

Peer Review File

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Reviewer A

Comment 1: A strong rationale for compiling the review article is lacking. For example, it has to be explained why these 8 Chinese herbs were selected. Did you aim to compare the pharmacological and clinical effects of these Chinese herbs commonly used for the prevention of diseases or promoting body function? In addition, the nomenclature of the herbs are not consistent; for example, both botanical names and pharmaceutical name (common name) should be shown.

Reply 1: Many thanks for the constructive comments by this reviewer. The eight herbs we have selected are all representative and well known to the public. The valuable herbs mentioned in the essay have been shown to have a variety of pharmacological activities from laboratory work. However, the clinical application seems to be more important and the research is still lacking. Therefore we tried to make a review on the current status of the clinical trials in order to provide a basis for broadening their clinical use in the future. We have made the corrections to the nomenclature of the herbs. Thank you!

Changes in the text: all chapters, abstract and the introduction.

Reviewer B

Comment 1: “Herbal medicines”. This review contains eight representative valuable herbs, but 3 of 8 herbs (Ophiocordyceps sinensis, Bird's Nest and Colla corii asini) are not plant-origin. I understand that this problem has been discussed repeatedly and WHO expresses these ones as "herbs". However, it is better to express these ones as “traditional medicines” in the title and some places of the main body text.

Reply 1: We have added explanation about it. Thanks!

Changes in the text: Line 36-38

Comment 2: Names of herbal medicines. There is some confusion about herbal names. In this article, there are scientific (Latin) herbal names of the plant (animal) (it also needs the part name of the herb) and general English name (In some cases, there is also a Chinese pronunciation name). In all the titles of chapters of the main body text, and the abstract and the introduction, the expression of herbal name should be standardized (Any name is acceptable if it is the scientific name or English name). And at the beginning of all chapters (or the introduction), the multiple herbal names should be shown, and select the one name which is usually used in this article. This selected name should be used also in the abstract and in the introduction. And be careful in the italic style of the scientific name (italic

part of the name) and check them again including the references.

Reply 2: We have made the corrections. Thanks!

Changes in the text: all chapters, abstract and the introduction.

Comment 3: Effects of herbal medicines in the main body text

In this article, there are many expressions about the effects of herbs. However, in some of them, they are ambiguous whether it is the result of animal study, in vitro study, clinical study, or traditional legend. In the ambiguous points, the authors should express the effect from which methods. Please check these points, and if it is ambiguous, add some proper sentences, such as "in the animal study", "in in vitro study", "in the non-clinical study".

Reply 3: In this review, we briefly described the pharmacological activities of these herbal medicines in vitro, but the focus is still on the clinical applications of these herbs. The clinical study information regarding the effects of herbs has been detailed in the text and tables. We hope that this is acceptable. Thank you!

Comment 4: Tables. Please show the criteria for the pick upping of clinical studies of the tables. Whether all the clinical studies which the authors picked up are the controlled studies that have the control (comparative) group or not? If all the studies have the control group, please express in the

main body text that you picked up only the controlled clinical studies. And show the control group such as “the placebo group”, “the patients who were taking the other medicine”, “the patients which did not take herb” in the new column or in the main conclusion (in this case, such as “## was improved than in the placebo group”). And it is better to also show the results of statistics (such as “## was statistically significantly improved than in the placebo group”). And in this case, it should make clear whether the “sample size“ in the table is the number only in the treatment group or the sum of the control and treatment groups. If the studies in the tables include studies that do not have the comparative group, they should be deleted. The evidence grade of these types of studies is low.

Reply 4: Although these valuable herbs have been shown to have a variety of pharmacological activities, the clinical data are still far from sufficient. In this review, we tried to thoroughly collect current clinical studies on these herbal medicines. The studies we selected all have the control group and are stated in tables. However, this essay is not a comprehensive review. Instead, it has a clear focus to discuss the current clinical application of the herbal medicines. The results of statistics from different trials are hard to display in a table. To remain focused, we hope to list the most important part in the tables to address our central questions. We have added the explanation about sample size.

Comment 5: References. The expressions of several references are incomplete (Ref No. 10, 12, 13, 88, 89, 90, 91, 92, 93, 94, 96, 97, 98). Please check all the references again. The letters in reference 98 are all capital. It should be revised.

Reply 5: We have made the corrections. Thanks!

Changes in the text: In the reference part.

Reviewer C

Comment 1: Most importantly, this manuscript needs a Methods section detailing how the included papers/trials were selected and assessed. Addressing the details specifically requested in the Narrative Review Checklist would be good start. The authors should note if they conducted any sort of bias assessment on the included papers as well, as the majority of the papers discussed showed favourable outcomes for the herbal medicines.

Reply 1: Thank you for the suggestions! We have added a Methodology part in the essay. Thank you!

Changes in the text: In the Methodology part.

Comment 2: What is the rationale for conducting a review of these TCM? Is there a specific key question the authors wish to answer? From other sections of the paper, it seems as though identifying herbal medicines for

evidenced clinical use and new drug development is important to the authors. If so, this should be stated more explicitly in the introduction.

Reply 2: The eight herbs we have selected are all representative and well known to the public. The valuable herbs mentioned in the essay have been shown to have a variety of pharmacological activities from laboratory work. However, the clinical application seems to be more important and the research is still lacking. Therefore we tried to make a review on the current status of the clinical trials in order to provide a basis for broadening their clinical use in the future.

Comment 3: I think it should be clearer to readers where the research reporting benefits of the individual compounds for each TCM comes from (e.g. is it laboratory studies or human studies?). For example, in the section on Cordyceps, many benefits are reported but then Table 1 shows only two clinical trials. A more nuanced discussion of these potential benefits would be valued, to avoid overstating claims.

Reply 3: In this review, we mainly focus on the clinical applications of valuable herbs. The structure of each part consist of a brief introduction to herbs, pharmacological activities and clinical studies. Many of the pharmacological activities have not yet been verified in the clinic yet. The logic of each paragraph is quite clear and we also stated the limitations. We hope the current description is acceptable. Thank you!

Comment 4: Though the TCM may have traditional uses based on TCM theory, the authors should still be wary of saying further clinical trials are needed to successfully obtain evidence of efficacy, rather than using clinical trials to determine if the herbal medicine is effective or not.

Reply 4: We have stated the limitations of the current studies and provided an outlook. Thanks!

Changes in the text: In the discussion part.

Comment 5: The Tables throughout the manuscript could be improved by including more detail regarding study design, such as blinding, placebo or untreated control, dosage, participant characteristics, for each trial. Footnote should be used to describe acronyms and explain the columns on 'test sample', 'conditions', and 'effect'.

Reply 5: We have supplemented the tables. However, some trial descriptions are vague and there is no single standard for these clinical trials. We tried to provide the details and hope the current tables are acceptable. Thank you!

Changes in the text: Tables "Dosage" part

Comment 6. Could the authors provide more detailed information in the abstract to draw readers to the paper?

Reply 6: Done. Many thanks!

Changes in the text: In the abstract part.