Cytotoxic and Proapoptotic Activity of Diterpenoids from *in vitro* Cultivated *Salvia sclarea* Roots. Studies on the Leukemia Cell Lines

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Four diterpenoids, ferruginol, salvipisone, aethiopinone and 1-oxoaethiopinone, were isolated from transformed roots of *Salvia sclarea*. Salvipisone and aethiopinone showed relatively high cytotoxicity against HL-60 and NALM-6 leukemia cells (IC_{50} range 0.6–7.7 μg/mL which is equal to 2.0–24.7 μM), whereas 1-oxoaethiopinone and ferruginol were less active in this regard. Moreover, we have found that all four diterpenoids of *S. sclarea* had equal cytotoxic activity against parental HL-60 and multidrug-resistant HL-60 ADR cells, what indicates that they are poor substrates for transport by multidrug resistance-associated protein (MRP1). Caspase-3 activity determinations showed that salvipisone and aethiopinone were able to induce apoptosis in a time- and concentration-dependent manner. The results obtained in this study show that *S. sclarea* diterpenoids aethiopinone and salvipisone may be useful in the treatment of human cancers, especially in the case of drug resistance.

Key words: Diterpenoids, Cytotoxicity, Leukemia Cells