Van Veterinary Journal

https://dergipark.org.tr/tr/pub/vanvetj

Cite this article as: **Yaman T, Akkoyun HT, Keleş ÖF, Bayramoğlu Akkoyun M (2024).** Effect of Bee Bread (Perga) on Histopathological Changes and Immunohistochemical Expression of Apoptosis Markers in the Kidney of Rats Exposed to Cadmium. *Van Vet J*, 35 (2), 101-108. DOI: https://doi.org/10.36483/vanvetj.1431490

ISSN: 2149-3359 **Original Article** e-ISSN: 2149-8644

Effect of Bee Bread (Perga) on Histopathological Changes and Immunohistochemical Expression of Apoptosis Markers in the Kidney of Rats Exposed to Cadmium

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Received: 05.02.2024 Accepted: 03.04.2024

ABSTRACT Cadmium (Cd) is an environmental and industrial pollutant that causes toxicity in various organs in humans and animals. Bee bread (perga) is a natural flavonoid with a wide range of pharmacological properties. This study was conducted to examine the effects of perga on Cd-induced nephrotoxicity. Thirty-two male Wistar rats were randomly divided into 4 groups, as the Control group, Cd group (5 mg/kg/day, orally), Perga group (0.5 g/kg/day, orally), and Cd + Perga group. At the end of the 28-day experiment, kidney tissue samples were taken and histopathological, immunohistochemical, and biochemical analyses were performed. Histopathologically, severe tubular and glomerular damage occurred as a result of Cd exposure in the Cd group. Immunohistochemically, there was an increase in caspas-3 and Bax expression in the renal tissue in the Cd group. According to the biochemical results, while the catalase, superoxide dismutase, and glutathione peroxidase antioxidant enzyme levels decreased in the Cd group, and the malondialdehyde levels increased. However, most of the above-mentioned Cd-induced changes were attenuated by treatment with perga in the Perga + Cd group. In conclusion, perga supplementation may alleviate Cd-induced renal injury through inhibition of apoptosis in renal tissue.

Keywords: *Cadmium, Histopathology, Kidney, Perga, Rat.*

ÖZ

Arı Ekmeğinin (Perga) Kadmiyuma Maruz Kalan Sıçan Böbreğindeki Histopatolojik Değişiklikler ve Apoptoz Belirteçlerinin İmmünohistokimyasal Ekspresyonu Üzerine Etkisi

Kadmiyum (Cd), insanlarda ve hayvanlarda çeşitli organlarda toksisiteye neden olan çevresel ve endüstriyel bir kirleticidir. Arı ekmeği (perga), çok çeşitli farmakolojik özelliklere sahip doğal bir flavonoiddir. Bu çalışma, perganın Cd kaynaklı nefrotoksisite üzerindeki etkilerini incelemek amacıyla yapıldı. Otuz iki adet erkek Wistar sıçanı kontrol grubu, Cd grubu (5 mg/kg/gün, oral), Perga grubu (0.5 g/kg/gün, oral) ve Cd+Perga grubu olmak üzere rastgele 4 gruba ayrıldı. 28 günlük deneme süresi sonunda böbrek dokusu örnekleri alınarak histopatolojik, immünohistokimyasal ve biyokimyasal analizler yapıldı. Histopatolojik olarak Cd grubunda, Cd maruziyeti sonucu ciddi tübüler ve glomerüler hasar meydana geldi. İmmünohistokimyasal olarak Cd grubunda böbrek dokusunda caspas-3 ve Bax ekspresyonunda artış vardı. Biyokimyasal sonuçlara göre Cd grubunda katalaz, süperoksit dismutaz ve glutatyon peroksidaz antioksidan enzim seviyeleri azalırken, malondialdehit seviyeleri arttı. Ancak yukarıda belirtilen Cd'nin neden olduğu değişikliklerin çoğu, Perga + Cd grubunda perga tedavisiyle azaldı. Sonuç olarak, perga takviyesi böbrek dokusunda apoptozun inhibisyonu yoluyla Cd kaynaklı böbrek hasarını hafifletebilir.

Anahtar Kelimeler: *Böbrek, Histopatoloji, Kadmium, Perga, Rat.*

INTRODUCTION

Cadmium (Cd) is an important trace element released into aquatic and terrestrial environments from both natural sources and anthropogenic activities (mining, smelting, electroplating, battery manufacturing using Cd) (Chora et al. 2009). People are exposed to Cd through food, water, and cigarette smoke (Waisberg et al. 2003). Cd has a long biological half-life and accumulates in the liver and kidney (Ercal et al. 2001). It is a toxic metal that can cause toxicity in many tissues, such as nephrotoxicity, immunotoxicity, reproductive toxicity, and osteotoxicity (Liu et al. 2009; Gong et al. 2019).

The kidney is thought to be the target organ in Cd toxicity

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because it does not have an effective mechanism for Cd elimination and is one of the organs where Cd accumulates (Fouad and Jresat 2011). Metallothionein (MT), a small metal-binding protein induced by Cd, that binds most of the Cd in the form of the Cd-MT complex (Nordberg 2009). After Cd exposure, Cd-MT is produced in the liver and released into the bloodstream (Wolff et al. 2008). The nephrotoxic effect of Cd occurs as a result of the Cd-MT complex released from damaged liver cells, filtering through the glomerulus, and passing into the urinary cavity, where it is endocytosed by proximal tubular cells and broken down by lysosomes, resulting in the release of Cd (Morales et al. 2006).

Oxidative stress is an important possible mechanism in Cd-induced nephrotoxicity (Watjen and Beyermann 2004). Cd causes oxidative stress damage by inducing excessive amounts of reactive oxygen species (ROS) (Jomova and Valko 2011). It was reported that Cd induces tubular epithelial cell apoptosis in the kidney and the underlying mechanism is excessive ROS production (Almeer et al. 2019). In addition, Cd-induced oxidative stress damage activates mitochondrial signals that cause apoptosis (Wilmes et al. 2011).

Bee bread (perga) consists of pollen, honey, and the secretions of the salivary glands of bees (Vásquez and Olofsson 2009). Bees place the ingredients into the honeycomb cells, then coat the mixture with beeswax and honey. The content is then subjected to lactic fermentation caused by bacteria and yeasts, resulting in perga (Kieliszek et al. 2018). Perga is a source of polyphenols with antioxidant activity due to rich compounds such as α-tocopherol, kaempferol, p-coumaric acid, and isorhamnetin (Isidorov et al. 2009). Due to its antioxidant properties, antimicrobial (Zerdani et al. 2011), anti-inflammatory (Kosedag and Gulaboglu 2023), and antihypertensive (Nagai et al. 2005) activities have been demonstrated. Perga also has properties that help to remove various toxins from organisms (Nagai et al. 2005).

The aim of this study was to investigate the protective effect of perga against Cd-induced nephrotoxicity in rats using histopathological, immunohistochemical, and biochemical methods.

MATERIAL AND METHODS

Animals

The Experimental Animal Research Centre at Van Yuzuncu Yil University (Van, Türkiye) provided 32 male Wistar albino rats that were approximately 2 months old with an average weight of 200–250 g The rats were randomly divided into 4 groups, with 8 in each group (n=8). They were housed at 25±2 °C with a daily light/dark photoperiod of 10:14. The rats were fed a wheat-soybean-based diet ad libitum and housed in stainless steel cages. Humane care, according to the criteria expressed in the Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Science and published by the National Institute of Health, was followed throughout the experiment period. The ethics regulations followed were in accordance with national and institutional guidelines for the protection of animal welfare during the experiments. The local ethics committee of Van Yuzuncu Yil University Animal Experiments approved the study (01/06/2023, 2023/07-12).

Experimental Design

The 32 male rats were randomly divided into 4 groups, with each containing 8 rats. The experiment was conducted for 28 days. Freshly procured perga was dried at 35 °C for 4 h, and then ground into a fine powder using a blender and stored at −20 °C until use (Zakaria et al. 2021). During the 4-week trial period, perga was given daily via oral gavage at a dose of 0.5 g/kg body weight (Kosedag and Gulaboglu 2023). Cd was administered daily via orogastric gavage at 5 mg/kg body weight throughout the trial period (Fang et al. 2021). The rats were grouped as shown in Table 1.

Table 1: Animal groups.

Group	Treatment	Route of Administration
1. Control group	Distilated water	via orogastric gavage
2. Perga group	0.5 g/kg perga	via orogastric gavage
3. Cd group	5 mg/kg Cd	via orogastric gavage
4. Cd + Perga	0.5 g/kg perga + 5 mg/kg Cd	via orogastric gavage

A standard pellet diet ad libitum was available during the experiment.

At the end of the 28-day experiment, the rats were anesthetized using ketamine (50 mg/kg) (Arion Pharmacy, İstanbul, Türkiye) and xylazine (10 mg/kg) (Mefar Pharmacy, İstanbul, Türkiye). Kidney tissue was removed after median laparotomy. Samples taken for histopathological examination were stored in 10% formaldehyde solution. Samples taken for biochemical [malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px)] analysis were washed with phosphate-buffered saline (PBS) and stored in a deep freezer (–80 °C).

Histopathological Examination

Kidneys from the animals were fixed in 10% neutral buffered formalin and embedded in paraffin using routine methods. Sections measuring 5 µm thick were cut for histological examination. Histopathological evaluation was performed for findings such as glomerular damage, tubular degeneration and necrosis, hyperemia, and hemorrhage (Renugadevi and Prabu 2009). The histopathological findings were evaluated on hematoxylin and eosin (H&E)-stained tissue slides using a light microscope (E-400; Nikon, Corp., Minato City, Tokyo, Japan) equipped with a DS-Ri2 video camera (DS-U3; Nikon Corp). Histopathological findings were evaluated subjectively as negative (–), mild (+), moderate (++), and intense (+++) (Yaman and Kömüroğlu 2018).

Immunohistochemical Staining

Immunohistochemistry was performed according to the streptavidin-biotin-peroxidase (avidin–biotin peroxidase complex) method. Briefly, the sections were deparaffinized (2 times for 5 min in xylol) and rehydrated using a series of ethanol solutions. Subsequently, tissue endogenous peroxidase activity was quenched with 3% H_2O_2 (v/v) for 20 min followed by washing 3 times in PBS for 5 min. Antigen retrieval was performed with citrate buffer (pH 6.0) for 30 min at 95 °C using a water bath, and then cooled for 20 min. Subsequently, the slides were incubated with blocking serum (Histostain Plus Bulk Kit, Zymed Laboratories Inc., Oxnard, CA, USA) for 15 min to block nonspecific binding sites. The sections were incubated with caspase-3, and Bax primary antibodies at 4 °C overnight (Table-2). The next day, the slides were washed

four times with PBS, incubated with a biotinylated secondary antibody (Histostain Plus Bulk Kit, Zymed) for 20 min at room temperature, and washed four times with PBS for 5 min. Next, the sections were incubated with horseradish-streptavidin peroxidase (HRP) conjugate (Histostain Plus Bulk Kit, Zymed) at room temperature for 20 min. Finally, the slides were incubated for 5–15 min with diaminobenzidine (DAB), rinsed 3 times for 5 min in distilled water, and counterstained with Gill's hematoxylin for 3 min. Then, the sections were passed through a series of alcohol and xylene and mounted directly with Entellan mounting medium. Immunohistochemical findings were evaluated subjectively according to the intensity of the staining in the tissue as negative (–), mild (+), moderate (++) and intense (+++), using a light microscope (E-400; Nikon Corp.) equipped with a DS-Ri2 video camera (DS-U3, Nikon Corp.) (Yaman and Aydemir 2021).

Preparation of Kidney Tissue Homogenate

Kidney tissue samples, weighed at 0.5 g on a precision scale, were placed in tubes. Then, 10 times the weight of cold buffer (1 mmol/L EDTA, 0.32 mol/L sakaroz and 10 nmol/L Tris-HCl, pH 7.4) was added to the tissue samples. Samples were digested using a homogenizer. After the vortexing process, the samples placed into porcelain crucibles were subjected to advanced disintegration in an ultrasanitizer at 20 KHz. After the disintegration process, the upper clear part was removed by centrifugation at 9500 rpm for 30 min. The collected supernatants were transferred into Eppendorf tubes. All of these processes were carried out at 4 °C (Akkoyun et al. 2023).

Antioxidant Enzyme Activity Determinations and Determination of the Total Protein Concentration.

Antioxidant enzyme activity levels in the kidney tissues were determined spectrophotometrically. Superoxide dismutase (SOD (EC 1.15.1.1) activity was measured according to the method by Sun et al. (1988), glutathione peroxidase GSH-Px (E.C.1.11.1.9) tissue enzyme activity was measured based on the method by Paglia and Valentine (1967), and the catalase CAT (EC 1.11.1.6) activity was measured according to the method used by Aebi (1984). The MDA level, which is the most important indicator of lipid peroxidation, was determined according to the method of Ohkawa et al. (1979). The total protein concentration of the kidney tissue homogenates was determined spectrophotometrically using standard bovine serum albumin solution (Lowry et al. 1951).

Statistical Analysis

The biochemical findings obtained as a result of the study were analyzed using analysis of variance (ANOVA) with the JMP statistical package program. Standard deviation (X ± SD) values were also calculated with the JMP package program. According to the results of ANOVA, statistically significant factor averages were compared using the least significant differences student's t test ($p<0.01$) and lettered.

RESULTS

Histopathological Results

Normal histological structure of the kidney tissue was observed in the Control (Figure 1A) and Perga groups (Figure 1B). After 4 weeks of Cd treatment, swelling of the glomeruli was observed in some sections from the Cd group, so that there was no space between the glomerulus and the Bowman capsule (Figure 1C). Shrinkage and atrophy were observed in the glomeruli in some sections. This resulted in an expansion of the Bowman space (Figure 1D). Tubular damage manifested by fragmented tubular epithelium and loss of brush border was observed. Dilation was detected in the tubules. Necrosis and cloudy swelling were observed in the tubule epithelium (Figure 1E). Cd also caused hyperemia and hemorrhagic foci and inflammatory cell infiltration. The histopathological changes caused by Cd were significantly reduced by the application of perga. In particular, the atrophic glomeruli were barely detected. However, glomerular swelling was partially present (Figure 1F). The frequency and severity of histopathological lesions in kidney tissue in all of the groups are presented in Table 3.

Table 2: Antibody specificity, host, dilution rates and incubation times.

Antibody	Host	Dilution	Incubation	Source
Caspase-3	Rabbit/ Polyclonal	1:100 dilution	Overnight	PA5-16335; Thermo Fisher Sci.
Bax	Rabbit/ polyclonal	1:100 dilution	Overnight	ab53154; abcam

Heat-induced antigen retrieval was performed with citrate buffer.

Table 3: Incidence and severity of the lesions in the kidneys of the Control, Perga, Cd, and Cd + Perga groups.

Changes/lesions in kidney	Control	Perga	Cd	Cd + Perga
Tubular degeneration and necrosis	0/8	0/8	8/8	8/8
Mild	0	0	1	2
Moderate	0	0	4	5
Intense	0	0	3	1
Damaged glomeruli	0/8	0/8	8/8	8/8
Mild	0	0	2	3
Moderate	0	0	2	3
Intense	0	0	4	2
Inflammatory cells infiltration	0/8	0/8	8/8	5/8
Mild	0	0	5	4
Moderate	0	0	3	1
Intense	0	0	0	0
Hyperemia and/or hemorrhage	0/8	0/8	8/8	7/8
Mild	0	0	1	4
Moderate	0	0	3	2
Intense	0	0	4	1

Number of rats with lesions among all of the animals examined (8 rats per group)

Immunohistochemical Results

Immunohistochemically, the caspase-3 and Bax immunoexpressions were evaluated in the kidney tissue. There was no expression of caspase-3 in the Control (Figure 2A) or Perga (Figure 2B) group sections. Strong caspase-3 expression was detected in the glomerular and tubular cells in the Cd group sections (Figure 2C). Expression was present in the Cd + Perga group, but it was less than that in the Cd group (Figure 2D). Bax expression was not observed in the Control (Figure 3A) or Perga group (Figure 3B) sections. Expression was determined in the tubule epithelium in the Cd group sections. However, there was no reaction in the glomerular cells (Figure 3C). In the Cd + Perga group, there was lower Bax expression compared to the Cd group (Figure 3D).

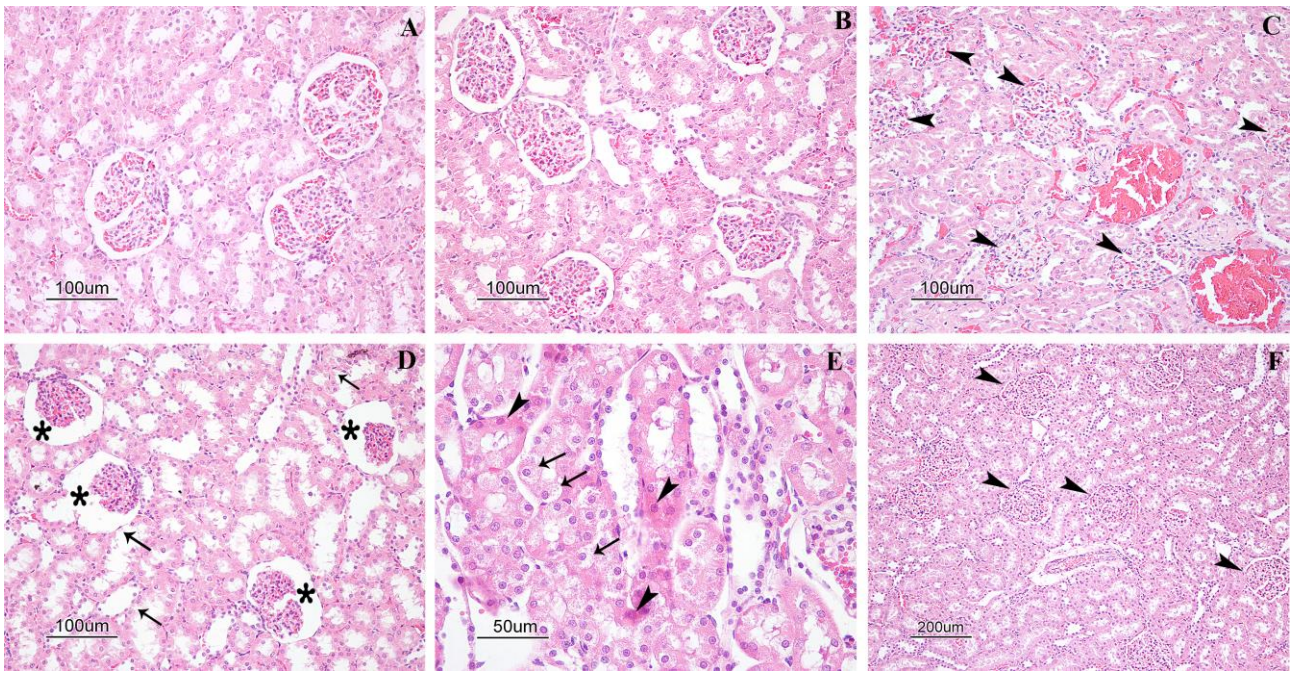

Figure 1: Effects of perga on Cd-induced changes in the kidney sections (H&E).

A) Control group: Normal histological appearance of the kidney. B) Perga group: Normal glomeruli and tubules. C) Cd group: Swelling of the glomerulus and absence of space between the glomerulus and Bowman's capsule (arrowhead). D) Cd group: Shrinkage of the glomerulus, increase in the space between the glomerulus and Bowman's capsule (Stars), and tubuler damage (arrows). E) Cd group: Necrosis (arrows) and cloudy swelling (arrowhead) of the tubular epithelium. F) Cd + Perga group: Treatment with perga prominently attenuated the damage caused by Cd (arrowhead).

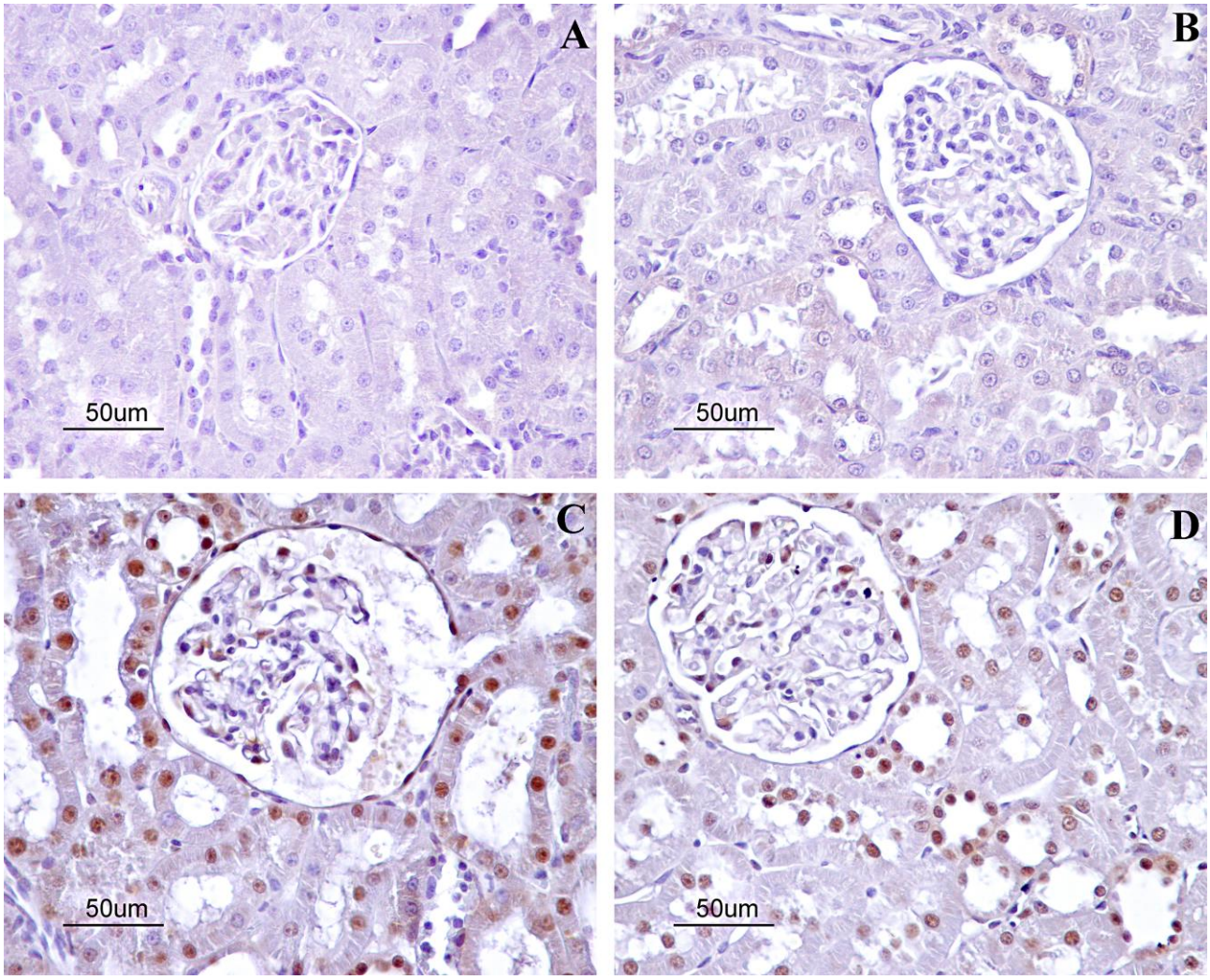

Figure 2: Effect of Cd and perga on the immune-expression of caspase-3 in the kidney tissue of rats.

A) Control group; B) Perga group; C) Cd group; D) Cd + Perga group. ABC method, counterstained with hematoxylin.

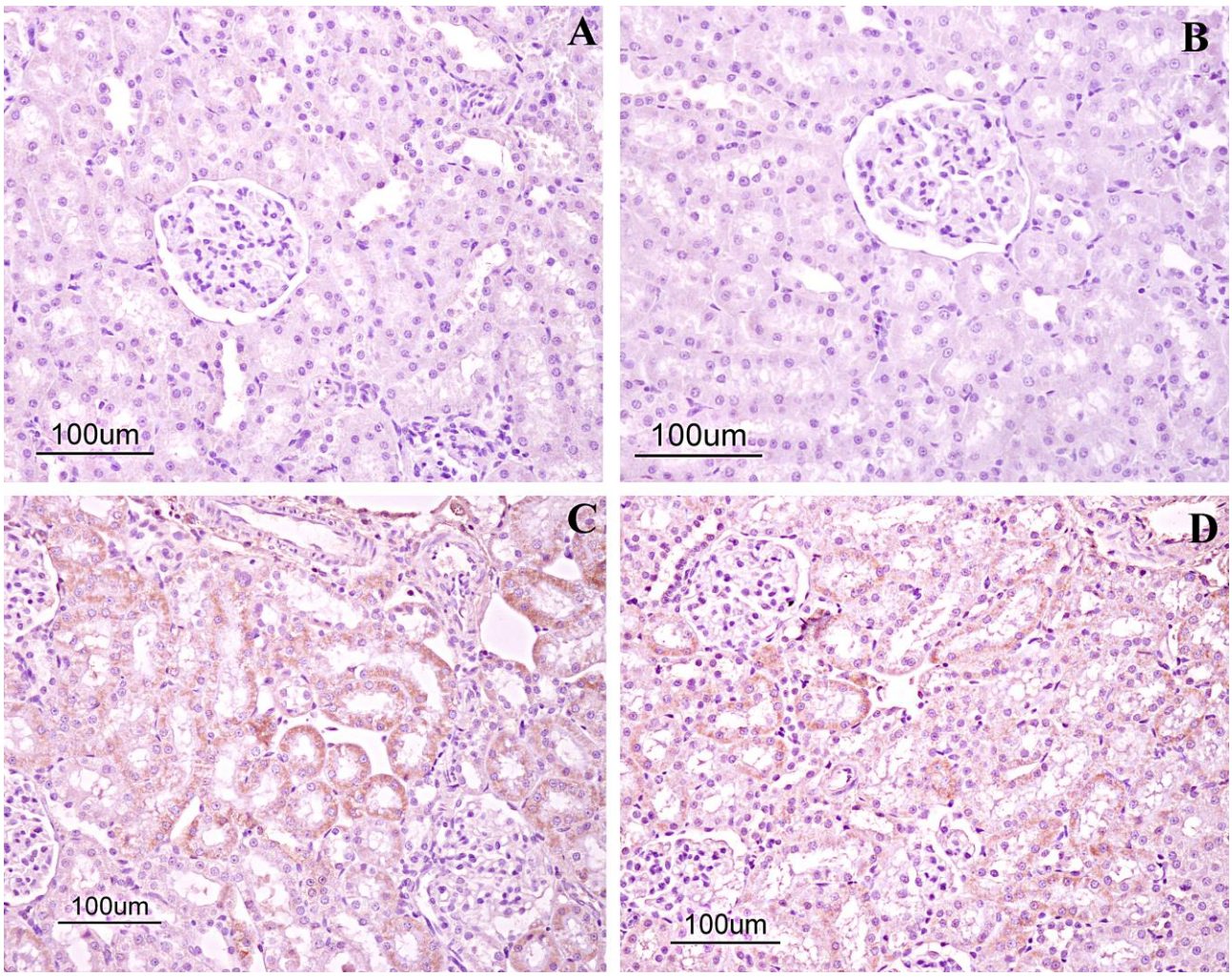

Figure 3: Effect of Cd and perga on the immune-expression of Bax in the kidney tissue of rats.
A) Control group; B) Perga group; C) Cd group; D) Cd + Perga group. ABC method, counterstained with hematoxylin.

Biochemical Results

When the results were evaluated, the SOD, CAT, and GSH-Px enzyme activity decreased in the Cd group compared to the Control group ($p<0.01$). The SOD and GSH-Px activity in the Cd + Perga group increased significantly compared to the Cd group ($p<0.01$). Enzyme activities in the Perga group were close to those in the control group (Figures 4–6). When the MDA level was evaluated, an increase was observed in the Cd group compared to the Control group ($p<0.01$). Compared to the Cd group, the MDA level decreased significantly in the Cd + Perga group ($p<0.01$) (Figure 7).

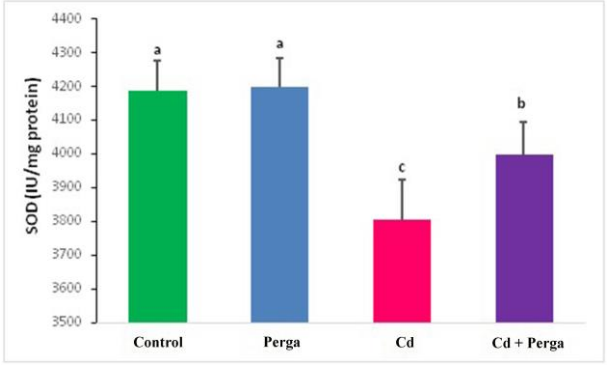

Figure 4: Effect of Cd and perga on SOD levels in the kidney tissue of rats (IU/mg protein) ($p<0.01$).

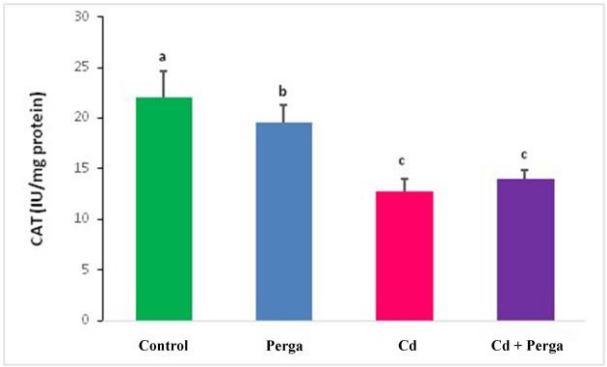

Figure 5: Effect of Cd and perga on CAT levels in the kidney tissue of rats (IU/mg protein) ($p<0.01$).

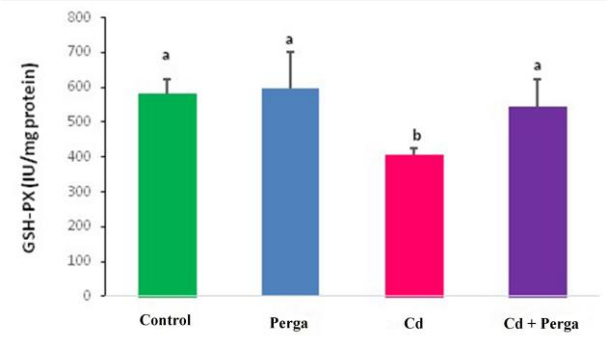

Figure 6: Effect of Cd and perga on GSH-PX levels in the kidney tissue of rats (IU/mg protein) ($p<0.01$).

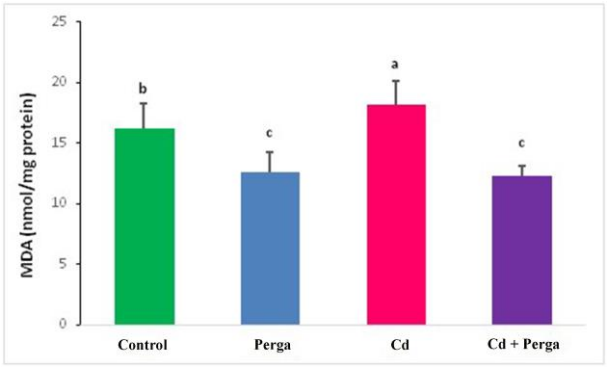

Figure 7: Effect of Cd and perga on MDA levels in the kidney tissue of rats (nmol/mg protein) ($p<0.01$).

DISCUSSION AND CONCLUSION

Cd causes ROS production by triggering the production of pro-inflammatory cytokines and signaling molecules in the kidney (Fouad and Jresat 2011). The toxic effects caused by Cd are closely related to this ROS production, which can activate signaling pathways that cause cell apoptosis (Pathak and Khandelwal 2006). Additionally, antioxidant deficiency occurs with ROS production (Waisberg et al. 2003). It has been reported that a diet rich in natural flavonoids may be useful to prevent Cd-induced kidney damage (Morales et al. 2006). This study described evidence of the protective efficacy of perga in Cd-induced nephrotoxicity.

Cd accumulates in proximal tubule cells through glomerular filtration and disrupts the structure of the kidney (Ge et al. 2019). Marked tubular necrosis, cloudy degeneration of the tubular epithelium, and tubular dilatation have been reported in rat kidneys as a result of exposure to Cd (Pari et al. 2007; Renugadevi and Prabu 2010; Fang et al. 2021). Multiple hemorrhage foci, inflammatory cell infiltration (Renugadevi and Prabu 2010), and the accumulation of eosinophilic debris (hyaline cylinders) in the tubules are other known findings (Tripathi and Srivastav 2011). In the current study, similar histopathological findings were detected in the Cd group. Tubular degeneration, necrosis and dilatation after exposure to toxic substances may be the result of hydraulic changes (Tripathi and Srivastav 2011). Tubular dilatation may be a compensatory mechanism after the loss of function of nephrons due to tubular damage (Sanchez-Chardi et al. 2009).

Cd affects the glomeruli as well as the tubules. In the present study, exposure to Cd caused atrophy of the glomeruli in some sections. The glomerular shrinkage observed in this study was consistent with that in previous studies reporting glomerular shrinkage in rats administered Cd at the same dose and duration as that herein (Renugadevi and Prabu 2009; Renugadevi and Prabu 2010). However, in rats administered Cd at the same dose and duration as in the current study, it was reported that the Bowman's space narrowed as a result of swelling in the glomeruli following exposure to Cd (Tripathi and Srivastav 2011). Herein, similar findings were detected in some of the tissues.

In the present study, the perga treatment showed improvement in some of the histopathological changes caused by Cd in the kidney. Perga has been reported to alleviate oxidant-mediated kidney damage caused by various heavy metals. Ethanolic extract of perga (100 mg/kg) given to rats for 1 month contributed positively to histopathological and biochemical parameters in the liver, kidney, and brain as a detoxifying agent against titanium dioxide nanoparticles and other xenobiotics (Bakour et al. 2021). Perga extract has been shown to significantly ameliorate aluminum-induced hepato-renal toxicity (Bakour et al. 2017).

An important factor for Cd-induced kidney damage is apoptosis (Zhuang et al. 2019). Cd-induced apoptosis involves multiple pathways (Shao et al. 2014). Bax, and caspase-3 play a role in the mitochondria-mediated intrinsic apoptosis pathway. The pro-apoptotic protein Bax can change mitochondrial permeability and cause apoptosis (Amanpour et al. 2019). Caspase-3 is the final protease that activates apoptotic DNA degradation (Abdel Moneim 2016). In the current study, it was found that the caspase-3 and Bax immunoexpression increased in the kidney tissue sections of the Cd group. This evidence are consistent with previous research reporting an increase in caspase-3 and Bax immunoexpression in the kidney of mice (Almeer et al. 2019) and rats (Yuan et al. 2014) exposed to Cd. Previous studies have suggested that antioxidant supplements such as vitamin E (Fang et al. 2021) and selenium (Wang et al. 2013) have a protective effect against Cd-induced apoptosis by reducing Bax and caspase-3 mRNA expression levels. In this presented study, the perga treatment effectively reversed this Cd-induced process.

Vitamins C, E, and selenium may be very important factors in terms of the protective effect against Cd damage (Karabulut-Bulan et al. 2008). Perga is an important source of nutrients and bioactive compounds such as vitamins (C, B, K, P, E H, P, nicotinic acid, and folic acid) and polyphenols (flavonoids, phenolic acids) (Vásquez and Olofsson 2009). It has also been reported that perga contains many micro and macro elements with antioxidant activity such as selenium, zinc, calcium, phosphorus, copper, and magnesium (Nagai et al. 2005). Studies have reported that vitamin C and E, zinc, and selenium reduce oxidative stress and damage caused by Cd (Karabulut-Bulan et al. 2008; Çilenk et al. 2016). Vitamin C supplementation has been shown to reduce Cd uptake from the gastrointestinal tract (Grosicki 2004). It has been shown that vitamin E acts as an antioxidant in cells, interrupting the spread of LPO in the plasma membrane to maintain membrane integrity (Karabulut-Bulan et al. 2008). It has been observed that selenium treatment may protect kidney tissue against Cd toxicity by increasing the activity of antioxidant enzymes in these tissues (EI-Sharaky et al. 2007). Zinc supplementation may partially protect against Cd-induced lipid peroxidation (Jemai et al. 2007). In this study, the significant improvement in histopathological findings and apoptotic markers in the kidney as a result of perga treatment may be related to the content of perga.

Oxidative stress is defined as a disorder in the balance between ROS and antioxidant defenses systems (Akkoyun 2019). Oxidative stress can cause significant interrelated disorders in cellular metabolism, including changes in the protein and nucleic acid structures, an increase in intracellular free calcium, and the destruction of cells by lipid peroxidation (Szymonic-Lesiuk et al. 2003; Akkoyun et al. 2023). Studies have shown that Cd administration significantly reduced SOD, CAT, and GSH-Px activities and increased MDA levels compared to control rats (Messaoudi et al. 2009; Renugadevi and Prabu 2010). In the presented study, the SOD, CAT, and GSH-Px enzyme activities decreased significantly in the Cd and Cd + Perga groups compared to the Control group ($p<0.01$). The SOD, CAT,

and GSH-Px activities in the Cd + Perga group increased significantly compared to the Cd group ($p<0.01$).

MDA is known to be one of the most abundant aldehydes formed as a byproduct of lipid peroxidation (Soltaninejad et al. 2003). A significant increase in MDA level due to Cd exposure has been reported in the kidney tissue of rats (Suhartono et al. 2015). In the presented study, the MDA level increased in the Cd group compared to the Control group ($p<0.01$). The MDA level, which increased in the Cd group, decreased significantly in the Cd + Perga group ($p<0.01$).

In the literature, no studies could be found evaluating the effects of perga against Cd toxicity. It was reported that propolis, another bee product, acts as a protective agent against Cd-induced testicular toxicity (Çilenk et al. 2016). In a study evaluating the protective properties of propolis and royal jelly against the negative effects of Cd on kidney and liver function, it was concluded that both products have the ability to contribute to Cd chelation and the reduction of oxidative stress (Omar et al. 2023). In the presented study, the SOD and GSH-Px activity values in the Cd + Perga group were significantly increased compared to the Cd group. This results shows that perga has preventive effects against Cd-induced oxidative damage due to its antioxidant properties.

In conclusion, perga appears to have a protective role in Cd-induced nephrotoxicity, as it causes a decrease in caspase-3 and Bax immune expressions, reduces the MDA level, and increases serum antioxidant enzyme activities. Therefore, perga could have a potential role as an antioxidant and antiapoptotic agent in food supplementation or the pharmaceutical industry. However, further studies are needed to fully understand the nephroprotective effects of perga.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Idea / Concept: TY, HTA
Supervision / Consultancy: TY, HTA, ÖFK
Data Collection and / or Processing: TY, HTA, MBA
Analysis and / or Interpretation: TY, HTA, ÖFK, MBA
Writing the Article: TY, HTA
Critical Review: TY, HTA, ÖFK, MBA

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