Evaluation of anticancer activity in vitro of a stable copper(I) complex with phosphine-peptide conjugate

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Streszczenie

[CuI(2,9-dimethyl-1,10-phenanthroline)P(p-OCH_3-Ph)$_2$$CH_2$SarcosineGlycine] (1-MPSG), highly stable in physiological media phosphino copper(I) complex—is proposed herein as a viable alternative to anticancer platinum-based drugs. It is noteworthy that, 1-MPSG significantly and selectively reduced cell viability in a 3D spheroidal model of human lung adenocarcinoma (A549), in comparison with non-cancerous HaCaT cells. Confocal microscopy and an ICP-MS analysis showed that 1-MPSG effectively accumulates inside A549 cells with colocalization in mitochondria and nuclei. A precise cytometric analysis revealed a predominance of apoptosis over the other types of cell death. In the case of HaCaT cells, the overall cytotoxicity was significantly lower, indicating the selective activity of 1-MPSG towards cancer cells. Apoptosis also manifested itself in a decrease in mitochondrial membrane potential along with the activation of caspases-3/9. Moreover, the caspase inhibitor (Z-VAD-FMK) pretreatment led to decreased level of apoptosis (more pronouncedly in A549 cells than in non-cancerous HaCaT cells) and further validated the caspases dependence in 1-MPSG-induced apoptosis. Furthermore, the 1-MPSG complex presumably induces the changes in the cell cycle leading to G2/M phase arrest in a dose-dependent manner. It was also observed that the 1-MPSG mediated intracellular ROS alterations in A549 and HaCaT cells. These results, proved by fluorescence spectroscopy, and flow cytometry, suggest that investigated Cu(I) compound may trigger apoptosis also through ROS generation.

Adres publiczny

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