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

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Version: 3 Date: 24 August 2015

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Reviewer's report

Reviewer's report

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

Version:2   Date:8 May 2015

Reviewer: Piyali Bhattacharyya

Reviewer's report:

The author (s) revised carefully the previous revision requested by reviewers.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests.

Reviewer's report

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

Version: 2  Date: 15 May 2015

Reviewer: Shanthi Palanivelu

Reviewer's report:

Minor essential revisions

Line 46: the hepatoprotection effects of unmodified SHSST : “hepatoprotection may be replaced by hepatoprotective”  
The word was changed to “hepatoprotective” in revised manuscript at line 46.

Line 129 pretreated with the test material –pretreated should be replaced by pretreatment.  
The word was changed to “pretreatment” in revised manuscript at line 129.

Line: 131 scarification: the meaning is not clear.  
The worlds were removed in revised manuscript at line 131.

143 sections were cut into slices from these paraffin-embedded tissue blocks.  
The words “into slices”may be deleted.  
The worlds were removed in revised manuscript at line 142.

Lines 144 145 146 All slices were dyed with hematoxylin and eosin (H&E) and then rinsed with water. Each slide was 146 dehydrated through graded alcohols. Samples were soaked in xylene twice.: should be written as : Sections were stained with hematoxylin and eosin (H&E), immersed in graded alcohols followed by xylene and mounted in ------- .  
The sentences was corrected in revised manuscript at line 144 to 146.

Line 153: were cut into slices from these paraffin-embedded tissue blocks :The words into slices should be deleted.  
The worlds were deleted in revised manuscript at line 152.
Line 157: MT satin was used to investigate eliverhisto-logical and fibrotic: please correct the spelling mistake in the underlined portions.
The spelling mistake was corrected in revised manuscript at line 156.

Lines 226 227 However, the products after CCl4 oxidation also include radicals. The authors should mention what radicals they are referring to.
The radicals were trichloromethyl radical and trichloromethylperoxyl radical. The descriptions were added in the revised manuscript at line 226 to 227.

**MAJOR COMPULSORY REVISIONS**

1. Lines 186 187 After 24h CCl4 intraperitoneal injection treatment, the AST, ALT, TC and cholesterol parameters did not show statistical change- the results stated here do not match with those in the relevant table-table 1, which indicates a change in the parameters. This has been pointed out by one of the reviewers(Dr.Bishayee) in his previous comments.
The description should not included ALT and AST, and this sentence was corrected in revised manuscript at line 185.

2. lines 189, 190, 191, 192 Further, HE staining showed abnormal morphology adipocyte around the smallvascular in the liver 24h after CCl4 treatment. The SHSSTc and silymarin efficiently protected the hepatocytes and decreased the cell death number around the small vascular. (Figure 1): Abnormal morphology adipocyte imply the presence of fat cells –the cells with vacuolated cytoplasm may be hepatocytes with steatosis- the authors should re-examine the slides and confirm.
The section was refined in revised manuscript at line 189 to 190.

4. Lines 190, 191, 192 The SHSSTc and silymarin efficiently protected the hepatocytes and decreased the cell death number around the small vascular. (Figure 1): Cell death could mean necrosis or apoptosis-this should be specified. Furthermore, cell death in the group with ccl4 injection (Group2) is not mentioned in the results, nor in the figure legend. The area of cell death in group 2 should be indicated directly on the figure with the help of arrows etc.
The description about the cell death in figure 1 was eliminated in revised manuscript at line 190. The cell necrosis or apoptosis need to be proved by more experimental evidences.

5. Line p- 419 and 420 IGF1R/p-PI3K/p-Akt/p-Bad protein expressions decreased in CCl4-induced acute hepatotoxicity group and reduced in SHSSTc treatment: This sentence should be rewritten after correct interpretation. The mistake was corrected in revised manuscript at line 422.

6. Fig.1. As pointed out by Dr.Bishayee in his earlier comments, subpanels of the Figure may be labeled as A,B,C etc. and these be referred to in the results. Also,
fibrosis is mild in group 2—this may be mentioned in the results and discussion. A review of relevant literature shows that fibrosis is not a prominent finding in acute ccl4 toxicity. The authors should review relevant articles again and accordingly modify their discussion. The Figure 1 was labeled as (A) and (B) in revised manuscript. The discussion was also modified at line 239 to 242.

**Level of interest:** An article of importance in its field

**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