

Fraxin as a promising molecule in the pharmacological treatment of acute mesenteric ischemia: an experimental study

İsmail Aydın,¹ Furkan Ali Uygur,¹ Ömer Emecen,² Demet Şengül³

¹Department of General Surgery, Giresun University Faculty of Medicine, Giresun-Türkiye

²Department of Biochemistry, Giresun University Faculty of Medicine, Giresun-Türkiye

³Department of Pathology, Giresun University Faculty of Medicine, Giresun-Türkiye

ABSTRACT

BACKGROUND: Ischemia-reperfusion (I-R) injury associated with acute mesenteric vascular occlusion can lead to severe impairment of intestinal tissue and may become a life-threatening condition if not treated in the early clinical stages. Previous studies have suggested that fraxin may exert protective effects against I-R-induced mesenteric injury due to its antioxidant and anti-inflammatory properties.

METHODS: This experimental study was conducted using healthy male Wistar albino rats. The animals were divided into four groups: a Sham group (superior mesenteric artery [SMA] isolated but not occluded), a Control group (SMA isolated and I-R induced), a 10 mg/kg Fraxin group, and a 50 mg/kg Fraxin group (fraxin administered before reperfusion). Total antioxidant status (TAS), total oxidant status (TOS), superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) activities were evaluated. Histopathological examinations and inflammatory markers, including tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and myeloperoxidase (MPO), were also analyzed.

RESULTS: In the Sham group, SOD activity was 135.2 ± 10.5 U/mg protein, GPx activity was 65.3 ± 4.7 U/mg protein, and CAT activity was 85.1 ± 5.8 U/mg protein. In the Control group, these values were 95.4 ± 7.9 , 45.7 ± 3.6 , and 60.3 ± 4.2 U/mg protein, respectively. In 10 mg/kg Fraxin group, SOD, GPx, and CAT activities were 115.6 ± 8.4 , 55.8 ± 4.2 , and 75.6 ± 5.5 U/mg protein, respectively; in the 50 mg/kg Fraxin group, the corresponding values were 130.8 ± 9.7 , 60.2 ± 4.8 , and 90.4 ± 6.3 U/mg protein. Significant decreases in TNF- α , IL-6, and MPO levels were observed in the Fraxin-treated groups ($p < 0.05$).

CONCLUSION: Fraxin administration preserved tissues and improved antioxidant parameters by reducing oxidative stress and inflammation in the acute mesenteric artery ischemia-reperfusion injury (AMAIRI) model. Based on these findings, fraxin may be considered a potential therapeutic option for mesenteric ischemia-reperfusion-related injuries.

Keywords: Acute mesenteric vascular occlusion; anti-inflammatory activity; antioxidant activity; fraxin; Ischemia-reperfusion injury.

INTRODUCTION

Experimental models of acute mesenteric vascular occlusion with ischemia-reperfusion (I-R) injury in small intestinal tissues cause severe tissue damage and may develop into a potentially lethal surgical emergency if not diagnosed at an early

clinical stage. Acute mesenteric ischemia (AMI) has been reported in 0.11% of all patients presenting to the emergency department (ED), corresponding to a frequency of nearly 1 in 1,000 patients.^[1] However, despite significant advances in diagnostic techniques, perioperative management, and surgical interventions over the past decades, the mortality rate

Cite this article as: Aydın İ, Uygur FA, Emecen Ö, Şengül D. Fraxin as a promising molecule in the pharmacological treatment of acute mesenteric ischemia: An experimental study. *Ulus Travma Acil Cerrahi Derg* 2026;32:413-419.

Address for correspondence: Furkan Ali Uygur

Department of General Surgery Giresun University Faculty of Medicine, Giresun, Türkiye

E-mail: druygurfurkanali@gmail.com

Ulus Travma Acil Cerrahi Derg 2026;32(4):413-419 DOI: 10.14744/tjtes.2025.21860

Submitted: 21.01.2025 Revised: 14.08.2025 Accepted: 12.11.2025 Published: 13.04.2026

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of AMI remains between 32% and 69%.^[2] These rates may vary depending on geographical region, healthcare facilities, and population characteristics.^[3] This high mortality rate underscores the severity of AMI and highlights the importance of early diagnosis and timely management.

The most common pathophysiological mechanisms of I-R injury include superior mesenteric artery (SMA) embolism, superior mesenteric artery thrombosis associated with chronic atherosclerosis, non-critical mesenteric ischemia, abdominal aortic aneurysm surgery, cardiopulmonary bypass, strangulated hernia, neonatal necrotizing enterocolitis, intestinal transplantation, and hemorrhagic-hypovolemic shock.^[4] Interruption of blood circulation causes ischemic damage by rapidly disrupting tissue metabolism, whereas restoration of blood flow can further exacerbate tissue injury. Reperfusion following hypoperfusion leads to severe damage to the intestinal mucosa and cells and can trigger a range of pathological, molecular, and biochemical changes, particularly when diagnosis or treatment is delayed.^[5] While ischemic tissue injury primarily results from oxygen deprivation and cell death associated with energy depletion, reperfusion further increases oxidative stress and local tissue damage and may trigger systemic inflammation or widespread inflammatory responses.

These considerations suggest that I-R injury requires further investigation, as such injuries can cause substantial impairment in both quality of life and overall health. A better understanding of I-R injury may facilitate the development of new therapeutic strategies for the management of these injuries in clinical practice.

It has been hypothesized that fraxin may prevent or attenuate mesenteric I-R injury due to its antioxidant and anti-inflammatory properties. This hypothesis is based on the ability of fraxin to act as a radical scavenger, inhibit lipid peroxidation, and suppress the production of pro-inflammatory cytokines.^[6,7] Supporting this hypothesis, several studies have demonstrated that fraxin exerts protective effects against I-R injury in various organs and tissues. For example, previous studies have shown that fraxin reduces oxidative stress and exhibits anti-inflammatory activity in renal ischemia-reperfusion injury.^[8] Additionally, similar protective effects of fraxin have been demonstrated in lung tissue.^[9] Moreover, research findings indicate that fraxin has hepatoprotective effects against toxic injury in liver cells.^[10] Therefore, this study aimed to investigate the effects of fraxin administration on intestinal I-R injury.

The aim of this study was to evaluate the potential of fraxin to regulate or attenuate I-R-induced mesenteric injury in a rat model based on biochemical and pathological findings. Furthermore, the findings of the present study may contribute to the development of novel therapeutic approaches for the treatment of mesenteric ischemia-reperfusion injury.

MATERIALS AND METHODS

This study was conducted at the Giresun University Experi-

mental Animals Research and Application Center. Healthy young adult male Wistar albino rats with an initial body weight between 250 and 300 g were used in the study. To ensure experimental consistency, only rats weighing between 180 and 200 g were included. Inclusion and exclusion criteria were established to ensure that only healthy animals within the specified weight range were used in the experiments. To control for potential confounding variables, rats with any signs of disease, injury, or body weight outside the predefined range were excluded from the experiment. All procedures were conducted in accordance with these criteria to maintain the validity and consistency of the experimental groups, following commonly accepted research practices. The rats were assigned to four groups, each consisting of eight animals. Anesthesia was induced by intramuscular injection of ketamine HCl at a dose of 80 mg/kg (Ketalar®; Pfizer, İstanbul, Türkiye) and xylazine HCl at a dose of 3 mg/kg (Rompun®; Bayer, İstanbul, Türkiye).

Study Design

In this study, a controlled experimental design was used.

- **Group 1 (Sham group):** The superior mesenteric artery was identified but not ligated. The abdominal wall was closed in two layers using No. 2 polypropylene sutures, and the rats were euthanized after 1 hour and 45 minutes.
- **Group 2 (Control group):** The SMA was dissected, and ischemia was induced using a non-traumatic microvascular clip. The abdomen was then closed. The durations of ischemia and reperfusion were set at 45 minutes and 60 minutes, respectively, as established in previous studies. The effects of different durations were not investigated in this study; however, the selected durations are widely used in experimental models and provide reliable results.^[11,12] After 45 minutes of ischemia, laparotomy was performed, the clamp was released, and reperfusion was initiated. I-R injury was induced by reperfusion, and the rats were euthanized after 60 minutes.
- **Group 3 (Fraxin 10 mg/kg group):** The procedure was identical to that used in Group 2, with the addition of intraperitoneal administration of fraxin at a dose of 10 mg/kg prior to reperfusion. The rats were euthanized after 60 minutes of reperfusion.
- **Group 4 (Fraxin 50 mg/kg group):** The procedure was identical to that used in Group 2. Fraxin was administered intraperitoneally at a dose of 50 mg/kg prior to reperfusion. The rats were euthanized after 60 minutes of reperfusion.

Dose Selection

The doses of 10 mg/kg and 50 mg/kg fraxin were selected based on previous studies in the literature. These studies determined the effective dose range and demonstrated the efficacy of these doses in I-R injuries in different organs and tissues.^[8,9]

This study design was carefully planned and implemented to ensure that the experimental groups were as comparable as

possible and that the results obtained would be reliable and valid.

Interventions, Experiments, or Treatments

All animals received intramuscular injection of cefuroxime at a dose of 20 mg/kg/day following the initial surgical procedures. Throughout the experiment, the body temperature of the rats was maintained at approximately 37.5°C using a heat lamp. At the end of the experimental period, the rats were anesthetized with ketamine and xylazine. Blood samples were then collected from the heart using a syringe and transferred into microcentrifuge tubes. The samples were centrifuged at 3,000 g to obtain serum for biochemical analysis. The abdomen was subsequently reopened, and intestinal tissue samples measuring approximately 6–8 cm in length were obtained from the terminal ileum. The samples were washed with cold saline and fixed in 10% neutral formaldehyde solution. Additional blood samples were collected in ethylenediaminetetraacetic acid (EDTA)-containing tubes to prevent clotting and centrifuged to obtain plasma for biochemical analysis; the plasma samples were stored at -80°C. The intestinal tissues were embedded in paraffin blocks, and 5 µm thick sections were prepared and stained with hematoxylin and eosin (H&E). Histological sections were examined under a microscope by a pathologist who was blinded to the experimental procedures. Total antioxidant status (TAS), total oxidant status (TOS), superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) activities in plasma and tissue samples were measured using spectrophotometric methods with commercial kits. At the end of the study, all rats were euthanized by the decapitation method.

Methods of Measurement and Calculations

Biochemical Tests

Total Antioxidant Status Measurement: TAS levels were measured using the Total Antioxidant Status kit (Rel Assay Diagnostics, Türkiye). In this method, ABTS (2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonate)) is oxidized to ABTS^{•+} by hydrogen peroxide in an acidic buffer solution (30 mmol/L, pH 3.6). The ABTS^{•+} forms a stable dark green-colored complex in an acetate buffer. During serial dilution, the dark green color gradually disappears upon dilution in a more concentrated, higher-pH acetate buffer solution (0.4 mol/L, pH 5). The loss of this color occurs at a rate proportional to the concentration of antioxidants present in the sample. This reaction can be monitored spectrophotometrically, and the rate of decolorization is inversely proportional to the total antioxidant capacity (TAC) of the sample. This reaction is quantified using Trolox™ (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), a water-soluble analog of vitamin E. The results obtained with this method are expressed as mmol Trolox equivalent/L.

Total Oxidant Status Measurement: TOS levels were measured using the Total Oxidant Status kit (Rel Assay Diagnostic, Türkiye). In this method, oxidant molecules in the

sample convert the ferrous ion (Fe²⁺)-o-dianisidine complex to ferric ions (Fe³⁺). The oxidation reaction is enhanced by glycerol molecules present in the reaction medium. Ferric ions then form a colored complex with xylenol orange in an acidic environment. The intensity of the color is proportional to the amount of oxidant molecules present in the sample. The assay is calibrated using hydrogen peroxide (H₂O₂). Results are expressed as micromolar hydrogen peroxide equivalents per liter (µmol H₂O₂ equiv./L).

SOD, GPx, and CAT Level Measurement Methods

• **SOD Activity:** SOD activity was measured using a spectrophotometric method based on the inhibition of nitroblue tetrazolium (NBT) reduction by superoxide generated by the xanthine-xanthine oxidase system. Results were expressed as units of SOD per milligram of protein (U/mg protein).

• **GPx Activity:** GPx activity was determined using a spectrophotometric method based on the oxidation of nicotinamide adenine dinucleotide phosphate (NADPH) to nicotinamide adenine dinucleotide phosphate (NADP⁺) in the presence of reduced glutathione, glutathione reductase, and hydrogen peroxide. The results were expressed as U/mg protein.

• **CAT Activity:** CAT activity was measured by monitoring the decomposition of hydrogen peroxide through the decrease in absorbance at 240 nm in the presence of catalase. Results were expressed as U/mg protein.

Histopathological Examination

Terminal ileum tissues were embedded in parallel wax, sectioned, and stained with hematoxylin and eosin. Histological sections were examined under light microscopy by a pathologist who was blinded to the experimental procedures. Intestinal lesions were graded according to a five-level ischemia-reperfusion injury scoring system adapted from Quaedackers et al.:

- Grade 0: Normal villi and mucosa
- Grade 1: Development of subepithelial space at the villus tip with villous edema and occlusion
- Grade 2: Development of a subepithelial space at the villus tip with bleeding and fragmentation at the villus tip
- Grade 3: Loss and fragmentation of the villus tip
- Grade 4: Complete separation of the villi from the lamina propria
- Grade 5: Necrosis of the entire wall with fragmentation of the lamina propria.

Statistical Analysis

A power analysis was performed to determine the appropriate sample size for the study. Based on the results of the power analysis, it was determined that eight rats per group were required. Experimental ischemia-reperfusion studies reported in the literature were used as references to deter-

mine the appropriate number of animals required for statistical evaluation. Based on these references, the optimal sample size was selected for this study. Statistical analyses were performed using MedCalc (MedCalc Software Ltd., Ostend, Belgium) and GraphPad Prism version 9.0.1. Variables were expressed as mean±standard deviation. The Kruskal-Wallis H test was used for comparisons among more than two groups, and Dunn's test was applied for post hoc comparisons. Statistical significance was defined as $p < 0.05$ (two-tailed).

The study was conducted in compliance with ethical standards for animal experimentation. The study protocol was approved by the Local Ethics Committee of Giresun University (approval number: 08.06.2020/6859/21). All procedures involving animals were carried out in accordance with the Guide for the Care and Use of Laboratory Animals and adhered to the principles outlined in the EU Directive 2010/63/EU on the protection of animals used for scientific purposes.

RESULTS

In this study, MDA and TAS levels were compared among the four groups. In the Sham group, the MDA level was 45.5 ± 9.0 $\mu\text{mol/L}$, whereas this value was 42.5 ± 10.8 $\mu\text{mol/L}$ in the Control group. In the Fraxin-treated groups, MDA level was 33.6 ± 11.4 $\mu\text{mol/L}$ at the 10 mg/kg dose and 56.3 ± 16.5 $\mu\text{mol/L}$

at the 50 mg/kg dose. In terms of TAS levels, the values were 1.21 ± 0.12 mmol Trolox equiv./L in the Sham group, 1.21 ± 0.15 mmol Trolox equiv./L in the Control group, 1.81 ± 0.91 mmol Trolox equiv./L in the 10 mg/kg Fraxin group, and 1.27 ± 0.28 mmol Trolox equiv./L in the 50 mg/kg Fraxin group (Table 1, Figure 1A-B).

Histopathological examinations revealed three normal, three edematous, and two fragmented villi in the Sham group. In the Control group, two normal, two edematous, two hemorrhagic, one fragmented, and one detached villus were observed. In the 10 mg/kg Fraxin group, three normal, one fragmented, one detached, and three necrotic villi were identified, whereas in the 50 mg/kg Fraxin group, five normal, one hemorrhagic, one fragmented, and one necrotic villus were observed (Table 2).

Regarding local and systemic inflammatory markers, the tumor necrosis factor alpha (TNF- α) level was 15.2 ± 2.1 pg/mL, the interleukin-6 (IL-6) level was 12.3 ± 1.8 pg/mL, and the myeloperoxidase (MPO) level was 10.5 ± 1.3 U/mg protein in the Sham group. In the Control group, these values were 35.4 ± 5.3 pg/mL, 40.6 ± 4.9 pg/mL, and 25.8 ± 3.6 U/mg protein, respectively. In the Fraxin-treated groups, the levels were TNF- α 20.7 ± 3.2 pg/mL, IL-6 22.4 ± 2.5 pg/mL, and MPO 14.2 ± 2.0 U/mg protein at the 10 mg/kg dose, and TNF- α

Table 1. Malondialdehyde (MDA) and total antioxidant status (TAS) levels across the four study groups

Group	MDA ($\mu\text{mol/L}$)	TAS (mmol Trolox equiv./L)	p-value (MDA)	p-value (TAS)
Group 1 (Sham)	45.5 ± 9.0	1.21 ± 0.12	0.045	0.510
Group 2 (Control)	42.5 ± 10.8	1.21 ± 0.15	0.048	0.515
Group 3 (Fraxin 10 mg/kg)	33.6 ± 11.4	1.81 ± 0.91	0.036	0.475
Group 4 (Fraxin 50 mg/kg)	56.3 ± 16.5	1.27 ± 0.28	0.039	0.480

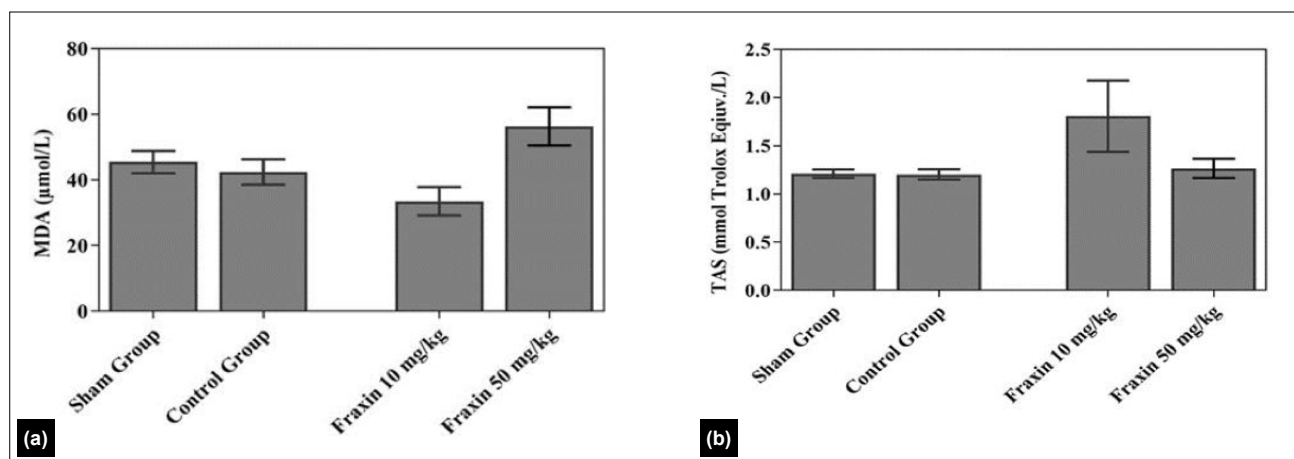


Figure 1. (a) Bar graph showing malondialdehyde (MDA) levels across the four groups (presented as mean±standard error). (b) Bar graph showing total antioxidant status (TAS) levels across the four groups (presented as mean±standard error).

Table 2. Histopathological grading and findings across the study groups

Group	Grade 0 (Normal)	Grade 1 (Edema)	Grade 2 (Hemorrhage)	Grade 3 (Fragmentation)	Grade 4 (Separation)	Grade 5 (Necrosis)	Total (n)
Sham	3	3	0	2	0	0	8
Control	2	2	2	1	1	0	8
Fraxin 10 mg/kg	3	0	0	1	1	3	8
Fraxin 50 mg/kg	5	0	1	1	0	1	8

Table 3. Comparison of local and systemic inflammatory markers

Group	TNF- α (Mean \pm SD)	IL-6 (Mean \pm SD)	MPO (Mean \pm SD)	p-value (TNF- α)	p-value (IL-6)	p-value (MPO)
Sham	15.2 \pm 2.1	12.3 \pm 1.8	10.5 \pm 1.3	0.05	0.04	0.03
Control	35.4 \pm 5.3	40.6 \pm 4.9	25.8 \pm 3.6	0.02	0.01	0.01
Fraxin 10 mg/kg	20.7 \pm 3.2	22.4 \pm 2.5	14.2 \pm 2.0	0.04	0.03	0.02
Fraxin 50 mg/kg	18.3 \pm 2.8	19.8 \pm 3.1	13.1 \pm 1.7	0.03	0.02	0.02

18.3 \pm 2.8 pg/mL, IL-6 19.8 \pm 3.1 pg/mL, and MPO 13.1 \pm 1.7 U/mg protein at the 50 mg/kg dose (Table 3).

In our study, although biochemical assessments indicated a marked improvement in antioxidant capacity, the rate of tissue necrosis was higher in the Fraxin-treated groups (particularly the low-dose group) compared to the other groups. This finding appears inconsistent with the observed biochemical improvement. We believe that studies with longer follow-up periods and larger sample sizes may provide clearer results.

In conclusion, Fraxin treatment reduced oxidative stress and inflammation while enhancing antioxidant defense mechanisms. These findings demonstrate a protective role of fraxin in acute mesenteric ischemia-reperfusion injury.

DISCUSSION

The aim of this study was to evaluate the protective effects of fraxin against ischemia-reperfusion injury of the small intestine. The results demonstrated that Fraxin exerted a protective effect against I/R-induced tissue damage by reducing oxidative stress and inflammation and by enhancing antioxidant defense mechanisms. In the present study, Fraxin-treated groups showed increased levels of total antioxidant status and decreased levels of total oxidant status. Additionally, significant increases were observed in the activities of antioxidant enzymes, including SOD, GPx, and CAT. Moreover, compared with the control group, Fraxin-treated groups exhibited markedly reduced levels of inflammatory markers such as TNF- α , IL-6, and MPO. Histopathological examination also demonstrated that Fraxin reduced intestinal damage and helped preserve the structural integrity of villi. These

findings indicate that fraxin may serve as a potential therapeutic agent in mesenteric I/R injury.

The findings of this study demonstrate the protective effects of fraxin against acute mesenteric ischemia-reperfusion injury. Fraxin administration reduced oxidative stress and inflammatory responses while enhancing antioxidant defense mechanisms in tissues. Previous studies have also reported similar protective effects of fraxin in ischemia-reperfusion injury affecting other organs. For instance, Topdađı et al.^[8] reported that fraxin reduces oxidative stress and inflammation during renal ischemia-reperfusion injury. Similarly, Okubo et al.^[13] demonstrated its protective effects in lung ischemia-reperfusion injury. Nanayakkara et al.^[14] also showed that fraxin protects against ischemic tissue damage in cardiac muscle. Together, these findings suggest that fraxin could be used as an effective agent for treating mesenteric ischemia-reperfusion injuries.

The present research findings show that fraxin has protective effects by reducing inflammatory markers such as TNF- α , IL-6, and MPO in acute mesenteric ischemia-reperfusion injury. The effects observed with fraxin are consistent with findings from other studies on I/R injuries reported in the literature. For example, İçođlu Aksakal et al.^[15] demonstrated that umbelliferone reduced TNF- α , IL-6, and MPO levels. Similarly, the present study found that fraxin produced comparable reductions in these inflammatory markers.^[15] Ali et al.^[16] reported that raloxifene decreased TNF- α and IL-6 levels while increasing antioxidant capacity. These findings indicate that raloxifene reduces inflammation and oxidative stress, supporting effects similar to those observed with

fraxin.^[16] In another study, Karataş et al.^[17] investigated tocilizumab and reported reduced TNF- α and IL-6 levels along with an enhanced antioxidant defense system. This suggests that tocilizumab suppresses the inflammatory response, further supporting the anti-inflammatory effects observed with fraxin.^[17] Furthermore, Zengin et al.^[18] showed that cerium oxide nanoparticles decreased TNF- α and IL-6 levels and reduced MPO activity. The above findings demonstrate the anti-inflammatory properties of fraxin.^[18] Alvani et al.^[19] demonstrated that acacetin reduced TNF- α and IL-6 levels while increasing antioxidant enzyme activity. Taken together, these results demonstrate that fraxin has beneficial effects on inflammation and oxidative stress.^[19] In conclusion, this study, along with other research in the literature, indicates that fraxin is an effective protective agent against mesenteric ischemia-reperfusion injuries by reducing inflammatory markers and enhancing antioxidant defenses. These findings are supported by similar outcomes, as evidenced by decreased TNF- α , IL-6, and MPO levels.

The findings of this study indicate that acute mesenteric ischemia-reperfusion injury can be mitigated by fraxin through its ability to increase the levels of antioxidant enzymes such as SOD, GPx, and CAT. Other investigations on I/R injury also support these outcomes. In research conducted by Trocha et al.,^[20] liver I/R injury showed increased activities of SOD, CAT, and GPx when treated with sitagliptin. Hence, it can be inferred that these findings corroborate that fraxin has similar protective effects by enhancing the activity of these enzymes against free radicals that cause oxidative stress in cells.^[20] Demirhan .'s work on resveratrol demonstrated that MDA levels decreased while SOD and CAT activities increased; this is consistent with the observed effects of fraxin in strengthening antioxidant defense mechanisms.^[21] Similarly, Heidari .'s study on *Withania coagulans* root extract reported decreased MDA levels along with increased SOD, CAT, and GPx activity, thereby reducing oxidative stress. Fraxin demonstrated comparable effects by increasing antioxidant enzyme activities as well.^[11] CoQ10, together with berberine, was reported by Apaydin and Batil (2019) to provide protection against ischemia-reperfusion injury by increasing SOD, CAT, and GPx activities, indicating that fraxin may act through similar mechanisms.^[12] In light of these findings, it can be concluded from this study, as well as others reported in the literature, that mesenteric ischemia-reperfusion injuries are effectively prevented by fraxin acting as an inducer of antioxidant enzymes. Consistent with these findings, SOD, GPx, and CAT levels were shown to increase.

This study has certain limitations. First, the experimental study was conducted only in a rat model, which may limit the generalizability of these findings to humans. Additionally, the investigation assessed only short-term effects and did not examine long-term outcomes or potential adverse reactions associated with fraxin use. Moreover, specific doses were used in the experimental design without consideration of different

dosage ranges; therefore, the effects of varying doses on outcome measures were not explored. Finally, only biochemical and histopathological parameters were evaluated in this research, and a detailed analysis of the molecular mechanisms of action of fraxin was not performed.

CONCLUSION

Fraxin protected tissues and strengthened the antioxidant system by reducing oxidative stress and inflammation. It increased the activity of antioxidant enzymes such as SOD, GPx, and CAT, while reducing inflammatory markers including TNF- α , IL-6, and MPO. These findings are consistent with other studies reported in the literature. The results suggest that fraxin may be a potential therapeutic agent for mesenteric ischemia-reperfusion injury. Further studies with larger sample sizes and longer follow-up periods are needed to better clarify tissue necrosis at low doses and to determine the safety of this treatment.

Ethics Committee Approval: This study was approved by the Local Ethics Committee of Giresun University Ethics Committee (Date: 08.06.2020, Decision No: 6859/21).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: İ.A., Ö.E.; Design: İ.A., F.A.U.; Supervision: İ.A., F.A.U.; Resource: Ö.E.; Materials: İ.A., Ö.E.; Data collection and/or processing: İ.A., F.A.U.; Analysis and/or interpretation: F.A.U., D.Ş.; Literature review: D.Ş.; Writing: İ.A., F.A.U.; Critical review: İ.A., D.Ş.

Conflict of Interest: None declared.

Financial Disclosure: The author declared that this study has received no financial support.

REFERENCES

- Bala M, Kashuk J, Moore EE, Kluger Y, Biffl W, Gomes CA, et al. Acute mesenteric ischemia: guidelines of the World Society of Emergency Surgery. *World J Emerg Surg* 2017;12:38. [CrossRef]
- Kerzmann A, Haumann A, Boesmans E, Detry O, Defraigne JO. L'ischémie mésentérique aiguë [Acute mesenteric ischemia]. *Rev Med Liege* 2018;73:300–3. [In French]
- Acosta S, Björck M. Modern treatment of acute mesenteric ischaemia. *Br J Surg* 2014;101:e100–8. [CrossRef]
- Clair DG, Beach JM. Mesenteric Ischemia. *N Engl J Med* 2016;374:959–68. [CrossRef]
- Vollmar B, Menger MD. Intestinal ischemia/reperfusion: microcirculatory pathology and functional consequences. *Langenbecks Arch Surg* 2011;396:13–29. [CrossRef]
- Eltzschig HK, Eckle T. Ischemia and reperfusion--from mechanism to translation. *Nat Med* 2011;17:1391–401. [CrossRef]
- Whiting PH, Kalansooriya A, Holbrook I, Haddad F, Jennings PE. The relationship between chronic glycaemic control and oxidative stress in type 2 diabetes mellitus. *Br J Biomed Sci* 2008;65:71–4. [CrossRef]
- Topdağ Ö, Tanyeli A, Akdemir FNE, Eraslan E, Güler MC, Çomaklı S. Preventive effects of fraxin on ischemia/reperfusion-induced acute kidney injury in rats. *Life Sci* 2020;242:117217. [CrossRef]
- Ma X, Liu X, Feng J, Zhang D, Huang L, Li D, et al. Fraxin Alleviates LPS-induced ards by downregulating inflammatory responses and oxidative damages and reducing pulmonary vascular permeability. *Inflamma-*

- tion 2019;42:1901–12. [CrossRef]
10. Chang BY, Jung YS, Yoon CS, Oh JS, Hong JH, Kim YC, et al. Fraxin prevents chemically induced hepatotoxicity by reducing oxidative stress. *Molecules* 2017;22:587. [CrossRef]
 11. Heidari Z, Mahmoudzadeh-Sagheb H, Sarbishegi M, Gorgich EAC. Withania coagulans extract attenuates oxidative stress-mediated apoptosis of cerebellar purkinje neurons after ischemia/reperfusion injury. *Metab Brain Dis* 2021;36:1699–708. [CrossRef]
 12. Apaydin Yildirim B, Batil Annour A. The investigation of the preventive effects of Coenzyme Q10 and Berberine for tourniquet induced ischemia-reperfusion injury on skeletal muscle in rat hindlimb. *GSC Biol Pharm Sci* 2019;09:127–33. [CrossRef]
 13. Okubo K, Kosaka S, Isowa N, Hirata T, Hitomi S, Yodoi J, et al. Amelioration of ischemia-reperfusion injury by human thioredoxin in rabbit lung. *J Thorac Cardiovasc Surg* 1997;113:1–9. [CrossRef]
 14. Nanayakkara G, Alasmari A, Mouli S, Eldoumani H, Quindry J, McGinnis G, et al. Cardioprotective HIF-1 α -frataxin signaling against ischemia-reperfusion injury. *Am J Physiol Heart Circ Physiol* 2015;309:H867–79. [CrossRef]
 15. Icoğlu Aksakal F, Koc K, Geyikoglu F, Karakaya S. Ameliorative effect of umbelliferone in remote organ injury induced by renal ischemia-reperfusion in rats. *J Food Biochem* 2021;45:e13628. [CrossRef]
 16. Ali RAH, Altimimi M, Hadi NR. The potential renoprotective effect of Raloxifene in renal ischemia-reperfusion injury in a male rat model. *J Med Life* 2023;16:1274–81. [CrossRef]
 17. Karatas Y, Erdi ME, Kaya B, Keskin F, Cüce G, Kılınc I, et al. Neuroprotective effects of tocilizumab on experimentally-induced spinal cord ischemia-reperfusion injury. *World Neurosurg* 2019;124:e208–13. [CrossRef]
 18. Zengin A, Eriğiç A, Telli G, Gümüşel B, Kösemehmetoğlu K, Uçar G, et al. Anti-inflammatory effects of oral and intraperitoneal administration of cerium oxide nanoparticles on experimental hepatic ischemia-reperfusion injury. *Turk J Surg* 2022;38:255–65. [CrossRef]
 19. Alvani A, Jalili C, Shiravi A, Vaezi G, Ghanbari A. Acacetin inhibits oxidative stress and inflammation in renal ischemia-reperfusion injury. *Jentashapir J Cell Mol Biol* 2023;14:E136185. [CrossRef]
 20. Trocha M, Krzystek-Korpacka M, Merwid-Ląd A, Nowak B, Pieńiewska M, Dziegłiel P, et al. Sitagliptin-dependent differences in the intensity of oxidative stress in rat livers subjected to ischemia and reperfusion. *Oxid Med Cell Longev* 2019;2019:2738605. [CrossRef]
 21. Demirhan I, Kurutas EB, Oner E. Network pharmacology-based investigation and experimental discovery of resveratrol's mechanism of liver ischemia reperfusion-induced oxidative stress damage. *Indian J Animal Res* 2025;59:101–7.

DENEYSSEL ÇALIŞMA - ÖZ

Fraksin, akut mezenter iskemisinin farmakolojik tedavisinde umut veren molekül: Deneysel bir çalışma

AMAÇ: Akut mezenter iskemisi (AMI), ince bağırsağa kan akışının ani kesilmesi sonucu oluşan, bağırsak nekrozu ve karın ağrısının nadir nedenlerinden biridir. Tanı ve tedavideki gecikme mortalitede ciddi artışlara neden olmaktadır. Bu çalışmada, antiinflamatuar ve antioksidan etkileri olduğu bilinen fraksin'in bağırsak iskemisi-reperfüzyon hasarı üzerindeki etkilerinin araştırılması amaçlandı.

GEREÇ VE YÖNTEM: Bu çalışma, sağlıklı erkek Wistar Albino sıçanlar kullanılarak kontrollü deneysel tasarımda gerçekleştirildi. Sıçanlar dört gruba ayrıldı: Sham grubu (SMA izole edilmiş ancak kapatılmamış), Kontrol grubu (SMA izole edilmiş ve I-R ile indüklenmiş), 10 mg/kg fraksin grubu ve 50 mg/kg fraksin grubu (reperfüzyondan önce fraksin uygulandı). Toplam antioksidan kapasite (TAS), toplam oksidan durum (TOS), süperoksit dismutaz (SOD), glutatyon peroksidaz (GPx) ve katalaz (CAT) aktiviteleri değerlendirildi. Histopatolojik incelemeler ve enflamatuar belirteçler (TNF- α , IL-6 ve MPO) da analiz edildi.

BULGULAR: Sham grubunda SOD aktivitesi 135.2 ± 10.5 U/mg protein, GPx aktivitesi 65.3 ± 4.7 U/mg protein ve CAT aktivitesi 85.1 ± 5.8 U/mg protein olarak belirlendi. Kontrol grubunda ise bu değerler sırasıyla 95.4 ± 7.9 , 45.7 ± 3.6 ve 60.3 ± 4.2 U/mg protein olarak belirlendi. 10 mg/kg fraksin grubunda SOD 115.6 ± 8.4 , GPx 55.8 ± 4.2 ve CAT 75.6 ± 5.5 U/mg protein; 50 mg/kg fraksin grubunda SOD 130.8 ± 9.7 , GPx 60.2 ± 4.8 ve CAT 90.4 ± 6.3 U/mg protein. Fraksin uygulanan gruplarda TNF- α , IL-6 ve MPO düzeylerinde anlamlı düşüşler gözlemlendi ($p < 0.05$).

SONUÇ: Fraksin'in mezenterik iskemisi-reperfüzyon hasarında dokuları koruması, inflamasyonu ve oksidatif stresi azaltarak antioksidan göstergeleri güçlendirmesi nedeniyle bu hastalığın farmakolojik tedavisinde potansiyel bir ajan olarak kullanılabileceğinin akılda tutulması gerektiğini düşünüyoruz.

Anahtar sözcükler: Antiinflamatuar aktivite; antioksidan aktivite; fraksin; iskemisi-reperfüzyon hasarı; koruyucu etki; mezenterik iskemisi.

Ulus Travma Acil Cerrahi Derg 2026;32(4):413-419 DOI: 10.14744/tjtes.2025.21860