LIÈGE université
Center for Interdisciplinary Research on Medicines

Bioactive clerodanes diterpenoids from *Casearia coriacea* : cytotoxic activity on different human cell lines and toxicity on zebrafish embryos

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1 INTRODUCTION

- The genus *Casearia* (Salicaceae) encompasses more than 180 species known for possessing numerous bioactive compounds, including those with cytotoxic and antiparasitic activities [1].
- Clerodane-type diterpenoids are recognized as significant active constituents within this genus [2].
- Through a bioassay-guided fractionation approach applied to the dichloromethane extract of *C. coriacea* leaves, three known clerodane diterpenoids were isolated and identified : caseamembrin T (1), corymbulosin I (2), and isocaseamembrin E (3) [3].
- In this study, we evaluated the impact of these three compounds on a panel of human cancer cell lines, and the toxicity of one of those was also evaluated on an in vivo model of zebrafish embryos.

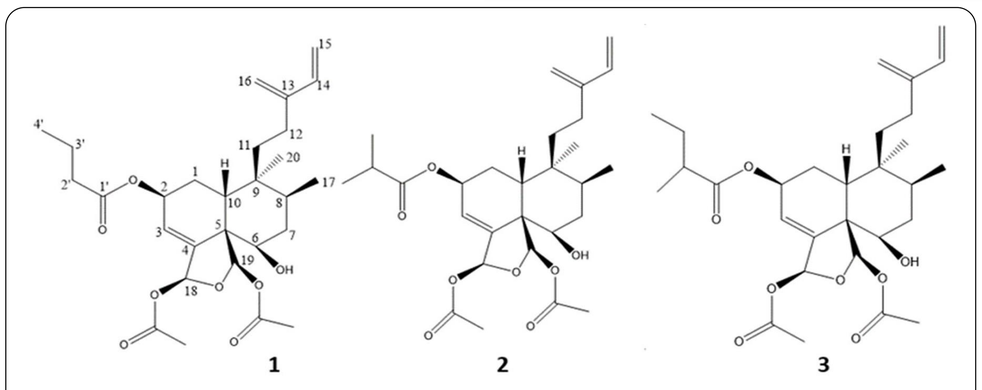


Figure 1: Structures of compounds 1–3 isolated from *Casearia coriacea* Vent.

2 EXPERIMENTAL SECTION

A

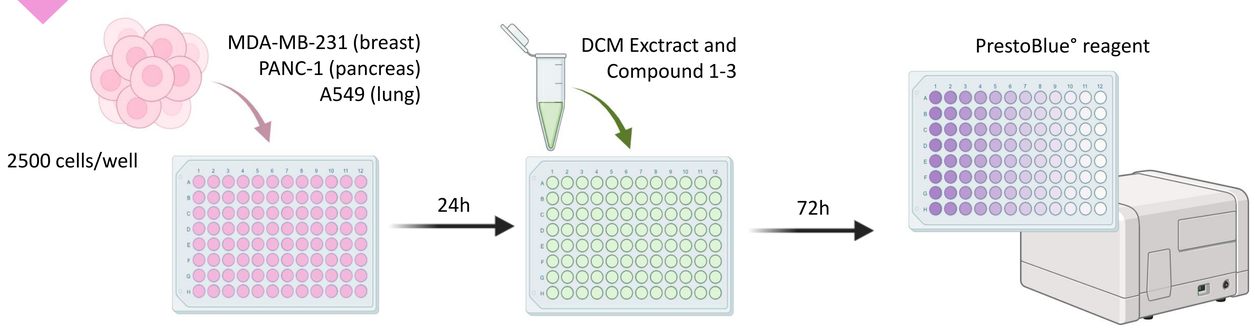


Figure 2: *In vitro* cell vitality assay.

B

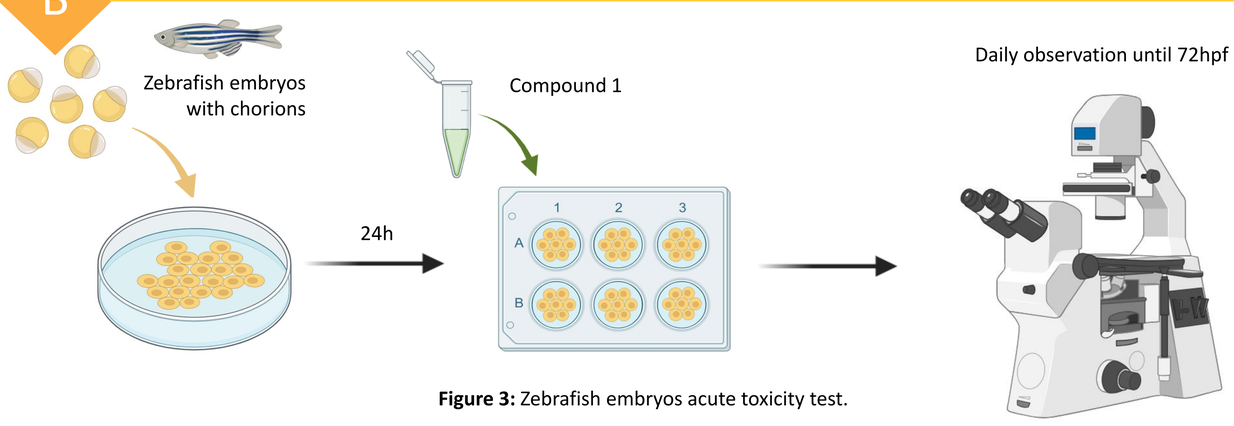


Figure 3: Zebrafish embryos acute toxicity test.

C

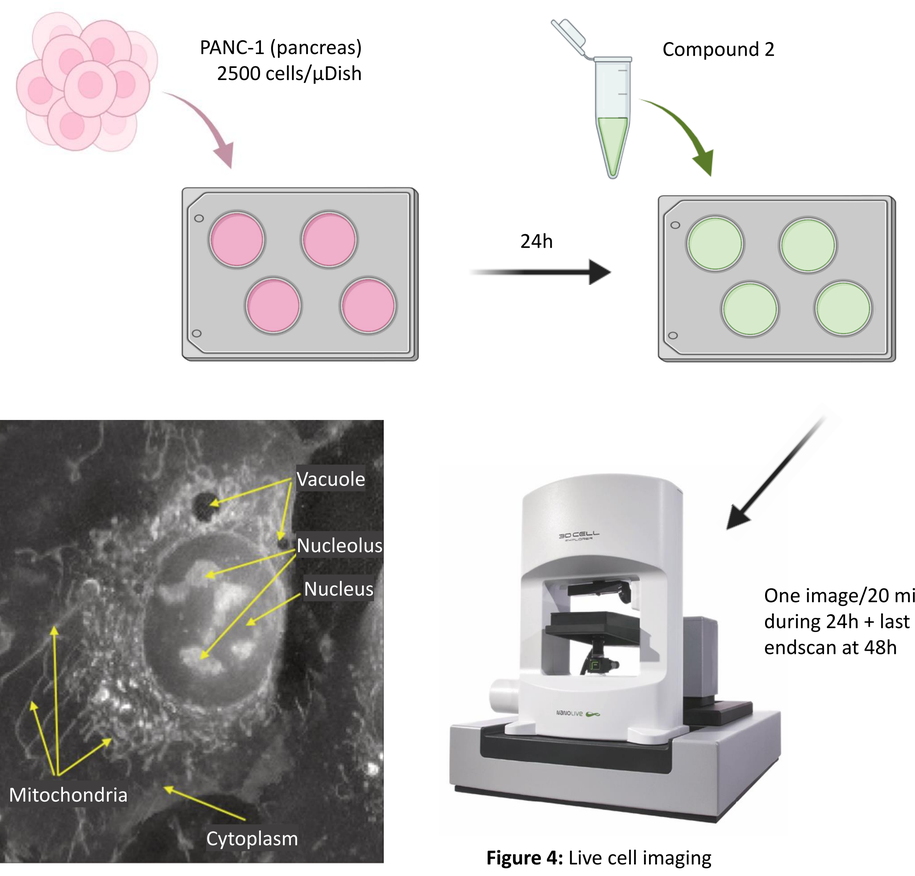


Figure 4: Live cell imaging

3 RESULTS & DISCUSSION

A

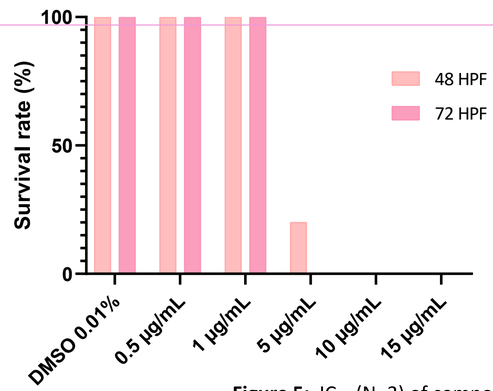


Figure 5: IC_{50} (N=3) of compounds 1–3 and the crude extract

The activity against PANC-1 cells differs from the other two cell lines.
The crude DCM extract shows moderate activity, whereas the isolated Corymbulosin I (2) is the most promising compound.
Compounds 1–3 exhibited slightly selective cytotoxic activity for the pancreatic carcinoma (PANC-1) cell line.

B

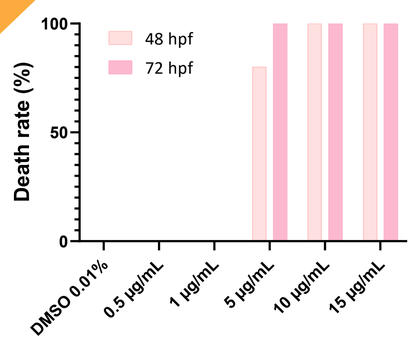
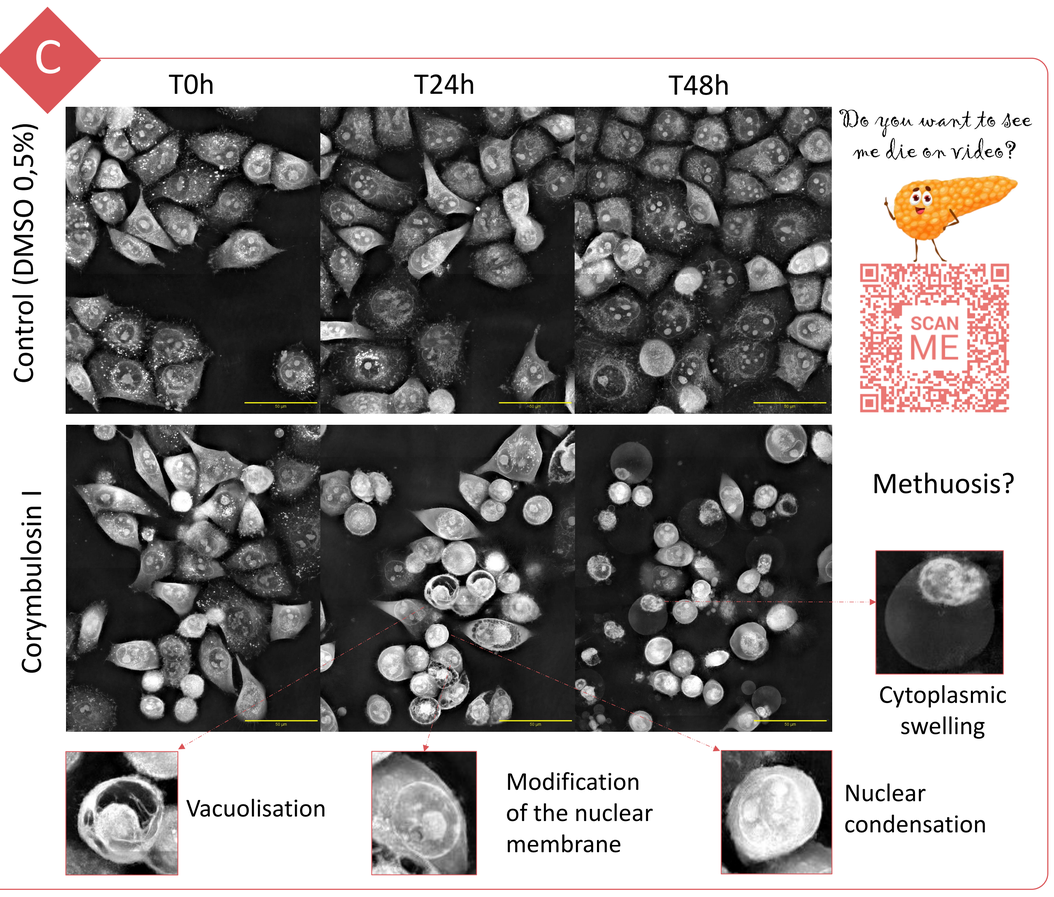


Figure 6: Survival (%) of the zebrafish at 48 and 72 hpf

Neither mortality nor morphological change were observed up to a concentration of 1 µg/mL.
At a dose of 5 µg/mL, mortality was observed, 20% of the embryos were alive at 48 hpf but were dead at 72 hpf.
Concentrations higher than 5 µg/mL were lethal for all embryos.
With a LC_{50} value in the range of 1 and 5 µg/mL, these results confirmed the important toxicity of compound 1.

C



4 CONCLUSION

This is the first time that the activity of caseamembrin T on PANC-1, A549 and MDA-MB231 cells has been highlighted. The activity of corymbulosin I and isocaseamembrin E has already been demonstrated against A549 and MDA-MB-231 cells [2], but it was the first time against the PANC-1 cells. It could be interesting to deeply investigate the potentialities of clerodane diterpenes, and more specifically corymbulosin I, for the targeting of pancreatic cancer cells. It would be interesting to perform real-time imaging on a pool of cells, which would contain both tumor cells (as PANC-1) and healthy cells (as fibroblasts), in order to have a detailed morphological analysis of the cells when they are put in contact with corymbulosin I, and to try to distinguish a difference in terms of mode of action.

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References:

[1] Xia, L., Guo, Q., Tu, P. & Chai, X. The genus Casearia: a phytochemical and pharmacological overview. Phytochem. Rev. 14, 99–135 (2015).
[2] Aimaiti, S. et al. Corymbulosins I–W, Cytotoxic Clerodane Diterpenes from the Bark of Laetia corymbulosa. J. Org. Chem. 83, 951–963 (2018).
[3] Ledoux, A. et al. Bioactive Clerodane Diterpenoids from the Leaves of Casearia coriacea Vent. Molecules 28, 1197 (2023).