

## *Two out of Three Musketeers Fight against Cancer: Synthesis, Physicochemical, and Biological Properties of Phosphino Cu<sup>I</sup>, Ru<sup>II</sup>, Ir<sup>III</sup> Complexes*

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### Kolekcja

Naukowa

### Streszczenie

Two novel phosphine ligands, Ph<sub>2</sub>PCH<sub>2</sub>N(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub> (**1**) and Ph<sub>2</sub>PCH<sub>2</sub>N(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub> (**2**), and six new metal (Cu(I), Ir(III) and Ru(II)) complexes with those ligands: iridium(III) complexes: Ir(η<sup>5</sup>-Cp\*)Cl<sub>2</sub>(**1**) (**1a**), Ir(η<sup>5</sup>-Cp\*)Cl<sub>2</sub>(**2**) (**2a**) (Cp\*: Pentamethylcyclopentadienyl); ruthenium(II) complexes: Ru(η<sup>6</sup>-p-cymene)Cl<sub>2</sub>(**1**) (**1b**), Ru(η<sup>6</sup>-p-cymene)Cl<sub>2</sub>(**2**) (**2b**) and copper(I) complexes: [Cu(CH<sub>3</sub>CN)<sub>2</sub>(**1**)BF<sub>4</sub>] (**1c**), [Cu(CH<sub>3</sub>CN)<sub>2</sub>(**2**)BF<sub>4</sub>] (**2c**) were synthesized and characterized using elemental analysis, NMR spectroscopy, and ESI-MS spectrometry. Copper(I) complexes turned out to be highly unstable in the presence of atmospheric oxygen in contrast to ruthenium(II) and iridium(III) complexes. The studied Ru(II) and Ir(III) complexes exhibited promising cytotoxicity towards cancer cells in vitro with IC<sub>50</sub> values significantly lower than that of the reference drug—cisplatin. Confocal microscopy analysis showed that Ru(II) and Ir(III) complexes effectively accumulate inside A549 cells with localization in cytoplasm and nuclei. A precise cytometric analysis provided clear evidence for the predominance of apoptosis in induced cell death. Furthermore, the complexes presumably induce the changes in the cell cycle leading to G2/M phase arrest in a dose-dependent manner. Gel electrophoresis experiments revealed that Ru(II) and Ir(III) inorganic compounds showed their unusual low genotoxicity towards plasmid DNA. Additionally, metal complexes were able to generate reactive oxygen species as a result of redox processes, proved by gel electrophoresis and cyclic voltamperometry. In vitro cytotoxicity assays were also carried out within multicellular tumor spheroids and efficient anticancer action on these 3D assemblies was demonstrated. It was proven that the hydrocarbon chain elongation of the phosphine ligand coordinated to the metal ions does not influence the cytotoxic effect of resulting complexes in contrast to metal ions type.

Język

Angielski

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Słowa kluczowe

iridium(III) complexes, ruthenium(II), cationic copper(I) complex, phosphines, lung cancer, DNA, reactive oxygen species, 3D spheroids

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