Author's response to reviews

Title: San Huang Shel Shin Tang beta-cyclodextrin complex augmented the hepatoprotective effects against carbon tetrachloride-induced acute hepatotoxicity in rats

Authors:

Wei-Syun Hu (duodenum222000@yahoo.com.tw)
Wei-Jen Ting (tim_sigeen@hotmail.com)
Dennis Jine-Yuan Hsieh (djh@csmu.edu.tw)
Hsi-Hsien Hsu (u596@mmc.edu.tw)
Yueh-Min Lin (YuehMinLin@outlook.com)
Chia-Yao Shen (x00003061@meiho.edu.tw)
Chung-Ho Chang (changch@nhri.org.tw)
Viswanadha Vijaya Padma (padma.vijaya@gmail.com)
Yuhsin Tsai (yhtsai@mail.cmu.edu.tw)
Chih-Yang Huang (cyhuang@mail.cmu.edu.tw)

Version: 2
Date: 16 April 2015

Author's response to reviews: see over
Author's response to reviews

Title: San Huang Shel Shin Tang beta-cyclodextrin complex augmented the hepatoprotective effects against carbon tetrachloride-induced acute hepatotoxicity in rats

Authors:
Wei-Syun Hu (duodenum222000@yahoo.com.tw)
Wei-Jen Ting (tim_sigeen@hotmail.com)
Dennis Jine-Yuan Hsieh (djh@csmu.edu.tw)
Hsi-Hsien Hsu (u596@mmc.edu.tw)
Yueh-Min Lin (YuehMinLin@outlook.com)
Chia-Yao Shen (x00003061@meiho.edu.tw)
Chung-Ho Chang (changch@nhri.org.tw)
Viswanadha Vijaya Padma (padma.vijaya@gmail.com)
Yuhsin Tsai (yhtsai@mail.cmu.edu.tw)
Chih-Yang Huang (cyhunag@mail.cmu.edu.tw)

Version: Date: 16 April 2015

Author's response to reviews: see over

Reviewer's report

Title: San Huang Shel Shin Tang cyclodextrin complex augmented the hepatoprotective-effects on CCl4-induced acute liver hepatotoxicity rats

Version: 2 Date: 19 November 2014

Reviewer: Shanthi Palanivelu

Reviewer's report:
Major compulsory revisions:
1. On the whole the paper lacks clarity partly due to grammatical errors. These should be corrected. Eg: Lines 266 – 271 – the last paragraph of the discussion – the meaning is not clear.
   The grammatical errors were corrected by English editing. Line 265-269 section was rebuilt in revised manuscript.

2. Line 77 – The similar liver protection effects ------ are due to the same bioactive compounds, a specific kind of flavonoid ----Do the authors mean the same or similar compounds. If same, they should specify the name of the compounds.
   The similar effect bioactive compound is baikalein, and this section from Line
78 was rewrite in revised manuscript.

3. Line 194 – The description of results of histopathology, especially of Masson’s Trichrome staining is inadequate and incomplete. This stain is particularly important in the interpretation of hepatic fibrosis.
   The section frome Line 187-191 was rewrite in revised manuscript.

4. Figure 1 – Legend is inadequate – it does not detail the changes in each photomicrograph separately.
   The legend of Figure 1 was rebuilt.

5. Figure 5 is referred to in the results, but the figure has not been submitted.
   The missing Figure 5 was uploaded in revised manuscript.

Minor essential revisions

1. The objectives of the study are not stated clearly.
   The objectives of the study were rewrite in revised manuscript.

2. The experimental design has to be detailed clearly. The authors have not clearly stated that pretreatment with SSHT and SSHT-βCD complex has been used in their experiments.
   The SHSST, SHSSTc and silymarin pretreatment was described at Animal Model section, Line 126.

3. Lines 147 – 149. The authors have not detailed the procedure used for Masson’s Trichrome stain nor have they cited a reference.
   The section was rewrite and procedure of MT satin was according to the kit protocol.

5. Line 178-179 ---- The last step of the protocol is missing.
   The section at Line 172-173, the last step of protocol was added in revised manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
I declare that I have no competing interests.
Reviewer's report
Title: San Huang Shel Shin Tang cyclodextrin complex augmented the hepatoprotective-effects on CCl4-induced acute liver hepatotoxicity rats

Version: 2
Date: 27 November 2014

Reviewer: Anupam Bishayee

Reviewer's report:
Yang and co-investigators reported a hepatoprotective effect and associated mechanisms of action of a complex of herbal medicine San Huang Shel Shin Tang with cyclodextrin. Although results are interesting, the manuscript suffers from numerous problems associated with presentation, organization and expression of English language. The following modifications are recommended to improve the quality of this manuscript:

1. The title needs revision, e.g.: San Huang Shel Shin Tang-cyclodextrin complex augmented the hepatoprotective effects against carbon tetrachloride-induced acute hepatotoxicity in rats
   The title was changed in revised manuscript.

2. Abstract and elsewhere: please use full forms for all abbreviations for the first time. Subsequently, just use the abbreviated form, if necessary.
   These mistakes were corrected in revised manuscript.

3. Page 5, line 119 and elsewhere: Please provide full vendor information (vendor name, city, state/province and country as applicable) for all chemicals, reagents, and major instrument/equipment.
   The information was added in revised manuscripts.

4. Page 6, line 124: Use “…treatment was performed on the 7th day following pretreatment with test materials.”
   This section was corrected in revised manuscript at line 128.

5. Please clearly indicate when and how the animals were sacrificed.
   This animal were sacrificed through decapitation, and this description was added in revised manuscript at line 130.

6. Page 6, line 127 (Blood biochemical analysis): Please mention that blood (not plasma) was collected from rats and also indicate if the animals were anesthetized or killed before blood collection.
   The correction and the description about the blood collection were added in revised manuscript at line 130-135.

7. Page 6, line 134 (H&E staining): How were the livers collected? Were the animals anesthetized or killed?
   The livers were collected after the animals were killed. This description was
8. It is confusing that the authors indicate measuring endpoints at 24 h as well as 7 days throughout the manuscript. The authors should avoid this discrepancy by clearly mentioning exactly when the animal experiments were terminated and various parameters were measured.
   The description was rebuilt more clearly in revised manuscript at line 130 and line 186.

9. Page 8: Please indicate (name) the antibodies procured from Santa Cruz Biotechnology instead of repeating the vendor name.
   This section was corrected in revised manuscript at line 174.

10. Page 9, line 184: Use Student’s t-test (t in italics).
    The “t” was in italics in revised manuscript.

11. Page 9, line 189: The statement “However….7 days treatment” does not match with the results in Table 1. Please revise as appropriate. Table 1 should be included as the main Table, not supplementary material.
    The table 1. was added in the revised manuscript.

12. Figure 1: A better description of results from various groups is needed. Use subpanels like A, B, C etc. and indicate several pathological characteristics directly on appropriate figure by using arrows.
    The pathological characteristic changes were indicated by arrows in revised manuscript figure 1.

    The mistake was corrected in revised manuscript. (line 199)

14. Page 10: a) line 202, Figure 3C should be Figure 2C; b) delete 3D; line 203, use “….reduction of CTGF….(Figure 2D)”.
    The mistakes were corrected in revised manuscript. (line 203-205)

15. Page 10, line 212: Figure 4C should be Figure 3C.
    The mistakes were corrected in revised manuscript. (line 213)

16. Page 10, line 220: Figure 5D and Figure 5E should be Figure 4D and Figure 4E, respectively.
    The mistakes were corrected in revised manuscript. (line 221)

17. Page 11, line 225: Delete “In toxicology”.
    The words unnecessary were deleted in revised manuscript. (line 226)

18. Page 11, line 234: Replace “eliminates” with “reduces”.
    The word was replaced at line 234 of revised manuscript.
19. Page 11, line 239: Figure 1, 3 should be Figures 1 and 2.
The mistakes were corrected in revised manuscript. (line 239)

20. Page 12, line 246: Figure 3, 5 should be Figure 4.
The mistake was corrected in revised manuscript. (line 246)

21. Page 12, line 252: Modify to “The bioactive compounds of SHSST represent antthraquinones…..”
The sentence was modified in revised manuscript. (line 252)

22. Page 12, line 257 and 258: Change as “The structures of bioactive compounds from SHSST belong to the flavone and flavonol groups.”
The sentence was modified in revised manuscript. (line 256-257)

23. Page 13, lines 266-268: not clear, please revise.
This section was modified in revised manuscript. (line 263-267)

24. Page 13, line 278: Replace “from” with “against”.
The word was replaced in revised manuscript. (line 274)

25. Figure 1: use + to indicate combination treatment.
The figure 1 was added + to indicate combination treatment in revised manuscript.

26. Figures 2-4: “Shame” should be “Sham” or “none”.
The “none” was used in Figure 2-4 in revised manuscript.

27. Figures 3B and 3D: please indicate statistical difference between control and SHSSTc.
There is no statistical difference between control and SHSSTc in Figure 3B and 3D.

28. Figures 4F: please indicate statistical difference between control and SHSSTc.
There is no statistical difference between control and SHSSTc in Figure 4F.

29. Table 1: A better descriptive title to capture the essence of the results is necessary.
The title of Table 1 was changed in revised manuscript.

30. This entire manuscript needs extensive editing, especially for proper organization, style, punctuation, and sentence construction. The use of language improvement service or native English speaker is recommended.
The revised manuscript was modified through English editing.
Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being Published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests.

Reviewer's report

Title: San Huang Shel Shin Tang cyclodextrin complex augmented the hepatoprotective-effects on CCl4-induced acute liver hepatotoxicity rats

Version: 2 Date: 17 November 2014

Reviewer: Piyali Bhattacharyya

Reviewer's report:
Major Compulsory Revisions: No need for major Compulsory Revision.
Minor Essential Revisions: Author need to put space in Animal Model section line No. 122 Example- “treatment(40mg/kg/day)”, it should be - “treatment (40mg/kg/day)”.

The mistakes were corrected in revised manuscript.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: 'I declare that I have no competing interests'.