Author's response to reviews

Title: Gastroprotective effect of the traditional herbal medicine, Sipjeon daebo-tang water extract, against ethanol-induced gastric mucosal injury.

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Version: 3 Date: 26 August 2014

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Version: 2 Date: 26 August 2014

Author's response to reviews:
Referee #1:
Referees' Comment.

Figure 4 looks a little bit confusing because the 2 lines are overlapping each other (between NC and 5000 mg/kg group), both in female and male groups. Can it be made clearer to the readers?

We appreciate your comment. As commented by referee, we corrected the Figure 4 (change to Figure 3) to distinguish between NC and 5000 mg/kg group, both in female and male groups.

Figure 3 (page 23).
Referee #2:
Referees’ comment.

Authors has to check the manuscript carefully. There is repetition of figures and images which don’t have explanation. If these figures are repetitive delete them to avoid confusion.

We appreciate your comment. As suggested by referee, we check the manuscript carefully and we delete or edited the figures to avoid confusion.
Referee #3:
Referees' comment.

1. General comment: The present manuscript studies the Gastroprotective effect of the traditional herbal medicine, Sipjeondaebo-tang water extract, against ethanol-induced gastric mucosal injury. The effort made by the researchers either in writing the manuscript or practical work is good. However, some errors need to be corrected. Blue color is used for word(s) to be added and Red for the word(s) to be deleted all over the attached manuscript. Acute toxicity study was not well done because there were defects in the biochemical tests and findings which show that this herbal medicine is not toxic. In other words, the results of acute toxicity study were not convincing.

   We appreciate your comment. As suggested by referee, we corrected the manuscript (page 02, line 04), (page 03, line 08), (page 04, line 03), (page 04, line 08), (page 06, line 11), (page 13, line 07), (page 13, line 10), (page 14, line 05). According to the OECD guidelines, we include the all data for acute toxicity study. For OEDC guides, biochemical, heamatology etcs results must include for repeated toxicity study. Our research groups already published the 13 weeks toxicity study for Sipjeondaebo-tang water extract (1), and the no-observed-adverse-effect level (NOAEL) was more than 2000 mg/kg/day for both genders.

2. Methods: The methodology used is quite good but the tests used for acute toxicity evaluation were not enough; biochemical tests after using different doses is much preferred in this case. Other methods were acceptable.

   We appreciate your comment. Before performing this study, we conducted the preliminary DRF (dose range finding) toxicity study according to OECD guideline. As results of acute DRF toxicity study, Sipjeondaebot-tang water extract did not exhibit any adverse effects at dose level of up to 5000 mg/kg (1250, 2500, or 5000 mg/kg) in both genders. Therefore, we are chosen the highest dose 5000 mg/kg. According to the OECD Guidelines for the Testing of Chemicals, maximum dosage is 2000 mg/kg. Also, this study conducted by OECD guideline. According to the OECD guidelines, we include the all data for acute toxicity study. For OEDC guides, biochemical, heamatology etcs results must include for repeated toxicity
study. Our research groups already published the 13 weeks toxicity study for Sipjeondaebo-tang water extract (1), and the no-observed-adverse-effect level (NOAEL) was more than 2000 mg/kg/day for both genders.


3. Results:

Although the findings are well presented, the following comments should be considered:

1) The results presented in figure 3 should be re-presented in a table form.

    We appreciate your comment. As suggested by referee, we corrected figure 3 to table 1 (page 25).

2) The unit of MDA was written in the method section as nmol of MDA/mg protein and in the results section µmol/mg protein (including figure 2A). The authors should correct this.

    We appreciate your comment. As suggested by referee, we corrected the unit of MDA as µmol/mg protein (page 7, line 12).

3) There is no indication in the results section for the use of the statistical test ANOVA, although it was stated in the Statistical analysis section.

    We appreciate your comment. As suggested by referee, we newly inserted additional description in results section (page 9, line 17) as follows:
Significance was determined using ANOVA. If the ANOVA showed a significant difference between groups, the data were analyzed further with a multiple-comparison procedure using Dunnett’s test. The level of significance was $p < 0.05$ or 0.01.

4. Discussion and conclusion:

The authors discussed the presented findings very well except that table 1 mentioned in the discussion section and shown in the manuscript was not necessary.

We appreciate your comment. As suggested by referee, we corrected and excluded the unnecessary description in discussion section (page 11, line 13) as follows:

Among the traditional herbal medicines, Sipjeondaebotang composed of 10 different herbs and its herbs exhibited various biological effects [18,19]. However, study on protective effect of Sipjeondaebotang on the gastric mucosal injury is rare. Hence, we aimed to determine whether SDTW has antioxidative and anti-inflammatory effects on ethanol-induced gastric mucosal injury.
Additional revision request:

Please include Email addresses of co-authors in the title page.

We newly inserted the additional Email addresses of co-authors in the title and Author’s contributions page.