

Peer Review File

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Reviewer A:

Comment 1: The manuscript contains several grammar and spelling mistakes to mention a few. A native English speaking person must edit the manuscript.

Reply 1: We are very sorry for our incorrect writing, and we polished the article in detail without changing the paper's frame and main content. Simultaneously, we contacted the native English editing company for language editing, and the proof of the editing was provided.

Changes in the text: There are many changes in the article about modifying grammar and spelling issues in the article without changing the frame and main content of the paper. We have modified our text as advised (see Page 4, line 16,17,18), et al.

Comment 2: There are a lot of statements made in the manuscript with no proper referencing. For example- a proper introduction on Traditional medicine and its sources such as natural products is required and the following references must be used: PMID: 33174654; PMID: 33173434; PMID: 33181660; PMID: 32654634; PMID: 29799486; PMID: 33178026.

Reply 2: It is true as the Reviewer suggested that many statements were made in the

manuscript with no proper referencing. The references mentioned above as well as those not cited in this article have been used. The above references have been used as reference 17, 18, 32, 46, 49, and 54, the references of a proper introduction on Traditional medicine and its sources have been used as reference 10, 15, 18, 20, and 47, and the references of natural products have been used as reference 32, and 46. The references of COVID-19 have been used as references 3, 4, 5, and 11. The references for database and method usage have been used as reference 29,30, and 31. The contexts of cytokine storm have been added, and the references have been used as references 6, 7, 8, 9, and 10. The reference of global infection has been used as reference 5. The contexts of some existing Chinese herbal medicine systematic review and meta analysis, and the references have been used as reference 49, 50, 51, 52, and 53.

Changes in the text: There are many changes in the article about modifying the citation of references without changing the frame and main content of the paper. We have modified our text as advised (see Page 18, line 16; Page 6), et al.

Comment 3: Page 6 –the Component Database Establishment – must be described further. The Figure given by the authors is not readable and not clear.

Reply 3: We are very sorry for our negligence of the description of Component Database Establishment. The database establishment's flow chart was finished as **Figure 2** to explain the database establishment process, and the key models and processes of database establishment are added. The result of the database establishment

was finished as **Figure 3** to explain the properties of active ingredients. Moreover, the Figures provided by us were replaced with high-resolution images, and the graphics comments have been modified and added.

Changes in the text: We have modified our texts as advised (see Page 8, line 5-18;), **Figure 2**, and **Figure 3** were added (see Page 38, line 4; Page 39, line 2).

Comment 4: Page 19- lines 398-401 on cytokines involvement in COVID19- More information must be given since the cytokine storm is associated with COVID19 serious cases- many studies have shown cytokines are involved and this has been published already. Please add the following references to this section: PMID: 33180935; PMID: 33180360; PMID: 32857671; PMID: 32293098; PMID: 32192578.

Reply 4: We have made correction according to the Reviewer's comments. The contexts of cytokines involvement in COVID19 have been added in the introduction. We introduce the cytokine storm concept, clinical data of cytokine storm in patients with COVID-19, the relationship of cytokine storm and COVID-19, and the treatment of cytokines involvement in COVID19 in detail. We also cited the necessary articles as references 6, 7, 8, 9, and 10.

Changes in the text: We have modified our texts as advised (see Page 5, line 8-22)

Comment 5: Most of the Figures are not clear and readable. These must be replaced with high resolution images.

Reply 5: It is confirmed as the Reviewer suggested that Most of the Figures are not clear and readable. The Figure provided by us was replaced with high-resolution images, and the graphics comments have been modified and added. Maybe because the file (docx) is too large (65.2 Mb), the pictures were compressed in the process of converting word to PDF, we have uploaded the picture separately and contacted the editor to ensure the picture is clear.

Changes in the text: We have modified our texts as advised (see Page 37-55, Figure), and the original high-resolution image has been uploaded, respectively.

Comment 6: Keys must be readable as well in order for readers to make sense of the Figures.

Reply 6: We are very sorry for our negligence. We modified the graphics' annotations and added line annotations so that reviewers, editors, and readers can clearly understand the image.

Changes in the text: We have modified our texts as advised (see Page 37-55, Figure)

Special thanks to you for your good comments.

Reviewer B:

Comment 1: When authors mention the global total numbers of COVID-19, and fatality cases, please add the date. Such as "As of Nov 1, 2020, there are....."

Reply 1: We have re-written this part according to the Reviewer's suggestion. In the

article, we changed the expression as suggested. "As of Nov 29, 2020, there are more than 62.34 million people have been diagnosed with COVID-19, and the number of deaths is close to 1,460,000."

Changes in the text: We have modified our text as advised (see Page 5, line 4-6)

Comment 2: In introduction or discussion part, please add some existing Chinese herbal medicine systematic review and meta analysis, as the evidence of Chinese herbal medicine does play an important role in the treatment of COVID-19 in mainland China. (Chinese herbal medicine for COVID-19: Current evidence with systematic review and meta-analysis. Fan AY, Gu S, Alemi SF; Research Group for Evidence-based Chinese Medicine. J Integr Med. 2020 Sep;18(5):385-394. doi: 10.1016/j.joim.2020.07.008. Epub 2020 Jul 31. PMID: 32792254).

Reply 2: Considering the Reviewer's suggestion, the mentioned article was used as reference 50, and we introduced some existing Chinese herbal medicine systematic review and meta-analysis in the discussion, and the corresponding articles were used as reference 49, 50, 51, 52, and 53. The evidence-based medicine and systematic reviews show that the combination of TCM and standard care can significantly improve the treatment outcome in COVID-19 cases. These findings have significant implications for the understanding of the clinical effect of HSBDF on COVID-19.

Changes in the text: We have modified our text as advised (see Page 17, line 10-22; Page 18, line 1-5)

Comment 3: In potential mechanism part, please add a discussion of the mechanism - Hua shi, Dampness-removal action.

Reply 3: We are very sorry for our negligence of describing a discussion of the mechanism -Hua shi, Dampness-removal action. In the discussion, we mentioned that the potential pharmacological mechanism of HSBDF on COVID-19 is based on the direct and indirect antiviral effects. The binding activity of active ingredients and crucial proteins related to SARS-CoV-2 plays the direct antiviral effects, and the key biological pathway mechanism of HSBDF on the body, such as AMPK signalling pathway, Arachidonic acid metabolism, NF-kappa B signalling pathway, serotonergic synapse, renin secretion, and the renin-angiotensin system, which plays the indirect antiviral effects.

Changes in the text: We have modified our text as advised (see Page 23, line 16-22; Page 24, line 1-15)