DOI: 10.37990/medr.1197782 Med Records 2023;5(2):400-5

MEDICAL RECORDS-International Medical Journal

Research Article

Rosmarinic Acid Ameliorates Deltamethrin Induced Hepatotoxicity and Nephrotoxicity

Eda Yildizhan[1], Burak Veli Ulger[2], Murat Akkus[1], Omer Faruk Katanalp[3], Ebru Gokalp Ozkorkmaz[1], Ibrahim Yildizhan[4]

[1]Dicle University, Faculty of Medicine, Department of Histology and Embryology, Diyarbakır, Türkiye
[2]Dicle University, Faculty of Medicine, Department of General Surgery, Diyarbakır, Türkiye
[3]Dicle University, Faculty of Veterinary, Department of Laboratory Animals, Diyarbakır, Türkiye
[4]Iğdır University, Faculty of Agricultural Technology, Department of Agricultural Technology, Iğdır, Türkiye

Abstract

Aim: Deltamethrin (DM) is an insecticide and is widely used around the world. Rosmarinic acid (RA) is found in herbs and spices in the Lamiaceae (mint) family and has antioxidant, antiinflammatory and antiapoptotic effects. We objective to examine the protecting efficacy of Rosmarinic acid in preventing the toxic effects of Deltamethrin.

Material and Methods: In ours study we used 28 male rats. Group 1: Control group, Group 2: RA group, RA was given 20 mg/kg peroral (p.o.) for 7 days, Group 3: DM group, 35 mg/kg/dose of DM was given 24 hours before sacrification as a single dose by gavage, Group 4: RA+ DM group.

Results: BUN, creatinine, AST and ALT values of the RA+DM group were lower than the DM group. TAS and TOS grades were higher in the DM group matched to the RA+DM group. The damage scores of the DM group were higher aacording as those of the RA+DM group.

Conclusion: RA has been shown to have predicative influence in the therapy of deltamethrin-induced nephrotoxicity and hepatotoxicity.

Keywords: Deltamethrin, rosmarinic acid, hepatotoxicity, nephrotoxicity

INTRODUCTION

Deltamethrin (DM) is a widely used insecticide for protecting plants against ants, insect, etc. Additionally, it is topically used as an ectoparasiticide to control vector-borne diseases in farm animals (1). DM is generally preferred in the first place among insects because it has rapid metabolism and high efficiency on harmful insects (2). Consuming water or food contaminated with DM can cause serious harm (3). In their studies, Tuzmen et al and Tos-Luty et al have revealed that DM administration to the rats affects hepatic lipid peroxidation and antioxidant defense system and this causes generation of free oxygen radicals, and the destructive effects in liver and kidney textures were occured owing to these free oxygen radicals (4,5).

RA was first isolated and purified in 1958 from Rosmarinus officinalis by two Italian chemists, Scarpati and Oriente, who then named it according to the plant that they isolated it from (6). RA is soluble in water and found in herbs and spices like Rosmarinus officinalis L. (rosemary), Thymus vulgaris L. (thyme) etc. (7). RA has multiple effects, such as antioxidant (8), antiinflammatory (9) and antiapoptotic (10) effects. RA was found to be effective in preventing liver damage due to diabetes (11), tertbutyl hydroperoxide (12), and carbon tetrachloride (13). Lee et al. revealed that Rosmarinic acid has protective effects against hydrogen peroxide-induced neurotoxicity, with Bcl-2 downregulated but Bax upregulated (14).

In this study, we examined to RA intake in the results of DM that occur on the liver and kidney tissue damage.

CITATION
Yidizhan E, Ulger BV, Akkus M, et al. Trosmarinic Acid Ameliorates Deltamethrin Induced Hepatotoxicity and Nephrotoxicity. Med Records. 2023;5(2):400-5. DOI:1037990/medr.1197782

Received: 01.11.2022 **Accepted:** 19.04.2023 **Published:** 02.05.2023
Corresponding Author: Eda Yildizhan, Dicle University, Faculty of Medicine, Department of Histology and Embryology, Diyarbakır, Türkiye
E-mail: blgc_eda@hotmail.com

MATERIAL AND METHOD

Chemicals

Deltamethrin (Butox® 50 mg/ml) was puechased from Intervet Co. (France), and RA was obtained from Sigma Aldrich Inc.

Animals and Experiment Procedure

Twenty-eight male Wistar Albino rats were used. Rats were permitted to eat standard chow ad libitum during the experiment. The rats were protected in steel cages, at 21 C, with alternating 12 hr light/dark cycles, subsequently all rats were placed under general anesthesia by intraperitoneal (i.p.) administration of Ketamine HCl (90 mg/kg, Pfizer Inc, USA) + Xylazine HCl (10 mg/kg, Bayer Health Care AG, Germany).

The animals were randomly divided into 4 equal groups:

Group 1 (n=7): Control Group; no experimental procedure was applied.

Group 2 (n=7): RA group; rats were administered 20 mg/kg/day of RA by gavage for 7 Days (15).

Group 3 (n=7): DM group; on the 7th day of the experiment, the rats were administered 35 mg/kg DM by gavage once, and 24 hours later the rats were sacrificed (16).

Group 4 (n=7): RA + DM group; the rats were administered RA for 7 days, 1 hour later a single dose of DM was given and 24 hours later the rats were sacrificed.

Collection and Staining of Tissue and Blood Samples

Liver tissues, kidney tissues were taken for pathological examination. We took blood samples from the all rats. The liver and kidney tissues taken were fixed in containers containing 10% buffered formol. Tissue samples washed in runing water after fixation were examined with routine histological examinations. routine histological examined with dyes Hematoxylin & Eosin (H&E) protocols for histological evaluation and Periodic Acid Schiff (PAS). Tumor Necrotizing Factor-α (TNF-α) (Santa Cruz, Cat no:sc-52746) antibodies were used to show inflammatory changes in immunohistochemical studies, and Apoptotic protease activating factor-1 (APAF-1) (Santa Cruz, Cat no:sc-65891) antibodies were used for proapoptotic changes.

Biochemical Analysis

Total Antioxidant (TAS) and Total Oxidant (TOS) Levels

Kits were used from Rel Assay Diagnostics for both TAS and TOS levels measurement with Erel's method (17,18).

Liver and Kidney Function Tests

On account of demonstrate liver functions, alanine aminotransferase (ALT) enzyme and aspartate aminotransferase (AST) enzyme levels were evaluated. Blood urea nitrogen (BUN) and Creatinine (Cre) levels were evaluated to evaluate kidney functions.

Histopathological analysis

Liver damage was classified as follows:

Hepatic damage was assessed using a grading system as follows:

• Grade 0: The tissues were normal.

•Grade 1: The injury was mild with pycnosis and cytoplasmic vacuoles.

•Grade 2: Moderate damage without cytoplasmic vacuoles, hepatocytes swelling, sinusoidal dilatation and congestion, and no obvious necrosis.

•Grade 3: Moderate damage with signs of extensive sinusoidal dilatation and congestion, with coagulation necrosis.

•Grade 4: There was severe damage with loss of tissue integrity (19).

Renal damage was classified as follows:

•Grade 0: The tissues were normal.

•Grade 1: Nuclear loss due to swelling in 1/3 of the cells in the tubules.

•Grade 2: Nuclear loss due to swelling in 2/3 of the cells in the tubules.

• Grade 3: Greater nuclear loss due to swelling in more than 2/3 of the cells in the tubules (20).

Immunohistochemical Analysis

After routine histological tissue follow-up, 5 µm thick sections of liver tissues was taken on positively charged slides. Sections were heated in ethylenediamine tetraacetic acid (EDTA) solution for 1 minute in a microwave oven for antigen retrieval treatment and then cooled at room temperature for 15 minutes. The sections were washed in buffered phosphate saline (PBS) solution. Then, the tissues in the sections were drawn with a hydrophobic pen and lined up on the bar. Endogenous peroxide blockade was performed for 20 minutes by dripping 3% H2O2 prepared in methanol on the sections. Sections were washed in PBS for 3x5 minutes.

The sections were incubated for 7 minutes by dripping in Ultra V Block solution (Thermo). The Blocking solution was then removed from the sections. The samples were incubated for a night at +4 °C with primary antibodies APAF-1 (Santa Cruz, Cat no:sc-65891) and TNF-α (Santa Cruz, Cat no:sc-52746) diluted 1/250 with antibody diluent (Thermo) without washing the samples.

In immunohistochemical analysis;

Immunoreactivity prevelance of the tissues were scored as; 0.1 (<25%), 0.4 (26-50%),

0.6 (51-75%), 0.9 (76-100%)

Immunoreactivity severity was leveled as; 0: none, +0.5: very little, +1: little, +2: moderate, +3: severe. The histoscore was created by using the formula:

Histoscore=PrevalencexSeverity (21).

Statistical Analysis

We used SPSS program for statistical analyzes (Chicago, IL, USA) . Normally distributed measurements was done by One-Way Analysis of Variance (ANOVA), and non-normally distributed measurements by Mann Whitney-U test. It was considered significant in case of p<0.05 value.

RESULTS

AST, ALT, BUN and Creatine Values

AST, ALT, BUN and Creatine values of the RA+DM group was lower than the DM

group's (p<0.05) (Table 1).

TAS and TOS Values

We found that TAS and TOS levels were higher in DM group then the RA+DM group (p<0.05) (Table 1).

Histopathological Evaluation

Histopathological evaluation of kidney tissues revealed fibrosis in the glomerular area, impairment in the tubules, pycnosis in the endothelial cells, and inflammatory cell infiltration and congestion in the DM group. In the RA+DM group; the glomeruli appeared near normal, and the proximal and distal tubules were normal. However, inflammatory cell infiltration continued at a mild score. We tracked that the kidney damage measuremed of the DM group was higher than the RA+DM group (p<0.05) (Figure 1). In liver tissues; Pycnotic cells were observed in the DM group. Inflammatory cell infiltration, dilatation and congestion were observed around the vena centralis, where the radial alignment of the cell cords was disrupted. In the RA+DM group, it was tracked that the radial alignment of the cell cords improved, while the congestion continued. Endothelial cells around the sinusoid were normal (Figure

Table 1. Mean±standard deviation values of AST, ALT, BUN, Creatine, TAS and TOS values

GROUPS	BUN (mg/dl)	Cre (mg/dl)	AST (u/l)	ALT (u/l)	TAS (µmol H2O2 equivalent/L)	TOS (mmol Trolox equivalent/L)
Control	54.42±2.37^{c,d}	0.58±0.02^{c}	168.85±12.81^{c,d}	61.14±9.42^{c}	1.29±0.07^{c,d}	19.86±9.67^{c,d}
RA	56.42±2.82^{c,d}	0.56±0.03^{c}	165.00±7.65^{c,d}	61.42±6.05^{c}	1.36±0.10^{c}	18.28±3.78^{c}
DM	95.28±18.14^{a,b,d}	0.85±0.09^{a,b,d}	524.71±81.16^{a,b,d}	91.57±6.80^{a,b,d}	1.90±0.08^{a,b,d}	82.66±18.27^{a,b,d}
RA+DM	67.85±4.52^{a,b,c}	0.60±0.04^{a,b,c}	225.85±32.57^{a,b,c}	70.00±5.68^{c}	1.48±0.10^{a,c}	46.44±12.26^{a,b,c}

AST; Aspartate aminotransferase, ALT; Alanine aminotransferase, Cre; Creatinine, BUN, TAS; total antioxidant capacity (µmol H2O2 equivalent/L), TOS; total oxidant capacity (mmol Trolox equivalent/L) results are expressed as Mean ±SD. a: There is a difference with the control group, b: There is a difference with the RA group, c: There is a difference with the DM group, d: There is a difference with the RA+DM group

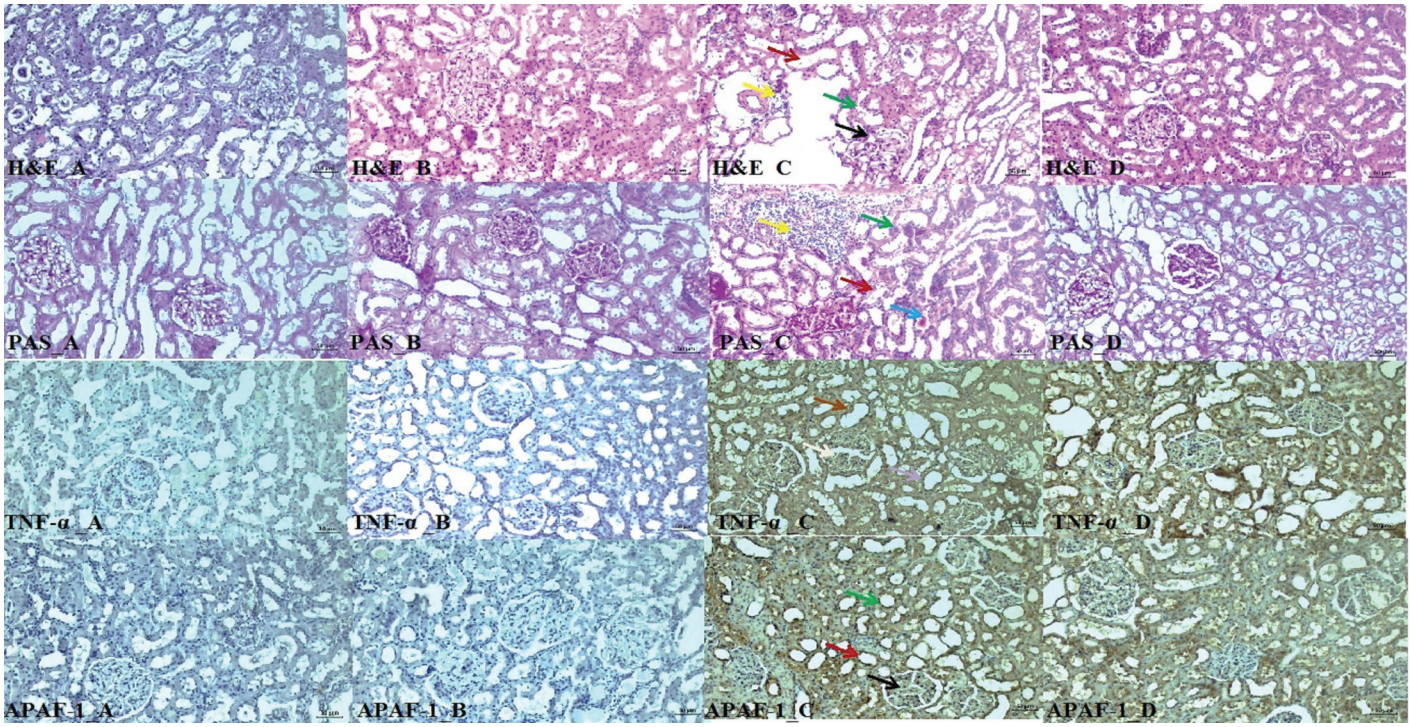

Figure 1. Light microscopic images of kidney tissues. First row: H&E, Second row: PAS, Third row: TNF-α, Fourth row: APAF-1. A: Control Group, B: RA Group, C: DM Group, D: RA+DM Group. Fibrosis in the glomerular area (black arrow), degeneration of the proximal tubules (red arrow), degeneration of the distal tubules (green arrow), inflammatory cell infiltration (yellow arrow), congestion (blue arrow). Intense expression in the glomerular area (white arrow), intense expression in the proximal tubules (Brown arrow), intense expression in the distal tubules (purple arrow)

2). The liver damage grade of the DM group was higher than that of the RA+DM group ($p<0.05$).

Examination of the Periodic acid Schiff (PAS) defilementing of kidney tissues under a light microscope revealed a narrowing in the Bowman's space in the DM group, while this narrowing improved in the RA+DM group (Figure 1). In the liver tissues, there was degeneration and deterioration in the basement membrane structure of the DM group, and the glycogen density decreased. It was observed that basement membrane integrity and glycogen density started to develop in the RA+DM group (Figure 2).

Immunohistochemical Evaluation

Immunohistochemical examinations of kidney tissues revealed that; while intense positive TNF-α expressions were observed in the cytoplasm of glomerular cells in the DM group, similarly intense positive TNF-α expressions were present in the tubules. The expressions were milder in the RA+DM group, than that in the DM group. When TNF-α and APAF-1 histoscoping was carried out, it was monitored that the expressions in the RA+DM group were lower than those in the DM group ($p<0.05$) (Figure 3). In immunohistochemical examinations of liver tissues; intense TNF-α and APAF-1 expressions were observed in hepatocyte nuclei and cytoplasm, while expressions were milder in the RA+DM group compared to the DM group (Figure 3).

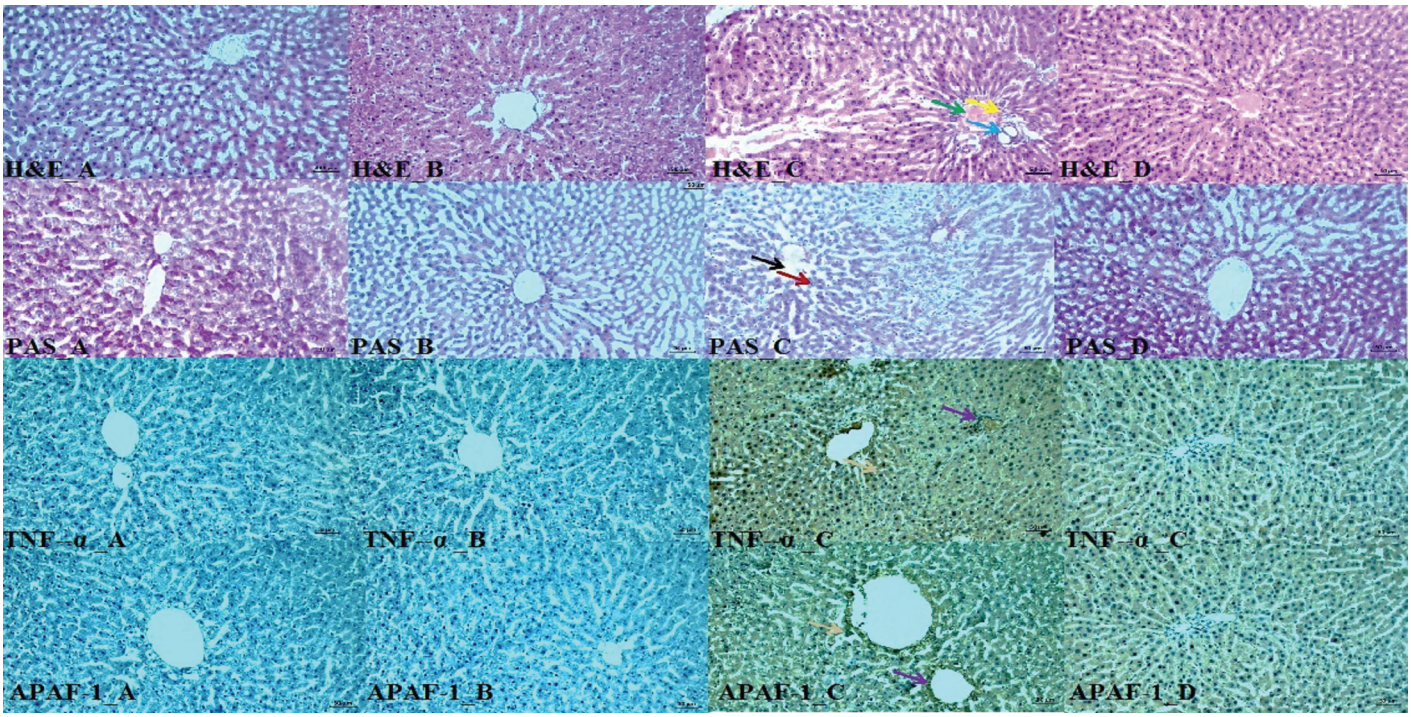

Figure 2. Light microscopic images of liver tissues. First row: H&E, Second row: PAS, Third row: TNF-α, Fourth row: APAF-1. A: Control Group, B: RA Group, C: DM Group, D: RA+DM Group. Congestion (green arrow), dilatation (blue arrow), mononuclear cell infiltration (yellow arrow), disruption of basement membrane integrity and degeneration (black arrow), decrease in glycogen density (red arrow). Intense expression in hepatocyte nuclei and cytoplasm (gray arrow), intense expression in endothelial cells (purple arrow)

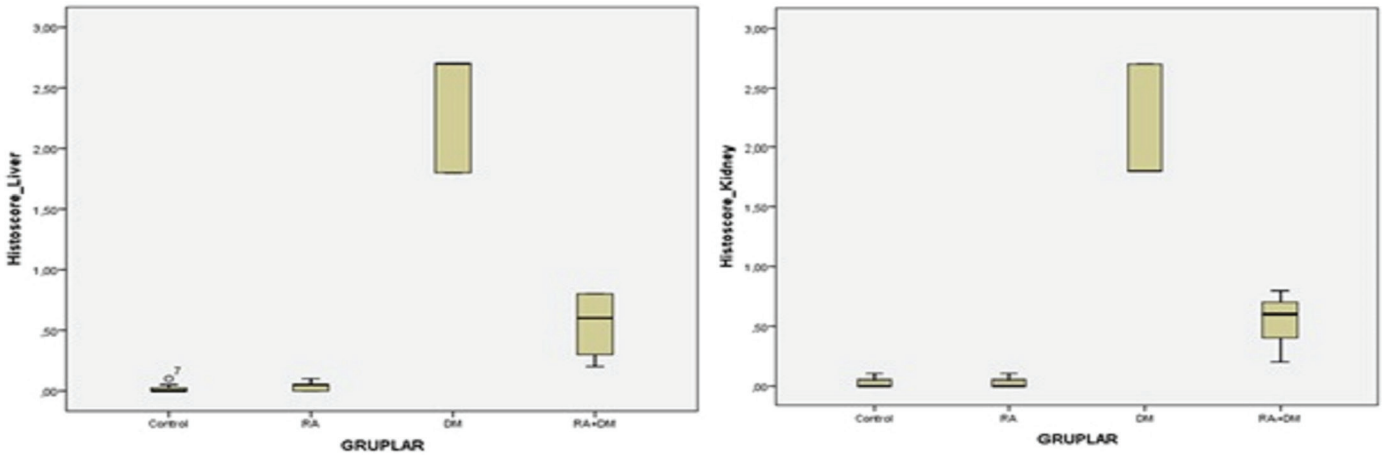

Figure 3. Average analysis graph of liver and kidney tissues with histoscoring

DISCUSSION

Rosmarinic acid (RA) is isolated from herbal balm mint plants, such as Rosmarinus officinalis, Melissa officinalis, and Prunella vulgaris L. (22, 23). It is a naturally occurring hydroxylated compound with anti-inflammatory, anticancer, antimutagenic, antibacterial, and antiviral activity (24, 25). Deltamethrin (DM) is a synthetic insecticide with a wide range of uses. Contaminated water and food are the leading sources of exposure to this pesticide (3). The main organ in which DM is metabolized is the liver, and the kidneys provide the excretion of its metabolites (26). We noted that DM showed toxic effects on either liver or kidney tissues after administering a dose of 35 mg/kg.

In their study, Yousef et al. and El-Demerdash et al observed that DM toxicity increased serum AST and ALT values (27, 28). In our study serum AST and ALT levels were seen to be higher in the DM group compared to the other groups. Domitrovic R et al. revealed that the serum ALT level of the RA group was close to normal (13). In our study, the serum AST and ALT levels of the RA+DM group were lower than the DM group.

In their study Aydin et al. a single acute thiacloprid dose of 112.5 mg/kg (aT) a subacute thiacloprid dose of 22.5 mg/kg (sT), a single acute deltamethrin dose of 15 mg/kg (aD), a subacute deltamethrin dose of 3 mg/kg (sD), or combined dose of these pesticides at the same rates by gavage to rats. They monitored that there was an improvement in serum BUN and creatine values when rats were subjected to DM at a dose of 3mg/kg for 30 days (29). These findings were compatible with our study. Ozturk et al. reported that RA reduced oxidative damage on kidney tissue and normalized serum creatinine and BUN levels of rats with RA compared to other groups in their kidney ischemia and reperfusion (I/R) study (30). The serum BUN and creatinine values in the RA group were close to normal in our study, and they were lower in the RA+DM group than that in the DM group.

Ramalho et al reported that RA protected the liver against I/R damage by showing a strong anti-inflammatory and antioxidant attachment in liver parenchymal cells (31). We observed that RA protects the liver endothelial cells against DM-induced liver damage in rats, reduces the number of pycnotic cells, and the radial arrangement in the cell cords begins to reappear. In addition, in the immunohistochemical examinations, we observed that the intense TNF-α and APAF-1 expressions in the hepatocyte nuclei and cytoplasm and endothelial cells were decreased in the RA+DM group compared to the DM group.

Abdel-Daim et al. found that DM administration increased lipid peroxidation by increasing hepatic and renal malondialdehyde (MDA) levels, and decreased hepatic and renal antioxidants (superoxide dismutase, catalase, GSH) (32). Similarly, we observed that the serum TAS level decreased and the serum TOS level increased in the DM group, and this balance changed in the opposite direction after RA application.

Al-Gerbed et al. observed that glomerular congestion, tubular degeneration, necrosis, swelling of the tubules and vacuolization in various regions along the renal cortex developed in the kidney tissues of rats administered DM (33). In our study, we observed that histopathological changes such as fibrosis in the glomerular area, degeneration in the tubules, inflammatory cell infiltration and congestion occurred in the kidney tissues of rats treated with DM. Our study showed consistent results with other studies in line with these findings.

Abdel- Daim et al. noticed an increase in lipid peroxidation, oxidative stress and proinflammatory cytokin levels (IL-1β, IL-6, TNF-α) in kidney tissues of rats given DM (32). Similarly, we observed intense positive TNF-α and APAF-1 expressions in the kidneys of the rats in DM group, and these expressions were decreased in the RA+DM group.

CONCLUSION

Our study revealed that Rosmarinic acid has positive effects in preventing deltamethrin induced nephrotoxicity and hepatotoxicity in terms of biochemical, histopathological and immunohistochemical examinations.

Financial disclosures: *The authors declared that this study has received no financial support.*

Conflict of Interest: *The authors have no conflicts of interest to declare.*

Ethical approval: *The ethics committee approval for this study was obtained from the Dicle University Local Ethics Committee (decision number: 2020/40).*

REFERENCES

1. Mehlhorn H, Schumacher B, Jatzlau A, et al. Efficacy of deltamethrin (Butox 7.5 pour on) against nymphs andadults of ticks (Ixodes ricinus, Rhipicephalus sanguineus) in treated hair of cattleand sheep. Parasitol Res. 2011;108:963-71.
2. Chargui I, Grissa I, Bensassi F, et al. Oxidative stress, biochemical and histopathological alterations in the liver and kidney off male rats exposed to low doses of deltamethrin (DM): a molecular assessment. Biomed Environ Sci. 2012;25:672-83.
3. Barlow SM, Sullivan FM, Lines J. Risk assessment of the use of deltamethrin on bednets for the prevention of malaria. Food Chem Toxicol. 2001;39:407-22.
4. Tuzmen N, Candan N, Kaya E, et al. Biochemical effects of chlorpyrifos and deltamethrin on altered antioxidative defense mechanisms and lipid peroxidation in rat liver. Cell Biochem. Funct. 2008;26:119-24.
5. Tos-Luty S, Haratym-Maj A, Latuszynska J, et al. Oral toxicity of deltamethrin and fenvalerate in Swiss mice. Ann Agric Environ Med. 2001;8:45-54.
6. Al-Dhabi NA, Arasu MV, Park CH, Park SU. Recent Studies On Rosmarinic Acid And Its Biological And Pharmacological Activities. EXCLI J. 2014;13:1192-5.

7. Rosmarinic Acid Biosynthesis and Mechanism of Action in "Functional Foods and Biotechnology" by Shetty K. 1st Edition. 2006; CRC Press.

8. Pietsch K, Saul N, Chakrabarti S, et al. Hormetins, antioxidants and prooxidants: defining quercetin, caffeic acid- and rosmarinic acid-mediated life extension in C. elegans. Biogerontol. 2011;12:329-47.

9. Chu X, Ci X, He J, et al. Effects of a natural prolyl oligopeptidase inhibitor, rosmarinic acid, on lipopolysaccharide-induced acute lung injury in mice. Molecules. 2012;17:3586-98.

10. Rizk HA, Masoud MA, Maher OW. Prophylactic effects of ellagic acid and rosmarinic acid on doxorubicin-induced neurotoxicity in rats. J Biochem Mol Toxicol. 2017;31:12.

11. Mushtaq N, Schmatz R, Ahmed M, et al. Protective effect of rosmarinic acid against oxidative stress biomarkersin liver and kidney of strepotozotocin-induced diabetic rats. J Physiol Biochem. 2015;71:743-51.

12. Yang SY, Hong CO, Lee GP, et al. The hepatoprotection of caffeic acid and rosmarinic acid, major compounds of Perilla frutescens, against t-BHP-induced oxidative liver damage. Food Chem Toxicol. 2013;55:92-9.

13. Domitrovic R, Škoda M, Marchesi VV, et al. Rosmarinic acid ameliorates acute liver damage and fibrogenesis in carbon tetrachloride-intoxicated mice. Food Chem Toxicol. 2013;51:370-8.

14. Lee HJ, Cho HS, Park E, et al. Rosmarinic acid protects human dopaminergic neuronal cells against hydrogen peroxide-induced apoptosis. Toxicol. 2008; 250:109-15.

15. Zhang ZK, Zhou Y, Cao J, et al. Rosmarinic acid ameliorates septic-associated mortality and lung injury in mice via GRP78/IRE1α/JNK pathway. J Pharm Pharmacol. 2021;73:916-21.

16. Gunduz E, Ulger BV, Ibiloglu I, et al. Glutamine provides effective protection against deltamethrin-induced acute hepatotoxicity in rats but not against nephrotoxicity. Med Sci Monit. 2015;21:1107-14.

17. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Clin Biochem. 2004;37:112–9.

18. Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem. 2005;38:1103–11.

19. Camargo Jr CA, Madden JF, Gao W, et al. Interleukin-6 protects liver against warm ischemia/reperfusion injury and promotes hepatocyte proliferation in the rodent. Hepatology. 1997;26:1513–20.

20. Chatterjee PK, Cuzzocrea S, Brown PA, et al. Tempol, a membrane permeable radical scavenger, reduces oxidant stress-mediated renal dysfunction and injury in the rat. Kidney Int. 2000;58:658–73.

21. Erdogan MA, Yalcin A. Protective effects of benfotiamine on irisin activity in methotrexate-induced liver injury in rats. Arch Med Sci. 2018;16:205-11.

22. Sahu A, Rawal N, Pangburn MK. Inhibition of complement by covalent attachment of rosmarinic acid to activated C3b. Biochem Pharmacol. 1999;57:1439–46.

23. Xu Y, Jiang Z, Ji G, Liu J. Inhibition of bone metastasis from breast carcinoma by rosmarinic acid. Planta Med. 2010;76:956–62.

24. Wu HP, Wang HL, Zhang Z, et al. [Analyze on the component of rosmarinic acid in Prunella vulgaris and its effect on alpha-glycosidase activity]. Zhong Yao Cai. Chinese. 2011;34:1712-5.

25. Qiao S, Li W, Tsubouchi R, et al. Rosmarinic acid inhibits the formation of reactive oxygen and nitrogen species in RAW264.7 macrophages. Free Radic Res. 2005;39:995–1003.

26. Anand SS, Bruckner JV, Haines WT, et al. Muralidhara S, Fisher JW, Padilla S. Characterization of deltamethrin metabolism by rat plasma and liver microsomes. Toxicol Appl Pharmacol. 2006;212:156-66.

27. El-Demerdash FM, Yousef MI, Kedwany FS, et al. Role of α-Tocopherol and β-Carotene in ameliorating the Fenvalerate-Induced Changes in Oxidative Stress, Hemato-Biochemical Parameters, and Semen Quality of Male Rats. J Environ Sci Health. 2004;39:443-59.

28. Yousef MI, El-Demerdash FM, Al-Salhen KS. Protective role of isoflavones against the toxic effect of cypermethrin on semen quality and testosterone levels of rabbits. J Environ Sci Health. 2003;38:463-78.

29. Aydın B. Effects of thiacloprid, deltamethrin and their combination on oxidative stress in lymphoid organs, polymorphonuclear leukocytes and plasma of rats. Pesticide Biochemist Physiol. 2011;100:165-71.

30. Ozturk H, Ozturk H, Terzi EH, et al. Protective effects of rosmarinic acid against renal ischaemia/reperfusion injury in rats. J Pak Med Assoc. 2014;64:260–5.

31. Ramalho LN, Pasta ÂA, Terra VA, et al. Rosmarinic acid attenuates hepatic ischemia and reperfusion injury in rats. Food Chem Toxicol. 2014;74:270-8.

32. Abdel-Daim MM, Abuzead SMM, Halawa SM. Protective role of Spirulina platensis against acute deltamethrin-induced toxicity in rats. PLoS One. 2013;8:e72991.

33. El-Gerbed MSA. Protective effect of lycopene on deltamethrin-induced histological and ultrastructural changes in kidney tissue of rats. Toxicol Ind Health. 2014;30:160–73.