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Chemometric and transcriptomic profiling, microtubule disruption and cell death induction by secalonic acid in tumor cells

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ABSTRACT

The aim of the work: Nature represents an indispensable source providing bioactive natural products with potential for cancer therapy [1]. The present study aims to assess cytotoxicity and modes of action of a naturally occurring ergochrome pigment secalonic acid F (SAF) on various leukemia and multiple myeloma cells by using in silico and in vitro methods. We used resazurin assay for the determination of cytotoxicity. Cell cycle analysis and cell death mode (apoptosis/necrosis) were analyzed by using flow cytometry. COMPARE and cluster analyses were performed to discover the association between the gene expression patterns and the drug responsiveness measured by the NCI developmental therapeutic program and to determine cell lines from different origin exhibiting different degrees of sensitivity to secalonic acid, respectively. Fluorescence microscopy was used to observe the alterations in the microtubule formation. SAF exhibited cytotoxic activity on both leukemia and multiple myeloma cells. Generally, multiple myeloma cells were more sensitive to SAF than leukemia cells. NCI-H929 cells were the most affected cells among the tested panel of multiple myeloma cell lines and were taken for further studies to assess the mode of action of SAF on those cells. Cell cycle analysis revealed that SAF induced S and G2/M arrest in NCI-H929 cells. SAF-associated apoptosis and necrosis resulted in cytotoxicity. SAF further inclined the disassembly of the tubulin network, which may also account for its cytotoxicity. COMPARE and hierarchical cluster analyses of transcriptome-wide expression profiles of the NCI tumor cell line panel identified genes involved in numerous cellular processes (e.g., cell differentiation, cell migration, and other numerous signaling pathways) notably correlated with log10IC50 values for secalonic acid. Jointly use of in silico and in vitro methods enabled the evaluation of cytotoxicity and molecular mechanisms of SAF on multiple myeloma cells. Thus, the present study supported the therapeutic potential of SAF to treat multiple myeloma.

BIOGRAPHY

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