Electronic Supplementary Information (ESI)

Water-soluble copper(II) 5-fluorouracil complexes bearing polypyridyl co-ligands: Synthesis, structures and anticancer activity

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Table S1 Crystallographic data and structure refinement for **1**–**5**

	1	**2**	**3**	**4**	**5**
empirical formula	$C_{16}H_{16}ClCuFN_4O_3S$	$C_{32}H_{28}CuF_2N_8O_8$	$C_{24}H_{25}CuFN_9O_{7.5}$	$C_{16}H_{17}CuFN_6O_6$	$C_{19}H_{13}ClCuFN_5O_2$
formula weight	462.38	700.13	642.07	471.89	461.33
crystal system	monoclinic	monoclinic	monoclinic	triclinic	monoclinic
space group	$P2_1/n$	$I2/a$	$P2/c$	$P\bar{1}$	$P2_1/n$
a, Å	8.1412(4)	13.1277(13)	15.6860(11)	7.8385(7)	11.6071(9)
b, Å	21.3384(13)	19.623(3	9.7121(9)	8.4548(9)	13.0317(14)
c, Å	11.1897(6)	24.848(3)	18.3253(18)	15.5138(10)	12.3107(11)
α, deg	90	90	90	84.255(7)	90
β, deg	93.746(4)	95.728(10)	104.091(9)	77.099(7)	91.472(8)
γ, deg	90	90	90	70.084(9)	90
V, Å^3	1939.72(18)	6369.0(14)	2707.7(4)	941.93(16)	1861.5(3)
T, K	292(2)	293(2)	292(2)	292(2)	295(2)
Z	4	8	2	2	4
ρ_{calc} (g cm^{-3})	1.450	1.460	1.575	1.664	1.646
μ (mm^{-1})	1.583	0.752	0.878	1.218	1.354
F(000)	940	2856	1320	482	932
θ (°)	3.151-25.027	3.296-25.027	3.107-25.039	3.129-25.681	3.126-26.370
collected refls	6500	9494	8982	6029	7139
R_{int}	0.0471	0.0670	0.0614	0.0343	0.0330
data/parameters	3397/250	5577/436	4614/403	3421/293	3800/262
goodness-of-fit	1.006	1.024	0.709	0.865	1.077
R_1 [$I>2\sigma(I)$]	0.0526	0.1103	0.0466	0.0436	0.0462
R_1 (all data)	0.1130	0.1655	0.1481	0.0745	0.0679
wR_2 [$I>2\sigma(I)$]	0.0789	0.2640	0.0566	0.0808	0.1032
wR_2 (all data)	0.0968	0.2998	0.0659	0.0851	0.1142

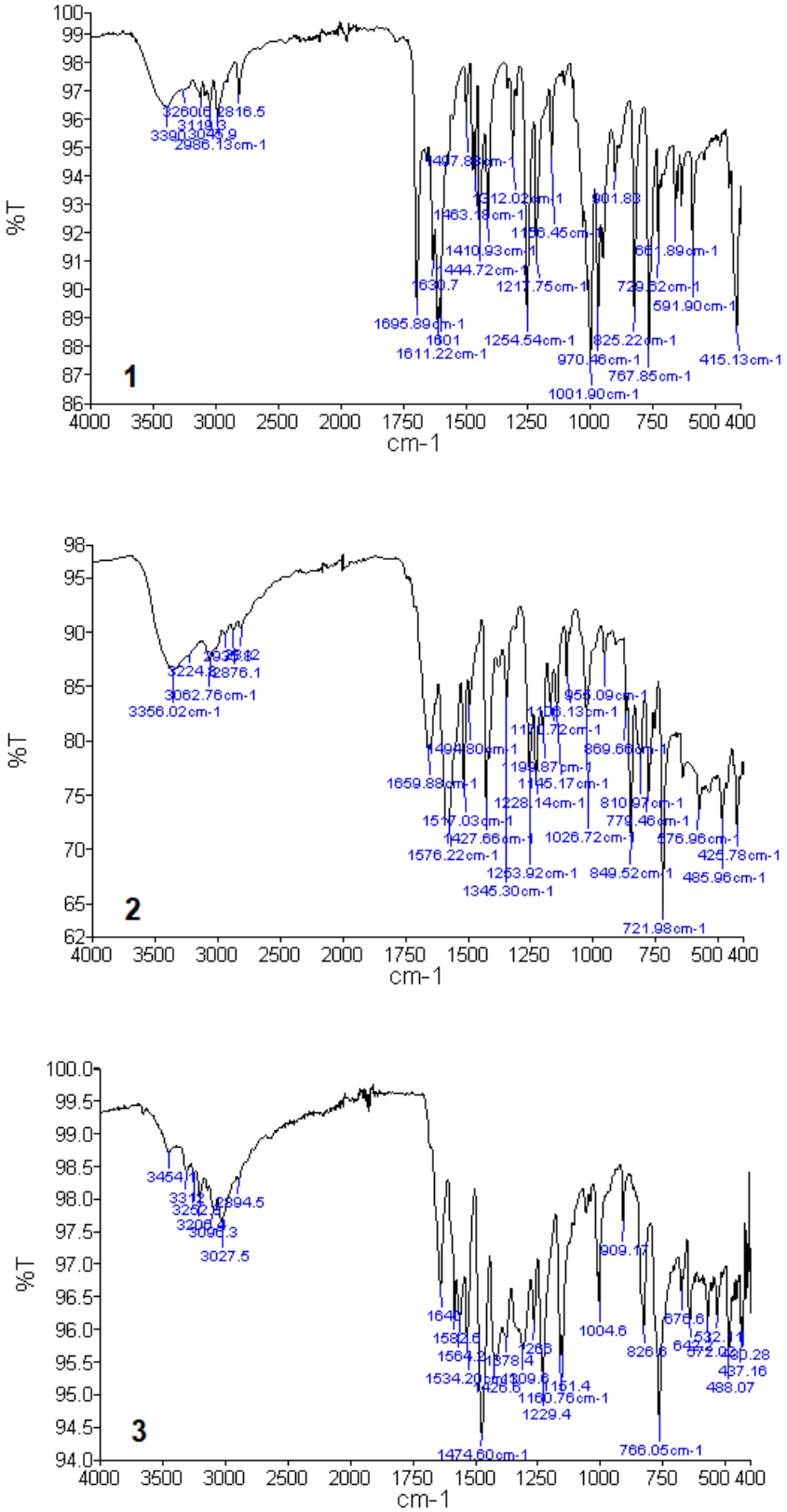

Fig. S1 (continued)

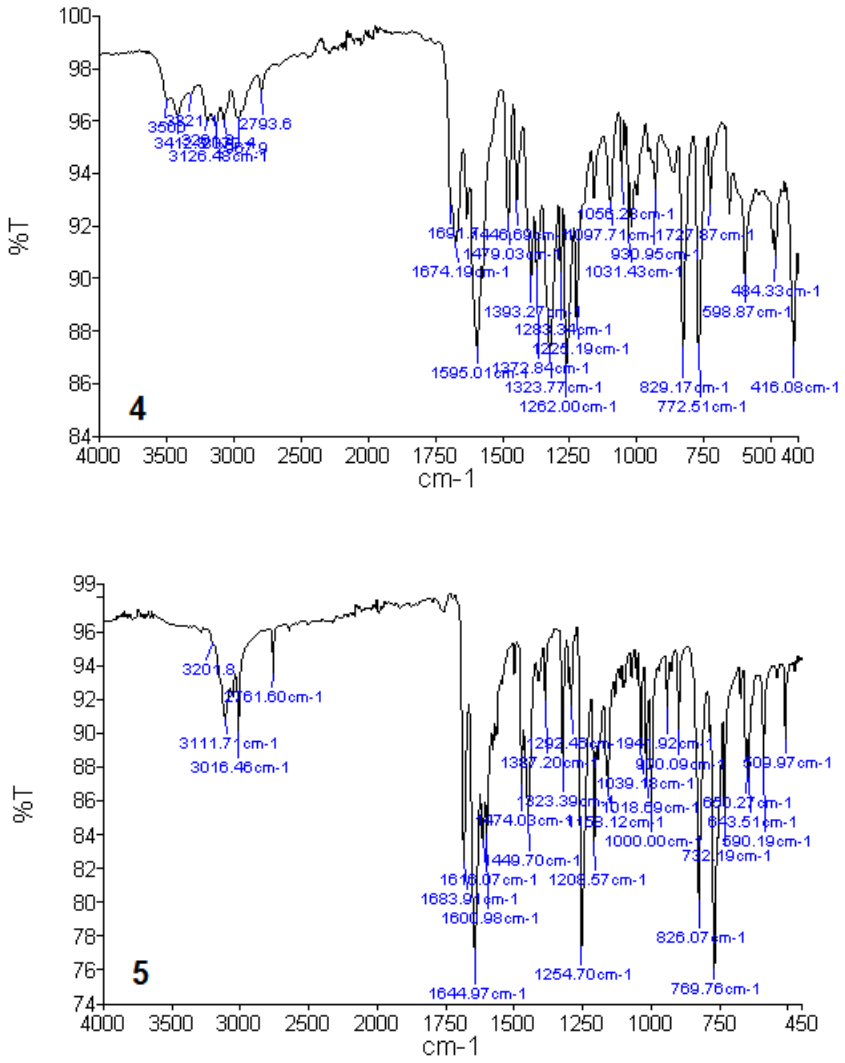

Fig. S1 FTIR spectra of **1**–**5**.

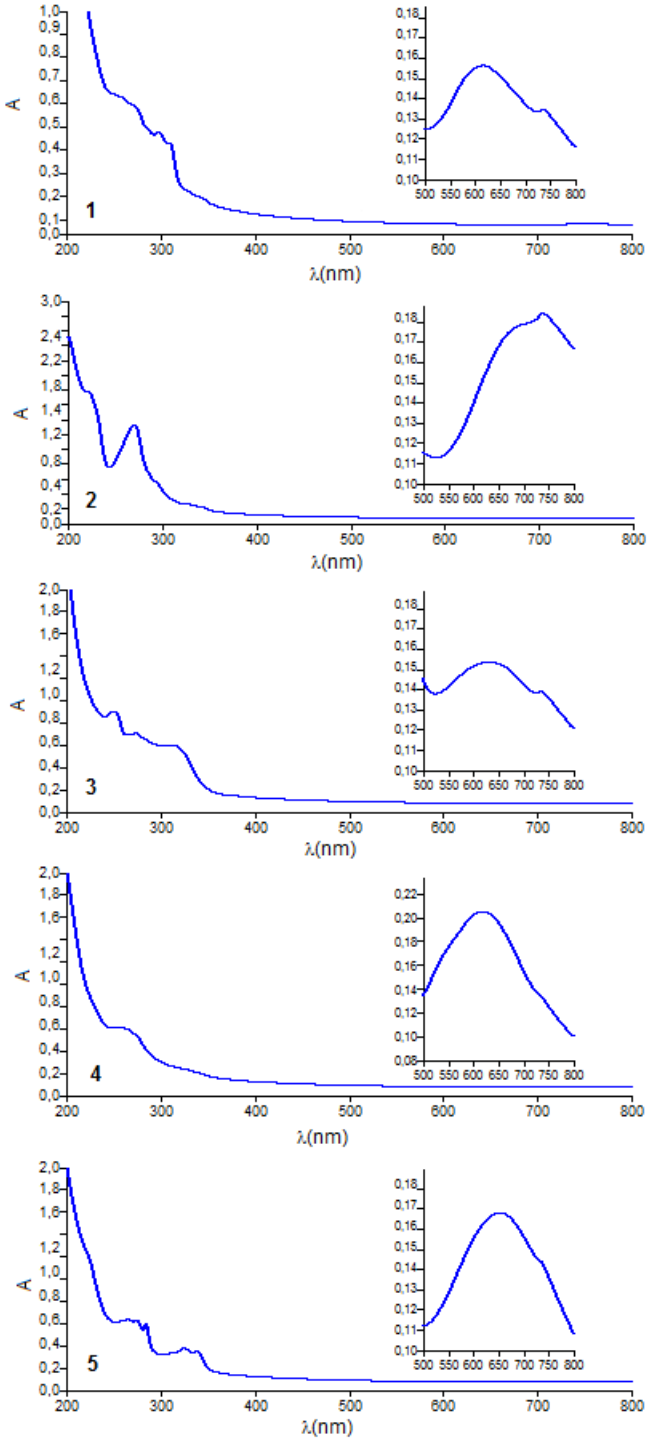

Fig. S2 UV-Vis spectra of **1**–**5** (10 μM) in water.

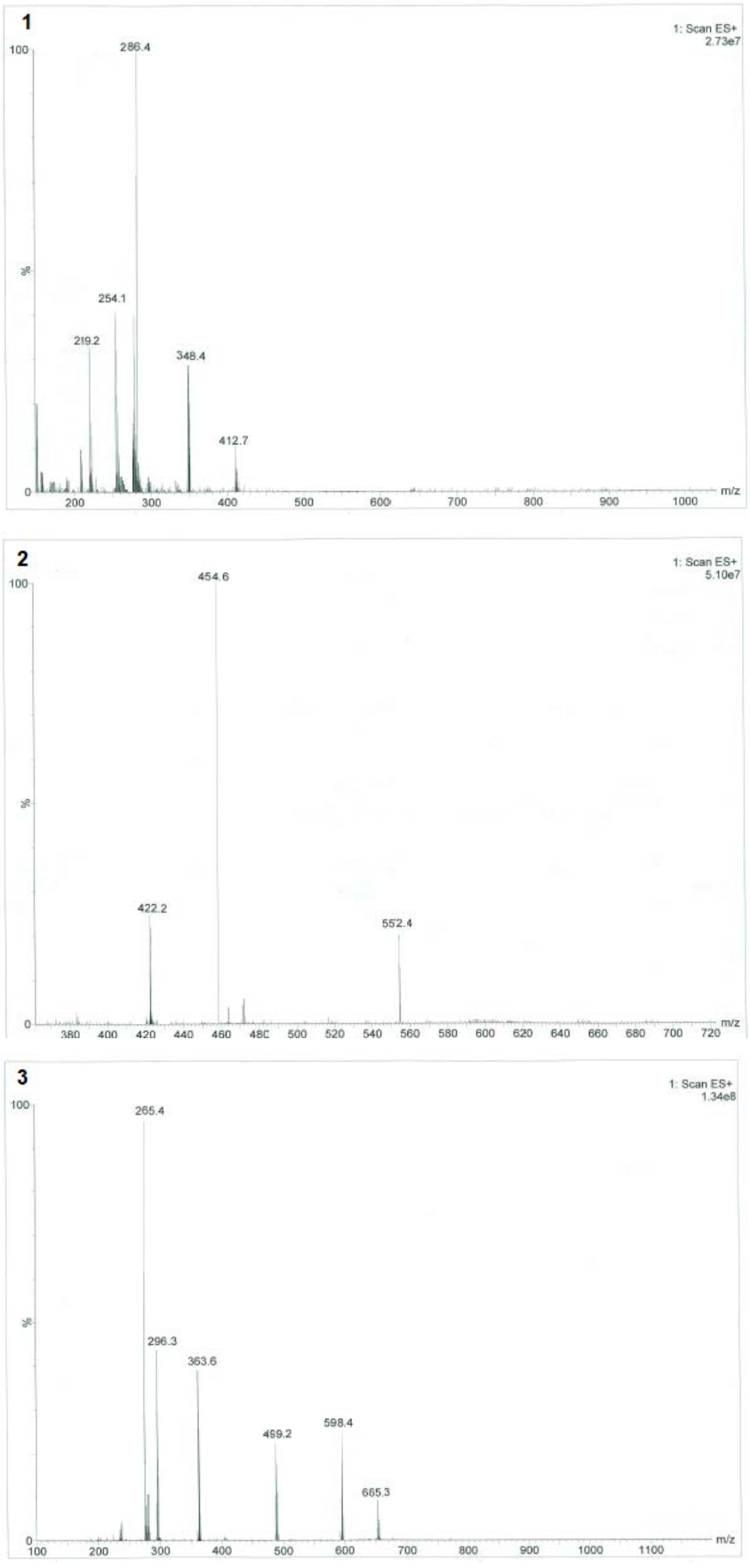

Fig. S3 (continued)

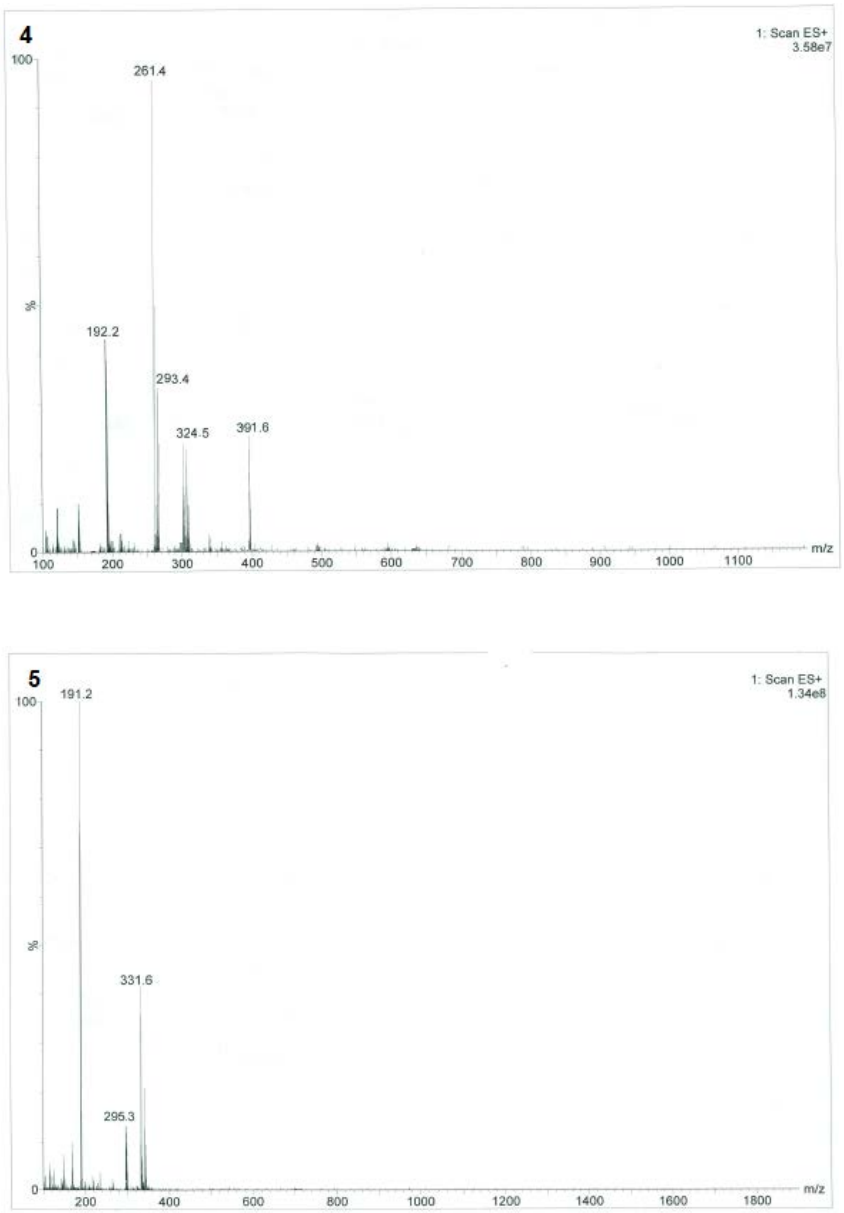

Fig. S3 ESI-MS spectra of **1**–**5**.

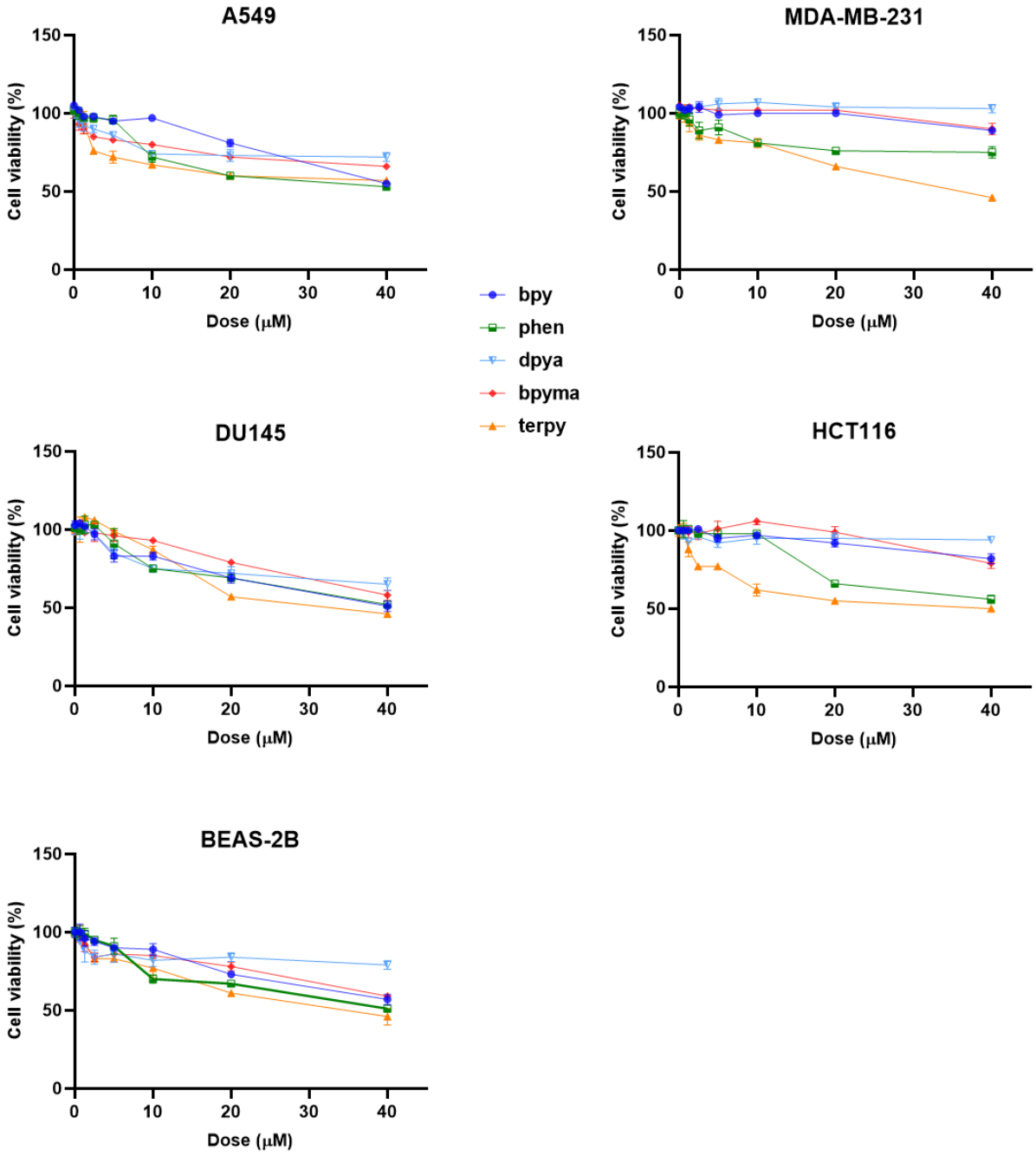

Fig. S4 (continued)

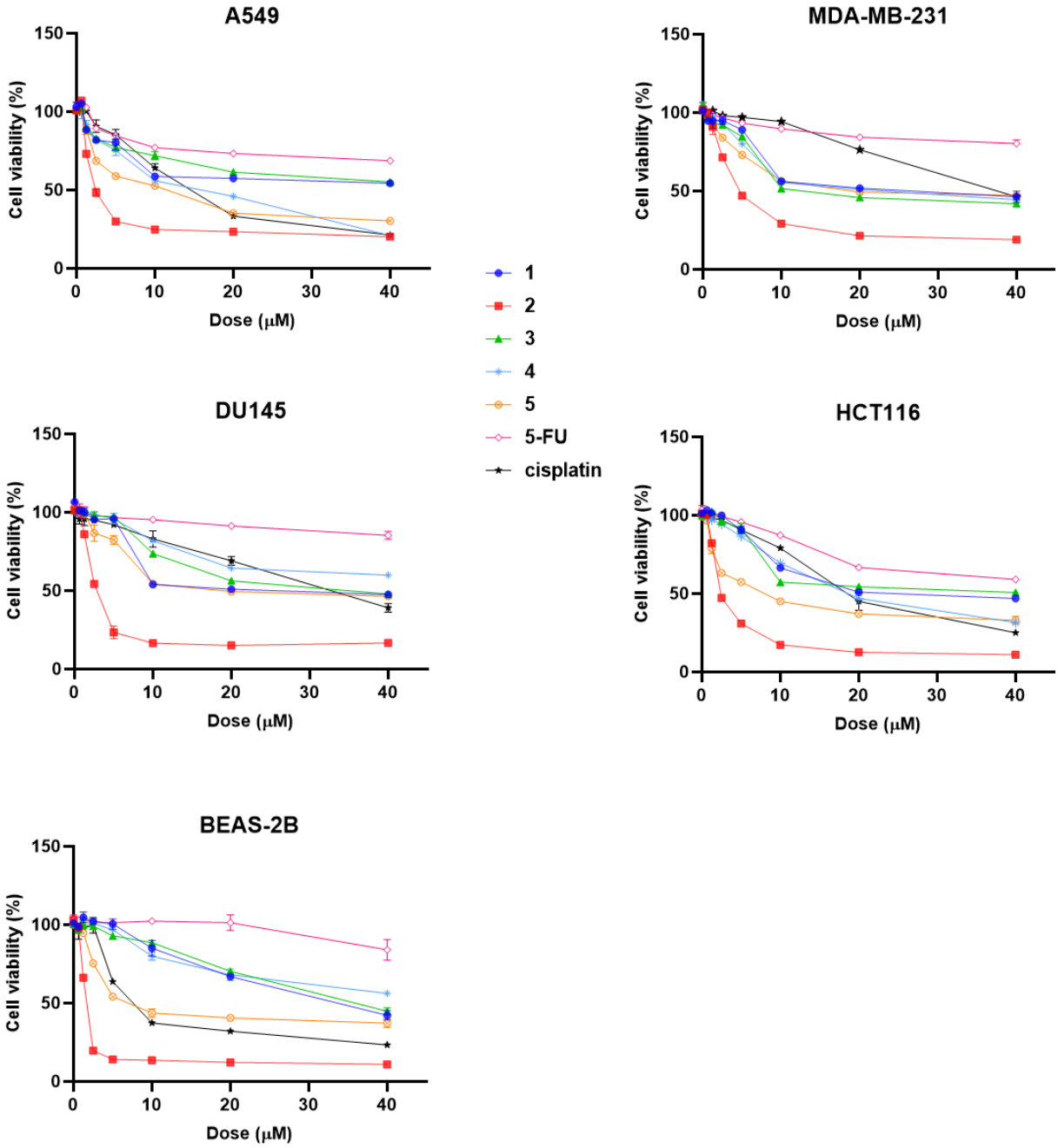

Fig. S4 Dose-response curves of complexes **1**–**5**, polypyridyl ligands, 5-FU and cisplatin against cancer and normal cell lines after 48 h treatment. Results are represented as mean ± standard deviation (n = 3).

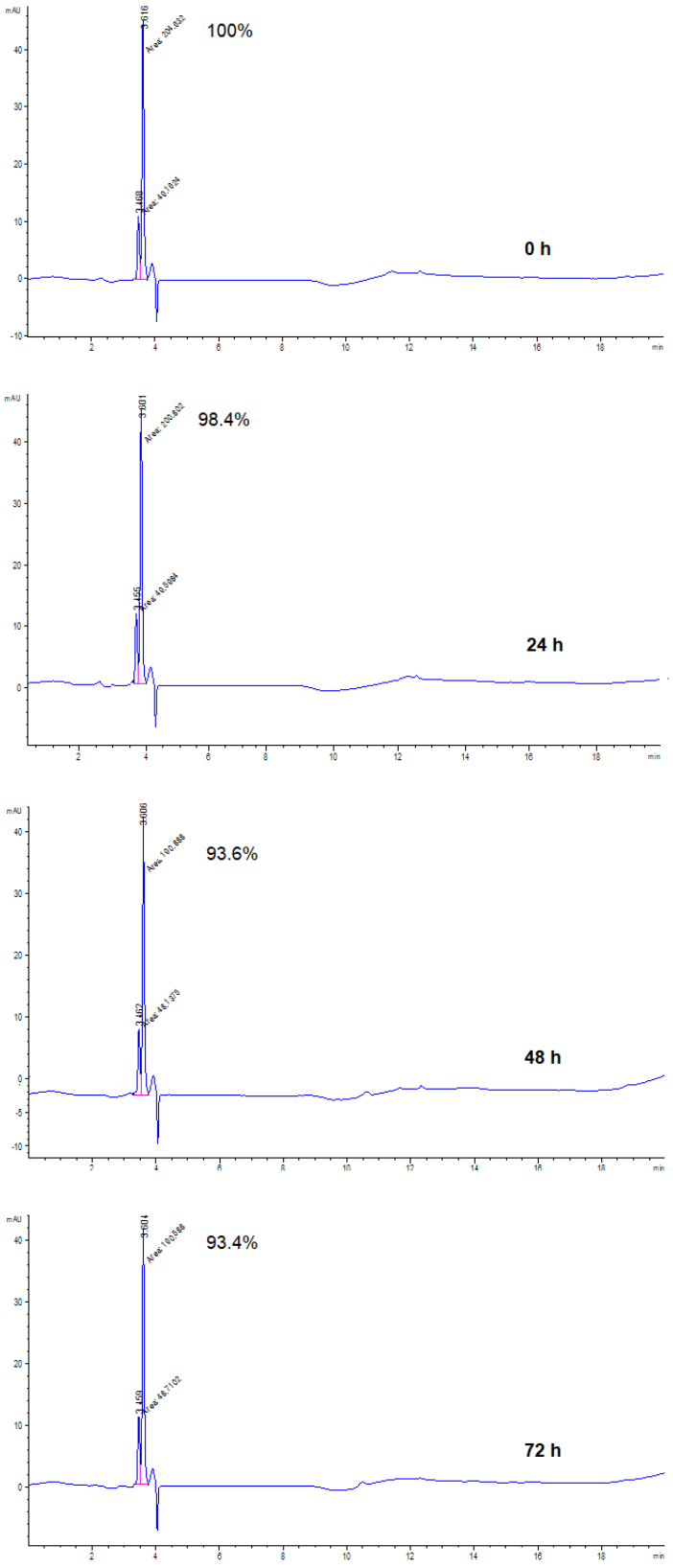

Fig. S5 The HPLC chromatograms, showing the time-dependent stability of **2** in a saline solution (0.9% NaCl). The amount of **2** was measured by the reverse phase HPLC at 267 nm, and stability values were expressed as the percentage of the complex remaining in the solution.

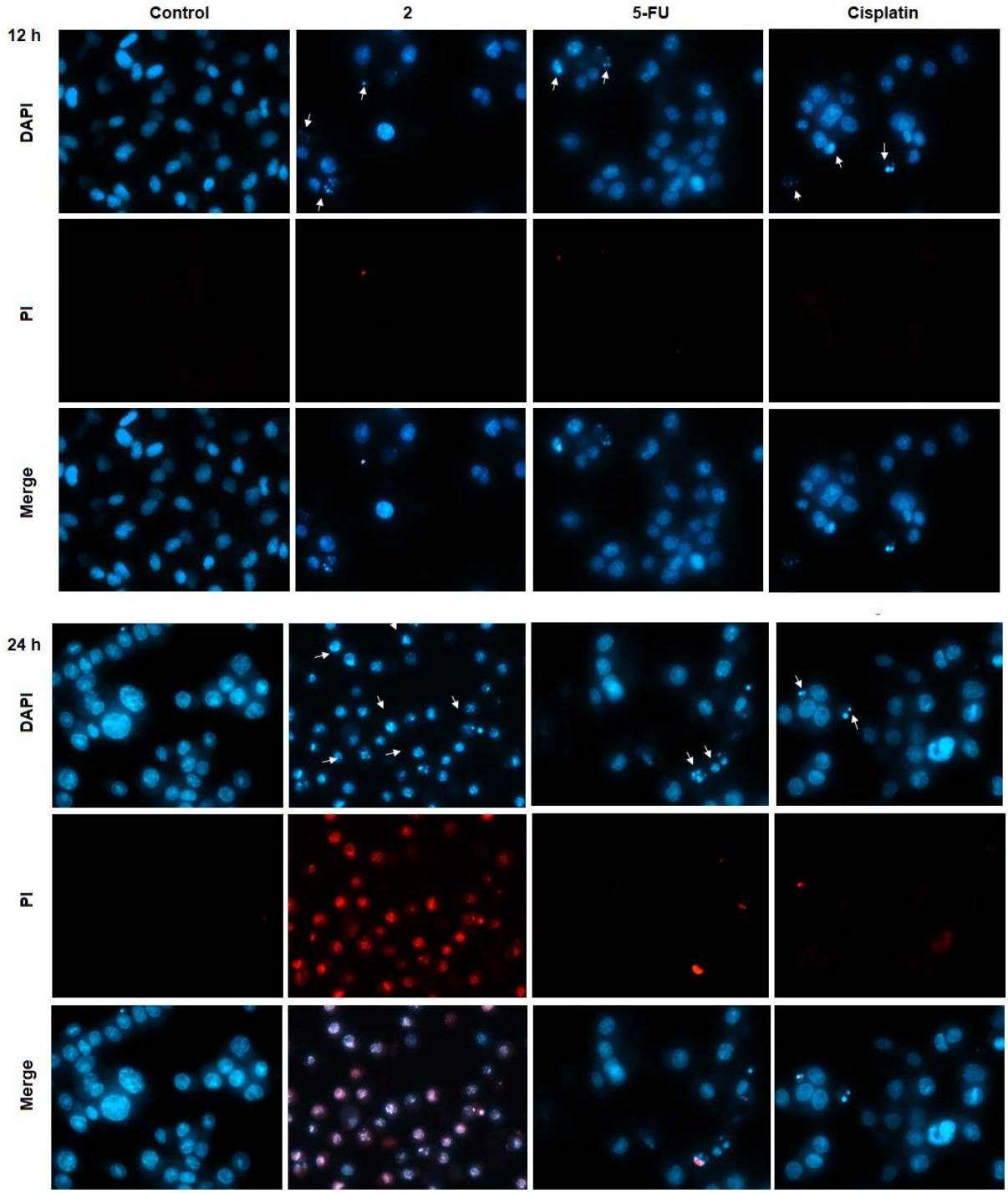

Fig. S6 DAPI/PI double staining of HCT116 cells treated with **2** (10 μM), 5-FU (172 μM) and cisplatin (33.9 μM), respectively, for 12 and 24 h. Cells were stained with DAPI/PI followed by detection using a fluorescence microscope. DAPI stained the live cells with intact plasma membrane (blue fluorescence), while PI stained dead and apoptotic ones (red fluorescence) with disrupted plasma membrane. Magnification: 40×.

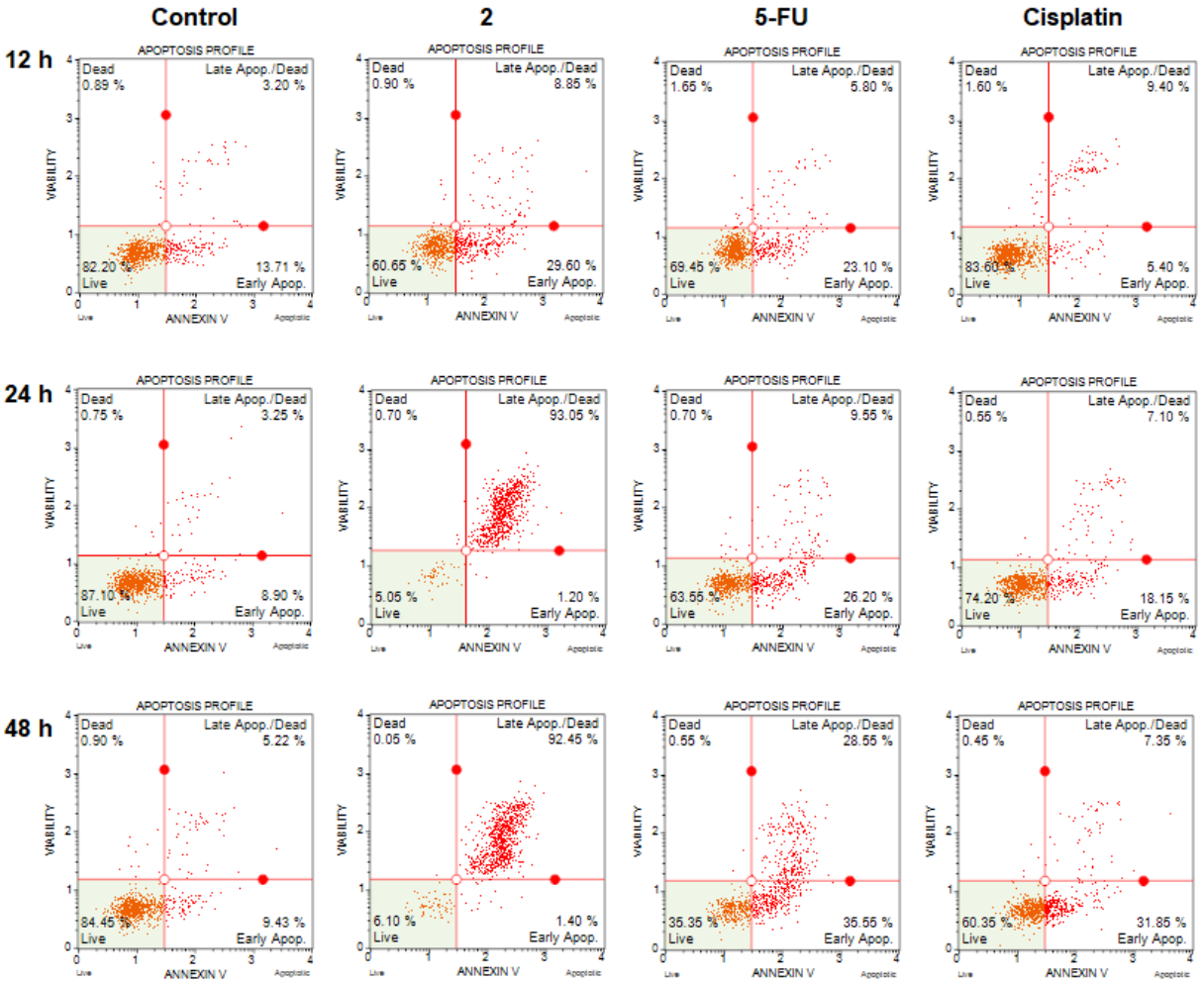

Fig. S7 Annexin-V/7-AAD assay of HCT116 cells treated with **2** (10 μM), 5-FU (172 μM) and cisplatin (33.9 μM), respectively, for 12, 24 and 48 h. 5-FU and cisplatin were used as positive controls. The quadrants show populations for HCT116 cells in four stages treated by the compounds.

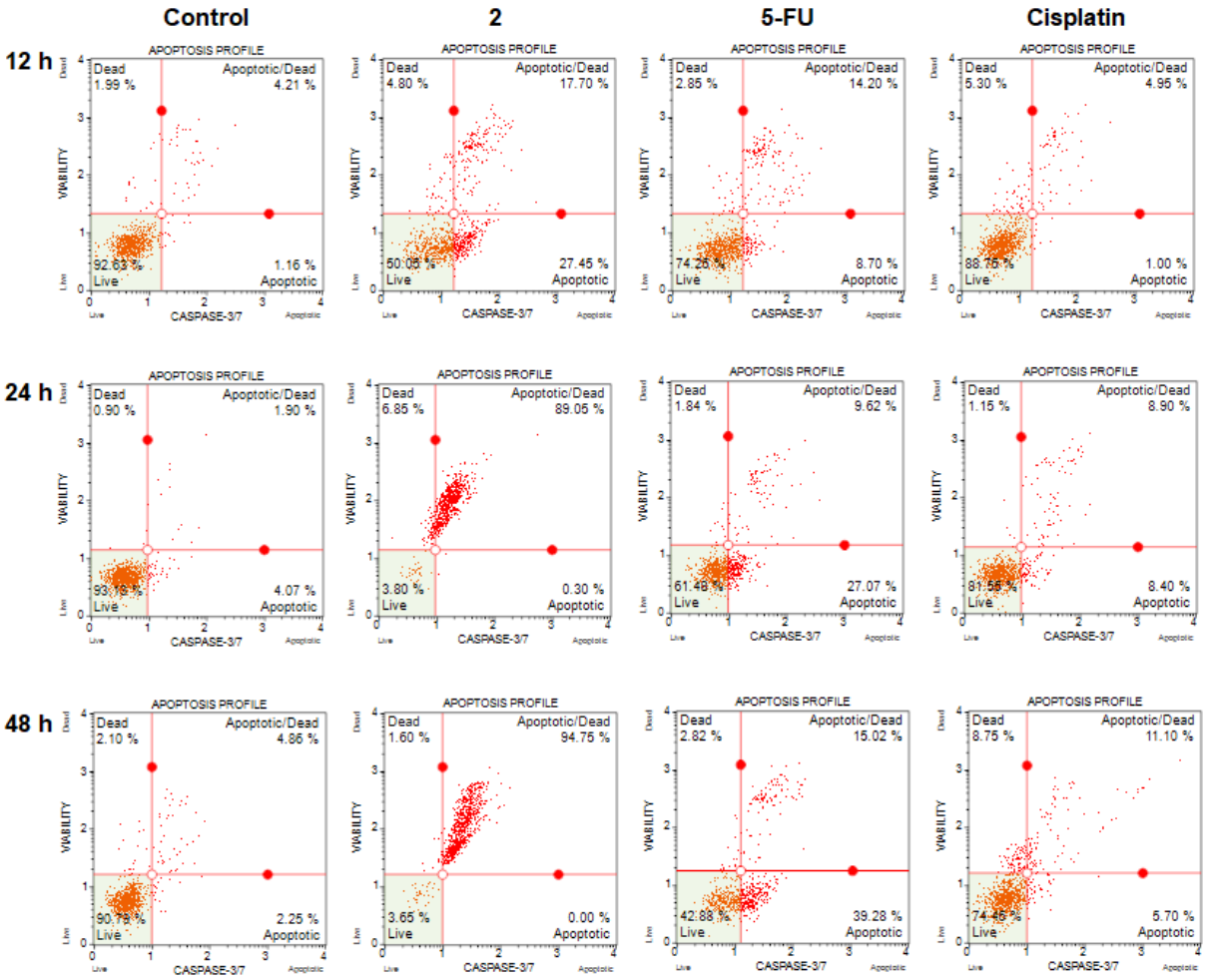

Fig. S8 Caspase 3/7 activity in HCT116 cells treated with **2** (10 µM), 5-FU (172 µM) and cisplatin (33.9 µM), respectively, for 12, 24 and 48 h. 5-FU and cisplatin were used as positive controls. The quadrants show populations for A549 cells in four stages treated by the compounds.

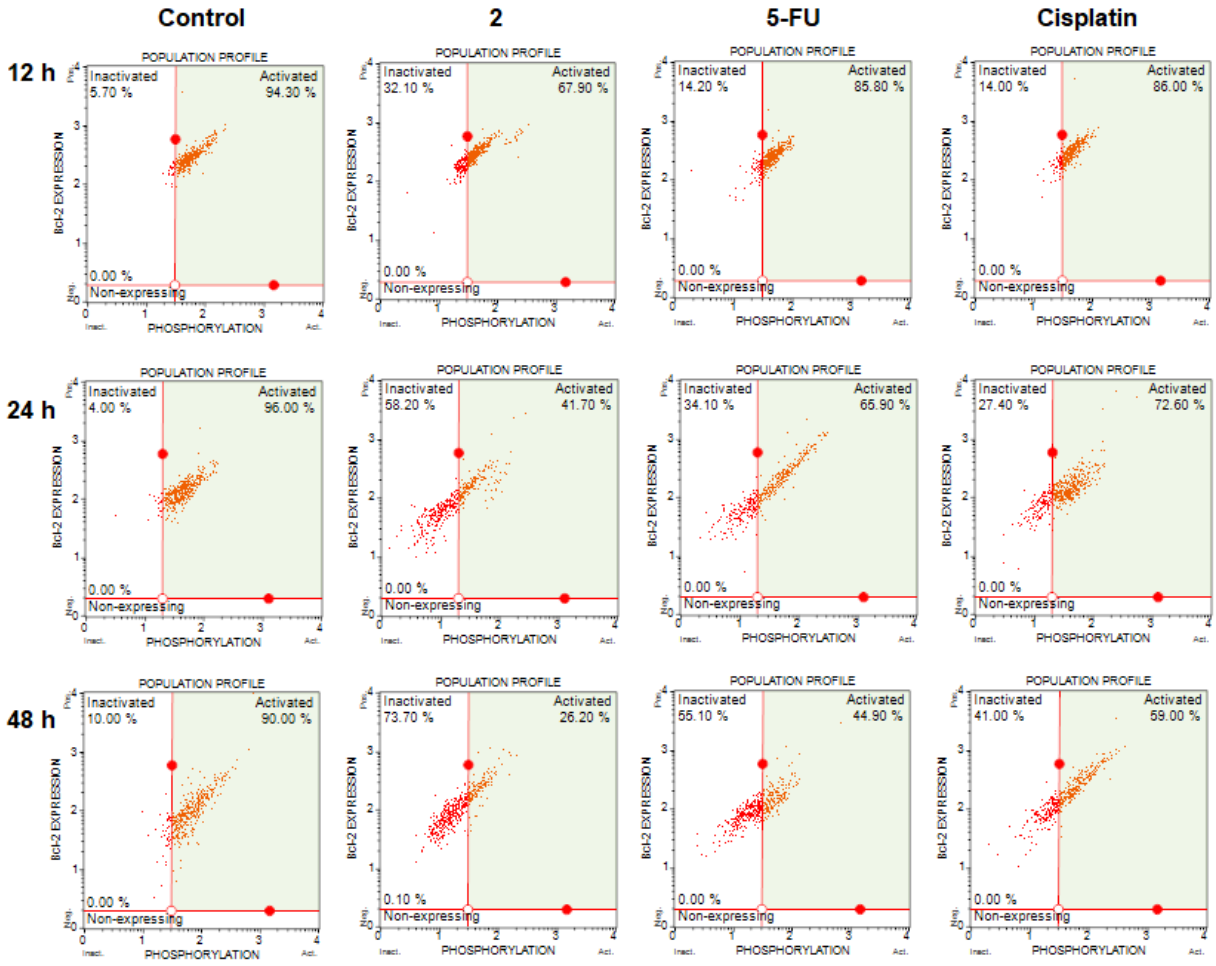

Fig. S9 Bcl-2 expression levels in HCT116 cells treated with **2** (10 μM), 5-FU (172 μM) and cisplatin (33.9 μM), respectively, for 12, 24 and 48 h. 5-FU and cisplatin were used as positive controls.

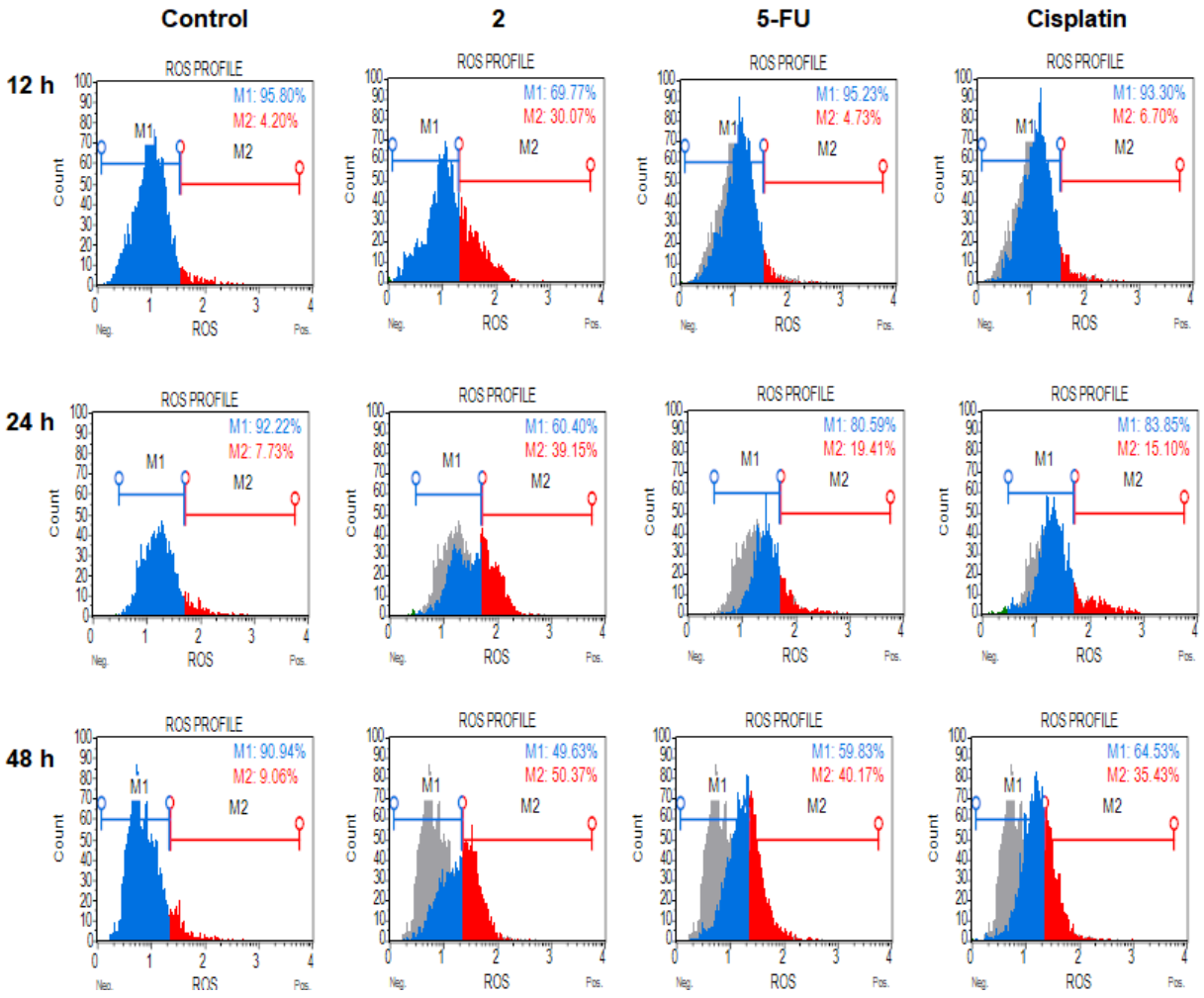

Fig. S10 ROS generation in HCT116 cells treated with **2** (10 µM), 5-FU (172 µM) and cisplatin (33.9 µM), respectively, for 12, 24 and 48 h. 5-FU and cisplatin were used as positive controls. M1 and M2 correspond to unstressed and oxidatively stressed cells.

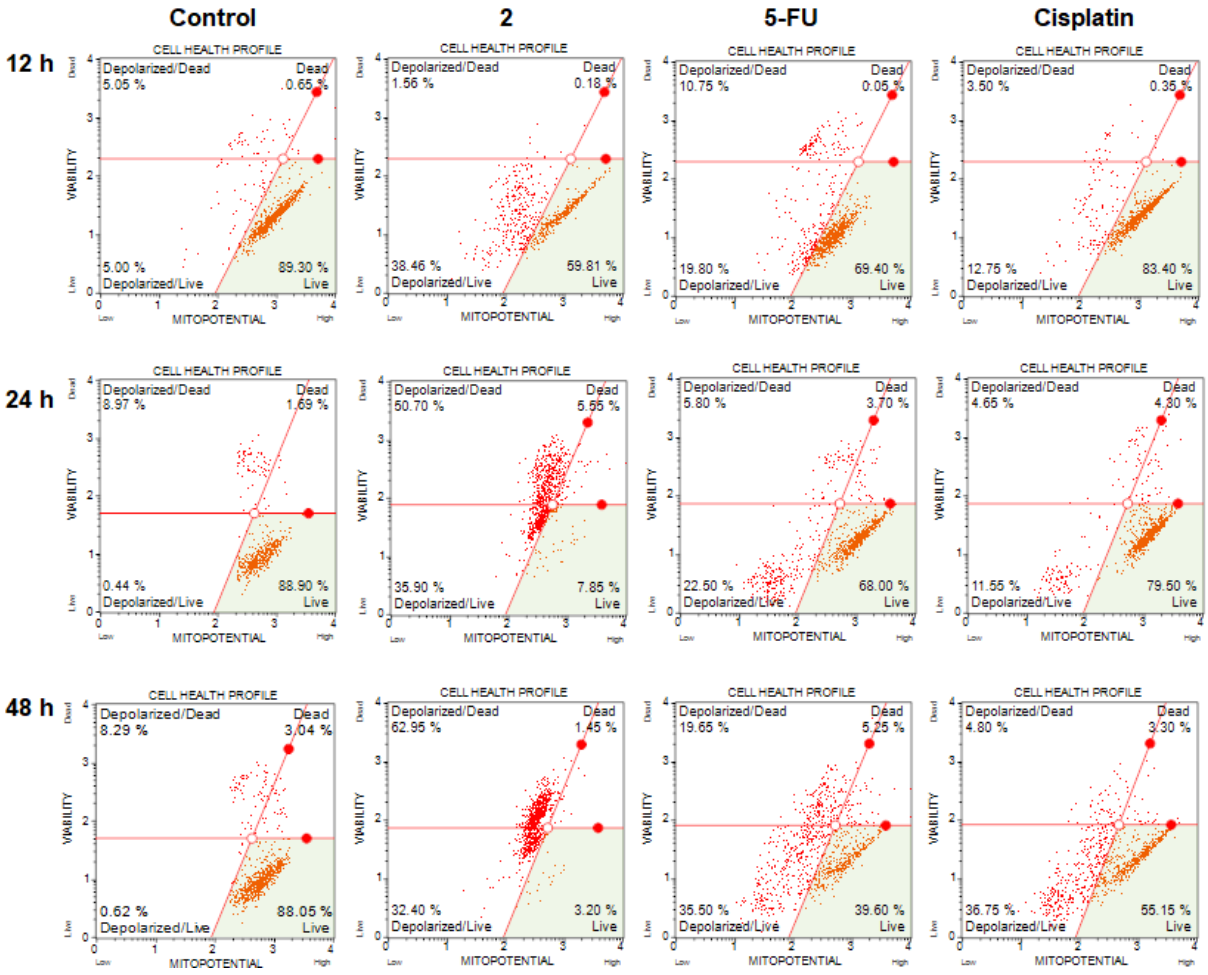

Fig. S11 Mitochondrial membrane depolarization in HCT116 cells treated with **2** (10 µM), 5-FU (172 µM) and cisplatin (33.9 µM), respectively, for 12, 24 and 48 h. 5-FU and cisplatin were used as positive controls.

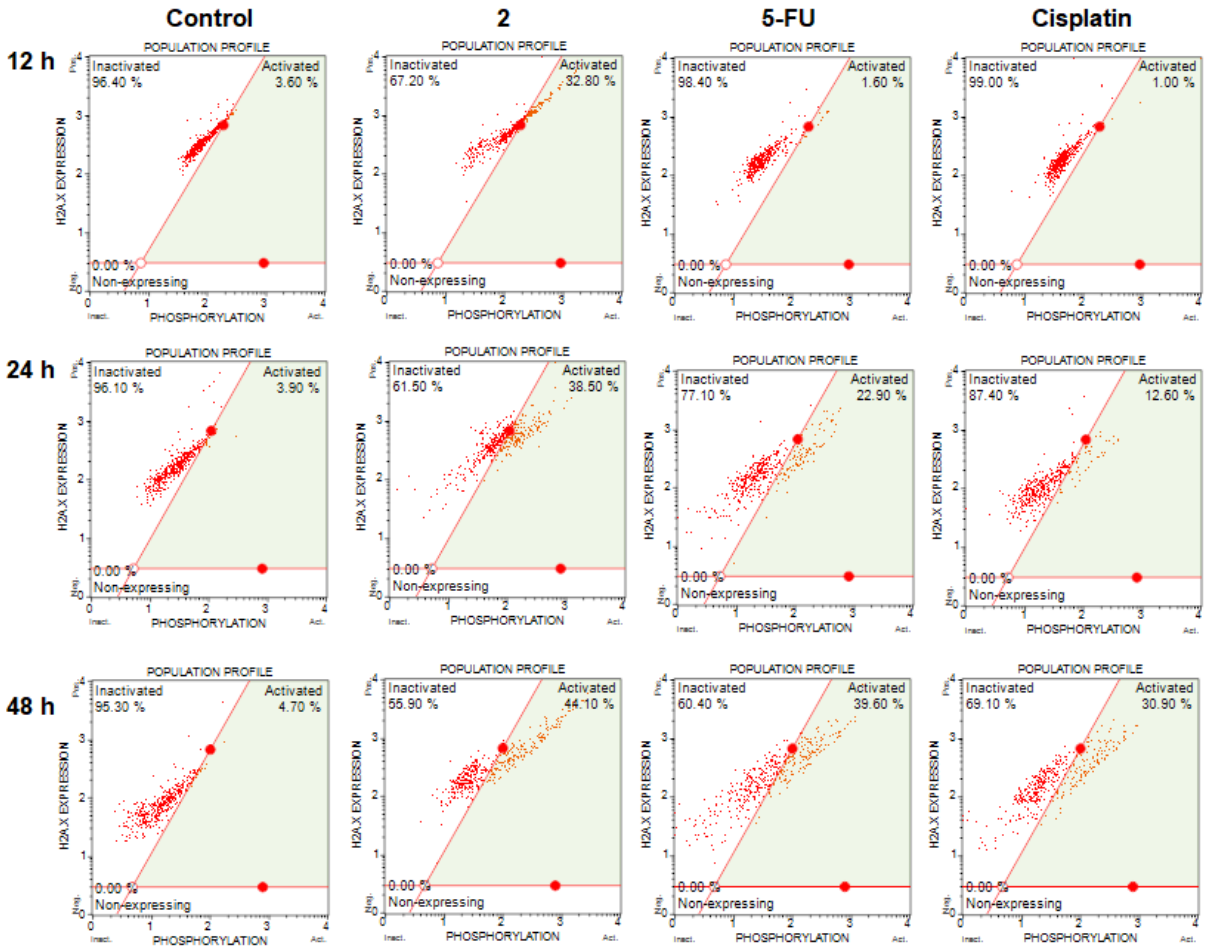

Fig. S12 H2AX expressions in HCT116 cells treated with **2** (10 μM), 5-FU (172 μM) and cisplatin (33.9 μM), respectively, for 12, 24 and 48 h. 5-FU and cisplatin were used as positive controls.