

## ANSWERING REVIEWERS

May 14, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 17472-review.docx).

**Title: Mechanism of aqueous fructus aurantii immaturus extracts in neuroplexus of cathartic colons**

(old title: A research about the effect and mechanism of fructus aurantii immaturus (FAI) aqueous extracts towards intestinal plexus in cathartic colon of rats)

**Author:** Shi-Yi Wang, Yan-Ping Liu, Yi-Hong Fan\*, Lu Zhang, Li-Jun Cai, Bin Lv

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 17472

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

We thank the reviewers for the critical review and the helpful comments. Please find our point-to-point response and appropriate revision below:

### **Point-by-Point Response to Reviewers**

#### **Reviewer's comment #1 (40631) :**

*Dear Editor, the topic and the findings of this paper are interesting but it is too long, nobody will read it like this, it looks more like a PhD Thesis. It should be halved, then in the results of the abstract the authors should report numbers and terms such as "defecation is a little bit more" are not scientific. Please come back to me only if the authors cancelled AT LEAST 50% of the text*

#### **Answer:**

Thank you for your suggestion. We now have deleted some repeated and unnecessary contents. We also have simplified our language with the help of language polishing company.

#### **Reviewer's comment #2 (3001572) :**

*In this study, authors investigated the effect and mechanism of FAI treating rat model. This topic is interesting and important and authors provide sufficient evidence to support it. However, the manuscript should be reorganization and editing. For example: The abbreviation of STC is first mentioned. Authors should explain what it is? In the result section, authors might consider to use more specific description as the sub-title. For example: 3.2 FAI could significantly improve ITR. In addition, the figure or table labeled following sub-title is inappropriate. Authors should more precisely to embed in text.*

#### **Answer:**

- 1) The abbreviation of STC is explained in the article.
- 2) In the result part, we have already changed our sub-title, which is more specific and general.

- 3) We have changed the label of figure or table in the content, which have embedded in the text following the corresponding results.

**Reviewer's comment #3 (68594) :**

*I am unable to review this manuscript in its current form. As an example, I tried to revise the abstract, and it took considerable time. Please see attachment. The results are very promising and hence I am willing to review this manuscript, if the authors work on the language.*

**Answer:**

Thank you very much for your serious and precise revision of our article. In order to make up the deficiency of language, we seek help from AmEdition, a famous language polishing company, to polish our article. This manuscript has been checked and edited by AmEdition, Inc.

**Reviewer's comment #4 (68404) :**

*In this article, authors investigated the role of FAI on gastrointestinal tract movement. They concluded that FAI extracts can improve the movement of GI tract in a 5-HT<sub>4</sub>-independent manner. There are several important problems that authors haven't clearly stated. 1. In animal model preparation, Dahuang was used. Authors used increasing doses to let the rats have loose stools. Why didn't authors apply certain dose during STC model preparation? More importantly, it's strange that loose stools of the rats were considered as a symptom for slow transit constipation. As this controversy, authors assessed the hard stools in later experiment for STC in this article. Animal model is a key problem for animal experiments. So, authors must make it clear. 2. 60 rats were chosen in the STC model group. However, the total number of these rats were not 60 in "12 in model group, 14 in positive drug group, Chinese medicine with low, medium and high dosages respectively." Authors should be cautious in calculation. 3. In figure 1 and 2, markers should be added in the images to let readers easier to understand. 4. Only 2 or 4 cm colons around anus were taken for further analysis. So only distal colons were assessed. It's not accurate to conclude FAI improved the whole colon movement. 5. English writing is not good enough. It's better to ask specialists to modify the article writing.*

**Answer:**

- 1) The reason to apply increasing dose not certain dose to make STC model is that the clinical manifestation of cathartic colon is laxative-dependent defecation, which indicates that the more dose STC patients are taking, the worse effect STC patients have. Eventually, no laxatives, no defecation. Thus, applying certain dose is not in accordance with clinical rule and increasing dose is more close to real condition. The index of increasing the dose is based on rat stool condition: if 50% of rats appear loose stool, it indicates that the laxative exerts its effect on rats. This dose is maintained until 80% rats' loose stools disappeared, which indicates that rats develop laxative tolerance. Then, the dose of laxative increases until 50% of rats appears loose stool again (the laxative exerts its catharsis effect again).  
We have conducted large numbers of fundamental works using this modeling method. (Fan YH, et al. Chinese Journal of Digestion, 2009 (12): 845-846. Fan YH, et al. Chinese journal of digestive diseases, 2006, 7(4): 225-229). Furthermore, other researcher's works are also based on this model (Li HY, et al. WJG, 2007, 13(1): 141-145). Thus, we think that this is a mature model to study cathartic colon.
- 2) The number of rats is 68, not 60. Thank you for pointing out such mistakes.
- 3) In order to let readers have a better understanding, we have put markers on figure1 and 2.
- 4) Cathartic colon is a disease that involves the whole colon. Thus, selecting 2 to 4cm colon tissue can manifest the whole colon lesion.
- 5) As the language is not scientific, this manuscript has been checked and edited by AmEdition, Inc.

**Reviewer's comment #5 (61678) :**

*Dear editor, Authors Thanks for sending manuscript "A research about the effect and mechanism of fructus aurantii immaturus (FAI) aqueous extracts towards intestinal plexus in cathartic colon of rats" to be revised, please accept the following comments. - Title should be modified (I think no need for starting by "a research") - Paper is well written, organized - Few grammatical errors Thanks*

**Answer:**

Thank you for your appreciation of our manuscript. We really agree with your suggestion about revising our title. However, WJG requires us that the title should be no more than 12 words. Thus, we revise our title as follows: Mechanism of aqueous fructus aurantii immaturus extracts in neuroplexus of cathartic colons. Wish it can fit your taste.

**Reviewer's comment #6 (51081) :**

*The authors studied the effects of FAI in a colonic cathartic animal model. This is a very interesting study. I want to review this study again after following revisions and missing files are completed. 1- The introduction is very long and should be revised accordingly. 2-The references are not in WJG style, this should be corrected. 3-Abbreviations should not be used in abstract and the abstract should be more compact requiring revision. 3- In page 8 under subtitle: "2.7.2 intestinal transit rate (ITR) testing" the ITR formula given as "ITR (%) = ??×100" is faulty and should be corrected 4- The number of animals in study group is very high. In order to keep consistency with the Helsinki declaration, the institutional board approval should also seen. Therefore, a copy of hand-signed board approval given with a board approval serial number should be sent as a different file. Also a contact name of the board secretary should be addressed in case of any further questions. This is a high priority issue. 4- The language needs polishing. There are countless typos and grammatical errors throughout the text.*

**Answer:**

- 1) Introduction has been simplified.
- 2) The format of references has been changed, which fits WJG style.
- 3) Abbreviations in abstract have been revised, which fits the rule of abstract required by WJG.
- 4) In "2.7.2 intestinal transit rate (ITR) testing" the ITR formula given as "ITR (%) = ??×100". This mistake is because of Microsoft Word version. The right one is  $ITR (\%) = (\text{pushing length}/\text{total length}) \times 100$ , which has been shown in article.
- 5) The Institutional Animal Care and Use Committee (IACUC) statement and animal care and use statement is placed in the attachment.
- 6) The language of our manuscript has been checked and edited by AmEdition, Inc. All typos and grammatical errors have been corrected.

3 References and typesetting were corrected—We have included the PubMed ID/DOI.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



Yi-Hong Fan, Associate Professor  
Department of Gastroenterology  
1st Affiliated Hospital of Zhejiang Chinese Medical University  
54 Youdian Road

Hangzhou, China

Fax: +86 571 87077785

E-mail: yhfansjr@163.com