Antitumoral Effect of N(4)-Tolyl-2-Acetylpyridine Derived Thiosemicarbazones and their Gallium (III) Complexes Against Glioma Tumors

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Glioblastoma multiforme (GBM), an aggressive brain tumor, is well known for its radio and chemoresistance. The development of new therapeutic compounds against these tumors constitutes a strategy to improve prognosis and health quality for malignant glioma patients, given their low survival rate. Thiosemicarbazones have drawn great pharmaceutical interest for their broad biological activities, including an antitumoral one. We have previously reported that N(4)tolyl-2-acetylpyridine derived thiosemicarbazones are very potent against glioblastomas. The aim of this work was to determine if gallium (III) coordination to N(4)tolyl-2-acetylpyridine derived thiosemicarbazones (GaLac, GaLacm, GaLacpt) can improve the antitumoral activity of their related free thiosemicarbazones. This was evaluated through the MTT assay and analysis of photomicrographies. All thiosemicarbazones proved to have high cytotoxic effect against human glioblastoma cell lines even at very low concentrations. Also, morphological alterations such as rounding of the cells, chromatin condensation and the diminishing of cytoplasmic volume indicated the apoptotic cell death mechanism. All compounds were more potent than clinically used drugs such as cisplatin and etoposide. Taken together, these data strongly suggest that N(4)tolyl-2-acetylpyridine derived thiosemicarbazones constitute promising anticancer agents and that gallium complexation is a good strategy to improve antitumoral activity of their respective free thiosemicarbazones.

Keywords: chemotherapy, gallium, glioblastoma, thiosemicarbazone

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