Name of journal: *World Journal of Diabetes*

Manuscript NO: 95055

Title: Network pharmacology and molecular dynamics study of the effect of the Astragalus-Coptis drug pair on diabetic kidney disease

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

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Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor, Doctor

Reviewer’s Country/Territory: Italy

Author’s Country/Territory: China

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In this paper, the authors adopted a comprehensive approach integrating network pharmacology, molecular docking technology, and molecular dynamics simulation was adopted to elucidate the material basis and mechanism by which Astragalus-Coptis drug pair treats DKD. One of the strengths of this study is the clarity and coherence of the data presented. The findings are well-organized and clearly elucidate the characteristics of multiple ingredients, targets, and signaling pathways involved in the treatment of DKD with the Astragalus-Coptis drug pair. The identification of Quercetin as a potent active ingredient, specifically targeting AKT1 and TNF, is particularly noteworthy. This finding not only provides a theoretical foundation for further exploration but also offers potential therapeutic avenues for DKD treatment. Overall, this manuscript is well-organized and the topic is of great significance. Furthermore, minor comment that I would to proposed: 1. In the method 1.2, please check the “|logFC| > 1”, is it log2FC? 2. The font in all the figures of this article needs to be adjusted and enlarged, so that readers can easily obtain the information. 3. In Supplementary Figure 2 A-C, please indicate the meanings represented by red and cyan.
PEER-REVIEW REPORT

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SPECIFIC COMMENTS TO AUTHORS

This is a potentially significant paper. This study represents a contribution to the field of integrative pharmacology, particularly in the context of diabetic kidney disease (DKD) treatment. The authors have undertaken a heavy workload, employing a comprehensive approach that integrates network pharmacology, molecular docking technology, and molecular dynamics simulation. This rigorous methodology underscores the depth of their investigation into the material basis and mechanism of action of the Astragalus-Coptis drug pair in treating DKD. This study not only advances our understanding of the molecular mechanisms underlying the therapeutic effects of the Astragalus-Coptis drug pair but also demonstrates a novel approach that could be applied to other traditional Chinese medicine formulations. A very nice study with comprehensive set of work. I have only a few comments on the discussion: The discussion briefly mentions the implications of the study findings, such as the identification of Quercetin as a potent active ingredient targeting AKT1 and TNF. However, it could be expanded to include a more in-depth analysis of the potential clinical relevance and therapeutic implications of these findings. Discuss how targeting
AKT1 and TNF with Quercetin may impact the pathogenesis or progression of DKD and how this could inform future research or clinical practice.