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The Effects of *Ficus carica* Seed Oil Administration on Renal TAS, TOS, OSI, PON and Total Thiol Values in Renal Ischemia Reperfusion Damage

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ABSTRACT

Background and Objective: Renal ischemia-reperfusion is an important health condition that occurs for various reasons and causes kidney losses, and protective activities are especially important due to the short duration of the process. Studies with Ficus carica seed oil have shown that it has high antioxidant and anti-inflammatory effects. The aim of the study is to determine the protective effects of fig seed oil on renal ischemia-reperfusion injury.

Material and Method: The study was formed by dividing 30 Wistar Albino rats into 3 groups as control, ischemia reperfusion and ischemia reperfusion group performed after intragastric administration of 3 ml/kg Ficus carica seed oil for 14 days. At the end of the study, TOS, TAS, OSI, PON and total thiol levels were biochemically measured from the kidney tissues.

Results: Obtained results showed that 14-day fig seed oil application reduced oxidative damage (TOS, OSI) and increased antioxidant level (TAS, PON and total thiol) in kidneys exposed to ischemia-reperfusion injury statistically ($p<0.05$).

Conclusion: It has been determined that fig seed oil provides protective properties due to its ability to reduce oxidative damage, and has positive effects against ischemia-reperfusion injury that can occur randomly.

Keywords:
Antioxidant, Ficus carica seed oil, Oxidative damage, Renal ischemia reperfusion damage

1. INTRODUCTION

The worldwide production of seed oils is growing exponentially, encouraging the use of new plant sources for oil production and the provision of raw materials to meet growing demand (1). Seed oils are known to contain high levels of unsaturated fat, and consumption of unsaturated fatty acids is linked to improving human health. Studies have revealed the relationship between dietary intake of unsaturated fatty acids and coronary heart disease (2). The health-improving effects of such seeds and seeds, which are currently included in diets, have led to intensification of scientific studies. Therefore, the seeds of many fruits have been studied for potential industrial or food uses as newer sources of bioactive compounds. A new perspective has been gained especially for industrial oils such as Ficus carica (fig), Opuntia ficus-indica, papaya, honeydew, mangosteen, rambutan, durian, palm tree, etc. (3). Ficus carica, known as fig, is a plant that grows in our country, especially in the Aegean region Aydın, and its fruit is frequently consumed. It is known that fig, which is one of the most important fruits that provide high concentrations of phytochemicals and antioxidant compounds in the

Mediterranean diet, contains a significant amount of seeds that differ in their number and size and contribute to the taste and aroma of fresh dried figs (4). In figs, antioxidants such as vitamin C, vitamin E, beta-carotene, and polyphenols are present. Additionally, figs contain various phytochemicals, including flavonoids, carotenoids, and tannins. There are few data on the fatty acid composition of fig seed oils and almost no reports on their antioxidant properties. It is seen that existing studies have been realized in the last 10 years (1,5–7). The results of studies on fig and fig seed oil indicate that it is used for many different purposes with a wide variety of health benefits such as antipyretic, anti-inflammatory, antiplatelet, anthelmintic, hepatoprotective, hypoglycemic, hypocholesterolemic, anticancer, antituberculosis and antioxidant effects (8–11).

Renal ischemia-reperfusion injury (IR) is a complex pathophysiological process and there are many conditions that cause it. For example; kidney transplantation, surgical interventions, revascularization of the renal artery are important for renal IR. In addition, renal IR is the main cause of acute renal failure (12,13). Oxygenation is essential for the vitality of the tissue. Therefore, reperfusion is vital for ischemic kidney tissue. However, the reactive oxygen radicals generated create additional damage and complicate the process even more (14). The mechanisms underlying renal IR injury are multifactorial and interdependent, including inflammatory responses, hypoxia, radical-induced damage, vascular endothelial damage, tubular obstruction, endothelial-epithelial cell dysfunction, and apoptosis (15). A better understanding of the cellular and molecular mechanisms of injury is needed to improve current therapeutic approaches (16). Scientific studies on IR damage mostly focused on neutrophil function, effects of inflammatory cytokines, tissue factor and free oxygen radicals (13,16).

The aim of our study is to determine the possible protective effects of fig seed oil application against ischemia-reperfusion injury in kidney tissue.

MATERIALS AND METHODS

In the study, 30 female Wistar albino rats with an average weight of 250-400 grams, which were obtained from the Experimental Animal Production Center of Aydın Adnan Menderes University Faculty of Medicine, were used. Experiments were carried out with the approval number 64583101/2023/69 from ADU HADYEK. The rats were kept in semi-climatized laboratory conditions with an ambient temperature of 22±1˚C, a 12/12 hour light/dark cycle, relative humidity (40-50%) and ventilation.

Experimental groups were divided into 3 groups with 10 animals in each group.

Sham control (Control) group: In sham animals, the right kidney was removed by nephrectomy, and the left kidney was not exposed to IR damage with nontraumatic clamping.

Ischemia-reperfusion (IR) group: In animals in the IR group, the right kidney was removed by nephrectomy, and the left kidney was exposed to IR damage by clamping.

Fig seed oil + ischemia-reperfusion (FC) group: The rats in this group were given 3ml/kg Ficus carica seed oil (ONEVA, Aydin, Türkiye) orally by intragastric gavage for 14 days. The right kidney was removed by nephrectomy on the day of the procedure, and the left kidney was exposed to IR damage by clamping.

Establishment of Ischemia-Reperfusion Injury: Right nephrectomy was first performed in rats whose experimental kidney IR model was to be performed. Right after the nephrectomy, the left renal artery was closed with a clamp. The ischemia time of the left renal artery was applied as 45 minutes. At the end of 45 minutes, the clamp was removed and a 60-minute reperfusion period was started.

At the end of the experiment, TAS, TOS, OSI, PON and Total Thiol levels were measured in the left kidneys.

Total oxidant status (TOS) level was measured spectrophotometrically using Rel Assay brand commercial kit (Rel Assay Kit Diagnostics, Gaziantep/ Türkiye). The results were expressed as μmol H_2O_2 equiv/lt. Total antioxidant status (TAS) level in tissue homogenates was measured using Rel Assay brand

Table 1: Biochemistry analysis results of left kidney tissues.

	TOS (mmol H_2O_2 Eq/L)	TAS (mmol Trolox Eq/L)	OSİ (Arbitrary Unit	PON (U/L)	Total thiol (μmol/L)
Control Group	8.86±1.85	1.52±0.14	0.58	17.72±3.12	438±80
IR Group	12.47±2.87*	1.27±0.12*	0.98*	14.37±2.19*	301±62*
FC Group	9.85±2.76*#	1.33±0.13*#	0.74*#	15.77±2.69*#	348±69*#

commercial kit (Rel Assay Kit Diagnostics, Gaziantep/ Türkiye). Results are expressed as mmol Trolox equiv/lt. The oxidative stress index (OSI), expressed as the ratio of TOS levels to TAS levels, was calculated. Results are expressed as "arbitrary units" (AU) (17).

Thiol oxidative stress test, which has been used in recent years, is one of the methods used to determine the role of oxidative stress in the etiology of erectile dysfunction. While only one side of this bilateral balance has been measured since 1979, with the new method developed by Erel & Neşelioğlu, both variable levels can be measured separately and additively and evaluated both individually and holistically (18).

Commercial kits (RelassayR, Gaziantep, Türkiye) were used to measure paraoxonase activities and the results were given as U/L serum. In the measurement of arylesterase activity, phenylacetate was used as the substrate and one unit of arylesterase activity was defined as 1 μmol of phenol produced/min under current conditions and given as KU/L serum (19).

Statistical analysis

IBM SPSS Statistics 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) program was used for statistical analysis. The distributions of biochemical measurements were evaluated with the Shapiro-Wilk test and skewness/kurtosis statistics. The homogeneity of variances between groups for these measurements was examined by Levene's test. p value <0.05 was considered statistically significant. All these measurements were provided with mean±standard deviation (mean±SD). The four groups in the study were compared with ANOVA based on biochemical measurements. Tukey HSD test was performed if necessary.

RESULTS

It was obtained by comparing the control and IR groups with the FC group treated with fig seed oil (Table 1). According to these results;

When the total oxidant status was examined, the highest levels were determined in the IR group. The results of the FC group were found to be significantly lower than the IR group in which ischemia-reperfusion injury was performed ($p \leq 0.05$).

Total antioxidant status levels were highest in the Control group, which was not exposed to ischemia-reperfusion injury. It was determined that these levels decreased significantly in the IR group, and FC application caused an increase in TAS levels ($p \leq 0.05$).

When the oxidative stress index was examined, the highest levels were found in the IR group, parallel to the TOS and TAS levels. The results of the FC group were found to be significantly lower than the IR group in which ischemia-reperfusion injury was performed ($p \leq 0.05$).

Paraoxonase levels were highest in the Control group, which was not exposed to ischemia-reperfusion injury. It was determined that these levels decreased significantly in the IR group, and FC application caused an increase in TAS levels ($p \leq 0.05$).

Total thiol levels were also found to be highest in the Control group, similar to Paraoxonase levels. It was determined that these levels decreased significantly in the IR group, and FC application caused an increase in TAS levels ($p \leq 0.05$).

DISCUSSION

Scientific literature on Ficus carica seed oil reveals that effective dosage is a minimum of 1 ml/kg and an optimum of 3 ml/kg. Therefore, in our study, a dosage of 3 ml/kg of fig seed oil was administered. Furthermore, it was determined that this dosage was effective as a result of the applied treatment (10,20). The damage caused by ischemia-reperfusion injury in kidney tissue has been shown biochemically and histopathologically (12,16,21). In the resulting damage, it was determined that especially oxidative stress parameters increased and antioxidant parameters decreased and tissue deterioration was observed (22,23). In studies investigating total oxidant status, it was determined that TOS levels increased in renal ischemia-reperfusion injury (24,25). In our study, it was determined that TOS levels increased statistically significantly as a result of ischemia-reperfusion injury.

The increase in oxidative markers also brings about a decrease in antioxidant capacity. Walker et al. (2001) showed in their study that reactive oxidative and nitrogen derivatives that occur in the 3 and 6 hour reperfusion stages following 40 minutes of ischemia are accompanied by decreased glutathione levels (23). Serteser et al. (2002) observed that SOD, CAT and reduced glutathione levels decreased significantly after 30-minute ischemia followed by 1-hour reperfusion and 1-hour ischemia followed by 2-hour reperfusion injury (21). In our study, a decrease was found in TAS levels in relation to increased TOS levels.

In the study conducted by Bozkurt et al. (2012), it was determined that OSI levels increased significantly after 45 minutes of ischemia and 60 minutes of reperfusion (26). In the study of Toprak et al. (2020), it was determined that the OSI values were significantly higher in the ischemia-reperfusion group than in the other groups after 4 hours of reperfusion following 45 minutes of ischemia (27). The results obtained in our study showed that OSI levels were highest in rats exposed to ischemia-reperfusion injury without fig seed oil applied.

In the renal ischemia reperfusion study conducted by Tavafi et al. (2020), it was observed that the PON values decreased in the kidney tissues reperfused for 24 hours after being exposed to ischemia for 45 minutes, and the PON value increased in the group treated with the therapeutic agent (28). In the study of Kulah et al. (2007), 0, 24, 48 and 72 hours reperfusion was performed after 90 minutes of renal ischemia, and the results obtained in the study showed that PON-1 was at the highest level in the 24-hour reperfusion group. It was concluded that PON-1 has a lipid peroxidation inhibitory role in parallel with lipid peroxidation and other parameters (29). The results obtained in our study showed the protective properties of PON together with other parameters. The fact that fig seed oil application causes an increase in PON results supports the protective feature of fig seed oil.

In our study, it was determined that the total thiol level was at the lowest level in the group with renal ischemia-reperfusion injury. In the group to which fig seed oil was applied, it was determined that the thiol level increased significantly and approached the results of the control group. In the study of Hosseinzadeh et al. (2005), it was observed that the total thiol level decreased after 90 minutes of reperfusion following 60 minutes of ischemia, and this level increased in the group administered with saffron extract (30). In the study of Volti et al. (2007), the effects of Heme Oxygenase-1 application on 30-minute, 1-hour and 3-hour reperfusion injury following 45 minutes of renal ischemia were investigated and normalization was found in thiol levels in all three groups with this administration (31). These results show the protective efficacy of total thiol levels and their effect as a damage marker.

CONCLUSION

As a result, it is clear that the administration of fig seed oil applied for 14 days has therapeutic effects against renal ischemia-reperfusion injury. The decreased TOS and OSI levels, increased TAS, PON and total thiol levels observed in the treatment group compared to the ischemia-reperfusion group showed the protective efficacy of fig seed oil. Investigating which pathways are involved in molecular studies in further studies may determine the effectiveness of fig seed oil and allow it to be used in the elimination of ischemia-reperfusion injury.

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