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Cellular Mechanistic Considerations on Cytotoxic Mode of Action of Phosphino Ru(II) and Ir(III) Complexes

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Streszczenie

Two piano-stool ruthenium(II) complexes Ru(η6 -pcymene)Cl2PPh2CH2OH (RuPOH) and Ru(η6 -p-cymene)Cl2P(pOCH3Ph)2CH2OH (RuMPOH) and two half-sandwich iridium(III) complexes Ir(η5 -Cp*)Cl2PPh2CH2OH (IrPOH) and Ir(η5 -Cp*)Cl2P(pOCH3Ph)2CH2OH (IrMPOH) have been studied in terms of potential anticancer activity on previously selected cell line (human lung adenocarcinoma). Based on experimental results obtained in monoculture in vitro model mechanistic considerations on the possible cellular modes of action have been carried out. ICP-MS analysis revealed the higher cellular uptake for less hydrophobic Ir(III) complexes in comparison to the corresponding Ru(II) compounds. Cytometric analysis showed a predominance of apoptosis over the other types of cell death for all complexes. The apoptotic pathway was confirmed by a decrease in mitochondrial membrane potential and the activation of caspases-3/9 for both Ru(II) and Ir(III) complexes. It was concluded that in the case of Ru(II) complexes the intense ROS generation is mainly responsible for the resulting cytotoxicity. The corresponding Ir(III) complexes trigger simultaneously at least three different cytotoxic pathways i. e., depletion of mitochondrial potential, activation of caspases-dependent apoptosis, and ROS-associated oxidation. Thus, it can be assumed that the final accumulation of toxic effects over time via parallel activation of different pathways results in the highest cytotoxicity in vitro exhibited by Ir(III) complexes when compared with Ru(II) complexes.

Słowa kluczowe

Cellular mechanism of action, Chemotherapeutics, Iridium(III), Phosphines, Ruthenium(II)

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