Anti-proliferative effects of Cynaropicrin on anaplastic thyroid cancer cells

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Sesquiterpene lactones are a large group of plant-derived compounds characterized by a wide spectrum of biological effects including anti-tumor, anti-ulcer, anti-inflammatory, neuro-cytotoxic and cardiotonic activities and for this reason have often been used in traditional medicine against inflammation and cancer. Recently, in vitro anti-proliferative effects have been reported for Cynaropicrin, one of the main sesquiterpene lactones present in Cynarascolymus leaves extracts.

In this study we evaluated the effects of Cynaropicrin on three human thyroid cancer cell lines (CAL-62, 8505C, SW1736), widely used as preclinical model of anaplastic thyroid carcinoma (ATC), a very aggressive neoplasia for which there are not effective treatments.

Cell viability was investigated by cell counting and MTT assay, cell cycle by FACS assay and apoptosis by annexin V-FACS assay. Moreover, after treatment, we measured reactive oxygen species (ROS) and malonyldealdeyde (MDA) levels by cytofluorimetric analysis and using a commercial kit (Sigma Aldrich, Italy) respectively.

Cynaropricrin was able to block the proliferation of cancer cells after 24 and 48 h of treatment in a concentration- and time-dependent way. Treatment with 2.5, 5 and 10 µM of Cynaropicrin reduced the growth of CAL-62, 8505C, and SW1736 cells with a similar trend. In particular, after 24 h of treatment, the strongest inhibiting effect (about 70%) was obtained using the 10 µM concentration. After 48 h of treatment, a significant reduction of the viability was observed already at the concentration of 1 µM (about 70% inhibition) in CAL-62 and 8505C, and 2.5 µM in SW1736 cells. As determined by cytofluorimetric analysis, Cynaropicrin caused a block in the G2/M phase of the cell cycle, accompanied by apoptosis in all cell lines. In all cell lines, no changes in ROS production were observed after treatment with all the concentrations of this compound. Finally, MDA levels resulted significantly enhanced in CAL-62, 8505C and SW1736 cells treated with Cynaropicrin at the concentration of 10 µM. These latter finding suggest the presence of a damage caused by the onset of lipid peroxidation despite the absence of ROS production.

These results demonstrate the effectiveness of Cynaropicrin in blocking the growth of ATC cells, suggesting for this compound a potential use as adjuvant in the treatment of thyroid cancer.