

## Response to Editorial Office

Dear Editorial Office, thank you for the warm reception of our work and your comments on how to improve the paper. We have carefully considered them, similar to the Reviewers' suggestions. Below this page, as well as a section containing responses to Reviewers, we provided a manuscript version that is accompanied by comments that indicate where the content was modified to be in line with helpful suggestions from you and the Reviewers. Please note that the comments can be easily removed just by one click in the "Review" tab of MS Word and the manuscript can then serve (similar to the "Auto\_Edited" file in the system) as a ready-to-publish document since this was prepared according to journal's guidelines. Taking this chance, I would like to mention a few details that will probably ease further processing of this submission:

1) To answer this part of your letter:

*"If your manuscript has supportive foundations, the approved grant application form(s) or funding agency copy of any approval document(s) must be provided. Otherwise, we will delete the supportive foundations."*

→ **We confirm that this research received no external funding.**

2) To answer this part of your letter:

*"If your manuscript has no "Video" or "Supplementary Material", you do not need to submit those two types of documents."*

→ **We confirm that "Supplementary material" and "Video" files are not applicable for our submission.**

3) To answer this part of your letter:

*"Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. [...] If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint [...]."*

→ **We have uploaded the main Figures in a decomposable form (all components are movable and editable) and organized them into a single PowerPoint file (with relevant copyright information). The same applies to the newly created Table.**

4) To answer this part of your letter:

*"When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript."*

→ **We confirm that the new language certificate is now uploaded into the system. During the time between the submission and receipt of peer-review reports, we contacted the relevant institute and improved the paper with the help of a native speaker.**

5) To answer this part of your letter (specific Editorial Office comments):

*"The author(s) must add a table/figure to the manuscript."*

→ **We have added three new objects: two figures and one table. Please see the last three pages of the manuscript.**

6) To answer this part of your letter:

*"All authors should accept and sign the Copyright License Agreement (CLA) [...]."*

→ **We provided a PDF file with CLA signed in by all authors; however, as I mentioned in my e-mails from 2nd February 2024, some of the co-authors did not receive unique links to their inbox, even after the re-sending by the Editorial Office. Therefore, all co-authors provided handwritten signatures with a date of signing in. Those who accepted CLA via unique links have the electronic form of date (generated from the system), whereas those who were unable to receive links provided a handwritten date next to their signature. We hope such a solution is acceptable, please contact the first author and the corresponding author if additional steps are needed.**

Contact me anytime if needed, the Authors are open to further improvements if anything is still not publication-ready.

With kind regards and on behalf of all Authors,

Żaneta Kałuzińska-Kołat

## Response to Reviewer 1 Comments

*"Scientific Quality: Grade C (Good)*

*Language Quality: Grade B (Minor language polishing)*

*Conclusion: Minor revision*

*This minireview compiled and discussed the advance in Britanin in gastrointestinal tumors and outlined new research directions for Britanin in gastrointestinal research using data from outside scope of the digestive system. These contribute to the development of Britanin as a novel anti-tumor chemotherapeutic agent."*

**Answer(s):** We would like to thank Reviewer 1 for your kind opinion on our paper. Since your report was mainly summarizing the content of our study, we presumed it is our duty to decide which parts of manuscript require amendments. Scientific Quality should be improved since we provided an additional discussion on why Britanin is a promising anti-tumor compound in gastrointestinal tumors. Moreover, we provided two new figures and one new table that recapitulates the main message of our work. As for the Language Quality, we contacted a native English speaker and performed language editing of the entire manuscript. In general, the document is filled with multiple comments related to language improvements, but the ones unrelated to English but rather associated with other improvements can be found: in the last comment in the Abstract on page 3, in the last paragraph on page 8, in the last sentence of second paragraph in Future Prospects on page 9, in the last two paragraphs of Future Prospects on page 10/11, and in the middle comment in Conclusions on page 11/12, as well as on pages 17-19. We also hope that all improvements contributed to the overall reception of the paper. If you are interested in these changes, they are highlighted in the main text, with the previous form provided as a comment. Once again, thank you so much.

## Response to Reviewer 2 Comments

*"Scientific Quality: Grade D (Fair)*

*Language Quality: Grade B (Minor language polishing)*

*Conclusion: Major revision*

*The authors introduced us the natural compound britanin, a bioactive sesquiterpene lactone, having powerful anti-tumor activity in several tumors via multiple signal pathways. As mentioned by the authors, the compound britanin could also enhance T cell activity by inhibiting PD-L1 transcription. In the end of this review, the authors also emphasized the possibility of britanin as a promising anti-cancer drug in gastrointestinal carcinoma in future. In my opinion, one or two diagrams should be supplemented to describe the mechanism of britanin suppressing tumors. Also, the content of this review should be much more closed to the title. As my advice, the authors could try to answer the question why do you think britanin can be used as a promising anti-tumor drug in gastrointestinal tumor."*

**Answer(s):** We would like to thank Reviewer 2 for your kind opinion on our paper. In response to your specific comment from the end of the peer-review report (to answer why Britanin can be used as a promising anti-tumor drug in gastrointestinal tumors), we discussed it in new paragraphs or sentences located in various parts of the manuscript. Please see the last comment in the Abstract on page 3, the last paragraph on page 8, the last sentence of the second paragraph in Future Prospects on page 9, the last two paragraphs of Future Prospects on page 10/11, and the middle comment within Conclusions on page 11/12. This elaboration, alongside new two figures (which you also suggested) and one new table (which was suggested by the Editorial Office), should improve Scientific Quality. As for the Language Quality, we contacted a native English speaker and performed language editing of the entire manuscript. In general, the document is filled with multiple comments related to language improvements, but the ones unrelated to English but rather associated with other improvements can be found on pages 3, 8, 9, 10/11, and 11/12 (as we mentioned above), as well as on pages 17-19. To find comments dedicated to You, please search for "Comment to Reviewer 2" instead of "To Reviewers and Editorial Office". We also hope that all improvements contributed to the overall reception of the paper. If you are interested in these changes, they are highlighted in the main text, with the previous form provided as a comment. Once again, thank you so much.