Review of: "Anti-metastasis After Bee Venom and Melittin by Upregulation of BRMS1 and DRG1 Genes, With Downregulation of WNT7B in Breast Cancer Cells"

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Potential competing interests: No potential competing interests to declare.

Authors analyze the effects of bee venom and melittin (main active component of bee venom) on MDA-MB-231 (metastatic breast cancer) and MCF10A (epithelial breast) cells and compare these compounds with the anticancer agent cisplatin.

They used different concentrations and an incubation time of 24 hours for analysis of cell viability and determinate IC50 values for each compound.

To evaluate wound healing, cells were exposed to different concentrations of compounds for distinct times.

Expression of anti-metastatic (BRMS1, DRG1, and KAI1/CD82) and pro-metastatic (WNT7B and EGFR) genes in cells treated for 24 h with bee venom and melittin was also evaluated.

The conclusion considers the suggestion that bee venom or melittin may be applied with an EGFR inhibitor to enhance selective activity.

Comments:

The conclusion seems inadequate considering the approach that the authors proposed in the introduction and methodology.

In the discussion section, it is necessary to emphasize the results obtained with cisplatin, since it is the reference compound in terms of the effect on cancer cells. This antineoplastic agent is only commented on in terms of its effect on cell viability.

I would ask the authors to define the use of the terms IC50 and EC50 to apply them correctly in their research.

In the results section, it is indicated that the IC50 value of cisplatin was 12 µg/ml for both MCF10A and MDA-MB-231 cells, but in Figure 1, it is indicated that the IC50 value of cisplatin for MCF10A cells was 25 µg/ml.

The methodological description for gene expression analysis is not provided.

Milliliters are expressed as “ml” and “mL”; it is necessary to uniformize.

The legend text of the figure corresponding to the cytotoxicity profiles indicates that it is Figure 3 but should be indicated as Figure 1.

It is necessary to include a graph that shows the percentage viability data (quantitative data) since the images in Figure 1 are only qualitative.

In addition, the legend text could be improved. My suggestion is the following:

Figure 1. Cytotoxicity profiles of MCF10A and MDA-MB-231 cells after cisplatin, bee venom, and melittin treatments. Cells were treated with cisplatin and bee venom at 8, 12, 25, 50, or 100 µg/ml for 24 hours, and with melittin at 0.375, 0.75, 1.5, 3, 6, or 12 µg/ml for 24 hours. IC50 values are given for each agent in the cells.

In Figure 3, the incubation times are not the same for the three panels shown (panel B has 7 times).

Figure 3 does not completely correspond to Figure 2 since the incubation times are not the same, even though the results come from the same parameter evaluated. The same comment applies to Figures 4 and 5.

The change values should be included in Table 3, not only the symbols that indicate the direction of the changes.

The following texts could be improved:

Legend text of Figures 2, 3, 4, 5, 6 (include methodological and statistical details).

The heading text of Table 2.

The following text (at the end of “Bee venom, melittin and cisplatin treatments” section:

Cisplatin (Koçak Pharma, TURKIYE, Cat. No. 19111614) was treated similar to bee venom as MTT concentrations (8, 12, 25, 50, or 100 µg/mL for 24 h) and wound healing (1, 2, 4, and 8 µg/mL for 6, 24, 30, 48, 54, 72, and 96 hours).

Finally, I comment that this manuscript is similar to one published in 2019 (Uzuner SC, et al. Investigation of long-term effect of Black Sea bee’s venom on the cytotoxicity of pancreatic cancer cells. J Apit Nat 2019;2(1):1-6).