



## The Effect of Resveratrol on The Oxidative Stress in Rats Treated with Irradiation

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**Abstract:** The antioxidant and protective effect of resveratrol against irradiation induced oxidative damage were researched. Twenty-one rats were separated into 3 groups; First group was the control group. Second group was the irradiation group; received physiological saline intraperitoneally (i.p.) for three days, then 9 Gray (Gy) irradiation was applied. Third group was irradiation+Resveratrol group; received 10 mg/kg resveratrol i.p. for three days and then the same dose of radiation was applied. As a result of irradiation, a significant increase was found in the level of malondialdehyde (MDA) in the liver, kidney and brain tissues of rats ( $P<0.001$ ). Glutathione peroxidase (GSH-Px) activity in all the tissues and superoxide dismutase (SOD) activity, Glutathione (GSH) levels in liver decreased ( $P<0.01$ ), GSH levels in kidney, spleen and ovarium tissues significantly increased ( $P<0.05$ ). The giving of resveratrol significantly reduced the MDA levels increasing in liver, kidney, and brain as a result of irradiation ( $P<0.001$ ) and the liver MDA levels reached to the control levels. By giving resveratrol, it was determined that all the antioxidants studied reduced significantly compared to the control group and/or the irradiation group ( $P<0.05$ ). According to the data obtained as a result; It was concluded that resveratrol shows a corrective effect by changing the oxidant/antioxidant balance against oxidative stress caused by irradiation, therefore resveratrol is a powerful antioxidant.

**Keywords:** Irradiation, Oxidative stress, Resveratrol.

## Radyasyona Maruz Kalan Ratlarda Oksidatif Stres Üzerine Resveratrolün Etkisi

**Öz:** Radyasyonun yarattığı oksidatif hasar üzerine resveratrolün antioksidan ve koruyucu etkisi araştırıldı. Yirmi bir rat 3 gruba ayrıldı; Birinci grup, Kontrol grubu. İkinci grup, Radyasyon grubu; Üç gün fizyolojik tuz solüsyonu intraperitoneal (i.p.) olarak verildi ve sonra 9 Gray (Gy) radyasyon uygulandı. Üçüncü grup, Radyasyon + Resveratrol grubu; Üç gün 10 mg/kg olacak şekilde resveratrol i.p. verildi ve sonra aynı dozda radyasyon uygulandı. Radyasyon sonucu ratların karaciğer, böbrek ve beyin dokularında malondialdehit (MDA) seviyesinde önemli artış saptandı ( $P<0.001$ ). Çalışılan tüm dokularda glutatyon peroksidaz (GSH-Px) aktivitesinde ( $P<0.01$ ), yine karaciğer süperoksit dismutaz (SOD) aktivitesi ve glutatyon (GSH) seviyesinde azalış ( $P<0.01$ ), böbrek, dalak ve ovarium dokularında GSH düzeyinde ise önemli artış tespit edildi ( $P<0.05$ ). Resveratrol verilmesi radyasyon sonucu karaciğer, böbrek ve beyinde artan MDA düzeylerini önemli azalttı ( $P<0.001$ ) ve karaciğer MDA düzeyleri kontrol düzeylerine ulaştı. Resveratrol verilmesiyle çalışılan tüm antioksidanların kontrol ve/veya radyasyon uygulanan gruba göre önemli azalma gösterdiği tespit edildi ( $P<0.05$ ). Sonuç olarak elde edilen verilere göre; resveratrolün radyasyona bağlı oluşan oksidatif strese karşı oksidan/antioksidan dengeyi değiştirerek düzeltici bir etki gösterdiği, bu nedenle resveratrolün güçlü bir antioksidan olduğu kanaatine varılmıştır.

**Anahtar Kelimeler:** Oksidatif stres, Radyasyon, Resveratrol.

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## INTRODUCTION

Ionizing radiation (X,  $\gamma$ -ray) has drawn a great deal of attention in terms of its advantages and possible harmful effects to human population (1,2). The reactive oxygen species (ROS) is produced by ionizing radiation as a result of the decomposition of cellular water, like superoxide anion radical ( $\cdot\text{O}_2^-$ ), hydrogen peroxide ( $\text{H}_2\text{O}_2$ ), hydroxyl radical ( $\cdot\text{OH}$ ), nitric oxide (NO), and nitrogen dioxide ( $\cdot\text{NO}_2$ ). These ROS significantly take part in cell damage by causing lipid peroxidation, protein modification, and DNA strand breaks, and eventually leading to physical and chemical damage in tissues if not scavenged (3). The malondialdehyde (MDA), which is an end-product of lipid peroxidation, is among the markers of oxidative damage (4). Aerobic cells develop their own defense systems and the antioxidant system against to ROS. The antioxidant system has low molecular weight antioxidant molecules such as Ascorbic acid,  $\alpha$ -Tocopherol, glutathione (GSH) and various antioxidant enzymes such as glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) (5).

One of currently proposed strategies is to use the addition of antioxidants for enhancing the efficacy of radiotherapy since antioxidants are able to scavenge free radicals from the radiolysis of water and to protect cells from damage (6). Resveratrol is a natural non-flavonoid, polyphenolic compound some plants contain like the skin of red grapes, peanuts, blueberries, and cranberries. Resveratrol realized several biological activities such as antioxidant and anticancer (7). As a polyphenolic compound, Resveratrol is also a scavenger of superoxide, hydroxyl, and metal-induced radicals (8). It is known that irradiation causes oxidative damage in the liver (1,9-11). The objective of study, the effect of resveratrol on oxidant (MDA) and antioxidant (SOD, GSH-Px, GSH) state of the kidney, heart, spleen, brain and ovarium tissues of the irradiated rats as well as their liver tissues was researched.

## MATERIALS and METHODS

### Animals

Female fertile Wistar albino rats ( $200 \pm 10$  g) aged between 4–5 months were supplied from the

Animal Care Unit of Firat University. They were kept in plastic cages with stainless-steel grid tops. The experimental conditions were environmentally controlled in terms of temperature ( $23 \pm 2$  °C), humidity ( $50 \pm 5\%$ ), and light (12 h of light and dark cycle). The animals were fed with pellet diet and water ad libitum. Three rats were kept together in polypropylene cages containing sterile husk bedding during the experiment. The experiments were carried out after the approval of the Local Ethics Committee of the Veterinary Research Institute (Official form date and number: 18.04.2013 and 2013/4-1) in Elazığ. Chemicals were supplied from companies such as Sigma, Merck, Fluka.

### Irradiation of the Rats

A  $\gamma$ -ray source was used to perform whole-body irradiation. The animals were put in Plexiglass<sup>R</sup> cages and irradiated in groups of seven rats, simultaneously. The source-to-skin distance was 291 cm with a dose of 0.0233 Gy/s and absorbed dose of 9 Gy (12). They were irradiated by a 160 MLC LINAC (Siemens Artiste linear accelerator, using 6 MV photons). The rats were irradiated under continuous isoflurane anesthesia in a specially fabricated plexiglass chamber radiating out from the center.

### Experimental Design

The rats were separated into three groups including 7 rats in each.

Control group, rats did not receive any treatment.

Irradiation group, rats were treated with intraperitoneal injection (i.p.) containing a physiologic saline solution for three days. All rats in this group were irradiated with gamma-rays at dose of 9 Gy.

Irradiation + Resveratrol group, rats were treated with i.p. injection containing Resveratrol (resVida, DSM, Basel, Switzerland) at dose of 10 mg/

kg body weight (9) for three days. Then, all rats were irradiated with gamma-rays at dose of 9 Gy.

Ketamine (ketamine hydrochloride, 50 mg/kg [Ketalar® 5%, Parke-Davis]) and xylazine (8 mg/kg [Rompun® 2%, Bayer]) mixture was done i.p. in order to anesthetize the rats. All rats were sacrificed at 24th hour after irradiation exposure. After decapitation, whole liver, spleen, kidney, brain, heart and ovarium tissues were rapidly resected. The tissues were stored at -80°C.

### Biochemical Analysis in Tissues

The tissues were homogenized by using a Teflon-glass homogenizer (CAT, Germany) with 1.15% KCl to prepare 1: 10 (w /v) homogenate. Malondialdehyde (MDA) concentration of tissue homogenates expressed as the thiobarbituric acid reactive substances (TBARS) was assayed spectrophotometrically according to the method of Placer et al. (13). GSH concentration of tissue homogenates was measured by an assay using the dithionitrobenzoic acid recycling method by Sedlak and Lindsay (14). The GSH-Px activity was determined according to the method of Lawrance and Burk (15) which records the decrease of NADPH at 340 nm. The SOD activity was performed based on the method by

Sun et al. (16). The SOD enzyme activity was measured based on the nitroblue tetrazolium (NBT) degradation by the superoxide radical, which was produced with the xanthine- xanthine oxidase system. The Formazan obtained at the end of the reactions exhibited a blue colour and was maximally absorbed at 560 nm. Tissue protein contents were determined in accordance with the method of Lowry et al. (17).

### Statistical Analysis

The SPSS statistical software (SPSS for windows, version 22.0) was used for all statistical analyses. All the data were given in mean ( $\pm$ ) and standard error (SE). Analysis of variance (ANOVA) followed by Duncan test was done to determine whether there were significant differences among the groups. The 5% level of significance was used to establish differences.

### RESULTS and DISCUSSION

The effect of resveratrol on lipid peroxidation (MDA), nonenzymatic antioxidants (GSH) and enzymatic activities (SOD, GSH-Px) in the tissues of the irradiated rats were presented in Table 1.

**Table 1.** The effect of resveratrol on MDA and some antioxidant levels in the tissues of the irradiated rats.

**Tablo 1.** Radyasyon uygulanan ratların tüm dokularında MDA ve bazı antioksidanlar üzerine resveratrolün etkisi.

	Control	Irradiation	Irradiation + Resveratrol	P
LIVER				
MDA (nmol/g prot)	4.56 $\pm$ 0.38 <sup>b</sup>	12.57 $\pm$ 0.56 <sup>a</sup>	5.50 $\pm$ 0.74 <sup>b</sup>	***
GSH-Px (U/g prot)	2.12 $\pm$ 0.33 <sup>a</sup>	0.75 $\pm$ 0.16 <sup>b</sup>	0.85 $\pm$ 0.14 <sup>b</sup>	***
GSH (nmol/g prot)	0.59 $\pm$ 0.05 <sup>a</sup>	0.35 $\pm$ 0.04 <sup>b</sup>	0.41 $\pm$ 0.05 <sup>b</sup>	**
SOD (U/g prot)	1.8 $\pm$ 0.19 <sup>a</sup>	1.13 $\pm$ 0.04 <sup>b</sup>	1.22 $\pm$ 0.11 <sup>b</sup>	**
KIDNEY				
MDA (nmol/g prot)	9.10 $\pm$ 0.42 <sup>b</sup>	22.57 $\pm$ 2.86 <sup>a</sup>	5.67 $\pm$ 0.78 <sup>b</sup>	***
GSH-Px (U/g prot)	2.54 $\pm$ 0.27 <sup>a</sup>	1.10 $\pm$ 0.17 <sup>b</sup>	1.05 $\pm$ 0.50 <sup>b</sup>	***
GSH (nmol/g prot)	0.41 $\pm$ 0.02 <sup>b</sup>	1.92 $\pm$ 0.43 <sup>a</sup>	0.50 $\pm$ 0.11 <sup>b</sup>	***
SOD (U/g prot)	1.52 $\pm$ 0.11 <sup>a</sup>	1.64 $\pm$ 0.09 <sup>a</sup>	1.05 $\pm$ 0.09 <sup>b</sup>	***
HEART				
MDA (nmol/g prot)	12.24 $\pm$ 0.98 <sup>a</sup>	15.02 $\pm$ 1.37 <sup>a</sup>	3.92 $\pm$ 0.6 <sup>b</sup>	***
GSH-Px (U/g prot)	45.29 $\pm$ 1.58 <sup>a</sup>	22.61 $\pm$ 1.56 <sup>b</sup>	9.60 $\pm$ 0.92 <sup>c</sup>	***
GSH (nmol/g prot)	0.73 $\pm$ 0.06 <sup>ab</sup>	0.82 $\pm$ 0.096 <sup>a</sup>	0.50 $\pm$ 0.06 <sup>b</sup>	*
SOD (U/g prot)	3.36 $\pm$ 0.33 <sup>a</sup>	2.76 $\pm$ 0.24 <sup>a</sup>	1.67 $\pm$ 0.21 <sup>b</sup>	***

**Table 1.** The effect of resveratrol on MDA and some antioxidant levels in the tissues of the irradiated rats (Continued).**Tablo 1.** Radyasyon uygulanan ratların tüm dokularında MDA ve bazı antioksidanlar üzerine resveratrolün etkisi (Devamı).

	Control	Irradiation	Irradiation + Resveratrol	P
SPLEEN				
MDA (nmol/g prot)	14.09 ± 1.15 <sup>a</sup>	16.76 ± 0.7 <sup>a</sup>	5.16 ± 0.25 <sup>b</sup>	***
GSH-Px (U/g prot)	18.35 ± 1.12 <sup>a</sup>	11.23 ± 1.11 <sup>b</sup>	8.05 ± 0.26 <sup>b</sup>	***
GSH (nmol/g prot)	0.41 ± 0.02	0.55 ± 0.05	0.33 ± 0.02	NS
SOD (U/g prot)	1.4 ± 0.05 <sup>a</sup>	1.5 ± 0.13 <sup>a</sup>	0.85 ± 0.03 <sup>b</sup>	***
BRAIN				
MDA (nmol/g prot)	13.07 ± 0.86 <sup>b</sup>	21.65 ± 2.02 <sup>a</sup>	7.47 ± 1.38 <sup>c</sup>	***
GSH-Px (U/g prot)	38.41 ± 1.98 <sup>a</sup>	21.36 ± 1.77 <sup>b</sup>	20.24 ± 2.03 <sup>b</sup>	**
GSH (nmol/g prot)	0.5 ± 0.1 <sup>ab</sup>	0.67 ± 0.04 <sup>a</sup>	0.48 ± 0.038 <sup>b</sup>	*
SOD (U/g prot)	1.97 ± 0.14 <sup>a</sup>	1.97 ± 0.11 <sup>a</sup>	1.16 ± 0.12 <sup>b</sup>	***
OVARIIUM				
MDA (nmol/g prot)	12.93 ± 0.82 <sup>a</sup>	14.64 ± 1.4 <sup>a</sup>	9.48 ± 0.53 <sup>b</sup>	***
GSH-Px (U/g prot)	57.76 ± 2.99 <sup>a</sup>	38.74 ± 0.97 <sup>b</sup>	34.56 ± 0.69 <sup>b</sup>	***
GSH (nmol/g prot)	0.82 ± 0.03 <sup>b</sup>	1.33 ± 0.15 <sup>a</sup>	0.91 ± 0.15 <sup>ab</sup>	*
SOD (U/g prot)	3.78 ± 0.15 <sup>a</sup>	4.01 ± 0.24 <sup>a</sup>	2.84 ± 0.25 <sup>b</sup>	**

MDA: Malondialdehyde; GSH-Px: Glutathione peroxidase; GSH: Glutathione; SOD: Superoxide dismutase

\*P&lt;0.05, \*\*P&lt;0.01, \*\*\*P&lt;0.001, NS: No Significant

<sup>ab</sup> Mean values with different superscripts within a row differ significantly.

As a result of irradiation, a significant increase was determined in MDA of liver, kidney and brain tissues of the rats ( $P<0.001$ ). As a result of irradiation, a significant decrease in GSH-Px activity in all the tissues and SOD activity, GSH concentration in the liver was determined ( $P<0.01$ ); whereas a significant increase was observed in GSH level in the kidney, spleen and ovary tissues ( $P<0.05$ ) (Table 1).

The giving of Resveratrol significantly reduced the MDA increasing in liver, kidney, and brain caused by irradiation ( $P<0.001$ ) and the liver MDA levels reached to the control levels. In addition, by giving resveratrol, the MDA values in the tissues other than liver decreased compared to the control group ( $P<0.001$ ). By giving resveratrol, it was determined that all the antioxidants studied reduced compared to the control group and/or the irradiation group ( $P<0.05$ ) (Table 1).

Oxidative stress emerges in case of increased production of ROS and/or deficiencies of antioxidants and leads to structural and functional modifications and chemical alterations of biomolecules (18). Irradiating biological material causes a rapid burst of ROS, generated mainly due to

the ionizing of water molecules, which then interact with biological target molecules, resulting in lipid peroxidation, DNA damage and later cell killing and mutations (9, 19). The malondialdehyde is among the markers of oxidative damage and this is one of results of reaction of ROS with the unsaturated free fatty acids of membrane lipids (1). In several studies, it was revealed that irradiation caused oxidative damage by causing an increase in MDA levels and a decline in antioxidants such as SOD, GSH, GSH-Px depending on time and dosage (1,9,10,20-23). In this study, MDA levels in liver, kidney, and brain increased as a result of  $\gamma$ -radiation; whereas, a significant reduction in the GSH-Px activity in these tissues and also in the SOD activity and GSH levels in liver was determined. Also, as a result of  $\gamma$ -radiation, significant decreases in GSH-Px activity were determined in the heart, spleen and ovarium tissues, where MDA had an insignificant increase. The antioxidant enzymes reduce because of the depletion of enzymes during oxidative stress induced by irradiation (1,10). When compared to studies reporting the decreased GSH in the kidney, ovarium and spleen (23-26), a significant increase was observed in GSH levels in these tissues as a result

of  $\gamma$ -radiation in the present study. Şimsek et al. (27) stated that while irradiation did not change the ovarium MDA level, it increased GSH-Px and CAT activities. Hermes-Lima et al. (28) suggested that the activation of antioxidant defenses was a protective mechanism against the oxidative stress in order to reduce the production of oxyradicals.

As is seen, irradiation causes oxidative stress in more than one tissue and usually depletes the antioxidants. Cell's capability to counter increased ROS production is based on the endogenous antioxidant defenses; on the other hand, radiation exposure changes the balance of antioxidant defense systems (29). Exogenous antioxidants are able to effectively counteract the oxidative-stress state (30). Phenolic hydroxyl groups of resveratrol enable electrons to stabilize free radicals and ROS (20). In this study, MDA levels increasing in liver, kidney, and brain tissues as a result of irradiation decreased significantly upon addition of resveratrol and also MDA values were found to be significantly low in all the other tissues, except for liver, compared to the control values. The significant decreases in MDA levels in the tissues studied as a result of addition of resveratrol may be directly associated with the ROS scavenging characteristic of resveratrol. The fact that these results were common for all the tissues indicates a strong protective effect of resveratrol against the oxidative damage. Li et al. (19) reported that the ROS levels increasing in the hippocampal tissue of the irradiated rats were reversed by giving resveratrol. In various studies, it was determined that the administration of resveratrol decreased MDA levels increasing in liver and ileum (9), and salivary glands (31,32) as a result of irradiation and elevated the decreasing antioxidant levels such as GSH (9,31) and SOD (32). Also, the addition of the extracts obtained from grape or grape seed decreased MDA levels increasing in heart and skin as a result of irradiation (20,33,34) and increased the decreased antioxidant activities such as GSH-Px, CAT, SOD, and GSH (33,34). On the other hand, the fact that the addition of resveratrol caused a reduction in the

antioxidants compared to the control and/or irradiation group may be associated with the fact that resveratrol decreased the need for enzymatic and nonenzymatic antioxidants directly due to its ROS scavenging characteristic (8,20). As a result, we may mention that resveratrol may be an important antioxidant that may be used for the disorders including more than one tissue and causing common oxidative damage.

As a result, as the administration of resveratrol created a significant decrease in MDA contents of all the tissues studied compared to the control group and/or the irradiation group, it may be asserted that resveratrol is a strong herbal antioxidant.

#### Conflict of interest

The authors declare that they have no conflict of interest.

#### REFERENCES

1. Mansour HH., Hafez HF., Fahmy NM., Hanafi N., 2008. Protective effect of N-acetylcysteine against radiation induced DNA damage and hepatic toxicity in rats. *Biochem Pharmacol*, 75, 773-780.
2. Jagetia GC., Shirwaikar A., Rao SK., Bhilegaonkar PM., 2003. Evaluation of the radioprotective effect of *Ageratum conyzoides* Linn. extract in mice exposed to different dose of gamma radiation. *J Pharm Pharmacol*, 55, 1151-1158.
3. Liu Y., Zhang H., Zhang L., Zhou Q., Wang X., Long J., Dong T., Zhao W., 2007. Antioxidant N-acetylcysteine attenuates the acute liver injury caused by X-ray in mice. *Eur J Pharmacol*, 575, 142-148.
4. Bardak Y., Ozerturk Y., Ozguner F., Durmus M., Delibas N., 2000. Effect of melatonin against oxidative stress in ultraviolet-B exposed rat lens. *Curr Eye Res*, 20, 225-230.
5. Sies H., 1993. Strategies of antioxidant defense. *Eur J Biochem*, 215, 213-219.
6. Barker S., Weinfeld M., Zheng J., Li L., Murray D., 2005. Identification of mammalian proteins

- cross-linked to DNA by ionizing gradiation. *J Biol Chem*, 280, 33826-33838.
7. Sener TE., Tavukcu HH., Atasoy BM., Cevik O., Kaya OT., Cetinel S., Dagli Degerli A., Tinay I., Simsek F., Akbal C., Buttice S., Sener G., 2018. Resveratrol treatment may preserve the erectile function after radiotherapy by restoring antioxidant defence mechanisms, SIRT1 and NOS protein expressions. *Int J Impot Res*, 30, 179-188.
  8. Bradamante S., Barengi L., Villa A., 2004. Cardiovascular protective effects of resveratrol. *Cardiovasc Drug Rev*, 22, 169-188.
  9. Velioğlu-Oğünç AI., Sehirli O., Toklu HZ., Ozyurt H., Mayadağlı A., Ekşioğlu-Demiralp E., Erzik C., Cetinel S., Yeğen BC., Sener G., 2009. Resveratrol protects against irradiation-induced hepatic and ileal damage via its anti-oxidative activity. *Free Radic Res*, 43, 1060-1071.
  10. Khattab HAH., Abdallah IZA., Yousef FM., Huwait EA., 2017. Efficiency of borage seeds oil against gamma irradiation-induced hepatotoxicity in male rats: possible antioxidant activity. *Afr J Tradit Complement Altern Med*, 14, 169-179.
  11. Radwan RR., Mohamed HA., 2018. *Nigella sativa* oil modulates the therapeutic efficacy of mesenchymal stem cells against liver injury in irradiated rats. *J Photochem Photobiol B*, 178, 447-456.
  12. Benkovic V., Knezevic AH., Dikica D., Lisicic D., Orsolc N., Basic I., Kosalec I., Kopjar N., 2008. Radioprotective effects of propolis and quercetin in gamma-irradiated mice evaluated by the alkaline comet assay. *Phytomedicine*, 15, 851-858.
  13. Placer ZA., Cushman LL., Johnson BC., 1966. Estimation of product of lipid peroxidation (malonyldialdehyde) in biochemical systems. *Anal Biochem*, 16, 359-364.
  14. Sedlak J., Lindsay RH., 1968. Estimation of total, protein-bound, and nonprotein sulfhydryl groups in tissue with Ellman's reagent. *Anal Biochem*, 25, 192-205.
  15. Lawrence RA., Burk RF., 1976. Glutathione peroxidase activity in selenium-deficient rat liver. *Biochem Biophys Res Commun*, 71, 952-958.
  16. Sun Y., Oberley WL., Li Y., 1988. A simple method for clinical assay of superoxide dismutase. *Clin Chem*, 34, 497-500.
  17. Lowry OH., Rosebrough NJ., Farr AL., Randall RJ., 1951. Protein measurement with folin phenol reagent. *J Biol Chem*, 193, 265-275.
  18. Cuzzocrea S., Reiter RJ., 2001. Pharmacological action of melatonin in shock, inflammation and ischemia/reperfusion injury. *Europ J Pharmacol*, 426, 1-10.
  19. Li J., Feng L., Xing Y., Wang Y., Du L., Xu C., Cao J., Wang Q., Fan S., Liu Q., Fan F., 2014. Radioprotective and antioxidant effect of resveratrol in hippocampus by activating Sirt1. *Int J Mol Sci*, 15, 5928-5939.
  20. de Freitas RB., Boligon AA., Rovani BT., Piana M., de Brum TF., da Silva Jesus R., Rother FC., Alves NM., Teixeira da Rocha JB., Athayde ML., Barrio JP., de Andrade ER., de Freitas Bauerman L., 2013. Effect of black grape juice against heart damage from acute gamma TBI in rats. *Molecules*, 18, 12154-12167.
  21. Xie Y., Zhao QY., Li HY., Zhou X., Liu Y., Zhang H., 2014. Curcumin ameliorates cognitive deficits heavy ion irradiation-induced learning and memory deficits through enhancing of Nrf2 antioxidant signaling pathways. *Pharmacol Biochem Behav*, 126, 181-186.
  22. Karami M., Asri-Rezaei S., Dormanesh B., Nazarizadeh A., 2018. Comparative study of radioprotective effects of selenium nanoparticles and sodium selenite in irradiation-induced nephropathy of mice model. *Int J Radiat Biol*, 94, 17-27.
  23. Sener G., Kabasakal L., Atasoy BM., Erzik C., Velioğlu-Oğünç A., Cetinel S., Gedik N., Yeğen BC., 2006. Ginkgo biloba extract protects against ionizing radiation-induced oxidative organ damage in rats. *Pharmacol Res*, 53, 241-252.
  24. Ekici K., Temelli O., Parlakpınar H., Samdancı E.,

- Polat A., Beytur A., Tanbek K., Ekici C., Dursun IH., 2016. Beneficial effects of aminoguanidine on radiotherapy-induced kidney and testis injury. *Andrologia*, 48, 683-692.
25. Cheng C., Yi J., Wang R., Cheng L., Wang Z., Lu W., 2018. Protection of Spleen Tissue of  $\gamma$ -ray Irradiated Mice against Immunosuppressive and Oxidative Effects of Radiation by Adenosine 5'-Monophosphate. *Int J Mol Sci*, 19, E1273.
26. Said RSI., Nada AS., El-Demerdash E., 2012. Sodium selenite improves folliculogenesis in radiation-induced ovarian failure: a mechanistic approach. *PLoS One*, 7, e50928.
27. Simsek Y., Gurocak S., Turkoz Y., Akpolat N., Celik O., Ozer A., Yilmaz E., Turhan U., Ozyalin F., 2012. Ameliorative effects of resveratrol on acute ovarian toxicity induced by total body irradiation in young adult rats. *J Pediatr Adolesc Gynecol*, 25, 262-266.
28. Hermes-Lima M., Storey JM., Storey KB., 1998. Antioxidant defenses and metabolic depression. The hypothesis of preparation for oxidative stress in land snails. *Comp Biochem Physiol B-Biochem Mol Biol*, 120, 437-448.
29. Black HS., 2004. Reassessment of a free radical theory of cancer with emphasis on ultraviolet carcinogenesis. *Integr Cancer Ther*, 3, 279-293.
30. Kucukoglu K., Nadaroglu H., 2014. Assessment of the antioxidant and antiradical capacities in vitro of different phenolic derivatives. *Free Rad Antiox*, 4, 24-31.
31. Simsek GI., Gurocak S., Karadag N., Karabulut AB., Demirtas E., Karataş E., Pepele E., 2012. Protective effects of resveratrol on salivary gland damage induced by total body irradiation in rats. *Laryngoscope*, 122, 2743-2748.
32. Xu L., Yang X., Cai J., Ma J., Cheng H., Zhao K., Yang L., Cao Y., Qin Q., Zhang C., Zhang Q., Sun X., 2013. Resveratrol attenuates radiation-induced salivary gland dysfunction in mice. *Laryngoscope*, 123, E23-29.
33. Saada HN., Said UZ., Meki NH., Abd El., Azime AS., 2009. Grape seed extract *Vitis vinifera* protects against radiation-induced oxidative damage and metabolic disorders in rats. *Phytother Res*, 23, 434-438.
34. Cho BO., Che DN., Shin JY., Kang HJ., Jang SI., 2018. Ameliorative effects of fruit stem extract from Muscat Bailey A against chronic UV-induced skin damage in BALB/c mice. *Biomed Pharmacother*, 97, 1680-1688.