Author’s response to reviews

Title: Protective effect of Xuebijing injection on paraquat-induced pulmonary injury via down-regulating the expression of p38 MAPK

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RESPONSES TO REVIEWER COMMENTS

1. Positive control group is needed so as to prove the clinical meanings.
Response: A positive control group has been used to prove the effect of Xuebijing on paraquat-induced pulmonary injury.

2. The chart of the mechanism is suggested to illustrate better.
Response: The chart of the mechanism has been added.

Major points
1. The dose of paraquat: in abstract, the author described that paraquat was intraperitoneally injected by 35mg/kg. However, in “animal groups and drug administrations” in materials and methods, the dose of paraquat was 10mg/kg. Why?
Response: This was an error and has been corrected. The experimental dose of paraquat was 35 mg/kg.

2. The dose of Xuebijing: why the author chose 2.5g/kg as the dose for Xuebijing? Is there any preliminary study for selecting the dose? Otherwise, the author should evaluate the protective effect of Xuebijing with different doses.
3. The model of acute lung injury: the author described that paraquat was intraperitoneally injected to induce acute lung injury. However, in “Xuebijing inhibited the expression of p-p38 MAPK, NF-κB65, HIF-1α, Nrf2 and TGF-β1 in paraquat-induced lung tissue” in results, the author also described CLP challenge. Since CLP (cecal ligation and puncture) challenged acute lung injury is another model, it makes me quite confusing.

Response: We have changed “CLP challenge” to “paraquat challenge” in the revised manuscript.

4. About lung histopathology: the description of lung injury score was unclear. The content of the score should be listed as a table. I wonder whether the histopathological evaluation score was made by the author.

Response: A table has been added to the revised manuscript describing the content of lung injury scores.

5. In order to clarify the role of NF-κB p65 in acute lung injury, p-κB-# should also be tested in western blotting analysis.

Response: In light of this comment, we have tested p-κB-# to clarify the role of NF-κB65 in acute lung injury using western blotting.

6. The poor qualities of the lung pathological graphs and immunohistochemical staining graphs in figure 2 and figure 4. Furthermore, the standards were not visible.

Response: The graphs in Figures 2 and 4 have been redrawn to improve their quality.

7. The discussion should be rewritten to clarify the main points of the authors.

Response: The discussion has been rewritten in the revised manuscript.

Minor points
1. It is necessary to add protein size marker in every blot.

Response: Protein size markers have been added.

2. The expression of paraquat +Xuebijing group should be in concord both in articles and in figures. NF-κB and NF-κκ65 both appeared in the article. I think the correct expression is NF-κB p65.

Response: This has been changed for consistency.

3. In paragraph 3 in background, “promote qi and blood circulation” should be corrected as “promote gas and blood circulation”.

Response: This has been corrected in the revised manuscript.

4. In “Animal groupings and drug administration” in materials and methods, “ALI was induced by and intraperitoneal paraquat injection” should be corrected as “ALI was induced by an intraperitoneal paraquat injection”.

Response: This has been corrected in the revised manuscript.
5. In paragraph 1 of “Xuebijing inhibited the activation of NF-#B65 in paraquat-induced lung tissue” in results, “At 48 h after Xuebijing administration, activation of NF-#B65 markedly inhibited the activation of NF-#B65 in the Xuebijing + paraquat group.” could not be understood.

Response: This paragraph has been revised for clarity. It now reads: “Lung activation of NF-#B65 was very weak at 48 h in the control group (Figure 4). However, NF-#B65 expression was markedly increased in the paraquat and Xuebijing + paraquat groups. At 48 h after Xuebijing administration, activation of NF-#B65 was markedly inhibited in the Xuebijing + paraquat group, and compared with the dexamethasone + paraquat group, there were no significant differences.”

6. In figure legend 4 and 5, “Data re expressed” should be corrected as “Data are expressed”.

Response: This has been corrected in the revised manuscript.

7. In the sixth paragraph of discussion, “the expression of p83MAPK” should be corrected as “the expression of p38 MAPK”.

Response: This has been corrected in the revised manuscript.