

Dear editor and reviewers,

Thanks for your comments, we have carefully edited our manuscript. The edited parts have been highlighted with yellow color in our revised manuscript. The point-by-point responses of your comments are shown as follows,

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors:

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? - Yes, the title reflects the main subject/hypothesis of the manuscript.

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? - Yes, the abstract summarizes the contents of the manuscript quite nicely.

3 Key Words. Do the key words reflect the focus of the manuscript? Yes.

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? -In my opinion, yes. However, controlling blood glucose levels, reducing blood pressure, and improving microcirculation can prevent diabetic nephropathy to a certain extent. In line 92, "the above treatments cannot impede the progression of DN." This needs to be expressed more rigorously.

Response: Thanks for your suggestion. We have modified the above statement to make it more rigorous.

Conventional treatments of DN include controlling blood glucose levels, reducing blood pressure, and improving microcirculation. The above treatments using Western drugs (e.g., antihypertensives) can prevent DN to a certain extent, however, have negligible effects on patients with advanced DN

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? - Yes. The authors described the experiments and material details fully.

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? - Yes. The authors experimentally evaluated the therapeutic effects and possible mechanisms of spleen-strengthening and kidney-stabilizing soup (JPGS) in mice with diabetic nephropathy and showed that JPGS significantly ameliorated renal injury, controlled inflammation and oxidative stress, and improved renal metabolites by regulating renal metabolites, decreasing TLR4/NF- κ B/NLRP3-mediated inflammation, and inhibiting JNK/P38-mediated apoptosis, which resulted in improved diabetic nephropathy. This is an interesting finding.

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? - Generally, yes. However, the discussion section can be appropriately streamlined by removing content that is not relevant to the results.

Response: Thanks for your suggestion. We have adjusted the content of the discussion section to make it more relevant to the results section. The adjusted content was highlighted in red in the article.

8 Illustrations and tables. Are the figures, diagrams, and tables sufficient, good quality and appropriately illustrative, with labeling of figures using arrows, asterisks, etc, and are the legends adequate and accurately reflective of the images/illustrations shown? - I did not notice any manipulations.

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? - Yes.

10 Units. Does the manuscript meet the requirements of use of SI units? - Yes.

11 References. Does the manuscript appropriately cite the latest, important and authoritative references in the Introduction and Discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? - I did not notice any incorrectly cited.

12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? - Yes.

13 Research methods and reporting. Authors should have prepared their manuscripts according to BPG's standards for manuscript type and the appropriate topically-relevant category, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. For (6) Letters to the Editor, the author(s) should have prepared the manuscript according to the appropriate research methods and reporting. Letters to the Editor will be critically evaluated and only letters with new important original or complementary information should be considered for publication. A Letter to the Editor that only recapitulates information published in the article(s) and states that more studies are needed is not acceptable? - Yes, the authors had provided the ARRIVE Guidelines.

14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? - I did not notice any ethics issues.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

Diabetic nephropathy is a serious complication of diabetes mellitus, making the search for drugs that could be used to treat it an important challenge.

Comments:

1. In the introduction it is recommended to reword the sentence "... and Western drugs (e.g., antihypertensives) may cause side effects in DN patients", as the wording used is not correct and will not be understood by a wide range of readers.

Response: Thanks for your suggestion. We have modified the above statement to make it more rigorous. Conventional treatments of DN include controlling blood glucose levels, reducing blood pressure, and improving microcirculation. The above treatments using Western drugs (e.g., antihypertensives) can prevent DN to a certain extent, however, have negligible effects on patients with advanced DN.

2. It is recommended to correct the sentence "can invigorate the spleen, strengthen the kidneys, disperse blood stasis, and dredge collaterals, corresponding to the pathogenesis of DN", as it uses terms specific to traditional medicine, which will not be understood by a wide range of readers.

Response: Thanks for your suggestion. We have corrected it. JPGS is highly efficacious clinically on DN.

3. It is not clear from the materials and methods whether Huanglian Jiedu Decoction is a fixed combination. It is also recommended that the Latin names of medicinal plants, descriptions of the parts of these plants, and methods of extracting the active ingredients from them be described. It is not clear what is meant by leeches, and rhubarb (stir-fried with wine). In the current form, the exact composition and methods of obtaining JPGS are not clear. What components are used to standardize and dose JPGS (low doses, high doses)?

Response: Thanks for your suggestion. We included the Latin names of JPGS medicinal plants in the last paragraph of the introduction, and we included JPGS preparation methods in the Methods section, with more detailed quality control included in the supplementary material.

4. I did not find Supplementary material.

Response: Thanks for your suggestion. The supplementary material has been uploaded to the submission system.

5. In Figure 6C are the processed or original Western blotting results?

Response: Thanks for your suggestion. We used the automatical exposure image in our manuscript. Because the chemiluminescence imaging system adjust the indicators such as exposure time, gamma value etc. automatically during the imaging acquisition process, which could enhance the visibility of

WB bands. We have attached the original image of WB with markers to the submission system.

OTHER COMMENTS

1 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

Response: Thanks for your suggestion. Our revised manuscript has been polished by a professional English language editing company, and the proof of language polishing has been uploaded to the submission system.

2 ABBREVIATIONS

Response: Thanks for your suggestion. We have carefully reviewed the full text and made modifications to the abbreviations.

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

The manuscript has been peer-reviewed, and it is ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Response: Thanks for your suggestion. Our revised manuscript has been polished by a professional English language editing company, and the proof of language polishing has been uploaded to the submission system.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, please provide and upload the following important documents:

- **Biostatistics Review Certificate**, a statement affirming that the statistical review of the study was performed by a biomedical statistician;

Response: Biostatistics Review Certificate has been uploaded to the submission system.

- **Institutional Review Board Approval Form or Document**, the primary version (PDF) of the Institutional Review Board's official approval, prepared in the official language of the authors' country;
- **Institutional Animal Care and Use Committee Approval Form or Document**, the primary version (PDF) of the Institutional Animal Care and Use Committee's official approval in the official language of the authors' country;

Response: Institutional Animal Care and Use Committee Approval Form or Document has been uploaded to the submission system.

- The ARRIVE Guidelines, an important document related to manuscript writing of basic research using animals.

Response: The ARRIVE Guidelines has been uploaded to the submission system.

- The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, it is recommended that the authors provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend:
<https://www.wjgnet.com/bpg/gerinfo/240>.

Response: Thanks for your suggestion. Our revised manuscript has been polished by a professional English language editing company, and the proof of language polishing has been uploaded to the submission system.

- Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

Response: Thanks for your suggestion. We have made the required changes to figure legends.

- Please provide the original figure documents.

Response: The original figure documents has been uploaded to the submission system.

- Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the

author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Response: The PPT containing figures has been uploaded to the submission system.

- Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: The format of the table meets the above requirements.

- Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: The approved grant application form has been uploaded to the submission system.

If you have more comments on our manuscript, please contact us as soon as possible.

Best regards,

Huantian Cui