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Activity of novel semisynthesized sesquiterpene lactones towards NF-B in a her2 breast cancer cell line

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The NF-B signalling pathway is constitutively activated in Cancer Stem Cells (CSCs) inducing the expression of genes that regulate proliferation, invasion, and metastasis. Plant-derived Sesquiterpene Lactones (SLs) have been suggested to inhibit this transcription factor. SLs are found in plants from the Asteraceae family and one species in this family, *Ambrosia arborescens*, contains a high concentration of damsine. We have previously shown that treatment with damsine reduces the CSC population of the HER2 breast cancer cell line JIMT-1. Damsine was used as a starting material for the synthesis of the SL analogue DCS3 followed by the synthesis of four DCS3 SL analogues. The toxicity of DCS3 and the analogues was investigated in the normal-like human breast epithelial cell line MCF-10A and in the JIMT-1 breast cancer cell line. Inhibitory concentration 50 (IC₅₀) values were obtained from MTT-based dose response curves. Immunofluorescence microscopy was used to evaluate if the compounds inhibited TNF-induced translocation of NF-B to the cell nucleus. All compounds were more toxic to JIMT-1 cells than to MCF-10A cells as shown by lower IC₅₀ values in the former cells. DCS3 was more toxic than damsine and the DCS3 SL analogues were more toxic than DCS3. At IC₅₀, all compounds inhibited TNF-induced translocation of NF-B to the cell nucleus. The compounds reduce the CSC sub-population of JIMT-1 cells. Our results suggest that these compounds should be further investigated to find efficient CSC inhibiting compounds that may be used in the clinic.

Biography

Wendy Soria is a Doctoral student of Functional zoology at Lund University, Sweden. Her research focus is Anti-cancer stem cell activity of a sesquiterpene lactone isolated from *Ambrosia arborescens* and of a synthetic derivative.

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