EXPERIMENTAL STUDY

The protective effects of sesamin on the ileum in superior mesenteric artery ischemia induced in rats

Hikmet Özesmer,[1] Mehmet Tolga Kafadar,[2] Eda Yıldızhan,[3] Murat Akkuş[3]

[1]Department of Surgical Medical Sciences, University of Health Sciences, Gazi Yaşargil Training and Research Hospital, Diyarbakır-*Türkiye*
[2]Department of General Surgery, Faculty of Medicine, Dicle University, Diyarbakır-*Türkiye*
[3]Department of Histology And Embryology, Dicle University, Faculty of Medicine Hospital, Diyarbakır-*Türkiye*

ABSTRACT

BACKGROUND: Acute mesenteric artery ischemia is recognized as a significant cause of mortality and morbidity, with its incidence increasing with age. This study aims to investigate the efficacy of sesamin in mitigating the histological, immunological, and biochemical damage associated with superior mesenteric artery ischemia and reperfusion (SMA I/R) injury in the ileum.

METHODS: Twenty-eight Sprague-Dawley rats were randomly assigned into four equal groups. Group I (Control group): Received no treatment. Group II (SMA I/R group): Carboxymethylcellulose was mixed with distilled water and administered orally via gavage at a dose of 1 mL/kg/dose for three weeks. At the end of the third week, SMA ischemia was induced for 60 minutes followed by 120 minutes of reperfusion. Group III (Sesamin group): Received sesamin orally at a dose of 30 mg/kg via gavage for three weeks. Group IV (Sesamin + SMA I/R group): Received sesamin followed by SMA I/R.

RESULTS: Serum malondialdehyde (MDA) levels were highest in the SMA I/R group, while lower levels were observed in the Sesamin + SMA I/R group ($p<0.05$). Similarly, total oxidant status (TOS) was significantly reduced in the Sesamin + SMA I/R group compared to the SMA I/R group ($p<0.05$). Consistent with these findings, Bax expression, a pro-apoptotic marker, was less intense in the Sesamin + SMA I/R group than in the SMA I/R group.

CONCLUSION: Our findings indicate that the administration of sesamin prior to SMA I/R effectively reduces oxidative damage and prevents histological alterations, as demonstrated by histological, immunohistochemical, and biochemical parameters.

Keywords: Ischemia and reperfusion; sesamin; oxidative stress; apoptosis.

INTRODUCTION

Acute mesenteric ischemia (AMI) is one of the most critical acute abdominal conditions, with a high mortality rate of approximately 60%, primarily affecting older adults (typically between 58 and 63 years of age). The incidence is higher in males compared to females.[1] It has been reported that approximately 50% of mesenteric ischemia cases are due to superior mesenteric artery (SMA) embolism, 25% are caused by atherosclerotic vessel thrombosis, and the remaining 25% result from non-occlusive venous thrombosis.[2] AMI caused by arterial embolism is often associated with a history of cardiac dysrhythmias, whereas arterial thrombosis typically develops in patients with critical vascular stenosis.[3] Common symptoms of mesenteric ischemia include abdominal pain, changes in bowel habits, nausea, and vomiting. Early diagnosis is challenging, especially before the appearance of peritoneal irritation signs. Once peritoneal irritation develops, the ischemia, initially affecting the mucosa, progresses transmurally to involve the bowel serosa.[4] With the exception of non-occlu-

Cite this article as: Özesmer H, Kafadar MT, Yıldızhan E, Akkuş M. The protective effects of sesamin on the ileum in superior mesenteric artery ischemia induced in rats. Ulus Travma Acil Cerrahi Derg 2025;31:317-323.

Address for correspondence: Eda Yıldızhan
Department of Histology and Embryology, Dicle University, Faculty of Medicine Hospital, Diyarbakır, Türkiye
E-mail: edayildizhan21@gmail.com

Ulus Travma Acil Cerrahi Derg 2025;31(4):317-323 DOI: 10.14744/tjtes.2025.97340
Submitted: 10.12.2024 Revised: 09.01.2025 Accepted: 10.01.2025 Published: 28.03.2025

sive cases, treatment for acute mesenteric ischemia typically involves laparotomy, resection of necrotic bowel segments, and revascularization.[2-4]

Restoration of blood flow impaired by ischemia is known as ischemia-reperfusion (I/R) injury.[5,6] However, reperfusion may exacerbate the damage caused by ischemia. It has been observed that arterio-venous occlusion of the gastrointestinal system develops following reperfusion.[7] I/R injury is a significant cause of morbidity and mortality, particularly in organ transplantation and resuscitation settings.[5] The small intestine is considered one of the most susceptible organs to I/R injury.[8] Intestinal I/R can result from mesenteric ischemia, disseminated infections, traumatic shock, or surgical procedures. Following I/R injury, an uncontrolled inflammatory response and multiple organ dysfunction may occur.[9] This is because, during reperfusion, the ischemic organ is suddenly flooded with blood, leading to a surge in reactive oxygen species (ROS). The increase in ROS contributes to inflammation, immune cell activation, and apoptosis.[10] Oxidative stress also disrupts the balance between anti-inflammatory factors in the ischemic tissue.[11] Bax molecules trigger the release of cytochrome c, initiating caspase-9 activation. Bax protein is considered one of the key markers of cell death following I/R injury.[12]

To date, many studies have suggested that certain herbs and drugs may protect against I/R injury by exerting antioxidant effects. However, studies demonstrating the anti-apoptotic activity of sesamin in I/R injury are limited. Sesamin, a flavonoid found in sesame oil, is believed to be effective in reducing oxidative stress.[13]

Sesame (Sesamum indicum L.), a member of the Pedaliaceae family, has a long history, having been first cultivated in Babylon approximately 4,000 years ago.[14] Several studies have reported the antioxidative, anti-inflammatory, and neuroprotective effects of sesame oil.[15] Additionally, sesamin, one of the key components of sesame oil, has been shown to offer protective effects against oxidative stress.[16]

Our aim was to demonstrate, through histopathological and biochemical markers, that sesamin administration prior to I/R may protect against and ameliorate I/R-induced injury by reducing oxidative stress, inflammation, and apoptosis. For this purpose, malondialdehyde (MDA), a marker of oxidative stress, along with total oxidant status (TOS), total antioxidant capacity (TAS), and oxidative stress index (OSI), will be evaluated to assess the antioxidant potential of sesamin and compared between the groups. Additionally, histological changes in ileum tissues will be evaluated in relation to the expression of Bax proteins.

MATERIALS AND METHODS

All experimental protocols were conducted in accordance with the guidelines for the ethical use and care of experimental animals. The study was approved by the Dicle University Prof. Dr. Sabahattin Payzın Health Sciences Research and Application Center Animal Experiments Local Ethics Committee (Protocol Number: 2022/25, Approval Number: 2, Date: 31.05.2022). The study was carried out on 28 Sprague-Dawley rats, weighing between 180 and 300 grams.

Preparation of Sesamin

The sesamin used in this study (purity: ≥98%) was obtained from Dalian Meilun Biotech Co., Ltd. (Dalian, China). It was dissolved in a carboxymethyl cellulose solution and administered orally (p.o.) via gavage at a daily dose of 30 mg/kg for three weeks. Previous studies have shown that administering sesamin at this dose and duration, for up to eight weeks, does not produce toxic effects.[17]

Preparation of Carboxymethyl Cellulose

Carboxymethyl cellulose was prepared by dissolving 0.5% of it in distilled water. This solution was administered orally via gavage at a daily dose of 1 mL/kg.[18]

Surgical Procedure for Inducing SMA I/R

Rats were fasted for twelve hours prior to surgery, with access to water only. General anesthesia was induced via intraperitoneal (i.p.) injection of 90 mg/kg ketamine hydrochloride (Ketalar; Pfizer, Istanbul, Türkiye) and 10 mg/kg xylazine hydrochloride (Rompun; Bayer, Istanbul, Türkiye). The depth of anesthesia was periodically monitored using skin and toe pinch responses. Under anesthesia, the rats were placed in a supine position and secured to the surgical table. The abdominal skin was shaved and disinfected with 10% povidone-iodine. A midline laparotomy was performed to expose the abdominal cavity, and the intestines were exteriorized to visualize the superior mesenteric artery. The Treitz ligament was identified and incised, and the site where the SMA branches from the aorta was clamped using an atraumatic microvascular clamp for 60 minutes to induce ischemia in the ileum. Following the ischemic period, the clamp was released to initiate a 120-minute reperfusion period. Finally, a 2 cm segment of the terminal ileum was resected.[17]

Experimental Animal Grouping and Protocol

The rats were housed in stainless steel cages at 22±2°C with 60% humidity and a 12-hour light/dark cycle. They were fed a standard diet, with no restrictions on movement, food, or water. Food was provided in steel containers, and water was supplied in glass bottles filled with tap water. The rats were divided into four groups, with seven rats per group. Drug dosages were calculated individually based on the body weight of each rat, in accordance with literature recommendations.

• Group I (Control Group): 0.5% carboxymethyl cellulose was mixed with distilled water and administered orally via gavage at a dose of 1 mL/kg/dose for three weeks.

• Group II (SMA I/R Group): 0.5% carboxymethyl cellulose was mixed with distilled water and administered orally via gavage at a dose of 1 mL/kg/dose for three weeks. At the end of the third week, SMA was subjected to 60 minutes of ischemia followed by 120 minutes of reperfusion.

• Group III (Sesamin Group): Sesamin was administered orally (p.o.) via gavage at a dose of 30 mg/kg for three weeks.

• Group IV (Sesamin + SMA I/R Group): Sesamin was administered orally at a dose of 30 mg/kg via gavage for three weeks. At the end of the third week, the rats were placed under general anesthesia, followed by 60 minutes of ischemia and 120 minutes of reperfusion after the clamps were released.

At the end of the experiment, a 2 cm segment of the distal terminal ileum was resected from all groups.

Biochemical Analyses

Measurement of Serum Malondialdehyde Levels

For the measurement of serum malondialdehyde levels, commercially available kits (BT LAB, Zhejiang, China) were used. Blood samples were collected intracardially and centrifuged at 3000 rpm for 15 minutes. The plasma was separated and stored in individual tubes at -80°C for subsequent MDA analysis. During the MDA analysis, 0.5 mL of plasma was mixed with 2.5 mL of 20% trichloroacetic acid (TCA) and vortexed. Then, 1 mL of 0.6% thiobarbituric acid (TBA) was added to the mixture, which was vortexed for 10 minutes and subsequently incubated in boiling water for 30 minutes. After cooling, the absorbance of the mixture was measured at 532 nm using a spectrophotometer. Results were calculated in µmol/L, considering the extinction coefficient ($1.56x10^5$) and dilution factors.

Total Antioxidant Capacity and Total Oxidant Status

Venous blood samples were collected into EDTA (ethylenediaminetetraacetic acid) tubes and centrifuged at 3000 rpm for 10 minutes. The plasma samples were then separated and stored at -80°C. Prior to analysis, the serum samples and assay kits were brought to room temperature (+25°C). TAS levels were measured using the method developed by Erel, utilizing a Rel Assay Diagnostics kit (Gaziantep, Türkiye). TAS results were expressed in µmol/L and analyzed using a Beckman Coulter AU5800 analyzer.[19,20]

Measurement of Oxidative Stress Index

The OSI was calculated using the following formula:

OSI = TOS (µmol H_2O_2 equivalent/L) / TAS (mmol Trolox equivalent/L) x 100.[21]

Histological Tissue Examination

Ileum tissues obtained from the sacrificed animals were fixed in 10% formalin (Sigma #SZBE2450V) for 24 hours and then washed in running water for 12 hours. For dehydration, the tissues were passed through a graded alcohol series (70%, 80%, 96%). Following dehydration, the tissues were treated with xylene for 2 x 15 minutes and then embedded in paraffin. Sections 5 µm thick were cut from the paraffin blocks and mounted on positively charged slides. Routine histological evaluation was performed using hematoxylin and eosin staining. The degree of tissue damage was assessed using the Chiu scoring system.[22]

Bax Analysis

Sections 5 µm thick were cut and mounted on positively charged slides, then deparaffinized in xylene for 2 x 15 minutes and rehydrated through a decreasing alcohol series to distilled water. Antigen retrieval was performed using an EDTA solution. The sections were rinsed in phosphate-buffered saline (PBS) for 3 x 5 minutes, and the tissue boundaries were outlined using a hydrophobic pen. The specimens were incubated overnight at +4°C with the primary Bax antibody (Santa Cruz), diluted at 1:250 in antibody diluent (Thermo). Histoscore analysis was used to evaluate the degree of damage in the ileum tissue.[23]

Statistical Analysis

Statistical analysis was performed using SPSS version 20 (SPSS Inc., USA). The Shapiro-Wilk test was used to determine whether the data followed a normal distribution. For data not conforming to a normal distribution, the Kruskal-Wallis H test was applied. Pairwise comparisons between groups were performed using the Mann-Whitney U test. A p value of <0.05 was considered statistically significant.

RESULTS

Biochemical Analyses

MDA Analysis

The highest mean MDA levels were observed in the SMA I/R group, while significantly lower levels were found in the Sesamin + SMA I/R group (1.36±0.19 and 1.11±0.08, respectively; p=0.002) (Table 1).

TAS and TOS Values Analysis

There was no significant difference in TAS values among the groups (p>0.05).

The highest TOS values were observed in the SMA I/R group, while significantly lower values were recorded in the Sesamin + SMA I/R group (125.20±57.75 vs. 36.14±22.32, p=0.006) (Table 1).

OSI Analysis

No significant differences were found among the groups in the OSI comparison (p>0.05) (Table 1).

Histological Evaluation

Based on the Chiu scoring system, the highest mean tissue

Table 1. Mean ± standard deviation values of statistically analyzed malondialdehyde (MDA), total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress ındex (OSI)

Groups	MDA	TAS	TOS	OSI
G I (n=7): Control	0.91±0.21	0.92±0.25	20.61±12.29	2409.64±1783.88
G II (n=7): SMA I/R	1.36±0.19*	0.99±0.18	125.20±57.75*	12353.14±4787.41
G III (n=7): Sesamin	1.03±0.09	0.87±0.09	17.29±13.58	1835.80±1770.63
G IV (n=7): Sesamin + SMA I/R	1.11±0.08	0.76±0.08	36.14±22.32	4841.55±2634.40

SMA I/R: Superior mesenteric artery ischemia and reperfusion; n: Number of subjects; MDA: Malondialdehyde (µmol/L); TAS: Total antioxidant status (µmol H_2O_2 equivalent/L); TOS: Total oxidant status (mmol Trolox equivalent/L); OSI: Oxidative stress index (AU). Sesamin + SMA I/R *p<0.05.

Table 2. Average±Standard deviation values of statistically analysed Histological and Immunohistochemical damage.

Groups	Histological Damage	Immunohistochemical Damage
G I (n=7): Control	0.14±0.37*	0.01±0.02*
G II (n=7): SMA I/R	4.57±0.53*	1.54±0.32*
G III (n=7): Sesamin	0.14±0.37*	0.02±0.03*
G IV(n=7): Sesamin+ SMA I/R	2.00±0.57	0.74±0.29

SMA I/R: Superior mesenteric artery ischemia and reperfusion; n: Number of subjects. Sesamin + SMA I/R *p<0.05.

damage score was observed in the SMA I/R group. The Sesamin + SMA I/R group had lower damage scores (1.54±0.32 vs. 0.74±0.29, p=0.001) (Table 2).

Microscopic examination under a light microscope revealed normal histological structures in both the Sham and Sesamin groups. The tunica mucosa, submucosa, muscularis, and serosa layers appeared intact and unaffected in these groups. In contrast, the SMA I/R group showed severe disruption of tissue integrity, including reduced villus height, numerous pyknotic cells, congestion, muscular layer damage, and injury to the intestinal glands. In the Sesamin + SMA I/R group, signs of villus regeneration and restoration of the muscular layer were observed. Although mild congestion remained, sesamin demonstrated a protective and reparative effect at the microscopic level (Fig. 1).

Immunohistochemical Evaluation

The highest immunohistochemical scores were observed in the SMA I/R group, while the mean score was lower in the Sesamin + SMA I/R group (4.57±0.53 vs. 2.00±0.57, p=0.002) (Table 2).

Microscopic examination under a light microscope showed generally negative immunoreactivity in both the Sham and Sesamin groups. In contrast, intense Bax-positive expression was observed in the ileum tissues of the SMA I/R group, whereas the expression intensity was reduced in the Sesamin + SMA I/R group (Fig. 1).

DISCUSSION

In mesenteric ischemia, the lack of specific biochemical markers and pathognomonic physical examination findings can lead to misdiagnosis and delays in treatment. Even when a rapid and accurate diagnosis is made, there is no specific treatment currently available. It is well established that tissue damage primarily occurs during reperfusion rather than during ischemia. Parks et al.[24] demonstrated that four hours of ischemia caused less mucosal damage in tissues compared to three hours of ischemia followed by one hour of reperfusion. Reactive oxygen species primary contributors to cellular damage during reperfusion.[25] Lipid peroxidation initiated by ROS disrupts cell membrane structure, leading to cellular damage.[26] Furthermore, lipid peroxidation impairs the function of affected cells.[27] MDA, a byproduct of lipid peroxidation, serves as an indicator of reactive oxygen species. Toxic enzymes released from activated neutrophils during I/R injury further exacerbate tissue damage.[8] However, the body possesses endogenous antioxidant defense systems to counteract the harmful effects of increased ROS levels.[28,29] The degree of ischemia and reperfusion damage in tissues depends on the balance between oxidant and antioxidant substances.[30] However, this system is often insufficient to eliminate the excessive amount of free oxygen radicals generated during reperfusion. As a result, many agents have been tested to reduce reperfusion injury, but the desired success has not yet been achieved.[31]

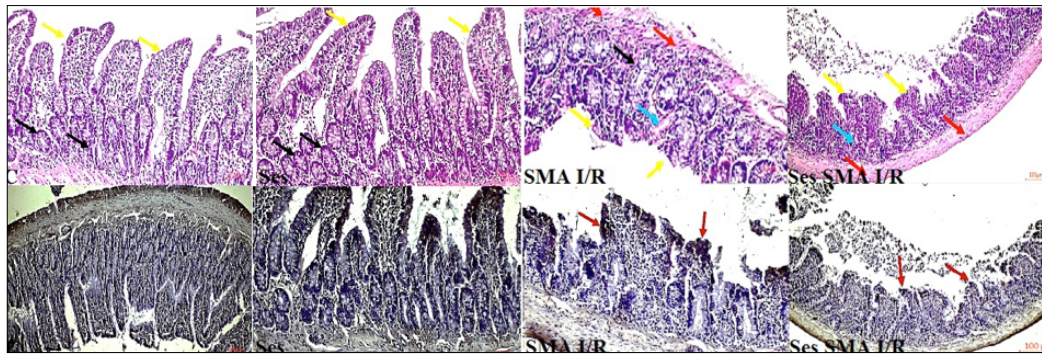

Figure 1. Light microscopic images of ileal tissue micrographs:
• C (Control group): Normal ileum tissue.
• Ses (Sesamin group): Ileum tissue showing intestinal glands (black arrow) and villus tips (yellow arrow).
• SMA I/R (Superior Mesenteric Artery Ischemia and Reperfusion Group): Tissue showing congestion (blue arrow), degeneration at the villus tips (yellow arrow), damage in the muscular layer (red arrow), and degeneration in intestinal glands (black arrow).
• Ses + SMA I/R (Sesamin + Superior Mesenteric Artery Ischemia and Reperfusion Group): Tissue demonstrating regeneration of the muscular layer (red arrow) and reformation and repair of villus tips (yellow arrow), although congestion (blue arrow) is still present (Staining: Hematoxylin & Eosin (H&E); Scale Bar: 50-100 μm).
Second row:
• C (Control group): No Bax-positive expression observed in the ileum tissue.
• Ses (Sesamin group): Very mild Bax-positive expression in the ileum tissue (red arrow).
• SMA I/R (Superior Mesenteric Artery Ischemia and Reperfusion Group): Widespread Bax-positive expression (red arrow).
• Ses + SMA I/R (Sesamin + Superior Mesenteric Artery Ischemia and Reperfusion Group): Milder Bax-positive expression (red arrow) (Staining: Bax immunohistochemistry; Counterstaining: Hematoxylin; Scale Bar: 50-100 μm).

In most models evaluating I/R injury, 60 minutes for ischemia followed by 120 minutes of reperfusion is considered sufficient to induce and assess reperfusion injury.[32] In our study, we applied 60 minutes of ischemia followed by 120 minutes of reperfusion period. Zheng et al.[33] reported that MDA levels increased in intestinal tissue due to lipid peroxidation caused by oxidative damage, while Shen et al.[34] found elevated MDA levels in a group with brain I/R injury. Similarly, Sener et al.[35] reported a significant increase in MDA during ischemia and reperfusion in their study of renal I/R injury. In our rat model of SMA I/R injury, we also observed increased MDA levels, in line with findings from these studies.

Sesamin, the primary active component of sesame oil, is known to have numerous beneficial effects, particularly due to its antioxidant properties.[36] However, studies investigating the protective efficacy of sesamin in ischemia-reperfusion injury are limited. Chang et al.[37] demonstrated the antioxidant and anti-inflammatory effects of sesamin in their study. Khan et al.[38] and Ahmad et al.[39] suggested that sesamin has neuroprotective and antioxidant effects in cerebral I/R injury. Similarly, Utsunomiya et al.[25] also demonstrated the antioxidant properties of sesamin. Akimoto et al.[40] reported that sesamin accelerated recovery in liver injury induced by ethanol toxicity. In parallel with these findings, our study showed that sesamin reduced oxidative stress and increased serum antioxidant levels in SMA I/R injury.

In the early 1990s, a test was developed to measure total antioxidant capacity, referred to as TAS. This test allows for the evaluation of the overall antioxidant capacity of all antioxidants present in a biological sample. Due to the damage caused during ischemia, oxidant levels increase and antioxidant levels decrease, leading to oxidative stress. TAS reflects the overall antioxidant effect in all body fluids, whereas TOS reflects the total oxidant effect.[41] Dobashi et al.[42] showed that antioxidant levels significantly decreased in I/R injury, while Yurtcu et al.[43] found that TAS levels were low and TOS levels were high in ischemia studies. In some experimental studies with sesamin, it was observed that sesamin significantly increased TAS levels after oxidative stress. However, in one renal I/R study, sesamin did not cause a significant change in serum and tissue TAS values.[44] In our study, we found that sesamin significantly reduced serum TOS levels, even when administered over a three-week period prior to SMA I/R.

Chiu et al.[22] developed a scoring system for the histopathologic classification of intestinal I/R injury. In our study, ileum tissue sections obtained from each group were examined under a light microscope after H&E staining, and it was observed that tissue integrity was severely impaired in the SMA I/R group. However, the damage was reduced in the Sesamin + SMA I/R group. The Bax gene, a member of the Bcl-2 family, promotes cell death.[45] In their study, Li et al.[46] reported that the Bcl-2/Bax ratio was significantly decreased in the I/R group compared to the control group. Aslan et al.[47] demonstrated that melatonin increased Bcl-2 levels and significantly decreased Bax levels in a myocardial I/R model. We found that strong Bax-positive expression was common in the ileum tissues of the SMA I/R group, whereas the expression intensity was lower in the group that received sesamin prior to SMA I/R.

CONCLUSION

Sesamin administered prior to AMI reduced oxidative stress parameters, mitigated histopathological changes in ileum tissues, and prevented apoptosis, owing to its antioxidant properties. However, as current studies exploring the protective mechanisms of sesamin against AMI are limited, we recommend further research on this subject.

Acknowledgments: This study was supported by the Dicle University Scientific Research Platform (DÜBAP) under project number TIP. 22.028. The authors gratefully acknowledge the contributions of the DÜBAP.

Ethics Committee Approval: This study was approved by the Dicle University Prof. Dr. Sabahattin Payzın Health Sciences Research and Application Center Animal Experiments Local Ethics Committee (Date: 31.05.2022, Decision No: 2022/25).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: O.H., K.M.T., Y.E., A.M.; Design: O.H., K.M.T., Y.E.; Supervision: O.H., K.M.T.; Resource: O.H., K.M.T., Y.E., A.M.; Materials: Y.E., A.M.; Data Collection and/or Processing: O.H., K.M.T.; Analysis and/or Interpretation: O.H., K.M.T., Y.E., A.M.; Literature Review: O.H., K.M.T., Y.E., A.M.; Writing: O.H., K.M.T., Y.E., A.M.; Critical Review: O.H., K.M.T., Y.E., A.M.

Conflict of Interest: None declared.

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

REFERENCES

1. Levy PJ, Krausz MM, Manny J. Acute mesenteric ischemia: Improved results—a retrospective analysis of ninety-two patients. Surgery 1990;372–80. [CrossRef]
2. Schwartz L, Gewertz B. Mesenteric ischemia. Surg Clin North Am 1997;77:275—502. [CrossRef]
3. Wilson C, Gupta R, Gilmour DG, Imrie CW. Acute superior mesenteric ischaemia. Br J Surg 1987;74:279–81. [CrossRef]
4. Kazmers A. Operative management of acute mesenteric ischemia. Part 1. Ann Vasc Surg 1998;12:187–97. [CrossRef]
5. Aydın İ, Yücel AF, Pergel A, Karakaya A, Oğullar S, Şahin DA, et al. Acute mesenteric arterial embolus: Early diagnosis and embolectomy. Kocatepe Med J 2024;17:69–71. [CrossRef]
6. Sitges-Serra A, Mas X, Roqueta F, Figueras J, Sanz F. Mesenteric infarction: An analysis of 83 patients with prognostic studies in 44 cases undergoing a massive small-bowel resection. Br J Surg 1988;75:544–8. [CrossRef]
7. Tapuria N, Kumar Y, Habib MM, Abu Amara M, Seifalian AM, Davidson BR. Remote ischemic preconditioning: A novel protective method from ischemia reperfusion injury--A review. J Surg Res 2008;150:304–30. [CrossRef]
8. Mallick IH, Yang W, Winslet MC, Seifalian AM. Ischemia-reperfusion injury of the intestine and protective strategies against injury. Dig Dis Sci 2004;49:1359–77. [CrossRef]
9. Grootjans J, Lenaerts K, Buurman WA, Dejong CH, Derikx JP. Life and death at the mucosal-luminal interface: New perspectives on human intestinal ischemia-reperfusion. World J Gastroenterol 2016;22:2760–70. [CrossRef]
10. Quesnelle KM, Bystrom PV, Toledo-Pereyra LH. Molecular responses to ischemia and reperfusion in the liver. Arch Toxicol 2015;89:651–7. [CrossRef]
11. Matsuyama M, Yoshimura R, Hase T, Kawahito Y, Sano H, Nakatani T. Study of cyclooxygenase-2 in renal ischemia-reperfusion injury. Transplant Proc 2005;37:370–2. [CrossRef]
12. Zhao Y, Li S, Childs EE, Kuharsky DK, Yin XM. Activation of pro-death Bcl-2 family proteins and mitochondria apoptosis pathway in tumor necrosis factor-alpha-induced liver injury. J Biol Chem 2001;276:27432–40. [CrossRef]
13. Latha RC, Daisy P. Insulin-secretagogue, antihyperlipidemic and other protective effects of gallic acid isolated from terminalia bellerica roxb. in streptozotocin-induced diabetic rats. Chem Biol Interact 2011;189:112–8. [CrossRef]
14. Bedigian D, Harlan JR. Evidence for cultivation of sesame in the ancient world. Econ Bot 1986;40:137–54. [CrossRef]
15. Liu CM, Zheng GH, Ming QL, Chao C, Sun JM. Sesamin protects mouse liver against nickel-induced oxidative DNA damage and apoptosis by the PI3K-Akt pathway. J Agric Food Chem 2013;61:1146–54. [CrossRef]
16. Abou-Gharbia HA, Shahidi F, Shehata AAY, Youssef MM. Oxidative stability of extracted sesame oil from raw and processed seeds. J Food Lipids 1996;3:59–72. [CrossRef]
17. Ghaderi S, Rashno M, Nesari A, Khoshnam SE, Sarkaki A, Khorsandi L, et al. Sesamin alleviates diabetes-associated behavioral deficits in rats: The role of inflammatory and neurotrophic factors. Int Immunopharmacol 2021;92:107356. [CrossRef]
18. Bozkurt G. Susam yağının antioksidan özellikteki başlıca bileşenlerinin nitelik ve nicelikleri üzerine araştırmalar. [Master's Thesis]. Ege Üniversitesi; 2006. [CrossRef]
19. Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem 2005;38:1103–11. [CrossRef]
20. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Clin Biochem 2004;37:112–9. [CrossRef]
21. Tüfek A, Tokgöz O, Aliosmanoglu I, Alabalik U, Evliyaoglu O, Çiftçi T, et al. The protective effects of dexmedetomidine on the liver and remote organs against hepatic ischemia reperfusion injury in rats. Int J Surg 2013;11:96–100. [CrossRef]
22. Chiu CJ, McArdle AH, Brown R, Scott HJ, Gurd FN. Intestinal mucosal lesion in low-flow states. I. A morphological, hemodynamic, and metabolic reappraisal. Arch Surg 1970;101:478–83. [CrossRef]
23. Erdogan MA, Yalcin A. Protective effects of benfotiamine on irisin activity in methotrexate-induced liver injury in rats. Arch Med Sci 2018;16:205–11. [CrossRef]
24. Parks DA, Granger DN. Contributions of ischemia and reperfusion to mucosal lesion formation. Am J Physiol 1986;250:G749–53. [CrossRef]
25. Utsunomiya T, Shimada M, Rikimaru T, Hasegawa H, Yamashita Y, Hamatsu T, et al. Antioxidant and anti-inflammatory effects of a diet supplemented with sesamin on hepatic ischemia-reperfusion injury in rats. Hepatogastroenterology 2003;50:1609–13. [CrossRef]
26. Gülçin İ. Antioxidant activity of food constituents: An overview. Arch Toxicol 2012;86:345–91. [CrossRef]
27. Moslen MT. Reactive oxygen species in normal physiology, cell injury and phagocytosis. Adv Exp Med Biol 1994;366:17–27. [CrossRef]
28. Gülünç İ. Antioxidant properties of resveratrol: A structure-activity insight. Innov Food Sci Emerg Technol 2010;11:210–8. [CrossRef]
29. Ercan G, İlbar Tartar R, Solmaz A, Gulcicek OB, Karagulle OO, Meric S, et al. Examination of protective and therapeutic effects of ruscogenin on cerulein-induced experimental acute pancreatitis in rats. Ann Surg Treat Res 2019;97:271–81. [CrossRef]
30. Onder A, Kapan M, Gümüş M, Yüksel H, Böyük A, Alp H, et al. The protective effects of curcumin on intestine and remote organs against mesenteric ischemia/reperfusion injury. Turk J Gastroenterol 2012;23:141–7. [CrossRef]

31. Yildiz Y, Kose H, Cecen S, Ergin K, Demir EM, Serter M. Protective effects of leflunomide on intestinal ischemia-reperfusion injury: Leflunomide against intestinal ischemia-reperfusion. Dig Dis Sci 2010;55:245–52. [CrossRef]
32. Zhang W, Zhu W, Zhang J, Li N, Li J. Protective effects of glucagon-like peptide 2 on intestinal ischemia-reperfusion rats. Microsurgery 2008;28:285–90. [CrossRef]
33. Zheng X, Mao Y, Cai J, Li Y, Liu W, Sun P, et al. Hydrogen-rich saline protects against intestinal ischemia/reperfusion injury in rats. Free Radic Res 2009;43:478–84. [CrossRef]
34. Shen H, Kuo CC, Chou J, Delvolve A, Jackson SN, Post J, et al. Astaxanthin reduces ischemic brain injury in adult rats. FASEB J 2009;23:1958–68. [CrossRef]
35. Sener G, Sener E, Sehirli O, Oğünç AV, Cetinel S, Gedik N, et al. Ginkgo biloba extract ameliorates ischemia reperfusion-induced renal injury in rats. Pharmacol Res 2005;52:216–22. [CrossRef]
36. Ikeda T, Nishijima Y, Shibata H, Kiso Y, Ohnuki K, Fushiki T, et al. Protective effect of sesamin administration on exercise-induced lipid peroxidation. Int J Sports Med 2003;24:530–4. [CrossRef]
37. Chang CY, Chen YL, Yang SC, Huang GC, Tsi D, Huang CC, et al. Effect of schisandrin B and sesamin mixture on CCl(4)-induced hepatic oxidative stress in rats. Phytother Res 2009;23:251–6. [CrossRef]
38. Khan MM, Ishrat T, Ahmad A, Hoda MN, Khan MB, Khuwaja G, et al. Sesamin attenuates behavioral, biochemical and histological alterations induced by reversible middle cerebral artery occlusion in the rats. Chem Biol Interact 2010;183:255–63. [CrossRef]
39. Ahmad S, Yousuf S, Ishrat T, Khan MB, Bhatia K, Fazli IS, et al. Effect of dietary sesame oil as antioxidant on brain hippocampus of rat in focal cerebral ischemia. Life Sci 2006;79:1921–8. [CrossRef]
40. Akimoto K, Kitagawa Y, Akamatsu T, Hirose N, Sugano M, Shimizu S, et al. Protective effects of sesamin against liver damage caused by alcohol or carbon tetrachloride in rodents. Ann Nutr Metab 1993;37:218–24. [CrossRef]
41. Aslan R, Kutlu R, Civi S, Tasyurek E. The correlation of the total antioxidant status (TAS), total oxidant status (TOS) and paraoxonase activity (PON1) with smoking. Clin Biochem 2014;47:393–7. [CrossRef]
42. Dobashi K, Ghosh B, Orak JK, Singh I, Singh AK. Kidney ischemia-reperfusion: Modulation of antioxidant defenses. Mol Cell Biochem 2000;205:1–11. [CrossRef]
43. Yurtcu E, Togrul C, Ozyer S, Uzunlar O, Karatas YH, Seckin KD, et al. Dose dependent protective effects of vardenafil on ischemia-reperfusion injury with biochemical and histopathologic evaluation in rat ovary. J Pediatr Surg 2015;50:1205–9. [CrossRef]
44. Zhang JX, Yang JR, Chen GX, Tang LJ, Li WX, Yang H, et al. Sesamin ameliorates arterial dysfunction in spontaneously hypertensive rats via downregulation of NADPH oxidase subunits and upregulation of eNOS expression. Acta Pharmacol Sin 2013;34:912–20. [CrossRef]
45. Wei MC, Zong WX, Cheng EH, Lindsten T, Panoutsakopoulou V, Ross AJ, et al. Proapoptotic BAX and BAK: A requisite gateway to mitochondrial dysfunction and death. Science 2001;292:727–30. [CrossRef]
46. Li J, Hu HP, Li Y, Shao W, Zhang JZ, Wang LM. Influences of remifentanil on myocardial ischemia-reperfusion injury and the expressions of Bax and Bcl-2 in rats. Eur Rev Med Pharmacol Sci 2018;22:8951–60. [CrossRef]
47. Aslan G, Gül HF, Şahna E, Önalan E. Melatonin may regulate apoptotic pathway via affecting Bax, Bcl2I1, and XIAP levels in myocardial ischemia-reperfusion injury. Firat Med J 2021;25:111–6. [CrossRef]

DENEYSEL ÇALIŞMA - *ÖZ*

Sıçanlarda oluşturulan süperior mezenterik arter iskemisinde sesamin'in ileum üzerindeki koruyucu etkinliği

AMAÇ: Akut mezenterik arter iskemi yaşla birlikte insidansı artan mortalite ve morbidite nedenlerinden biri olarak görülmektedir. Bu çalışmada süperior mezenter arter (SMA) iskemi ve reperfüzyonuna (I/R) bağlı ileumda gelişen histolojik, immünolojik ve biyokimyasal hasarın giderilmesinde sesamin'in etkinliği incelenecektir.

GEREÇ VE YÖNTEM: Çalışmada 28 adet, Sprague-Dawley cinsi sıçan kullanıldı. Sıçanlar rastgele seçilip eşit 4 gruba ayrıldı. Grup I (Sham/Kontrol grubu), grup II (SMA I/R grubu); % 0.5 karboksimetil selüloz 3 hafta süreyle 1 ml/kg dozdan gavaj yoluyla peroral (p.o.) verildi. Üçüncü haftanın sonunda 60 dk iskemi ve 120 dk reperfüzyon uygulandı. Grup III (Sesamin grubu); sesamin 3 hafta süreyle 30 mg/kg dozdan gavaj yoluyla peroral verildi. Grup IV (Sesamin+SMA I/R grubu) olarak belirlendi.

BULGULAR: Serum malondialdehit (MDA) düzeyleri en yüksek SMA I/R grubunda görülürken, sesamin+SMA I/R grubunda ortalamanın daha düşük olduğu izlendi ($p<0.05$). Serum total oksidan seviyelerini (TOS) karşılaştırdığımızda yine sesamin+SMA I/R grubunun ortalaması SMA I/R grubundan daha düşük hesaplandı ($p<0.05$). Bulgularımıza paralel şekilde proapoptotik faktör olan Bax ekspresyonların SMA I/R grubuna kıyasla sesamin+SMA I/R grubunda daha az yoğunlukta olduğu izlendi.

SONUÇ: Histolojik, immünohistokimyasal ve biyokimyasal parametreler doğrultusunda yapılan araştırmamızda sesamin'in SMA I/R öncesinde uygulanması, oluşan oksidatif hasarın giderilmesine ve histolojik değişikliklerin önlenmesine karşın etkin olduğu görülmektedir.

Anahtar sözcükler: İskemi ve reperfüzyon; sesamin; oksidatif stres; apoptozis.

Ulus Travma Acil Cerrahi Derg 2025;31(4):317-323 DOI: 10.14744/tjtes.2025.97340