Supplementary information

Mixed–Ligand copper(II)–sulfonamide complexes: Effect of the sulfonamide derivative on DNA binding, DNA cleavage, Genotoxicity and Anticancer activity

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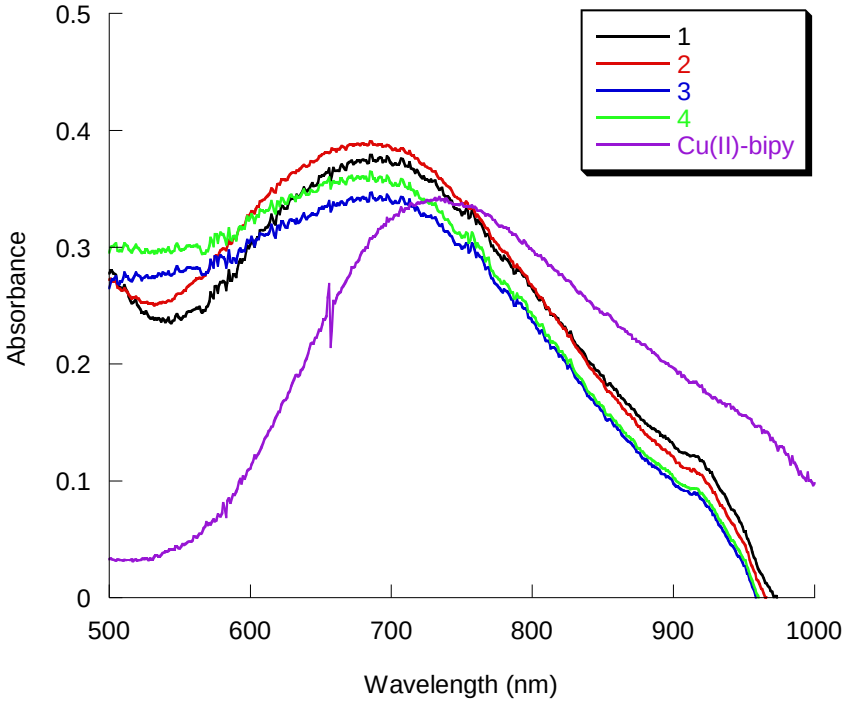


Fig. S1. Electronic spectra of compounds **1**–**4** and Cu(II)-bipy (1:1) in DMF solution.

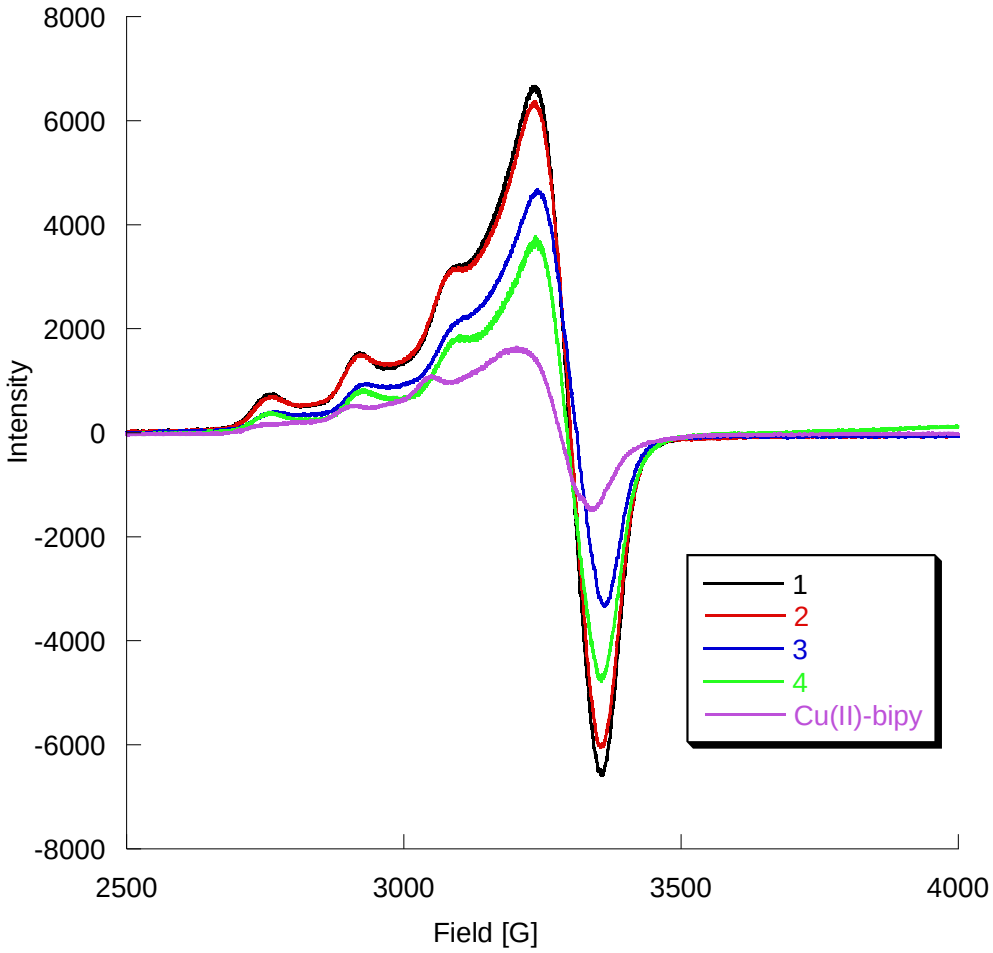


Figure S2. X–band EPR spectra of the complexes **1**–**4** in DMF solution at 40 K.

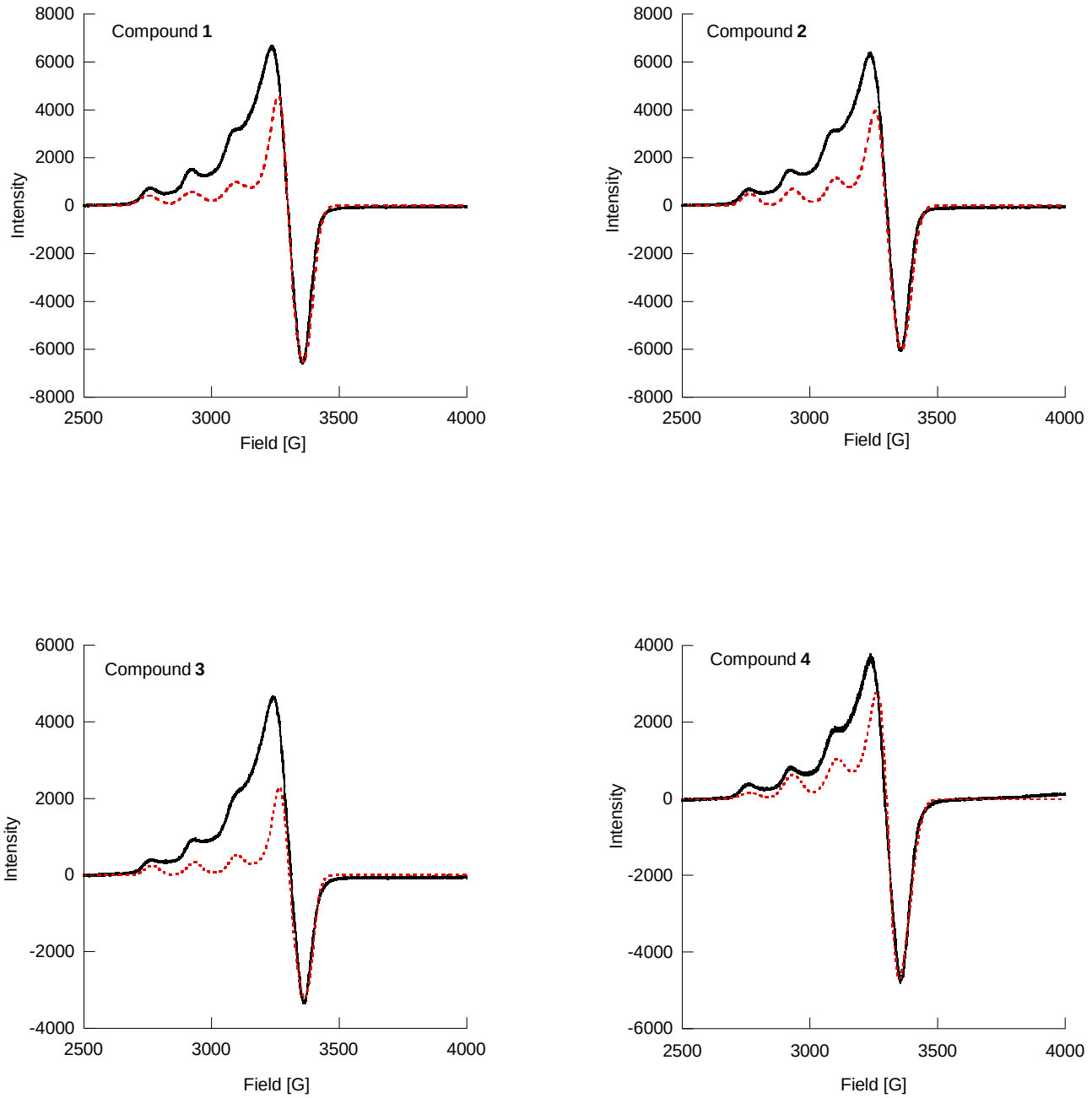


Fig. S3. X–band EPR spectra of compounds **1**–**4** in DMF solution (40 K).

Experimental (black line); simulated (dashed– red line).

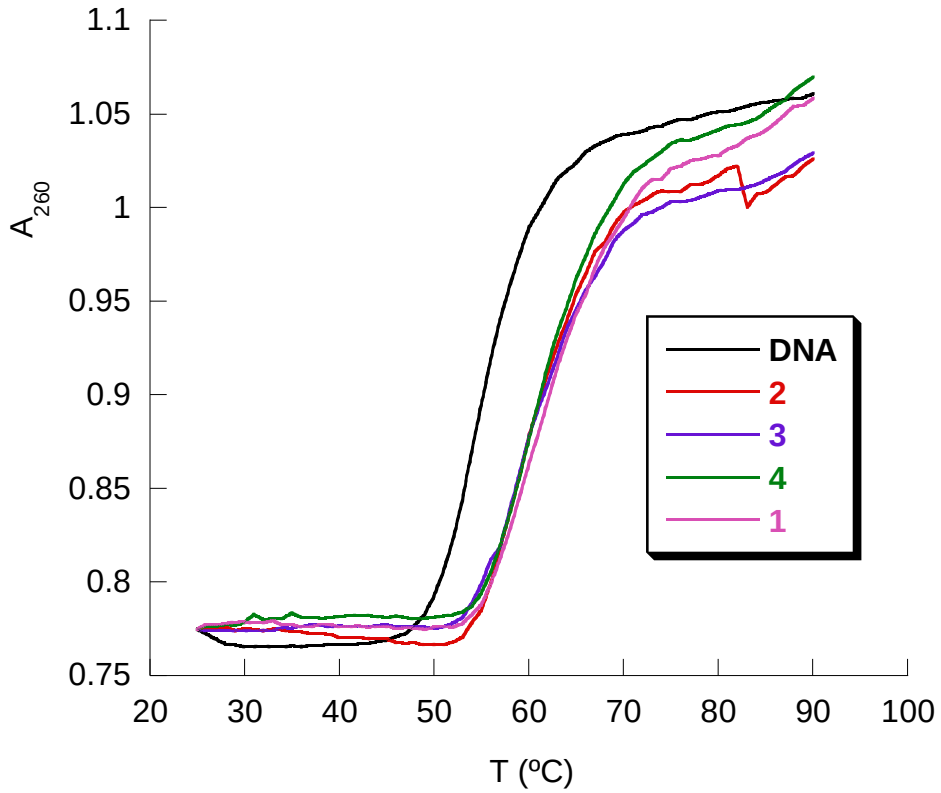


Fig S4. Thermal denaturation of CT-DNA in the absence and in the presence of the complexes **1**, **2**, **3** or **4**.

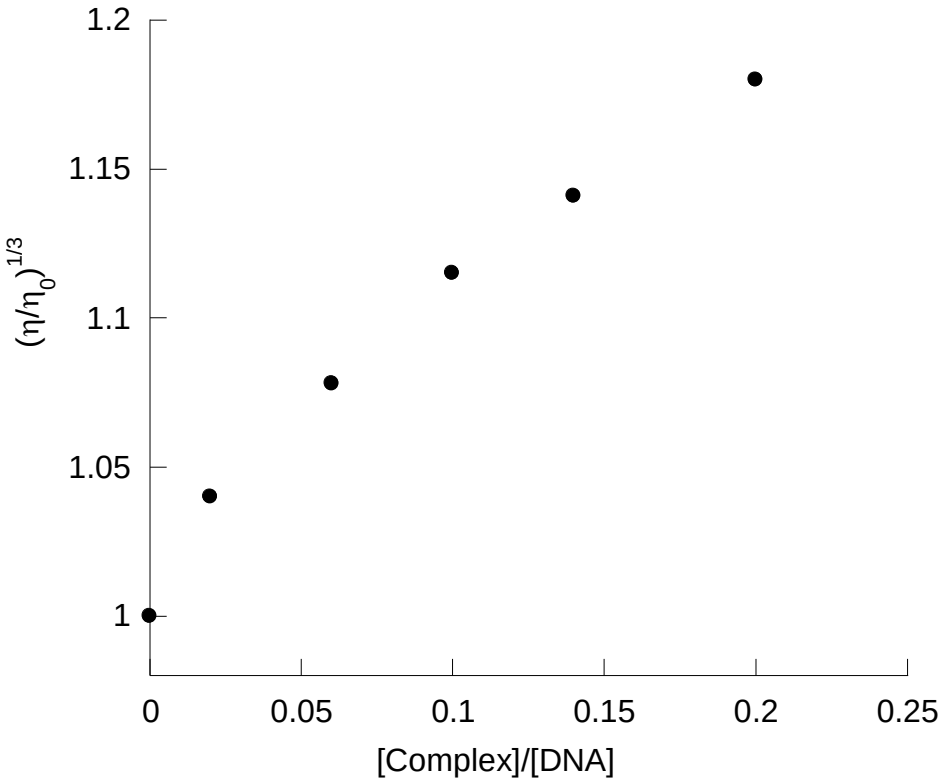
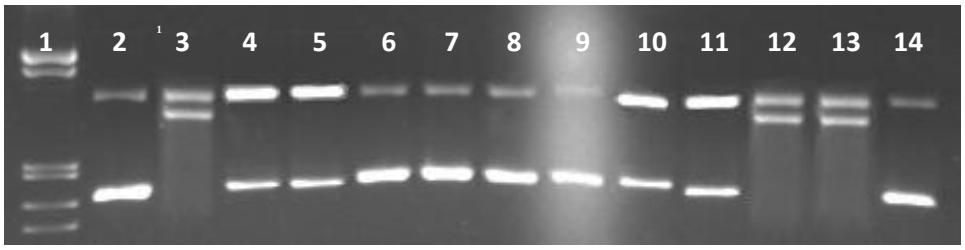
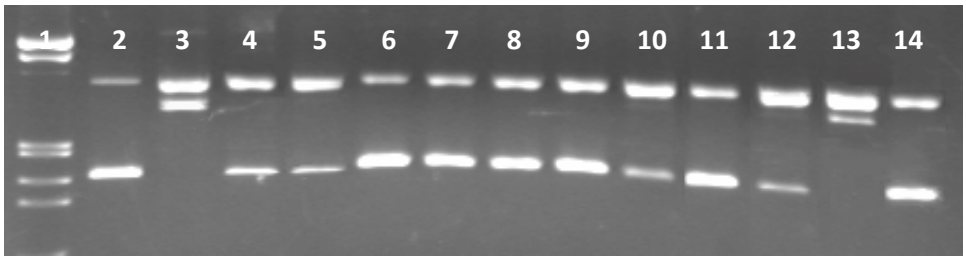


Fig. S5. Effect of $[Cu(L2)_2(bipy)]$ (**2**) on the relative viscosity of CT-DNA (50 μM base pairs) in cacodylate buffer 0.1 M (pH = 6.0).

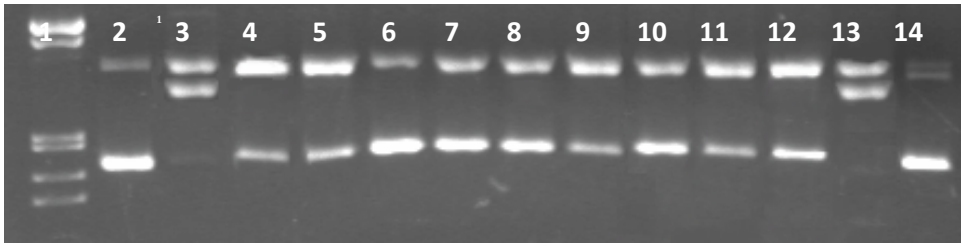
a)



b)



c)



d)

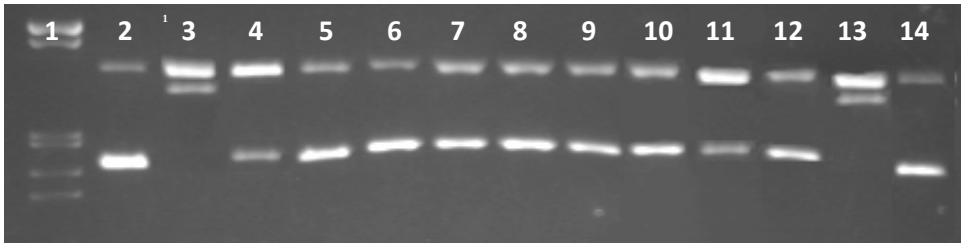


Fig. S6. Agarose gel electrophoresis of pUC18 plasmid treated with **1**, **2**, **3** or **4** and ascorbate in the presence of potential inhibitors. Incubation time 60 min (37 ºC). Complex 24 μM, ascorbate (25 ×). a) complex **1**, b) complex **2**, c) complex **3** d) complex **4**: 1. λDNA/EcoR1+HindIII Marker; 2: pUC18 control + ascorbate, 3: complex without inhibitors, 4: dmso 0.4 M, 5: *tert*–butyl alcohol 0.4 M, 6: sodium formate 0.4 M, 7: KI 0.4 M, 8: sodium azide 100 mM, 9: 2,2,6,6–tetramethyl–4–piperidone 100 mM, 10: Tiron 10 mM, 11: neocuproine 75 μM, 12: distamycin 8 μM, 13: methyl green (2.5 μL of a 0.01 mg/mL solution), 14: Catalase 10 μg/mL (6.50 units).

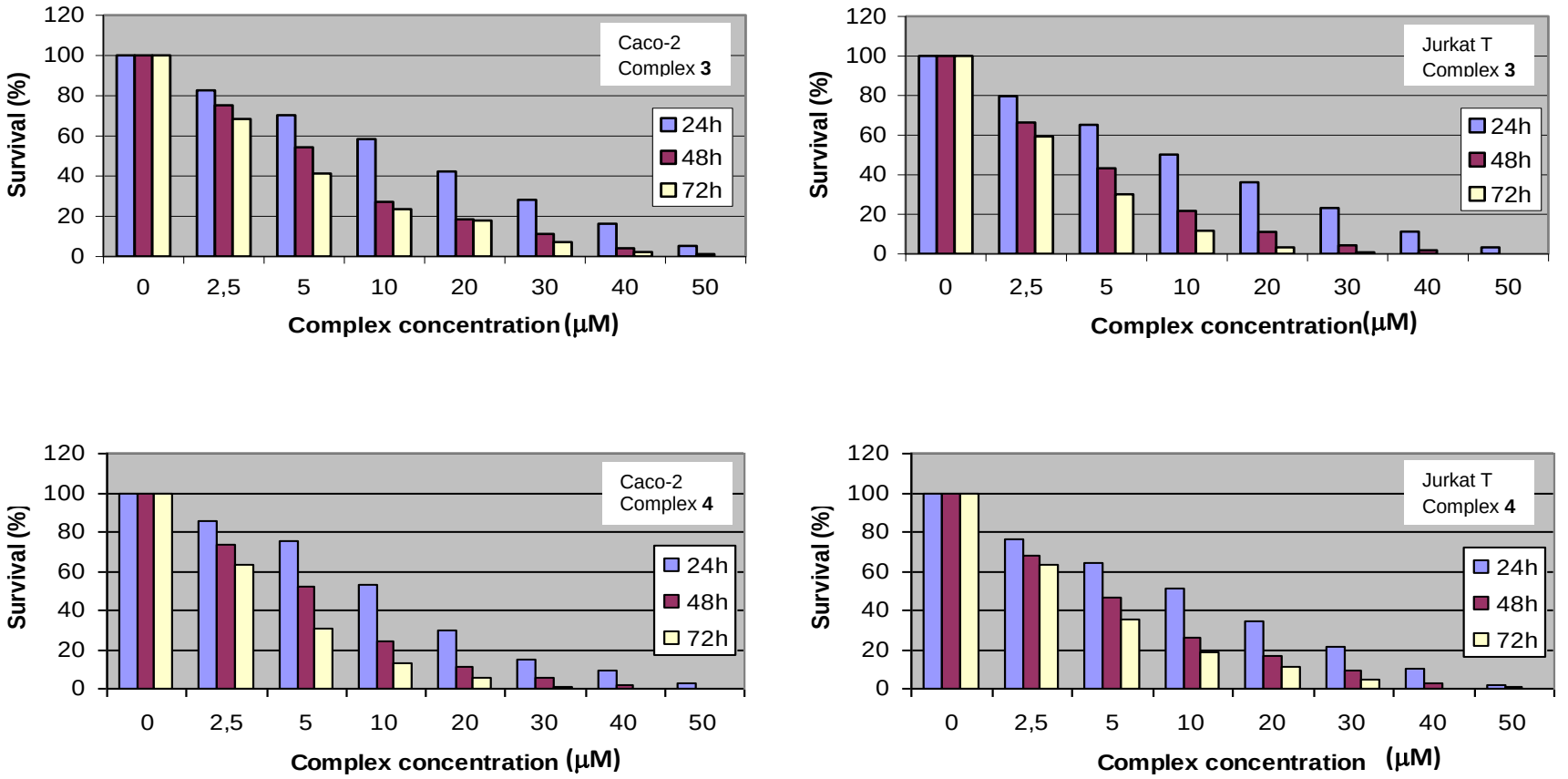


Fig. S7. Percentage of survival of Caco-2 cells or Jurkat T lymphocytes after treatment with complexes **3** or **4** for 24 h, 48 h or 72 h. Data represent the means of experiments performed in triplicate.

Table S1. EPR parameters for the compounds **1**-**4** and Cu(II)-bipy (1:1) calculated through simulation (ref. 63)

Compound	$\mathbf{g_{\parallel}}$	$\mathbf{g_{\perp}}$	$\mathbf{A_{\parallel}\ (cm^{-1})}$	$\mathbf{g_{\parallel}/A_{\parallel}(cm)}$
1	2.251	2.050	167×10^{-4}	135
2	2.244	2.051	167×10^{-4}	134
3	2.241	2.047	166×10^{-4}	135
4	2.252	2.041	170×10^{-4}	132
Cu(II)-bipy (1:1)	2.250	2.055	144×10^{-4}	156

Table S2. IC_{50} values of the complexes **1-4** against Caco-2 cells or Jurkat T lymphocytes (results obtained by the trypan blue exclusion method)

Cells	Complex	IC_{50} (μM)		
		24 h	48 h	72 h
Caco-2 cells	**1**	15.66±0.29	7.16±0.32	4.85±0.13
	2	8.89 ± 0.65	4.57±0.40	2.89±0.13
	3	11.95±1.67	5.97± 0.62	3.78±0.69
	4	12.64±1.15	5.22±0.22	3.81±0.28
Jurkat T lymphocytes	**1**	11.46±0.12	6.60±0.57	4.39±0.19
	2	4.81±0.65	3.85±0.23	2.20±0.56
	3	10.09±1.37	4.34±0.26	3.78±0.20
	4	10.16±0.23	4.70±0.17	3.23±0.36

Data represent the means ± SD of experiments carried out in triplicate