

Liposomal Binuclear Ir(III)–Cu(II) Coordination Compounds with Phosphino-Fluoroquinolone Conjugates for Human Prostate Carcinoma Treatment

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Novel heteronuclear Ir^{III}–Cu^{II} coordination compounds ([Ir(η^5 -Cp*)Cl₂Pcfx-Cu(phen)](NO₃)·1.75(CH₃OH)·0.75(H₂O) (**1**), [Ir(η^5 -Cp*)Cl₂Pnfx-Cu(phen)](NO₃)·1.75(CH₃OH)·0.75(H₂O) (**2**), [Ir(η^5 -Cp*)Cl₂Plfx-Cu(phen)](NO₃)·1.3(H₂O)·1.95(CH₃OH) (**3**), [Ir(η^5 -Cp*)Cl₂Psfx-Cu(phen)] (**4**)) bearing phosphines derived from fluoroquinolones, namely, sparfloxacin (Hsfx), ciprofloxacin (Hcfx), lomefloxacin (Hlfx), and norfloxacin (Hnfx), have been synthesized and studied as possible anticancer chemotherapeutics. All compounds have been characterized by electrospray ionization mass spectrometry (ESI-MS), a number of spectroscopic methods (*i.e.*, IR, fluorescence, and electron paramagnetic resonance (EPR)), cyclic voltammetry, variable-temperature magnetic susceptibility measurements, and X-ray diffractometry. The coordination geometry of Ir^{III} in all complexes adopts a characteristic piano-stool geometry with the η^5 -coordinated and three additional sites occupied by two chloride and phosphine ligands, while Cu^{II} ions in complexes **1** and **2** form a distorted square-pyramidal coordination geometry, and in complex **3**, the coordination geometry around Cu^{II} ions is a distorted octahedron. Interestingly, the crystal structure of [Ir(η^5 -Cp*)Cl₂Plfx-Cu(phen)] features the one-dimensional (1D) metal–organic polymer. Liposomes loaded with redox-active and fluorescent [Ir(η^5 -Cp*)Cl₂Pcfx-Cu(phen)] (**1L**) have been prepared to increase water solubility and minimize serious systemic side effects. It has been proven, by confocal microscopy and an inductively coupled plasma mass spectrometry (ICP-MS) analysis, that the liposomal form of compound **1** can be effectively accumulated inside human lung adenocarcinoma and human prostate carcinoma cells with selective localization in nuclei. A cytometric analysis showed dominance of apoptosis over the other cell death types. Furthermore, the investigated nanoformulations induced changes in the cell cycle, leading to S phase arrest in a dose-dependent manner. Importantly, *in vitro* anticancer action on three-dimensional (3D) multicellular tumor spheroids has been demonstrated.

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