Reviewer’s report

Title: The synergistic antitumor effect of Huaier combined with 5-florouracil in human cholangiocarcinoma cells

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Reviewer: Ying-Ray Lee

Reviewer's report:

The manuscript "The synergistic antitumor effect of Huaier combined with 5-florouracil in human cholangiocarcinoma cells", authors demonstrated that Huaier extract alone exhibits anticancer effects including growth inhibition, cell cycle arrest, apoptosis induction and suppression of tumor migration/invasion in human cholangiocarcinoma. Moreover, combination treatment with 5-florouracil and Huaier extract can elevate the anticancer activity with a synergistic effect in Hs68 cells. Finally, they also show the activation of STAT-3 can be regulated under the treatment with agent alone or combination. This study provides a novel knowledge in the anti-human cholangiocarcinoma of Huaier extract alone or combination treatment with 5-Fu. However, below are some comments to improve the quality of this article.

1. The resolution of figures are too low, authors need to provide highly resolution data if the article has been accepted for publish.
2. Fingerprint analysis has been accepted by WHO as a methodology for the quality control of herbal samples. Therefore, authors have to provide the fingerprint of Huaier extract in the present study.
3. The manuscript should be revised for linguistic and style errors.
4. In this article, authors determined the effect of Huaier extract alone or combining with 5-FU on the cell proliferation, cell cycle regulation, apoptosis, and cellular migration/invasion. It is straightforward.; however, authors also evaluated the activation of STAT-3 under treatment. IL-6 is used to be inducer of STAT-3 activation in the figure 5 and as a control. Therefore, it is recommended to examine whether agents-reduced STAT-3 activation is the reason involved in the cellular proliferation, cell cycle, apoptosis as well as cellular migration and invasion.
5. In this study, title "The synergistic antitumor effect of Huaier combined with 5-florouracil in human cholangiocarcinoma cells", authors verify the anticancer activity of these agents in only one cell line. It is also recommended to provide the effects of these agents in two or three human cholangiocarcinoma cell lines.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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