Oncology Insights

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Anticancer activity of diphenyltin(IV) compounds bearing carboxylato N-functionalized 2-quinolones

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Background: The limited efficacy of conventional metal-based chemotherapeutic drugs is attributed to resistance, high toxicity, and numerous side effects, thus providing a platform for the design of new metal-based drugs with enhanced properties. Organotin(IV) compounds have already been recognized as promising agents due to their ability to inhibit tumor growth both in vitro and in vivo. Following this concept, new diphenyltin(IV) complexes incorporating carboxylato N-functionalized 2-quinolones ligands were assessed on different cancer cell lines. Material and Methods: Evaluation of anticancer activity in vitro of the newly synthesized diphenyltin(IV)complexes bis (3-(4-methyl-2-oxoquinolin-1(2H)-I)propanoato)diphenyltin(IV), and bis (2-(4-hydroxy-2-oxoquinolin-1(2H)-yI)ethanoato)diphenyltin(IV) (1-3, respectively) as well as ligand precursors (HL1, HL2, and HL3) was determined after 72 h on a panel of cancer cell lines of human and mouse origin (MCF-7, A375, HCT116, 4T1, B16, CT26) using MTT and CV assays.Complex 1 and HCT116 cells were selected for further analysis of the potential mechanism, Flow cytometry for the assessment of cell death, proliferation, caspase activation and production of active oxygen/nitrogen species as well as fluorescent microscopy for detection of nuclei morphology were employed. Results: Obtained results showed a dose-dependent viability decrease in all cell lines exposed to complexes 1-3 with IC50 values in the low micromolar range. Ligand precursors, HL1-HL3 showed no activity up to 200 μM. Complex 1 inhibited cell proliferation and provoked caspase-dependent apoptosis in HCT116 cells. The enhanced presence of autophagosomes determined after the treatment with complex 1 was found to be protective, opposing apoptosis. The scavenging potential of tested complex 1 on ROS/RNS production can be connected with abolished viability and suppressed proliferation, since HCT116 cells are potent producers of ROS. Conclusion: Taking all together, novel diphenyltin(IV) complexes present promising anticancer agents and should be further tested in vivo.

Keywords: apoptosis, cancer, cytotoxicity, melanoma



Bismuth ferrite nanoparticles increase ROS production and p62 expression in A375 melanoma and HeLa cells

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Background: Cancer nanomedicine is a rapidly developing field that uses nanoparticles (NPs) for the diagnosis and treatment of cancer. Currently, many nanomaterials with different shapes, sizes, structures, and compositions have been investigated to produce effective anticancer NPs. The interest in the biomedical applications of bismuth-containing nanoparticles, such as bismuth ferrite (BFO-NP) is a result of their promising properties such as cost-effectiveness, chemical inertness, high stability, and simplicity of functionalization. Material and Methods: A375 human melanoma and HeLa cervical carcinoma cells were used to study the antitumor activity of BFO-NP. Clonogenicity of treated cells was analyzed by colony forming assay, while cell death was examined using flow cytometry. DCF-DA fluorescent assay was applied to measure ROS production. Protein expression of p62 and TfR1 was detected by Western blot. Cell migration was analyzed using a wound scratch assay, while an SRB assay was used to assess cell adhesion. Results: BFO-NP (200 ng/ μ L) significantly reduced the clonogenicity of A375 and HeLa cells by 46 and 60%, respectively. Detected ROS production was increased considerably, especially for A375 melanoma cells, and amounted to 400%. The number of late apoptotic and/or necrotic cells increased by 10-12%, compared to the control. Significantly increased expression of autophagy-related protein p62 was observed in both cell lines after BFO-NP treatment. Ferroptosis-related transferrin