Author’s response to reviews

Title: Role of limonin in anticancer effects of Evodia rutaecarpa on ovarian cancer cells

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Reviewer reports:

Muhammad Sajid Hamid Akash, PhD (Reviewer 1): 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.

The authors have performed excellent in which they have tried to find out the role of limonin on anti-cancer effects of Evodia rutaecarpa. The current research work is interesting and it has sufficient data that should be published in this journal. The publication of this data will definitely help the researchers working in this area to focus on the development of new treatment strategies. But overall, the English language is very poor and it is very hard to understand even the purpose of the study. It is advised that the whole manuscript should be critically revised in order to improve its English quality so that the reader may be able to understand it easily. Moreover, I also suggest the authors to draw a schematic representation for the mechanistic role of limonin on anticancer effects of evodia rutaecapra in ovarian cancer. This will help to understand the mechanistic role of limonin in cancer.

Thank you for your comments. The manuscript has been rechecked for grammar and spelling, and we have added a figure (Fig. 8) explaining the potential mechanism of action of limonin in ovarian cancer. Figure 8 has been cited in line 276, and the Fig. 8 legend has been cited in line 483.
Haji Akber Aisa, Ph.D (Reviewer 2): Subject Appropriateness of the Manuscript

The topic of this manuscript falls within the scope of BMC Complementary Medicine and Therapies

Recommendation

Consider After Minor Changes

Comments

The study by Jae Ryul Bae et al., investigated the anti-cancer effects of Evodia rutaecarpa (ER) in the ovarian cancer cell line, SKOV-3, and demonstrated that ER has anti-cancer effects as ER treatment led to a significant reduction of the viability of SKOV-3 cells. Moreover, limonin, an ER-derivative, induced apoptosis via activation of the p53 signaling pathway. The study as a whole is interesting, but the authors need to address the following questions before it has been accepted for the publication.

1. In introduction part, line 35, author mentioned that limonin is a known major constituent of limonoids groups compounds mainly found in seeds. Does any plant seed contain limonin, or the author should indicate the source of the plant.

Thank you for your comments. We have added a sentence and references to address these issues (line 65).

2. In introduction part, line 43, "cancer lines" should be written as "cancer cell lines".

We have corrected the expression based on your comment (line 73).

3. In figure 1b and 1c, the concentration of the ER treatment should be displayed as same as in figure legend (µg/mL).

We have corrected the units in Figure 1b and 1c according to your comment.

4. If it's possible, insert the concentration of the ER treatment ER (100 µg/mL) in figure 1a and 1d.

We have provided the concentration of ER in Figure 1a and 1d according to your comment.

5. In the first result section, author evaluated anti-cancer effects of ER extract in SKOV-3 cells. It would be better if the author briefly described the preparation method of the ER extract.
In lines 89–91, we described the source of ER as follows: “A water extract of ER was obtained from the National Development Institute of Korean Medicine (Kyungsan, Republic of Korea), and synephrine and limonin were purchased from ChemFaces (Wuhan, China). DMSO (Sigma–Aldrich) was used to dissolve the ER extract, synephrine, and limonin.” Because we bought the ER extract from an external source, we do not have the details of the preparation process.

6. In the conclusion, author mentioned limonin contributes to the anti-cancer effect of ER via activation of p53. In this case, author should explain how much limonin dose the extract contains. It could be done by quantification of limonin in ER extract.

Thank you for your insightful comments. However, it is difficult to perform additional experiments because the first author has recently moved to another institute. We added sentences regarding the content of limonin in ER (Lines 295–297).

7. The manuscript needs careful editing by someone with expertise in technical English paying particular attention to the choice of words, English grammar, spelling and sentence structure so that the goals and results of the study are clear to the reader.

The manuscript has been rechecked for grammar and spelling.