Effects of Monoterpenes as a Novel Proton Pumps Inhibitors in Melanoma Tumor Cells

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Recent studies have indicated that proton pumps (H⁺-ATPases) can play an important role in cancer progression and metastasis by inducing a cell acidification in tumor microenvironment. In this work, we analyzed the monoterpenes Citral and Myrtenal as putative inhibitors of the H⁺ pumps, F- and V-type H⁺-ATPases, in two melanoma cell lines with distinct metastatic potential and using a transformed macrophage cell line as a control. It was analyzed the enzyme activities, cell viability, and the type of cell death, using spectrophotometry, electron microscopy, flow cytometry, and further molecular approaches. It was observed an inhibition of both, F-ATPases and V-ATPases, by the monoterpenes tested, but the inhibition of V-ATPases were more pronounced in cell lines with higher metastatic potential. Such an inhibition could also be related to apoptosis and secondary necrosis verified in monoterpenes treated melanoma cells. In conclusion, the results suggest that Citral and Myrtenal can induce apoptosis by inhibiting the main H⁺ pumps involved in acidification of the tumor microenvironment. Innovative anti-cancer therapies could be putatively developed based in the blockage of the V-ATPase, inhibiting the growth and metastasis by induction of death programmed cell.

KeysWord: Monoterpenes, Proton Pumps, Melanoma Cells.
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