[Pt(*O*,*O*'-acac)(*γ*-acac)(DMS)]: Alternative Strategies to Overcome Cisplatin-Induced Side Effects and Resistance in T98G Glioma Cells

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This article has been updated

Abstract

Cisplatin (CDDP) is one of the most effective chemotherapeutic agents, used for the treatment of diverse tumors, including neuroblastoma and glioblastoma. CDDP induces cell death through different apoptotic pathways. Despite its clinical benefits, CDDP causes several side effects and drug resistance.[Pt(*O*,*O*'-acac)(*γ*-acac)(DMS)], namely PtAcacDMS, a new platinum(II) complex containing two acetylacetonate (acac) and a dimethylsulphide (DMS) in the coordination sphere of metal, has been recently synthesized and showed 100 times higher cytotoxicity than CDDP. Additionally, PtAcacDMS was associated to a decreased neurotoxicity in developing rat central nervous system, also displaying great antitumor and antiangiogenic activity both in vivo and in vitro. Thus, based on the knowledge that several chemotherapeutics induce cancer cell death through an aberrant increase in $[Ca^{2+}]_i$, in the present in vitro study we compared CDDP and PtAcacDMS effects on apoptosis and intracellular Ca^{2+} dynamics in human glioblastoma T98G cells, applying a battery of complementary techniques, i.e., flow cytometry, immunocytochemistry, electron microscopy, Western blotting, qRT-PCR, and epifluorescent Ca^{2+} imaging. The results confirmed that (i) platinum compounds may induce cell death through an aberrant increase in $[Ca^{2+}]_i$ and (ii) PtAcacDMS exerted stronger cytotoxic effect than CDDP, associated to a larger increase in resting $[Ca^{2+}]_i$. These findings corroborate the use of PtAcacDMS as a promising approach to improve Pt-based chemotherapy against gliomas, either by inducing a chemosensitization or reducing chemoresistance in cell lineages resilient to CDDP treatment.