2-Acetylpiridine -Derived Thiosemicarbazones: Antitumoral Effect Against Malignant Glioblastoma

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Glioblastoma multiforme (GMB) is the most commonly diagnosed primary tumours of the brain in humans and always culminates in death within 1–2 years of diagnosis. Despite decades of intensive clinical and laboratory research, progress in clinical treatment has been slow, in part because of tumour heterogeneity. For this reason, the development of alternative drugs is relevant in the attempt to increase the patient survival. 2-acetylpiridine –derived thiosemicarbazones present a wide range of bioactivities but their pharmacological applications for brain tumours treatment have not so far been investigated. The aim of this work was to identify and characterize the antitumoral effect of 2-acetylpiridine -derived thiosemicarbazones (Lac, Lacm, Lacpt, LacPh and LacClPh) on malignant glioblastoma cells (RT2 and T98 cells). The results showed that the 2- acetylpiridine -derived thiosemicarbazones possess a powerful antitumoral effect with IC_{50} at nanomolar concentrations. LacClPh presented the higher cytotoxic effect (IC_{50} = 1nM for both tumour cells lineages) and was much more potent than the antitumor agent cisplatin (IC_{50} = 17 and 5 μM for RT2 and T98 cells, respectively). Tumour cells treated with 2- acetylpiridine -derived thiosemicarbazones acquired round shapes and presented cell shrinkage, blebs formation and nuclear changes characteristics of apoptosis. Moreover, all studied compounds presented a low haemolytic activity ($IC_{50} > 10^{-3}$M), near that of the control sample, indicating no detectable disturbance of red blood cell membrane. These results show that 2- acetylpiridine -derived thiosemicarbazones have a good potential to be developed into novel drug candidates for brain tumour therapy and further investigations on their pharmacological behaviour should be carried out.

Key words: Thiosemicarbazones, acetylpiridine, antitumoral effect.
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