

Palavras-chave: valproic acid, pharmacodynamics, pharmacokinetics, forensics

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POSTER 39

Sodium Dichloroacetate and 3-Bromopyruvate induce loss of cell viability and metabolic alterations in melanoma and breast cancer cells

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Resumo

Introduction: The majority of tumor cells presents a metabolic reprogramming, changing to a glycolytic phenotype, even under aerobic conditions, which is named "Warburg effect", that is essential for their survival and proliferation [1,2]. This metabolic switch is associated to abnormal vascularization, hypoxic state, and activation of oncogenic signaling pathways. In cancer cells, pyruvate is preferentially converted to lactate which is rapidly exported by specific transporters. This leads to a hyper-glycolytic acid-resistant phenotype, that favors cancer proliferation and invasion as well as chemoresistance to several conventional anti-tumor drugs [1,3]. **Objectives:** Evaluate the effect of anti-glycolytic compounds on two models of tumor cells (breast cancer and melanoma), namely concerning cell viability and metabolism. **Materials and Methods:** SRB assays were performed to evaluate the effect of DCA and 3-BP in MCF7 (breast) and A375-C5 (melanoma) cell viability. To study their effect in metabolism, cancer cells were grown in RPMI medium supplemented with fetal bovine serum (FBS) until 80% confluence in 24-well plates, and then incubated 24h

in fresh RPMI medium without FBS with ½ IC50 or IC50 of the compound. The culture medium was collected and for glucose and lactate levels were determined by an enzymatic colorimetric kit and normalized to the respective cell biomass. **Results:** The different cell lines were incubated with different concentrations of 3-bromopyruvate (3-BP) and sodium dichloroacetate (DCA) for 24h and the cell viability and the respective IC50 were determined by the SRB assay. In both cell lines, it was observed that both compounds decrease the percentage of viable cells in a dose-dependent way, although differently, depending on the cell line and the compound, being both cell lines more sensitive to 3-BP. Glycolysis inhibitors are reported to lead to a decrease in lactate production and efflux and in glucose consumption. As expected, the inhibitors tested proved to be effective decreasing the lactate produced. However, even with higher compound concentrations, the glucose concentration remained similar. **Conclusion:** The anti-tumoral drugs were able to alter the metabolism of tumor cells and consequently the cancer proliferation.

Keywords: cancer; cellular metabolism; Warburg effect; 3-bromopyruvate; sodium dichloroacetate.

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