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S-allyl cysteine protects against kidney injury induced by myocardial ischemia-reperfusion in ovariectomized rats

S-allyl cysteine protege contra la lesión renal inducida por isquemia-reperfusión miocárdica en ratas ovariectomizadas

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Abstract

Acute kidney injury secondary to myocardial ischemia-reperfusion is a serious complication driven by oxidative stress and inflammation. Although reperfusion restores oxygenation, it also increases reactive oxygen species generation, worsening renal injury. S-allyl cysteine, a garlic-derived organosulfur compound, exerts antioxidative effects by enhancing endogenous antioxidant defenses. Hence, this study investigates the effects of S-allyl cysteine in ovariectomized rats subjected to myocardial ischemia-reperfusion injury. Thirty-two female Wistar rats underwent either ovariectomy (n=24) or sham surgery (n=8). After a 3-week recovery, myocardial ischemia-reperfusion injury was induced by 30 min of left anterior descending coronary artery ligation followed by 2 h of reperfusion. S-allyl cysteine or propargylglycine was administered via the right carotid artery at reperfusion onset. Kidney tissues were analyzed biochemically and histologically. S-allyl cysteine significantly reduced malondialdehyde levels and insignificantly increased both glutathione level and catalase activity in renal tissues. However, no changes were observed in superoxide dismutase activity and hydrogen sulfide levels. Renal histology revealed that S-allyl cysteine preserved renal morphology in ovariectomized rats, likely via reactive oxygen species scavenging and Nrf2 pathway activation. This study concludes that S-allyl cysteine attenuates myocardial ischemia-reperfusion-induced kidney injury in estrogen-deficient rats by reducing oxidative stress and enhancing antioxidant defenses, suggesting potential as a therapeutic supplement to reduce risk of acute kidney injury in menopausal women.

Resumen

La lesión renal aguda secundaria a la isquemia-reperfusión miocárdica constituye una complicación grave impulsada por el estrés oxidativo y la inflamación. Aunque la reperfusión restablece la oxigenación, también incrementa la generación de especies reactivas de oxígeno, agravando el daño renal. La S-alil cisteína, un compuesto organosulfurado derivado del ajo, ejerce efectos antioxidantes al potenciar las defensas antioxidantes endógenas. Por ello, este estudio investiga los efectos de la S-alil cisteína en ratas ovariectomizadas sometidas a lesión por isquemia-reperfusión miocárdica. Treinta y dos ratas Wistar hembras fueron sometidas a ovariectomía (n=24) o cirugía simulada (n=8). Tras un período de recuperación de tres semanas, se indujo la lesión por isquemia-reperfusión miocárdica mediante 30 minutos de ligadura de la arteria coronaria descendente anterior izquierda, seguidos de 2 horas de reperfusión. La S-alil cisteína o la propilglicina se administraron a través de la arteria carótida derecha al inicio de la reperfusión. Los tejidos renales fueron analizados bioquímica e histológicamente. La S-alil cisteína redujo significativamente los niveles de malondialdehído y aumentó de manera no significativa tanto el nivel de glutatión como la actividad de la catalasa en los tejidos renales. Sin embargo, no se observaron cambios en la actividad del superóxido dismutasa ni en los niveles de sulfuro de hidrógeno. La histología renal reveló que la S-alil cisteína preservó la morfología renal en ratas ovariectomizadas, probablemente mediante la eliminación de especies reactivas de oxígeno y la activación de la vía Nrf2. Este estudio concluye que la S-alil cisteína atenúa la lesión renal inducida por la isquemia-reperfusión miocárdica en ratas con deficiencia de estrógenos al reducir el estrés oxidativo y potenciar las defensas

antioxidantes, lo que sugiere su potencial como suplemento terapéutico para disminuir el riesgo de lesión renal aguda en mujeres posmenopáusicas.

Introduction

Acute kidney injury (AKI) is a frequently reported complication following myocardial ischemia reperfusion, with an incidence of approximately 26 % among patients with acute myocardial infarction and an associated mortality rate of 20.5 %, compared with only 0.6 % in patients without AKI[1]. Myocardial infarction and post cardiac arrest related cardiac dysfunction reduce renal perfusion, thereby predisposing the kidneys to ischemic injury. During reperfusion therapies especially percutaneous coronary intervention (PCI), restoration of blood flow results in the abrupt reintroduction of molecular oxygen, leading to excessive generation of reactive oxygen species (ROS). This oxidative surge further exacerbates cellular and molecular damage within renal tissues[2]. Consequently, the ischemia reperfusion cascade culminates in AKI, ultimately impairing renal function and precipitating AKI[3]. Patients developing AKI following reperfusion procedures are often associated with poor short-term prognosis, with higher rates of developing major bleeding, reinfarction and stroke within 30 days and death[4]. Interestingly, sex hormones disturbance, particularly estrogen, may influence susceptibility to AKI during myocardial ischemia-reperfusion events, thereby placing females in a predisposing condition for developing AKI following reperfusion interventions[5]. Menopause is a natural process caused by cessation of menstruation and ovarian hormone depletion due to follicle development loss. Estrogen deficiency, a hallmark of menopause, increases the risk of developing AKI during myocardial ischemia-reperfusion events[6]. While menopause itself is not a direct cause of cardiovascular disease, however the associated hormonal changes that occur during the transition (particularly the decline in estrogen levels) contribute to the adverse alterations in lipid profiles, lipoprotein and vascular function. These changes ultimately increase the risk of developing cardiovascular disease in postmenopausal women[7]. Estradiol, a primary estrogen steroid hormone mainly produced in the ovaries, had showed renoprotective effects. These protective effects are potentially mediated via transforming growth factor (TGF)-β1 inhibition[8] and nitric oxide-mediated vasodilatation[9]. The renoprotective role of estrogen is further supported by findings from Ji et al.[10], which showed that estrogen deficiency activates renin-angiotensin system (RAS), promotes oxidative stress and inflammation, and exacerbates myocardial ischemia-reperfusion-induced renal hypoperfusion and AKI.

S-allyl cysteine (SAC) is an organosulfur compound derived from aged garlic (*Allium sativum*). Previous studies have shown that SAC exhibits antioxidant, anti-inflammatory, as well as cardioprotective properties. Due to its powerful antioxidative properties, SAC attenuates lipid peroxidation, mitigates oxidative stress in damaged tissues[11]. Studies by Khajevand-Khazaei et al.[12] demonstrated that SAC administration reduces malondialdehyde (MDA) levels while enhancing glutathione, superoxide dismutase

(SOD), and catalase (CAT) levels in lipopolysaccharide-induced AKI mouse model, resulting in the improvement of antioxidant defenses while lowering serum creatinine and blood urea nitrogen. This demonstrates its potential benefits in reducing oxidative stress conditions and indirectly improving AKI. Additionally, SAC exerts anti-inflammatory effects by NF-κB inhibition which suppresses pro-inflammatory cytokines (tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6) and attenuates immune cell infiltration into renal tissue[12]. Together with its potent antioxidative properties, SAC moderates oxidative injury, inflammation, and apoptosis, preserving renal function following myocardial ischemia-reperfusion injury. Therefore, SAC demonstrates therapeutic potential in mitigating the risk of postmenopausal AKI induced by myocardial ischemia-reperfusion. Although many studies have been conducted on SAC and its general health benefits, there is still a lack of specific research on the effects of SAC on myocardial ischemia-reperfusion-induced kidney injury. Thus, this research aims to investigate the effects of SAC on kidney injury induced by myocardial ischemia-reperfusion in ovariectomized rats, providing insights into its potential as a natural supplement to reduce kidney damage.

Materials and methods

A total of 32 female Wistar rats weighing between 200-250 g underwent either ovariectomy (n=24) or sham (n=8) surgery and left to recover for 3 weeks. The sham-operated rats served as the normal control (*Sham*, normal saline). The ovariectomized rats were randomly divided into 3 groups; (1) *OVX-IR***:** ovariectomized rats with ischemia-reperfusion, administered with normal saline; (2) *OVX-IR-SAC*: ovariectomized rats with ischemia-reperfusion administered with SAC (98 % purity; lot number, WWHCI OC; Tokyo Chemical Industry) at 10 mM/kg; and (3) *OVX-IR-SAC-PAG*: ovariectomized rats with ischemia-reperfusion supplemented with SAC (10 mM/-kg) and *DL*-propargylglycine (PAG) (98 % purity; batch number, 102544340; Sigma Aldrich) (1 mM/-kg), with PAG serving as a negative control owing to its inhibitory effect on cystathionine γ-lyase. All treatments were administered to their respective group intravenously through the jugular vein at perfusion onset following myocardial ischemia. Prior to myocardial ischemia-reperfusion procedure, estrogen deficiency was achieved by performing ovariectomy procedure. Under general anesthesia (ketamine-xylazine cocktail via intraperitoneal injection), all ovariectomized groups underwent complete bilateral ovariectomy while the Sham group underwent a sham surgical procedure without ovarian excision. A 21-day recovery period was given to ensure estrogen depletion[13]. Myocardial ischemia-reperfusion protocol was performed according to left anterior descending artery ligation as described by[14]. Following this method, the left anterior descending coronary artery was directly ligated for 30 minutes, followed by 120 minutes of reperfusion. At reperfusion onset, treatment was administered via the right carotid artery according to their respective group. After the myocardial ischemia-reperfusion procedure was completed, the rats were sacrificed, and kidneys were harvested for biochemical analysis and histopathological observation.

Renal oxidative stress was assessed by measuring antioxidants and peroxidation products in kidney homogenates. Homogenates were prepared in buffer and centrifuged to obtain supernatants for assays. MDA was quantified via thiobarbituric acid (TBA) reactive substances assay at 532 nm[15]. Hydrogen sulfide (H_2S) was measured by methylene blue formation at 665 nm[16]. Reduced glutathione was determined using the Ellman method at 415 nm[17]. SOD

activity was evaluated by inhibition of nitroblue tetrazolium reduction at 560 nm[18], and CAT activity by hydrogen peroxide breakdown at 240 nm[19]. Chromogenic products were analyzed colorimetrically with a microplate reader, except catalase, measured by spectrophotometer, with all assays standardized using controls and calibration curves.

Kidney tissue collected were immediately fixed in 10 % formalin, followed by dehydration through a graded alcohol series and paraffin embedding. Sections of 5 µm thickness were prepared and stained with hematoxylin and eosin. Images were captured using light microscopy. Finally, one-way analysis of variance (ANOVA) statistical analysis was used to compare the means of all parameters measured across groups, with data expressed as mean ± standard error of means (SEM). Significance was set at $p<0.05$.

Results

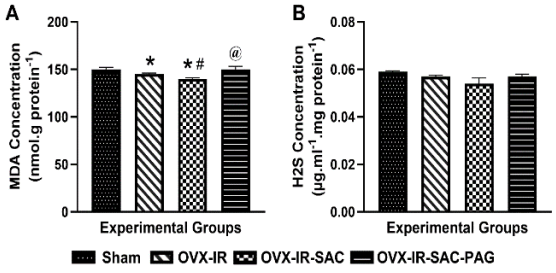

Figure 1 A Comparison of MDA concentration between study groups. *p<0.05 vs. *Sham*, $^{\#}$p<0.05 vs. *OVX-IR* and $^{@}$ p<0.05 vs. *OVX-IR-SAC.* B Comparison of hydrogen sulfide (H_2S) concentration between study groups

The findings show that the *Sham* group (157.6±1.523 nmol/g), which served as the control, exhibited the highest level of MDA compared to the *OVX-IR* group (147.5±0.854 nmol/g) and the *OVX-IR-SAC* group (140.2±0.566 nmol/g). Notably, treatment with SAC significantly reduced oxidative stress relative to all groups, including the *OVX-IR-SAC-PAG* group (151.5±3.861 nmol/g) (Figure 1A).

Statistical analysis revealed no significant differences ($p > 0.05$) in the H_2S levels among all groups, namely *Sham* (0.05813±0.001 µg/mL/mg), *OVX-IR-SAC* (0.05350±0.002 µg/mL/mg), *OVX-IR-SAC-PAG* (0.05645±0.001 µg/mL/mg), and *OVX-IR* (0.05631±0.001 µg/mL/mg) (Figure 1B).

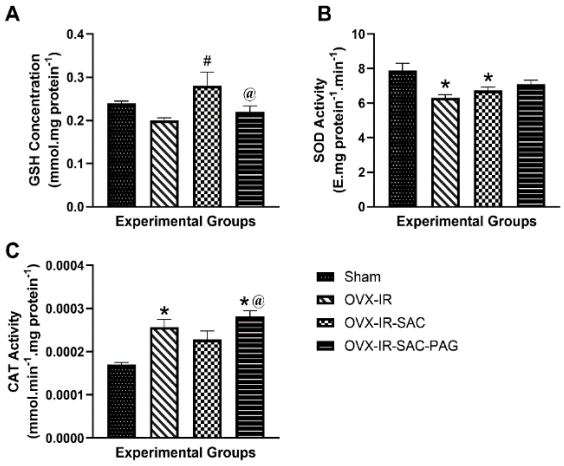

Figure 2 A Comparison of reduced glutathione (GSH) concentration between study groups. B Comparison of superoxide dismutase (SOD) activity between study groups. C Comparison of catalase (CAT) activity between study groups. *p<0.05 vs. *Sham*, $^{\#}$p<0.05 vs. *OVX-IR*, $^{@}$ p<0.05 vs. *OVX-IR-SAC*

Figure 2A shows renal GSH levels. The O*VX-IR-SAC* group (0.2843±0.03206 mmol/mg) demonstrated a significant increase compared to *OVX-IR* (0.1982±0.00741 mmol/mg) and *OVX-IR-SAC-PAG* (0.2101±0.01204 mmol/mg). Although higher than Sham (0.2361±0.00421 mmol/mg), the increase was not significant.

Figure 2B presents renal SOD activity. Both *OVX-IR* (6.313±0.1690 E/mg/min) and *OVX-IR-SAC* (6.612 ±0.1856 E/mg/min) showed significantly lower activity ($p < 0.05$) compared with *Sham* (7.843±0.4684 E/mg/min). No significant differences were observed *between OVX-IR-SAC-PAG* (6.835±0.1995 E/mg/min) and other groups.

Figure 2C depicts renal CAT activity. *OVX-IR* (0.000251±0.000017 mmol/min/mg) and *OVX-IR-SAC* (0.000224±0.000021 mmol/min/mg) showed significantly higher activity compared with *Sham*

(0.000170±0.000006 mmol/min/mg). The *OVX-IR-SAC-PAG* group (0.000284±0.000013 mmol/min/-mg) exhibited a further significant increase relative to SAC treatment.

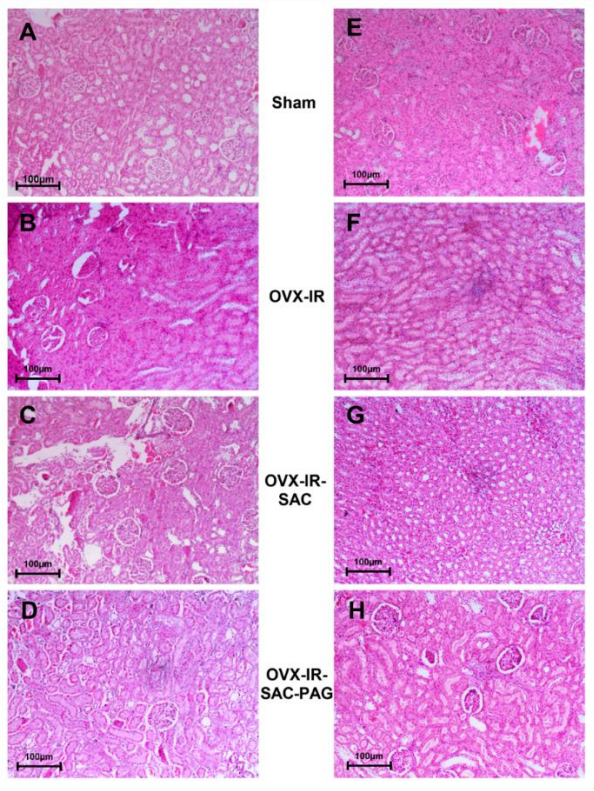

Figure 3 Histopathological differences in kidney tissue sections stained with hematoxylin and eosin (H&E) staining (40x magnification; scale bar: 100 µm). A and E *Sham*; B and F *OVX-IR*; C and G *OVX-IR-SAC*; D and H *OVX-IR-SAC-PAG*

Figure 3 shows representative H&E-stained kidney sections (400×). The *Sham* group (A and E) exhibited largely normal glomerular morphology with occasional degeneration and mild tubular epithelial swelling. The *OVX-IR* group (B and F) demonstrated marked tubular dilatation, epithelial swelling, and prominent interstitial inflammatory infiltration. The *OVX-IR-SAC* group (C and G) showed preserved glomerular morphology with mild tubular dilatation and epithelial swelling. Normal tubular structures were evident within the kidney. The *OVX-IR-SAC-PAG* group (D and H) exhibited interstitial edema, tubular dilatation, epithelial swelling, and glomerular degeneration with Bowman's space expansion.

Discussion

This study manifested that SAC exerts antioxidant effects in ovariectomized rats with AKI induced by myocardial ischemia and reperfusion. SAC treatment significantly reduced MDA levels compared to other ovariectomized groups, suggesting ROS scavenging effect and inhibition of lipid peroxidation. These effects are potentially mediated by activation of nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, which enhances the synthesis of endogenous antioxidants[20]. Although a more detailed discussion of Nrf2 involvement follows, it is worth noting here that enhanced antioxidant levels observed with SAC treatment may reflect, at least in part, this pathway's activation.

Despite SAC administration, H_2S levels remained unchanged, possibly due to myocardial ischemia-reperfusion- and AKI-induced downregulation of cystathionine γ-lyase which is an enzyme involved in H_2S synthesis[21,22]. Interestingly, SOD activity was significantly reduced in SAC-treated ovariectomized rats. This decline may reflect the absence of estrogen, which is necessary for optimal activation of antioxidant pathways[23]. A similar trend was observed with CAT activity, which was also reduced following SAC treatment, presumably due to decreased oxidative burden and reduced need for compensatory upregulation of catalase. CAT activity is dynamically regulated in response to cellular oxidative burden, with expression and activity changing according to ROS levels as part of redox homeostasis[24]. While increase in reduced glutathione levels in the SAC-treated group was not statistically significant compared to *Sham*, a positive trend was noted. This may be attributed to the thiol groups present in SAC,

which directly neutralize ROS and thereby reduce glutathione consumption during oxidative stress[25]. Additionally, SAC may support glutathione restoration by acting as a cysteine donor.

Estrogen is crucial for redox homeostasis by modulating antioxidant defenses[26]. It upregulates cystathionine γ-lyase, which is necessary for H_2S synthesis, an essential activator of the Nrf2 pathway[27]. Estrogen also influences Nrf2 activity via estrogen receptor signaling. In ovariectomized rats, the lack of estrogen suppresses the Nrf2 pathway, leading to decreased expression of antioxidant genes such as glutathione synthase and SOD, which worsens oxidative stress during myocardial ischemia-reperfusion injury[28,29]. The effectiveness of the Nrf2 pathway closely depends on H_2S-mediated regulation. Under physiological conditions, H_2S sulfhydrates Keap1 which stabilizes Nrf2 and promoting its nuclear translocation and antioxidant response element (ARE)-driven gene transcription, subsequently stimulates the production of antioxidant including glutathione and SOD. However, during myocardial ischemia-reperfusion with estrogen depletion, H_2S deficiency impairs this mechanism, hence weakening antioxidant defenses[27,28].

Despite SAC, H_2S levels in the *OVX-MIR-SAC* group remained statistically unchanged compared to sham-operated rats. This is notable because myocardial ischemia-reperfusion and estrogen deficiency are typically associated with downregulation cystathionine γ-lyase[27]. The maintenance of H_2S at near-physiological levels in the SAC treated group suggests that S-allyl cysteine may compensate for this suppression by acting as a cysteine donor, thus supporting cystathionine γ-lyase's functions and H_2S production despite the absence of estrogen. This restoration of H_2S may have helped maintain Nrf2 activation and mitigate ROS accumulation. Moreover, thiol group in S-allyl cysteine directly scavenge ROS, thereby preserving mitochondrial function and reducing inflammatory cytokines like TNF-α and IL-6, which further protects against renal damage[30]. PAG or propargylglycine serves as a negative control that specifically inhibits cystathionine γ-lyase, blocks H_2S synthesis, and inhibits the antioxidant and anti-inflammatory pathways[31]. In other words, it negates the renoprotective effects of S-allyl cysteine. As seen in *OVX-IR-SAC-PAG* rats, PAG removes the S-allyl cysteine's ability to suppress lipid peroxidation, thus confirming that ROS scavenging capacity of SAC is disabled due to Nrf2 pathway inactivation.

Histopathological observation expresses severe tubular dilation, tubular edema, and glomerular atrophy similar to untreated *OVX-IR* oxidative damage. In contrast, SAC treatment to ovariectomized rats was observed to preserve glomerular structure integrity with only mild tubular dilation, similar to findings in previous study[32]. The renoprotective effect of SAC against renal structural alterations may be mediated, at least in part, through mechanisms known to influence tissue injury in ischemia reperfusion induced AKI, including attenuation of ROS, reduction of inflammatory cytokines, preservation of adenosine triphosphate (ATP) levels, and maintenance of Na^+/K^+-ATPase activity, which collectively contribute to minimizing morphological damage[12,30,33,34]. Additionally, SAC-mediated protection likely involves activation of the Nrf2 pathway via H_2S signaling. The presence of mild tubular dilation suggests that residual hypoxic damage had occurred from endothelial dysfunction and probable peritubular capillary congestion[35].

In conclusion, SAC effectively attenuates myocardial ischemia-reperfusion-induced renal injury in estrogen-depleted rats by reducing oxidative stress, enhancing antioxidant defenses, and preserving renal morphology (Figure 4). These findings highlight the

potential of SAC as a natural and effective therapeutic supplement for mitigating myocardial ischemia-reperfusion-associated renal damage, particularly in postmenopausal women. SAC may thus offer a promising strategy for supporting renal antioxidant capacity and managing estrogen deficiency related kidney injury.

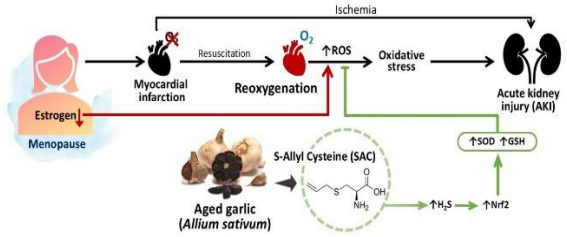

Figure 4 Potential of SAC in protecting the kidneys against myocardial infarction reperfusion injury

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Conflicts of interest

The authors declare no competing interests.

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Ethical considerations

All experimental protocol were reviewed and approved by the Universiti Kebangsaan Malaysia Animal Ethics Committee (UKMAEC), ethic approval number CORE/FSK/UKM/2024/SATIRAHZAINA LABIDIN/27-MAC./1418-APR.-2024-SEP.-2025.

Limitations in research

Several limitations of the present study should be acknowledged. First, renal profile parameters were not assessed; therefore, the potential protective effects of SAC against ischemia/reperfusion induced AKI could not be evaluated. Inclusion of renal function assays, such as serum creatinine and blood urea nitrogen, would have provided valuable insights into the systemic and renal responses to SAC treatment. Second, this study employed a single dose of SAC, which limits conclusions regarding dose response relationships. Evaluation of multiple SAC dosages would be beneficial to determine the optimal therapeutic dose that confers maximal protective effects.

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Not applicable.

Contribution of the authors in the article

Satirah Zainalabidin, conception & design of study, supervision, funding acquisition. *Chai Yi Ping*, acquisition of data, analysis and interpretation of data, drafting. *Muhamad Adib Abdul Ghani*, *Izatus Shima Taib* and *Mohd Kaisan Mahadi*, project administration and resources, revising manuscript critically for intellectual content. *Fatin Farhana Jubaidi*, interpretation, drafting, writing and revision. All authors have read and consented to the final version of the manuscript.

Use of artificial intelligence

Artificial intelligence (OpenAI) was used to assist in language editing (English to Spanish) and improvement of grammar and clarity. All content has been reviewed and approved by the authors to ensure ac-

curacy and originality.

Cited Literature

1. Wang C, Pei YY, Ma YH, Ma XL, Liu ZW, Zhu JH, et al. Risk factors for acute kidney injury in patients with acute myocardial infarction. Chin Med J (Engl) 2019;132(14):1660-5. DOI: https://doi.org/10.1097/CM9.0000000000000029. PMID: 31261199; PMCID: PMC6759102.
2. Anzai A, Anzai T, Naito K, Kaneko H, Mano Y, Jo Y, et al. Prognostic significance of acute kidney injury after reperfused ST-elevation myocardial infarction: synergistic acceleration of renal dysfun ction and left ventricular remodeling. J Card Fail 2010;16(5):381-9. DOI: https://doi.org/10.1016/j.cardfail.2009.12.020. PMID: 20447573.
3. Bonventre JV, Yang L. Cellular pathophysiology of ischemic acute kidney injury. J Clin Invest 2011;121(11):4210-21. DOI: https://doi.org/10.1172/JCI45161. PMID: 22045571; PMCID: PMC3204829.
4. Tsai TT, Patel UD, Chang TI, Kennedy KF, Masoudi FA, Matheny ME, et al. Contemporary incidence, predictors, and outcomes of acute kidney injury in patients undergoing percutaneous coronary interventions: insights from the NCDR Cath-PCI registry. JACC Cardiovasc Interv 2014;7(1):1-9. DOI: https://doi.org/10.1016/j.jcin.2013.06.016. PMID: 24456715; PMCID: PMC4122507.
5. Kunadian V, Qiu W, Lagerqvist B, Johnston N, Sinclair H, Tan Y, et al. Gender differences in outcomes and predictors of all-cause mortality after percutaneous coronary intervention (Data from United Kingdom and Sweden). Am J Cardiol 2017;119(2):210-6. DOI: https://doi.org/10.1016/j.amjcard.2016.09.052. PMID: 27816119.
6. Farahmand M, Ramezani Tehrani F, Khalili D, Cheraghi L, Azizi F. Endogenous estrogen exposure and chronic kidney disease: a 15-year prospective cohort study. BMC Endocr Disord 2021;21(1):155. DOI: https://doi.org/10.1186/s12902-021-00817-3. PMID: 34348694; PMCID: PMC8336110.
7. El Khoudary SR, Aggarwal B, Beckie TM, Hodis HN, Johnson AE, Langer RD, et al. Menopause transition and cardiovascular disease risk: implications for timing of early prevention: A Scientific Statement From the American Heart Association. Circulation 2020;142(25):e506-e532. DOI: https://doi.org/10.1161/CIR.0000000000000912. PMID: 33251828.
8. Ren L, Li F, Di Z, Xiong Y, Zhang S, Ma Q, et al. Estradiol ameliorates acute kidney ischemia-reperfusion injury by inhibiting the TGF-βRI-SMAD pathway. Front Immunol 2022;13:822604. DOI: https://doi.org/10.3389/fimmu.2022.822604. PMID: 35281024; PMCID: PMC8907449.
9. Satake A, Takaoka M, Nishikawa M, Yuba M, Shibata Y, Okumura K, et al. Protective effect of 17 β-estradiol on ischemic acute renal failure through the PI3K/Akt/eNOS pathway. Kidney Int 2008;73(3):308-17. DOI: https://doi.org/10.1038/sj.ki.5002690. PMID: 18004295.
10. Ji H, Menini S, Zheng W, Pesce C, Wu X, Sandberg K. Role of angiotensin-converting enzyme2 and angiotensin (1-7) in 17β-oestradiol regulation of renal pathology in renal wrap hypertension in rats. Exp Physiol 2008;93(5):648-57. DOI: https://doi.org/10.1113/expphysiol.2007.041392. PMID: 18296494.
11. Padmanabhan M, Prince PS. Preventive effect of S-allylcysteine on lipid peroxides and antioxidants in normal and isoproterenol-induced cardiotoxicity in rats: a histopathological study. Toxicology 2006;224(1-2):128-37. DOI: https://doi.org/10.1016/j.tox.2006.04.039. PMID: 16757080.
12. Khajevand-Khazaei MR, Azimi S, Sedighnejad L, Salari S, Ghorbanpour A, Baluchnejadmojarad T,

et al. S-allyl cysteine protects against lipopolysaccharide-induced acute kidney injury in the C57BL/6 mouse strain: Involvement of oxidative stress and inflammation. Int Immunopharmacol 2019;69:19-26. DOI: https://doi.org/10.1016/j.intimp.2019.01.026. PMID: 30665040.

13. Yousefzadeh N, Kashfi K, Jeddi S, Ghasemi A. Ovariectomized rat model of osteoporosis: a practical guide. EXCLI J 2020;19:89-107. DOI: https://doi.org/10.17179/excli2019-1990. PMID: 32038119; PMCID: PMC7003643.
14. Yusof NLM, Yellon DM, Davidson SM. Novel selective cardiac myosin-targeted inhibitors alleviate myocardial ischaemia-reperfusion injury. Cardiovasc Drugs Ther 2025. DOI: https://doi.org/10.1007/s10557-024-07663-0. PMID: 39754660.
15. Ledwozyw A, Michalak J, Stepień A, Kadziołka A. The relationship between plasma triglycerides, cholesterol, total lipids and lipid peroxidation products during human atherosclerosis. Clin Chim Acta 1986;155(3):275-83. DOI: https://doi.org/10.1016/0009-8981(86)90247-0. PMID: 3708856.
16. Xie YH, Zhang N, Li LF, Zhang QZ, Xie LJ, Jiang H, et al. Hydrogen sulfide reduces regional myocardial ischemia injury through protection of mitochondrial function. Mol Med Rep 2014;10(4):1907-14. DOI: https://doi.org/10.3892/mmr.2014.2391. PMID: 25198340.
17. Ellman GL. Tissue sulfhydryl groups. Arch Biochem Biophys 1959; 2(1):70-7. DOI: https://doi.org/10.1016/0003-9861(59)90090-6. PMID: 13650640.
18. Beyer WF Jr, Fridovich I. Assaying for superoxide dismutase activity: some large consequences of minor changes in conditions. Anal Biochem 1987; 161(2):559-66. DOI: https://doi.org/10.1016/0003-2697(87)90489-1. PMID: 3034103.
19. Aebi H. Catalase in vitro. Methods Enzymol 1984; 105:121-6. DOI: https://doi.org/10.1016/s0076-6879(84)05016-3. PMID: 6727660.
20. Basu C, Sur R. S-Allyl cysteine alleviates hydrogen peroxide induced oxidative injury and apoptosis through Upregulation of Akt/Nrf-2/HO-1 signaling pathway in HepG2 cells. Biomed Res Int 2018;2018:3169431. DOI: https://doi.org/10.1155/2018/3169431. PMID: 30515391; PMCID: PMC6236807.
21. Han SJ, Kim JI, Park JW, Park KM. Hydrogen sulfide accelerates the recovery of kidney tubules after renal ischemia/reperfusion injury. Nephrol Dial Transplant 2015;30(9):1497-506. DOI: https://doi.org/10.1093/ndt/gfv226. PMID: 26142397.
22. Wijerathne CUB, Madduma Hewage S, Siow YL, Karim O. Kidney Ischemia-reperfusion decreases hydrogen sulfide and increases oxidative stress in the heart. Biomolecules 2020;10(11):1565. DOI: https://doi.org/10.3390/biom10111565. PMID: 33212962; PMCID: PMC7698428.
23. Talat A, Satyanarayana P, Anand P. Association of superoxide dismutase level in women with polycystic ovary syndrome. J Obstet Gynaecol India 2022;72(1):6-12. DOI: https://doi.org/10.1007/s13224-021-01430-z. PMID: 35125733; PMCID: PMC8804132.
24. Elliot SJ, Catanuto P, Pereira-Simon S, Xia X, Pastar I, Thaller S, et al. Catalase, a therapeutic target in the reversal of estrogen-mediated aging. Mol Ther 2022;30(2):947-62. DOI: https://doi.org/10.1016/j.ymthe.2021.06.020. PMID: 34174444; PMCID: PMC8821897.
25. Maher P, Lewerenz J, Lozano C, Torres JL. A novel approach to enhancing cellular glutathione levels. J Neurochem 2008;107(3):690-700. DOI: https://doi.org/10.1111/j.1471-4159.2008.05620.x. PMID: 18702664; PMCID: PMC2644427.
26. Mohamad NV, Ima-Nirwana S, Chin KY. Are oxidative stress and inflammation mediators of bone

loss due to estrogen deficiency? A review of current evidence. Endocr Metab Immune Disord Drug Targets 2020;20(9):1478-87. DOI: https://doi.org/10.2174/1871530320666200604160614. PMID: 32496996; PMCID: PMC8383467.

27. Montano MM, Deng H, Liu M, Sun X, Singal R. Transcriptional regulation by the estrogen receptor of antioxidative stress enzymes and its functional implications. Oncogene 2004;23(14):2442-53. DOI: https://doi.org/10.1038/sj.onc.1207358. PMID: 14676828.
28. Zhu X, Tang Z, Cong B, Du J, Wang C, Wang L, et al. Estrogens increase cystathionine-γ-lyase expression and decrease inflammation and oxidative stress in the myocardium of ovariectomized rats. Menopause 2013;20(10):1084-91. DOI: https://doi.org/10.1097/GME.0b013e318287473. PMID: 23571523.
29. Xiang M, Lu Y, Xin L, Gao J, Shang C, Jiang Z, et al. Role of oxidative stress in reperfusion following myocardial ischemia and its treatments. Oxid Med Cell Longev 2021;2021:6614009. DOI: https://doi.org/10.1155/2021/6614009. PMID: 34055195; PMCID: PMC8149218.
30. Colín-González AL, Santana RA, Silva-Islas CA, Chánez-Cárdenas ME, Santamaría A, Maldonado PD. The antioxidant mechanisms underlying the aged garlic extract- and S-allylcysteine-induced protection. Oxid Med Cell Longev 2012;2012:907162. DOI: https://doi.org/10.1155/2012/907162. PMID: 22685624; PMCID: PMC3363007.
31. Sun Q, Collins R, Huang S, Holmberg-Schiavone L, Anand GS, Tan CH, et al. Structural basis for the inhibition mechanism of human cystathionine γ-lyase, an enzyme responsible for the production of H_2S. J Biol Chem 2009;284(5):3076-85. DOI: https://doi.org/10.1074/jbc.M805459200. PMID: 19019829.
32. Segoviano-Murillo S, Sánchez-González DJ, Martínez-Martínez CM, Cruz C, Maldonado PD, Pedraza-Chaverrí J. S-allylcysteine ameliorates ischemia and reperfusion induced renal damage. Phytother Res 2008;22(6):836-40. DOI: https://doi.org/10.1002/ptr.2396. PMID: 18381751.
33. Li Z, Ludwig N, Thomas K, Mersmann S, Lehmann M, Vestweber D, et al. The pathogenesis of ischemia-reperfusion induced acute kidney injury depends on renal neutrophil recruitment whereas sepsis-induced aki does not. Front Immunol 2022;13:843782. DOI: https://doi.org/10.3389/fimmu.2022.843782. PMID: 35529856; PMCID: PMC9069608.
34. Kwiatkowska E, Kwiatkowski S, Dziedziejko V, Tomasiewicz I, Domański L. Renal microcirculation injury as the main cause of ischemic acute kidney injury development. Biology 2023;12(2):327. DOI: https://doi.org/10.3390/biology12020327. PMID: 36829602; PMCID: PMC9953191.
35. Ehling J, Bábíčková J, Gremse F, Klinkhammer BM, Baetke S, Knuechel R, et al. Quantitative micro-computed tomography imaging of vascular dysfunction in progressive kidney diseases. J Am Soc Nephrol 2016;27(2):520-32. DOI: https://doi.org/10.1681/ASN.2015020204. PMID: 26195818; PMCID: PMC4724942.