Copper(I) phosphine-polypiridyl complexes: DNA/HSA binding study and antiproliferative activity

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Copper(I, II) coordination compound have been also tested as promising candidates for cancer treatment, searching for better and less toxic (based on the premise that copper is an essential trace metalloelement for plant and animal including human being) than platinum anticancer metallodrugs[1]. We present the DNA/HSA interaction and biological activity of five copper(I) phosphine-polypiridyl complexes with the general formula $[Cu(PPh_3)_2(N\text{-}N)]NO_3$, (where N-N = 1,10-phenantroline (phen) (**1**), dipyrido[3,2-a: 2',3'-h]quinoxoline (dpq) (**2**), dipyrido[3,2-a: 2',3'-c]phenazine (dppz) (**3**), 11-carboxy-dipyrido(3,2-a:2,3-c)phenazine (dppa) (**4**), dipyrido[3,2-a:2',3'-c]phenazine-11-carboxylic acid methyl ester (dppme) (**5**). The interactions between these copper complexes and the DNA have been investigated using UV-Vis titrations, thermal denaturation, circular dichroism, viscosity measurements, electrophoresis in gel and competitive fluorescent intercalator displacement assays. The results of our studies suggested that these copper(I) complexes interact with the DNA by intercalative way, as reported for other copper-dppz complexes. Furthermore, their high protein binding affinities toward human serum albumin (HSA) were determined by fluorescence studies. Additionally, cytotoxicity of all complexes against several cancel cell lines (human breast: MDA-MB-231 and MCF-7, human lung: A549, human prostate: DU-145, and Chinese hamster lung: V79-4) and health cell line from mouse L929 were performed. The finding results showed in Table 1 reveled that copper(I)-phosphine-polypyridyl complexes are more cytotoxic than the corresponding planar ligand and also showed to be more active than cisplatin. A good correlation was observed between the cytostatic activity and lipophilicity of the copper(I) complexes here studied, showed that these copper(I) complexes have potential antitumoral for drug development.

Table 1. IC_{50} values in μM for copper- polypyridyl complexes **1-5,** its respective organic ligands and cisplatin towards tumor cells: A549, MCF-7, DU-145 and non-tumor cells: V79-4 and MRC-5 after 48 h.

Compound	A549	MCF-7	DU-145	V79-4	MRC-5	IS	Log D
(**1**)	0.47±0.04	1.75±0.35	1.34±0.04	0.40±0.06	0.70±0.03	1.48	0.41±0.01
(**2**)	0.38±0.02	3.50±0.50	1.24±0.03	0.47±0.02	3.57±0.90	9.40	0.41±0.01
(**3**)	0.36±0.01	2.63±0.25	0.78±0.04	0.34±0.04	0.52±0.02	1.44	0.96±0.03
(**4**)	0.92±0.08	5.25±0.25	2.20±0.15	1.05±0.05	1.83±0.13	1.98	-0.33±0.01
(**5**)	0.32±0.01	3.50±0.40	0.80±0.01	0.31±0.06	0.71±0.06	2.20	0.78±0.03
phen	>50	>50	>50	>50	>50	-	-
dpq	>50	>50	>50	>50	>50	-	-
dppz	>100	>100	>100	>100	>100	-	-
Cisplatin	14.42±1.45	13.98±2.02	2.33±0.40	21.60±1.28	29.09±0.78	2.01	-

Selectivity index IC_{50} MRC-5/IC_{50} A549.

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