Protective effects of artichoke (*Cynara scolymus* L.) extract on ionizing radiation-induced hepatic injury

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Abstract
This study investigated the protective effects of artichoke extract (ENG) on ionizing radiation-induced liver damage in rats. Thirty-two 8-week-old male Wistar albino rats were divided into four groups (n=8). The control group received a standard pellet diet for 10 days. The radiation group (RAD) was exposed to 5 Gy single-dose radiation and fed a pellet diet for 10 days. The radiation + artichoke extract group (RAD+ENG) received the same radiation dose and then a pellet diet supplemented with 25 mL/kg ENG for 10 days. The ENG group was fed only a pellet diet enriched with 25 mL/kg ENG for 10 days. At the end of the study, animals were sacrificed, and blood and liver samples were collected. Biochemical assays measured serum and hepatic levels of MDA, GSH, GSH-Px, CAT, and SOD, while serum AST and ALT were also determined. Histopathological evaluations assessed liver lesions, and immunohistochemistry was used to detect Caspase-3 expression. Findings indicated that the RAD group exhibited pronounced hepatic degeneration and necrosis, characterized by significant elevations in MDA, AST, and ALT levels, together with a marked reduction in the antioxidant parameters GSH, GSH-Px, CAT, and SOD. In contrast, ENG administration following radiation reduced AST, ALT, and MDA levels while restoring antioxidant enzyme activities. Histological analysis demonstrated milder lesions in the RAD+ENG group, and immunohistochemistry revealed reduced Caspase-3 expression compared to the RAD group. In conclusion, artichoke extract mitigated ionizing radiation-induced oxidative stress, preserved antioxidant defenses, and provided hepatoprotective effects.

Keywords: *Artichoke, caspase-3, histopathology, oxidative stress, radiation*

INTRODUCTION

Ionizing radiation is a well-established modality in the treatment of various tumor types. Globally, approximately 14 million individuals are diagnosed with cancer each year, and half of these patients undergo radiotherapy either for curative or palliative purposes (Beyzadeoglu, 2010). The primary aim of radiotherapy is to deliver the maximum possible dose to tumor tissues while sparing normal tissues. Although dose escalation enhances local tumor control, it simultaneously increases the risk of complications in normal tissues. Therefore, tumor control largely depends on the tolerance of normal tissues to radiotherapy (Alkis et al., 2015).

The biological effects of ionizing radiation are primarily mediated through DNA damage. Cell death occurs not only through direct ionization of DNA but also indirectly via free oxygen radicals (ROS) generated by radiolysis of water molecules (Taysi et al., 2008). Under physiological conditions, free radicals are essential for life and are tightly regulated within the organism. However, disruption of the oxidant–antioxidant balance results in oxidative stress, which leads to disturbances in cellular metabolism, inflammatory damage, accelerated aging, and tissue injury in vital organs (Halliwell, 1994).

Various radioprotective agents have been developed to mitigate radiation-induced damage. Radioprotectors are compounds that protect living organisms from the harmful effects of radiation by enhancing cellular resistance (Hall, 2000). These agents are generally categorized into three groups: (i) chemical compounds (e.g., amifostine, amino sulfides, thiol derivatives) (Giambarresi and Jacobs, 1987), (ii) naturally occurring molecules (e.g., vitamin A, melatonin, beta-glucan) (Kumar et al., 2002; Kuntić et al., 2013), and (iii) plant-derived constituents (Çakır et al., 2020). This classification provides a comparative framework for evaluating the mechanisms of action, safety, and bioavailability of different radioprotectors.

Research on minimizing radiation-induced damage is of great importance for preventing the adverse effects of radiotherapy. In recent years, experimental animal studies have highlighted the therapeutic potential of natural products in alleviating radiation-induced cellular injury (Jit et al., 2022). Plant extracts with high antioxidant capacity can neutralize the harmful effects of free radicals and support cellular defense mechanisms. In this context, the artichoke (*Cynara scolymus* L.), rich in phenolic compounds, has attracted particular interest in studies targeting liver tissue (Zhu et al., 2004).

Cynara scolymus L. (artichoke) has historically been consumed as part of the Mediterranean diet and used for therapeutic and supportive purposes. It is also documented in various monographs (Curadi et al., 2007). Phytochemical studies on artichoke leaves using high-performance liquid chromatography (HPLC) have

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identified monocaffeoylquinic acid (0.48–4.24%) and dicaffeoylquinic acid derivatives (0.03–0.52%) (Comino et al., 2009). These phenolic compounds are classified as caffeic acid derivatives. Leaves also contain chlorogenic acid, neochlorogenic acid, cryptochlorogenic acid, and cynarin; approximately 0.5% flavonoids; and 0–4% sesquiterpene lactones (Meriçli and Seyhan, 1998). In addition, phytosterols, tannins, sugars, starch, and inulin are present (Joy and Haber, 2007). Among the major caffeic acid derivatives, cynarin (1,3-dicaffeoylquinic acid) and chlorogenic acid (5-O-caffeoylquinic acid) are particularly notable (Llorach et al., 2002). Flavonoids such as cynaroside and scolymoside, and sesquiterpene lactones such as cynaropicrin, are among the key compounds (Curadi et al., 2007). Cynarin, in particular, exhibits hepatoprotective and regenerative properties similar to silymarin. For this reason, artichoke leaves have long been used in the management of digestive complaints and liver disorders (Azzini et al., 2007).

Extracts prepared from artichoke leaves have been reported to accelerate liver regeneration after hepatectomy and to stimulate bile production and secretion (Speroni et al., 2003). Moreover, antioxidant, antispasmodic (Holtmann et al., 2003), antifungal, antimicrobial, and diuretic effects of the plant have been demonstrated in various studies (Zhu et al., 2004). Leaf extracts are also widely used for alleviating digestive system disorders and reducing blood cholesterol levels (Fritsche et al., 2002). Both *in vitro* and *in vivo* studies have confirmed the anticholesterolemic (Bundy et al., 2008), antifungal, antibacterial, anticancer, and antioxidant properties of artichoke. The antioxidant activity is largely attributed to its major phenolic constituents, with flavonoids contributing synergistically (De Paolis et al., 2008).

In the present study, the protective effects of artichoke extract, a natural product, on radiation-induced hepatic tissue injury in rats were investigated through biochemical, histopathological, and immunohistochemical approaches.

MATERIALS AND METHODS

Experimental animals

Thirty-two male Wistar albino rats, aged 4–5 weeks and weighing approximately 180–210 g, were used for the study. The animals were housed in polypropylene cages under standard laboratory conditions, including 45±5% relative humidity, a temperature of 22±1 °C, and a 12 h light/dark cycle. Throughout the experimental period, rats were provided ad libitum access to drinking water and standard pellet feed. All experimental procedures were conducted in accordance with the Guide for the Care and Use of Laboratory Animals.

Preparation of plant extract and dietary administration

Artichoke (*Cynara scolymus*) was used as the plant material. Dried samples were ground in an electric mill for extraction. For each kilogram of artichoke, 2 L of ethanol was added. The mixture was shaken in a separatory funnel for 15 min and then left to stand for 24 h. After centrifugation, the supernatant was collected and the precipitate discarded. The supernatant was concentrated by evaporating ethanol in a rotary evaporator, yielding the extract. Finally, the extract was incorporated into ground pellet feed at a ratio of 25 mL/kg, re-pelleted, and dried (Yener et al., 2009).

Radiation procedure

For radiation planning, a rat of the same age, sex, and weight as the experimental animals was used as a simulation model. At the Department of Radiation Oncology, Faculty of Medicine, Yüzüncü Yıl University, the rat was anesthetized with intraperitoneal (IP) ketamine (50 mg/kg) and xylazine (10 mg/kg), then positioned prone on a Siemens® Sensation4 CT simulator table. Axial CT images with a slice thickness of 2.5 mm were obtained to encompass the entire body. The CT images were transferred to the Prowess Panther® treatment planning system (TPS), and all tissues and organs were contoured. Whole-body irradiation was planned using 6 MV photon energy with equal weighting from anterior and posterior fields. The dose planning targeted delivery of 5 Gy in a single fraction to at least 95% of the liver volume. The three-dimensional plan was then transferred to a Siemens® Artiste (160 MLC) linear accelerator, and whole-body irradiation was performed in the predetermined position for both RAD and RAD+ENG groups (Figure 1) (Çakır et al., 2020; Yıldızhan et al., 2020).

Experimental design

The animals were randomly divided into four groups (n=8 per group):

Control (CONT) group: Rats were fed a standard pellet diet for 10 days.

Radiation (RAD) group: Rats received a single dose of 5 Gray (Gy) radiation on day 1, followed by 10 days of a standard pellet diet.

Artichoke (ENG) group: Rats were fed pellet feed supplemented with 25 mL/kg artichoke extract for 10 days.

Radiation + Artichoke (RAD+ENG) group: Rats re-

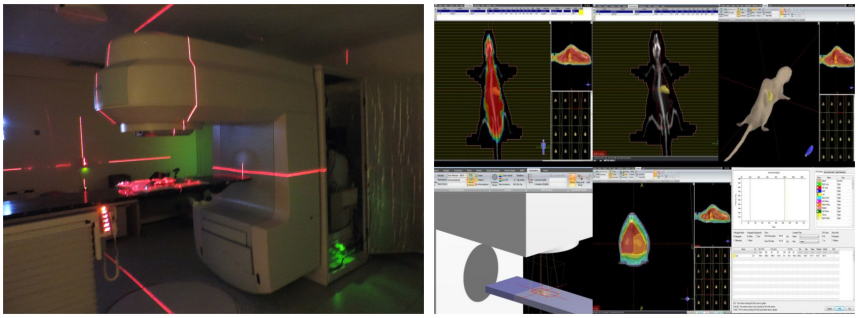


Figure 1. *Simulation of radiation application and dose distribution in the treatment planning system (TPS).*

ceived a single 5 Gy radiation dose on day 1, followed by 10 days of a pellet diet supplemented with 25 mL/kg artichoke extract.

Twenty-four hours after the last treatment, the body weights of all rats were measured. Subsequently, under anesthesia with ketamine (50 mg/kg) and xylazine (10 mg/kg), intracardiac blood samples were collected. Necropsies were performed, and liver tissues were harvested. A portion of the tissues was fixed in 10% buffered formalin for histopathological and immunohistochemical examinations, while the remaining samples were washed with physiological saline and stored at -80 °C for lipid peroxidation and oxidative stress analyses.

Biochemical analyses

Blood samples were centrifuged at 4,000 × g for 15 min at +4 °C to obtain serum. Portions of the liver tissue were fixed in 10% buffered formalin for histopathology, while the remaining tissues were washed with 0.9% NaCl and stored at -80 °C for oxidative stress and antioxidant activity analyses. Tissue samples were incubated for 5 min in ice-cold potassium dihydrogen phosphate (KH_2PO_4) solution (1:5 w/v), then homogenized at 20 kHz for 5 min using a stainless-steel probe homogenizer (Jencons Scientific Co., Bedfordshire, UK), and centrifuged at 7,000 × g for 15 min. All procedures were carried out at 4 °C. Supernatants were analyzed spectrophotometrically. Lipid peroxidation was determined by thiobarbituric acid-reactive substances, with malondialdehyde (MDA) levels used as an indicator and expressed as nmol/g protein at 532 nm (St-Laurent-Thibault et al., 2011). Glutathione (GSH) levels were measured at 412 nm according to the method of Sedlak and Lindsay (Sedlak and Lindsay, 1968) and expressed as nmol/g protein. Glutathione peroxidase (GSH-Px) activity was determined by the method of Lawrence and Burk (Lawrence and Burk, 1976), and catalase (CAT) activity by the method of Aebi (1984). Both enzyme activities were expressed as units/g protein. Superoxide dismutase (SOD) activity was measured at 505 nm by calculating the percentage inhibition of formazan dye formation (McCord and Fridovich, 1969).

Additionally, alanine transaminase (ALT) and aspartate transaminase (AST) levels were measured in serum using an autoanalyzer (Architect 16200, Abbott Park, IL, USA).

Histopathological examination

Liver tissue samples were fixed in 10% buffered formaldehyde for 72 h, dehydrated through graded alcohols, cleared in xylene, and embedded in paraffin blocks using an automated tissue processor (Leica TP 1020, Leica Biosystems Nussloch GmbH, Germany). Sections of 5 µm thickness were obtained with a microtome (Leica RM 2135, Leica Biosystems Nussloch GmbH, Germany) and stained with hematoxylin and eosin (H&E) (Luna, 1968). Preparations were examined and photographed under a light microscope (Olympus BX50).

Immunohistochemical examination

Immunohistochemistry was performed according to the avidin–biotin peroxidase complex method. Briefly, the sections were deparaffinized in xylene (2 times for 5 min) and rehydrated through graded alcohols. After rinsing in distilled water, sections were washed in phosphate-buffered saline (PBS, pH 7.2, P4417, Sigma-Aldrich, USA) for 5 min. The slides were boiled accordingly in a citrate buffer solution for the antigen retrieval at pH: 6 in a microwave oven (750 W) for 30 min and then cooled for 20 min. They were washed with PBS for 3 × 5 min. Then, in order to prevent endogenous peroxidase activity, the tissues were incubated with a hydrogen peroxide block solution (hydrogen peroxide block, TA-125-HP, Lab Vision Corporation, USA) for 5 min. After applying Ultra V Block solution to the tissues that were washed with PBS for 5 min to prevent floor staining, caspase-3 primary antibody (PA5-16335; Thermo Fisher Sci, Pittsburgh, PA, USA) diluted 1:100 was incubated in a humid environment for 60 min. Then, after being washed with PBS for 3 × 5 min, the tissues were incubated with a secondary antibody (Biotinylated Goat anti-Polyvalent (anti-mouse/rabbit IgG), TP-125-BN, Lab Vision Corporation, USA) for 30 min at room temperature and in a humid environment. After incubating with a secondary antibody, the tissues were incubated with streptavidin peroxidase (TS-125-HR, Lab Vision Corporation, USA) for 30 min after being washed with PBS for 3 × 5 min and then taken into PBS. 3,3′-diaminobenzidine (DAB; Vector Labs, SK-4100, CA, USA) chromogen solution was applied to the tissues. The sections were then washed with PBS, followed by distilled water, and counterstained with Mayer's hematoxylin. 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 (Olympus CX31, Olympus Corporation, Tokyo, Japan) equipped with video camera (Olympus DP12, Olympus Corporation, Tokyo, Japan.)

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 23. One-way analysis of variance (ANOVA) was used to compare group means, and Tukey's post hoc test was applied to identify intergroup differences. A value of $P \leq 0.05$ was considered statistically significant.

RESULTS

Body weight

Changes in body weight of rats during the experimental period are presented in Table 1. At the beginning of the

Table 1. *Effect of artichoke (Cynara scolymus l.) extract on body weight changes in rats exposed to ionizing radiation*

Period	CONT	RAD	ENG	RAD+ENG
First day	194.12 ± 5.21	196.43 ± 3.14	192.14 ± 3.45	195.28 ± 5.24
End of trial	268.68 ± 4.17 [a]	229.55 ± 16.08 [b]	270.92 ± 5.12 [a]	259.10 ± 4.90 [ab]

Data are expressed as mean ± SD. Different superscript letters indicate significant differences ($p \leq 0.05$).

study, no statistically significant differences were observed among the groups (P > 0.05). At the end of the experiment, body weights in the RAD group were significantly reduced compared to the control group (P ≤ 0.05). In contrast, the body weights of the RAD+ENG group were closer to those of the control group and exhibited partially comparable values (P ≤0.05).

Biochemical findings

Serum AST and ALT enzyme levels are shown in Table 2, while lipid peroxidation and antioxidant parameters in serum and liver tissues are presented in Table 3. Analysis of serum AST and ALT levels revealed that these parameters were significantly elevated in the RAD group compared to the other groups (P ≤ 0.05). In the RAD+ENG group, values were slightly higher than those of the control group but significantly lower than those of the RAD group (P ≤ 0.05). These results indicate that radiation impaired liver function, whereas artichoke extract markedly mitigated this effect.

***Table 2**. Effect of artichoke (Cynara scolymus l.) extract on AST and ALT levels in rats exposed to ionizing radiation*

Group	AST (IU/L)	ALT (IU/L)
CONT	74.3 ± 3.5^{a}	53.5 ± 4.8^{a}
RAD	117.5 ± 5.2^{b}	67.6 ± 4.1^{b}
ENG	67.8 ± 2.9^{a}	50.8 ± 3.3^{b}
RAD+ENG	96.2 ± 4.9^{ab}	64.7 ± 3.8^{c}

Data are expressed as mean ± SD. Different superscript letters indicate significant differences (p ≤ 0.05). AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

As shown in Table 3, serum MDA levels were significantly increased in the RAD group (2.80 ± 0.42), accompanied by a marked decrease in antioxidant parameters (GSH, GSH-Px, CAT, SOD) (P ≤ 0.05). This demonstrates that radiation induced oxidative stress and suppressed the antioxidant defense system. In the ENG group, MDA levels were significantly reduced (1.43 ± 0.3), while particularly GSH-Px (64.85 ± 1.6) and CAT (5.91 ± 0.2) activities were markedly increased (P ≤ 0.05). In the RAD+ENG group, MDA levels were lower than in the RAD group (1.98 ± 0.3), while antioxidant parameters were moderately higher.

Findings from liver tissue were consistent with those of serum. MDA levels were significantly higher in the RAD group (3.86 ± 0.21), whereas antioxidant parameters were reduced (P ≤ 0.05). In the ENG group, MDA levels decreased (2.64 ± 0.16), and antioxidant parameters exceeded those of the control group. In the RAD+ENG group, MDA levels (3.12 ± 0.16) were significantly lower, and antioxidant parameters were significantly higher compared with the RAD group (P ≤ 0.05). Overall, these results demonstrated that artichoke extract reduced radiation-induced oxidative stress and enhanced antioxidant defense capacity both in serum and liver tissue.

Histopathological findings

In the control group, hepatocytes exhibited regular alignment, normal cytoplasmic staining characteristics, and preservation of the general lobular architecture (Fig. 2A). In the RAD group, the most prominent morphological alterations included degenerative and necrotic changes in hepatocytes, particularly in centrilobular and midzonal regions, accompanied by disruption (dissociation) of the hepatic cord structure. Loss of cytoplasmic integrity and staining properties was observed in these hepatocytes, with nuclei showing pyknosis (shrinkage and hyperchromasia) and, in some cases, karyolysis. Mild sinusoidal dilatation and congestion were also noted (Fig. 2B).

In the ENG group, the histological appearance resembled that of the control group, with only limited activation of perisinusoidal cells (Fig. 2C). In the RAD+ENG group, the overall histological structure of the liver was largely preserved. No prominent dissociation was observed, and most hepatocytes maintained cytoplasmic integrity with normal eosinophilic staining. Although the nuclei were more hyperchromatic compared to the control group, de-

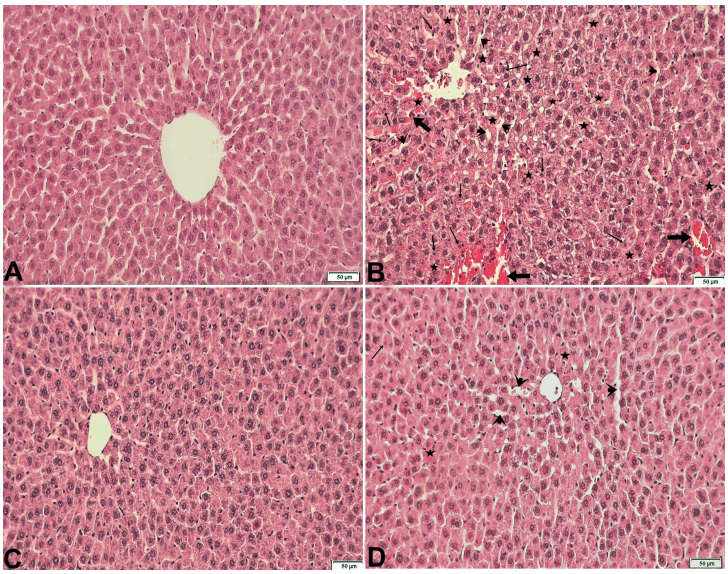


***Figure 2.** Representative histopathological images of liver tissues stained with hematoxylin and eosin (H&E). (A) Control group: normal hepatic architecture. (B) RAD group: moderate degenerative and necrotic changes. (C) ENG group: normal hepatic architecture. (D) RAD+ENG group: markedly reduced degenerative and necrotic alterations. Thin arrows denote pyknotic nuclei; thick arrows represent sinusoidal and vascular congestion; arrowheads mark sinusoidal dilatation; stars highlight degenerated hepatocytes. (Scale bar = 50 µm.)*

generative and necrotic alterations in hepatocytes and sinusoidal dilatation were markedly reduced. Additionally, partial activation of perisinusoidal cells was noted (Fig. 2D). Histopathological findings related to the protective effect of artichoke extract against radiation-induced liver injury are presented statistically in Table 4.

Immunohistochemical findings

Microscopic images and scorings of immunohistochemical staining with Caspase-3 antibody are shown in Figures 3 (A–D) and Figure 4. No caspase-3 immunopositive hepatocytes were observed in the control and ENG groups (Fig. 3A, 3C). In the RAD group, however, caspase-3 immunoexpression was markedly increased in liver tissue (Fig. 3B). In the RAD+ENG group, the number of caspase-3 immunopositive hepatocytes was significantly reduced compared to the RAD group (Fig. 3D).

DISCUSSION

Radiation interacts with drug toxicities, chemical agents, and various diseases, leading to increased free radical production, which exerts harmful effects on cellular components (Halliwell and Gutteridge, 1989). The severity of the damage depends on the applied dose and the size of the exposed area. Although modern radiotherapy has improved treatment success rates in cancer, its toxic effects on normal tissues cannot be completely eliminated. Therefore, the development of radioprotective agents capable of shielding organisms from the adverse effects of radiation has gained increasing importance. Classical radioprotectors include thiol compounds (cysteine, cysteamine), substances containing -SH groups (thioureas, sulfones), certain pharmacological agents (serotonin, hormones), and synthetic compounds (WR-638, WR-2721, WR-44923, adenosine) (Copp et al., 2013; Grdina et al., 2002). In recent years, attention has shifted toward the protective potential of natural compounds and enzyme systems (Nurlu et al., 2025).

In the present study, the potential radioprotective effects of artichoke extract (*Cynara scolymus*) against ionizing radiation-induced hepatic injury in rats were investigated through biochemical, histopathological, and immunohistochemical analyses.

In the radiation-exposed group (RAD), serum AST and

Table 3. *The effect of artichoke (Cynara scolymus l.) extract on MDA, GSH contents and antioxidant enzyme activities in rats exposed to ionizing radiation*

		GROUPS			
Tissues	**Parameters**	**CONT**	**RAD**	**ENG**	**RAD+ENG**
Serum	MDA	1.79 ± 0.2^{a}	2.80 ± 0.42^{b}	1.43 ± 0.3^{a}	1.98 ± 0.3^{ab}
	GSH	1.31 ± 0.5^{a}	0.85 ± 0.13^{b}	1.43 ± 0.05^{c}	1.23 ± 0.07^{a}
	GSH-Px	57.26 ± 2.7^{a}	43.95 ± 2.8^{b}	64.85 ± 1.6^{a}	54.41 ± 1.6^{ab}
	CAT	3.69 ± 0.3^{a}	2.56 ± 0.1^{b}	5.91 ± 0.2^{c}	4.34 ± 0.2^{ac}
	SOD	5.49 ± 0.52^{a}	4.69 ± 0.19^{b}	6.09 ± 0.23^{c}	5.07 ± 0.22^{ab}
Liver	MDA	3.08 ± 0.42^{a}	3.86 ± 0.21^{b}	2.64 ± 0.16^{c}	3.12 ± 0.16^{a}
	GSH	2.08 ± 0.25^{a}	1.95 ± 0.12^{b}	2.11 ± 0.14^{a}	2.03 ± 0.12^{a}
	GSH-Px	4.08 ± 0.46^{a}	3.75 ± 0.12^{b}	4.15 ± 0.22^{a}	3.86 ± 0.12^{ab}
	CAT	0.72 ± 0.10^{a}	0.67 ± 0.05^{a}	0.73 ± 0.06^{a}	0.72 ± 0.03^{a}
	SOD	2.43 ± 0.15^{a}	2.18 ± 0.20^{b}	2.55 ± 0.19^{a}	2.25 ± 0.09^{b}

Data are expressed as mean ± SD. Different superscript letters indicate significant differences ($p \leq 0.05$). MDA: Malondialdehyde; GSH: Reduced glutathione; GSHPx: Glutathione peroxidase CAT: Catalase. SOD: *Superoxide dismutase*

Table 4. *The effect of artichoke (Cynara scolymus l.) extract on histopathological lesions in rats exposed to ionizing radiation*

Lesion		**CONT**	**RAD**	**ENG**	**RAD+ENG**
Degeneration		*/8 ^{b}	8/8 ^{b}	*/8 ^{b}	2/8 ^{b}
	Mild	*	2	*	2
	Moderate	*	6	*	*
	Severe	*	*	*	*
Congestion		*/8 ^{b}	8/8 ^{a}	*/8 ^{b}	2/8 ^{ab}
	Mild	*	5	*	2
	Moderate	*	3	*	*
	Severe	*	*	*	*
Necrosis		*/8 ^{b}	8/8 ^{a}	*/8 ^{b}	2/8 ^{ab}
	Mild	*	6	*	2
	Moderate	*	2	*	*
	Severe	*	*	*	*

*: None

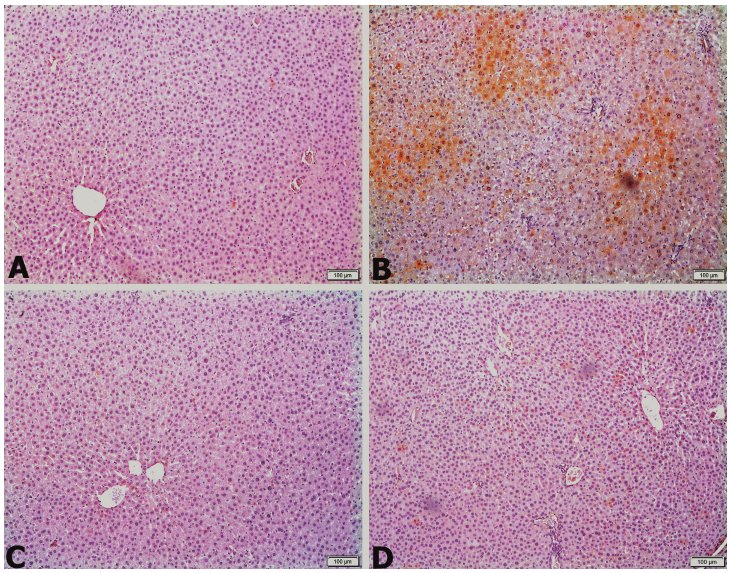


Figure 3. *Immunohistochemical detection of Caspase-3 expression in liver tissues using the ABC-peroxidase method. (A) Control group. (B) RAD group. (C) ENG group. (D) RAD+ENG group. (Scale bar = 100 µm.)*

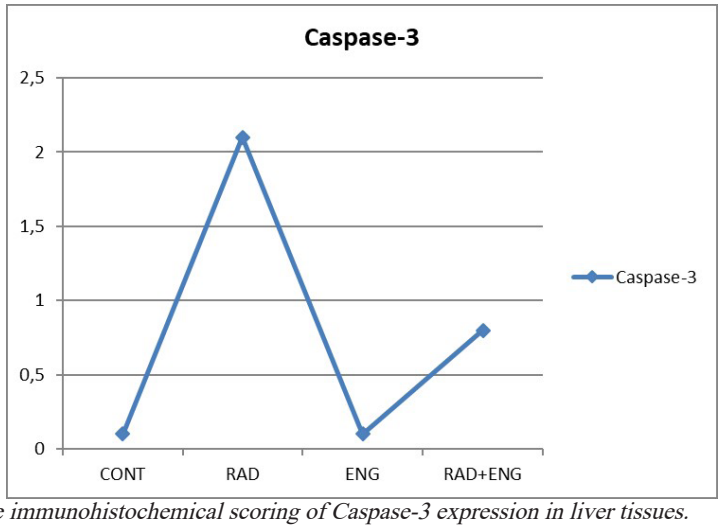


Figure 4. *Semi-quantitative immunohistochemical scoring of Caspase-3 expression in liver tissues.*

ALT levels were significantly elevated, indicating that radiation disrupted hepatocyte membrane integrity, leading to the release of cellular enzymes into the circulation. These findings are consistent with previous reports demonstrating that ionizing radiation enhances lipid peroxidation in the cell membrane via oxidative stress, thereby inducing hepatocellular damage (El-Hady et al., 2024; Jameel and Mohammed, 2021; Thabet et al., 2020; Yahyapour et al., 2018). In the group treated with artichoke extract alongside radiation (RAD+ENG), enzyme levels were significantly reduced and approached those of the control group, clearly demonstrating the hepatoprotective effect of the extract. Phenolic compounds found in artichoke, including chlorogenic acid, cynarin, and flavonoids, are well known for their free radical scavenging properties and their ability to attenuate oxidative damage in hepatocytes (Akkaya Albayrak et al., 2022; Lupattelli et al., 2004; Miccadei et al., 2008). The reduction in AST levels observed in this study was more pronounced than that of ALT, suggesting that artichoke extract may exert stronger effects on preserving mitochondrial integrity. This is supported by the fact that AST is localized in both the cytosol and mitochondria, whereas ALT is primarily confined to the cytoplasm (Giannini et al., 2005). Such a distinction implies that the extract's antioxidant effects may be particularly effective in mitigating mitochondrial oxidative stress. Taken together, our findings support these biochemical mechanisms and demonstrate that the antioxidant activity of artichoke extract contributes to the preservation of liver cell integrity under radiation-induced stress.

The results of this study, which investigated the protective effects of artichoke extract on oxidative stress marker (MDA) and antioxidant defense system parameters (GSH, GSH-Px, CAT, SOD) in serum and liver tissue exposed to ionizing radiation, demonstrate that ionizing radiation increases free radical generation, elevates lipid peroxidation, and suppresses antioxidant defense mechanisms. In our study, the significant elevation of serum and hepatic MDA levels in the radiation group (RAD) compared to the control group indicates pronounced oxidative damage. These findings suggest that ionizing radiation disrupts cellular integrity by inducing peroxidation of membrane lipids. Previous studies have also reported that ionizing radiation increases lipid peroxidation in a dose-dependent manner and that this process is a major mechanism underlying hepatotoxicity (Jameel and Mohammed, 2021; Tan et al., 2020). Yıldızhan et

al. (2020) similarly demonstrated that ionizing radiation significantly increased MDA levels in rats, while the administration of nettle extract concomitantly with radiation reduced oxidative stress and markedly decreased MDA concentrations. Consistent with these findings, in the present study, concomitant administration of artichoke extract (RAD+ENG) significantly lowered serum and hepatic MDA levels. This protective effect can be attributed to the strong free radical scavenging properties of phenolic compounds contained in the extract (Miccadei et al., 2008). When the radiation or radiocontrast agents-induced overproduction of free radicals exceeds the capacity of antioxidant enzymes, the cellular redox balance is disrupted and oxidative stress is exacerbated. The suppressive effects of radiation on critical components of the antioxidant defense system-namely GSH, GSH-Px, CAT, and SOD-were clearly evident (Cellat and İşler, 2022; Okunieff et al., 2008). In the radiation group, serum GSH levels declined to 0.84 ± 0.03, reflecting depletion of the intracellular antioxidant reservoir. Similarly, significant reductions in GSH-Px, CAT, and SOD activities were observed. These results are consistent with earlier studies reporting radiation-induced suppression of antioxidant enzyme activity (Miccadei et al., 2008; Yıldızhan et al., 2020). Notably, co-administration of artichoke extract with radiation improved antioxidant parameters. For instance, in the RAD+ENG group, serum GSH levels increased compared with the RAD group, suggesting that the extract supports glutathione metabolism. Furthermore, higher activities of GSH-Px and SOD in the RAD+ENG group imply that phenolic compounds may stimulate endogenous antioxidant enzyme expression. Similarly, artichoke extract enhanced hepatic GSH and SOD levels, thereby mitigating radiation-induced oxidative injury. These findings are in agreement with previous reports demonstrating the antioxidant and hepatoprotective properties of artichoke extract (Gebhardt, 1997; Mehmetçik et al., 2008). Indeed, several investigators have reported that plant-derived antioxidants attenuate radiation-induced oxidative stress and support antioxidant enzyme activities (Miccadei et al., 2008; Weiss and Landauer, 2000). In conclusion, the present study demonstrates that ionizing radiation induces oxidative stress and suppresses the antioxidant defense system, whereas artichoke extract exerts a hepatoprotective role by reducing lipid peroxidation and supporting antioxidant parameters.

Histopathological alterations induced by radiation are generally associated with oxidative stress mechanisms. Reactive oxygen species generated by radiation trigger lipid peroxidation in hepatocyte membranes, leading to cytoplasmic and nuclear degeneration (Zhu et al., 2021). In the present study, histopathological examination revealed substantial degenerative and necrotic changes in hepatocytes of the RAD group, whereas fibrotic alterations were not observed. Similar observations have been reported in previous studies (Karahan et al., 2008; Yıldızhan et al., 2020; Zhu et al., 2021). The absence of a fibrotic response in our study can be attributed to the short duration of exposure, supporting the notion that fibrosis typically develops following prolonged or high-dose radiation exposure (Baran et al., 2021; Farhood et al., 2019). In the RAD+ENG group, the overall hepatic architecture was largely preserved, with only a limited number of hepatocytes showing mild degenerative changes. This protective effect can be attributed to the phenolic compounds present in artichoke extract, such as chlorogenic acid, luteolin, and apigenin, which neutralize free radicals, maintain cellular membrane integrity, and limit degenerative processes. Consequently, artichoke extract substantially mitigated radiation-induced lesions, demonstrating a hepatoprotective role (Salem et al., 2015; Wang et al., 2003). Literature reports similarly indicate that artichoke extract supports hepatocyte structure through its phenolic constituents (Zapolska-Downar et al., 2022).

The biological effects of ionizing radiation are primarily mediated by the excessive production of reactive oxygen species (ROS) and the consequent development of oxidative stress. Excessive ROS generation leads to lipid peroxidation of cellular membranes, protein oxidation, and DNA damage, thereby activating multiple intracellular signaling pathways. One of the most critical outcomes of these processes is the induction of apoptosis via the mitochondrial (intrinsic) pathway (Halliwell and Gutteridge, 1989; Yahyapour et al., 2018). In the present study, the marked increase in Caspase-3 expression observed in the radiation-exposed group (RAD) indicates that radiation-induced oxidative stress activates intrinsic apoptotic pathways at the cellular level. Disruption of mitochondrial membrane potential, release of cytochrome c, and subsequent activation of the caspase cascade are well-established mechanisms underlying radiation-induced hepatic injury (Baran et al., 2021; Han et al., 2019). Previous studies have reported a direct association between increased lipid peroxidation, suppression of antioxidant defense systems, and activation of Caspase-3–mediated apoptosis. In line with these findings, the elevated MDA levels and decreased GSH, GSH-Px, CAT, and SOD activities observed in our biochemical analyses demonstrate that ionizing radiation induces severe oxidative stress in liver tissue. The concomitant evaluation of these biochemical alterations together with increased Caspase-3 immunopositivity strongly supports the existence of a close pathophysiological link between oxidative stress and apoptosis. Similarly, Baran et al. (2022) and Yıldızhan et al. (2020) reported that radiation-induced impairment of oxidative stress parameters in animal models closely parallels an increase in apoptotic cell numbers. In contrast, in the radiation plus artichoke extract–treated group (RAD+ENG), a significant improvement in oxidative stress markers accompanied by a marked reduction in Caspase-3 expression was observed. These findings suggest that artichoke extract, owing to its rich phenolic composition, suppresses ROS generation, preserves mitochondrial integrity, and thereby attenuates oxidative stress–induced apoptotic signaling. Phenolic compounds have been shown not only to exert potent free radical–scavenging activity but also to stabilize mitochondrial membranes, reduce cytochrome c release, and inhibit caspase activation, as reported in previous studies (Huang et al., 2010; Miccadei et al., 2008). Taken together, the findings of the present study demonstrate that ionizing radiation triggers apoptosis in hepatic tissue through oxidative stress–mediated mechanisms, whereas artichoke extract effectively suppresses this process at both biochemical and cellular levels through its antioxidant properties.

This study demonstrates that ionizing radiation induces

significant hepatic damage, including increased oxidative stress, elevated lipid peroxidation, impaired antioxidant defense, enzyme release, activation of apoptosis, and disruption of histological integrity. Administration of artichoke extract markedly mitigated these adverse effects by reducing lipid peroxidation, enhancing antioxidant defenses, suppressing apoptosis, and preserving histological architecture.

CONCLUSION

The findings indicate that artichoke extract possesses potent antioxidant and hepatoprotective properties and may serve as a potential protective agent against radiation-induced liver injury. However, further experimental studies incorporating different doses and treatment durations are warranted to elucidate the long-term efficacy of the extract and to clarify its underlying molecular mechanisms in greater detail.

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Conflict of interest

The authors declared that there is no conflict of interest.

Ethical statement or informed consent

The study was approved by the Yüzüncü Yıl University Animal Experiments Local Ethics Committee (25.06.2015, Decision No: 2015/08).

Author contributions

AU: Conceptualization, Investigation, Methodology, Formal analysis, Writing, Supervision; TÇ: Radiation dose plan and radiation application to rats; MY: Formal analysis (Immunohistochemistry); ZY: Conceptualization, Formal analysis, Writing.

Availability of data and materials

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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