

Original Research Article

***Garcinia forbesii* King leaf extract protects against renal tubular injury in ischemia- reperfusion injury via IL-18 and oxidative stress reduction**

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Abstract

Purpose: To evaluate the protective effects of *Garcinia forbesii* King leaf extract against renal tubular injury induced by Renal ischemia–reperfusion injury (IRI) and to assess its association with inflammatory and oxidative stress markers, including interleukin-18 (IL-18), superoxide dismutase 2 (SOD2), and malondialdehyde (MDA).

Methods: Male Wistar rats were subjected to renal IRI and treated with *Garcinia forbesii* King leaf extract at doses of 2.5, 25, and 250 mg/kg. Renal IL-18 levels, SOD2 expression, serum MDA levels, and histopathological tubular injury scores were evaluated.

Results: Renal IL-18 levels were significantly increased in IRI group compared with the sham-operated group. Treatment with *Garcinia forbesii* King leaf extract at doses of 25 and 250 mg/kg significantly reduced renal IL-18 levels. The medium dose (25 mg/kg) significantly increased renal SOD2 expression and reduced serum MDA levels. Histopathological analysis showed that low- and medium-dose treatments attenuated renal tubular injury, whereas the high dose did not provide additional histological protection.

Conclusion: *Garcinia forbesii* King leaf extract exerts nephroprotective effects against IRI-induced renal injury, likely through modulation of inflammatory responses and oxidative stress.

Keywords: *Garcinia forbesii*, AKI, IRI, Inflammation, Oxidative stress

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INTRODUCTION

Renal ischemia-reperfusion injury (IRI) frequently leads to acute kidney injury (AKI) and is marked by oxidative stress and inflammation. IRI is a pathological condition characterized by an initial reduction or cessation of renal blood flow (ischemia), followed by its restoration (reperfusion), which paradoxically exacerbates

cellular and tissue damage. The main mechanisms of damage to IRI involve excessive oxidative stress, the production of reactive oxygen species (ROS), and a massive inflammatory response [1-3]. Oxidative stress damages cellular components, including membrane lipids, which may be assessed by malondialdehyde (MDA) levels, and disrupts endogenous antioxidant defenses [4,5]. In renal

IRI, decreased superoxide dismutase 2 (SOD2) activity has been reported, which contributes to excessive oxidative stress and subsequent kidney damage [6,7].

Beyond oxidative stress, the inflammatory response plays a significant role in the pathogenesis of IRI. This process involves the release of pro-inflammatory cytokines, including interleukin-18 (IL-18), which contributes to renal tubular damage by activating inflammatory signaling pathways and apoptosis [1,8]. Renal tubular damage is a key pathological feature of IRI and leads to kidney dysfunction, in severe cases, organ failure. Therefore, therapeutic strategies targeting oxidative and inflammatory stress pathways are essential to mitigating IRI-induced tubular injury [1,4].

Medicinal plants have long been a source of bioactive compounds with pharmacological potential. *Garcinia forbesii* King is a plant that is widely found in the tropics and is traditionally used for a variety of medicinal purposes. Studies on *Garcinia* genus have revealed the existence of phenolic, flavonoid, and xanthone compounds, which are recognized for their potent antioxidant and anti-inflammatory effects [9,10], however, the potential of *Garcinia forbesii* King leaf extract in protecting renal tubule injury due to IRI through IL-18 modulation and oxidative stress markers such as SOD2 and MDA has not been comprehensively investigated.

This study aimed to evaluate the nephroprotective effects of *Garcinia forbesii* King leaf extract in renal IRI, with a particular focus on inflammatory modulation via IL-18 and oxidative stress markers, including SOD2 and MDA.

METHODS

Animal groups and protocols

The Ethics Committee of the Faculty of Medicine, Lambung Mangkurat University, approved the procedure (approval no. 189/KEPK-FKIK ULM/EC/X/2024). This study involved twenty-five male Wistar rats, weighing 200 – 260 g and aged six weeks. All animals were housed under standard laboratory conditions with free access to food and water. The rats were randomly assigned to five groups (n = 5 per group): (1) Sham-operated (SO) group receiving distilled water; (2) IRI group receiving distilled water; (3) IRI + low-dose group receiving *Garcinia forbesii* King leaf extract at 2.5 mg/kg; (4) IRI + medium-dose group receiving the extract at 25 mg/kg; and (5) IRI + high-dose group receiving the extract at 250 mg/kg. After a 3-day recovery

period, the animals were administered *Garcinia forbesii* King leaf extract for 7 consecutive days via oral gavage. On day 10 postoperatively, the animals were sacrificed for serum and kidney collection.

Preparation of *Garcinia forbesii* King leaf extracts

The fresh leaves of *Garcinia forbesii* King were picked from Biih Village in the Banjar district. Plant identification was performed at the Basic Laboratory, Faculty of Mathematics and Natural Sciences, University Lambung Mangkurat (ULM), South Kalimantan, Indonesia. The leaves were cleaned, dried at 45 - 55 °C, and ground into powder. This powder was soaked in 70 % methanol. Fresh leaves of *Garcinia forbesii* King (approximately 10 kg wet weight) were cleaned, oven-dried at 45 – 55 °C for three days, and ground into powder (2,133.4 g). The powder was extracted by maceration in 70 % methanol for 3 × 24 h with occasional stirring, with filtration performed every 24 h. The combined filtrates were concentrated using a rotary evaporator, further thickened in a water bath, and freeze-dried to obtain a stable crude extract (200.44 g).

Animal model of renal I/R injury

The rats were anesthetized by intraperitoneal injection of ketamine (100 mg/kg) and xylazine (10 mg/kg). Renal IRI was induced by occluding the renal artery and vein using a non-traumatic vascular clamp (Hammacher®) for 45 minutes, followed by clamp removal to allow reperfusion. The incision was closed using 3/0 silk sutures (One Med®). Rats in SO group underwent the same surgical procedures without renal vascular occlusion [11,12].

Blood sample collection and kidney sample collection

Rats were anesthetized with intraperitoneal ketamine (100 mg/kg) and xylazine (10 mg/kg) before abdominal and thoracic incision. Blood was collected by cardiac puncture, followed by perfusion via the left ventricle with 0.9 % NaCl. Both kidneys were collected; one was stored in RNA later for RNA extraction, and the other was fixed in 4 % paraformaldehyde (PFA) in *Phosphate-Buffered Saline* (PBS) before paraffin embedding [12].

Biochemical assay of IL-18 in kidney homogenates

Each renal cortex was thoroughly rinsed with cold phosphate-buffered saline (PBS; 0.01 M, pH

= 7.4) to remove residual blood. Kidney tissues were homogenized in phosphate-buffered saline (Sigma-Aldrich; Cat. no. P2272) at a tissue-to-buffer ratio of 1:9 (w/v) using a glass homogenizer on ice. The homogenates were stored at -80°C until further analysis.

Renal IL-18 levels were measured using a rat IL-18 ELISA kit (Reed Biotech Ltd., Cat. no. RE1123R). For the assay, 100 μL of each sample was added to each well of a 96-well plate and processed according to the manufacturer's instructions. All samples were analyzed in duplicate, and IL-18 concentrations were expressed as pg/mg protein. Biochemical assay of MDA in serum

Serum malondialdehyde (MDA) levels were measured using the thiobarbituric acid (TBA) method with a commercial assay kit (Elabscience, Cat. No. E-BC-K025-M-96T), according to the manufacturer's instructions. Blood samples were collected from rats by cardiac puncture, and serum was separated by centrifugation prior to analysis.

Reverse transcriptase PCR (RT-PCR)

Total RNA was extracted using Genezol solution (Cat no. GZR100) according to the manufacturer's instructions. RNA concentration and purity were measured using a NanoDrop spectrophotometer. Complementary DNA (cDNA) was synthesized using random primers (Toyobo, Japan; Cat no. 3801) and ReverTra Ace reverse transcriptase (Toyobo, Japan; Cat no. TRT-101). Reverse transcription polymerase chain reaction (RT-PCR) was performed using GoTaq Green Master Mix to evaluate the expression of superoxide dismutase 2 (SOD2) and β -actin. Gene expression levels were analyzed by densitometry using ImageJ software and normalized to β -actin as the housekeeping gene. Primer sequences and annealing temperatures are listed in Table 1.

Histological analysis and tubular injury quantification

The tubular injury score was evaluated using PAS staining and determined through a semi-quantitative scoring system across 15 fields for each specimen at 400x magnification. Tubular injury was graded on a scale from 0 to 4, where a

score of 0 indicated normal histology; score 1 indicated mild injury (< 25 %); score 2 indicated moderate injury (25 – 50 %); score 3 indicated severe injury (50 – 75%); and score 4 indicated extensive injury (> 75 %) [3,11].

Statistical analysis

Statistical analysis was performed on biochemical and histopathological data using the SPSS software Version 25.0. Data normality was assessed using the Shapiro-Wilk test. Non-normally distributed data were analyzed using the Kruskal-Wallis test. While normally distributed data were analyzed using one-way analysis of variance (ANOVA). Post hoc comparisons between groups were conducted using the Bonferroni test. Results are presented as mean $\pm$ standard deviation (SD), with $p < 0.05$ considered statistically significant.

RESULTS

Effect of *Garcinia forbesii* King leaf extract on kidney IL-18

Renal IL-18 levels were significantly higher in IRI group compared with SO group ($p = 0.014$). Administration of *Garcinia forbesii* King leaf extract following IRI significantly reduced renal IL-18 levels in the medium-dose (25 mg/kg) and high-dose (250 mg/kg) groups compared with IRI group ($p < 0.001$ for both comparisons). The medium-dose group (25 mg/kg) exhibited significantly lower renal IL-18 levels than the low-dose group (2.5 mg/kg; $p < 0.001$), whereas no significant difference was observed between the medium-dose and high-dose groups ($p = 1.00$). Despite these reductions, renal IL-18 levels in the medium- and high-dose groups remained significantly higher than those in SO group ($p < 0.05$). These results are shown in Figure 1.

Effect of *Garcinia forbesii* King leaf extract on oxidative stress

Renal SOD2 expression was significantly lower in IRI group compared with SO group ($p = 0.015$). Administration of *Garcinia forbesii* King leaf extract following IRI, significantly increased renal SOD2 expression compared with IRI group ($p = 0.03$).

Table 1: Primer sequences used for RT-PCR at annealing temperature of 60°C

Gene	Primer forward (5'-3')	Primer reverse (5'-3')
SOD2	ATGTTGTGTCGGGCGCGTGCAGC	GCGCCTCGTGGTACTTCTCCTCGGTG
β -actin	GCAGATGTGGATCAGCAAGC	GGTGTAACGCAGCTCAGTAA

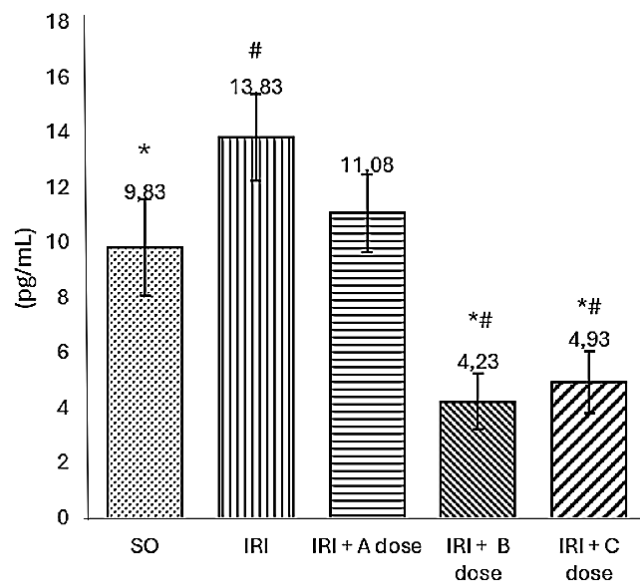


Figure 1: Effects of *Garcinia forbesii* King leaf extract at different doses on renal IL-18 (pg/mL) levels following renal ischemia-reperfusion injury (IRI). # $P < 0.05$ vs sham-operated (SO) group; * $P < 0.05$ vs IRI group

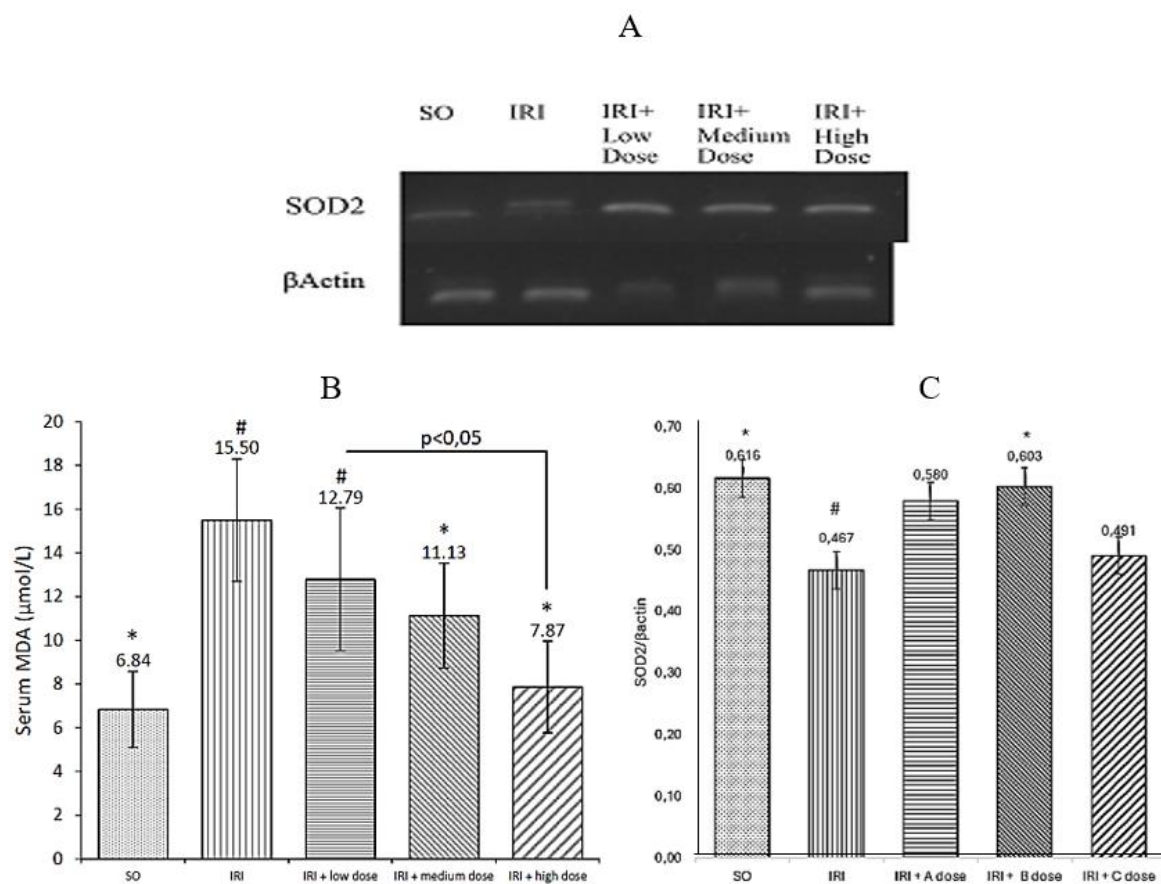


Figure 2: Effects of *Garcinia forbesii* King leaf extract at different doses on (A and C) renal SOD2 expression and (B) serum malondialdehyde (MDA) levels following renal ischemia-reperfusion injury (IRI) application. * $P < 0.05$ vs IRI group; # $p < 0.05$ vs SO group

Dose-specific analysis showed that administration of the medium dose (25 mg/kg) significantly increased renal SOD2 mRNA expression relative to IRI group ($p = 0.03$), whereas administration of low dose (2.5 mg/kg) and high dose (250 mg/kg) did not result in significant differences. These results are shown in Figure 2.

Effect of *Garcinia forbesii* King leaf extract on renal tubular injury following IRI

Renal tubular damage score was significantly higher in IRI group compared to SO group ($p < 0.001$). Administration of *Garcinia forbesii* King leaf extract following IRI significantly reduced tubular damage scores in the low-dose (2.5 mg/kg) and medium-dose (25 mg/kg) groups compared with IRI group ($p < 0.001$ for both comparisons).

The medium-dose group exhibited significantly lower renal tubular damage scores than the high-dose group ($p < 0.001$), while no significant difference was observed between the medium-dose and low-dose groups ($p = 0.23$). These results are shown in Figure 3.

DISCUSSION

The present finding indicates that the *Garcinia forbesii* King leaf extract following IRI is associated with reduced renal inflammation, as reflected by decreased renal IL-18 expression compared with IRI group (Figure 1). Interleukin-18 (IL-18) is a member of the IL-1 cytokine family and is produced by hematopoietic and nonhematopoietic cells, including renal tubular epithelium and podocytes, as an inactive precursor (pro-IL-18). This precursor is subsequently cleaved. Activated caspase-1 processes pro-IL-18 into mature IL-18, which is then secreted by immune cells, including monocytes and macrophages [17,18]. Previous studies have demonstrated that IL-18 contributes to neutrophil and macrophage infiltration in the kidney and promotes apoptotic pathways following IRI. Consistent with these findings, experimental studies employing genetic manipulation or therapeutic inhibition of IL-18 have shown attenuation of renal injury after ischemia–reperfusion [8,13].

Renal ischemia-reperfusion injury (IRI) induces the generation of reactive oxygen species (ROS), resulting in oxidative stress and subsequent tissue damage, including lipid peroxidation, protein, and DNA damage. These processes ultimately contribute to apoptosis and necrosis of renal cells. Mitochondria's antioxidant defense

systems play a crucial role in limiting oxidative stress by detoxifying superoxide radicals. One of the key enzymes involved in this process, superoxide dismutase 2 (SOD2), is crucial for converting superoxide radicals into less harmful molecules, thereby reducing oxidative stress. Enhanced SOD activity has been shown to ameliorate renal damage markers and improve renal function following IRI [7,14,15]. This interpretation is further supported by elevated serum malondialdehyde (MDA) levels in IRI group, which were significantly reduced after treatment with medium and high doses of *Garcinia forbesii* King leaf extract. Serum malondialdehyde MDA results from lipid peroxidation due to ROS-induced oxidative stress. Excessive ROS during kidney IRI causes extensive damage to various cellular components. Several studies have reported increased MDA levels following IRI. MDA is widely recognized as a reliable biomarker of oxidative stress, particularly lipid peroxidation [4,16]. Increased SOD2 expression and reduced serum MDA levels in the treatment group suggest that *Garcinia forbesii* King leaf extract may attenuate free radical activity and lipid peroxidation.

Histopathological analysis using periodic acid–Schiff (PAS) staining demonstrated significantly greater tubular injury in IRI group compared with SO group. Renal tubular injury is closely related to oxidative stress and inflammation. Oxidative stress refers to damage caused by reactive oxygen species (ROS), highly reactive molecules that damage cellular components. In the kidneys, oxidative stress is triggered by various factors, including IRI. In renal IRI, in addition to an increase in ROS, there is an inflammatory response as a defense mechanism against oxidative damage [4,17]. However, this inflammatory response also promoted further ROS generation, creating a vicious cycle that worsens kidney injury. Renal tubular epithelial cells are highly susceptible to oxidative stress and inflammation, damage to these cells leading to apoptosis and necrosis, leading to functional impairment and contributing to the development of acute kidney injury (AKI) and progression to chronic kidney disease (CKD). Oxidative stress disrupts mitochondrial function, resulting in energy deficits and exacerbating cell death and inflammation responses [1,2]. Mitochondrial antioxidant defense systems play a critical role in limiting oxidative injury. One of the key enzymes involved is SOD2, which converts superoxide radicals into less harmful molecules and thereby protects cells from oxidative damage.

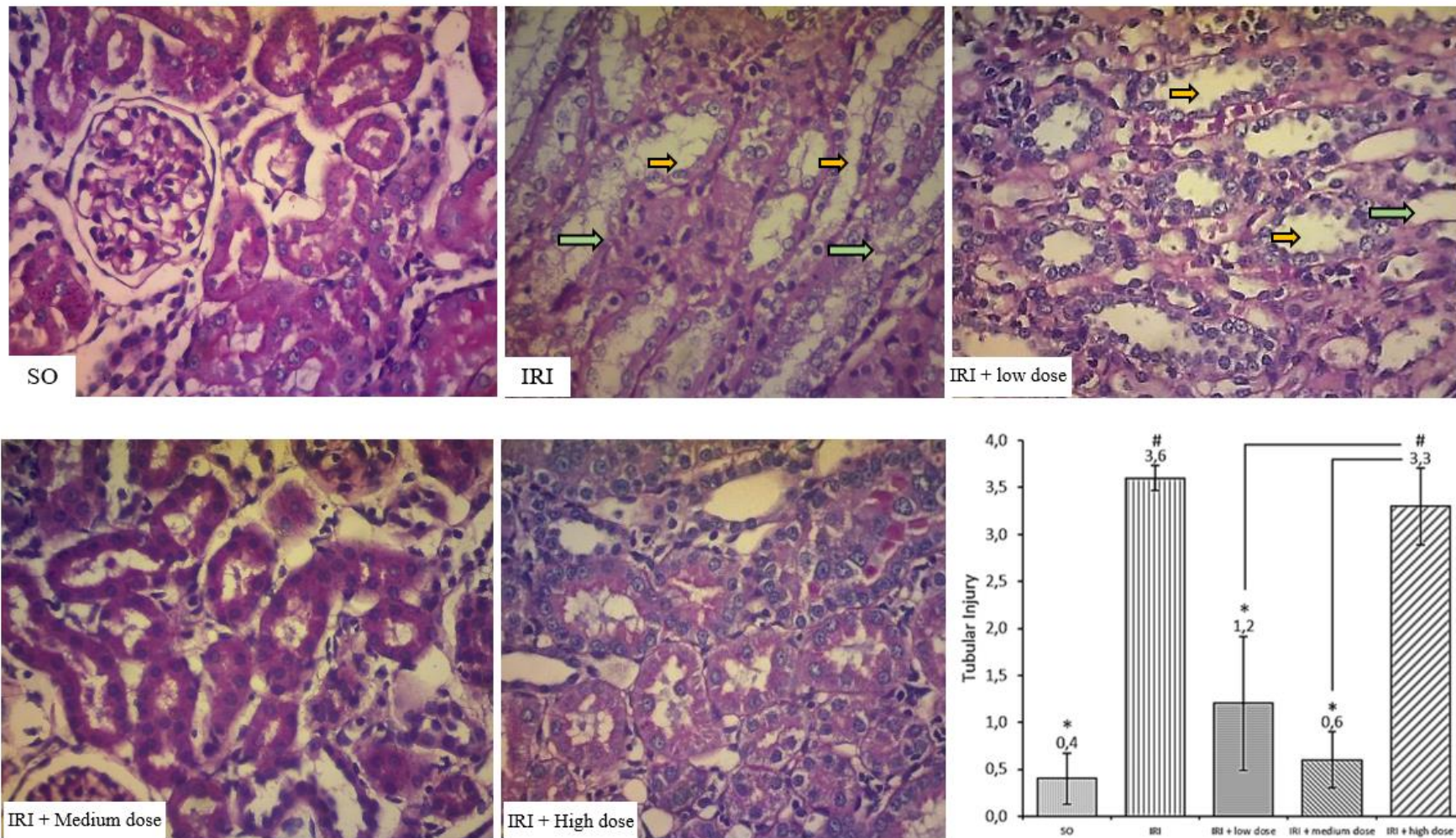


Figure 3: Effect of different doses of *Garcinia forbesii* King leaf extract on renal tubule injury after renal ischemia-reperfusion (I/R) application. * $P < 0.05$ vs IRI group; # $p < 0.05$ vs SO group

In addition, modulation of inflammatory pathways, including inhibition of IL-18, contributes to attenuation of the inflammatory response and protects against renal tubule injury [5,7]. In the present study, administration of *Garcinia forbesii* King leaf extract at doses of 2.5 mg/kg and 25 mg/kg resulted in significantly lower tubular injury scores compared with IRI group. In contrast, no significant difference in tubular injury scores was observed between the high-dose group (250 mg/kg) and the Tubular injuries in this study were characterized by tubular dilatation, intraluminal cast formation, thinning of tubular epithelial cells, and loss of the brush border. Histopathological evaluation revealed that administration of *Garcinia forbesii* King leaf extract at a dose of 250 mg/kg produced tubular injury patterns comparable to those observed in IRI group without extract treatment.

This study is the first to explore the nephroprotective potential of *Garcinia forbesii* King leaf extract in renal ischemia-reperfusion injury model. The findings provide experimental evidence supporting the potential use of *Garcinia forbesii* King as natural nephroprotective agent, which may exert its effect through anti-inflammatory and antioxidant mechanisms.

This study has several limitations. Renal function parameters, such as serum creatinine levels, were not evaluated and therefore could not be correlated with the observed histopathological changes. Consequently, the assessment of kidney injury in this study was primarily based on histological analysis rather than functional biomarkers. Future studies incorporating renal function markers are warranted to further validate these findings.

CONCLUSION

Administration of *Garcinia forbesii* King leaf extract at 2.5 and 25 mg/kg significantly reduces renal IL-18 levels compared with IRI group. In addition, treatment with *Garcinia forbesii* King leaf extract at 25 mg/kg, significantly increased renal SOD2 expression and reduced serum malondialdehyde (MDA) levels relative to IRI group. Furthermore, administration of *Garcinia forbesii* King leaf extract at doses of 2.5 mg/kg and 25 mg/kg attenuated renal tubular injury compared with IRI I group. These findings indicate that *Garcinia forbesii* King leaf extract exerts nephroprotective effects against ischemia-reperfusion-induced renal injury, likely through modulation of inflammatory responses and oxidative stress.

DECLARATIONS

Acknowledgment/Funding

None.

Ethical approval

This study was approved by the Ethics Committee of FKIK ULM (approval no. 189/KEPK-FKIK ULM/EC/X/2024)

Conflicts of interest

No conflict of interest is associated with this work.

Use of Artificial Intelligence/Large language models

Artificial Intelligence was used for editorial purposes, including language editing, writing assistance, and translation. The authors reviewed and approved the final version of the manuscript and take full responsibility for its content.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Contributions of Authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

Azma Rosida, Nia Kania, and Mohammad Rudiansyah conceptualized and designed the study. Azma Rosida drafted the initial version of manuscript. All authors contributed to the experimental work, data analysis, critical review, and approval of the final version.

REFERENCES

1. Maher SA, Fawzy MA, El-Rehany MA, Fathy M. Renal ischemia-reperfusion injury: molecular mechanisms and therapeutic targets. *Minia J Med Res* 2021; 32(2): 42–49.
2. Chen Y, Li Z, Zhang H, Chen H, Hao J, Liu H, Li X. Mitochondrial metabolism and targeted treatment strategies in ischemia-induced acute kidney injury. *Cell Death Discov* 2024; 10(1): 69.

3. Dhanarasu S, Almuqati AF. Allicin-mediated renal protection in mitigating streptozotocin-induced diabetic nephropathy in rats through comprehensive restoration of kidney function and morphology. *Trop J Pharm Res* 2024; 23(12): 2025–2033.
4. Saini V. The role of oxidative stress in kidney diseases. In: Maurya PK, Qamar I, editors. *Novel Therapeutic Approaches Targeting Oxidative Stress*. 1st ed. Oxford: Academic Press 2022: 119–141.
5. Zhang M, Liu Q, Meng H, Duan H, Liu X, Wu J, Gao F, Wang S, Tan R, Yuan J. Ischemia-reperfusion injury: molecular mechanisms and therapeutic targets. *Signal Transduct Target Ther* 2024; 9(1): 12.
6. Rashid H, Jali A, Akhter MS, Abdi SAH. Molecular mechanisms of oxidative stress in acute kidney injury: targeting the loci by resveratrol. *Int J Mol Sci* 2023; 25(1): 3.
7. Hou Y, Lin S, Xia J, Zhang Y, Yin Y, Huang M, Xu Y, Yang W, Zhu Y. Alleviation of ischemia-reperfusion induced renal injury by chemically modified SOD2 mRNA delivered via lipid nanoparticles. *Mol Ther Nucleic Acids* 2023; 34: 102067.
8. Exconde PM, Hernandez-Chavez C, Bourne CM, Richards RM, Bray MB, Lopez JL, Srivastava T, Egan MS, Zhang J, Yoo W, et al. The tetrapeptide sequence of IL-18 and IL-1 β regulates their recruitment and activation by inflammatory caspases. *Cell Rep* 2023; 42(12): 113581.
9. Tauchen J, Frankova A, Manourova A, Valterova I, Lojka B, Leuner O. *Garcinia kola*: a critical review on chemistry and pharmacology of an important West African medicinal plant. *Phytochem Rev* 2023; 22(5): 1305–1351.
10. Ismail MM, Appah J, Bello A, Mohammed UA. Hepatoprotective and nephroprotective effects of aqueous extract of *Garcinia kola* (Bitter Kola) in indomethacin-induced poisoning in Wistar rats. *Arid-Zone J Basic Appl Res* 2024; 3(4): 125–135.
11. Arfian N, Wahyudi DAP, Zulfatima IB, Citta AN, Anggorowati N, Multazam A, Romi MM, Sari DCR. Chlorogenic acid attenuates kidney ischemic/reperfusion injury via reducing inflammation, tubular injury, and myofibroblast formation. *Biomed Res Int* 2019; 2019(1): 5423703.
12. Sari FT, Arfian N, Sari DCR. Effect of kidney ischemia/reperfusion injury on proliferation, apoptosis, and cellular senescence in acute kidney injury in mice. *Med J Malaysia* 2020; 75(Suppl 1): 20–23.
13. Kim YG, Kim SM, Kim KP, Lee SH, Moon JY. The role of inflammasome-dependent and inflammasome-independent NLRP3 in the kidney. *Cells* 2019; 8(11): 1389.
14. Guerrero-Hue M, Rayego-Mateos S, Vázquez-Carballo C, Palomino-Antolín A, García-Caballero C, Opazo-Rios L, Morgado-Pascual JL, Herencia C, Mas S, Ortiz A, et al. Protective role of Nrf2 in renal disease. *Antioxidants* 2021; 10(1): 39.
15. Trambas IA, Bowen L, Thallas-Bonke V, Snelson M, Sourris KC, Laskowski Am Tauc M, Rubera I, Zhenh G, Harris DCH, et al. Proximal tubular deletion of superoxide dismutase-2 reveals disparate effects on kidney function in diabetes. *Redox Biol* 2025; 82: 103601.
16. Wu L, Xiong X, Wu X, Ye Y, Jian Z, Zhi Z, Gu L. Targeting oxidative stress and inflammation to prevent ischemia-reperfusion injury. *Front Mol Neurosci* 2020; 13: 28.
17. Li C, Yu Y, Zhu S, Hu Y, Ling X, Xu L, Zhang H, Guo K. The emerging role of regulated cell death in ischemia and reperfusion-induced acute kidney injury: Current evidence and future perspectives. *Cell Death Discov* 2024; 10(1): 216.
18. Yu Z, Zhou Y, Zhang Y, Ning X, Li T, Wei L, Wang Y, Bai X, Sun S. Cell profiling of acute kidney injury to chronic kidney disease reveals novel oxidative stress characteristics in the failed repair of proximal tubule cells. *Int J Mol Sci* 2023; 24 (14): 11617.