

Dear Dr. Ma,

Thank you very much for your letter and advice. We revised the manuscript and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the revisions are highlighted in red in the revised manuscript. The article highlight is demonstrated in page 16 to 17, and we have updated the references. Our study is about traditional Chinese medicine, Chinese literature would inevitably be cited, and we have highlighted these references in the manuscript. The point-by-point responses to the reviewers' comments are listed below (in blue).

We hope that the revised version of the manuscript is currently acceptable for publication in your journal.

We look forward to hearing from you soon.

Best regards,

Yours sincerely,

Mei-hua Wan

## Replies to reviewer #1 (ID: 05098861)

First of all, thank you for the patient review and praise of our work, and we appreciate the constructive comments you have made.

**Comments:** 1. In my point of view, you can emphasize the observed decrease in TNF and IL-10 levels.

**Response:** The pro-inflammatory cytokine TNF- $\alpha$  and anti-inflammatory cytokine interleukin-10 (IL-10) are usually regarded as an early predictor of SAP severity and prognoses<sup>[1]</sup>. The results in our experiment showed the serum TNF- $\alpha$  and IL-10 increased significantly when SAP occurred, while YBT intervention could reduce TNF- $\alpha$  but have no effect on IL-10 levels. From these results, we can deduce that YBT could decrease production of TNF- $\alpha$  and inhibit inflammation, while YBT does not interfere with anti-inflammatory ability of SAP rats. We have added this part in [page13, line 10 to 16](#).

**Comments:** 2. On the other hand, unfortunately, your results did not demonstrate changes in creatinine levels, at the experimental level we usually use tubular damage markers such as KIM-1, N-GAL, maybe you can use surrogates like those.

**Response:** We have added the results of creatinine of our experiment in [page 10, line 10 to 14](#). We had detected mRNA and protein expression of KIM-1, but found no significant difference in the three experimental groups ([in page 11, line 31; page 12, line 7-8](#)). The vimentin expression in kidney of SAP rats was increased in our experiment, which was reported could reflect cell inflammatory injury<sup>[2]</sup>, thus, we think the vimentin change in the model group can also reflect kidney injury ([in page 11, line 28 to 30](#)).

**Comments:** 3. Lastly, I would like to add that as a clinician, I would like to have a more accurate model of acute respiratory distress syndrome (ARDS) where changes in the relation of blood pressure of oxygen in relation to the Fraction inspired by oxygen, as used in the definition of Berlin of ARDS.

**Response:** You did provide us an important advice for our experimental scheme, the relationship between blood pressure of oxygen change and fraction inspired by oxygen change play a vital role in ARDS diagnosis, and we think in our further research we will add these markers to reflect lung injury, thank you very much for patient review of our manuscript!

**Reference:**

- 1 Zhang Y, Liang D, Dong L, Ge X, Xu F, Chen W, Dai Y, Li H, Zou P, Yang S, Liang G. Anti-inflammatory effects of novel curcumin analogs in experimental acute lung injury. *Respiratory research* 2015; **16**: 43 [PMID: 25889862 PMCID: PMC4391684 DOI: 10.1186/s12931-015-0199-1]
- 2 Carrier N, Cossette P, Daniel C, de Brum-Fernandes A, Liang P, Ménard HA, Boire G. The DERRA HLA-DR alleles in patients with early polyarthritis: protection against severe disease and lack of association with rheumatoid arthritis autoantibodies. *Arthritis Rheum* 2009; **60**(3): 698-707 [PMID: 19248090 DOI: 10.1002/art.24353]

## **Replies to reviewer #2 (ID: 02441672)**

We thank you so much for your patient review and such a good evaluation you have given us “Specific Comments to Authors: The study has an adequate methodology and the results were discussed appropriately. Although the study has limitations, mainly in relation to the fact that it is an experimental study and its results could not be reproduced and human, YBT can regulate water metabolism to reduce pulmonary and renal edema in SAP rats, decreasing inflammatory tissue damage .The results offer an excellent contribution to the study of inflammatory mechanisms in severe acute pancreatitis and its therapeutic possibilities. Scientific Quality: Grade B (Very good); Language Quality: Grade A (Priority publishing); Conclusion: Accept (General priority).” With your encouragement and recognition, we will try our best to revise the manuscripts, thank you again!

**Replies to reviewer #3 (ID: 02940086):**

Thank you for the patient review, all the comments you have raised about our manuscript are worth pondering over and will help us to improve the quality of our manuscript.