Author’s response to reviews

Title: The genotoxicity of an aqueous extract of Gyejibokryeong-hwan

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The genotoxicity of an aqueous extract of Gyejibokryeong-hwan

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BMC Complementary and Alternative Medicine.

Dear Suengmok

Thank you very much for your editorial decision letter, which also included the reviews of our manuscript by referees. We have made the changes as suggested by the reviewers. The changes are marked in blue in the revised text. We have made during the revision in a point-by-point response to each of the comments.

We hope the revisions made the responses provided are satisfactory, and our manuscript is now acceptable for publication in the BMC Complementary and Alternative Medicine.

Please, let us know if further revisions are needed.
Once again, thank you for all your help. We look forward to hearing from you.

Sincerely yours

Arun Yadav (Reviewer 5): - Needs extensive copy editing for English language and grammar corrections.
- Gyejibokryeong-hwan - what parts of plants are used, mention clearly.
- We appreciate your comment. As commented by reviewer, we added the used parts of plants in the Table 1 as below.

Table 1. The combination of crude components of Gyejibokryeong-hwan aqueous extract (GJBRHE)

<table>
<thead>
<tr>
<th>Herbal name</th>
<th>Scientific name</th>
<th>Family</th>
<th>Used parts</th>
<th>Original region</th>
<th>Amount (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinnamomi Ramulus</td>
<td>Cinnamomum cassia</td>
<td>Lauraceae</td>
<td>Ramulus</td>
<td>Vietnam</td>
<td>3.75</td>
</tr>
<tr>
<td></td>
<td>Presl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hoelen</td>
<td>Poria cocos</td>
<td>Polyporaceae</td>
<td>Sclerotium</td>
<td>Pyeongchang,</td>
<td>3.75</td>
</tr>
<tr>
<td></td>
<td>Wolf</td>
<td></td>
<td></td>
<td>Korea</td>
<td></td>
</tr>
<tr>
<td>Moutan Cortex Radicis</td>
<td>Paeonia suffruticosa</td>
<td>Paeoniaceae</td>
<td>Bark</td>
<td>Jecheon,</td>
<td>3.75</td>
</tr>
<tr>
<td></td>
<td>Andrews</td>
<td></td>
<td></td>
<td>Korea</td>
<td></td>
</tr>
<tr>
<td>Paeoniae Radix</td>
<td>Paeonia lactiflora</td>
<td>Paeoniaceae</td>
<td>Root</td>
<td>Uiseong,</td>
<td>3.75</td>
</tr>
<tr>
<td></td>
<td>Pallas</td>
<td></td>
<td></td>
<td>Korea</td>
<td></td>
</tr>
<tr>
<td>Persicae Semen</td>
<td>Prunus persica</td>
<td>Rosaceae</td>
<td>Seed</td>
<td>South Africa</td>
<td>3.75</td>
</tr>
<tr>
<td></td>
<td>Batsch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total amount</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>18.75</td>
</tr>
</tbody>
</table>
- Mention proper reference in support of use of this herbal formula in traditional medicine.

- We appreciate your comment. As commented by reviewer, we added the proper reference in Page 3, line 112-13 as below.

‘climacteric symptoms caused by blood stasis and mass uterine disorders [38, 39].


- IACUC data are repeating in more than one place, for different animal experiments. Just see, if IACUC data can be written only at one place (like- after details about Experimental Animals)

- We appreciate your comment. In this manuscript, acute toxicity and in vivo MN test were experimented at one place (KIT). However, the IACUC approve was different. Please let us know, if further revision are needed.

- Acute toxicity studies have been done following OECD guidelines, please include proper OECD reference to this effect.

- We appreciate your comment. We added reference in Page 6, line 12 as below.

‘and OECD guidelines [40].

40. OECD (1997): Principles of Good Laboratory Practice’

- The conclusion written in the last part of ms seem better presented; try to write, something same in the conclusion for 'Abstract' section.

- We appreciate your comment. As commented by reviewer, we edited the Abstract section as below.

‘GJBRHE did not cause detectable genotoxic effects in the bacterial mutation test or the in vivo MN test, however genotoxic effect was detected in the in vitro chromosomal aberration assay. Our results suggest that GJBRHE may be associated with a low risk of carcinogenesis. Thus, further detailed experiments would be needed to clarify the compound responsible for inducing this genotoxicity of GJBRHE and to determine its mechanism.’
Deniz Vardar (Reviewer 6): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

- We appreciate your comment. As commented by reviewer, we will include all comments in this box and upload annotated versions of manuscripts and tables.

Please, let us know if further revision are needed.