Reviewer’s report

Title: Jacarehyperol A induced apoptosis in leukaemia cancer cell through inhibition the activity of BCL2 Proteins

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Reviewer: Bernhard Gillissen

Reviewer’s report:

In the resubmitted manuscript “Jacarehyperol A induced apoptosis in leukaemia cancer cell through inhibition the activity of Bcl-2 Proteins” by Zhang et al. the authors changed their manuscript according to some of the critical comments by the reviewer. Missing information regarding data and methods were added, inappropriate labeling of figures was corrected. Furthermore, additional data that underline the author’s hypothesis that Jacarehyperol A (Jac-A) induces the mitochondrial apoptosis signaling pathway by disrupting the interaction of pro- and anti-apoptotic Bcl-2 family proteins were added to the manuscript. In conclusion, the changes made by the authors substantially improve the scientific value of the manuscript. However, the authors must address the following points before the manuscript can be accepted for publication.

Major Compulsory Revisions

1. The authors claim “Jac-A possesses a broad antitumor effect for all tested cancer cells and remarkably inhibited the proliferation of leukaemia cells”. However, for the solid tumor cell lines, only inhibition of proliferation by Jac-A is shown, but no data regarding an antitumor effect is presented. As already mentioned in the first review process, to conclude on a broad and general role of Jac-A as a potential inducer of apoptosis and to identify Jac-A as potent anti-cancer drug the authors should at least need to perform Annexin/PI staining with the solid tumor cell lines. Especially LOVO cells are of interest as they are resistant to a variety of stimuli due to loss of Bax expression. It would be interesting to know if Jac-A can induce apoptosis in these cells or if Jac-A can sensitize LOVO cells to drug induced apoptosis. If the solid tumor cell lines were conserved too long to be used for test (as mentioned by the authors) they can easily obtained from commercial or academic sources.

Minor Essential Revisions

2. Figure S1: scattergrams of the controls are missing
3. Figure 3F: partitioning for the quadrants differs compared to figure 3A-E.
4. A number of times: Bcl-XL instead of Bcl-xL
5. As there is no figure S2 figure S3 should be renamed to S2.
6. Line 274: “...leukemia cells HL-60 and THP-1 (Figure S1_C, Figure S1_D); regarding the legend of the figure, data for HL-60 and THP-1 are shown in Figure S1_A and Figure S1_B.”
7. Gossypol data in figure S1 is not mentioned in the main text.
8. Reference 13: a comment instead the original paper was cited.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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'