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Sesquiterpene lactones affect G2/M cell cycle arrest and apoptosis in human soft tissue sarcoma cell lines

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Uncontrolled proliferation, metastasis and failure in apoptosis constitute crucial elements in the development and progression of tumors. Several studies have demonstrated the efficacy of plant-derived agents in the treatment of various malignant entities. The present study investigated the anti-tumor effects of costunolide and dehydrocostus lactone isolated from *Saussurea lappa* in three human soft tissue sarcoma (STS) cell lines of various origins.

Cell proliferation was determined using the MTS assay and xCELLigence technology. Cell cycle distribution, cleaved caspase-3, and Annexin V/PI were analysed by FACS analysis. The protein expression level of PARP and cleaved-PARP, G1- and G2/M cell cycle checkpoints were analysed using western blotting.

Both compounds inhibited cell proliferation of STS cell lines at concentrations ranging from 0.5 to 100 µg/ml and incubation periods from 24 to 72 h. After costunolide treatment, no significant changes in cell cycle distribution were detected compared to untreated control groups. However, dehydrocostus lactone caused a significant reduction of the G1 phase and an increase in S and G2/M phases, as well as high levels of cleaved caspase-3 and PARP cleavage. The expression levels of CDK2, CDK1 (cdc2), cyclin B1, and p27 decreased significantly after dehydrocostus lactone treatment in a dose-dependent manner. Thus, G2/M arrest via the CDK1 down-regulation may be an important molecular mechanism by which dehydrocostus lactone inhibits cancer cell growth.

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