

The Effect of Cinnarizine Pretreatment on Gastric Ischemia-Reperfusion-Induced Oxidative Damage in Rats

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ABSTRACT

Objective: Gastric ischemia-reperfusion (I/R) injury is a significant clinical condition occurring in settings such as peptic ulcer bleeding, hemorrhagic shock, and surgery. Its pathogenesis involves oxidative imbalance and increased intracellular calcium. Cinnarizine, a calcium channel blocker with antioxidant properties, may exert protective effects. This study investigated the effect of cinnarizine pretreatment on gastric I/R injury.

Methods: Twenty-four male Wistar albino rats were randomly allocated to four groups (n=6): healthy group (HG), sham-operated (SOG), gastric I/R (GIR), and cinnarizine + I/R (C+GIR). The C+GIR group received cinnarizine orally at 10 mg/kg. One hour later, the SOG, GIR, and C+GIR groups were anesthetized with thiopental sodium (25 mg/kg, intraperitoneally). Access to the stomach was achieved via a ~2-2.5 cm midline laparotomy. In the GIR and C+GIR groups, the celiac artery was temporarily occluded to induce 1 hour of ischemia, whereas the SOG underwent no clamping. Reperfusion lasted 3 hours. Euthanasia was performed using thiopental sodium (50 mg/kg, intraperitoneally) and gastric tissues were subsequently excised. These tissues were assessed for malondialdehyde (MDA), total glutathione (tGSH), superoxide dismutase (SOD), and catalase (CAT) levels.

Results: The GIR group demonstrated significantly elevated MDA levels and decreased levels of tGSH, SOD, and CAT compared with the HG group (p<0.001). Conversely, pretreatment with cinnarizine in the C+GIR group markedly lowered MDA levels while maintaining tGSH levels and SOD and CAT activities (p<0.001).

Conclusion: Cinnarizine pretreatment may protect gastric tissue against I/R-induced oxidative damage by preserving redox balance.

Keywords: Cinnarizine, ischemia-reperfusion, oxidative stress, antioxidant

INTRODUCTION

Gastric ischemia-reperfusion (I/R)-induced injury is a clinically significant condition encountered in various pathological and surgical contexts, including peptic ulcer disease, severe blood loss, operative procedures.¹ I/R injury has been described as a stepwise process that begins with hypoxic damage and is exacerbated by the overproduction of reactive oxygen species

(ROS).² Reduced or interrupted blood flow causes cells to shift toward anaerobic metabolism to produce adenosine triphosphate (ATP), resulting in intracellular acidosis and energy depletion.^{2,3} In addition, impairment of ATPase-dependent ion transport disrupts intracellular calcium (Ca²⁺) homeostasis, leading to Ca²⁺ overload.³ Elevated intracellular Ca²⁺ levels are closely associated with the activation of



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apoptotic signaling pathways, Ca^{2+} -dependent proteolytic enzymes, and ultimately cellular injury.^{2,4,5} Reperfusion, although essential for restoring oxygen supply to ischemic tissues, paradoxically exacerbates tissue damage.⁶ This phenomenon is largely attributed to the accumulation of hypoxanthine and xanthine oxidase during the ischemic phase.² Upon reperfusion, tissue reoxygenation activates xanthine oxidase-mediated metabolism of hypoxanthine, resulting in excessive ROS production.^{3,7} When ROS generation exceeds the capacity of endogenous antioxidant defense systems, oxidative stress develops.⁶ Consequently, excessive ROS targets various biomolecules, including membrane lipids, proteins, and deoxyribonucleic acid, leading to cellular damage.⁶ Experimental studies have demonstrated increased levels of the oxidant marker malondialdehyde (MDA) and a decline in endogenous antioxidant defenses, such as glutathione (GSH) and superoxide dismutase (SOD), in gastric tissues exposed to I/R injury in rats.^{1,8} Previous research has reported that gastric I/R injury is associated with elevated intracellular Ca^{2+} levels, which contribute to the development of acute mucosal lesions.⁹ Given the underlying mechanisms of I/R injury, current evidence suggests that pharmacological agents possessing antioxidant and Ca^{2+} channel-blocking activities may confer protection against gastric damage induced by I/R. Cinnarizine, a piperazine-based compound examined in this study for gastric I/R-related effects, possesses antihistaminic, antioxidant, antiserotonergic, antidopaminergic, and Ca^{2+} channel-blocking properties.¹⁰ It is used primarily to treat nausea, vomiting, and vertigo associated with vestibular disorders.^{10,11} Experimental trials have indicated that cinnarizine exerts protective effects against oxidative stress by limiting MDA elevation and preserving GSH levels in various tissues.¹² Accumulating evidence indicates that lipophilic Ca^{2+} channel blockers, such as cinnarizine, may inhibit lipid peroxidation in cellular membranes.^{11,13} In addition, cinnarizine has been reported to prevent oxidative cell death by inhibiting intracellular Ca^{2+} influx.¹³ Moreover, it has been shown to reduce indomethacin-induced gastric lesions by improving mucosal blood flow.¹⁴ These findings suggest that cinnarizine may have therapeutic or preventive effects against I/R-induced gastric injury. Despite the growing interest in pharmacological modulation of ischemia-reperfusion injury, no direct evidence is available regarding the effects of cinnarizine in gastric I/R models. For this reason, we aimed to examine the effect of cinnarizine pretreatment on the extent of gastric damage induced by I/R.

MAIN POINTS

- Gastric ischemia-reperfusion (I/R) increased malondialdehyde and decreased total glutathione, superoxide dismutase and catalase levels.
- Cinnarizine pretreatment attenuated oxidative stress in gastric I/R.
- Cinnarizine preserved the endogenous antioxidant defense system.
- Cinnarizine may have therapeutic potential against gastric I/R injury.

MATERIALS AND METHODS

Animals

A total of twenty-four male Wistar albino rats (250-270 g) were procured from the Experimental Animals Application and Research Center of Erzincan Binali Yıldırım University, Türkiye. Before experimental procedures, all animals were maintained under standardized laboratory conditions and subjected to a 7-day acclimatization period to minimize environmental stress. After adaptation, rats were randomly assigned to four groups. Throughout the study, animals were housed under controlled environmental conditions, including a temperature of 22 ± 2 °C, relative humidity of 45-65%, and a 12-hour light/dark cycle. Standard laboratory chow and tap water were supplied ad libitum. All experimental procedures were carried out in the same institutional animal research facility. All experimental procedures were carried out following approval from the Erzincan Binali Yıldırım University Local Ethics Committee for Animal Experiments (date: 25.12.2025, decision no.: 66).

Experimental Groups

An equal number of rats ($n = 6$) were randomly assigned to each of the four experimental groups: healthy group (HG), sham-operated group (SOG), I/R group (GIR), and cinnarizine-pretreated GIR (C+GIR).

Chemicals

Cinnarizine (Nobel Pharmaceuticals, Düzce, Türkiye) and thiopental sodium (I.E. Ulagay, İstanbul, Türkiye) were used in this study.

Experimental Design

Prior to the experimental procedures, all rats were fasted for 12 hours with free access to water. After completion of the fasting period, animals in the C+IRG group received cinnarizine (10 mg/kg) by oral gavage. The dose of cinnarizine was determined based on previously published studies in rats demonstrating its gastroprotective effects.¹⁴ The HG, SOG, and GIR groups each received equivalent volumes of physiological saline via the same route. One hour after administration of cinnarizine or physiological saline, rats in the SOG, GIR, and C+GIR groups were anesthetized with thiopental sodium (25 mg/kg, intraperitoneally). Under anesthesia, a 2-2.5 cm midline abdominal incision was made to access the stomach. Meanwhile, in the SOG group, no manipulation of the celiac artery was performed, and the surgical incision was closed with sutures. In the GIR and C+GIR groups, following the 1-hour ischemic period, the vascular clips were removed, and a 3-hour reperfusion phase was initiated in the gastric tissue.¹ Upon completion of the protocol, all animals were euthanized by intraperitoneal injection of a lethal dose of thiopental sodium (50 mg/kg). Levels of MDA, tGSH, SOD, and catalase (CAT) were determined in the harvested tissues.

Biochemical Analyses

Sample Preparation

Gastric samples were rapidly frozen in liquid nitrogen and pulverized to obtain a fine powder. The powdered tissues were homogenized on ice in 50 mM phosphate buffer (pH 7.4) using a 1:10 (w/v) dilution. Subsequently, centrifugation was carried out at $10,000 \times g$ for 10 minutes under refrigerated conditions (4°C). Following centrifugation, the supernatants were carefully collected and stored for biochemical analyses. Prior to analysis, all samples were stored at -80°C .

Analysis of MDA, tGSH, SOD, and CAT in Gastric Tissues

Gastric tissue levels of MDA (Cat. No. 10009055), GSH (Cat. No. 703002), and SOD (Cat. No. 706002) were measured using rat-specific enzyme-linked immunosorbent assay kits obtained from Cayman Chemical Company (Ann Arbor, MI, USA). All experimental procedures were performed in strict accordance with the manufacturer's guidelines. CAT activity in tissue samples was determined spectrophotometrically following the method described by Góth.¹⁵ The Bradford¹⁶ technique was employed to quantify total protein levels in the tissues for normalization purposes.

Statistical Analysis

Data analysis was carried out using IBM SPSS Statistics (version 27, IBM Corp., Armonk, NY, USA), while graphical outputs were prepared with GraphPad Prism (version 9, GraphPad Software, San Diego, CA, USA). Results are expressed as mean $\pm$ standard deviation. Prior to statistical comparisons, the data distribution was evaluated using the Shapiro-Wilk test to verify normality. Since all variables met the assumption of normality, intergroup differences were examined using One-Way analysis of variance. The assumption of homogeneity of variance was checked with Levene's test, and multiple comparisons were subsequently performed using Tukey's post-hoc test. Statistical significance was defined at a threshold of $P < 0.05$.

RESULTS

Analysis of MDA Levels in Gastric Tissues

HG and SOG exhibited comparable MDA levels, with no statistically significant difference (Figure 1, Table 1; $P = 0.944$). In contrast, MDA levels were significantly elevated in the GIR

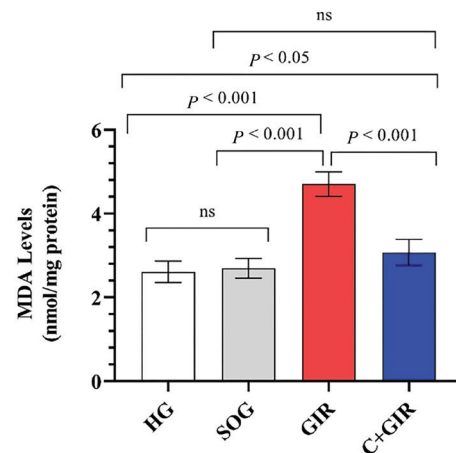


Figure 1. Effects of cinnarizine on MDA levels in gastric I/R injury. Bars represent mean $\pm$ standard deviation, $n = 6$ /each group. Statistical analysis was performed using One-Way ANOVA followed by Tukey's HSD post-hoc test. A P value < 0.05 was considered statistically significant.

Ns, non-significant; MDA, malondialdehyde; HG, healthy control; SOG, sham-operated group; GIR, ischemia-reperfusion group; C+GIR, cinnarizine pretreated ischemia-reperfusion group; I/R, ischemia-reperfusion.

compared with those in both the HG and SOG ($P < 0.001$). On the other hand, cinnarizine pretreatment in the C+GIR significantly attenuated the I/R-induced increase in MDA levels ($P < 0.001$). Following cinnarizine pretreatment, MDA levels in the C+GIR approached those observed in the HG ($P = 0.042$) and the SOG ($P = 0.125$).

Analysis of tGSH Levels in Gastric Tissues

As presented in Figure 2 and Table 1, no significant difference in tGSH levels was observed between the HG and SOG ($P = 0.445$). A marked reduction in tGSH content was observed in the GIR compared with both control groups (HG and SOG) ($P < 0.001$). Cinnarizine pretreatment effectively counteracted this ischemia-reperfusion-induced depletion of tGSH ($P < 0.001$). In the C+GIR group, tGSH values were restored toward those of the HG ($P = 0.092$) and SOG ($P = 0.768$).

Table 1. Effects of Cinnarizine on Oxidative Stress Parameters in Gastric Ischemia-Reperfusion Injury

Biochemical Variables		Experimental groups (n=6 /each group)			
		HG	SOG	GIR	C + GIR
		Mean ± SD			
Gastric tissues	MDA (nmol/mg protein)	2.61 ± 0.26 ^a	2.70 ± 0.24 ^{ac}	4.70 ± 0.29 ^b	3.07 ± 0.31 ^c
	tGSH (nmol/mg protein)	5.61 ± 0.42 ^a	5.34 ± 0.22 ^a	2.53 ± 0.21 ^b	5.17 ± 0.33 ^a
	SOD (U/mg protein)	6.80 ± 0.30 ^a	6.55 ± 0.37 ^a	2.89 ± 0.29 ^b	5.44 ± 0.30 ^c
	CAT (U/mg protein)	5.96 ± 0.27 ^a	5.84 ± 0.20 ^a	3.62 ± 0.26 ^b	5.32 ± 0.22 ^c

^{a, b, c}: Within the same row, groups sharing the same letter are not significantly different ($P > 0.05$), whereas groups with different letters differ significantly ($P < 0.05$). Statistical analysis was performed using One-Way ANOVA followed by Tukey's HSD post-hoc test. A P value < 0.05 was considered statistically significant.

SD, standard deviation; MDA, malondialdehyde; tGSH, total glutathione; SOD, superoxide dismutase; CAT, catalase; HG, healthy control; SOG, sham-operated group; GIR, ischemia-reperfusion group; C+GIR, cinnarizine pretreated ischemia-reperfusion group.

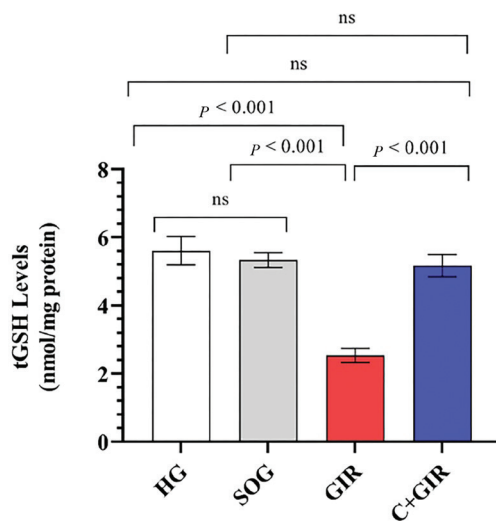


Figure 2. Effects of cinnarizine on tGSH levels in gastric I/R Injury. Bars represent mean $\pm$ standard deviation, $n = 6$ /each group. Statistical analysis was performed using One-Way ANOVA followed by Tukey's HSD post-hoc test. A P value < 0.05 was considered statistically significant.

ns, non-significant; tGSH, total glutathione; HG, healthy control; SOG, sham-operated group; GIR, ischemia-reperfusion group; C +GIR, cinnarizine pretreated ischemia-reperfusion group; I/R, ischemia-reperfusion.

Analysis of SOD and CAT Activities in Gastric Tissues

As shown in Figure 3A-B and Table 1, no statistically significant differences in SOD ($P = 0.542$) or CAT ($P = 0.845$) activities were observed between the HG and SOG. In contrast, both SOD and CAT were reduced in the GIR compared with the HG and SOG

($P < 0.001$). Cinnarizine pretreatment markedly attenuated this I/R-induced decline, leading to a significant improvement in antioxidant enzyme activities ($P < 0.001$). However, SOD and CAT in the C+GIR still differed significantly from those observed in the HG and SOG ($P < 0.05$).

DISCUSSION

In rats subjected to gastric I/R injury, the effect of cinnarizine on tissue protection was examined. Exposure to I/R alone resulted in higher MDA levels in gastric tissue, whereas tGSH content and activities of SOD and CAT were markedly reduced. These alterations indicate enhanced lipid peroxidation and suppression of the endogenous antioxidant defense system. In the cinnarizine + I/R group, oxidative stress-related alterations were substantially mitigated. Although both groups underwent the same ischemic insult, lower levels of oxidative damage markers were observed in the cinnarizine-treated group, suggesting a potential protective effect against I/R-induced tissue injury.

The findings of the current trial indicate that oxidative stress plays a central role in the development of gastric I/R injury. In tissues exposed to I/R, excessive ROS production occurs during both ischemia and, particularly, during reperfusion. This leads to the activation of lipid peroxidation, ultimately resulting in the disruption of cellular membrane integrity.¹⁷ MDA, a key end product of lipid peroxidation, is closely associated with cellular damage and cell death. Previous studies have demonstrated increased MDA levels in gastric tissues affected by I/R injury.^{8,18} I/R-induced augmentation of MDA levels in gastric tissues was confirmed, whereas cinnarizine treatment significantly suppressed this increase. To the best of our knowledge, The impact of cinnarizine on gastric MDA levels has not been directly addressed in the literature. However, cinnarizine has

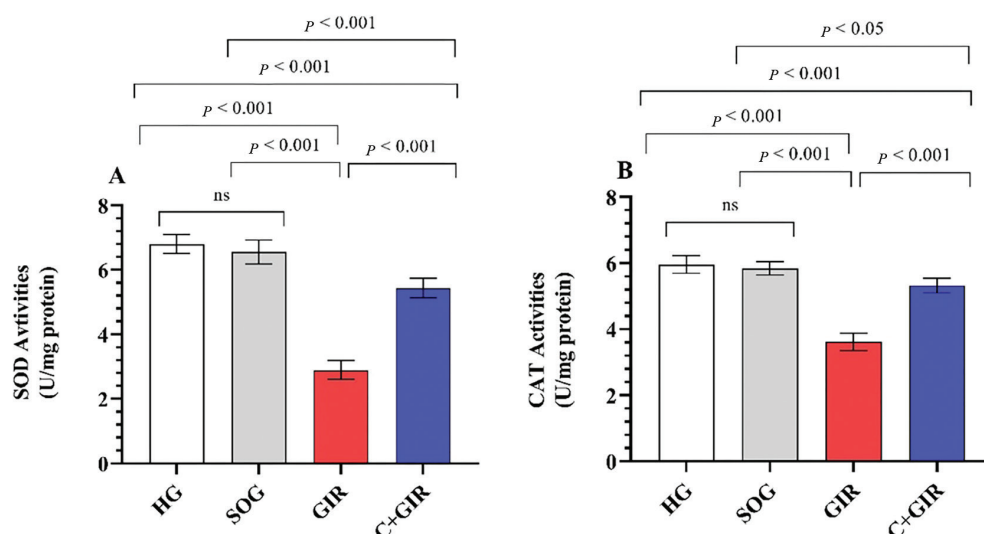


Figure 3A, B. Effects of cinnarizine on SOD and CAT activities in gastric I/R Injury. Bars represent mean $\pm$ standard deviation, $n = 6$ /each group. Statistical analysis was performed using one-way ANOVA followed by Tukey's HSD post-hoc test. A P value < 0.05 was considered statistically significant.

ns, non-significant; SOD, superoxide dismutase; CAT, catalase; HG, healthy control; SOG, sham-operated group; GIR, ischemia-reperfusion group; C +GIR, cinnarizine pretreated ischemia-reperfusion group; I/R, ischemia-reperfusion.

been reported to significantly reduce naphthalene-induced increases in MDA levels in liver and lung tissues as well as in plasma.¹⁹ The extent of tissue injury and the maintenance of cellular viability during I/R exposure largely depend on the capacity of endogenous antioxidant defense systems. When the excessive production of ROS cannot be adequately neutralized by antioxidant mechanisms, oxidative stress develops, leading to subsequent cellular damage.²⁰ Therefore, in the present study, gastric tissues were also evaluated for endogenous antioxidants, including tGSH, SOD, and CAT.

GSH is a major endogenous antioxidant synthesized in mammalian cells.⁸ It contributes to the maintenance of cellular redox homeostasis by directly reacting with ROS and serving as a cofactor in antioxidant enzyme systems.²¹ Previous studies have reported that I/R injury induces a marked reduction in GSH levels in gastric tissues as a consequence of increased oxidative stress and excessive ROS production.^{7,8} In the present study, gastric tGSH levels were significantly decreased following I/R, whereas cinnarizine treatment effectively prevented this decline. Despite the lack of direct evidence regarding the effects of cinnarizine on gastric GSH levels, cinnarizine has been reported to reverse GSH depletion in lung tissue in an experimental model of asthma, supporting its modulatory role in antioxidant defense systems.²²

Gastric tissues were further evaluated for SOD and CAT activities. SOD and CAT are sequential and complementary antioxidant enzymes. SOD acts on superoxide radicals by converting them into hydrogen peroxide and oxygen. This intermediate is subsequently broken down by CAT into water and oxygen, thereby preventing the generation of highly reactive hydroxyl radicals.²³ Experimental studies have shown that gastric I/R injury significantly reduces SOD and CAT activities, thereby weakening the antioxidant defense capacity of the tissue against oxidative stress.^{1,24} Consistent with the literature, the present findings demonstrated a decrease in SOD and CAT following I/R in gastric tissues. However, cinnarizine pretreatment appeared to be effective in preserving SOD and CAT activities despite I/R exposure. Existing literature indicates that no studies have evaluated the effects of cinnarizine on gastric SOD and CAT activities. Nevertheless, cinnarizine has been reported to prevent the reduction in SOD activity in lung tissue in an experimental model of asthma.²² In addition, flunarizine, a Ca²⁺ channel antagonist, has been shown to significantly attenuate I/R-induced reductions in gastric SOD activity. Its gastroprotective effect has been associated with its antioxidant properties and inhibition of cytoplasmic Ca²⁺ accumulation.²⁵

Study Limitations

This study has several limitations. Inflammatory cytokines, apoptotic markers, mitochondrial function parameters, and molecular Ca²⁺-signaling pathways were not evaluated. The absence of histopathological assessment is another limitation of this study. Furthermore, the use of a single dose and a single reperfusion time point limits the ability to determine dose-response relationships and time-dependent effects. Future studies employing different doses and varying reperfusion

durations may provide further insight into the optimal protective dose range of cinnarizine and the temporal profile of its effects.

CONCLUSION

A rat model of gastric I/R injury was used to investigate the protective effects of cinnarizine. The findings demonstrated that exposure to I/R resulted in a significant increase in the oxidant marker MDA in gastric tissues, accompanied by a marked reduction in key components of the endogenous antioxidant defense system, namely tGSH, SOD, and CAT. In contrast, cinnarizine-treated rats exhibited a significant attenuation of the I/R-induced increase in MDA levels and substantially prevented decreases in tGSH, SOD, and CAT activities. These results indicate that cinnarizine is effective in reducing oxidative stress and supporting the endogenous antioxidant defense system in gastric I/R injury.

Ethics

Ethics Committee Approval: All experimental procedures were carried out following approval by the Erzincan Binali Yıldırım University Local Ethics Committee for Animal Experiments (decision no.: 66, date: 25.12.2025).

Informed Consent: Since this is an animal experiment study, patient consent is not required.

Footnotes

Author Contributions: Concept Design – S.B., H.S.; Data Collection or Processing – S.B., T.A.Ç.; Analysis or Interpretation – S.B., T.A.Ç.; Literature Review – S.B., Z.S.; Writing, Reviewing and Editing – S.B., Z.S., H.S.

Declaration of Interests: The authors declare no conflict of interest.

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REFERENCES

1. Kuyruklyildiz U, Delen LA, Onk D, Yazici GN, Gulaboglu M, Suleyman H. The effect of dexmedetomidine on gastric ischemia reperfusion injury in rats. *Biochemical and histopathological evaluation. Acta Cir Bras.* 2021;36(1):e360104. [\[CrossRef\]](#)
2. Yapca OE, Borekci B, Suleyman H. Ischemia-reperfusion damage. *Eurasian J Med.* 2013;45(2):126-127. [\[CrossRef\]](#)
3. Kalogeris T, Baines CP, Krenz M, Korthuis RJ. Ischemia/reperfusion. *Compr Physiol.* 2016;7(1):113-170. [\[CrossRef\]](#)
4. Orrenius S, Burkitt MJ, Kass GE, Dypbukt JM, Nicotera P. Calcium ions and oxidative cell injury. *Ann Neurol.* 1992;32:S33-42. [\[CrossRef\]](#)
5. Ajike RA, Ajayi AF, Oyekunle OS, et al. Potential therapeutic targets in the prevention of testicular ischemia-reperfusion injury. *Front Reprod Health.* 2025;7:1706914. [\[CrossRef\]](#)
6. Jurcau A, Ardelean IA. Molecular pathophysiological mechanisms of ischemia/reperfusion injuries after recanalization therapy for acute ischemic stroke. *J Integr Neurosci.* 2021;20(3):727-744. [\[CrossRef\]](#)
7. Koç A, Kuyruklyildiz U, Gazi M, et al. The effects of sugammadex on gastric ischemia-reperfusion injury in rats: biochemical and

- histopathological evaluation. *Gen Physiol Biophys*. 2023;42(1):67-75. [\[CrossRef\]](#)
8. Cui J, Liu L, Zou J, et al. Protective effect of endogenous hydrogen sulfide against oxidative stress in gastric ischemia-reperfusion injury. *Exp Ther Med*. 2013;5(3):689-694. [\[CrossRef\]](#)
9. Hayashi N, Tsujii M, Itoh T, et al. Changes in the intracellular calcium ion concentration in the gastric mucosa in a rat ischemia-reperfusion model. *Scand J Gastroenterol Suppl*. 1989;162:43-46. [\[CrossRef\]](#)
10. Haress NG. Cinnarizine: comprehensive profile. *Profiles Drug Subst Excip Relat Methodol*. 2015;40:1-41. [\[CrossRef\]](#)
11. Fernandes AC, Filipe PM, Coelho H, Manso CF. The inhibition of lipid peroxidation by cinnarizine. Possible implications to its therapeutic and side-effects. *Biochem Pharmacol*. 1991;41(5):709-714. [\[CrossRef\]](#)
12. Abdel-Salam OM, El-Sayed El-Shamarka M, Salem NA, El-Mosallamy AE, Sleem AA. Amelioration of the haloperidol-induced memory impairment and brain oxidative stress by cinnarizine. *EXCLI J*. 2012;11:517-530. [\[CrossRef\]](#)
13. Çeçen ŞŞ, Cengiz G, Aktay G, Söylemezoğlu T. The effectiveness of N-acetylcysteine and cinnarizine on paraquat-induced neuro and hepato-toxicity in mice. *J Fac Pharm Gazi*. 2001;18(1):49-57. [\[CrossRef\]](#)
14. Abdel-Salam OM. Modulation of visceral nociception, inflammation and gastric mucosal injury by cinnarizine. *Drug Target Insights*. 2007;2:29-38. [\[CrossRef\]](#)
15. Góth L. A simple method for determination of serum catalase activity and revision of reference range. *Clin Chim Acta*. 1991;196(2-3):143-151. [\[CrossRef\]](#)
16. Bradford MM. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem*. 1976;72:248-254. [\[CrossRef\]](#)
17. Ozyigit F, Deger AN, Kocak FE, Ekici MF, Simsek H, Arık O. Protective effects of hesperidin in gastric damage caused by experimental ischemia-reperfusion injury model in rats. *Acta Cir Bras*. 2024;39:e391124. [\[CrossRef\]](#)
18. Wang T, Leng YF, Zhang Y, Xue X, Kang YQ, Zhang Y. Oxidative stress and hypoxia-induced factor 1α expression in gastric ischemia. *World J Gastroenterol*. 2011;17(14):1915-1922. [\[CrossRef\]](#)
19. Çeçen ŞŞ, Cengiz G, Aktay G, Söylemezoğlu T. The protective effects of cinnarizine and nitrendipine on naphthalene-induced oxidative stress in mice tissues. *FABAD J Pharm Sci*. 2002;27(4):197-203. [\[CrossRef\]](#)
20. Özcan O, Erdal H, Yönden Z. İskemi reperfüzyon hasarı ve oksidatif stres ilişkisine biyokimyasal bakış. *Mustafa Kemal Univ Tıp Derg*. 2015;6(23):27-33. [\[CrossRef\]](#)
21. Averill-Bates DA. The antioxidant glutathione. *Vitam Horm*. 2023;121:109-141. [\[CrossRef\]](#)
22. Abdel-Fattah MM, Messiha BA, Salama AA. Assessment of the mechanistic role of cinnarizine in modulating experimentally-induced bronchial asthma in rats. *Pharmacology*. 2015;96(3-4):167-174. [\[CrossRef\]](#)
23. Fukai T, Ushio-Fukai M. Superoxide dismutases: role in redox signaling, vascular function, and diseases. *Antioxid Redox Signal*. 2011;15(6):1583-1606. [\[CrossRef\]](#)
24. Rao ChV, Vijayakumar M. Protective effect of (+)-catechin against gastric mucosal injury induced by ischaemia-reperfusion in rats. *J Pharm Pharmacol*. 2007;59(8):1103-1107. [\[CrossRef\]](#)
25. Muthuraman A, Ramesh M, Chauhan A. Mitochondrial dependent apoptosis: ameliorative effect of flunarizine on ischemia-reperfusion of celiac artery-induced gastric lesions in the rat. *Dig Dis Sci*. 2011;56(8):2244-2251. [\[CrossRef\]](#)