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Protective Effects of Different Doses of Ficus Carica Seed Oil Against Renal Ischemia-Reperfusion Injury

Efectos Protectores de Diferentes Dosis de Aceite de Semilla de Ficus Carica Contra la Lesión por Isquemia-Reperfusión Renal

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RESUMEN

Introducción: La lesión por isquemia-reperfusión renal (IRI), en ausencia de un tratamiento eficaz, exhibe una fisiopatología compleja basada en el estrés oxidativo y la inflamación. El aceite de semilla de Ficus carica (FC), que tiene efectos protectores y terapéuticos, tiene propiedades antioxidantes y antiinflamatorias. **Objetivo:** El objetivo de este estudio fue investigar los efectos protectores de diferentes dosis de aceite de semilla de Ficus carica contra IRI. **Materiales y métodos:** Veinticuatro ratas albinas Wistar macho se dividieron aleatoriamente en cuatro grupos iguales: grupo de control, grupo IRI, grupo FC+IRI 3 ml/kg (FC3+IRI) y grupo FC+IRI 6 ml/kg (FC6+IRI). **Resultados:** En los grupos IRI, los niveles de malondialdehído y albúmina modificada por isquemia (IMA) y las puntuaciones de edema fueron más altas, mientras que los niveles de catalasa y glutatión peroxidasa fueron más bajos que en el grupo control. Los niveles de malondialdehído y mieloperoxidasa, el foco hemorrágico y las puntuaciones de edema fueron más bajos en los grupos suplementados con FC que en el grupo IRI, mientras que los niveles de glutatión peroxidasa fueron más altos. Además, el grupo FC6+IRI los niveles de IMA, tasas de inhibición de superóxido dismutasa y puntuaciones de nefrona necrótica fueron más bajos y los niveles de catalasa más altos que en el grupo IRI. Además, no hubo diferencias significativas entre el grupo FC6+IRI y el grupo control en términos de niveles de mieloperoxidasa, tasas de inhibición de superóxido dismutasa, nefrona necrótica y puntuaciones de foco hemorrágico. **Conclusiones:** FC tiene un efecto protector contra la IRI.

Palabras Clave: Ficus carica; albúmina modificada por isquemia; lesión por isquemia-reperfusión; malondialdehído; aceite de semilla.

ABSTRACT

Introduction: Renal ischemia-reperfusion injury (IRI), which lacks effective treatment, has a complex pathophysiology driven by oxidative stress and inflammation. Ficus carica seed oil (FC), which has protective and therapeutic effects, has antioxidant and anti-inflammatory properties. **Objectives:** The aim of this study was to investigate the protective effects of different doses of Ficus carica seed oil against IRI.

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Materials and Methods: Twenty-four Wistar albino type male rats were randomly divided into 4 equal groups: control group, IRI group, 3 ml/kg FC+IRI (FC3+IRI), and 6 ml/kg FC+IRI (FC6+IRI). **Results:** Malondialdehyde and ischemia-modified albumin (IMA) levels and edema scores of the IRI groups were higher, and catalase and glutathione peroxidase levels were lower than in the control group. Malondialdehyde and myeloperoxidase levels, hemorrhagic focus, and edema scores were lower in the Ficus carica seed oil supplemented groups compared to the IRI group, while glutathione peroxidase levels were higher. In addition, IMA levels, superoxide dismutase inhibition rates, and necrotic nephron scores of the FC6+IRI group were lower than those of the IRI group, while catalase levels were higher. Furthermore, there was no significant difference between the FC6+IRI group and the control group in terms of myeloperoxidase levels, superoxide dismutase inhibition rates, and necrotic nephron and hemorrhagic focus scores. **Conclusion:** FC has a protective effect on IRI.

Keywords: Ficus carica; ischemia modified albumin; ischemia reperfusion injury; malondialdehyde; seed oil.

INTRODUCTION

Renal ischemia-reperfusion injury (IRI) is a serious medical condition that contributes to acute kidney injury and leads to rapid renal dysfunction and high mortality. There is no effective treatment for renal ischemia-reperfusion injury, which is commonly seen in shock, kidney transplantation, trauma, and urologic and cardiovascular surgery. Cell injury and death are generally related to the ischemia-reperfusion rate [1] IRI, which is caused by sudden and temporary obstruction of blood flow to the kidney, has significant morbidity and mortality, but no effective treatment is available [2]. Because of the lack of effective therapy and the complex pathologic processes that characterize IRI, the search for treatment or preventive strategies has been the subject of many recent studies [3,4].

IRI, a complex pathophysiological event, is the most common cause of acute kidney injury. The molecular and pathological events in acute kidney injury include IRI, oxidative stress, apoptosis, inflammation, fibrosis, and changes in gene expression that activate different signaling pathways. The cascade of inflammatory events is an important mediator of IRI, including the inflammatory response, complement activation, and innate immune activation. In addition, IRI results from peroxidation of membrane lipids, oxidative damage to proteins and DNA, and causes apoptosis and necrosis [5]. Additionally, the expression of proteins involved in pathways closely related to oxidative stress and ferroptosis is increased in IRI. IRI-induced oxidative stress and ferroptosis lead to progression to renal fibrosis [6]. Moreover, acute kidney injury may progress to chronic kidney disease through this renal fibrosis and inflammation. Therefore, some treatment strategies have focused on improving inflammation, oxidative stress, and fibrosis [7].

Ficus carica seeds are an important source of mineral oils with strong antioxidant properties and high levels of unsaturated fatty acids. Ficus carica seeds have significant nutritional benefits as a food source rich in lipids, minerals, and proteins [8]. A recent study reported that Ficus carica seed oil has a protective effect on tissues due to its antioxidant activity [9]. Similarly, another recent study reported that intestinal histopathological findings induced by acute mesenteric ischemia can be reversed by Ficus carica seed oil. It has also been reported that this effect is probably due to the anti-inflammatory and antioxidant compounds in Ficus carica seed oil [10].

In a recent study conducted on experimental diabetic rats, it was reported that Ficus carica seed oil is a promising therapeutic adjuvant due to its rich composition of fatty acids, phenolics, antioxidants and anti-inflammatory compounds and exhibited neuroprotective and protective effects by inactivating the mechanisms leading to diabetic neuropathy [11] In another study conducted using an acute kidney injury animal model, it was reported that Ficus carica seed oil improved functional damage and eliminated morphological damage by increasing antioxidant capacity [12] On the other hand, in a study investigating the phototoxic potential of plants used in Eastern medicine, it was reported that Ficus carica showed positive phototoxicity in vitro. In addition, it was stated that phototoxicity was not only a negative side effect but could

also constitute one of the therapeutic effects of Eastern medicine [13]

Ficus carica, which grows in tropical and subtropical regions and has a wide range of pharmacological activities, is widely used in traditional medicine. Studies have found its use in more than 40 areas [14]. In addition, Ficus carica seed oil, which can be used by everyone and integrated into people's diets, has both protective and therapeutic effects against kidney damage, making it a long-term, accessible option. On the other hand, more studies are needed to explain the molecular mechanisms underlying its activity and to determine its pharmacokinetic properties [15] .

The failure to effectively treat IRI, the most common cause of acute kidney injury, is due to its complex pathophysiology involving oxidative stress, inflammation, and fibrosis. Given its potent antioxidant and anti-inflammatory properties, Ficus carica seed oil is increasingly being investigated as a potential therapeutic agent in complementary medicine. Although recent studies highlight its protective effects in several disease models, including diabetes and acute kidney injury, the exact mechanisms of action remain largely unknown. Ficus carica seed oil, a widely available dietary supplement with promising pharmacological activity, deserves further investigation for its potential role in kidney protection. This study aims to evaluate the protective effects of different doses of orally administered Ficus carica seed oil against renal IRI and contribute to the growing body of evidence supporting its therapeutic potential in complementary medicine.

MATERIALS AND METHODS

Animals

The necessary ethics committee decision for the study was obtained from the Animal Experiments Local Ethics Committee of Aydın Adnan Menderes University (ADUHADYEK). (Decision number: 64583101/2021/030). ADUHADYEK is an organization that monitors the conduct of experimental studies in accordance with ethical rules, and the study was approved and supervised by ADUHADYEK. All experimental procedures were carried out in strict accordance with the relevant guidelines and regulations, including the ARRIVE guidelines and the EU Directive 2010/63/EU for animal experiments. Throughout the study, rats were kept in an environment with a controlled ambient temperature of 22±2 ºC, 40-50% average humidity, and a 12-hour light-dark cycle. Feeding and experimental procedures were performed according to these standardized conditions. Twenty-four Wistar albino type male rats weighing between 300 and 350 grams, obtained from Aydın Adnan Menderes University Experimental Animals Laboratory, were included in the study. These rats were randomly divided into 4 groups: a control group, an ischemia-reperfusion injury (IRI) group, and 3 ml/kg Ficus carica seed oil+IRI (FC3+IRI) and 6 ml/kg Ficus carica seed oil+IRI (FC6+IRI) groups, with equal numbers of rats in each group.

Supplementation

The right kidneys of the rats in the control group were removed by nephrectomy. IRI was not applied to the left kidney. The right kidneys of the rats in the IRI group were removed by nephrectomy. IRI was applied by clamping the left kidney. Ficus carica seed oil was obtained from ONEVA® (Istanbul, Turkey). Rats in the FC3+IRI group were given 3 ml/kg Ficus carica seed oil by intragastric gavage for 14 days. The right kidney was removed by nephrectomy on the day of the experiment. IRI was applied by clamping the left kidney. Rats in the FC6+IRI group were given 6 ml/kg Ficus carica seed oil by intragastric gavage for 14 days. The right kidney was removed by nephrectomy on the day of the experiment. IRI was applied by clamping the left kidney. In the experimentally induced renal ischemia-reperfusion injury model, right nephrectomy was performed in all animals. Then, the left renal artery was closed with a clamp in rats exposed to IRI, and the first step, ischemia, was performed. Ischemia applied to the left kidney lasted 45 minutes. After the clamp was removed, the second step of the experimental model was completed by perfusing for 60 min.

Biochemical analyses

At the end of the 14-day experimental period, rats were euthanized under deep anesthesia to minimize pain and distress. Chemical euthanasia

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was performed using a combination of ketamine (10%, Alfamine, Alfasan IBV) at a dose of 80 mg/kg and xylazine (2%, Alfazin, Alfasan IBV) at a dose of 10 mg/kg, administered intraperitoneally. This combination was selected because of its effectiveness in inducing deep anesthesia while minimizing distress. Before proceeding with sample collection, animals were closely monitored for signs of deep anesthesia, such as loss of the right-turning reflex and unresponsiveness to a tail pinch. Euthanasia was completed by maintaining deep anesthesia until cardiorespiratory arrest occurred, ensuring no recovery or distress.

While the animals were fully anesthetized, equal amounts of kidney tissue were collected from the experimental animals for biochemical and histopathological analyses. Euthanasia was performed under deep anesthesia with extension to ensure no recovery or distress. Since the animals were euthanized under deep anesthesia, no postoperative care was required. Tissues taken for biochemical analyses were stored at -80 °C until the study was performed. For histopathological analyses, tissues were fixed in 10% neutral formaldehyde at 24 °C. For biochemical analyses, tissues thawed at room temperature were homogenized in an appropriate phosphate buffer (50 mM, pH 7.0). Tissue homogenates were centrifuged at 4 °C for 15 minutes. Supernatants obtained after centrifugation were analyzed for malondialdehyde (K739-100, Biovision, USA), superoxide dismutase inhibition rate (K335-100, Biovision, USA), myeloperoxidase (K744-100, Biovision, USA), glutathione peroxidase (K762-100, Biovision, USA), and ischemia-modified albumin (IMA) (ER1108, Tebubio, China). The protocols for the kits used were followed, and readings were taken on the ELISA device.

Histopathological analyses

Fixed tissues were embedded in paraffin blocks. Paraffin blocks were cut at 5 microns using a microtome. Hematoxylin and eosin staining was performed. Sections were examined with a normal light microscope. The routine staining method was used to stain the samples. Using hematoxylin and eosin staining, samples were kept in xylene pools for 5 minutes, and then for 4 minutes, for a total of 9 minutes. For washing, samples were kept in 100% and 80% alcohol solutions for 2 minutes, respectively, and then washed with distilled water. All samples were immersed in hematoxylin stain for 3 minutes, then washed, and then immersed in eosin stain for 1 minute to prepare for microscopic analysis.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 22.0 (IBM SPSS Statistics for Windows, Version 22.0. IBM Corp., Armonk, NY, USA). The distributional properties of biochemical variables were assessed using the Shapiro-Wilk test, along with skewness and kurtosis statistics. Levene's test was used to assess the equality of variances between groups for these variables. Results were reported as mean ± standard deviation. Intergroup differences in the variables were examined using an independent-samples t-test. The Pearson correlation test was used for correlation analysis. P values less than 0.05 were determined as statistically significant.

RESULTS

Effect of ischemia-reperfusion injury on histopathological and biochemical parameters

The highest mean levels of malondialdehyde, IMA, myeloperoxidase, and the superoxide dismutase inhibition rate were observed in the IRI group, while the lowest mean levels were observed in the control group. Mean malondialdehyde, IMA, myeloperoxidase, and superoxide dismutase inhibition rate levels were higher in the IRI group than in the control group ($p<0.001$, $p=0.004$, $p<0.001$, $p<0.001$, respectively) (Table 1). The lowest mean catalase and glutathione peroxidase enzyme activity levels were found in the IRI group, while the highest mean was found in the control group. Mean catalase and glutathione peroxidase enzyme activity levels were lower in the IRI group than in the control group ($p=0.003$, $p<0.001$, respectively) (**Table 1**).

In the histopathological staining comparison of kidney tissue samples from the groups, the highest mean scores for necrotic nephron, hemorrhagic focus, and edema were observed in the IRI group, while the lowest mean scores were observed in the control group. Mean

scores for necrotic nephron, hemorrhagic focus, and edema were higher in the IRI group than in the control group (p<0.001) (**Figure 1** and **Table 2**).

Effect of 3 ml/kg Ficus Carica seed oil supplementation on ischemia-reperfusion injury

Mean malondialdehyde and myeloperoxidase enzyme activity levels were lower in the FC3+IRI group than in the IRI group (p=0.005, p=0.003, respectively) (**Table 1**). Mean glutathione peroxidase enzyme activity levels were higher in the FC3+IRI group than in the IRI group (p=0.001) (**Table 1**). Mean hemorrhagic focus and edema scores were lower in the FC3+IRI group than in the IRI group (p<0.001, p=0.011, respectively) (**Figure 1** and **Table 2**).

Effect of 6 ml/kg Ficus Carica seed oil supplementation on ischemia-reperfusion injury

Mean malondialdehyde, IMA, myeloperoxidase, and superoxide dismutase inhibition rate levels were lower in the FC6+IRI group than in the IRI group (p<0.001, p=0.020, p=0.001, p=0.001, respectively) (**Table 1**). Mean catalase and glutathione peroxidase enzyme activity levels were higher in the FC6+IRI group than in the IRI group (p=0.020, p=0.007, respectively) (Table 1). Mean scores for necrotic nephron, hemorrhagic focus, and edema were lower in the FC6+IRI group than in the IRI group (p<0.001) (**Figure 1** and **Table 2**).

Comparison of FC3+IRI and FC6+IRI groups with each other and with the control group

Mean malondialdehyde and IMA levels were higher in the FC6+IRI group than in the control group (p=0.003, p=0.046, respectively) (**Table 1**). Mean catalase and glutathione peroxidase enzyme activity levels were lower in the FC6+IRI group than in the control group (p=0.022, p=0.015, respectively) (Table 1). Mean score for edema was higher in the FC6+IRI group than in the control group (p=0.022) (**Figure 1** and **Table 2**).

Mean malondialdehyde, IMA, and superoxide dismutase inhibition rate levels were higher in the FC3+IRI group than in the control group (p=0.002, p=0.011, p=0.005, respectively) (**Table 1**). Mean catalase and glutathione peroxidase enzyme activity levels were lower in the FC3+IRI group than in the control group (p=0.011, p=0.001, respectively) (**Table 1**). Mean scores for necrotic nephron and edema were higher in the FC3+IRI group than in the control group (p=0.001, p=0.013, respectively) (**Figure 1** and **Table 2**).

The mean score for necrotic nephron was lower in the FC6+IRI group than in the FC3+IRI group (p=0.011) (**Figure 1** and **Table 2**). No statistically significant difference was found between these two groups in other parameters.

Relationship between group scoring and analyzed parameters

The groups were scored as IRI group = 1, FC3+IRI group=2, FC6+IRI group=3, and control (healthy) group = 4, and the relationship between this scoring and the analyzed parameters was examined. Catalase and glutathione peroxidase enzyme activity levels were positively correlated with this scoring, whereas malondialdehyde, IMA, myeloperoxidase, superoxide dismutase inhibition rate, and histopathological scores were negatively correlated (**Table 3**).

Table 1: Biochemical parameter results of groups

Parameters	Control n=6	IRI n=6	FC3+IRI n=6	FC6+IRI n=6
MDA (nmol/g)	105.67±21.39	307.17±67.32	191.33±43.65	152.33±19.65
MPO (mU/mL)	376.00±98.09	676.50±103.21	453.33±100.21	407.00±48.92
IMA (U/mL)	1027.20±167.71	1923.20±466.97	1639.20±398.73	1319.73±256.91
SOD (%)	21.28±11.25	57.87±11.14	44.80±11.19	32.33±8.55
CAT (mU/mL)	172.00±46.46	77.45±19.20	100.93±30.35	111.00±22.77
GPx (mU/mL)	854.83±98.41	431.17±93.97	641.50±64.94	654.16±132.81

IRI: Ischemia-reperfusion injury, FC3: 3 mL/kg Ficus carica seed oil, **FC6**: 6 mL/kg Ficus carica seed oil, **MDA**: Malondialdehyde, **MPO**: Myeloperoxidase, **IMA**: Ischemia modified albumin, **SOD**: Superoxide dismutase (Inhibition rate), **CAT**: Catalase, **GPx**: Glutathione peroxidase

Table 2: Mean histopathological scores of the groups

Parameters	Control n=6	IRI n=6	FC3+IRI n=6	FC6+IRI n=6
Necrotic nephrons	0.17±0.41	2.50±0.55	1.83±0.75	0.67±0.82
Haemorhagic focus	0.17±0.41	2.83±0.41	0.67±0.82	0.67±0.82
Edema	0.00	2.33±0.52	1.17±0.75	0.83±0.75

IRI: Ischemia-reperfusion injury, **FC3**: 3 mL/kg Ficus carica seed oil, **FC6**: 6 mL/kg Ficus carica seed oil

Table 3: Correlation of group scoring with analysed parameters

Parameter		Group scoring*
Malondialdehyde	Correlation coefficient	-0.855
	P	<0.001
Myeloperoxidase	Correlation coefficient	-0.737
	P	<0.001
Ischemia modified albumin	Correlation coefficient	-0.732
	P	<0.001
Superoxide dismutase (Inhibition rate)	Correlation coefficient	-0.816
	P	<0.001
Catalase	Correlation coefficient	0.726
	P	<0.001
Glutathione peroxidase	Correlation coefficient	0.817
	P	<0.001
Necrotic nephrons	Correlation coefficient	-0.862
	P	<0.001
Haemorrhagic focus	Correlation coefficient	-0.777
	P	<0.001
Edema	Correlation coefficient	-0.823
	P	<0.001

*: The groups were scored as ischemia-reperfusion injury group = 1, 3 ml/kg Ficus carica seed oil+ischemia-reperfusion injury group = 2, 6 ml/kg Ficus carica seed oil+ ischemia-reperfusion injury group = 3 and control (healthy) group = 4.

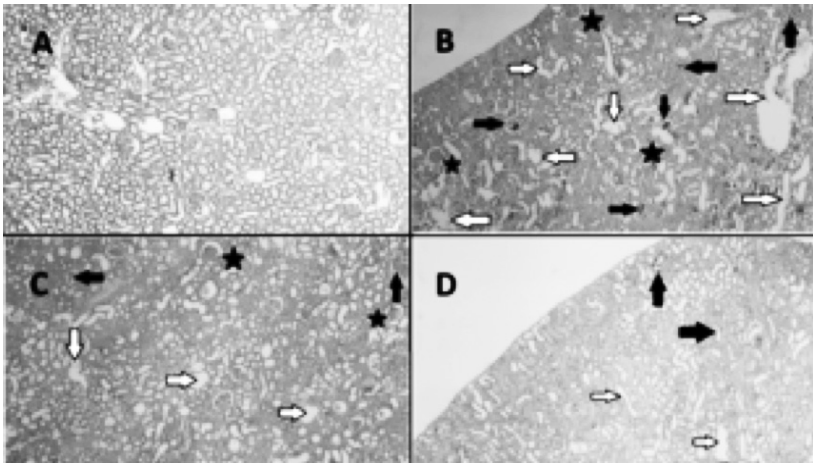

Figure 1: Histopathological kidney tissue images. A) Control group, B) Ischemia-reperfusion injury group, C) 3 ml/kg Ficus carica seed oil+ischemia-reperfusion injury group, D) 6 ml/kg Ficus carica seed oil+ischemia-reperfusion injury group. Black stars indicate necrotic nephrons. White arrows indicate oedema. Black arrows indicate haemorrhagic focus

DISCUSSION

Ferroptosis, which is closely related to the pathophysiological processes of many diseases, including IRI, kidney damage, tumors, blood diseases, and nervous system diseases, is a recently discovered form of cell death. This cell death process is accompanied by lipid peroxidation and large amounts of iron accumulation. Accumulation of lipid-reactive oxygen species in cells and a decrease in antioxidant capacity occur [16]. Excessive lipid-reactive oxygen species accumulation and redox imbalances lead to lipid peroxidation and disrupt cell membrane integrity. Accumulation of lipid peroxidation, increased bilayer membrane density, and mitochondrial shrinkage eventually lead to oxidative cell death [17]. In addition, malondialdehyde, a biomarker of lipid peroxidation, tends to increase in IRI, which is closely associated with lipid peroxidation and causes secondary organ damage [18].

In this study, increased malondialdehyde levels were observed in the kidney tissue of rats with IRI. This increase observed in rats with IRI was reduced by different doses of Ficus carica seed oil. Furthermore, group scoring from the IRI group to the healthy group showed a negative correlation with malondialdehyde levels.

Myeloperoxidase, whose levels increase during inflammation and oxidative stress, plays an important role in neutrophil antimicrobial activity and in human defense against various pathogens, especially through phagocytosis [19]. Myeloperoxidase reacts with superoxide, the substrate of superoxide dismutase. Superoxide acts as a cofactor to maintain the production of hypochlorous acid by myeloperoxidase, and superoxide as a substrate causes the formation of other less reactive oxygen species by the enzyme superoxide dismutase [20] In addition, overproduction of superoxide, which is used as a cofactor by myeloperoxidase and a substrate by superoxide dismutase, leads to increased damage in IRI [21] On the other hand, increased IMA levels due to decreased antioxidant systems and excessive production of free radicals leading to oxidative stress may contribute significantly to oxidative stress [22] . In addition, serum IMA values increase in parallel with ischemia duration in IR, and this increase is supported by histopathological damage findings. Therefore, IRI can also estimate IMA as an indicator of oxidative stress [23].

In this study, an increase in myeloperoxidase and IMA levels, and a decrease in the superoxide dismutase inhibition rate, were observed in kidney tissue from rats with IRI. These increases in rats with IRI were reduced by high-dose supplementation with Ficus carica seed oil. In addition, this reduction did not result in a significant difference in myeloperoxidase levels or in the superoxide dismutase inhibition rate between the high-dose Ficus carica seed oil group and the healthy control group. Similarly, the increase in myeloperoxidase levels in rats with IRI was reduced with low-dose supplementation with Ficus carica seed oil. Additionally, group scoring from the IRI group to the healthy group showed negative correlations with myeloperoxidase, IMA levels, and superoxide dismutase inhibition rate.

Dysfunction of glutathione peroxidase 4, which is defined as a lipid repair enzyme, lipid peroxidation of polyunsaturated fatty acids, and large amounts of iron accumulation, are characteristic of ferroptosis. Ferroptosis is closely related to IRI, acute renal failure, tumors, neurodegenerative diseases, and liver fibrosis [24]. Ferroptosis aggravates IRI. In contrast, increased glutathione peroxidase 4 expression prevents ferroptosis, providing a potential avenue for IRI management [25]. On the other hand, IRI can also lead to renal dysfunction through hydrogen peroxide-induced pathophysiological mechanisms. Overexpression of catalase enzyme by adenoviral catalase gene transfection prevents hydrogen peroxide-induced IRI [26]. In addition, an enzyme therapy based on catalase and superoxide dismutase for effective alleviation of IRI and pathogen-induced liver injury provides a treatment for organ transplantation and other diseases [27].

In this study, a decrease in catalase and glutathione peroxidase enzyme activities was observed in the kidney tissue of rats with IRI. This decrease observed in rats with IRI was increased by different doses of Ficus carica seed oil. Additionally, group scoring from the IRI group to the healthy group showed a positive correlation with catalase and glutathione peroxidase enzyme activities.

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Tubular cell death through necrosis and apoptosis is a fundamental feature of renal IRI [28]. Glutathione peroxidase 4 dysfunction sensitizes the kidney to tubular ferroptosis, leading to a distinct morphological pattern of tubular necrosis. Acute kidney injury, characterized by the simultaneous rupture of plasma membranes in a specific segment of the nephron, is therefore also called acute tubular necrosis [29]. Additionally, renal histology of renal IRI shows diffuse cell swelling and erythrocyte congestion in both cortex and medulla, and cell necrosis/apoptosis and cast formation in the medulla [30].

In this study, an increase in necrotic nephrons, hemorrhagic foci, and edema scores was observed in kidney tissue from IRI rats. This increase in hemorrhagic foci and edema scores was reduced with different doses of Ficus carica seed oil. In addition, the increase in necrotic nephrons scores was reduced with high doses of Ficus carica seed oil. Moreover, this decrease in necrotic nephrons and hemorrhagic foci scoring was not significant between the high-dose Ficus carica seed oil group and the healthy control group. Furthermore, this decrease in hemorrhagic foci scoring did not result in a significant difference between the low-dose Ficus carica seed oil group and the healthy control group. Additionally, group scoring from the IRI group to the healthy group showed negative correlations with necrotic nephron, hemorrhagic focus, and edema scores.

CONCLUSION

As a result, the levels of malondialdehyde, IMA, myeloperoxidase, superoxide dismutase inhibition rate, necrotic nephron, hemorrhagic focus, and edema scores increased with IRI, whereas they decreased with Ficus carica seed oil supplementation. In addition, catalase and glutathione peroxidase enzyme activities decreased with IRI, whereas they increased with Ficus carica seed oil supplementation. So much so, that the levels of myeloperoxidase and hemorrhagic foci scores were not different from the values of normal healthy kidney tissue with different Ficus carica seed oil supplementation despite IRI. In addition, the superoxide dismutase inhibition rate and necrotic nephron scores were not different from those of normal healthy kidney tissue with high-dose Ficus carica seed oil supplementation despite IRI. Ficus carica seed oil supplementation can be evaluated as a protective supplement against IRI.

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AUTHOR CONTRIBUTIONS

FS: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing–original draft, Writing–review and editing, Supervision.

GC: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing–original draft, Writing–review and editing.

AK: Methodology, Validation, Formal analysis, Investigation, Resources, Writing-review & editing.

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Ethics approval: The study was ethically approved by Aydın Adnan Menderes University Animal Experiments Local Ethics Committee, Aydin, Turkey (Decision number: 64583101/2021/030).

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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