplementation of CoQ10 to DM intoxicated broiler chickens significantly improves both enzymatic (SOD) and non-enzymatic (GSH) antioxidants and diminishes MDA production in liver tissues. Our results confirm previous studies (Gopi et al. 2014; Huang et al. 2011; Maalej et al. 2017). Many possible explanations might explain our findings. CoQ10 suppresses ROS overproduction, and endogenous antioxidant maintenance (Hussein et al. 2021; Ratliff et al. 2016) .

The current study demonstrated that cotreatment with Co10 was followed by downregulation in *caspase-3* and up-regulation in *BCL2* expression of hepatic tissues. These results agreed with Abdeen et al. (2020) and Allam et al. (2022). The anti-apoptotic activity of CoQ10 could be attributed to its capability to regulate the perturbation electrochemical gradients on the mitochondrial level (Allam et al. 2022) .

CoQ10 acts as a potent antioxidant free radical scavenger, thus limiting damage associated with oxidative stress (Abdeen et al. 2020; Ali et al. 2022; Okuden et al. 2022). CoQ10 in the diet improved reproductive performance (Rafieian-Naeini et al. 2021).

Conclusions

DM caused problems with hepatic function, lipid peroxidation, glutathione activity, and antioxidant enzymes. CoQ10 can counteract the negative effects of DM on the liver of chickens by improving antioxidant state.

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