Peer Review File

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Reviewer A

The authors have chosen an interesting topic and overall this manuscript is well written, however, the following points need to be corrected.

In the introduction, explain at least one paragraph about the SZC010.
Answer: SZC010 is the OA fused heterocycle derivative synthesised by us, we have added the explain of SZC010(see Page4, line87)

What is the gender of mice?
Answer: Female, we have added the information(see Page6, line172)

On what basis is the SZC010 dose selected?
Answer: Based on our pre-laboratory.
Changes in the text:None

In the discussion section: Please explain the following sentence by mentioning the reference. These results demonstrated that SZC010 treatment in MDA-MB-453 cells resulted in the inhibition of the PI3K/Akt/mTOR signaling pathway andNF-kBactivation
Answer: SZC010 inhibited the PI3K/Akt/mTOR signaling pathway and NF-kBactivation.
Changes in the text:None

Reviewer B

Dear Authors, Please find and revise the following comments
Line 78 needs to add a Reference for poor water solubility of OA
Answer: We have added the Reference(see Page3, line81)

Line 92 (methodology), method of synthesis, there is no reference to the synthesis of different derivatives of OA (seven types) and there aren't any clarifications or validation for those components, Fig.1 shows only chemical structure, please add the Reference for this methods OR a validation charts.
Answer: OA derivatives were synthesized by Professor Shisheng Wang from the Dalian University of Technology. We just discussed the activity and mechanism of these

derivatives.

Changes in the text:None

Line (95-105): Regarding media preparation, even MEM or DMEM, why didn't you add Antimycotic Antibiotic agents in Media?

Answer: We routinely don't add antifungal agents to our cultures, and the cells are not infected by fungi under aseptic conditions.

Changes in the text:None

Line 112: why didn't you apply the new conc. of the selected SZC010 on the third type of cells (MDA-MB-231)?

Answer: Because we determined that SZC010 was the most active for MDA-MB-453 cells by previous concentrations, all subsequent experiments were performed using MDA-MB-453.

Changes in the text:None

Line 123: Who is the manufacturer's instructions??? Company Name!

Answer: The company is Beyotime Institute of Biotechnology(see Page5, line130)

Line 132: Who is the manufacturer's instructions (PI) ??? Company Name

Answer: The company is Beyotime Institute of Biotechnology(see Page5, line141)

Lines (131-1139): why do you use MDA-MB-453 only in cell cycle analysis?

Answer: Because we determined that SZC010 was the most active for MDA-MB-453 cells by previous concentrations, all subsequent experiments were performed using MDA-MB-453.

Changes in the text:None

Line 171: why do you use the dose 10 mg/kg SZC010, depending on any rule and how you calculate it?

Answer: Based on our pre-laboratory.

Changes in the text:None

Line 199: the SZC009 and SZC010 have a potent effect on MCF7, please add their IC50 values as shown in the relative figure

Answer: We think that SZC009 and SZC010 did not have a potent effect on MCF7 cells (significant inhibition only at 80 μ M, which we consider to be meaningless), and SZC012 and SZC014 for 24 h significantly inhibited MCF-7 cells , IC50 values: 22.95 and 26.07 μmol/L,

respectively.

Changes in the text:None

Line 202: depending on your figure the SZC013 and SZC017 have a significant effect for 24 h on the MDA-MB-231 cell, please add their IC50 values

Answer: We think that SZC013 and SZC017 did not have a potent effect on MDA-MB-231 cells (significant inhibition only at 80 μ M, which we consider to be meaningless).

Changes in the text:None

Line 218: you didn't need to use a high dose 30 and 40 μmol/L, your initial IC50% dose at 24h was 17.14

Answer: We applied 30 and 40 μmol/L in order to determine the IC90 value of the drug and to establish that at this concentration, the drug had no inhibitory effect on normal cells.

Changes in the text:None

Line 299: what is the reference for this dose (10mg/kg/two Days), the period of treatment???

Answer: Based on our pre-laboratory.

Changes in the text:None

Line 614, Fig 8E, correct the spelling wehicle into Vehicle

Answer: We have corrected the spelling in Fig 8E.

Line 303, although there is no significant difference in body weight between the two groups, it can't be an accurate indicator for drug toxicity, maybe the increase in tumor weight covers the decreasing weight in the body, especially if there are a significant change in tumor weight between two groups

Answer: Thank you for your comments, we used body weight to side step the toxicity of the drug here, but that was not the focus of this article, so we did not delve into it.

Changes in the text:None

Line 304: regarding to the tumor weight, the error bar is huge in relative to the mean, if you see the figure, you can see the error bar nearly to the mean of the vehicle (0.564-0.118=0.446), please get out the out layers number before statistical analyses

Answer: Thank you for your comments, our findings show indeed a large variation in weight volume within the group, which we consider to be due to the inherent heterogeneity of the tumours. However, our statistical analysis showed that there was indeed a significant between the two groups

Changes in the text:None

<< Ethical Approval number and date to use experimental animals and the affiliation for this committee

Answer: We have completed to give our reply

Changes in the text: **“Ethical Statement”**