Author's response to reviews

Title: Xia-yu-xue decoction (XYXD) reduces carbon tetrachloride (CCl4)-induced liver fibrosis through inhibition hepatic stellate cell activation by targeting NF-kappaB and TGFbeta1 signaling pathways

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Author's response to reviews:

Re: Xia-yu-xue decoction (XYXD) reduces carbon tetrachloride (CCl4)-induced liver fibrosis through inhibition hepatic stellate cell activation by targeting NF-κB and TGF-β1 signaling pathways

Dear Editor,

We hereby submit the revised manuscript to be considered for publication in BMC Complementary Alternative Medicine.

We really appreciate you and two reviewers for your great efforts in evaluating and reviewing our manuscript. Your constructive comments and suggestions are very helpful for us to improve this manuscript.

After carefully studying each comment and suggestion, we have carefully revised our original manuscript by following the reviewers’ comments, which have been responded one by one with explanations as following. Also, we highlight all the changes in the revised manuscript.

Please do not hesitate to forward your queries and reviewers’ comments by e-mail [dongying11@citiz.net]

We are looking forward to hearing from you soon.

Yours Sincerely

Dongying Xue

Reviewer's report

Minor Essential Revisions

1. The authors reported that Xia-yu-xue decoction (XYXD) reduces carbon...
tetrachloride (CCl4)-induced liver fibrosis. In line 57, it was reported that XYXD could regulate the balance of MMPs/TIMPs in KCs [7] and in pig serum induced liver fibrosis [8]. This section was confused.

Answer: Thanks so much for your suggestions, we have revised this section.

It was reported that XYXD could regulate the balance of MMP2,9/TIMP1,2 in response to LPS stimulation in RAW264.7 cells and inhibit KC activation in pig serum induced liver fibrosis in rats. There was reported that XYXD exerts therapeutic effects by inhibiting HSC activation in carbon tetrachloride (CCl4)-induced liver fibrosis in mice.

2. In the methods, HSCs were serum starved for 12 h, the GFP-Col-HSCs first treated with XYXD (5, 25 µg/ml) for 1 hour. However, Zhang et al. reported that XYXD (50 µg/mL) suppressed the activation of HSCs and reversed the myofibroblastic HSCs into quiescent. The authors did not explain the medical measurement of XYXD in detail.

Answer: Thanks so much for your constructive suggestions, we have added the information of how to made XYXD. There were several reasons about the inhibitory effects on HSC activation between Zhang and us. First, the XYXD decoction from Zhang and I were different. Second, the HSC Zhang used is mice primary hepatic stellate cells. Here, we used GFP-Col-HSC cells. Third, the dose of XYXD used in our manuscript is 0.467g/100 g for mice, which is equally to human doses in clinical therapeutics daily. However, we did not see any information about the dose of XYXD used for animal in Zhang’s paper.

2. All significantly results should be marked as P<0.05 or P<0.01.

Answer: thanks so much, we have add the P<0.05 or P<0.01 in the manuscript.

Reviewer's report:

Reviewer comments:

The article by Liu and colleagues describes the effect of XYXD in vitro and in vivo liver fibrosis murine. The data are interesting well conducted and indicate the potential utility of this compound for the treatment of liver fibrosis by inhibiting HSC activation via inhibition of NF-κB and TGF-β1 signaling pathway. While the study might be of interest discretionary revisions have been clarified.

Discretionary Revisions:

1. In the In vivo CCl4-induced liver fibrosis experiments, it would be interesting to add the gender, age and weight of the animals.

Answer: thank you for your suggestion. We have added the gender, age, and weight of animals.

2) In Western blot methods, I suggest add the concentrations of proteins. Which control protein was used to normalize the response? Actin? Justify and I suggest add the text and figures.

Answer: thanks so much for your constructive suggestions. We have added the internal control GAPDH in the text and figures.
3) I suggest add scale bars in all Micrographs.
Answer: thanks so much for your suggestion. We have added magnification in figure legend.
4) Attention in the references according to the journal's guidelines.
Answer: Thanks so much. Y