

Ze-Mao Gong, Ph.D

Science Editor, *World journal of gastroenterology*

Dear Dr. Gong,

Enclosed please find a revised manuscript “Yangzheng Sanjie decoction regulates the proliferation and apoptosis of gastric cancer cells by enhancing let-7a expression” (NO: 34297). We thank you for giving us the opportunity to revise our manuscript, and we thank the reviewers for their careful review and insightful comments. We have made all required changes and highlighted all these modifications in the revised version. Here is a response to the reviewers:

Reviewer # 02549032 wrote that “This is an interesting basic study on new traditional Chinese medicine in regulation of proliferation and apoptosis of gastric cancer cells”, but asked some more details, as follows.

1. Please give more information about the Yangzheng Sanjie decoction (YZSJD). Where to find, how much dose should be given, which substance exactly if it is known etc. Give more information about preparation method of the YZSID.

Response: We have made some modifications to this section according to the suggestions of the reviewer.

2. Some parts of the discussion should be changed accordance to international scientific standards. E.g. In the second paragraph last sentence: << However, due to clear curative effects and low toxicity, traditional Chinese medicine has been recognized to have health and well-being benefits in cancer treatment>>. This is a basic study and this conclusion cannot be drained from the study. This is an hypothetical conclusion. For western medicine to be persuaded should be conducted further human studies.

Response: We apologize for the unclear expression mentioned above. To make our description more precise, two reviews (ref. 21, 22) assessing years of progress of Traditional Chinese Medicine in gastric cancer therapy were added.

3. The authors explain a lot the western medicine method but say very few regarding the preparation of the YZSJD.

Response: We have made some modifications to this section according to the suggestions of the reviewer.

4. Which of the components of the regimen the authors believe that have the anticancer effect?

Response: As we mentioned in the second paragraph of the introduction, It has been reported that several components of YZSJD such as Astragali Radix, Scutellariae Barbatae Herba and Arisaematis Rhizoma Preparatum exhibit anti-cancer activity (ref. 8-10). Screening and identifying effective components of YZSJD is an important part of our further research work.

5. The authors stated in the third paragraph of the discussion: << YZSJD is a Chinese herbal compound prescribed by Dr. Geng-Xin Chen and has been used to treat gastric precancerous lesions for more than a decade.>>. Is there any experience with this medicine outside China? So if this medicine is used only in China it is difficult to make generalized conclusion to all people. We have to study further. The authors should be more accurate.

Response: In the revised manuscript, we did some modification to the sentence to make its meaning more accurate.

6. Which is the possible hypothetical molecular anticancer mechanism of YZSJD ?

Response: Contrary to single-component drugs, the benefits of TCM drugs are often due to the synergistic interactions of multiple ingredients. The anticancer ability of YZSJD may occur through the activity of multiple ingredients with multiple targets. In

the present study, we found that regulation of the let-7a-c-Myc pathway may be a novel molecular mechanism through which YZSJD exerts anti-cancer effect.

comments of Reviewer #03002860. The manuscript is very interesting, I only detect two minimal details on it. First, In the Abstract, section Results, there is probably a mistake in the redaction of the sentence, because the YZSJD induces apoptosis (could change "induced" by "induces"). And the second issue is the preparation of the YZSJD, because is not clear how is made, quantities and proportions of constituents. Results are clear, I don't have objections.

Response:

1. It has been checked and revised.
2. Following the suggestions above, we added the corresponding content to the revised manuscript. Please see the “Preparation and quality control of YZSJD” section.

Thank you very much for your valuable advices and efforts with our submission.

Sincerely yours,

Geng-Xin Chen