Copper(I) complexes with phosphine derived from sparfloxacin. Part III: multifaceted cell death and preliminary study of liposomal formulation of selected copper(I) complex

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ABSTRACT: Cytotoxic effect of iodide or thiocyanate copper(I) complexes (**1-PSf**, **2-PSf**, **3-PSf**, **4-PSf**) with a phosphine derived from sparfloxacin (**HSf**) and 2,9-dimethyl-1,10-phenanthroline (**dmp**) or 2,2'-biquinoline (**bq**) as diimine auxiliary ligands was proved *in vitro* on somatic (MRC-5) and neoplastic (MCF7) human cell lines. Differences in mode of action were investigated in-depth for selected the **dmp** and the **bq** complexes (**1-PSf**, **3-PSf**, respectively) by elucidation of (*i*) efficiency to produce reactive oxygen species (ROS) in biological systems (cyclic voltammetry), (*ii*) their impact on mitochondrial membrane potential, (*iii*) potency to activation of caspases 3 and 9, and (*iv*) influence on the degree of DNA degradation (comet assay). It was concluded that the apoptosis of cancer cells is straightly connected with caspase-dependent mitochondrial pathway and supported by ROS production along with irreversible DNA fragmentations. Finally, it was demonstrated that the selected copper(I) complex encapsulated into liposomes (**1-PSf-L**) exhibited the enhanced accumulation inside cancer cells. This resulted in its higher cytotoxicity against cancer cells with therapeutic index even *ca.* 60. Increased selective accumulation in active neoplasm with simultaneous enhanced bioavailability and reduced systemic toxicity of liposomal formulations of copper(I) complexes can result in development of new copper-based therapeutics and their successful implementation in anticancer chemotherapy.

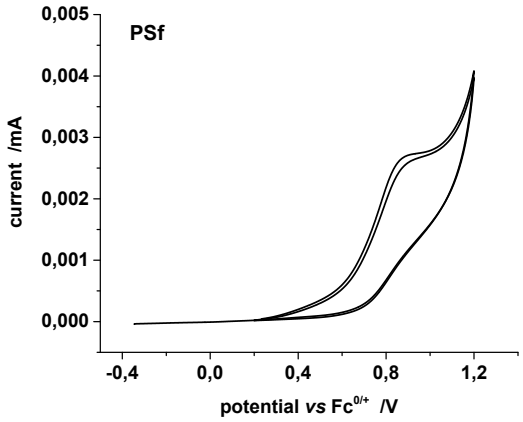

Fig. S1 Cyclic voltammogram of **PSf** ligand in dimethylformamide (DMF) with scan rate 10 mV s^{-1}.

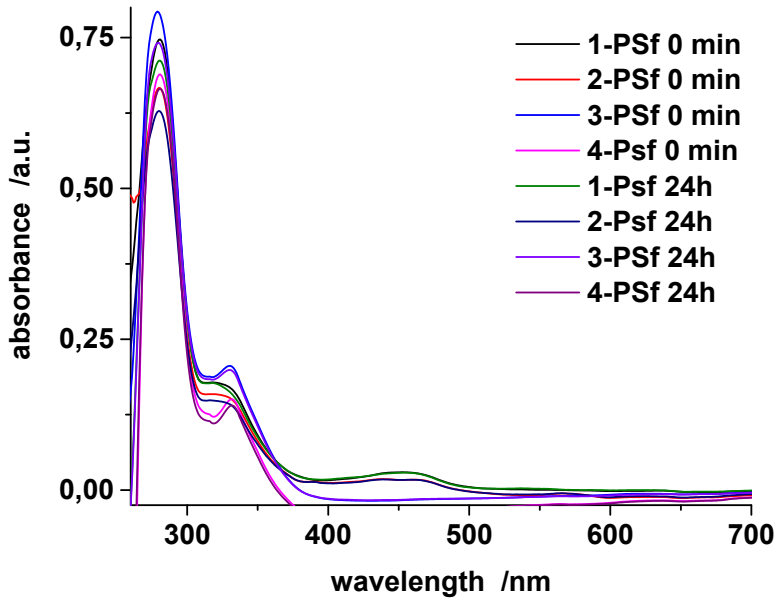

Fig. S2 UV-vis spectra of studied copper(I) complexes in dimethylformamide (DMF) recorded during 24 hours at 25ºC.

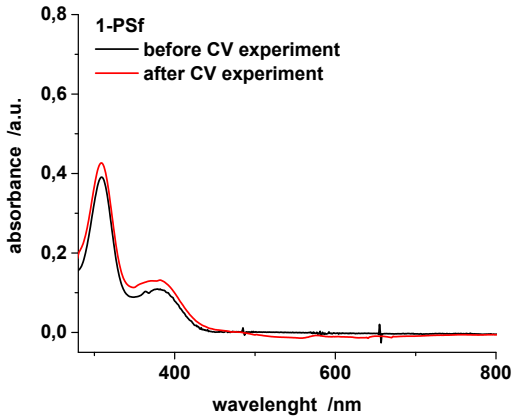

Fig. S3 UV-vis spectra before and after CV experiment for selected **1-PSf** copper(I) complex.

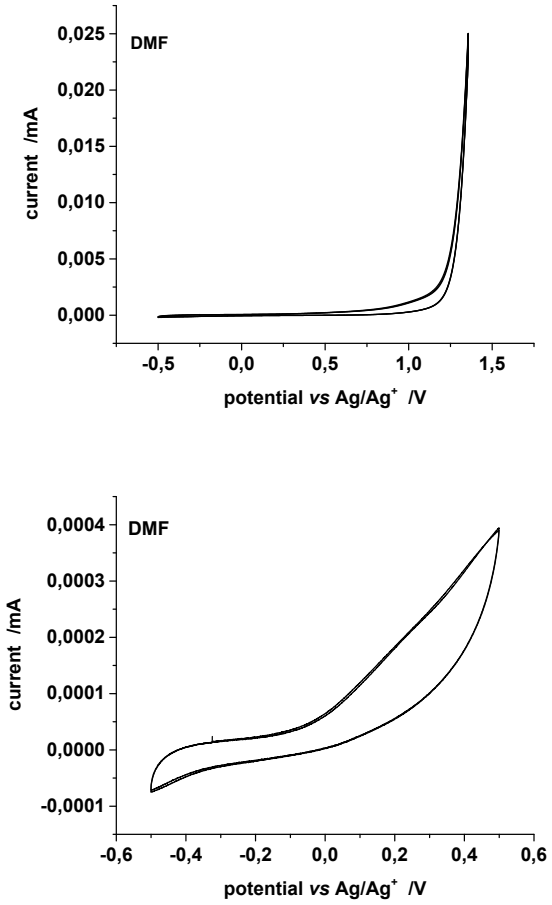

Fig. S4 CV voltammograms for DMF and CH_2Cl_2 in the range of potentials from -0.5 V to 1.4 V. Scan rate: 10 mV s^{-1}.

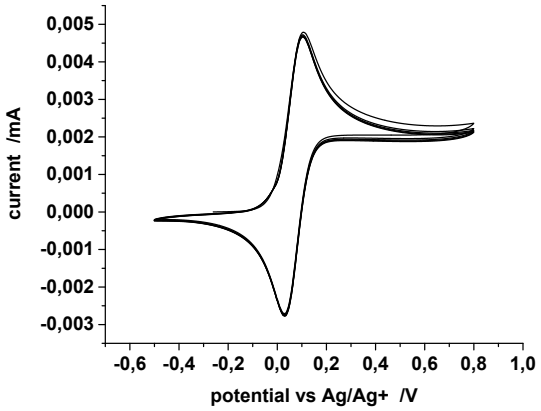

Fig. S5 CV voltammograms for ferrocene in DMF in the range of potentials from -0.5 V to 1.4 V. Scan rate: 10 mV s^{-1}.