

Peer Review File

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Reviewer A

This is a well written review that gives an interesting and clear insight into the possible effects from a molecular biology perspective of an ancient Chinese medicinal substance dubbed Icariin. The authors should be recommended for assembling this material in one place. The paper loyally refers a large body of work as taken as 'face value', however several measures could be taken for improving the value for the reader.

Thank you very much for your comments and suggestions, we have made a series of changes according to your suggestions as follows.

1) Which of these multiple molecular data are the most solid and believable? Which mechanisms are most likely? I miss a more critical voice and the authors should put forward an opinion so the paper becomes more than just a summary of data.

Reply1: Thank you very much for your advice. In this article, we highlight that “Regulating the proliferation and differentiation of tissue-resident stem cells to repair damaged tissues for ED therapy” is a hot and most solid and believable mechanism for current research. In addition we have summarized and mapped the well-documented signaling pathways from current studies. We have also revised parts of the article to include less data summary and more discussion of opinions and descriptions of possible limitation of these studies.

Changes in the text: we have modified our text as advised (see Page 8, line 174-178; Page 10, line 199-205, etc.)

2) A figure showing the most important pathways would be helpful

Reply2: Thank you very much for your advice. We have added a figure about the most important pathways to help better express.

Changes in the text: we have modified our text as advised (see Page 11, line 239) and added figure1.

3) A table would also increase clarity. This also give an easy way to take a more critical view where warranted

Reply3: Thank you very much for your advice. We have added a table to each of the three main mechanism content sections discussed in the article to help the reader obtain information more easily in conjunction with the article content.

Changes in the text: we have modified our text as advised (see Page 7, line 142; Page10, line 203; Page 17, line 372) and added table 1-3.

4) Finally, a couple of questions are pressing: what is the way forward for this field? Any human data?

Reply4: Thank you very much for your question. We add the future direction of this field based on the current state of research and the content of the article in the SUMMARY section at the end of the article. ICA and ICA derivatives are still in pre-clinical studies and no human data are available. This is likely to be the most important direction for future research.

Changes in the text: we have modified our text as advised (see Page 20, line 433-443) .

Reviewer B

The authors made a very nice narrative review about molecular biology of Icariin and Derivatives on treatment of erectile dysfunction. This is an important theme of investigation, because it can lead to the development of a new way of treating erectile dysfunction. Nevertheless, some points deserve revision:

Thank you very much for your comments and suggestions, we have made some changes according to your suggestions as follows.

1) In the title should be included the information about the type of article, in this case a narrative review

Reply1: Thank you very much for your advice. We agree with your suggestion and have indicated in the article title that this article belongs to "a narrative review" .

Changes in the text: we have modified our text as advised (see Page 1, line 2) .

2) Introduction: It's ok, but first paragraph could be shorter. The existing treatments for ED are not the focus of the article, therefore it's not necessary a detailed overview.

Reply2: Thank you very much for your advice. We originally overloaded this section and have streamlined it based on your suggestions.

Changes in the text: we have modified our text as advised (see Page 4, line 73-76) .

3) Discussion: I would suggest the confection of a table summing up the main articles of each topic with respective findings, limitations and quality of the research

Reply3: Thank you very much for your advice. We have added a table to each of the three main mechanism content sections discussed in the article to help the reader obtain information more easily in conjunction with the article content. The table summarizes the study design, ICA and ICA derivatives treatment results, drug dose and treatment duration, and STAIR list scores (evaluating the quality of experimental) for researches. Relevant experimental limitations have been highlighted and discussed in the text. Thank you again for your guidance for this article.

Changes in the text: we have modified our text as advised (see Page 7, line 142; Page9, line 190-194; Page10, line 203; Page 16, line ,340-349; Page 17, line 372) and added table 1-3.