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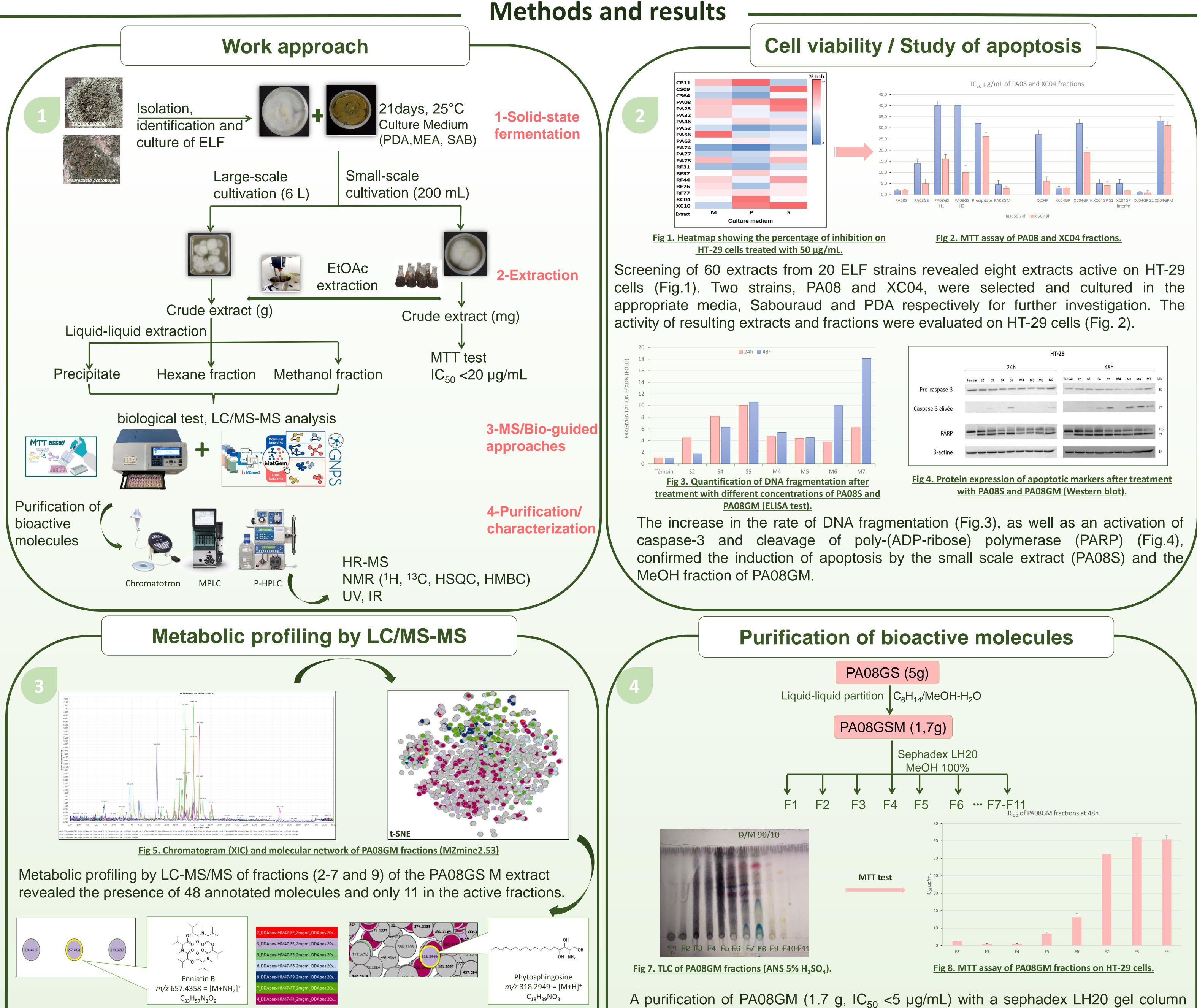
Apoptotic agents from the endolichenic fungi against chemoresistant cancers

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Introduction

Cancer is a major cause of death worldwide, with breast, lung and colon cancers being the most common. Chemoresistance is also a major obstacle in the treatment of cancer. Hence the importance of researching new treatments to diversify the therapeutic arsenal. Endolichenic fungi (ELF), non-pathogenic fungi located in the thallus of lichens, represent a niche of molecules with diverse biological activities, including antiproliferative activity^{1,2,3}. They offer a promising solution in the search for new bioactive compounds against colon cancer (HT-29) and triple-negative breast cancer (MDA-MB-231).



yielded 11 fractions (Fig.7), and an MTT test highlighted 5 active fractions including 2 (F3 and F4) with an IC₅₀ < 1 μ g/mL (Fig.8). According to the TLC, it was observed that the bioactive molecules are concentrated in the polar fractions. Their separation on RP18 column seemed not efficient and needed the use of other chromatographic phases (HILIC column).

Fig 6. some TSNE nodes of annotated molecules

Enniatin B and phytosphingosine were found in F3, the active fraction. Enniatin B is well known for its cytotoxicity on several human cancer cells⁴, and phytosphingosine for its induction of apoptosis via the caspase pathway⁵.

Conclusion

A screening of 60 extracts demonstrated the activity in vitro of 8 extracts of 7 strains on the HT-29 cells. The chemical investigation of two selected strains (PA 08 and XC 04) are in progress. The antiproliferative activity of fractions of the PA08GSM extract was evaluated and their involvement in the induction of an apoptotic process was demonstrated. In addition, LC-MS/MS analysis annotated very few known molecules from databases. This work shows that endolichenic fungi are a very interesting source of new molecules with antiproliferative activity which confirm their therapeutic potential.

References ¹Kellogg et al., «Endolichenic fungi: new source of rich bioactive secondary metabolites on the horizon », Phytochem Rev, 2017, (16), 271-293. ² Lagarde et al., « Antiproliferative and antibiofilm potentials of endolichenic fungi associated with the lichen Nephroma laevigatum », J.Appl. Micro, 2019 (126) 1044-1058. ³LI et al., "Tetramic Acids and pyridone alkaloids from the endolichenic fungus Tolypocladium cylindrosporum », J. Nat. Prod, 2015, (9), 2155–2160. ⁴ Prosperini et al. « A review of the mycotoxin enniatin B », Front. Public. Health, 2017, (3), 304. ⁵ Park et al. « Phytosphingosine induces apoptotic cell dearth via caspase 8 activation and bax translocation in human cancer cells », Clin. Cancer. Res, 2003, (9), 878-885.

