

*Original Scientific Article***THE IMPACT OF MICELLAR COENZYME Q10 AND LIPOSOMAL COENZYME Q10 ON TNF- $\alpha$  AND IL-1 $\beta$  IN CISPLATIN-INDUCED NEPHROTOXICITY IN RATS**

Icko K. Gjorgoski<sup>1</sup>, Emilija Shikole<sup>2</sup>, Marija Glavas Dodov<sup>3</sup>, Majlinda Ademi<sup>4</sup>,  
Elena Rafailovska<sup>4</sup>, Dushko Shalabalija<sup>3</sup>, Valdrina Ajeti<sup>5</sup>, Dimche Zafirov<sup>2</sup>,  
Jasmina Trojachanec<sup>2</sup>, Marija Cvijanovikj<sup>6</sup>

<sup>1</sup>*Department of Biochemistry and Physiology, Faculty of Natural Sciences and Mathematics Ss. Cyril and Methodius University, Arhimedova 8, Skopje, N. Macedonia*

<sup>2</sup>*Institute of Preclinical and Clinical Pharmacology and Toxicology, Ss. Cyril and Methodius University, Skopje, N. Macedonia*

<sup>3</sup>*Institute of Pharmaceutical Technology, Faculty of Pharmacy, Ss. Cyril and Methodius University, Skopje, N. Macedonia*

<sup>4</sup>*Faculty of Medical Sciences, University of Tetovo, Tetovo, N. Macedonia*

<sup>5</sup>*Department of Pharmacy, Alma Mater Europaea Campus College Rezonanca, Prishtina, Kosovo*

<sup>6</sup>*Food Lab, Boris Trajkovski 130, Skopje, N. Macedonia*

Received 8 May 2025; Received in revised form 22 August 2025; Accepted 15 October 2025

**ABSTRACT**

Cisplatin is a widely used chemotherapeutic agent, but its clinical application is often limited due to its nephrotoxic effects, largely mediated through proinflammatory cytokines. This study investigates the comparative effectiveness of micellar and liposomal formulations of Coenzyme Q10 (CoQ10) in modulating serum levels of tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-1 beta (IL-1 $\beta$ ) in a rat model of cisplatin-induced nephrotoxicity. Ninety Wistar rats were divided into control group and five experimental groups receiving various treatments, including cisplatin alone, micellar CoQ10, liposomal CoQ10, and combinations thereof. Serum concentrations of TNF- $\alpha$  and IL-1 $\beta$  were measured at defined intervals using ELISA. The results demonstrated that both formulations of CoQ10 significantly reduced cytokine levels compared to cisplatin-only treated rats, with the liposomal form yielding superior anti-inflammatory effects. These findings suggest that liposomal CoQ10 may offer a more effective strategy for mitigating inflammation and nephrotoxicity induced by cisplatin.

**Key words:** Coenzyme Q10, cisplatin-induced nephrotoxicity, TNF-alpha, IL-1 beta, rats

**INTRODUCTION**

Cisplatin is a first-line chemotherapeutic agent used in the treatment of various malignancies (1). Despite its efficacy, its clinical application is

limited due to significant side effects, particularly nephrotoxicity and myelosuppression (2, 3). One of the primary mechanisms of cisplatin-induced nephrotoxicity is inflammation, driven by proinflammatory cytokines such as tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-1 beta (IL-1 $\beta$ ). These cytokines are released by damaged renal cells and promote the recruitment of inflammatory cells to the injured kidneys (4, 5, 6). Elevated TNF- $\alpha$  levels have been observed as early as the first day following cisplatin administration (7).

A key upstream regulator of TNF- $\alpha$  and IL-1 $\beta$  expression is nuclear factor kappa B (NF- $\kappa$ B), which also contributes to oxidative stress and the

*Corresponding author:* Prof. Icko K. Gjorgoski, PhD

*E-mail address:* icko@pmf.ukim.mk

*Present address:* Department of Biochemistry and Physiology, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Arhimedova 8, Skopje, N. Macedonia

*Phone:* +38970273384

**Copyright:** © 2026 Gjorgoski I.K. This is an open-access article published under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Competing Interests:** The authors have declared that no competing interests exist.

**Available Online First:** 25 February 2026

**Published on:** 15 March 2026

<https://doi.org/10.2478/macvetrev-2026-0013>

inflammatory cascade (8). Cisplatin-induced renal damage is linked to mitochondrial dysfunction (9), leading to increased production of reactive oxygen species (ROS) and release of pro-apoptotic factors, ultimately causing tubular cell death (10).

Coenzyme Q10 (CoQ10), a lipid-soluble antioxidant molecule located in the inner mitochondrial membrane, has been shown to protect against nephrotoxicity (11, 12) through its ability to reduce ROS and inflammation. Its micellar structure increases the protective effect against nephrotoxicity. Its anti-inflammatory effects are believed to be mediated by suppression of NF- $\kappa$ B activation (13, 14). However, the therapeutic potential of CoQ10 is limited by its poor water solubility and low bioavailability.

Therefore, novel delivery systems such as liposomes have been explored. Liposomes, with their phospholipid bilayer structure, closely resemble cell membranes and offer improved stability, prolonged circulation time, and enhanced delivery of hydrophobic compounds like CoQ10 (15, 16). These systems may enhance the biological activity of CoQ10 and improve its efficacy in mitigating cisplatin-induced nephrotoxicity.

Given these considerations, the present in vivo study aims to compare the anti-inflammatory effectiveness of liposomal versus micellar formulations of CoQ10 in rats with cisplatin-induced nephrotoxicity, by evaluating serum levels of TNF- $\alpha$  and IL-1 $\beta$ . In the same time, the results obtained in this study can confirm the expectations that both formulations of CoQ10 significantly reduce cytokine levels.

## MATERIAL AND METHODS

### *Material and animals*

Cisplatin solution (1 mg/mL) was obtained from Accord, Latvia. Ascorbic acid and Tween 80 were purchased from Merck, Germany. Coenzyme Q10 (CoQ10) standard was acquired from Sigma-Aldrich, while thiopental sodium (500 mg) was procured from Ciron Drugs & Pharmaceuticals, India. The nanoliposomal formulations used in this study were previously formulated and optimized at the Faculty of Pharmacy, Skopje, with composition details available in Shalabalija et al. (16). All other chemicals were of analytical or pharmaceutical grade and were used without further purification.

Male Wistar rats (250–300 g) were obtained from the animal facility of the Faculty of Natural

Sciences and Mathematics, UKIM-Skopje. All procedures involving animals were conducted in accordance with the *Manual for the Care and Use of Laboratory Animals* and approved by the Institutional Animal Ethics Committee of the University “Ss. Cyril and Methodius”-Skopje (No. 10-3196/1 from 20.09.2022) in line with European Commission Directive 86/609/EEC and CIOMS guidelines.

### *Preparation of CoQ10 micellar solution*

A CoQ10 micellar solution (5 mg/mL) was prepared for intraperitoneal (i.p.) administration. Doses were adjusted based on the individual weight of each rat. CoQ10 powder was dissolved in 0.9% NaCl containing 1% Tween 80 and mixed continuously at 65 °C and 200 rpm for 15 min. Ascorbic acid (0.1% w/v) was added to preserve antioxidant stability.

### *Preparation of nanoliposomes with encapsulated CoQ10*

Nanoliposomes (5 mg/mL CoQ10) were prepared using a modified dry lipid film hydration technique as described in Shalabalija et al. (16). The resulting liposomes showed uniform size distribution (PDI: 0.26), an average diameter of 125 nm, and a sustained release of approximately 50% of the encapsulated CoQ10 within 24 h.

### *Animal grouping and treatment protocol*

Ninety male normotensive Wistar rats were randomly divided into six groups (n=15 per group):

- **Group 0** (control): received physiological saline with 1% Tween 80 and 0.1% ascorbic acid.
- **Group 1** (cisplatin): received a single dose of cisplatin (5 mg/kg, i.p.) on day 4.
- **Group 2** (micellar CoQ10): treated daily with CoQ10 (10 mg/kg, i.p.) for 11 days.
- **Group 3** (cisplatin+micellar CoQ10): received cisplatin (day 4) and daily micellar CoQ10 for 11 days.
- **Group 4** (liposomal CoQ10): received nanoliposomal CoQ10 (10 mg/kg, i. p.) on days 1, 3, 5, 7, 9, and 11.
- **Group 5** (cisplatin+liposomal CoQ10): received cisplatin (day 4) and liposomal CoQ10 on days 1, 3, 5, 7, 9, and 11.

### *Evaluation of TNF- $\alpha$ and IL-1 $\beta$ serum levels*

Blood samples were collected from the tail

vein on days 0, 2, 6, and 12. Serum levels of TNF- $\alpha$  and IL-1 $\beta$  were quantified using ELISA kits (Sigma-Aldrich, RAB0476-1KT, RAB0273-1KT), following the manufacturer's instructions. The assay involved standard steps of antibody binding, washing, substrate reaction (TMB), and colorimetric measurement at 450 nm. The minimum detectable concentrations were 30 pg/mL for TNF- $\alpha$  and 0.3 pg/mL for IL-1 $\beta$ .

#### Statistical analysis

Statistical analyses were performed using Statistica 7.1 software (StatSoft Inc., USA). Descriptive statistics included mean, standard deviation, and 95% confidence intervals. Intergroup comparisons of TNF- $\alpha$  and IL-1 $\beta$  levels across treatment groups and time points were performed using one-way ANOVA followed by LSD post-hoc tests. A p-value of <0.001 was considered statistically significant.

## RESULTS

#### TNF- $\alpha$ serum concentration

The results revealed significant differences in serum TNF- $\alpha$  levels among the six experimental groups ( $F=56.95$ ;  $p<0.001$ ). Group 1 (cisplatin only) exhibited the highest TNF- $\alpha$  concentration (145.32 pg/mL), which was significantly greater than that in the control group (114.58 pg/mL), as well as in all CoQ10-treated groups. The lowest TNF- $\alpha$  levels were recorded in Group 4

(liposomal CoQ10 alone; 113.59 pg/mL), which were even slightly lower than the control group, although this difference was not statistically significant ( $p=1.00$ ). Groups 3 and 5, treated with micellar and liposomal CoQ10 in combination with cisplatin, respectively, also showed significant reductions in TNF- $\alpha$  compared to Group 1 (Table 1).

Time-point measurements showed the highest TNF- $\alpha$  levels on day 2 (128.21 pg/mL), followed by gradual reductions by day 12 (121.02 pg/mL). The decrease from day 2 to day 12 was statistically significant ( $p<0.001$ ), confirming the time-dependent inflammatory response and the modulation of cytokine levels by treatment.

#### IL-1 $\beta$ serum concentration

Significant differences in serum IL-1 $\beta$  levels were also observed among the groups ( $F=308.63$ ;  $p<0.001$ ). Group 1 again exhibited the highest concentration (179.44 pg/mL), while Group 4 (liposomal CoQ10 alone) demonstrated the lowest (100.05 pg/mL), significantly lower than all other groups including the control (104.34 pg/mL). Groups treated with cisplatin plus either micellar or liposomal CoQ10 (Groups 3 and 5) showed substantial reductions in IL-1 $\beta$  levels compared to cisplatin-only rats, with liposomal CoQ10 performing better (Table 2).

Time-course data revealed no statistically significant changes in IL-1 $\beta$  levels over time (days 0, 2, 6, and 12), though day 6 showed a slight nonsignificant peak.

**Table 1.** TNF- $\alpha$  concentration across treatment groups (values in pg/mL, n=15 per group)

Group	Mean $\pm$ Std. Err.	95% CI
0	114.58 $\pm$ 1.43 <sup>a</sup>	111.27-117.89
1	145.32 $\pm$ 1.19 <sup>b</sup>	142.01-148.63
2	116.20 $\pm$ 1.66 <sup>a</sup>	112.89-119.51
3	132.13 $\pm$ 0.94 <sup>c</sup>	128.83-135.44
4	113.59 $\pm$ 1.14 <sup>a</sup>	110.28-116.90
5	127.93 $\pm$ 1.72 <sup>c</sup>	124.62-131.24

Groups with different superscripts (<sup>a,b,c</sup>) in a column indicate statistically significant difference in TNF- $\alpha$  concentration at  $p<0.001$

**Table 2.** IL-1 $\beta$  concentration across treatment groups (Values in pg/mL, n=15 per group)

Group	Mean $\pm$ Std. Err.	95% CI
0	104.34 $\pm$ 1.07 <sup>a</sup>	100.82-107.87
1	179.44 $\pm$ 1.96 <sup>b</sup>	175.91-182.97
2	108.06 $\pm$ 1.18 <sup>c</sup>	104.54-111.59
3	148.75 $\pm$ 1.41 <sup>d</sup>	145.22-152.27
4	100.05 $\pm$ 0.98 <sup>c</sup>	96.53-103.58
5	135.19 $\pm$ 1.24 <sup>d</sup>	131.66-138.72

Groups with different superscripts (<sup>a,b,c,d,e</sup>) in a column indicate statistically significant difference in IL-1 $\beta$  concentration at p<0.001

## DISCUSSION

This study demonstrates that both micellar and liposomal formulations of Coenzyme Q10 (CoQ10) significantly mitigate the cisplatin-induced increase in proinflammatory cytokines TNF- $\alpha$  and IL-1 $\beta$  in rats (Table 1 and Table 2). However, the liposomal formulation consistently showed superior effects in reducing these cytokines, suggesting improved bioavailability and efficacy compared to the micellar form.

The observed elevation in TNF- $\alpha$  and IL-1 $\beta$  in the cisplatin-only group aligns with prior studies indicating their key role in the pathophysiology of cisplatin-induced nephrotoxicity. These cytokines contribute to the recruitment of neutrophils and macrophages, generation of reactive oxygen species (ROS) (17, 18) and direct tissue injury in the renal parenchyma (19). NF- $\kappa$ B signaling, an upstream regulator of cytokine production, is known to be activated by cisplatin and serves as a target for anti-inflammatory agents.

CoQ10 exerts its effects by reducing NF- $\kappa$ B expression (20) and ROS levels, and by stabilizing mitochondrial function. Similar studies outline the positive effects of CoQ10 supplementation in reducing the levels of TNF- $\alpha$ , IL-1 $\beta$ , and NF- $\kappa$ B expression (11, 21, 22). However, its low solubility and rapid clearance hinder its clinical application. In this study, liposomal encapsulation of CoQ10 appears to overcome these limitations, leading to enhanced delivery and sustained release of the active compound (9). This is evidenced by lower serum cytokine levels in animals treated with liposomal CoQ10 compared to those receiving the micellar formulation.

These findings are consistent with previous reports showing that nano-formulated CoQ10 improves pharmacokinetics, circulation time, and cellular uptake (23). Liposomes, with their bilayer phospholipid membranes, mimic biological membranes, allowing for better interaction with cells and gradual intracellular release of CoQ10 (24).

Although both formulations were effective, liposomal CoQ10 showed a greater reduction in TNF- $\alpha$  and IL-1 $\beta$  levels than micellar CoQ10, particularly when co-administered with cisplatin. This suggests that the liposomal system may provide better tissue distribution and prolonged anti-inflammatory action (9).

The results support the potential use of liposomal CoQ10 as a protective agent in cisplatin-induced nephrotoxicity and possibly in other inflammatory conditions mediated by similar mechanisms.

## CONCLUSION

Coenzyme Q10 emerges as a promising therapeutic agent for alleviating cisplatin-induced inflammation and nephrotoxicity. Both micellar and liposomal formulations demonstrated significant reductions in serum TNF- $\alpha$  and IL-1 $\beta$  levels, indicative of anti-inflammatory effects. However, the liposomal CoQ10 formulation exhibited superior efficacy, likely due to enhanced bioavailability, sustained release, and targeted delivery. These findings highlight the potential of liposomal drug delivery systems to improve the therapeutic impact of CoQ10 and support further

investigation into its clinical application as a nephroprotective supplement during chemotherapy.

### CONFLICT OF INTEREST

The authors declare that they have no financial or non-financial conflict of interest regarding authorship and publication of this article.

### ACKNOWLEDGMENTS

The authors would like to express their gratitude to the technical staff and institutional support teams contributing to the animal care, laboratory analyses and statistical evaluation. No specific funding was received for this study.

### AUTHORS' CONTRIBUTION

All authors contributed substantially to the study design, experimental work, data analysis, and manuscript preparation. All authors have read and approved the final version of the manuscript.

### REFERENCES

- Brown, A., Kumar, S., Tchounwou, P.B. (2019). Cisplatin-based chemotherapy of human cancers. *J Cancer Sci Ther.* 11(4): 97.
- Hanigan, M.H., Devarajan, P. (2003). Cisplatin nephrotoxicity: molecular mechanisms. *Cancer Ther.* 1, 47-61.
- Shikole, E., Gjorgoski, I., Glavas Dodov, M., Kocheva, N., Trojchanec, J., Zafirov, D. (2022). The effect of Coenzyme Q10 in cisplatin induced myelosuppression in rats. *Maced Pharm Bull.* 68 (Suppl. 1): 385-386.  
<https://doi.org/10.33320/maced.pharm.bull.2022.68.03.186>
- Ramesh, G., Reeves, W.B. (2002). TNF- $\alpha$  mediates chemokine and cytokine expression and renal injury in cisplatin nephrotoxicity. *J Clin Invest.* 110(6): 835-842.  
<https://doi.org/10.1172/JCI200215606>  
PMid:12235115 PMCID:PMC151130
- Zhang, B., Ramesh, G., Norbury, C.C., Reeves, W.B. (2007). Cisplatin-induced nephrotoxicity is mediated by tumor necrosis factor- $\alpha$  produced by renal parenchymal cells. *Kidney Int.* 72(1): 37-44.  
<https://doi.org/10.1038/sj.ki.5002242>  
PMid:17396112
- Tripathi, P., Alshahrani, S. (2021). Mitigation of IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and markers of apoptosis by ursolic acid against cisplatin-induced oxidative stress and nephrotoxicity in rats. *Hum Exp Toxicol.* 40(12\_Suppl.): S397-S405.  
<https://doi.org/10.1177/096032712111045953>  
PMid:34569348
- Lee, S., Kim, W., Moon, S.-O., Sung, M.J., Kim, D.H., Kang, K.P., Jang, Y.B., Lee, J.E., Jang, K.Y., Park, S.K. (2006). Rosiglitazone ameliorates cisplatin-induced renal injury in mice. *Nephrol Dial Transplant.* 21(8): 2096-2105.  
<https://doi.org/10.1093/ndt/gfl194>  
PMid:16728429
- Aupperle, K.R., Bennett, B.L., Boyle, D.L., Tak, P.P., Manning, A.M., Firestein, G.S., (1999). NF-kappa B regulation by I kappa B kinase in primary fibroblast-like synoviocytes. *J Immunol.* 163(1): 427-433.  
<https://doi.org/10.4049/jimmunol.163.1.427>  
PMid:10384145
- Alhusaini, A., Fadda, L., Albogami, L., Alnaim, N., Sarawi, W., Mattar, D., Hasan, I., (2022). Liposomal coenzyme Q10 abates inflammation, apoptosis and DNA damage induced by an overdose of paracetamol in rat's liver. *J King Saud Univ-Sci.* 34(6): 102144.  
<https://doi.org/10.1016/j.jksus.2022.102144>
- Celik, B., Sağıroğlu, A.A., Özdemir, S. (2017). Design, optimization and characterization of coenzyme Q10- and D-panthenyl triacetate-loaded liposomes. *Int J Nanomedicine.* 12, 4869-4878.  
<https://doi.org/10.2147/IJN.S140835>  
PMid:28744121 PMCID:PMC5511013
- Fouad, A.A., Al-Sultan, A.I., Refaie, S.M., Yacoubi, M.T. (2010). Coenzyme Q10 treatment ameliorates acute cisplatin nephrotoxicity in mice. *Toxicology* 274(1-3): 49-56.  
<https://doi.org/10.1016/j.tox.2010.05.007>  
PMid:20510337
- Fatima, S., Al-Mohaimed, N., Al-Shaikh, Y., Tyagi, P., Banu, N., Hasan, S., Arjumand, S. (2016). Combined treatment of epigallocatechin gallate and Coenzyme Q10 attenuates cisplatin-induced nephrotoxicity via suppression of oxidative/nitrosative stress, inflammation and cellular damage. *Food Chem Toxicol.* 94, 213-220.  
<https://doi.org/10.1016/j.fct.2016.05.023>  
PMid:27265264

13. Mohamed, H.A., Said, R.S. (2021). Coenzyme Q10 attenuates inflammation and fibrosis implicated in radiation enteropathy through suppression of NF-kB/TGF- $\beta$ /MMP-9 pathways. *Int Immunopharmacol.* 92, 107347.  
<https://doi.org/10.1016/j.intimp.2020.107347>  
PMid:33418245
14. McRae, M.P. (2023). Coenzyme Q10 supplementation in reducing inflammation: an umbrella review. *J Chiropr Med.* 22(2): 131-137.  
<https://doi.org/10.1016/j.jcm.2022.07.001>  
PMid:37346240 PMCid:PMC10280088
15. Li, H., Chen, F. (2017). Preparation and quality evaluation of coenzyme Q10 long-circulating liposomes. *Saudi J Biol Sci.* 24(4): 797-802.  
<https://doi.org/10.1016/j.sjbs.2015.10.025>  
PMid:28490948 PMCid:PMC5415142
16. Shalabalija, D., Mihailova, L., Crcarevska, M.S., Karanfilova, I.C., Ivanovski, V., Nestorovska, A.K., Novotni, G., Dodov, M.G. (2021). Formulation and optimization of bioinspired rosemary extract loaded PEGylated nanoliposomes for potential treatment of Alzheimer's disease using design of experiments. *J Drug Deliv Sci Technol.* 63, 102434.  
<https://doi.org/10.1016/j.jddst.2021.102434>
17. Dinarello, C.A. (2000). Proinflammatory cytokines. *Chest* 118(2): 503-508.  
<https://doi.org/10.1378/chest.118.2.503>  
PMid:10936147
18. Semenzato, G. (1990). Tumour necrosis factor: a cytokine with multiple biological activities. *Br J Cancer.* 61(3): 354-361.  
<https://doi.org/10.1038/bjc.1990.78>  
PMid:2183871 PMCid:PMC1971301
19. Grace, P.A. (1994). Ischaemia-reperfusion injury. *Br J Surg.* 81(5): 637-647.  
<https://doi.org/10.1002/bjs.1800810504>  
PMid:8044536
20. Peng, J., Ma, J., Zhang, L., Lu, B. (2020). Coenzyme Q10 attenuates airway inflammation and oxidative stress in neonatal asthmatic rats. *Trop J Pharm Res.* 19(9): 1969-1975.  
<https://doi.org/10.4314/tjpr.v19i9.24>
21. Al-Megrin, W.A., Soliman, D., Kassab, R.B., Metwally, D.M., Moneim, A.E.A. El-Khadragy, M.F. (2020). Coenzyme Q10 activates the antioxidant machinery and inhibits the inflammatory and apoptotic cascades against lead acetate-induced renal injury in rats. *Front Physiol.* 11, 64.  
<https://doi.org/10.3389/fphys.2020.00064>  
PMid:32116774 PMCid:PMC7020615
22. Mantle, D., Heaton, R.A., Hargreaves, I.P. (2021). Coenzyme Q10 and immune function: an overview. *Antioxidants (Basel).* 10(5): 759.  
<https://doi.org/10.3390/antiox10050759>  
PMid:34064686 PMCid:PMC8150987
23. Pastor-Maldonado, C.J., Suárez-Rivero, J.M., Povea-Cabello, S., Álvarez-Córdoba, M., Villalón-García, I., Munuera-Cabeza, M., Suárez-Carrillo, A., et al. (2020). Coenzyme Q10: novel formulations and medical trends. *Int J Mol Sci.* 21(22): 8432.  
<https://doi.org/10.3390/ijms21228432>  
PMid:33182646 PMCid:PMC7697799
24. Zhang, Y. (2019). A review of the delivery system of coenzyme-Q10 based on nanotechnology. *IOP Conf Series: Earth and Environ Sci.* 242(4): 042003.  
<https://doi.org/10.1088/1755-1315/242/4/042003>

**Please cite this article as:** Gjorgoski I.K., Shikole E., Dodov M.G., Ademi M., Rafailovska E., Shalabalija D., Ajeti V., Zafirov D., Trojachanec J., Cvijanovikj M. The impact of micellar Coenzyme Q10 and liposomal Coenzyme Q10 on TNF- $\alpha$  and IL-1 $\beta$  in cisplatin-induced nephrotoxicity in rats. *Mac Vet Rev* 2026; 49 (1): 97-102. <https://doi.org/10.2478/macvetrev-2026-0013>