Reviewer's report

Title: Equol enhances tamoxifen's anti-tumor activity by induction of caspase-mediated apoptosis in MCF-7 breast cancer cells

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Reviewer: Rémy Bosviel

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After reading carefully the manuscript, I think it should be accepted for publication with the following corrections:

- Minor Essential Revisions

1-In the BACKGROUND part, 4th sentence, “in vitro” should be in italics.

2-The authors chose to show Standard Error to the Mean for their data... if they want to show the spread of their data, they should show Standard Deviation. If they want to show statistical significance of their data, they should show Confidence Intervals. Standard error of the mean is often misunderstood by readers and should at least be shown with the number of repetitions next to it.

3-In the RESULTS part, chapter “Equol and 4-OHT induce MCF-7 cell death via apoptosis”. The authors say the combination of 4-OHT and equol enhance cell death in an additive manner and cite the P value for [equol + 4-OHT] vs. 4-OHT... the P value for [equol + 4-OHT] vs. Equol should be cited too.

4-In the chapter “The combination of equol and 4-OHT promotes cytochrome-c release and reduction of bcl-2 expression” from the RESULTS part the authors talk about the release of cytochrome-c from mitochondria to the cytosol induced by the combination of Equol and 4-OHT… They should also point that this is not detected for Equol or 4-OHT alone. Maybe this could be discussed.

5-The authors showed an inhibition of equol and 4-OHT induced MCF-7 cell apoptosis with the pan-caspase inhibitor Z-VAD-FMK. However, this inhibition isn’t complete: the percentage of apoptotic cells is around 20% when Z-VAD-FMK is used against Equol and/or 4-OHT but around 5% when used alone. Could that mean Equol and 4-OHT do induce apoptosis not only using caspase-dependent pathway? This should be discussed in the article.

6-There is a unnecessary space in “bcl-2:bax” in the sentence before the last of the DISCUSSION.

7-Labels of the horizontal axis on figure 1A are not visible.

8-On figure 1 A, I think it would be interesting to show significant differences to the control for all results (with * for P<0.05, ** for P<0.005 and *** for P<0.0005).
9- On figure 1 B and C, please label with asterisks points where viability is significantly different from the no treatment control.

10- The number of repeats done for each experiment is missing in figures 1 and 3, please add them. In the same kind, the authors should indicate if western blot results were repeatable (and how many times they were repeated).

11- In the legend from figure 2, second sentence, 4-OHT is written with a zero and not an “O”.

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.