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Biological screening of meroterpenoids isolated from Moroccan marine algae *Cystoseira usneoids*

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Background: Seaweeds are potentially prolific sources of highly bioactive secondary metabolites with chemical compounds that might represent useful leads in the development of new pharmaceutical agents. The most prominent among these are meroterpenoids (MTs), a hybrid between terpenoids and polyketides. MTs are most often isolated from marine organisms (especially macroalgae) and exhibit various biological activities, some of which are promising, lead to new types of agents against cancer and infectious diseases. The chemical study of specimens of the brown alga *Cystoseira usneoides* has yielded twelve natural products, whose structures are characterized by possessing a phenolic moiety linked to an isoprenoid chain. The compounds differ in the length or in the functionalization of the isoprenoid chain.

Objectives: In this study we investigated the antitumoral, antiinflammatory and antioxidant capabilities of 12 MTs named MT-E, MT-F, MT-G, MT-H, MT-I, MT-isoS, MT-S, MT-T, MT-V, MT-X, MT-Y and MT-Z, all isolated from *Cystoseira usneoides*, using two human cells lines, HT-29 (adenoma cancer cell) and THP-1 (Human acute monocytic leukemia cell).

Materials and methods: HT-29 cells were grown in McCoy's and THP-1 cells in RPMI1640 medium, the both medium supplemented with 10% heat-inactivated fetal calf serum and penicillin/streptomycin (100µg/mL), maintained at 37℃ in 5% CO2 humidified atmo sphere. The anti-proliferative effect was investigated by cell viability(SRB) and apoptosis assays, as well as cell cycle analysis study, the cells were treated with different concentrations of MTs (6.25 to 100 µg/ml) and for different times (24, 48 and 72h). The antiinflammatory activity was assessed by TNF-α production (ELISA assay kit release). The antioxidant activity was measured by ABTS methods. Experiments were performed in duplicate in two independent experiments and results are expressed as mean ± standard deviation. (*p<0.05, **p<0.01, ***p<0.001) compared with control.

Results: All MTs showed a potent cytotoxic effect against HT-29 cells; the IC50 values ware estimated to range from 7 to 30µg/ml after 48h of treatment. Various compounds isolated demonstrated to induce apoptosis in HT-29; among them MT-S and MT-T showed highly potent promoted apoptosis in the HT-29 cells (44±0.99%* and 47.3±3.72%*, respectively). In cell cycle analysis, treatment with MTs (10, 20, 40µg/ml) for 24h resulted in a significant increase of cells in the G2/M phases; MT-G, MT-I and MT-X elevated the percentage of HT-29 cells in the G2/M phase from 19.2±0.02%, control cells, to 45±2.23%, 46.9±0.18%*** and 47.2±2.92%, respectively. TNF-α production by THP-1 (monocyte-derived macrophages) culture treated with LPS was found to be significantly inhibited by 5µg/ml of Cu-Z and Cu-E, and 4µg/ml of Cu-G. All MTs possessed considerable antioxidant activity, which was found to be nearly equivalent to Trolox in some cases; the EC50 values were 13.3±0.8, 16.1±1.1* and 17.2±0.6* µg/ml for MT-H, MT-G and MT-I, respectively.

Conclusion: The results from this study indicate that the MTs from *Cystoseira usneoides* can significantly inhibit HT-29 cell proliferation, induce apoptosis and block cells in G2/M phase. Similarly marine algae *C. usneoides* possess interesting antiinflammatory and antioxidative properties. These findings suggest that *C. usneoides* is a potential candidate for a novel therapeutic agent in the field of anticancer and antiinflammatory drug discovery, although its application as nutraceuticals and functional foods could be also considered.