Author’s response to reviews

Title: Protective effect of ethyl acetate fraction from Semen sojae germinatum, the processed sprout of Chinese black soybean, on rat experimental osteoarthritis

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Author’s response to reviews:

Dear Editor:

We have revised the manuscript (BCAM-D-19-00114R1) according to the suggestions and comments from you and the reviewers. Please see the response under following. We hope that the manuscript can fit the quality of the journal this time. Thank you very much for your consideration!

Yours sincerely,

Bingshu HE

Editor Comments:

1. Consent for publication refers to consent for the publication of identifying images or other personal or clinical details of participants that compromise anonymity. Seeing as this is not applicable to your manuscript please state “Not Applicable” in this section.

   Thank you very much for your kindly reminder! We state “Not Applicable” in the revised section of Consent for publication according to your suggestion.

2. Please clarify which animal handling guidelines were followed in this study and include this information in the Ethics approval and consent to participate section.
Thank you very much for your kindly reminder! The experiment protocols were approved and performed in accordance with the guidelines of the Animals Care and Use Committee of Wuhan University of Science and Technology, which has been added into the revised Ethics approval and consent to participate section.

3. The Availability of data and materials section refers to the raw data used in your study and presenting tables and figures is not sufficient to state that all data is contained within the manuscript and additional files. Please only use this statement if you have indeed provided all raw data on which your study is based. We strongly encourage all authors to share their raw data, either by providing it in a supplementary file or depositing it in a public repository and providing the details on how to access it in this section. If you do not wish to share your data, please clearly state this in this section along with a justification. Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
- The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.
- All data generated or analysed during this study are included in this published article [and its supplementary information files].
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].

Please also note that if you include your raw data as a supplementary file you will need to provide, after the References, a section titled “Additional files” where you list the following information about each of your supplementary files: * File name (e.g. Additional file 1), * Title of data, * Description of data. All additional files will also need to have been cited in the main manuscript.

Thank you very much for your kindly reminder! We have stated that “The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.” in the revised Availability of data and materials section according to your suggestion.

4. Please provide the raw/uncropped gel and microscopy images for the panel images in Figures 1-3 as Supplementary Material files.

Thank you very much for your kindly reminder! We have provided the raw images for the panel images in Figures 1-3 as Supplementary Material files.
Reviewer reports:

Rohit Agrawal, B. Pharmacy (Reviewer 1): First, I would like to congratulate the authors for their fine work. The study seems to have been well designed and conducted. The manuscript is even better and sound. The introduction comprised of the necessary elements well organized with no less or more information than required. I especially was attracted with the methods. All information required were mentioned correctly. Every elements like sample size, blinding, randomization, controls and so on have been well addressed in the methods. This makes this study reproducible. The discussion was quite good too. Authors have been able to give meaning to their results and lead it to a generalized concepts along with future recommendations. Overall, the manuscript was OK from all aspects and have no reason to be rejected.

Dear Reviewer:

Thank you for your review for our manuscript! And thank you very much for your consideration!

Yours sincerely,

Bingshu HE

Hyo Sang Bae, Ph.D., K.M.D. (Reviewer 2): This paper describes the protective effect of EAF from SSG on OA development via preventing the degeneration of articular cartilage, inhibiting chondrocyte apoptosis and suppressing synovial inflammation experimentally and is sufficient to present basic data.

Dear Reviewer:

Thank you for your review for our manuscript! And thank you very much for your consideration!

Yours sincerely,

Bingshu HE
Francisco Oliveira, Ph.D. (Reviewer 3): The article by Jun Wang et al. ("Protective effect of ethyl acetate fraction from Semen sojae germinatum, the processed sprout of Chinese black soybean, on rat experimental osteoarthritis") is well written, methodology is relevant and it is a good contribution to the knowledge of the anti-inflammatory activities of SSG on model of rheumatoid arthritis.

Dear Reviewer:

Thank you for your review for our manuscript! We have revised the manuscript (BCAM-D-19-00114R1) according to your suggestions and comments. Please see the response under following.

We hope that the manuscript can fit the quality of the journal this time. Thank you very much for your consideration!

Yours sincerely,

Bingshu HE

The manuscript, however, has some issues that need to be addressed by the authors:

Background Section

1) The authors must include the botanical family of the plant species mentioned (Line 50).

Thank you very much for your professional reminder! The botanical family of Glycine max L. Merr. is Leguminosae, which has been added into the revised manuscript (Background section, line 19, page 4).

Methods - Animals and groups Sections

1) According to the methodology, female rats were used in the study. So, did you have a control of the estrous cycle of the female rats? Is it possible that the estrous cycle of rats can affect the anti-inflammatory response? (Line 21).

Thank you very much for your professional reminder! This is indeed a limitation of this study.
There is a limitation in this study that the female rats used here were not in the control of estrous cycle stage. So the possibility that the estrous cycle of rats affects the anti-inflammatory response cannot be completely ruled out. However, because the majority of rats were synchronized in the breeding house, the observed differences in our study are probably not due to hormonal differences among the groups.

The above description has been added into the revised manuscript (the last paragraph of Discussion section).

Discussion Section

1) According to previous studies, daidzin and genistein (isoflavone compounds) are present in SSG (Bangladesh J Pharmacol 2013; 8: 365-370). However, the authors refer only to genistein as the probable substance responsible for the anti-inflammatory action observed in SSG (line 09).

Thank you very much for your responsible review for our manuscript and professional reminder! We have to apologize for this neglect! According to your reminder, we have added the statement on the anti-inflammatory activity of daidzin into Discussion section (line 6-8, page 12) as “In addition, daidzin as another isoflavone compound used for the quality control of SSG [5] has been shown to possess the anti-inflammatory activity in rat hemorrhagic cystitis [23] and dry eye rat model [24].” The corresponding statement in Discussion section (line 7, page 14) was also revised. And two references [23 and 24] have been added.

Reviewer 2 (Reviewer 4): PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable
OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?
Yes - current version is technically sound

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: Authors have been able to prove that the inflammatory status of the synovial membrane was improved, and the levels of inflammatory cytokines IL-1β and TNF-α in synovial fluid were decreased in rats administrated with EAF from the extract. This study has helped to show the antiosteoarthritis effect of a traditional extract using an in vivo model. This study is part of the continuous effort to elucidate the mechanism of this TCM. Other researchers can capitalize on these findings to develop any bioproduct with therapeutic properties. This study is well designed. The methodology is to an acceptable standard using several biochemical and histological techniques. The authors have performed an excellent experiment to validate the ethyl acetate fraction of Semen sojae germinatum. I have checked the published literature; the authors are proceeding with previous experiments from their team. The design is reproducible and the methodology well described. The scientific writing is of acceptable quality. The revisions undertaken also are satisfactory.

Dear Reviewer:

Thank you for your review for our manuscript! And thank you very much for your consideration!

Yours sincerely,

Bingshu HE