Electronic Supporting Information (ESI)

New Journal of Chemistry

Synthesis of two potential anticancer copper(II) complexes drugs: crystal structure, human serum albumin/DNA binding and anticancer mechanism

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Supplementary material

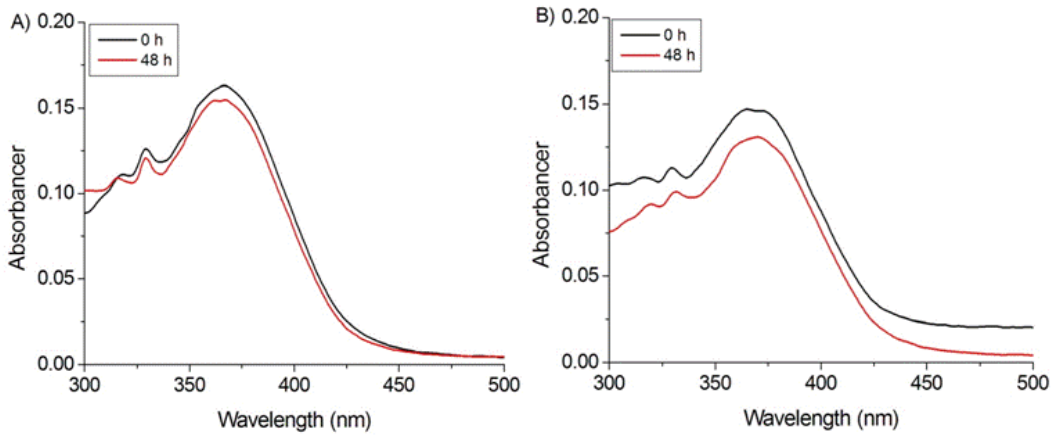


Fig.S1: UV-Vis absorption spectra of **1** (A) and **2** (B) (1.0×10^{-6} M) in TBS (0.1% DMSO) with time course 0 and 48 h, respectively.

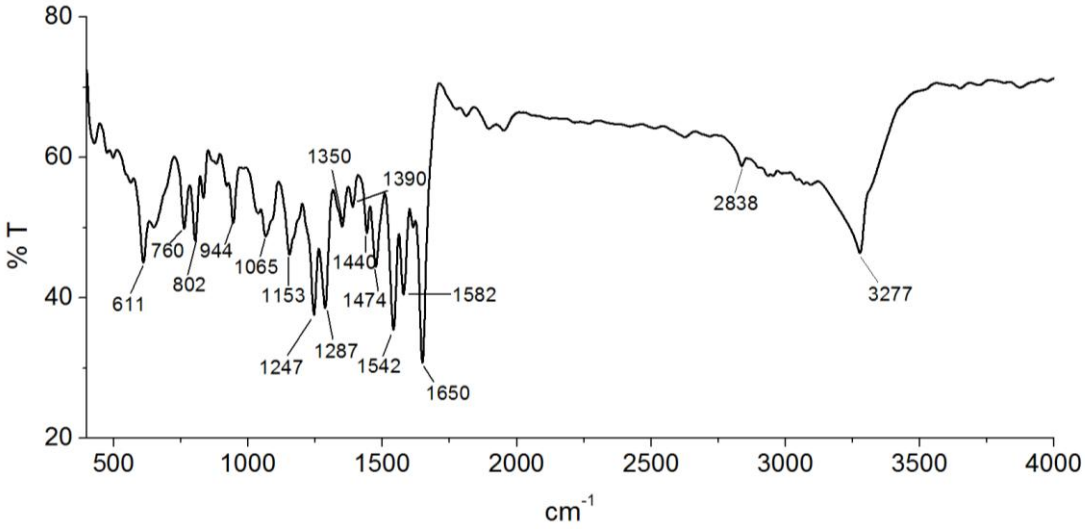


Fig. S2: FT-IR (KBr) spectra of L1.

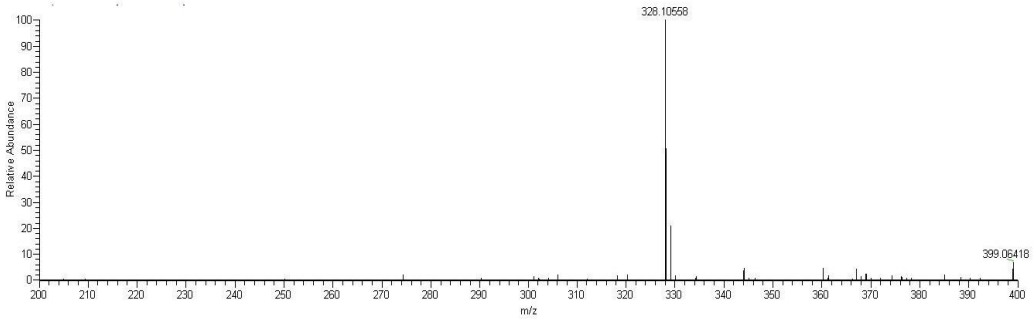


Fig. S3: HRMS(ESI) spectra of L1. Calcd. for $C_{18}H_{15}N_3O_2$ $[M+Na]^+$ 328.10620, found 328.10558.

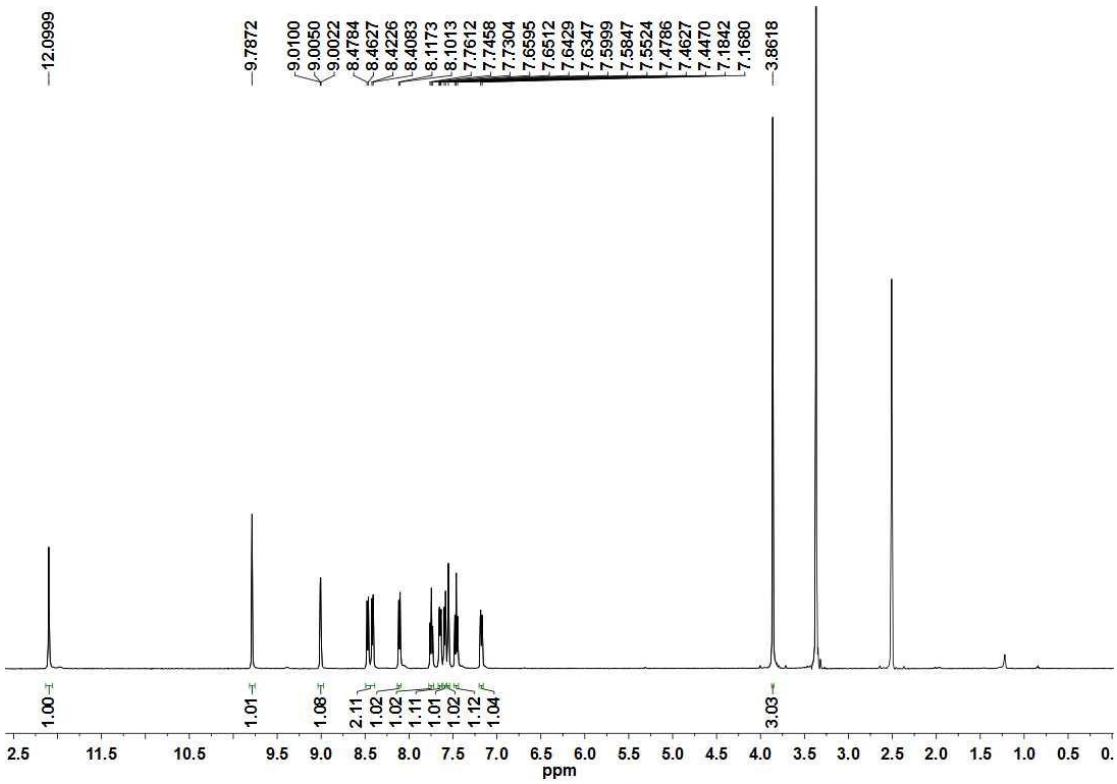


Fig. S4: ^{1}H NMR spectra of L1 in DMSO.

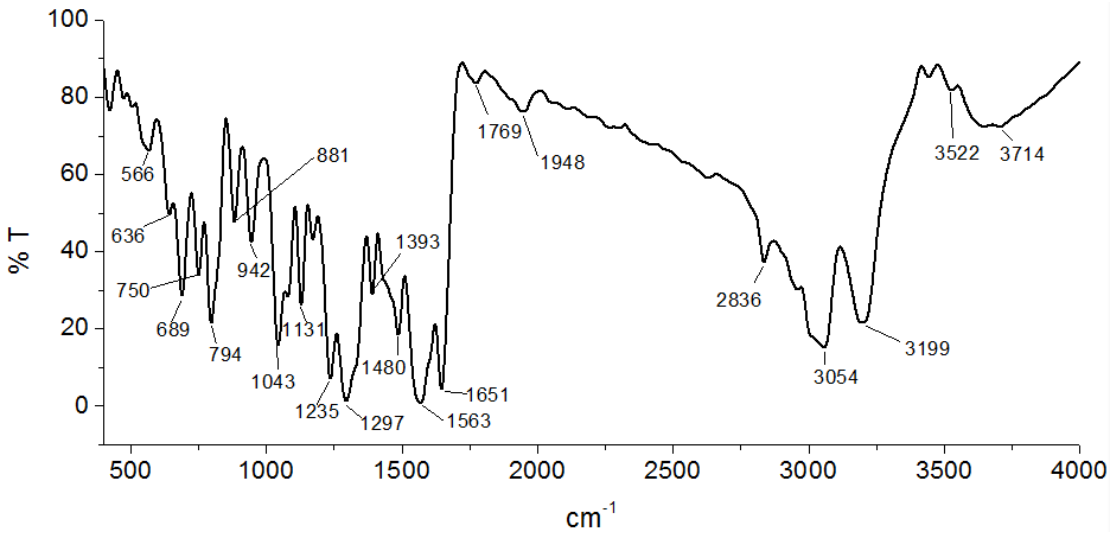


Fig. S5: FT-IR (KBr) spectra of L2.

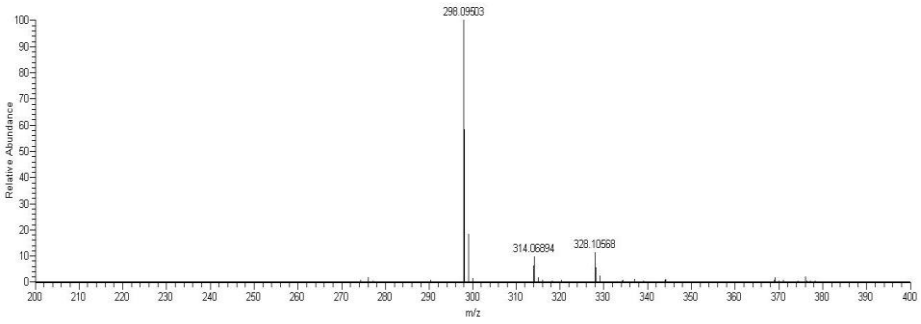


Fig. S6: HRMS(ESI) spectra of L2. Calcd. for $C_{17}H_{13}N_3O$ $[M+H]^+$ 298.09563, found 298.09603.

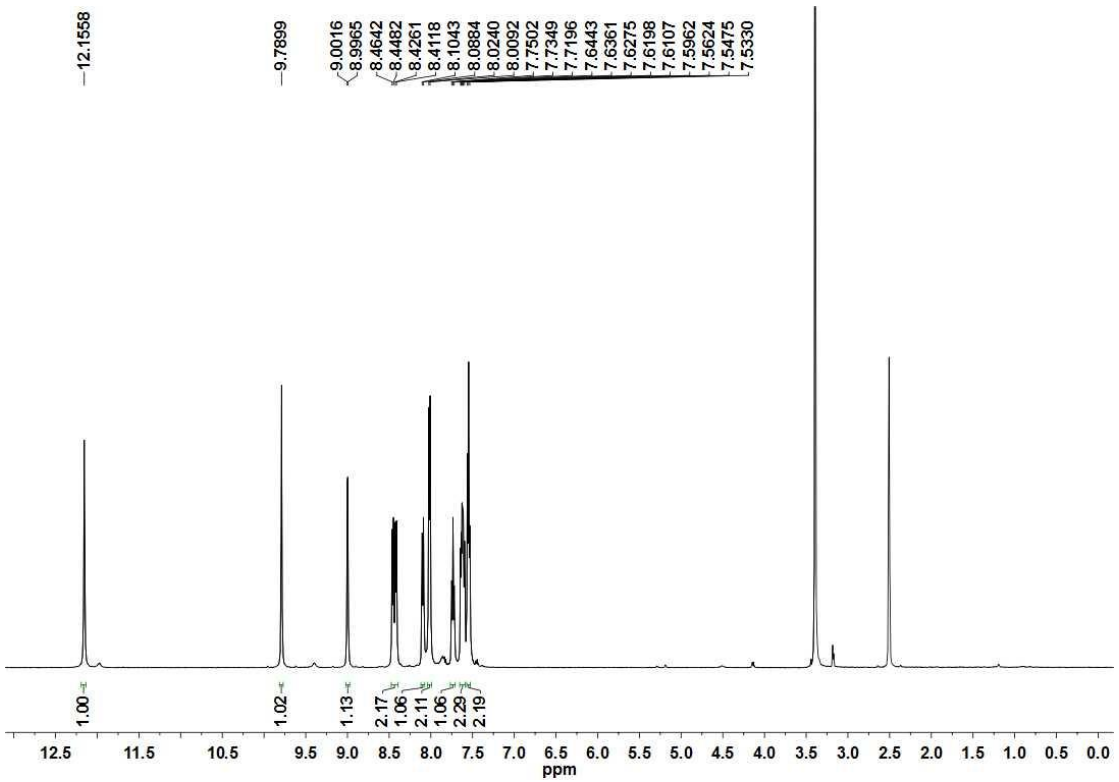


Fig. S7: ^{1}H NMR spectra of L2 in DMSO.

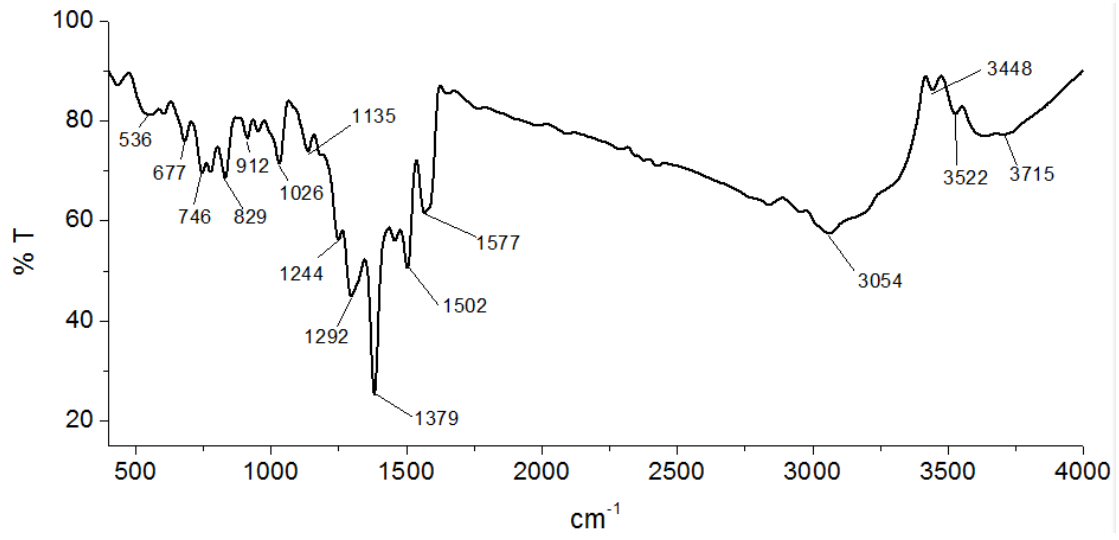


Fig. S8: FT-IR (KBr) spectra of complex **1**.

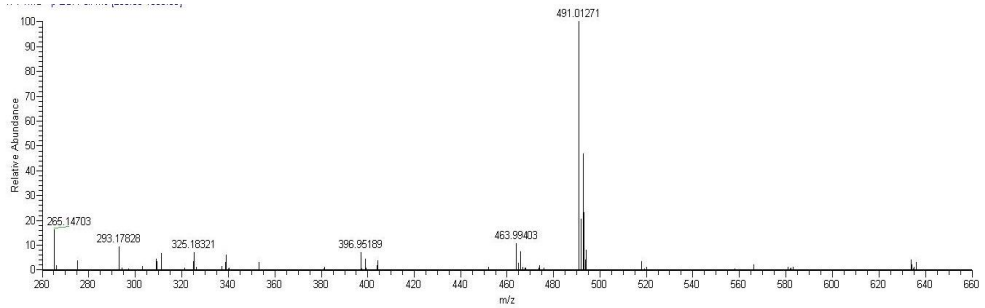


Fig. S9: HRMS (ESI) spectra of complex **1**. HRMS (ESI): Calcd. for $C_{18}H_{14}N_5O_8Cu$ $[M\text{-}H^+]^-$ 491.01384, found 491.01271.

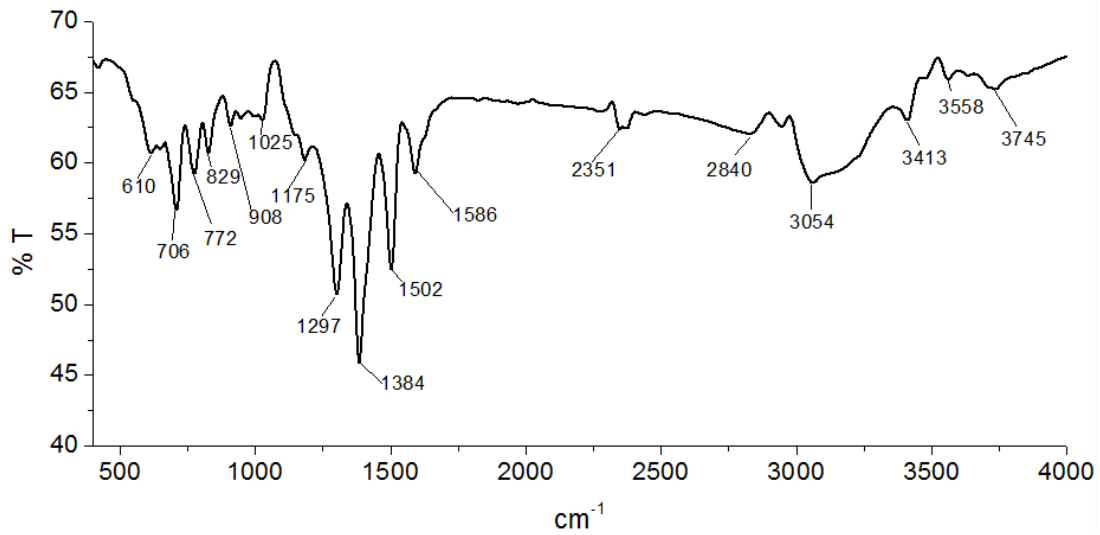


Fig. S10: FT-IR (KBr) spectra of complex **2.**

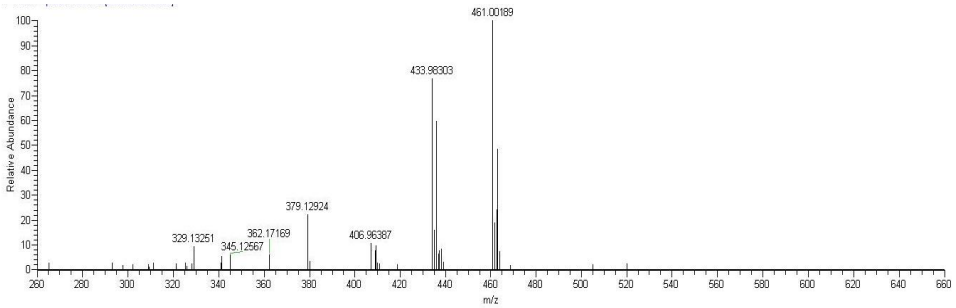


Fig. S11: HR-ESI-MS spectra of complex **2.** HRMS (ESI): Calcd. for $C_{18}H_{16}N_4O_5Cu$ $[M\text{-}CH_3O^-\text{+}NO_3^-\text{-}H^+]^-$ 461.00327, found 461.00189.

Table S1: DNA binding constant (K_b), Stern-Volmer constant (K_q) and the apparent binding constant (K_{app}) for ligands and complexes.

Compound	K_b (M^{-1})	K_q (M^{-1})	K_{app} (M^{-1})
L1	$4.63 \times 10^3 \pm 0.25$	$3.67 \times 10^4 \pm 0.12$	$4.10 \times 10^5 \pm 0.11$
L2	$6.79 \times 10^3 \pm 0.15$	$4.12 \times 10^4 \pm 0.22$	$4.48 \times 10^5 \pm 0.21$
1	$1.39 \times 10^4 \pm 0.32$	$5.91 \times 10^4 \pm 0.13$	$1.48 \times 10^6 \pm 0.02$
2	$1.67 \times 10^4 \pm 0.21$	$9.62 \times 10^4 \pm 0.32$	$1.97 \times 10^6 \pm 0.09$

Table S2: Stern-Volmer quenching constants and binding parameters of the HSA-complexes drug system at different temperatures.

	T (K)	Stern-Volmer quenching constants			Binding parameters		
		K_q ($M^{-1}s^{-1}$)	K_{sv} (M^{-1})	R	K_{bin} (M^{-1})	n	R
1	295	$3.70 \times 10^{13} \pm 0.03$	$1.85 \times 10^5 \pm 0.12$	0.9997	$3.06 \times 10^4 \pm 0.18$	0.85	0.9989
	305	$2.88 \times 10^{13} \pm 0.03$	$1.44 \times 10^5 \pm 0.09$	0.9876	$2.02 \times 10^4 \pm 0.10$		0.9987
	315	$2.36 \times 10^{13} \pm 0.02$	$1.18 \times 10^5 \pm 0.06$	0.9909	$1.47 \times 10^4 \pm 0.15$		0.9972
2	295	$4.48 \times 10^{13} \pm 0.03$	$2.24 \times 10^5 \pm 0.12$	0.9992	$1.63 \times 10^5 \pm 0.12$	0.97	0.9989
	305	$3.40 \times 10^{13} \pm 0.03$	$1.70 \times 10^5 \pm 0.13$	0.9992	$1.13 \times 10^5 \pm 0.10$		0.9985
	315	$2.74 \times 10^{13} \pm 0.02$	$1.37 \times 10^5 \pm 0.11$	0.9983	$0.89 \times 10^5 \pm 0.08$		0.9967

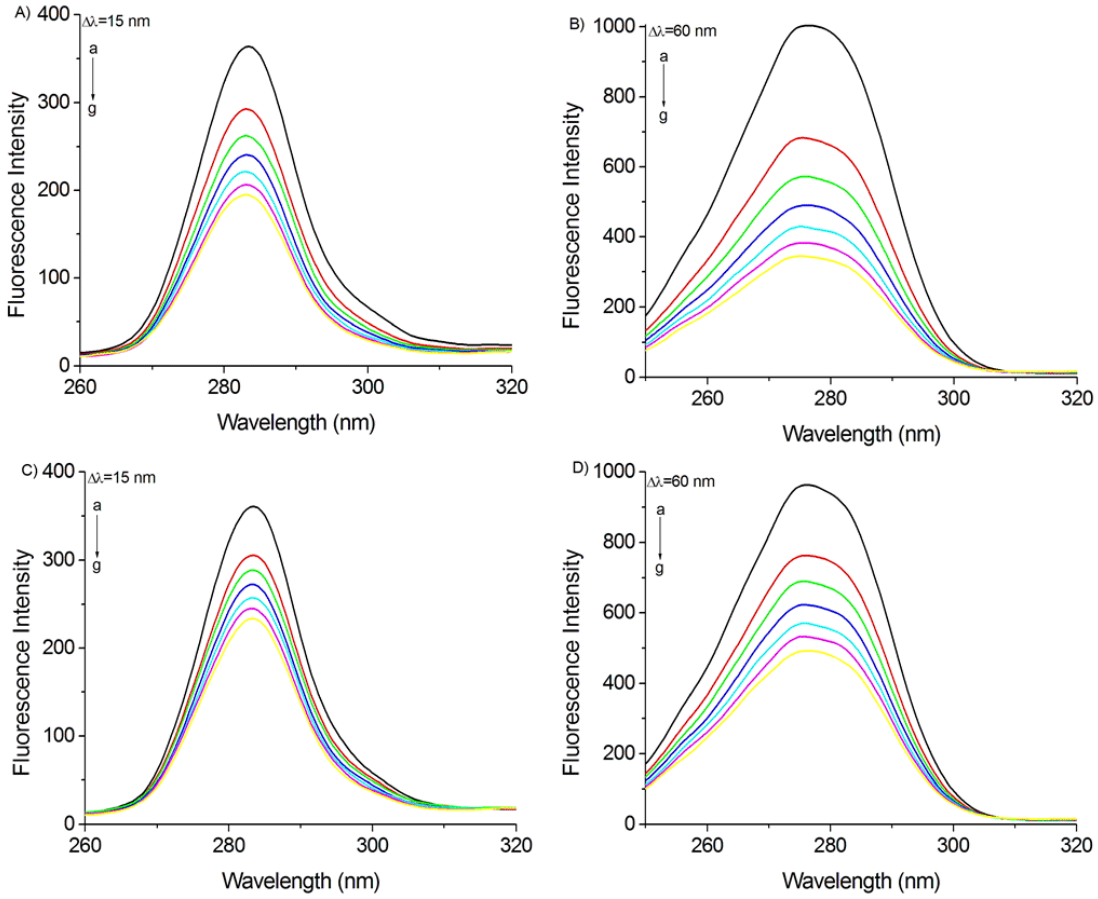


Fig. S12: Synchronous fluorescence spectra of HSA (1.0 µM, black line) in presence of increasing amounts of L**1 (**A, B**)** and **L2** (C, D) (0-6.0 µM; a to g) at the wavelength difference of Δλ= 15 and Δλ= 60 nm.

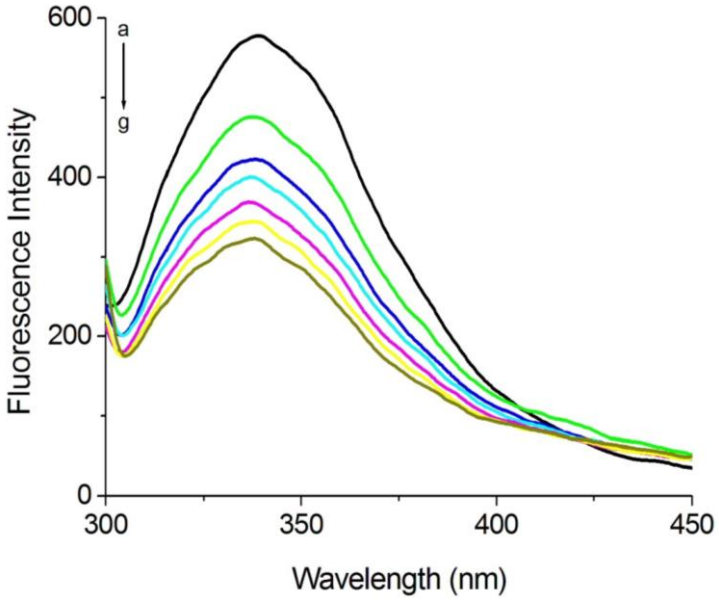


Fig. S13: The emission spectrum of HSA (1μM; λex=280 nm) in the absence and presence of the **2** with increasing concentrations (0, 1.0, 2.0, 3.0, 4.0, 5.0 and 6.0 μM) from a to g at pH=4.7.

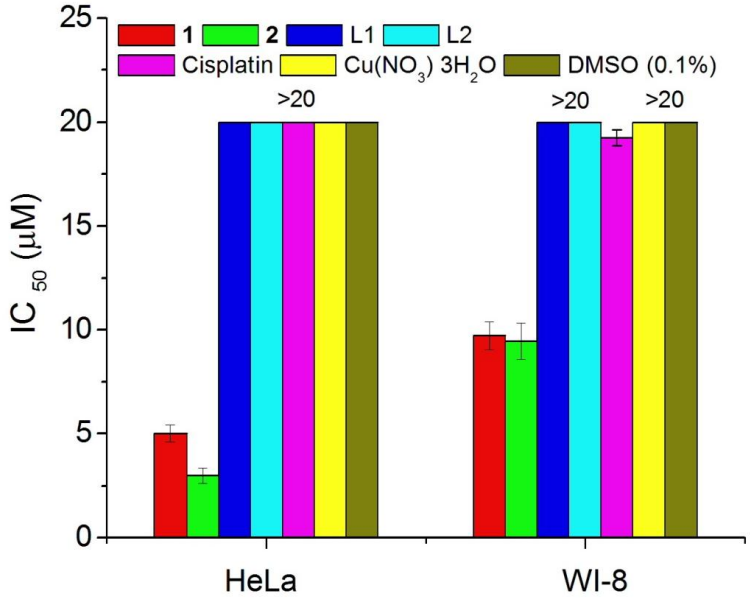


Fig. S14: The IC_{50} curves of L1, L2, **1**, **2** and cisplatin on the selected cells for 48 h.

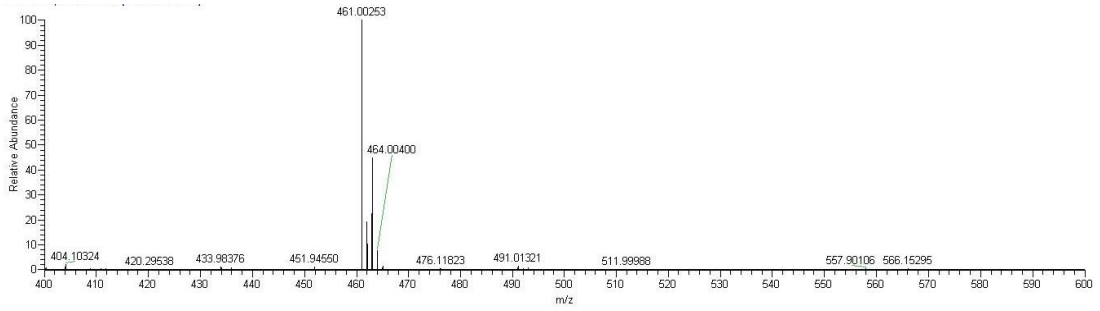
Table S3: IC_{50} (μM) values of L1, L2, 1, 2 and cisplatin on the selected cells for 48 h.

Compounds	HeLa	WI-8
1	5.01 ± 0.41	9.71 ± 0.67
2	2.98 ± 0.34	9.45 ± 0.87
L1	>20	>20
L2	>20	>20
Cisplatin	35.25 ± 1.88	19.25 ± 0.37
$Cu(NO_3)\cdot 3H_2O$	>20	>20
DMSO (0.1%)	>20	>20

Table S4: Log *P* values for the complexes **1, 2** in present system, $[Cu(L1)NO_3]$ and $[Cu(L2)NO_3]$(H-L1=8-quinolinecarbaldehyde o-vanilloylhydrazone, and H-L2=8-quinolinecarbaldehyde salicylhydrazone) in our previous work.

Compounds	Log *P*	
1	1.55 ± 0.12	In this work
2	1.62 ± 0.23	
$[Cu(L1)NO_3]$	1.52 ± 0.28	In our previous work
$[Cu(L2)NO_3]$	1.35 ± 0.25	

A)



B)

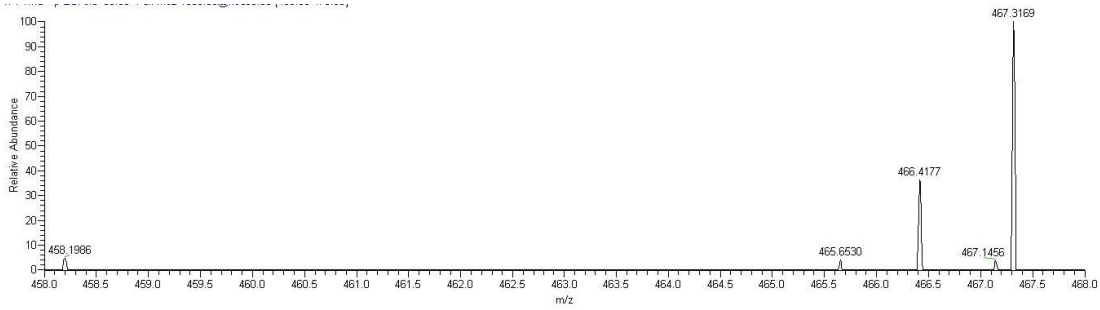


Fig. S15: Mass spectrometry detection of the interaction between complex **2** and mitochondria. A) Complex **2** was dissolved in DMSO and analyzed by electrospray ionization mass spectrometry at IC_{50} concentration $[M\text{-}CH_3O^-+NO_3^-\text{-}H^+]^-$ 461.00253. B) Complex **2** directly interacted with mitochondria. Mitochondria were extracted from HeLa cells with Mitochondrial Extraction Kit and incubated with complex **2** for 1 h. The mixture was eluted 3 times and then diluted with buffer solution to make 1.0 ml.

Table S5: The concentration of copper ion in HeLa cell (Control), and solution of complex 2 (at IC_{50} value concentration) and mitochondrial extracts of HeLa cell after incubating for 1 h (Mitochondrial).

Sample	Cu(II) (μg/L)
Control	2.53 ± 0.22
Mitochondrial	2.71 ± 0.18