

## Peer Review File

Article information: <https://dx.doi.org/10.21037/tau-23-562>

### Reviewer A

- 1) First, the abstract is not adequate. The background did not describe the clinical needs for this research focus and what the current knowledge gap is. The methods need to briefly describe the TCMSP. The results must provide data and statistics to support the findings. The conclusion needs comments for the clinical implications.

**Reply:** We have modified it. ""

**Changes in the text:** we have modified our text as advised (Page1/Line30-31; Page1-2/Line34-37;Page4-5/Line106-107;Page11/Line335-342). ( “Acute kidney injury (AKI) is a devastating clinical syndrome with high mortality rate attributed to lack of effective treatment”;“AR-RAS has certain protective effects on AKI in experiments, but the relevant mechanisms have yet to be clear. So this study aims to explore the mechanism of action of AR-RAS in AKI by combining network pharmacology and molecular docking methods”

- 2) Second, in the introduction, the authors need to provide clinical evidence that support the efficacy of AR and RAS for AKI, which is a prerequisite for this study. Please further describe the rationale and scientific soundness of network pharmacology to explain why this approach could answer the research questions.

**Reply:** We have modified it.

**Changes in the text:** We have modified our text as advised (Page4/Line90-93), “Modern clinical data have effectively confirmed that AR-RAS is a safe and effective herbs, which has significant effects on AKI and can profoundly promote recovery of renal function (10,11) ”.

- 3) Third, in the methodology of the main text, please first briefly summarize the procedures of this study, details of the TCMSP, and, a further question is how to validate the real-world effects of AR and RAS.

**Reply:** In Page5/Line110-117, the content is mentioned.

**Changes in the text:** None.

- 4) Finally, please cite several related studies: 1. Chia AXF, Pang PYK. Does the maze procedure predispose to acute kidney injury? J Thorac Dis 2023;15(2):223-225. doi: 10.21037/jtd-22-1709. 2. Guo S, Chen Y, Huo Y, Zhao C, Zhang K, Zhang X, Liu M, Hu Z. Comparison of early and delayed strategy for renal replacement therapy initiation for severe acute kidney injury with heart failure: a retrospective comparative cohort study. Transl Androl Urol 2023;12(5):715-726. doi: 10.21037/tau-23-146. 3. Zhang J, Lin J. Efficacy of artesunate in asthma: based on network pharmacology and molecular docking. J Thorac Dis 2023;15(4):1658-1674. doi: 10.21037/jtd-22-1437.

**Reply:** We have already cited 2. Guo S, Chen Y, Huo Y, Zhao C, Zhang K, Zhang X, Liu M, Hu Z. Comparison of early and delayed strategy for renal replacement therapy initiation for severe acute kidney injury with heart failure: a retrospective comparative cohort study. *Transl Androl Urol.* 2023 May 31;12(5):715-726. doi: 10.21037/tau-23-146. Epub 2023 May 9. PMID: 37305617; PMCID: PMC10251106.

**Changes in the text:** we have modified our text as advised (Page13/Line388-392)(“Guo S, Chen Y, Huo Y, Zhao C, Zhang K, Zhang X, Liu M, Hu Z. Comparison of early and delayed strategy for renal replacement therapy initiation for severe acute kidney injury with heart failure: a retrospective comparative cohort study. *Transl Androl Urol.* 2023 May 31;12(5):715-726. doi: 10.21037/tau-23-146. Epub 2023 May 9. PMID: 37305617; PMCID: PMC10251106.”)

#### **Reviewer B**

The paper titled “The effect of radix Astragali-radix Angelica sinensis on acute kidney injury: a network pharmacology and molecular docking study” is interesting. The described here the potential active ingredients, possible targets responsible for the efficacy of AR-RAS in AKI treatment, providing a theoretical basis for further research. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) The abstract is not sufficient and needs further modification. The research background did not indicate the clinical needs of the research focus.

**Reply:** We have modified it.

**Changes in the text:** we have modified our text as advised (Page1-2/Line30-37)(“Acute kidney injury (AKI) is a devastating clinical syndrome with high mortality rate attributed to lack of effective treatment. The herbal pair of Astragali radix (AR) and radix Angelica sinensis (RAS) is a commonly prescribed herbal formula or is added to other traditional Chinese medicine (TCM) prescriptions for the treatment of kidney diseases. AR-RAS has certain protective effects on AKI in experiments, but the relevant mechanisms have yet to be clear. So this study aims to explore the mechanism of action of AR-RAS in AKI by combining network pharmacology and molecular docking methods”)

2) Some fonts need to be enlarged, as shown in Figures 3 and 4.

**Reply:** We have modified it.

**Changes in the text:** we have modified our text as advised (Page21/Line582,Page22/Line588,as shown in Figure3 and Figure4)

3) Suggest increasing in vitro and in vivo experiments to prove the research results, which may be more credible.

**Reply:**there is a plan for experiments in the future.

**Changes in the text:**None.

4) How to carry out drug innovation and research through network pharmacology? Are there any difficulties to overcome? It is recommended to increase the discussion of related content.

**Reply:**This paper has already covered this content.(Page9/Line258-267)

**Changes in the text:**None.

5) It is recommended to add relevant possible mechanism to further enrich the content of the discussion.

**Reply:**This paper has already covered this content. (Page11/Line315-328)

**Changes in the text:**None.

6) Suggest increasing the analysis of differential metabolites closely related to AKI pathological processes and AR-RAS effects.

**Reply:**This paper has already covered this content.(Page10/Line303-314)

**Changes in the text:**None.

7) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “Yishen Xiezhuo formula ameliorates the development of cisplatin-induced acute kidney injury by attenuating renal tubular epithelial cell senescence, PMID: 36660714”. It is recommended to quote the articles.

**Reply:**We have modified it.

1. **Changes in the text:**we have modified our text as advised (Page13/Line395-399)(“Zhang Q, Qi J, Luo Q, Wu M, Zhang L, Qin L, Nie X. Yishen Xiezhuo formula ameliorates the development of cisplatin-induced acute kidney injury by attenuating renal tubular epithelial cell senescence. Ann Transl Med. 2022 Dec;10(24):1392. doi: 10.21037/atm-22-5415. PMID: 36660714; PMCID: PMC9843381.”)

8) It is suggested to increase the analysis and functional research of key genes, which may be more convincing and meaningful.

**Reply:**This paper has already covered this content (Page11/Line315-334).

**Changes in the text:**None.

