Evaluation of the cytotoxic activity of 2-Acetylpyridine-and 2-benzoylpyridine-derived hydrazones to healthy cells and glioma cells

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Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries. Although brain tumors constitute only 1-2% of tumors in adults, they have a poor prognosis and chance of survival of patients is generally very low. Gliomas, particularly glioblastomas, represent the most malignant primary brain tumor. Hydrazones are an important class of compounds that have numerous applications, including anti-tumor activity. In this present study 2-acetylpyridine-phenylhydrazone (H2AcPh), its para-chlorophenylhydrazone (H2AcpClPh) and para-nitrophenylhydrazone (H2AcpNO2Ph) analogues, derived from the corresponding 2-benzoylpyridine hydrazone (H2BzPh and H2BzpClPh H2BzpNO2Ph) were assayed for their cytotoxic activity against U87 and T98 glioma cells. Human Fetal Lung Fibroblast cells (MRC5) were used as a model of healthy cells. For this purpose, cytotoxicity was measured by 3 - (4,5-dimethyl-2-thiazolyl) -2,5-diphenyl-2H-tetrazolium bromide assay, which measures the metabolic cell viability. Cells stained with DAPI were visualized by phase contrast microscopy to assess whether the cells treated with hydrazides exhibit nuclear changes characteristic of apoptosis. The results showed that hydrazones were highly cytotoxic at nanomolar doses against U87 and T98 cells. 2-Acetylpyridine-derived hydrazones were more active than the 2-benzoylpyridine analogues against both cell lineages. Unlike H2BzpNO2Ph, all other hydrazones were more potent than the reference drug etoposide. IC50 values against MRC5 cells were much higher. In fact, the therapeutic indexes (TI = IC50MRC5/IC50 glioma) were 2-660 for T98 cells and 28-5000 for U87 cells. Due to their high therapeutic indexes the studied hydrazones revealed to be good as antitumor drug candidates to treat brain tumors.

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