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Gastrodin mitigates testicular ischemia-reperfusion injury in rats

Si-Ming Wei[1,2]*, Yu-Min Huang[3]

[1] Shulan International Medical College, Zhejiang Shuren University, Hangzhou, China; [2] School of Nursing, Zhejiang Chinese Medical University, Hangzhou, China; [3] Department of Sports Science, College of Education, Zhejiang University, Hangzhou, China.

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Abstract

Testicular ischemia-reperfusion is accompanied by elevated production of reactive oxygen species. It has been reported that reactive oxygen species are highly reactive to cellular carbohydrates, DNA, lipids, and proteins, and result in testicular ischemia-reperfusion injury. Gastrodin is the principal active ingredient isolated from the medicinal plant *Gastrodia elata* Blume and has anti-oxidative stress effect. The potential protective activity of gastrodin in rat testicular ischemia-reperfusion injury model and underlying mechanism were explored. Male rats were randomized into three groups, including sham control, testicular ischemia-reperfusion injury, and testicular ischemia-reperfusion injury along with gastrodin injection (n = 20). Testicular ischemia-reperfusion injury group received 2-hr period of left testicular torsion (720° and counterclockwise) and 4-hr or 3-month period of testicular detorsion. At the onset of testicular detorsion, gastrodin-treated rats were given 100 mg kg^{-1} gastrodin by intra-peritoneal route. Following testicular detorsion, testicular tissues were collected for enzymatic activity analysis, oxidative stress evaluation, and histopathological examination. The ipsilateral testicular xanthine oxidase activity (source of reactive oxygen species production) and malondialdehyde level (a precise biomarker of reactive oxygen species) were significantly increased in testicular ischemia-reperfusion injury group *versus* sham control group, while testicular spermatogenic function was decreased. Also, gastrodin administration reduced xanthine oxidase activity and malondialdehyde level in ipsilateral testicular tissue, while improving testicular spermatogenic function. Consequently, it is suggested that gastrodin plays a protective role in testicular torsion/detorsion-induced ischemia/reperfusion injury through inhibiting xanthine oxidase activity to decrease reactive oxygen species formation.

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Introduction

Testicular torsion is a severe emergency in the field of urology affecting about 1 out of every 4,000 men between the ages of 1 and 25.[1] It compromises blood supply of testis due to the rotation of testis on the spermatic cord. It is imperative that prompt operative testicular detorsion is performed to alleviate testicular ischemia. However, atrophy after testicular detorsion was observed in 12.00 - 50.00% of patients.[2,3] Oxidative stress plays a crucial role in testicular injury.[4] Testicular ischemia-reperfusion is accompanied by elevated production of reactive oxygen species, including hydrogen peroxide, hypochlorous acid, superoxide anions, singlet oxygen, hydroxyl radicals, alpha-oxygen, and so forth.[4] Reactive oxygen species are highly reactive to cellular carbohydrates, DNA, lipids, and proteins, and result in testicular ischemia-reperfusion injury.[4]

Till now, no known therapeutic agent is available to treat patients with testicular ischemia-reperfusion injury. Gastrodin is the principal active ingredient isolated from the medicinal plant *Gastrodia elata* Blume.[5] Its chemical formula is $C_{13}H_{18}O_7$ and molecular weight is 286.28.[6] It shows extensive pharmacological properties, like anti-oxidative stress, anti-inflammatory, anti-tumor, and anti-viral effects.[7] Its protective effects on ischemia-reperfusion injury have been demonstrated in some organs, including kidney, liver, heart, spinal cord, and brain.[8-12] To our best knowledge, treatment of testicular ischemia-reperfusion injury with gastrodin has not been explored yet. Therefore, the present study's aim was to ascertain the possible gonadoprotective ability of gastrodin in ischemia-reperfusion injury after rat testicular torsion-detorsion by examining the enzymatic activity, oxidative stress parameter, and histopathology in testicular tissue.

***Correspondence:**

Si-Ming Wei. MD, PhD
Shulan International Medical College, Zhejiang Shuren University, Hangzhou, China | School of Nursing, Zhejiang Chinese Medical University, Hangzhou, China
E-mail: 601357@zjsru.edu.cn

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Materials and Methods

Animals and ethical standards. Sixty male Sprague-Dawley rats (8 weeks old) weighing 250 - 300 g were selected in this study. They were procured from the SLAC Laboratory Animal Co. (Shanghai, China). All rats were hosted in hygienic plastic cages under controlled settings with the lighting regulation (12/12 hr light/dark cycle), moisture level maintained at 55.00 ± 5.00%, and environmental temperature being 21.00 ± 1.00 ˚C. Pellet rodent chow and normal tap water were provided for rats during the study. Before starting the experiment, rats spent 7 days for acclimation to the laboratory environment. After approval from the Zhejiang Chinese Medical University Ethics Committee, Hangzhou, China (Reference No. 10790), the study was carried out in strict compliance with the criteria for laboratory animal care and use.

Establishment of testicular ischemia-reperfusion model and gastrodin administration. The animals with similar body weights were randomly allocated into three experimental groups and assigned as sham control, testicular ischemia-reperfusion injury, and testicular ischemia-reperfusion injury along with gastrodin injection groups. Each group contained an equal number of rats (n = 20). First, all animals were given 50.00 mg kg^{-1} ketamine (Sigma-Aldrich, St. Louis, USA) through intra-peritoneal injection. Then, each rat had its left ilioinguinal and scrotal sites shaved and rinsed with 10.00% povidone-iodine solution. A small incision on the left ilioinguinal site was conducted, and the left testis was released. Rats in the sham control group were subjected to all surgical steps but without left testicular torsion-detorsion.[13] Next, the left testis was delivered to the scrotal sac and the incision site was sealed by 4-0 silk suture (Jumu Medical Equipment, Shanghai, China). In the testicular ischemia-reperfusion injury group, 720 degrees counterclockwise rotation of left testis led to testicular ischemia.[13] In order to maintain ischemic state, the torsional testis was secured to the scrotal wall with 11-0 polyamide suture (Jumu Medical Equipment) for 2 hr. At the end of the ischemia period, the suture was removed and testicular detorsion was done by reversing the torsional testis to its original position, thereby achieving testicular reperfusion. The gastrodin at a dose of 100 mg kg^{-1} body weight (Sigma-Aldrich) by intra-peritoneal route was given to gastrodin-treated group at detorsion of the testis. The dosage of gastrodin (100 mg kg^{-1}) was chosen considering earlier published literature reported that gastrodin conferred protection against oxidative damage in various diseases.[9,11,12] After 4 hr from reperfusion, 10 rats from each group were acquired. The testicular sample was harvested to analyze enzymatic activity and marker of oxidative stress. After 3 months from reperfusion, remaining 10 rats from each group were acquired. The testicular sample was harvested for histopathological examination.

Measurement of xanthine oxidase activity. The homogenate from testicular tissue was prepared in extraction solution on ice. Then, the homogenate was centrifuged at 8,000 *g* for 10 min at 4.00 ˚C to remove debris. The supernate was used for determination of xanthine oxidase activity. The xanthine oxidase activity was measured using commercial laboratory kit (Bioss Antibodies, Beijing, China).

Quantification of malondialdehyde (MDA) in testicular tissue. To determine tissue level of MDA, testicular tissue of rat was homogenized in MDA lysis buffer in 1 : 10 w/v on ice using a glass homogenizer. Next, the homogenate was centrifuged at 4.00 ˚C and 5,000 *g* for 15 min to separate the debris. After that, the supernatant was obtained and used for spectrophotometric detection of MDA activity using a testing kit (Jiancheng Bioengineering Institute, Nanjing, China).

Testicular histopathological analysis. Testicular spermatogenic function was evaluated by measuring the diameter of seminiferous tubule, testicular weight, Johnsen's biopsy score, and layer number of the germinal epithelium.[14] At the end of the experiment, both testes of rats were taken for weight analysis. For histological assessment, Bouin's fixative was employed to fix testicular specimen for a period of 4 hr. After fixation, the sample received a gradual alcohol dehydration process. Then, it was soaked in xylene for cleaning. The cleaned testicular sample was soaked in paraffin bath for impregnation and imbedded in paraffin. Section with thickness of 5.00 µm was incised from paraffin-imbedded specimen *via* a microtome. After xylene dewaxing and alcohol hydration, testicular slice was stained using Hematoxylin and Eosin (Sigma-Aldrich). A camera-attached to the light micro-scope was used to observe histopathological alterations in the section at a magnification of 200×. All testicular sections were independently analyzed by an expert pathologist being unfamiliar with the group assignment. The images of 20 transversely cut seminiferous tubules *per* section were examined in terms of the diameter of seminiferous tubule, Johnsen's biopsy score, and layer number of the germinal epithelium. Diameter of the seminiferous tubule was quantified in microns using an eyepiece micrometer. Testicular spermatogenesis in the seminiferous tubule was assessed using the 10-grade system defined by Johnsen.[15] Normal testicular spermatogenesis with dense spermatozoa and unobstructed tubular lumen was scored 10, whereas absence of both germ cells and Sertoli cells in the seminiferous tubule was scored 1.[15] From basement membrane to lumen, layer number of the germinal epithelium in each tubule was counted.

Statistical analysis. GraphPad Prism (version 4.0; GraphPad Software Inc., San Diego, USA) was utilized to conduct data analyses. For each group, continuous variables were recorded as mean ± standard deviation.

Variations were compared among three animal groups by one-way analysis of variance. Subsequently, multiple comparisons were carried out *via post-hoc* Student-Newman-Keuls test. The two-sided Student's *t*-test was utilized to assess the significance between ipsilateral and contralateral testes within group. Statistics were accepted as significant if the *p*-value was under 0.05.

Results

The impact of gastrodin on xanthine oxidase activity in testicular ischemia-reperfusion. The rats subjected to testicular ischemia-reperfusion injury showed a notable escalation in ipsilateral testicular xanthine oxidase activity ($p < 0.05$) in relation to the sham control group (Fig. 1). In contrast, gastrodin treatment at a dosage of 100 mg kg^{-1} led to a significant reduction in ipsilateral testicular xanthine oxidase activity in contrast with rats having testicular ischemia-reperfusion ($p < 0.05$).

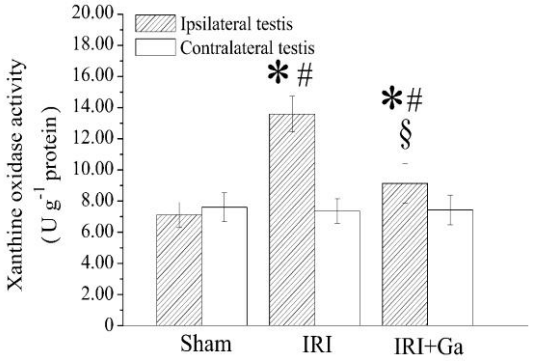

Fig. 1. Xanthine oxidase activity in rat testes across sham control, testicular ischemia-reperfusion injury (IRI), and gastrodin (Ga)-treated animal groups. The Ga treatment reduced xanthine oxidase activity in rat testicular ischemia-reperfusion. For each group, continuous variables (n = 10) were recorded as mean ± standard deviation. $^{*}p < 0.05$ *versus* sham control group; $^{§}p < 0.05$ *versus* ipsilateral testes in testicular IRI group; $^{\#}p < 0.05$ *versus* contralateral testes within group.

The differences among the three groups regarding contralateral testicular xanthine oxidase activity was not statistically significant ($p > 0.05$).

The impact of gastrodin on MDA concentration in testicular ischemia-reperfusion. Testicular ischemia-reperfusion exposure resulted in considerable ($p < 0.05$) increment in ipsilateral testicular MDA concentration relative to the rats received sham operation (Fig. 2). Conversely, gastrodin application at a dosage of 100 mg kg^{-1} displayed a noteworthy drop ($p < 0.05$) in ipsilateral testicular MDA concentration. Also, there was no marked variance ($p > 0.05$) in all groups in terms of contralateral testicular MDA concentration.

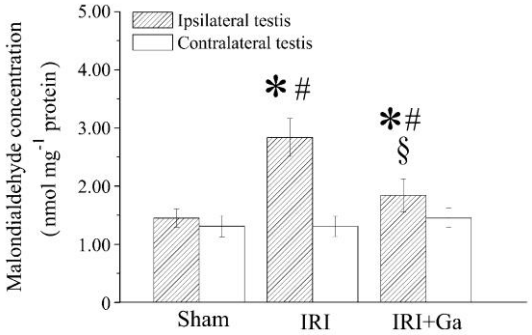

Fig. 2. Malondialdehyde concentration in rat testes across sham control, testicular ischemia-reperfusion injury (IRI), and gastrodin (Ga)-treated animal groups. The Ga treatment lowered malondialdehyde concentration in rat testicular ischemia-reperfusion. For each group, continuous variables (n = 10) were recorded as mean ± standard deviation. $^{*}p < 0.05$ *versus* sham control group; $^{§}p < 0.05$ *versus* ipsilateral testes in testicular IRI group; $^{\#}p < 0.05$ *versus* contralateral testes within group.

The impact of gastrodin on spermatogenic function in testicular ischemia-reperfusion. Testicular ischemia-reperfusion was associated with notable decline ($p < 0.05$) in ipsilateral testicular spermatogenesis, including diameter of seminiferous tubule, testicular weight, Johnsen's biopsy score, and layer number of the germinal epithelium, compared to the sham control rats (Figs. 3 and 4).

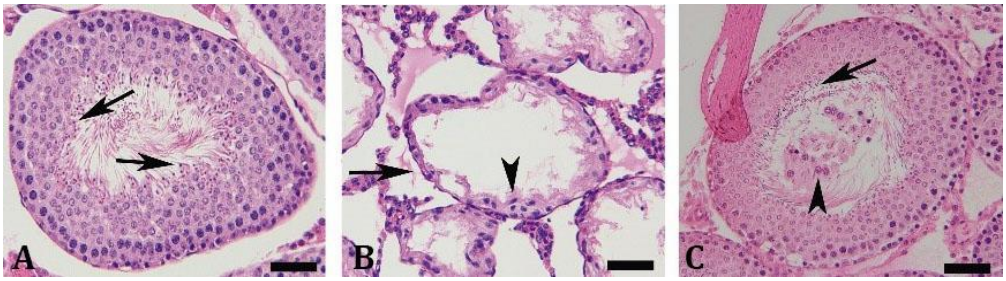

Fig. 3. Histopathological micrographs of rat testes from three different groups. **A)** The bilateral testes of sham control rats, and contralateral testes of testicular ischemia-reperfusion injury and gastrodin-treated rats displayed normal diameter of the seminiferous tubule, intact stratified seminiferous epithelium, and an open tubular lumen. The tubular lumen was plentiful with mature sperm cells (arrow). **B)** The photomicrograph of the ischemia-reperfusion testes exhibited narrowed diameter of the seminiferous tubule (arrow) and thinning seminiferous epithelium (arrowhead). The tubular lumen revealed azoospermia. **C)** The ipsilateral testes of gastrodin-treated rats resembled sham control group in the histopathology. Mature sperm cells (arrow) were detected in the tubular lumen. However, immature germ cells (arrowhead) spilled into the tubular lumen. The seminiferous tubule was stopped up easily by these spilled immature germ cells, (Hematoxylin and Eosin-staining; Scale bars = 40.00 µm).

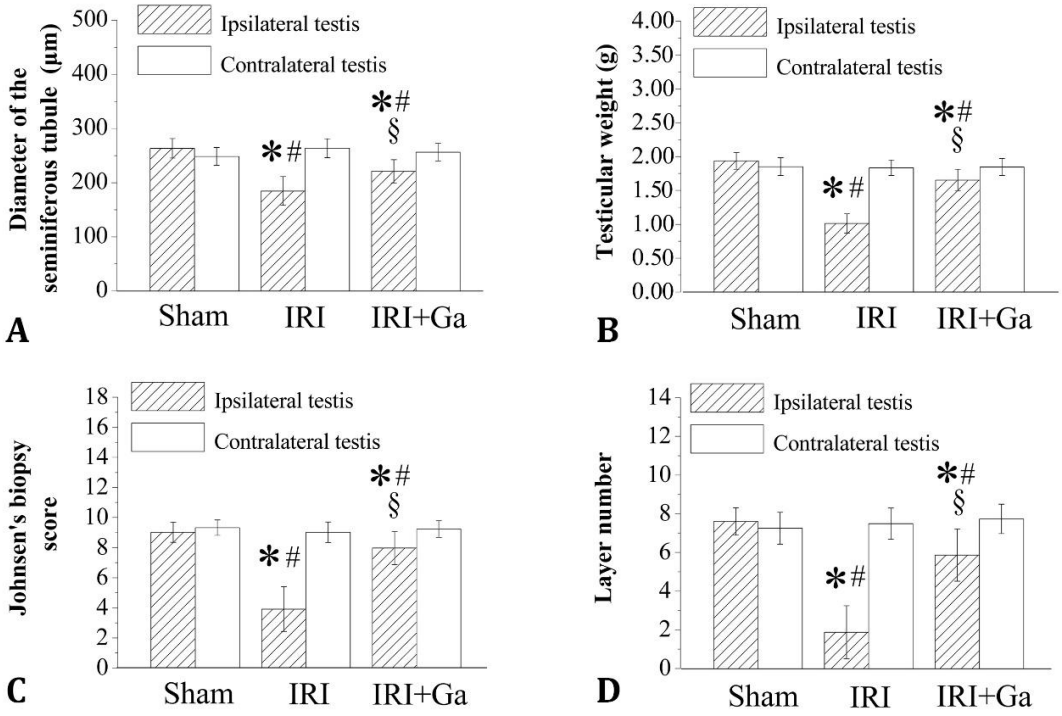

Fig. 4. Spermatogenic function including **A)** The diameter of seminiferous tubule, **B)** Testicular weight, **C)** Johnsen's biopsy score, and **D)** Layer number of the germinal epithelium across sham control, testicular ischemia-reperfusion injury (IRI), and gastrodin (Ga)-treated animal groups. The gastrodin treatment partly recovered spermatogenic function in rat testicular ischemia-reperfusion. For each group, continuous variables (n = 10) were recorded as mean ± standard deviation. * $p < 0.05$ *versus* sham control group; § $p < 0.05$ *versus* ipsilateral testes in testicular IRI group; # $p < 0.05$ *versus* contralateral testes within group.

However, the ipsilateral testicular spermatogenic function was reestablished markedly ($p < 0.05$) after administration of gastrodin at a dosage of 100 mg kg^{-1}. Contralateral testes displayed no discernible difference ($p > 0.05$) regarding testicular spermatogenic function among sham control, testicular ischemia-reperfusion injury, and gastrodin-treated animal groups.

Discussion

The management of testicular torsion requires urologists to perform surgical detorsion of torsional testis as soon as possible. If testicular detorsion is delayed, testicular necrosis may develop. When testicular detorsion is initiated within 6 hr after the beginning of testicular torsion, success rates for testicular salvage are between 90.00 and 100%.[16] Unfortunately, when testicular torsion persists beyond 12 hr, success rate falls to 50.00%.[16] When testicular torsion lasts for more than 24 hr, success rates decrease to < 10.00%.[16] However, 12.00 - 50.00% of patients received prompt testicular detorsion and successfully preserved testis, experienced testicular atrophy during follow-up.[2,3] In the current study, left testicular torsion of rat was induced for 2 hr. Though testicular detorsion was conducted rapidly, testicular damage still occurred 3 months after detorsion. Testicular injury was depicted by decreased diameter of the seminiferous tubule, testicular weight, Johnsen's biopsy score, and layer number of the germinal epithelium.

Testicular torsion-detorsion involves the increase in reactive oxygen species.[17] The reactive oxygen species have negative influence on cellular ingredients, including lipids, nucleic acids, proteins, and carbohydrates, causing testicular injury.[4] Due to the extremely high chemical reactivity and short life-span of reactive oxygen species, their direct detection is very difficult.[13] The increased reactive oxygen species are able to interact with polyunsaturated fatty acids in the cell membrane and result in a rise in lipid peroxidation content.[18] Malondialdehyde is a stable secondary product produced by lipid peroxidation.[19] Thus, MDA can serve as a precise biomarker of reactive oxygen species.[20] In this experiment, testicular ischemia-reperfusion rats exhibited increased MDA content along with diminished spermatogenic function in ipsilateral testes. The results from our experimental study indicate that testicular ischemia-reperfusion contributes to the accumulation of increased reactive oxygen species, severely destructing testicular spermatogenic function. Additionally, in gastrodin-treated group, MDA content was suppressed and spermatogenic function was elevated in ipsilateral testes. The results of our study reveal that gastrodin is testicular protective by inhibiting cellular oxidative stress in the testis. In clinical practice, gastrodin was sufficiently efficacious and had no

severe adverse effects in the treatment of myocardial injury after cardiac surgery, cognitive decline after mitral valve replacement operation with cardiopulmonary bypass, lower limb motor impairment after ischemic stroke, and refractory hypertension in old patients.[10,21-23] As a result, gastrodin has tremendous potential as a testicular protective drug against testicular ischemia-reperfusion injury in clinical setting. However, the precise underlying mechanisms through which gastrodin diminishes cellular oxidative stress in testicular ischemia-reperfusion remain poorly clarified.

During tissue ischemia-reperfusion, xanthine oxidase generates excessive reactive oxygen species.[24] Tissue ischemia induces a depletion of cellular adenosine triphosphate and triggers a transformation of xanthine dehydrogenase to xanthine oxidase.[25] Moreover, ischemia causes adenosine triphosphate degradation and increases hypoxanthine production.[26] During reperfusion, blood and oxygen are restored to ischemic tissue. Xanthine oxidase produces hydrogen peroxide and superoxide anion by catalyzing hypoxanthine and oxygen.[27] Hydroxyl radicals are formed by the interaction between superoxide anion and hydrogen peroxide.[28] Consequently, tissue ischemia-reperfusion provokes formation of reactive oxygen species. In this study, elevated xanthine oxidase activity and MDA content, and diminished testicular spermatogenic function were determined in ipsilateral testes of testicular ischemia-reperfusion injury rats relative to sham control ones. The present study's results show that testicular ischemia-reperfusion raises xanthine oxidase activity and exacerbates generation of reactive oxygen species, causing the deterioration of testicular spermatogenic function. In ipsilateral testes of gastrodin-treated group, a drop-in xanthine oxidase activity and MDA content, and an elevation in testicular spermatogenic function were noted. These data suggest that gastrodin confers a cytoprotective impact on testicular germ cells by inhibiting xanthine oxidase activity to lower reactive oxygen species production.

Whether unilateral testicular ischemia-reperfusion induces a deleterious impact on contralateral testis is disputable. Some findings indicated that unilateral testicular ischemia-reperfusion brought about low spermatogenesis of contralateral testis.[29,30] On the contrary, some studies reported that no any impairment was seen in contralateral testis.[31,32] Our research unveiled that testicular spermatogenic function, xanthine oxidase activity, and MDA concentration were similar in contralateral testes between sham control and testicular ischemia-reperfusion injury groups. Thus, our view is that unilateral testicular ischemia-reperfusion is not harmful to contralateral testis.

The present study clarifies, for the first time, that gastrodin can mitigate damage triggered by testicular ischemia-reperfusion. Therapeutic efficacy of gastrodin is attributed to the reactive oxygen species reduction by suppressing xanthine oxidase activity. These findings of our study indicate that gastrodin may become a new healing agent to ameliorate testicular dysfunction resulting from testicular ischemia-reperfusion. Nonetheless, the clinical applicability of gastrodin should be evaluated by additional clinical investigations.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Abu-Baih RH, Abu-Baih DH, Abdel-Hafez SMN, et al. Activation of SIRT1/Nrf2/HO-1 and Beclin-1/AMPK/mTOR autophagy pathways by eprosartan ameliorates testicular dysfunction induced by testicular torsion in rats. Sci Rep 2024; 14(1): 12566. doi: 10.1038/s41598-024-62740-6.
2. Chen P, Huang W, He Y, et al. A nomogram for predicting risk factors of testicular salvage after testicular torsion in children. Int J Urol 2024; 31(5): 568-574.
3. Komatsu S, Terui K, Takenouchi A, et al. Indocyanine green fluorescence imaging as a predictor of long-term testicular atrophy in testicular torsion: a pilot study. Surg Today 2025; 55(3): 386-392.
4. Azzam A, Karabulut R, Kaya C, et al. Effects of lupeol on experimental testicular ischemia-reperfusion damage in rats. Ulus Travma Acil Cerrahi Derg 2025; 31(2): 95-102.
5. Gong C, Fu X, Ma Q, et al. Gastrodin: Modulating the xCT/GPX4 and ACSL4/LPCAT3 pathways to inhibit ferroptosis after ischemic stroke. Phytomedicine 2025; 136: 156331. doi: 10.1016/j.phymed.2024.156331.
6. Xiao G, Tang R, Yang N, et al. Review on pharmacological effects of gastrodin. Arch Pharm Res 2023; 46(9-10): 744-770.
7. Yuan B, Huang H, Qu S, et al. Gastrodin pretreatment protects liver against ischemia-reperfusion injury via activation of the Nrf2/HO-1 pathway. Am J Chin Med 2020; 48(5): 1159-1178.
8. Zheng Y, Zhang N, Bai F. Gastrodin pretreatment alleviates renal ischemia-reperfusion injury. Urol Int 2022; 106(6): 630-637.
9. He SS, Huang HF, Shi SQ, et al. Gastrodin plays a protective role in alleviating hepatic ischemia reperfusion injury by regulating heme oxygenase-1

expression. Braz J Med Biol Res 2025; 58: e14248. doi: 10.1590/1414-431X2024e14248.
10. Chen L, Lv Y, Wu H, et al. Gastrodin exerts perioperative myocardial protection by improving mitophagy through the PINK1/Parkin pathway to reduce myocardial ischemia-reperfusion injury. Phytomedicine 2024; 133: 155900. doi: 10.1016/j.phymed.2024.155900.
11. Fang H, Zhang JC, Yang M, et al. Perfusion of gastrodin in abdominal aorta for alleviating spinal cord ischemia reperfusion injury. Asian Pac J Trop Med 2016; 9(7): 688-693.
12. Zhang M, Zhang Y, Peng J, et al. Gastrodin against oxidative stress-inflammation crosstalk via inhibiting mtDNA/TLR9 and JAK2/STAT3 signaling to ameliorate ischemic stroke injury. Int Immunopharmacol 2024; 141: 113012. doi: 10.1016/j.intimp.2024.113012.
13. Wei SM, Huang YM. Safranal ameliorates testicular ischemia-reperfusion injury in testicular torsion-detorsion rat model. Rev Int Androl 2024; 22(4): 33-41.
14. Wei SM, Huang YM. Effect of sulforaphane on testicular ischemia-reperfusion injury induced by testicular torsion-detorsion in rats. Sci Rep 2024; 14: 23420. doi: 10.1038/s41598-024-74756-z.
15. Johnsen SG. Testicular biopsy score count- -a method for registration of spermatogenesis in human testes: normal values and results in 335 hypogonadal males. Hormones 1970; 1(1): 2-25.
16. Azizoğlu M, Arslan S, Gökalp-Özkorkmaz E, et al. Protective effects of Passiflora Incarnata on ischemia-reperfusion injury in testicular torsion: an experimental study in a rat model. Cir Cir 2024; 92(2): 165-173.
17. Wei SM, Huang YM. Baicalein alleviates testicular ischemia-reperfusion injury in a rat model of testicular torsion-detorsion. Oxid Med Cell Longev 2022; 2022: 1603469. doi: 10.1155/2022/1603469.
18. Xiao J, Wan W, Zhang Y, et al. Administration of dexmedetomidine does not produce long-term protective effect on testicular damage post testicular ischemia-reperfusion injury. Drug Des Devel Ther 2021; 15: 315-321.
19. Celik M, Aydin P, Civelek MS, et al. Avanafil mitigates testicular ischemia/reperfusion injury via NLRP3 pathway modulation in rats. Reprod Sci 2024; 31(11): 3391-3399.
20. Kazak F, Akcakavak G, Alakus I, et al. Proanthocyanidin alleviates testicular torsion/detorsion-induced ischemia/reperfusion injury in rats. Tissue Cell 2024; 89: 102459. doi: 10.1016/j.tice.2024.102459.
21. Zhang Z, Ma P, Xu Y, et al. Preventive effect of gastrodin on cognitive decline after cardiac surgery with cardiopulmonary bypass: a double-blind, randomized controlled study. J Huazhong Univ Sci Technolog Med Sci 2011; 31(1): 120-127.
22. Yu Y, Tang L, Cui F, et al. Effect of Qizhitongluo capsule on lower limb rehabilitation after stroke: a randomized clinical trial. Pharmacol Res 2021; 165: 105464. doi: 10.1016/j.phrs.2021.105464.
23. Zhang Q, Yang YM, Yu GY. Effects of gastrodin injection on blood pressure and vasoactive substances in treatment of old patients with refractory hypertension: a randomized controlled trial [Chinese]. Zhong Xi Yi Jie He Xue Bao 2008; 6(7): 695-699.
24. Li T, Wang W, Liu W, et al. Macrophage membrane coated functionalized nanoparticles for targeted drug delivery and neural function repair in cerebral ischemia-reperfusion injury. Int J Pharm 2025; 672: 125329. doi: 10.1016/j.ijpharm.2025.125329.
25. Annesi L, Tossetta G, Borghi C, et al. The role of xanthine oxidase in pregnancy complications: a systematic review. Antioxidants (Basel) 2024; 13(10): 1234. doi: 10.3390/antiox13101234.
26. Mahanty A, Xi L. Utility of cardiac biomarkers in sports medicine: focusing on troponin, natriuretic peptides, and hypoxanthine. Sports Med Health Sci 2020; 2(2): 65-71.
27. Han C, Wu Y, Rong J, et al. Unveiling the emerging role of xanthine oxidase in acute pancreatitis: beyond reactive oxygen species. Antioxidants (Basel) 2025; 14(1): 95. doi: 10.3390/antiox14010095.
28. Teschke R, Eickhoff A. Wilson disease: copper-mediated cuproptosis, iron-related ferroptosis, and clinical highlights, with comprehensive and critical analysis update. Int J Mol Sci 2024; 25(9): 4753. doi: 10.3390/ijms25094753.
29. Wei S, Xiao J, Ju F, et al. Aloperine protects the testis against testicular ischemia/reperfusion injury in rats. Andrology 2025; 13(4): 934-954.
30. Balgetir MK, Tektemur NK, Tektemur A, et al. Determination of M1/M2 macrophage polarization in ipsilateral and contralateral rat testis tissue following unilateral torsion/detorsion. Reprod Sci 2024; 31(7): 2092-2102.
31. Alotaibi SR, Renno WM, Al-Maghrebi M. c-Jun N-terminal kinase supports autophagy in testicular ischemia but triggers apoptosis in ischemia-reperfusion injury. Int J Mol Sci 2024; 25(19): 10446. doi: 10.3390/ijms251910446.
32. Jafarova Demirkapu M, Karabag S, Akgul HM, et al. The effects of etomidate on testicular ischemia reperfusion injury in ipsilateral and contralateral testes of rats. Eur Rev Med Pharmacol Sci 2022; 26(1): 211-217.