Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Copper(II) Complexes of 2-methyl-8-hydroxyquinoline and tri/diimine Co-ligand: DFT Calculation, DNA and BSA Binding, DNA Cleavage, Cytotoxicity and Induction of Apoptosis

Somasundaram Sangeetha[1,2] · Tamilarasan Ajaykamal[3] · Mariappan Murali[1*]

Mariappan Murali
ma66mu@gmail.com

1 Coordination and Bioinorganic Chemistry Research Laboratory, Department of Chemistry, National College (Autonomous), Tiruchirappalli 620 001, Tamil Nadu, India
2 Department of Chemistry, Tamilavel Umamaheswaranar Karanthai Arts College, Thanjavur 613 002, Tamil Nadu, India
3 School of Chemistry, Bharathidasan University, Tiruchirappalli 620 024, Tamil Nadu, India

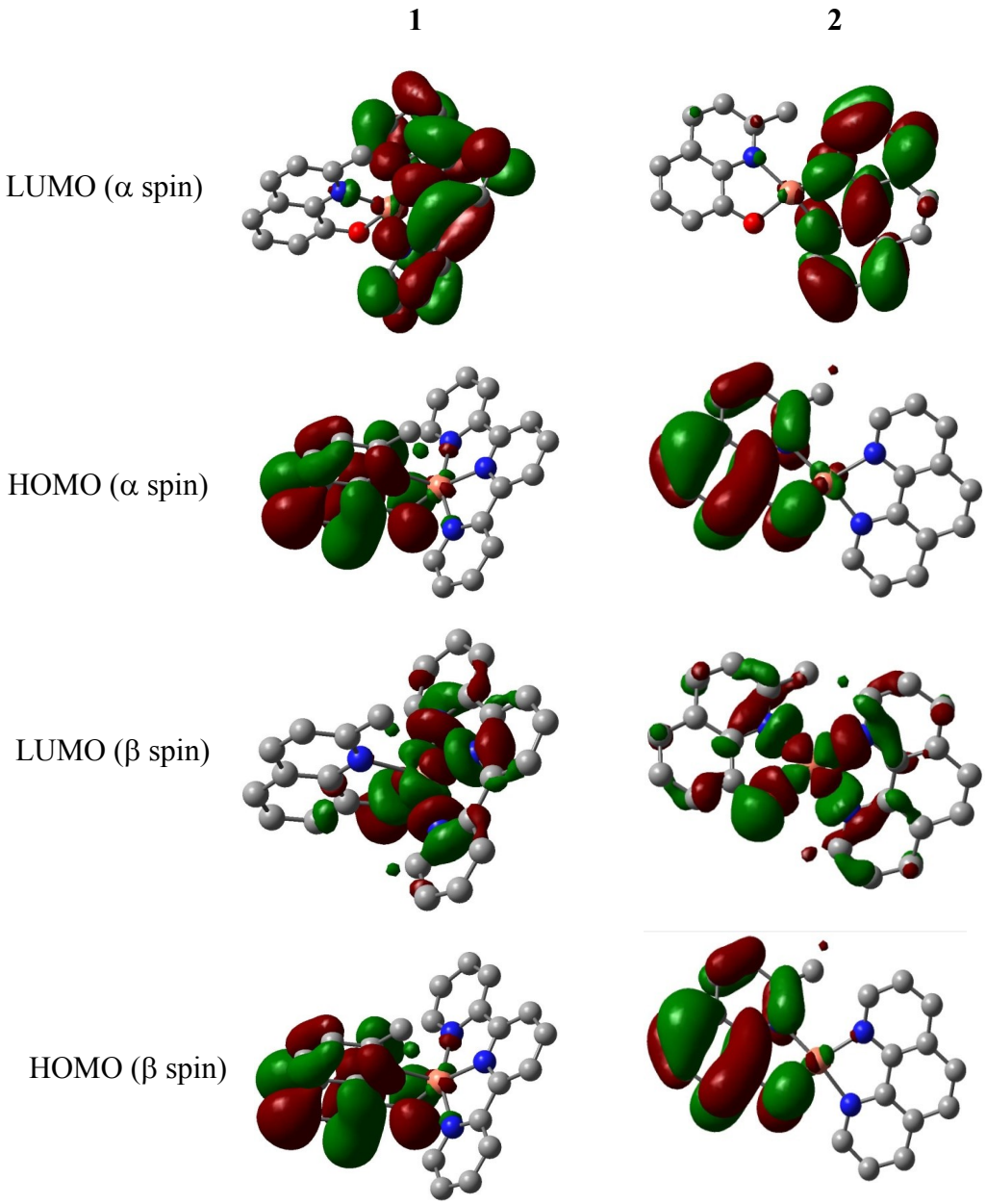

Fig. S1 Computed frontier molecular orbitals of complexes $[Cu(terpy)(mq)]^{1+}$ **1** and $[Cu(phen)(mq)]^{1+}$ **2** calculated at the B3LYP 6-31G/ LANL2DZ levels.

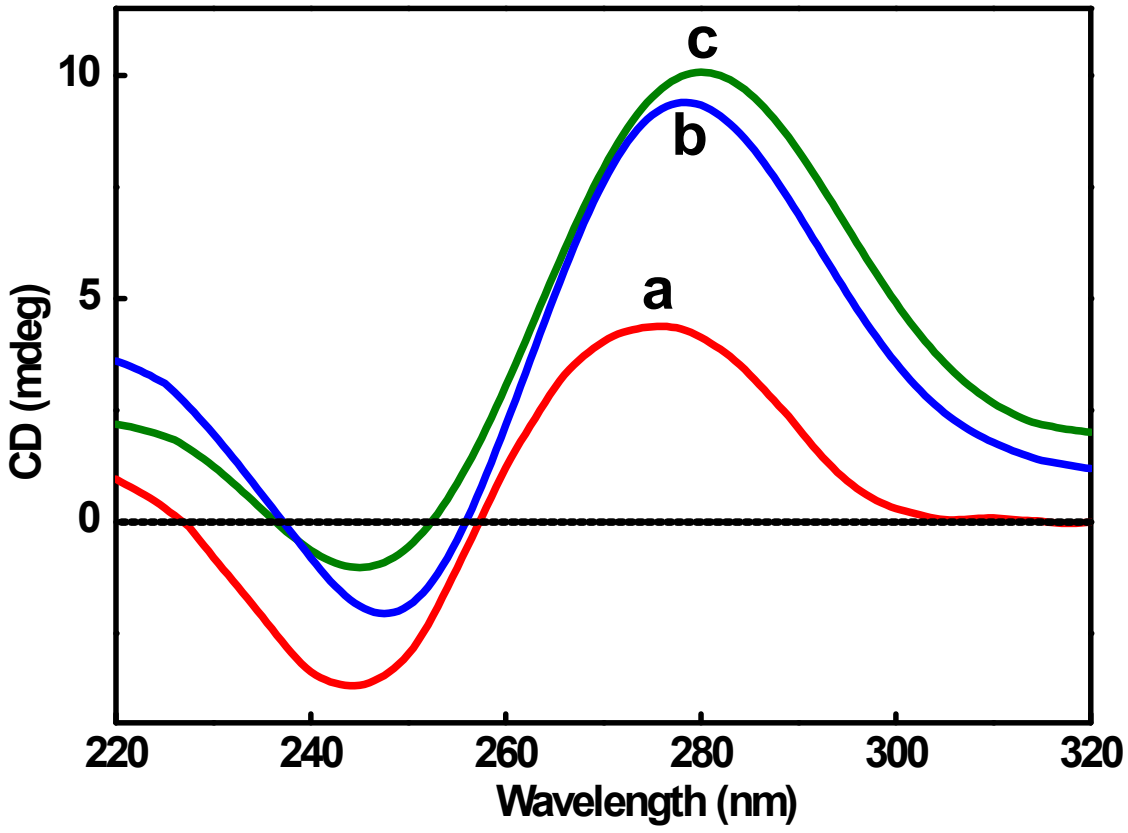

Fig. S2 Circular dichroism spectra of CT DNA in 2% DMF/5mM Tris-HCl/50 mM NaCl buffer at pH 7.1 and 25 °C in absence (a) and presence of **1** (b) and **2** (c) at 1/R value of 3.

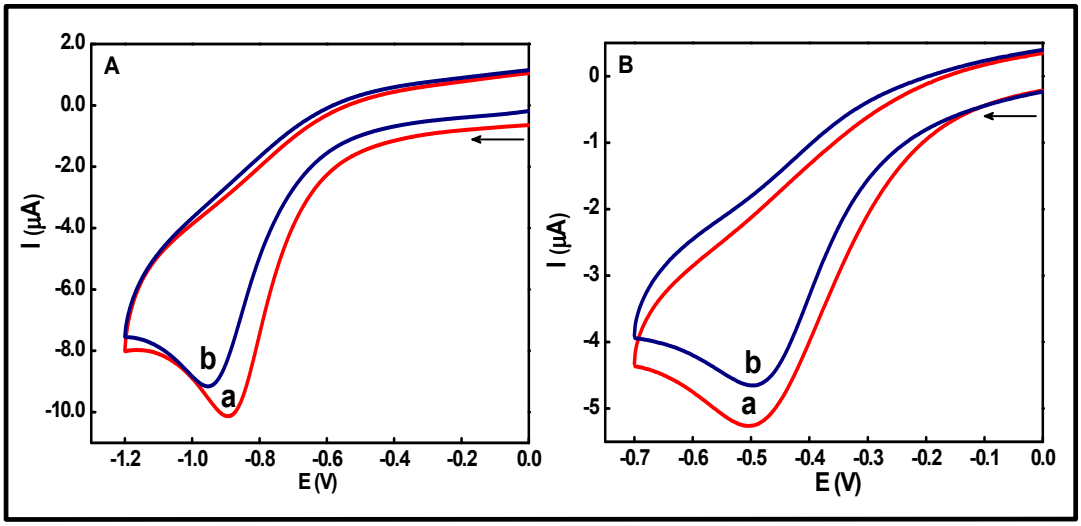

Fig. S3 Cyclic voltammograms of **1** (left, **A**) and **2** (right, **B**) (0.5 mM) in the absence (a) and presence (b) of CT DNA (R = 5) at 25.0 ± 0.2 °C at 50 mV s^{-1} scan rate in 2% DMF/5mM Tris-HCl/50 mM NaCl buffer at pH 7.1.

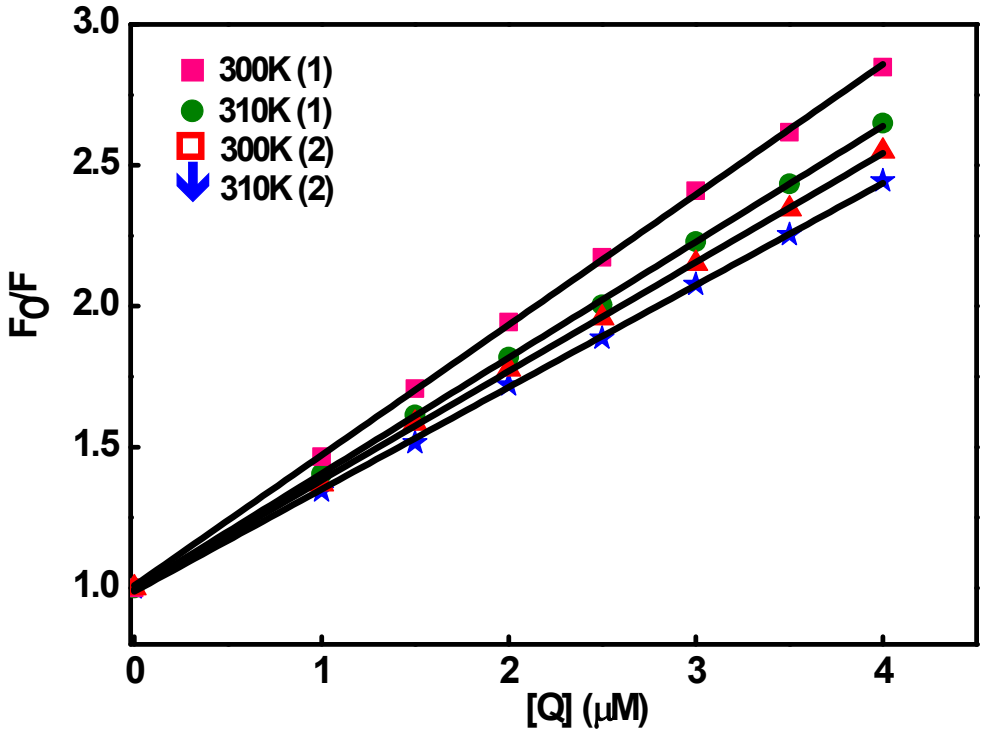

Fig. S4 The Stern-Volmer plots of BSA at different temperatures for addition of **1** and **2**. λ_{ex} = 280 nm; pH = 7.4.

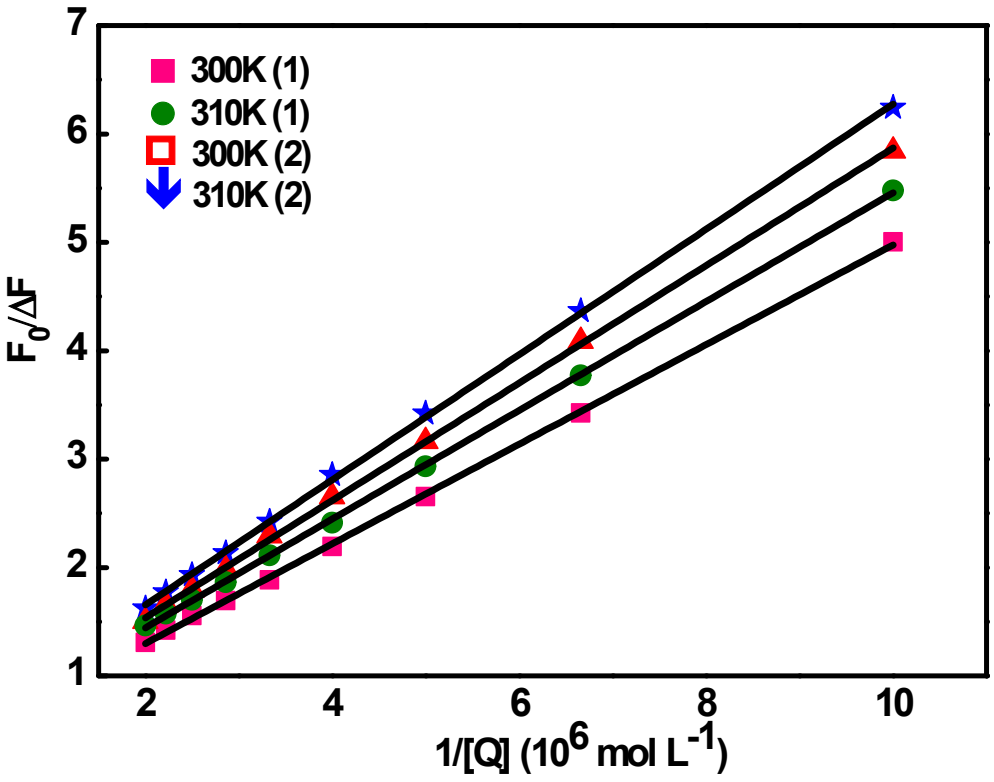

Fig. S5 The modified Stern-Volmer plots of BSA at different temperatures for addition of **1** and **2**. λ_{ex} = 280 nm; pH = 7.4.

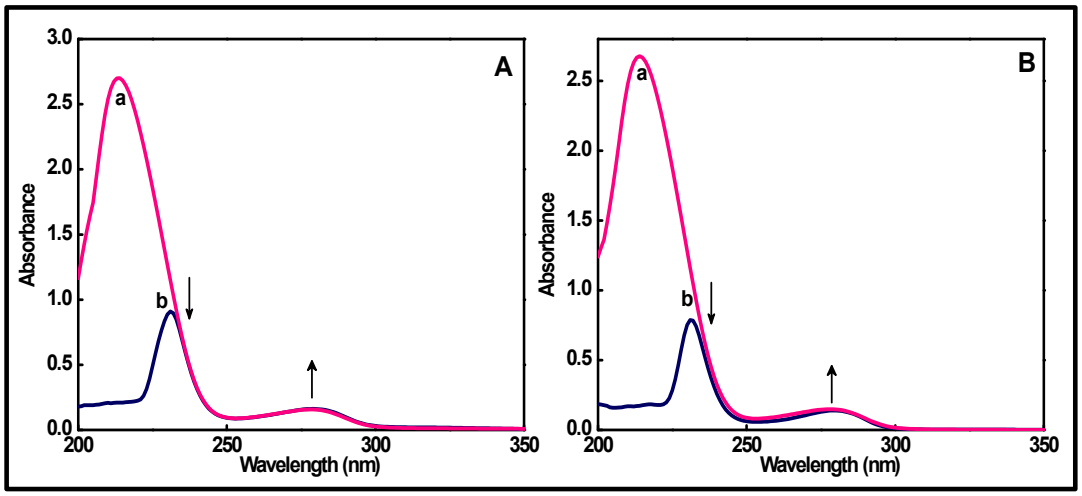

Fig. S6 UV-Vis absorption spectra of BSA in the absence and presence of **1** (left, **A**) and **2** (right, **B**). (a) Absorption spectrum of BSA. (b) Absorption spectrum of BSA in the presence of **1** and **2** at the same concentration, [BSA] = [Cu complex] = 3.5×10^{-6} mol L^{-1}.

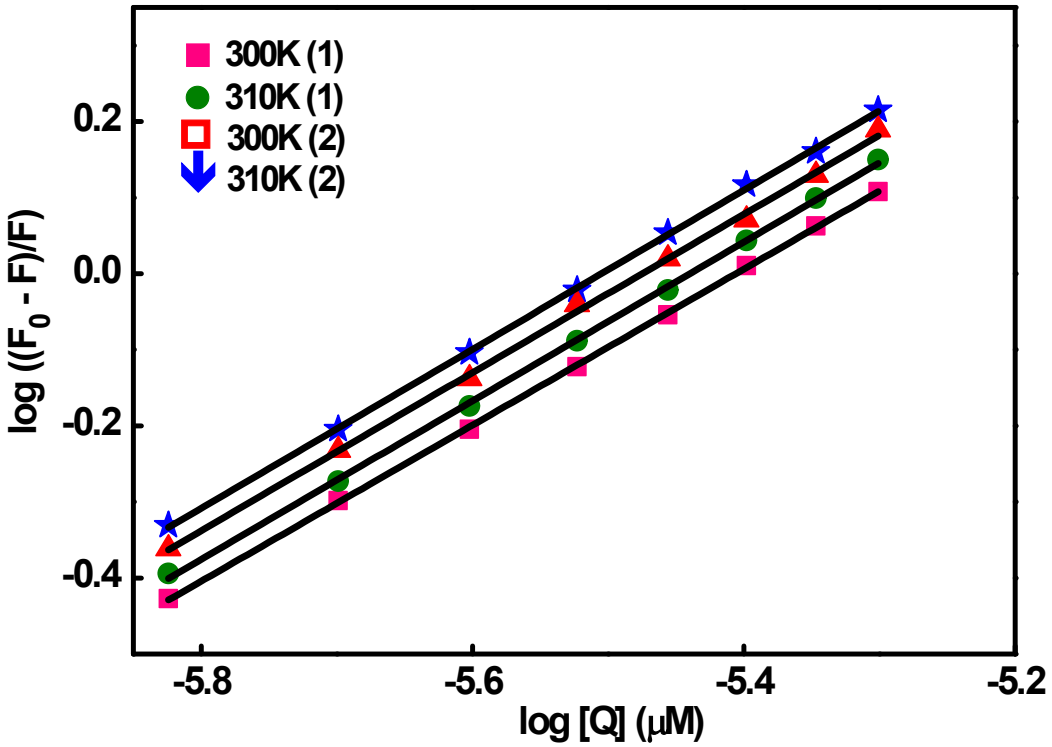

Fig. S7 Double-log plot of quenching effect of **1** and **2** on BSA fluorescence at pH = 7.4.

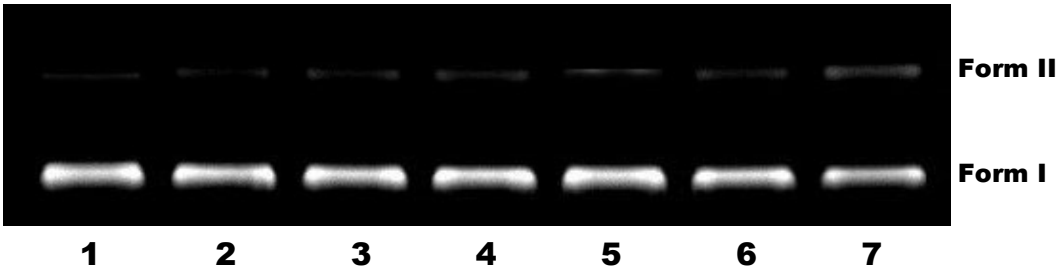

Fig. S8 Agarose gel showing cleavage of 20 μM SC ϕX174 RF DNA incubated with **1** in 0.1 M phosphate buffer (pH 7.2) at 37 °C for 1 h. Lane 1, DNA; Lanes 2-7, DNA + **1** (10,20,40,60,80,100 μM respectively). Form I and II are supercoiled and nicked circular forms of DNA respectively.

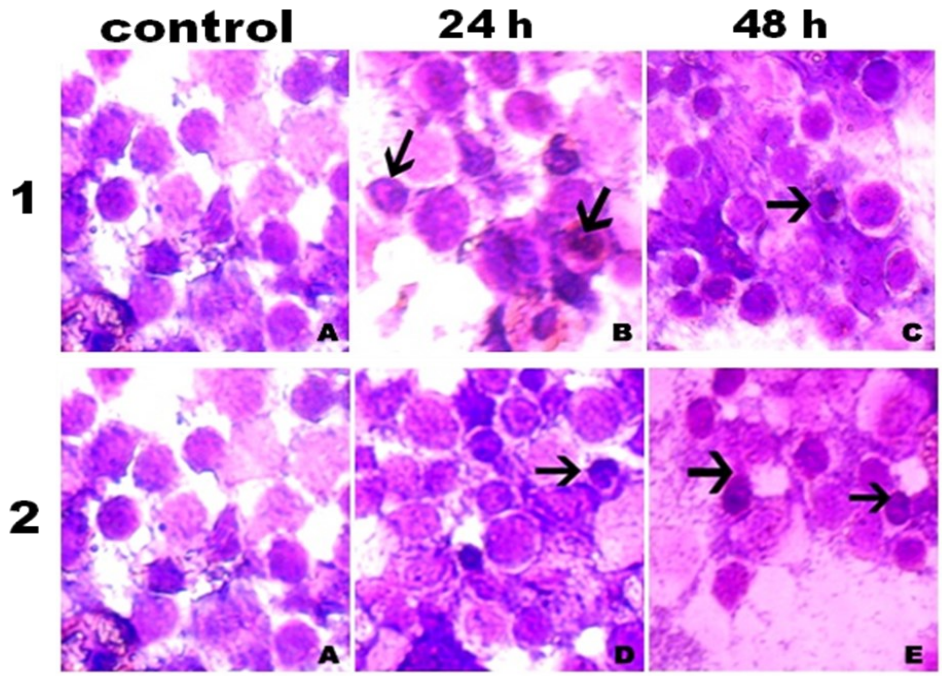

Fig. S9. Giemsa staining of MCF7 breast cancer cells untreated with **1** and **2** (**A**), treated with **1** and **2** at 24 (**B** and **D**) and 48 h (**C** and **E**) of incubation.

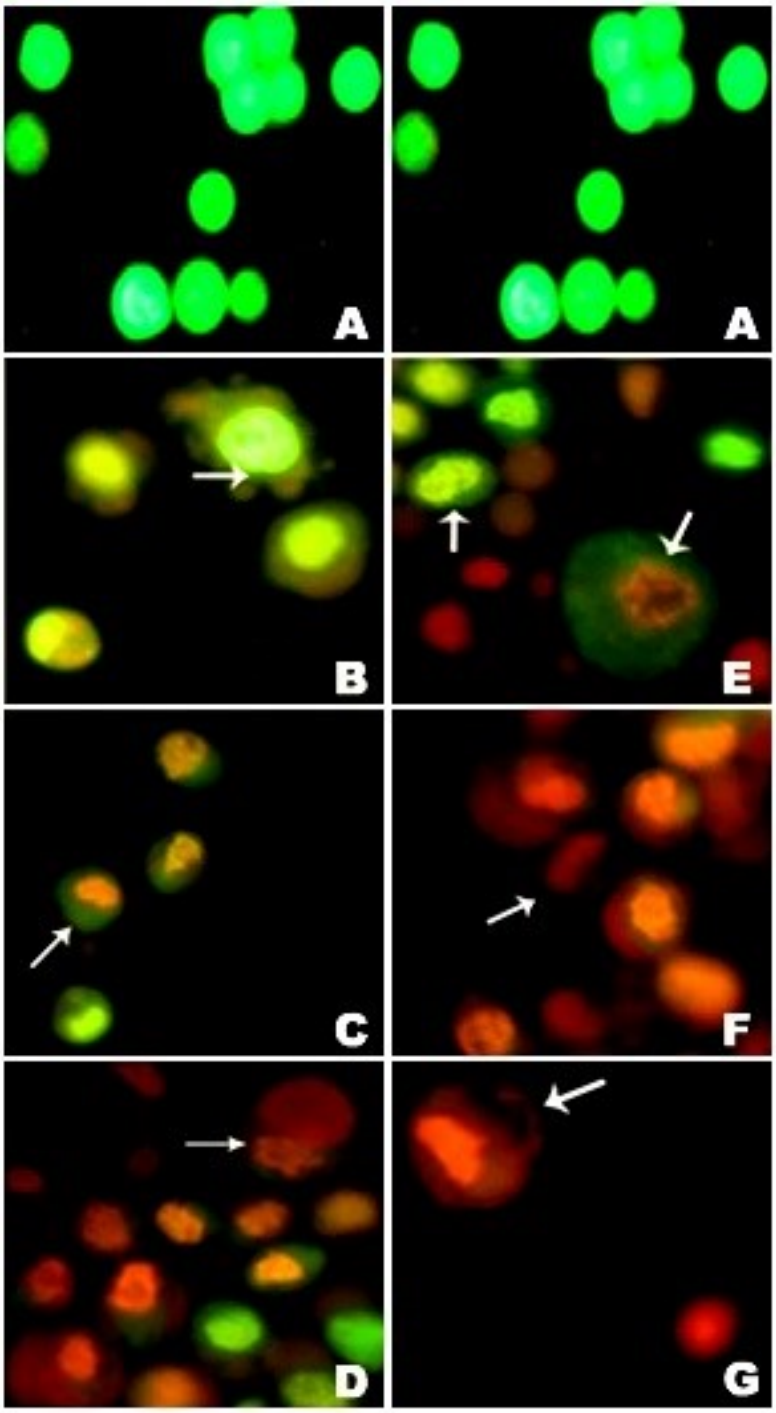

Fig. S10 AO/EB staining of MCF7 breast cancer cells untreated with **1** (**A**), treated with **1** at 24 (**B**, **C**, **D**) and 48 h (**E**, **F**, **G**) of incubation (arrow head indicate chromatin fragmentation, chromatin condensation and late apoptosis indication of apoptotic bodies)

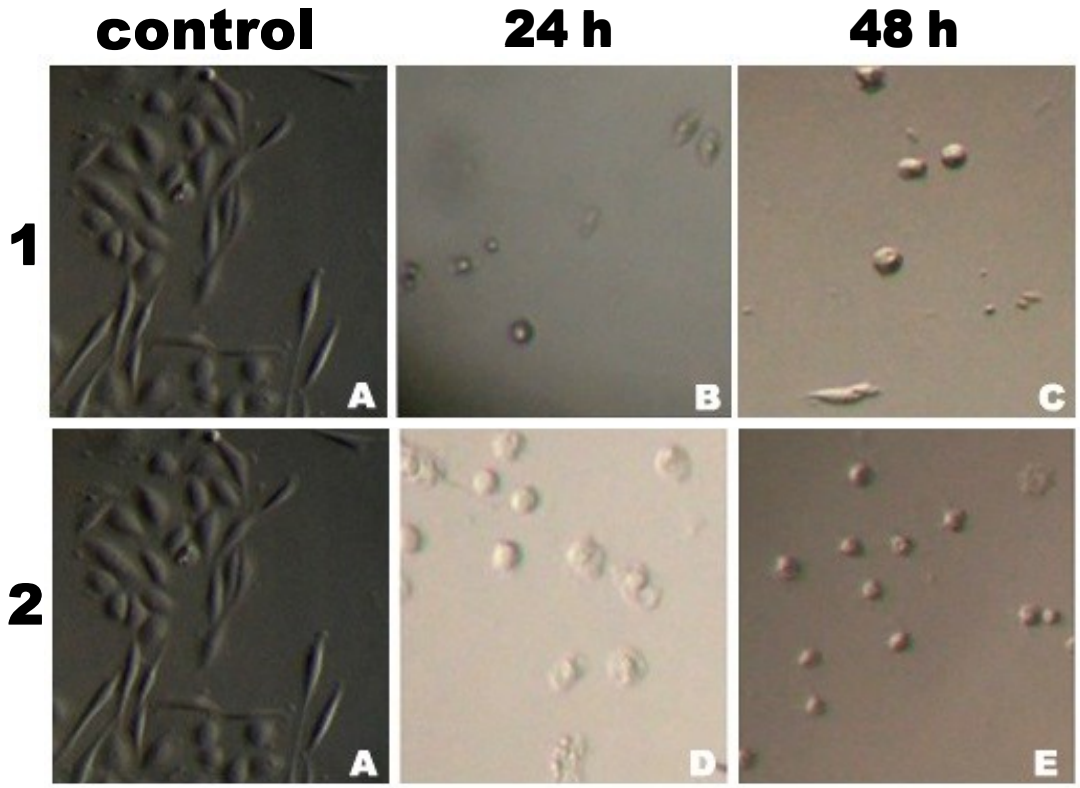

Fig. S11 Phase contrast of MCF7 breast cancer cells untreated with **1** and **2** (**A**), treated with **1** and **2** at 24 h of incubation (**B** and **D**) and 48 h of incubation (**C** and **E**).

Table S1. Selected crystal data and structure refinement parameters for **1**

Formula	$C_{25}H_{19}N_4ClO_5Cu$
Formula weight	554.53
Temperature (K)	293(2)
Wavelength (Å)	0.71069
Crystal system	Triclinic
Space group	*P*-1
a (Å)	7.3527(8)
b (Å)	12.8535(14)
c (Å)	13.2223(15)
α (°)	75
β (°)	79.635(2)
γ (°)	87
V (Å)^3, Z	1188.3(2), 2
D_{calc} (g cm^{-3})	1.550
μ (mm^{-1})	1.077
F(000)	566
Crystal size (mm)	0.18 x 0.10 x 0.09
θ (°)	1.62-29.01
Index ranges	-10≤h≤10, -17≤k≤17, -18≤l≤17
Reflections collected	17029
Independent reflections	6274
Reflections observed [I > 2σ(I)]	4623
R_{int}	0.0251
GOF	1.006
R_1 [I > 2σ(I)]	0.0341
wR_2 [I > 2σ(I)]	0.0890
R_1, wR_2 all data	0.0481/0.0939

Table S2. Electrochemical data[a] for the copper(II) complexes at 25.0 ± 0.2 °C

Complexes	R	E_{pc}(V)	E_{pa}(V)	$E_{1/2}$(V)		ΔE_p (mV)	i_{pa} / i_{pc}	D (10^{-6} cm^2 s^1)	K_+ / K_{2+}
				CV	DPV[b]				
1	0	-0.895	-0.674	-0.784	-0.805	221	0.52	6.59	
	5	-0.953	-0.623	-0.788	-0.799	330	0.54	6.02	1.30
2	0	-0.504	-0.312	-0.408	-0.413	192	0.62	7.62	
	5	-0.501	-0.295	-0.398	-0.390	206	0.57	7.45	2.30

[a]Measured vs. SCE electrode; scan rate: 50 mV s^{-1}, supporting electrolyte 2% DMF/5mM Tris-HCl/50mM NaCl; complex concentration: 2.5×10^{-4} M.
[b]Differential pulse voltammetry (DPV), scan rate: 2 mV s^{-1}, pulse height 50 mV.

Calculations of BSA binding parameters

Fluorescence quenching property can be described by the Stern-Volmer equation [1]:

$$F_0/F = 1 + K_{SV}[Q] = 1 + k_q\tau_0[Q]$$

where F_0 and F are the steady-state fluorescence intensities in the absence and the presence of quencher, respectively. K_{SV} is the Stern-Volmer quenching constant and [Q] is the concentration of quencher. The plot of F_0/F *versus* [Q] shows the value of K_{SV}. According to the above equation

$$K_{SV} = k_q/\tau_0$$

where K_q is the quenching rate constant and τ_0 is the fluorescence lifetime of protein in the absence of quencher, the value of τ_0 is considered to be 10^{-8} s [2].

The binding constant (K_b) and the numbers of binding sites (n) can be determined using the following equation [3]:

$$\log[F_0\text{-}F/F] = \log K_b + n\log[Q]$$

where K_b is the binding constant, reflecting the degree of interaction of the BSA and complex, and n is the number of binding sites. The plots of $\log[(F_0\text{-}F)/F]$ *versus* log[Q] gives a straight line. The values of n and K_b can be calculated from the slope and intercept of the linear plot respectively.

The thermodynamic parameters can be calculated from the following Van't Hoff equations [4, 5] to elucidate the binding forces between complex and BSA.

$$\ln(K_2/K_1) = (1/T_1 - 1/T_2)\,\Delta H°/R$$

$$\Delta G° = \Delta H° - T\Delta S° = -RT\ln K$$

where K_1 and K_2 are equilibrium binding constants at temperature T_1 and T_2, respectively, and R is the gas constant.

References

1. Lakowicz JR (2006) Principles of fluorescence spectroscopy, 3rd ed. (New York: Springer Science+Business Media).
2. Lakowicz JR, Webber G (1973) Biochemistry 12:4161-4170.
3. Divsalar A, Bagheri MJ, Saboury AA, Mansoori-Torshizi H, Amani M (2009) J. Phys. Chem. B 113:14035-14042.
4. Wang T, Zhao Z, Wei B, Zhang L, Ji L (2010) J. Mol. Struct. 970:128-133.
5. Bi S, Sun Y, Qiao C, Zhang H, Liu C (2009) J. Lumin. 129:541-547.