Reviewer's report

Title: Evaluation of a curcumin analog as an anti-cancer agent inducing ER stress-mediated apoptosis in non-small cell lung cancer cells

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Reviewer: Pithi Chanvorachote

Reviewer's report:

Dear Editor,

Wang et al. have provided the information regarding curcumin analog and its potential anti cancer effect in non-small cell lung cancer. They wished to address that the ER stress is the key mediating process in such an anticancer activity of compound. Even though the overall results are impressive, this work should be acceptable if all queries are clarified.

Major Compulsory Revisions
1. The siRNA CHOP only attenuated the apoptosis in the Fig. 3 but not completely abolished. What is the possible explanation on these results? Is there any possible of others apoptosis-mediating pathways?

2. The effect of curcumin and its analog on cancer cells apoptosis either by ER-stress or others have been intensively investigated. The authors should do more work on reviewing and added more informative information in the introduction as well as discussion parts. Also, the authors are asked to provide the explanation regarding the novelty.

Minor Essential Revisions
3. The results from Fig. 2 indicated that only late apoptosis increased in a dose-dependent manner. Please discuss why such compound did not alter the early apoptosis? Is it possible to decrease the time of the assay to assess only the early apoptosis?

4. The IC50 evaluation was carried out by incubating the cells with compounds for 72 h; however, the Annexin V/PI assay used 12 h for such treatments. It would be more precise if the authors could provide MTT results by the same treated condition. Also, at 12 h late apoptosis could be detected as shown in Fig. 2; what will happen if the cells were further exposed to the compound for 48 h more.

5. The results from Fig. 2 indicated that only late apoptosis increased in a dose-dependent manner. Please discuss why such compound did not alter the early apoptosis? Is it possible to decrease the time of the assay to assess only the early apoptosis?

6. What is the final concentration of DMSO used in the experiment? Fig. 2 clearly showed that vehicle alone can cause apoptosis?

7. Again the time for MTT assay in Fig 3 is not along with other experiments.
8. Other marker for apoptosis should be addressed.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests