

Format for ANSWERING REVIEWERS



October 20, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5356-review.doc).

Title: Protective role of hydrogen-rich water on aspirin-induced gastric mucosal damage in rats

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Four reviewers all pointed out that the English was not perfect enough, so we invited two friends in USA to improve my manuscript. The revised parts were marked in red.

(2)The reviewer 00008784—"The major concern regards the English text of the introduction and discussion sections: these parts of the paper should be accurately revised by English speaking supervisor."

Response.We invite two friends in USA to improve my manuscript. The revised parts are marked in red.

(3) The reviewer 00028038—"1. Although the paper showed that the effects of Aspirin in HRW upon gastric mucosal inflammation is significantly better than Aspirin alone, the mechanisms are not clear enough by just observing mucosal enzymatic activity and serum cytokine levels (TNF- α and IL-1 β) . Was the mucosal improvement after Aspirin in HRW treatment caused by combination of HRW and Aspirin? How did HRW enhance or reverse the effects of Aspirin? In other words, the specific targets of combination of HRW and Aspirin should be identified by a further study. Anti-oxidant and anti-inflammation activities could be distinguished through simple in vitro assays, for example, gastric immune cell or epithelial culture. Anyway, how Aspirin in HRW does its function was not studied in this paper, and the mechanistic studies of Aspirin in HRW are too descriptive. 2. Please justify why the animal experiment chose rat not mouse. Minor concerns 1. MPO data in Figure 2 and serum IL-1 β in Figure 3 were not shown completely. 2. Figure 5 has no negative controls, also should present the images with higher power magnification. 3. Author should consider if combine Figure 1 and 4. 4. Typos and grammatical problems should be fixed. 5. Paper should provide the detailed statistical analysis. 6. Too much introduction, methods and discussion distract audience attention. Suggest significantly trim down of them; meanwhile, add more result description"

Response: 1.In the study ,we found that hydrogen-rich water pretreatment could alleviate the aspirin-induced gastric lesions by inhibition of the oxidative stress, inflammatory reaction and reducing of COX-2 in the gastric tissues. So, we summarized a clue of "Hydrogen→ mitigating oxidative stress→alleviating inflammatory reaction→suppressing COX-2 expression→protecting aspirin-induced gastric injury" to explain the mechanism of hydrogen therapy. 2. Although the aspirin-induced gastric injury can be induced both in rat and mouse model, the rat model is more maneuverable and recipient for the researchers because of its large size. And most of the similar studies

preferred the rat model because it may succeed easily. **Minor concerns:** **1.** We will submit the whole picture separately. **2.** We have added the negative controls in the figure 5. **3.** We have combined Figure 1 and 4 in the revised manuscript. **4.** We have trimmed down of the “introduction, methods and discussion” parts and added more result description

(4)The reviewer 00006850–““3.5” Immunolocalization of COX-2 in gastric tissue. This is not corrected , I suggest to replace this title with “ immune histochemical analysis of COX-2 in gastric..”

Response.We have replaced the title with “ immune histochemical analysis of COX-2 in gastric.”

(5)The reviewer 00009292–“It is known that carboxy methyl cellulose reduces the levels of GSH in the liver of hamster (Brooks and Pong Biochem Pharmacol 1981) and mouse (Decorti et al Toxicol Appl Pharmacol 1983)..”

Response.First, using the carboxy methyl cellulose as the vehicle of medicines is widely used in rat models in the recent years because of its dissolution characteristic. Then ,the concentration of the carboxy methyl cellulose in our study is much lower than before, which can reduce the levels of GSH in the liver. Compared with other research on hydrogen therapy, a distinctive experimental design in our research was the delivery of hydrogen molecule. We designed the random oral intake of HRW to deliver hydrogen molecule, which was much closer to human physiological status.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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