Pro-apoptotic effects of a thiazoline-containing Pd(II) complex in human promyelocytic leukaemia HL-60 cells (maximum 200 characters, Times New Roman, 12 pt font, bold)

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Evading apoptosis represents the third hallmark of cancer. Cisplatin is a common chemotherapeutic agent used to treat cancer given that it can restore apoptotic mechanisms in cancer cells. However, cisplatin produces serious side effects as it also affects healthy cells, and certain cancers may acquire resistance to cisplatin. Thus, synthesis of new Pt(II) compounds as an alternative to cisplatin is warranted to avoid resistance and undesirable side effects. Pd(II) could be a Pt(II) surrogate given the similarity of coordination chemistry between them, thus widening the spectra of available anticancer drugs. The objective of this study was to test the potential cytotoxic and pro-apoptotic actions of a Pd(II) complex coordinated with the ligand PyTT (2-(2-pyridyl)imine-N-(2-thiazolin-2-yl)thiazolidine), a thiazoline derivative, with formula [PdCl2PyTT]. Its potential anticancer ability was evaluated in human promyelocytic leukaemia HL-60 cell line. To this aim, sub-confluent cultures of HL-60 cells were challenged with different doses (5-100 µM) of PyTT and PdPyTT for 24 h and cytotoxicity was then checked by means of MTS assay. The complex PdPyTT presented enhanced cytotoxicity, with a half-maximal (50%) inhibitory concentration (IC_{50}) of 20.7 µM for HL-60 cells. Nonetheless, the thiazoline derivative PyTT by itself did not show cytotoxic effects. Moreover, nuclear staining with Hoechst 33342 revealed that the complex PdPyTT produced nuclear condensation and DNA fragmentation, thus indicating that the main form of cell death was apoptosis. These findings were in line with activation of caspase-9 and caspase-3 observed after treating HL-60 cells with the complex PdPyTT for 24 h. On the other hand, exacerbated reactive oxygen species (ROS) production was also observed when HL-60 cells were incubated with 20.7 µM PdPyTT, ROS being mainly of mitochondrial origin. Although further studies are required to understand the underlying mechanisms, the present findings suggest that thiazoline-based Pd(II) complexes are promising alternatives to hamper cancer proliferation when common anticancer drugs fail.

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