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Cytotoxicity of triterpenoids-enriched extracts from bark of Eucalyptus nitens against colorectal HCT116 cancer cells

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Eucalyptus nitens crops are used in Portugal mainly by the pulp and paper industries, producing substantial bark residues with no added value use [1]. They can, however, be an interesting source of bioactive triterpenic compounds. Here, a lipophilic crude extract (CE) from bark of *E. nitens* prepared with dichloromethane [1] with about 70% (w/w) of triterpenoids, and a fraction of this (F2) more enriched in triterpenoids (93% w/w), as well as their main compounds betulinic acid (BiA) and betulonic acid (BoA), were used to determine their potential cytotoxicity against the colorectal HCT116 cancer cells. After 48h of incubation, the extracts/compounds inhibited significantly cell growth in a concentration-dependent manner (assessed by the MTT assay), with a GI50 s of 1.3 µg/mL and 2.2 µg/mL for F2 and CE extracts, respectively, and of 0.8µM and 3.9µM for BoA and BiA, respectively. The inhibition of cell growth was shown to be dependent on both the arrest of cell cycle at the G2/M phase, and the induction of cell death (assessed by PI staining). At the higher concentrations tested (up to 25µM), apoptosis was the major contributor to the observed cell death, and that was associated with JNK activation. Using the JNK inhibitor SP600125 and the pan-caspase inhibitor z-VAD, apoptosis induced by the extracts/compounds was shown to be dependent on JNK and caspases activation. At intermediate concentrations of extracts/compounds, a delayed and non-apoptotic type of cell death was present, which was associated with a significant activation of AMPK and a decrease of p53 levels. Altogether, these results demonstrate that the wasted bark of *E. nitens* can be used as a potential source of interesting cytotoxic natural triterpenoids against cancer cells.

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Keywords: Eucalyptus nitens, bark extracts, triterpenoids, HCT116 cancer cells, cytotoxicity, apoptosis, cell cycle arrest

References:

[1] Domingues RMA, Sousa GDA, Silva CM, Freire CSR, Silvestre AJD, Pascoal-Neto C (2011). High value triterpenic compounds from the outer bark of several Eucalyptus species cultivated in Brazil and in Portugal. Industrial Crops and Products 33: 158 – 164.