Perillyl alcohol (POH), a monoterpeno found in some vegetables, is used in treatment of various tumors, including gliomas. Our group demonstrated that POH is a Na\(^+\),K\(^+\)-ATPase inhibitor. Na\(^+\),K\(^+\)-ATPase participates in different physiological functions and is involved in cell signaling events. Therefore, changes in enzyme activity may have an important role in many biological and pathological processes. Here, we evaluated the effect of POH and perillyl acid (PA), the main POH metabolite, on the Na\(^+\),K\(^+\)-ATPase activity in three different human glioblastoma cell lines (U87, U251 and GBV). Our results, based on evaluation of Na\(^+\),K\(^+\)-ATPase activity by Rb\(^+\) ion incorporation showed a sensitivity to inhibition by POH similar among the three cell lines (IC\(_{50} \pm 1.9\)mM). However, PA was unable to inhibit the enzyme activity. Glioblastoma (GBM) cells overexpresses Na\(^+\),K\(^+\)-ATPase α\(_1\) isoform in the caveolar structure. This isoform modulates signaling mechanisms leading to apoptosis. Although the action mechanism of POH is not understood, some data indicate that it induces apoptosis in GBM cells. Therefore, we compared the cell viability by determining the activity of the enzyme lactate dehydrogenase present in the cell supernatants treated for 24 hours with POH and PA. PA did not reach citotoxic effect greater than 30% in the three cell lines even at 4mM, but POH caused cell death from the concentration of 1.5mM. Partial results obtained with flow cytometry showed apoptotic effect in GBM cells after 30 minutes of treatment with POH at 4.0mM, but not with PA.

Keywords: Na\(^+\),K\(^+\)-ATPase; perillyl alcohol; glioblastoma cell lines

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