

Copper(I) complexes with phosphines $P(p\text{-OCH}_3\text{-Ph})_2\text{CH}_2\text{OH}$ and $P(p\text{-OCH}_3\text{-Ph})_2\text{CH}_2\text{SarGly}$: synthesis, multimodal DNA interactions, and prooxidative and *in vitro* antiproliferative activity.

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Streszczenie

Phosphonium salt $(p\text{-OCH}_3\text{-Ph})_2\text{P}(\text{CH}_2\text{OH})_2\text{Cl}$ (**MPOHC**), derived phosphine ligands without and with SarGly (Sarcosine-Glycine) peptide carrier $P(p\text{-OCH}_3\text{-Ph})_2\text{CH}_2\text{OH}$ (**MPOH**) and $P(p\text{-OCH}_3\text{-Ph})_2\text{CH}_2\text{SarGly}$ (**MPSG**), respectively, and two copper(I) complexes $[\text{Cu}(\text{I})(\text{dmp})(\text{MPOH})]$ (**1-MPOH**; dmp = (2,9-dimethyl-1,10-phenanthroline)) and $[\text{Cu}(\text{I})(\text{dmp})(\text{MPSG})]$ (**1-MPSG**) were synthesized. The resulting compounds were characterized by elemental analysis, 1D and 2D NMR and UV–Vis absorption spectroscopies, mass spectrometry, cyclic voltammetry and by X-ray diffraction analysis. Cytotoxicity of all compounds was evaluated *in vitro* against colon, lung, breast, pancreatic, prostate tumor cell lines, as well as towards non-tumor cell lines: lung, kidney and keratinocyte. Stable in biological medium in the presence of atmospheric oxygen, Cu(I) complexes exerted a cytotoxic effect higher than that elicited by cisplatin against tested cancer cell lines. The introduction of methoxy group onto the phenyl rings of the phosphine ligand coordinated to the copper(I) ion resulted in a relevant increase of cytotoxicity in the case of breast, pancreatic and prostate tumor cell lines *in vitro*. Attachment of a peptide carrier significantly increased the selectivity towards cancer cells. Fluorescence spectroscopic data (calf thymus DNA: CT-DNA) titration, together with analysis of DNA fragmentation (gel electrophoresis) and molecular docking provided evidence for the multimodal interaction of copper compounds with DNA and showed their unusual low genotoxicity. Additionally, copper complexes were able to generate reactive oxygen species as a result of redox processes, proved by fluorescence spectroscopy and cyclic voltamperometry.

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