10.21608/avmj.2025.380543.1684 Assiut University web-site: www.aun.edu.eg

AMELIORATIVE EFFECT OF COENZYME Q 10 ON TITANIUM DIOXIDE NANOPARTICLES INDUCED HEPATOTOXICITY IN RATS

GHADA M. ABDALLAH; MOKHTAR TAHA AND KHALED M.A. HASSANEIN
Department of Pathology, Faculty of Veterinary Medicine, Assiut University, Assiut 71526, Egypt

Received: 5 May 2025; **Accepted:** 27 June 2025

ABSTRACT

This study aimed to explore the ameliorative effect of Coenzyme Q10 (CoQ10) on Titanium dioxide nanoparticles (TiO_2 NPs)-induced hepatotoxicity. Sixty adult male albino rats were divided into four groups, with 15 rats in each group. Group (A) was administered only a vehicle (1% Tween 80). Group (B) was administered TiO_2NPs daily by gastric tube (100 mg/kg.bwt) for three months. Group (C) was administered TiO_2NPs (100 mg/kg.bwt) and simultaneously administered CoQ10 (10 mg/kg.bw) daily by gastric tube for the same period. Group (D) was administered CoQ10 only. At the end of the experiment, serum samples and tissue samples from the liver were collected for the detection of liver enzyme markers and histopathological examination, respectively. The TiO_2 NPs-intoxicated $_2$NPs-intoxicated group showed elevation in the liver enzyme markers aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Also, the histopathological results revealed vascular and parenchymatous changes. The vascular changes were in the form of congestion and thrombosis of the blood vessels. The parenchymatous changes were vacuolar degeneration of hepatocytes, necrosis, apoptosis, hyperplasia of the bile duct epithelium and hepatic fibrosis. TiO_2NPs and CoQ10 treated group revealed a decrease in the levels of AST and ALT and an improvement of the histological architecture of the liver tissue. It was concluded that chronic toxicity of TiO_2NPs induced histopathological alterations in the liver. The administration of CoQ10 ameliorated the liver damage induced by TiO_2NPs via its antioxidative and anti-inflammatory properties.

Key words: TiO_2NPs, CoQ10, AST, ALT, histopathology

INTRODUCTION

With advances in nanotechnology, nanoparticles (NPs) are being used extensively in a wide variety of industrial and biomedical products. However, titanium dioxide nanoparticles (TiO_2NPs) are considered among the top five most hazardous NPs (Luo *et al.,* 2020; Cornu *et al.,* 2022 and Rajaiah *et al.,* 2022). They are being used in widespread applications to provide whiteness and opacity to products such as paints, plastics, papers and inks (Trouiller *et al.,* 2009). They are also used as a food colorant and white pigment in many products, including sauces, cheeses, skimmed milk and ice cream (Dudefoi *et al.,* 2017 and Baranowska-Wójcik *et al.,* 2020).

Corresponding author: GHADA M. ABDALLAH
E-mail address: Ghada_Mahmoud@aun.edu.eg
Present address: Department of Pathology, Faculty of Veterinary Medicine, Assiut University, Assiut . 71526, Egypt

TiO_2NPs induced toxicity in various organs, such as hepatotoxicity (Wang *et al.,* 2007; Hassanein and El Amir, 2017), nephrotoxicity (Hassanein and El Amir, 2018), pulmonary toxicity (Oberdörster *et al.,* 2000), testicular toxicity (Hassanein and El Amir, 2017) and neurotoxicity (Zhang et al., 2023).

It has been reviewed that TiO_2NPs can initiate several critical events in the liver, such as the formation of reactive oxygen species (ROS), induction of oxidative stress and inflammation (Brand *et al.,* 2020). Previous work reported that oral administration of TiO_2NPs and deposition of these particles in the liver induce several histopathological alterations in the hepatocytes (Wang *et al.,* 2007; Dhawan and Sharma, 2010; Jeon *et al.,* 2013; Fadda *et al.,* 2018; Javaheri *et al.,* 2023 and Choobchian *et al.,* 2024).

Coenzyme Q10 (CoQ10) is a vitamin-like benzoquinone compound, found in most eukaryotic cells, especially in the mitochondria. It acts as a cofactor, a component of the electron transport chain and participates in aerobic respiration and generating energy in the form of ATP (Lenaz *et al.,* 2007; Ghule *et al.,* 2009; Garrido-Maraver *et al.,* 2014 and El-Bassouny *et al.,* 2023).

CoQ10 acts as a powerful antioxidant that scavenges free radicals, prevents the initiation and propagation of lipid peroxidation and acts as a membrane stabilizer for the cell membrane and all intracellular membranes (Crane, 2001 and El-Bassouny *et al.,* 2023).

Researchers have discovered several biological activities of CoQ10, rather than its use as an antioxidant and a free radical scavenger. These biological activities include hepatoprotective effects, reduction of the endothelial cell impairments and anti-apoptotic, anti-fibrotic and anti-inflammatory properties (Çolak and Uysal, 2017; Mohamed *et al.,* 2019; Abdeen *et al.,* 2020 and Alhusaini *et al.,* 2022).

This study evaluated the liver function activities and histopathological changes induced by chronic toxicity of TiO_2NPs on the liver of male rats and evaluated the ameliorative effects of CoQ10.

MATERIALS AND METHODS

1. Materials

1.1. Drugs and chemicals:

Titanium dioxide nanoparticles (TiO_2NPs) and Coenzyme Q 10 (CoQ10) were purchased from Sigma Aldrich, Germany. The TiO_2NPs used in this study were titanium (IV) oxide and anatase with a purity of 99.7%, with a nanoparticle size of 21 nm. AST, ALT kits were obtained from Bio Diagnostic Co. Giza. Egypt**.** The additional chemicals were all analytical-grade compounds purchased from standard commercial sources.

1.2. Animals:

Sixty adult male albino rats (weighing 180 ± 20 gm at 12-14 weeks of age) were purchased from the Animal House of the Faculty of Veterinary Medicine, Assiut University, Egypt. The study protocol was authorized by the Animal Ethics Committee of the Faculty of Veterinary Medicine, Assiut University, Assiut, Egypt, according to the OLE standards for the use of animals in research under No. 06/2024/0209.

1.3. Experimental design:

Sixty adult male albino rats were assigned into 4 equal groups (n= 15 rats / group) as follows:

Group (A): Administrated the vehicle in a dose of (1% Tween 80).

Group (B): Administrated CoQ10 in a dose of (10 mg/kg.bw) daily dissolved in (1% Tween 80) by a gastric tube, according to (Fouad and Jresat, 2012). Rats were administered CoQ10 in advance, starting from day 1 till the end of the experiment.

Group (C): Administrated TiO_2NPs from day 16 till the end of the experiment in a dose of (100 mg/kg.bw) dissolved in (1% Tween 80) daily by a gastric tube, according to (Rajaiah *et al.,* 2022 and Kamal *et al.,* 2023). Rats were initially administered CoQ10 in advance, starting from day 1 till day 15 and continuing till the end of the experiment.

Group (D): Administrated TiO_2NPs as group B + CoQ10 in a dose of CoQ10 daily from day 1 till the end of the experiment in a dose of (10 mg/kg.bw) dissolved in (1% Tween 80) by a gastric tube, according to (Fouad and Jresat, 2012).

All rats were monitored for any clinical signs or mortality. At the end of the experimental period (105 days), rats were sacrificed under anesthesia with isoflurane 4% for sampling.

1.4 Blood and tissue sampling:
At the end of the experiment (day 105), the blood samples were collected from the medial canthus of the eyes, then the serum samples were collected and kept at -20°C for liver function markers. Tissue samples were collected from the liver for histopathological examination.

2. Methods
2.1. Biochemical analysis:
Determination of liver function markers (AST& ALT):
The levels of AST and ALT enzymes were estimated by the colorimetric method, described by **Reitman and Frankel (1957).**

2.2. Histopathological examination:
Liver tissue specimens were fixed in 10% neutral buffered formalin, dehydrated in ethyl alcohol, and then embedded in paraffin wax, according to Bancroft *et al.* (1996). Microscopic examinations involved 5-µ-thick sections stained with hematoxylin and eosin (H&E) and Masson's Trichrome stain. The slides were examined microscopically with an Olympus CX31 microscope and photographed with an Olympus SC30 camera adapted to the microscope. The histopathological lesion score is based on the incidence of lesions in 30 examined sections of 15 rats in each group.

2.3. Acridine orange stain for detection of apoptosis:
The procedure of Acridine orange stain (fluorescent stain) was performed according to Abd-Elhafeez *et al.* (2020). The sections were analyzed using a microscope (model Letiz DM 2500) with external fluorescent units (Leica EL 6000). Apoptotic cells stained with Acridine orange stain emit red and orange fluorescence, while normal and viable cells emit green fluorescence.

2.4. Statistical analysis
Statistical analysis was conducted using SPSS version 26 (SPSS Inc, Chicago, IL, USA) according to Borenstein *et al.* (1997). The data were expressed as mean ± standard error (SE). One-way ANOVA and the post-hoc Tukey HSD test were used for multiple comparisons. A difference of $P \leq 0.05\%$ was considered statistically significant. Graphs were plotted using GraphPad Prism 9.4.1.

RESULTS

1. Biochemical results
Liver function markers:
There was no significant difference in the level of ALT between the CoQ10 treated group and the control group. TiO_2NPs treated group showed a significant increased AST and ALT levels, compared to TiO_2NPs + CoQ10 treated group, CoQ10 treated group and control groups. The level of AST and ALT was significantly decreased in TiO_2NPs + CoQ10 treated group, compared to TiO_2NPs treated group. The level of AST was numerically increased in both TiO_2NPs +CoQ10 treated group, compared to CoQ10 treated group and control group. (Fig. 1).

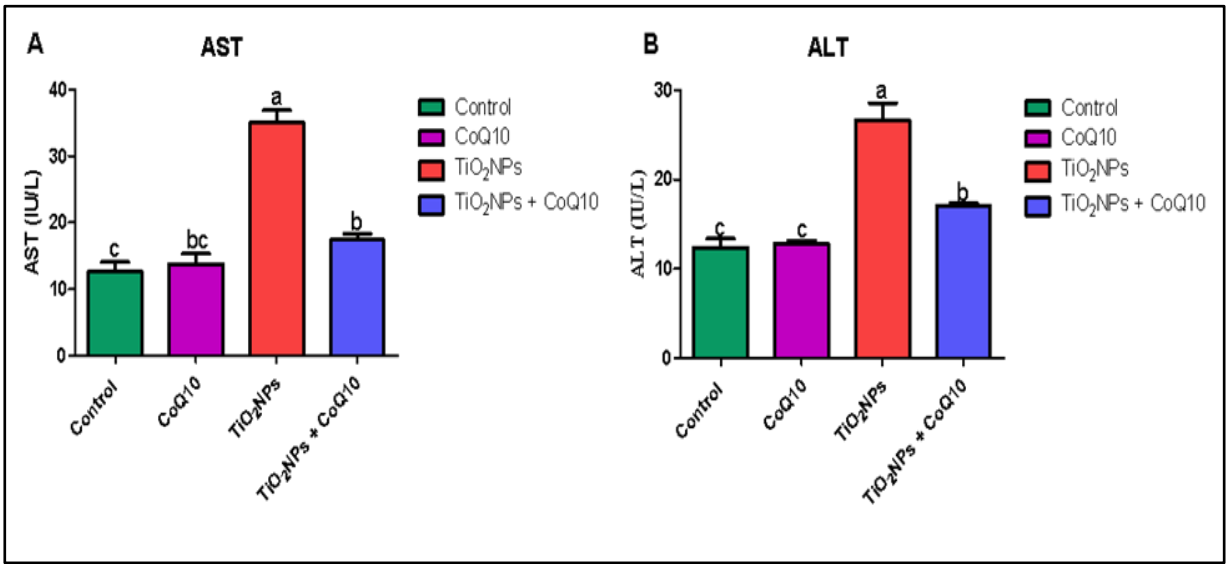

Fig. 1: Liver function markers in different treated groups. **A)** AST and **B)** ALT. Means with different superscripts are significantly different at P<0.05. Data are expressed as mean ± S.E., with n = 5.

2. Histopathological findings

The histopathological grades based on incidence of lesions in 30 examined sections of 15 rats in each group (- No lesion, + lesion present in 1- 6 sections, + + lesion present in 7- 14 sections, + + + lesion present in 15- 22 sections, + + + + lesion present in 23-30 sections) were summarized in Table (1)

Groups / Hepatic lesions	Group (A) Control group	Group (B) CoQ10 treated group	Group (C) TiO_2 NPs treated group	Group (D) TiO_2 NPS + CoQ10 treated group
1- Vascular changes:				
➢ **Congestion of blood vessels**	-	-	+ + + +	+ +
➢ **Thrombosis**	-	-	+ +	-
2- Parenchymal changes:				
➢ **Vacuolar degeneration of hepatocytes**	-	-	+ + + +	+ +
➢ **Lytic necrosis of hepatocytes**	-	-	+ +	+
➢ **Bile duct hyperplasia**	-	-	+ +	-
➢ **Kupffer cell activation**	-	-	+ + +	+
➢ **Mononuclear cell infiltration**	-	-	+ + + +	+
➢ **Fibrosis**	-	-	+ + +	-

Table 1: Lesion score of the histopathological results of the liver in all studied groups (- No lesion, + lesion present in 1- 6 sections, + + lesion present in 7- 14 sections, + + + lesion present in 15- 22 sections, + + + + lesion present in 23-30 sections / 15 rats in each group).

The histological architecture of the liver tissue sections stained with H&E stain in the control group and CoQ10 treated group revealed normal histology of the liver. The sections showed normal appearance of hepatocytes; they were polyhedral cells with vesicular nuclei and prominent nucleoli, arranged in cords and interspersed by hepatic sinusoids (Fig. 2).

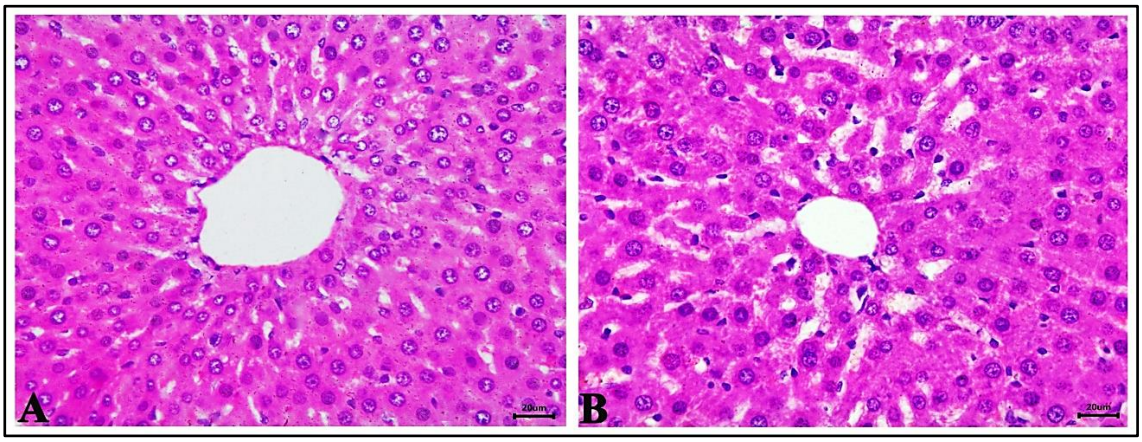

Fig. 2: Liver, A) Control group and B) CoQ10- treated group, both showing normal histological architecture of the liver (H&E stain).

The microscopical examination of liver tissue sections stained with H&E stain in TiO_2NPs treated group showed vascular and parenchymatous changes. The vascular changes were in the form of congestion of central veins, dilatation and congestion of hepatic sinusoids and portal blood vessels. Some blood vessels showed thrombosis, which consisted of fibrin threads, erythrocytes and leukocytes. Hyperplasia of the epithelial lining of the bile ducts, portal fibrosis and perivascular fibrosis were also noticed (Fig. 3). Fibrosis was confirmed by Masson's Trichrome stain, in which the fibrous connective tissue appeared blue in color against a reddish background (Fig. 4). There were several parenchymatous changes, including vacuolar degeneration of hepatocytes, a moderate increase in binucleated hepatocytes, Kupffer cell activation, focal area of lytic necrosis and focal necrosis infiltrated with mononuclear cells (Fig. 5).

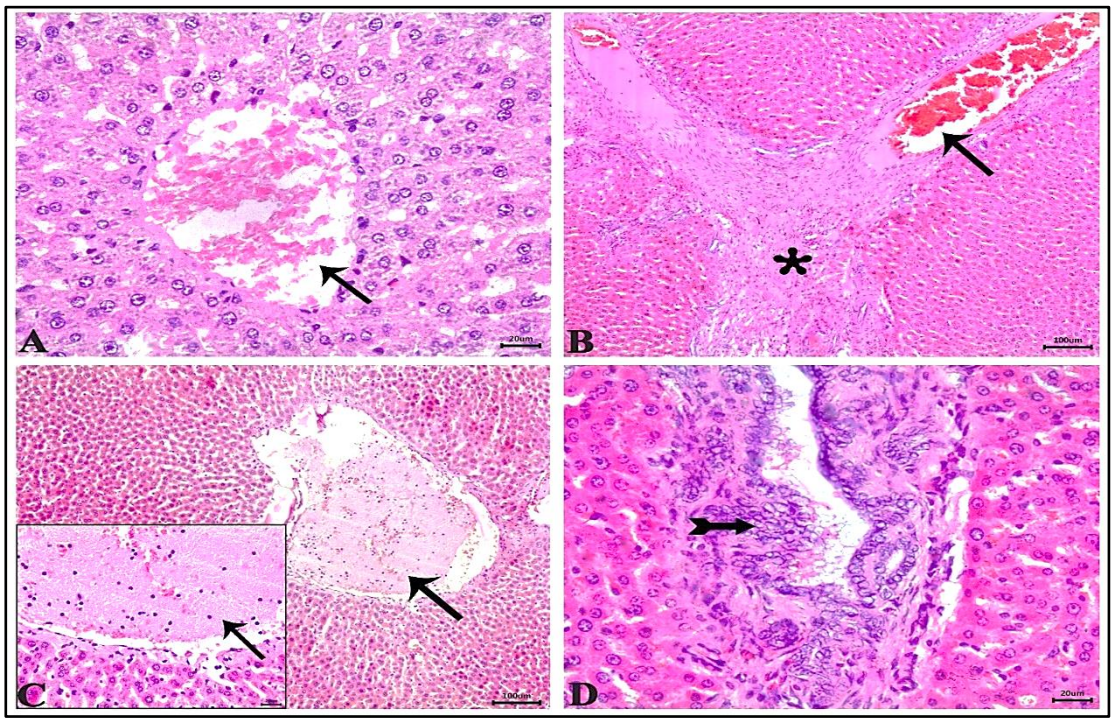

Fig. 3: Liver, TiO_2NPs treated group showing A) Congestion and dilatation of the central vein (arrow), B) Dilatation and congestion of the portal blood vessels (arrow) with fibrosis in the portal area (asterisk), C) Thrombus in the central vein (arrow). D) Hyperplasia of the epithelium lining of the bile duct (tailed arrow) (H&E stain).

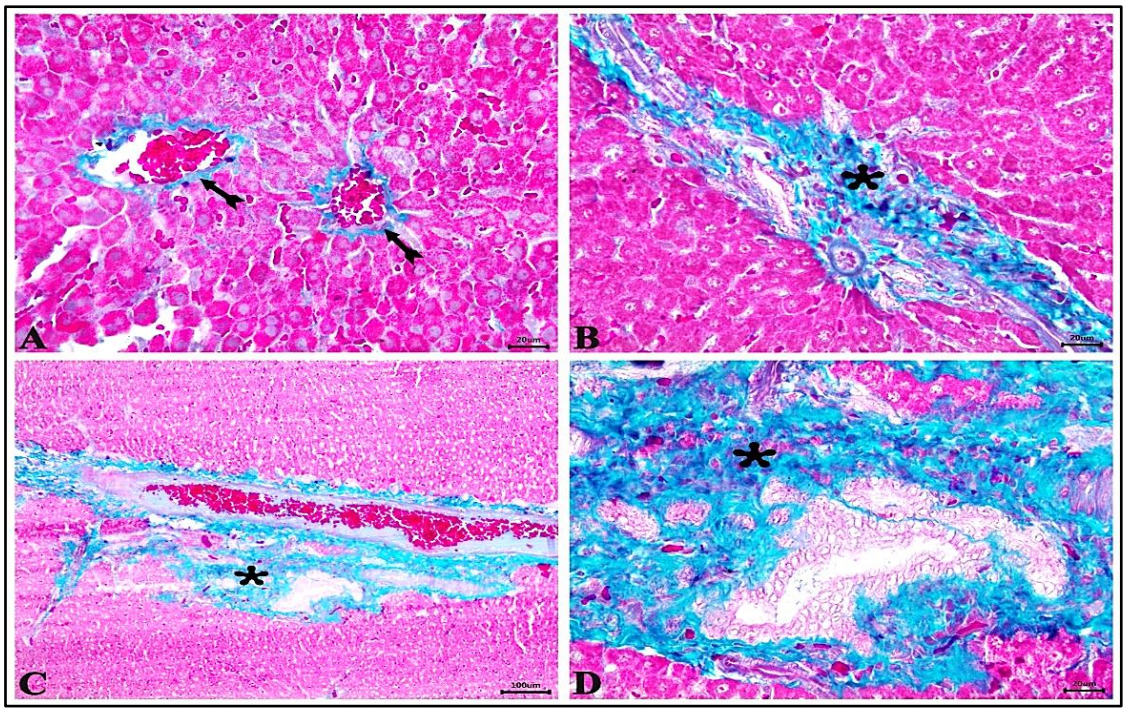

Fig. 4: Liver, TiO_2NPs treated group, (A) Perivascular fibrosis (tailed arrows); (B-D) Portal fibrosis (asterisks) that appears blue in color (Masson's Trichrome stain).

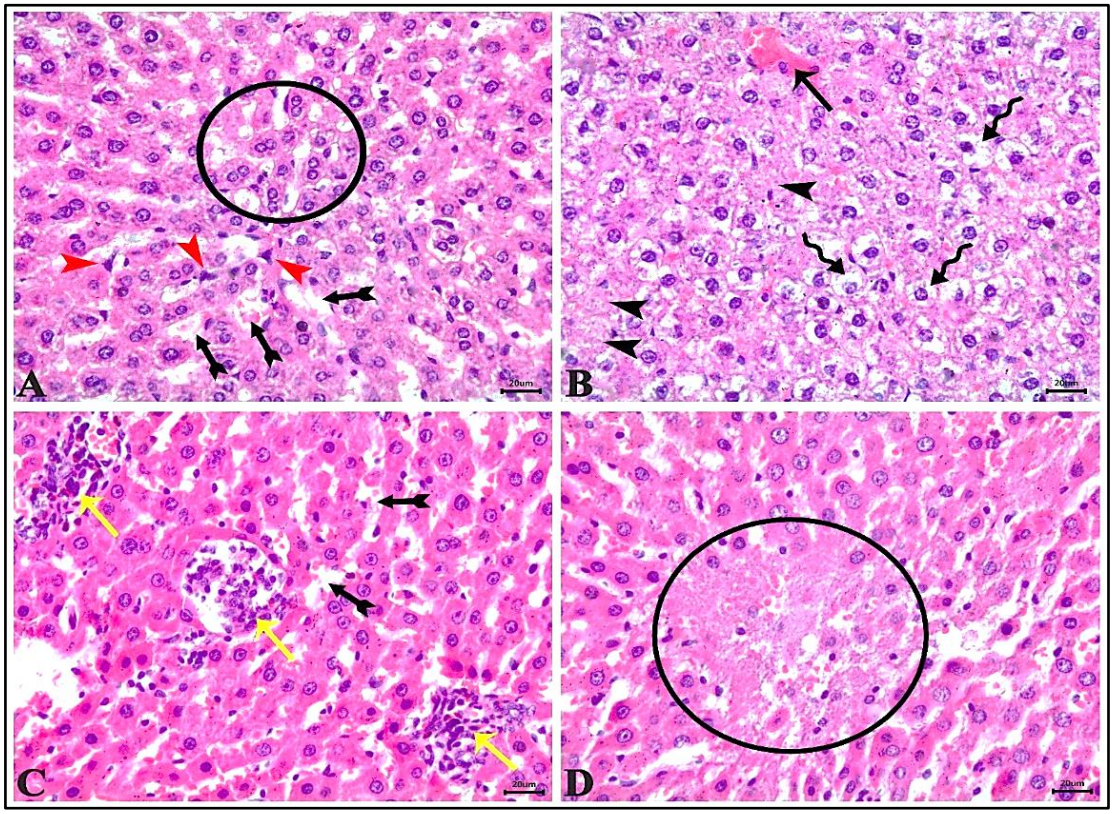

Fig. 5: Liver, TiO_2NPs treated group, (A) Binucleation of some hepatocytes (circle), Kupffer cell activation (red arrow heads) and hepatic sinusoidal dilatation (tailed arrows). (B) Dilatation and congestion of hepatic sinusoid (arrow), single-cell necrosis (black arrow heads) and vacuolar degeneration of hepatocytes (wavy arrows). (C) Focal area of necrosis infiltrated with inflammatory cells (yellow arrows) and sinusoidal dilatation also exists (tailed arrows). (D) Focal area of lytic necrosis (circle) (H&E stain).

The examined H&E-stained liver tissue sections of TiO_2NPs and CoQ10 treated group showed improvement of the general architecture of the liver with mild hepatic lesions. These lesions consisted of vascular changes, such as mild congestion of the portal blood vessel, moderate central vein congestion, hepatic sinusoidal dilatation and slight mononuclear cell infiltration (Fig.6).

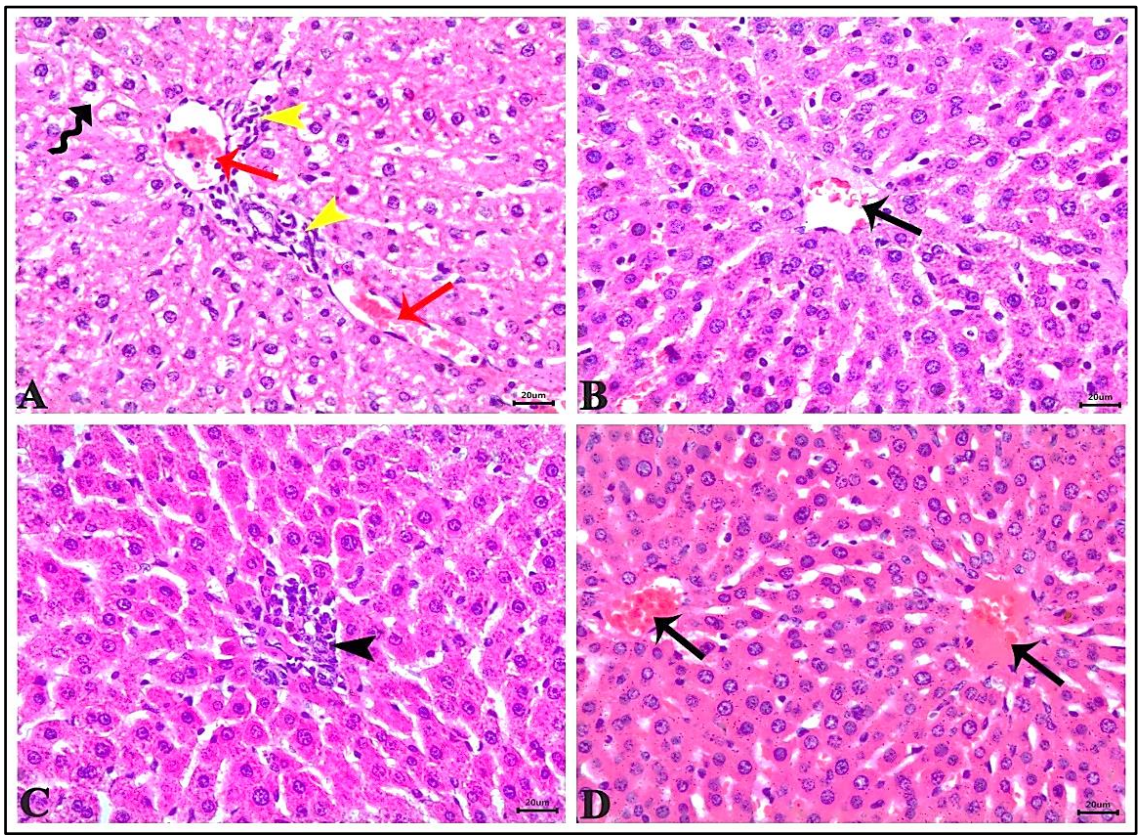

Fig. 6: Liver, (A- D) TiO_2NPs + CoQ10 treated group, (A) Congestion of the portal veins (red arrows), vacuolar degeneration of hepatocytes (wavy arrow) and perivascular mononuclear cell aggregation (yellow arrow heads); (B) Mild congestion of the central vein with slight normal appearance of hepatocytes (C) Focal aggregation of mononuclear cells (arrow head); (D) Congestion of central veins (arrows) with normal appearance of hepatocytes (H&E stain).

3. Acridine orange findings:

The apoptotic changes and also the lysosomal activity in the liver were detected by acridine orange stain, in which only green fluorescence was presented in both the control and CoQ10 treated group respectively (Fig. 7 A, B). TiO_2NPs treated group showed red and orange fluorescence that indicated high DNA damage, an increase in the number of apoptotic cells and lysosomal activity (Fig. 7 C, D). There was a reduction in the DNA damage and apoptotic cells, with an increase in the green fluorescence in TiO_2NPs and CoQ10 treated group (Fig. 7 E, F).

DISCUSSION

Nanoparticles have numerous properties that make them appropriate for use in a wide range of applications, such as biological and medical applications. Due to the quick growth of nanotechnology, different metal oxide nanoparticles are now used in a variety of industries and titanium dioxide nanoparticles are one of those metal oxides. Numerous investigations have demonstrated that the accumulation of TiO_2NPs in parenchymatous organs can cause inflammatory responses (Attia *et al.,* 2013 and Kumar *et al.,* 2016).

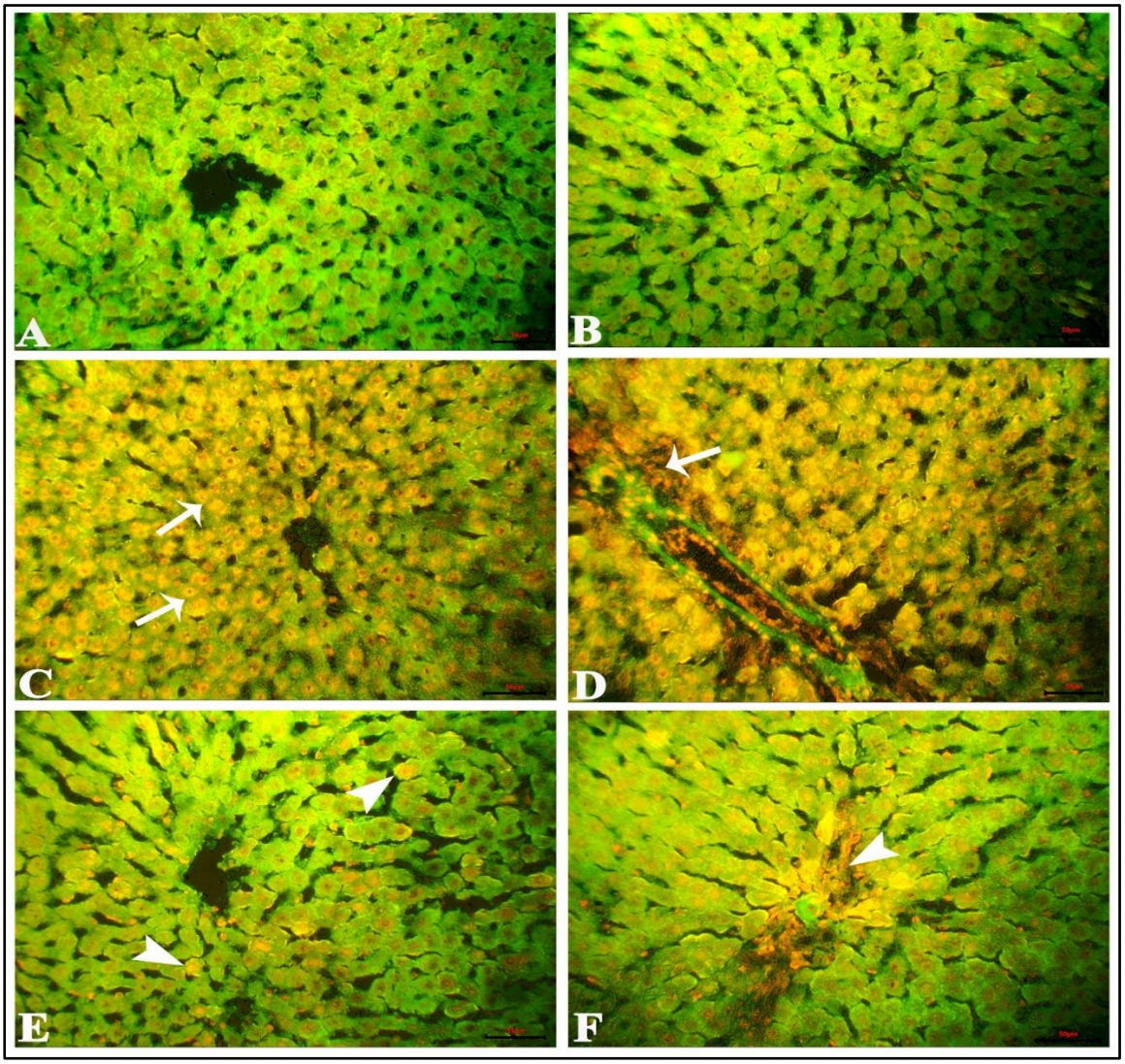

Fig. 7: Liver, acridine orange-stained paraffin section of the liver. A, B) CoQ10 treated group and the control group showing normal green fluorescence appearance of the hepatocytes. C, D) TiO_2NPs treated group showing red and orange fluorescence, which indicates apoptotic hepatocytes, DNA damage and lysosomal activity (white arrows). E, F) TiO_2NPs + CoQ10 treated group showing normal green fluorescence with the presence of some hepatocytes with orange fluorescence (arrow heads).

In the current study, the TiO_2NPs-administered rats showed a marked increase in the levels of AST and ALT liver enzymes, compared to the TiO2NPs and CoQ10-treated group and the control group. Many researchers reported that TiO_2NPs raise the oxidative stress indices, which consequently increases the liver function markers (Hassanein and El Amir, 2018; Fadda *et al.,* 2018 and Javaheri *et al.,* 2023).

Histopathological examination of the H&E-stained liver tissue sections in TiO_2NPs treated group revealed congestion and thrombosis of the central vein and portal blood vessels, vacuolar degeneration and lytic necrosis of hepatocytes, Kupffer cell activation, perivascular and periportal fibrosis and focal mononuclear cell infiltration. Similar results were reported by (Valentini *et al.,* 2019; Javaheri *et al.,* 2023 and Choobchian *et al.,* 2024).

The liver is the primary organ for the accumulation of TiO_2NPs, which produce oxidative stress and excessive release of reactive oxygen species (ROS) (Zhao *et al.,* 2021). Mohammed and Safwat, (2020)

concluded that oxidative stress is the principal mechanism by which TiO_2NPs induced hepatotoxicity. Subsequent to liver injury generated by TiO_2NPs, Ito cells (Hepatic stellate cells, HSC) exhibit smooth muscle α-actin, signifying their activation into myofibroblast-like cells, which is directly linked to experimental liver fibrogenesis (Li *et al.,* 2025).

Liver fibrosis was confirmed by Masson's Trichrome stain, in which the fibrous connective tissue appeared blue in color. TiO_2 has recently reclassified by the International Agency for Research on Cancer (IARC) as a group 2B carcinogen: "possibly carcinogenic to humans" (IARC, 2006). DNA damage and apoptotic hepatocytes in liver tissue were confirmed by acridine orange stain, TiO_2NPs treated group showed a significant increase of apoptotic cells, compared to other groups.

CoQ10 is a naturally occurring hydrophobic substance that is a potent antioxidant, in addition to being an essential part of the mitochondrial respiratory chain (Sohet *et al.,* 2009). CoQ10 has attracted significant study interest due to its role as a dietary supplement in producing cellular bioenergy and preventing tissue damage caused by oxidative stress (Akbari et al., 2020). TiO_2NPs and CoQ10 treated group revealed a marked decrease in the levels of AST and ALT liver enzymes. Histopathological examination of liver tissue in TiO_2NPs and CoQ10 treated group showed minimal histopathological changes and also an improvement of the histological appearance of the liver was observed. There was only moderate congestion of the central vein, minimal vacuolar degeneration and slight inflammatory cell infiltration. This improvement in histopathological changes could be attributed to CoQ10 demonstrating anti-inflammatory properties by lowering the release of pro-inflammatory cytokines during the inflammatory injury (Schmelzer *et al.,* 2008).

In liver tissue sections stained with acridine orange stain in TiO_2NPs and CoQ10 treated group, there was an increase in the green fluorescence with only a few hepatocytes with an orange fluorescence, which indicates a great improvement in the DNA damage, apoptosis and lysosomal activity of this group. Papucci *et al.* (2003) reported that CoQ10 inhibited the DNA fragmentation caused by all apoptotic triggers, significantly decreased apoptotic cell death and attenuated ATP decrease. The authors added that cytochrome C release, caspase 9 activation and mitochondrial depolarization were all inhibited by the action of CoQ10.

CONCLUSION

The current study showed that rats treated with TiO_2NPs for 3 months have strong hepatotoxicity of the liver, demonstrated by elevation of liver enzyme markers and histopathological alterations. CoQ10 improves the deleterious effect associated with TiO_2 NPs administration. This ameliorative effect may be due to their strong antioxidative activities.

REFERENCES

Abdeen, A.; Abdelkader, A.; Elgazzar, D.; Aboubakr, M.; Abdulah, O.A.; Shoghy, K. and El-Mleeh, A. (2020): Coenzyme Q10 supplementation mitigates piroxicam-induced oxidative injury and apoptotic pathways in the stomach, liver, and kidney. *Biomedicine & Pharmacotherapy*, *130*, 110627.

Abd-Elhafeez, H.H.; Abou-Elhamd, A.S. and Soliman, S.A. (2020): Morphological and immunohistochemical phenotype of TCs in the intestinal bulb of Grass carp and their potential role in intestinal immunity. *Scientific Reports*, *10*(1), 14039.

Akbari, A.; Mobini, G.R.; Agah, S.; Morvaridzadeh, M.; Omidi, A.; Potter, E. and Dehghani, S. (2020):

Coenzyme Q10 supplementation and oxidative stress parameters: a systematic review and meta-analysis of clinical trials. *European journal of clinical pharmacology*, *76*, 1483-1499.

Alhusaini, A.; Fadda, L.; Albogami, L.; Alnaim, N.; Sarawi, W.; Mattar, D. and Hasan, I. (2022): Liposomal coenzyme Q10 abates inflammation, apoptosis and DNA damage induced by an overdose of paracetamol in rat's liver. *Journal of King Saud University-Science*, *34*(6), 102144.

Attia, H.F.; Soliman, M.M.; Abdel-Rahman, G.H.; Nassan, M.A.; Ismail, S.A.; Farouk, M. and Solcan, C. (2013): Hepatoprotective effect of N-acetylcystiene on the toxic hazards of titanium dioxide nanoparticles. *American journal of pharmacology and toxicology*, *8*(4), 141.

Bancroft, J.; Stevens, A. and Turner, D. (1996): Theory and practice of histological techniques 4th Ed Churchill Living Stone, New York Edinburgh. *Madrid, Sanfrancisco*.

Baranowska-Wójcik, E.; Szwajgier, D.; Oleszczuk, P. and Winiarska-Mieczan, A. (2020): Effects of titanium dioxide nanoparticles exposure on human health—a review. *Biological trace element research*, *193*, 118-129.

Borenstein, M.; Rothstein, H. and Cohen, J. (1997): Analysis of variance. *SPSS Inc., Chicago*.

Brand, W.; Peters, R.J.; Braakhuis, H.M.; Maślankiewicz, L. and Oomen, A.G. (2020): Possible effects of titanium dioxide particles on human liver, intestinal tissue, spleen and kidney after oral exposure. *Nanotoxicology*, *14*(7), 985-1007.

Choobchian, R.; Raji, A.; Nourani, H.; Moghadam Jafari, A. and Moghtadari Esfahani, A. (2024): Histopathological effects of titanium dioxide nanoparticles on the liver in rats by light and transmission electron microscopy. *Iranian Journal of Toxicology*, *18*(4), 233-240.

Çolak, D.A. and Uysal, H. (2017): Protective effects of coenzyme Q10 and resveratrol on oxidative stress induced by various dioxins on transheterozigot larvae of Drosophila melanogaster. *Toxicology research, 6*(4), 521-525.

Cornu, R.; Béduneau, A. and Martin, H. (2022): Ingestion of titanium dioxide nanoparticles: a definite health risk for consumers and their progeny. *Archives of toxicology*, *96*(10), 2655-2686.

Crane, F.L. (2001): Biochemical functions of coenzyme Q10. *Journal of the American College of Nutrition*, *20*(6), 591-598.

Dhawan, A. and Sharma, V. (2010): Toxicity assessment of nanomaterials: methods and challenges. *Analytical and bioanalytical chemistry*, *398*, 589-605.

Dudefoi, W.; Moniz, K.; Allen-Vercoe, E.; Ropers, M.H. and Walker, V.K. (2017): Impact of food grade and nano-TiO2 particles on a human intestinal community. *Food and Chemical Toxicology*, *106*, 242-249.

El-Bassouny, D.R.; Mansour, A.A.; Ellakkany, A.S.; Ayuob, N.N. and AbdElfattah, A.A. (2023): Can coenzyme Q10 alleviate the toxic effect of fenofibrate on skeletal muscle? *Histochemistry and Cell Biology*, *160*(2), 147-158.

Fadda, L.M.; Hagar, H.; Mohamed, A.M. and Ali, H.M. (2018): Quercetin and idebenone ameliorate oxidative stress, inflammation, DNA damage, and apoptosis induced by titanium dioxide nanoparticles in rat liver. *Dose-Response*, *16*(4), 1559325818812188.

Fouad, A.A. and Jresat, I. (2012): Hepatoprotective effect of coenzyme Q10 in rats with acetaminophen toxicity. *Environmental toxicology and pharmacology*, *33*(2), 158-167.

Garrido-Maraver, J.; Cordero, M.D.; Oropesa-Avila, M.; Vega, A.F.; de la Mata, M.; Pavon, A.D. and Sanchez-Alcazar, J.A. (2014): Clinical applications of coenzyme Q10. *Front Biosci (Landmark Ed)*, *19*(4), 619-33.

Ghule, A.E.; Kulkarni, C.P.; Bodhankar, S.L. and Pandit, V.A. (2009): Effect of pretreatment with coenzyme Q10 on isoproterenol-induced cardiotoxicity and cardiac hypertrophy in rats. Current therapeutic research, 70(6), 460-471.

Hassanein, K.M. and El-Amir, Y.O. (2017): Protective effects of thymoquinone and avenanthramides on titanium dioxide nanoparticles induced toxicity in Sprague-Dawley rats. *Pathology-Research and Practice*, *213*(1), 13-22.

Hassanein, K.M. and El-Amir, Y.O. (2018): Ameliorative effects of thymoquinone on titanium dioxide nanoparticles induced acute toxicity in rats. *International journal of veterinary science and medicine, 6*(1), 16-21.

IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. (2006): Cobalt in hard metals and cobalt sulfate, gallium arsenide, indium phosphide and vanadium pentoxide. *IARC monographs on the evaluation of carcinogenic risks to humans*, *86*, 1.

Javaheri, R.; Raji, A.R.; Moghaddam Jafari, A. and Nourani, H. (2023): Effects of Oral Exposure to Titanium Dioxide Nanoparticles on the Liver, Small Intestine, and Kidney of Rats assessed by light microscopy and Transmission Electron Microscopy. *Iranian Journal of Veterinary Science and Technology*, *15*(1), 41-48.

Jeon, J.M.; Kim, W.J. and Lee, M.Y. (2013): Studies on liver damage induced by nanosized-titanium dioxide in mouse. *J Environ Biol*, *34*(2), 283-287.

Kamal, Z.; Ebnalwaled, A.A.; Al-Amgad, Z.; Saied, A.A.; Metwally, A.A. and Said, A.H. (2023): Immunomodulatory and antioxidant effect of green synthesized titanium dioxide nanoparticles on pregnant female albino rats and their fetuses. *Environmental science and pollution research*, *30*(19), 55455-55470.

Kumar, S.; Meena, R. and Paulraj, R. (2016): Role of macrophage (M1 and M2) in titanium-dioxide nanoparticle-induced oxidative stress and inflammatory response in rat. *Applied biochemistry and biotechnology*, *180*, 1257-1275.

Lenaz, G.; Fato, R.; Formiggini, G. and Genova, M.L. (2007): The role of Coenzyme Q in mitochondrial electron transport. *Mitochondrion*, *7*, S8-S33.

Li, J.; Guo, C.; Liu, Y.; Han, B.; Lv, Z.; Jiang, H. and Zhang, Z. (2025): Chronic arsenic exposure-provoked biotoxicity involved in liver-microbiota-gut axis disruption in chickens based on multi-omics technologies. *Journal of Advanced Research*, *67*, 373-386.

Luo, Z.; Li, Z.; Xie, Z.; Sokolova, I.M.; Song, L.; Peijnenburg, W.J. and Wang, Y. (2020): Rethinking nano-TiO2 safety: overview of toxic effects in humans and aquatic animals. *Small*, *16*(36), 2002019.

Mohamed, D.I.; Khairy, E.; Tawfek, S.S.; Habib, E.K. and Fetouh, M.A. (2019): Coenzyme Q10 attenuates lung and liver fibrosis via modulation of autophagy in methotrexate treated rat. *Biomedicine & Pharmacotherapy*, *109*, 892-901.

Mohammed, E.T. and Safwat, G.M. (2020): Grape seed proanthocyanidin extract mitigates titanium dioxide nanoparticle (TiO2-NPs)–induced hepatotoxicity through TLR-4/NF-κB signaling pathway. *Biological trace element research*, *196*(2), 579-589.

Oberdörster, G.; Finkelstein, J.N.; Johnston, C.; Gelein, R.; Cox, C.; Baggs, R. and Elder, A.C. (2000):

Acute pulmonary effects of ultrafine particles in rats and mice. *Research report (Health Effects Institute)*, (96), 5-74.

Papucci, L.; Schiavone, N.; Witort, E.; Donnini, M.; Lapucci, A.; Tempestini, A. and Capaccioli, S. (2003): Coenzyme q10 prevents apoptosis by inhibiting mitochondrial depolarization independently of its free radical scavenging property. *Journal of Biological Chemistry*, *278*(30), 28220-28228.

Rajaiah, S.G.; Nadoor, P.; Rao, S.; Poojari, R.; Rajashekaraiah, R.; Prasad, T.N.V.K.V. and Yegireddy, M. (2022): Comparative Studies on Dispersion Characters of Titanium Dioxide (TiO2) Nanoparticles for Rodent Toxicology Studies.

Reitman, S. and Frankel, S. (1957): A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. *American journal of clinical pathology*, *28*(1), 56-63.

Schmelzer, C.; Lindner, I.; Rimbach, G.; Niklowitz, P.; Menke, T. and Döring, F. (2008): Functions of coenzyme Q10 in inflammation and gene expression. *Biofactors*, *32*(1-4), 179-183.

Sohet, F.M.; Neyrinck, A.M.; Pachikian, B.D.; de Backer, F.C.; Bindels, L.B.; Niklowitz, P. and Delzenne, N.M. (2009): Coenzyme Q10 supplementation lowers hepatic oxidative stress and inflammation associated with diet-induced obesity in mice. *Biochemical pharmacology*, *78*(11), 1391-1400.

Trouiller, B.; Reliene, R.; Westbrook, A.; Solaimani, P. and Schiestl, R.H. (2009): Titanium dioxide nanoparticles induce DNA damage and genetic instability in vivo in mice. *Cancer research*, *69*(22), 8784-8789.

Valentini, X.; Rugira, P.; Frau, A.; Tagliatti, V.; Conotte, R.; Laurent, S. and Nonclercq, D. (2019): Hepatic and renal toxicity induced by TiO2 nanoparticles in rats: a morphological and metabonomic study. *Journal of toxicology*, *2019*(1), 5767012.

Wang, J.; Zhou, G.; Chen, C.; Yu, H.; Wang, T.; Ma, Y. and Chai, Z. (2007): Acute toxicity and biodistribution of different sized titanium dioxide particles in mice after oral administration. *Toxicology letters*, *168*(2), 176-185.

Zhang, X.; Song, Y.; Gong, H.; Wu, C.; Wang, B.; Chen, W. and Sun, M. (2023): Neurotoxicity of titanium dioxide nanoparticles: a comprehensive review. *International journal of nanomedicine*, 7183-7204.

Zhao, H.; Chang, J.; Havlík, P.; Van Dijk, M.; Valin, H.; Janssens, C. and Obersteiner, M. (2021): China's future food demand and its implications for trade and environment. *Nature Sustainability, 4*(12), 1042-1051.

دراسات باثولوجية علي التأثير الوقائى لمساعد الإنزيم كيو ١٠ علي السُمِّيَّة الكبدية المستحثة لجسيمات ثاني اكسيد التيتانيوم النانونية في الجرذان

غادة محمود عبد الله، مختار مصطفى طه ، خالد محمد أحمد حسانين
قسم الباثولوجيا، كليه الطب البيطري ،جامعه أسيوط ،أسيوط ، مصر،٧١٥٢٦

Email: Ghada_Mahmoud@aun.edu.eg Assiut University web-site: www.aun.edu.eg

تهدف هذه الدراسة إلى استكشاف التأثير التحسني لمساعد الإنزيم كيو ١٠ على السُمِّيَّة الكبدية المُستحثة بجسيمات ثاني أكسيد التيتانيوم النانونية. تم تقُسِّيم ستين جرذًا بالغًا إلى أربع مجموعات، كل مجموعة تضم ١٥ جرذًا. أُعطيت المجموعة (أ) المادة المذيبة فقط (توين٨٠ بتركيز١٪). أُعطيت المجموعة (ب) جسيمات ثاني أكسيد التيتانيوم النانونية يوميًا عن طريق أنبوب معدي بجرعة (١٠٠ ملغم/كجم من وزن الجسم) لمدة ثلاثة أشهر. أُعطيت المجموعة (ج) جسيمات ثاني أكسيد التيتانيوم النانونية بجرعة (١٠٠ ملغم/كجم من وزن الجسم) ومساعد الإنزيم كيو ١٠ بمقدار (١٠ ملغم/كجم من وزن الجسم) يوميًا عن طريق أنبوب معدي. أُعطيت المجموعة (د) مساعد الإنزيم كيو ١٠ فقط. في نهاية التجربة، تم تجميع عينات مصل وأنسجة من الكبد للكشف عن إنزيمات الكبد والفحص الهيستوباثولوجي. أظهرت المجموعة التي تسممت بجسيمات ثاني أكسيد التيتانيوم النانونية ارتفاعًا في معدل إنزيمات الكبد مثل ناقلة والأسبارتات أمينوترانسفيريز، وألانين أمينوترانسفيريز. كما كشفت نتائج الهستوباثولوجى عن تغيرات وعائية ونسيجية. كانت التغيرات الوعائية في شكل احتقان وتجلط في الأوعية الدموية بينما كانت التغيرات النسيجية عبارة عن فجوات داخل الخلايا الكبدية، ونخرللخلايا، وموت الخلايا المبرمج، زيادة عدد الخلايا في النسيج المبطن للقناة الصفراوية، وتليف الكبد، بينما أظهرت المجموعة المعالجة بجسيمات ثاني أكسيد التيتانيوم النانونية و مساعد الإنزيم كيو ١٠ انخفاضًا في مستويات لأسبارتات أمينوترانسفيريز، وألانين أمينوترانسفيريز وتحسنًا في البنية النسيجية لأنسجة الكبد. وقد خلصت الدراسة إلى أن السمية المزمنة لجسيمات ثاني أكسيد التيتانيوم النانونية تسبب تغيرات نسيجية مرضية في الكبد. وقد أدى تناول مساعد الإنزيم كيو ١٠ إلى تحسين تلف الكبد الناجم عن جسيمات ثاني أكسيد التيتانيوم النانونية من خلال خصائصه المضادة للأكسدة والمضادة للالتهابات.

الكلمات المفتاحية: جسيمات ثاني أكسيد التيتانيوم النانونية ، مساعد الإنزيم كيو١٠ ، أسبارتات أمينوترانسفيريز، ألانين أمينوترانسفيريز السُمِّيَّة الكبدية ،الهستوباثولوجى.