Synthesis, X-ray structure, antiproliferative activity, interaction with HSA and docking studies of three novels of mono and binuclear copper complexes containing maltol ligand

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Supplementary data:

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Table S1

Crystallographic data of the complexes (1), (2), and (3).

Compound	(1)	(2)	(3)
CCDC-number	1956605	1956606	1956607
Empirical formula	C_{16} H_{13} Br_2 Cu N_2 O_4, N O_3	C_{16} H_{26} Cu N_2 O_3, F_6 P	C_{36} H_{26} Cu_2 N_4 O_6, 2(F_6 P)
M (g mol^{-1})	582.65	489.79	1027.65
T (K)	293	293	293
Radiation	MoKα	MoKα	MoKα
λ (Å)	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	P 2_1/c	P 2_1/c	P -1
a (Å)	11.1803(2)	8.0772(2)	8.153(2)
b (Å)	11.3573(2)	14.8170(3)	11.328(3)
c (Å)	15.1698(3)	15.2106(3)	22.236(7)
α ( )	90	90	93.697(7)
β ( )	94.906(2)	101.928(2)	92.344(7)
γ ( )	90	90	107.709(7)
V ($Å^3$)	1919.17(6)	1781.10(7)	1948.3(10)
Z	4	4	2
D_{calc} (g/cm^3)	2.016	1.827	1.752
μ (mm^{-1})	5.348	1.399	1.283
F (000)	1140	980	1028
Crystal size (mm^3)	0.25 · 0.15 · 0.10	0.16 · 0.14 · 0.10	0.13 · 0.03 · 0.02
θ range for data collection ( )	3.24 – 26.37	3.35 – 26.37	2.53 – 25.68
Index ranges	-13 ≤ h ≤ 13 -14 ≤ k ≤ 14 -18 ≤ l ≤ 18	-10 ≤ h ≤ 10 -18 ≤ k ≤ 18 -19 ≤ l ≤ 19	-9 ≤ h ≤ 9 -13 ≤ k ≤ 13 -27 ≤ l ≤ 27
Reflections collected	43533	27438	60653
Independent reflections, R_{int}	3918, 0.0446	3637, 0.0269	7395 , 0.2219
Data/restraints/parameters	3918 / 3 / 271	3637 / 0 / 264	7395 / 0 / 561

Goodness-of-fit on F^2	1.104	1.051	1.179
Final R indexes [1≥2σ (1)]	0.0480	0.0485	0.1266
Final R indexes [all data]	0.1254	0.1399	0.2786
Largest difference,	1.085	0.894	0.738
peak/hole ($eÅ^{-3}$)	-0.928	-0.730	-0.705

Table S2

Selected bond lengths (Aº) and angles (º) of the complexes.

(1)		(2)		(3)	
Cu(1)-O(9)	1.906(4)	Cu(1)-O(8)	1.927(2)	Cu(1)-N(1)	1.99(1)
Cu(1)-O(10)	1.963(4)	Cu(1)-O(9)	1.962(2)	Cu(1)-N(2)	1.968(8)
Cu(1)-O(11)	2.292(5)	Cu(1)-N(10)	1.985(2)	Cu(1)-O(20)	1.910(8)
Cu(1)-N(16)	1.984(4)	Cu(1)-N(21)	1.972(3)	Cu(1)-O(21)	1.928(8)
Cu(1)-N(27)	1.984(3)	Cu(1)-O(8´)	2.472(4)	Cu(1)-O(20´)	2.554
				Cu(2)-N(22)	1.97(9)
				Cu(2)-N(33)	1.97(7)
				Cu(2)-O(43)	1.92(6)
				Cu(2)-O(44)	1.93(1)
				Cu(2)-O(43´)	2.51(4)
O(9)-Cu(1)-O(10)	85.5(2)	O(8)-Cu(1)-O(9)	85.3(1)	N(1)-Cu(1)-N(2)	83.5(3)
O(9)-Cu(1)-O(11)	99.0(2)	O(8)-Cu(1)-N(10)	94.5(1)	N(1)-Cu(1)-O(20)	178.2(4)
O(9)-Cu(1)-N(16)	161.9(2)	O(8)-Cu(1)-N(21)	176.2(1)	N(1)-Cu(1)-O(21)	95.4(4)
O(9)-Cu(1)-N(27)	96.3(2)	O(8)-Cu(1)-O(8)	89.72	N(1)-Cu(1)-O(20´)	89.2
O(10)-Cu(1)-O(11)	99.7(2)	O(9)-Cu(1)-N(10)	164.8(1)	N(2)-Cu(1)-O(20)	94.7(3)
O(10)-Cu(1)-N(16)	94.0(2)	O(9)-Cu(1)-N(21)	97.5(1)	N(2)-Cu(1)-O(21)	167.8(4)
O(10)-Cu(1)-N(27)	170.2(2)	O(9)-Cu(1)-O(8´)	100.32	N(2)-Cu(1)-O(20´)	87.6
O(11)-Cu(1)-N(16)	98.9(2)	N(10)-Cu(1)-N(21)	82.1(1)	O(20)-Cu(1)-O(21)	86.3(3)
O(11)-Cu(1)-N(27)	89.5(2)	N(10)-Cu(1)-O(8´)	94.90	O(20)-Cu(1)-O(20)	91.0

N(16)-Cu(1)-N(27)	81.3(2)	N(21)-Cu(1)-O(8´)	92.28	O(21)-Cu(1)-O(20´)	104.6
				N(22)-Cu(2)-N(33)	86.3(6)
Symmetry codes:				N(22)-Cu(2)-O(43)	177.6(2)
O(8´): 2-x, 1-y, 1-z				N(22)-Cu(2)-O(44)	95.4(7)
O(20´): -x, -y, 1-z				N(22)-Cu(2)-O(43´)	90.4(1)
O(43´): 2-x, 1-y, 1-z				N(33)-Cu(2)-O(43)	94.3(8)
				N(33)-Cu(2)-O(44)	167.3(3)
				N(33)-Cu(2)-O(43´)	88.1(7)
				O(43)-Cu(2)-O(44)	86.5(8)
				O(43)-Cu(2)-O(43)	90.2(4)
				O(44)-Cu(2)-O(43´)	104.4(6)

$[Cu(mal)(4,4\ dibromo\text{-}bpy)(H_2O)]^+$ (1), $[Cu(mal)(bpy)]_2^{+3}$ (2), $[Cu\ (mal)\ (1,10\ phen)]_2^{+3}$ (3) and . $[Cu(bpy)(mal)(NO_3)]$ (4)

Table S3

The selected hydrogen bond interactions. Selected bond lengths [Å] and angles [◦]

Complex	D-H···A	D-H	H···A	D···A	D-H···A
(1)	O11-H11A···O15	0.77	2.11	2.85	164.20
	O11-H11B···O14	0.77	2.16	2.90	161.08
	O11-H11B···O15	0.77	2.67	3.32	143.22
	C20-H20···O13	0.93	2.42	3.34	176.73
	C23-H23···O13	0.93	2.59	3.51	170.66
	C7-H7···Br1	0.93	2.92	3.70	141.89
(2)	C7-H7A···F5	0.96	2.57	3.38	142.52
	C11-H11···F4	0.93	2.41	3.18	140.13
	C12-H12···F6	0.93	2.62	3.49	154.92
	C14-H14···F1	0.93	2.63	3.01	105.09
	C19-H19···F3	0.93	2.62	3.15	117.29
	C20-H20···F5	0.93	2.64	3.52	159.17
(3)	C1-H1···F26	0.93	2.45	3.19	118.05
	C3-H3···F23	0.93	2.63	3.29	128.51
	C9-H9···F21	0.93	2.55	3.34	142.70
	C10-H10···F25	0.93	2.36	3.23	156.33
	C19-H19A···F25	0.96	2.55	3.39	146.85
	C27-H27···F24	0.93	2.44	3.31	157.14
	C42-H42C···F24	0.96	2.51	3.45	165.97

Table S4

K_{SV} and k_q values for the binding of HSA to the Cu(II) complexes and maltol at three different temperatures.

Compound	T(K)	K_{SV} ($\times 10^5$ M^{-1})	K_q ($\times 10^{12}$ $M^{-1}s^{-1}$)	R^2
	290	8.84	8.84	0.96
1	296	7.78	7.78	0.99
	310	5.16	5.16	0.99
	290	10.97	10.97	0.99
2	296	7.10	7.10	0.99
	310	5.62	5.62	0.99
	290	6.29	6.29	0.99
3	296	5.51	5.51	0.99
	310	4.46	4.46	0.99
	290	10.05	10.05	0.96
4	296	7.78	7.78	0.99
	310	5.16	5.16	0.99
	290	7.89	7.89	0.99
Maltol	296	6.79	6.79	0.99
	310	6.12	6.12	0.99

Table S5

K_b and n values for the binding of HSA to the Cu(II) complexes at three different temperatures.

Compound	T(K)	K_b ($\times 10^5$ M^{-1})	n	R^2
	290	13.18	1.03	0.96
1	296	8.51	1.01	0.99
	310	1.25	0.90	0.99
	290	102.33	1.16	0.99
2	296	26.92	1.09	0.99
	310	3.80	1.03	0.99
	290	27.54	1.1	0.99
3	296	22.38	1.1	0.99
	310	3.39	1.04	0.99
	290	144.54	1.18	0.96
4	296	41.69	1.12	0.99
	310	2.04	0.93	0.99
	290	1.95	0.90	0.99
Maltol	296	0.54	0.82	0.99
	310	0.38	0.80	0.99

Table S6

Thermodynamic parameters for the binding of HSA to the Cu(II) complexes at three different temperatures.

Compound	T(K)	ΔG°(kj mol^{-1})	ΔH° (kj mol^{-1})	ΔS° (j $mol^{-1}K^{-1}$)
	290	-27.06		
1	296	-29.59	95.32	422.35
	310	-35.50		
	290	-38.92		
2	296	-36.44	-80.77	-193.52
	310	-33.11		
	290	-35.75		
3	296	-35.98	-82.21	-158.71
	310	-32.82		
	290	-39.75		
4	296	-37.51	-144.17	-604.84
	310	-31.51		
	290	-29.37		
Maltol	296	-26.82	-53.84	-86.04
	310	-27.18		

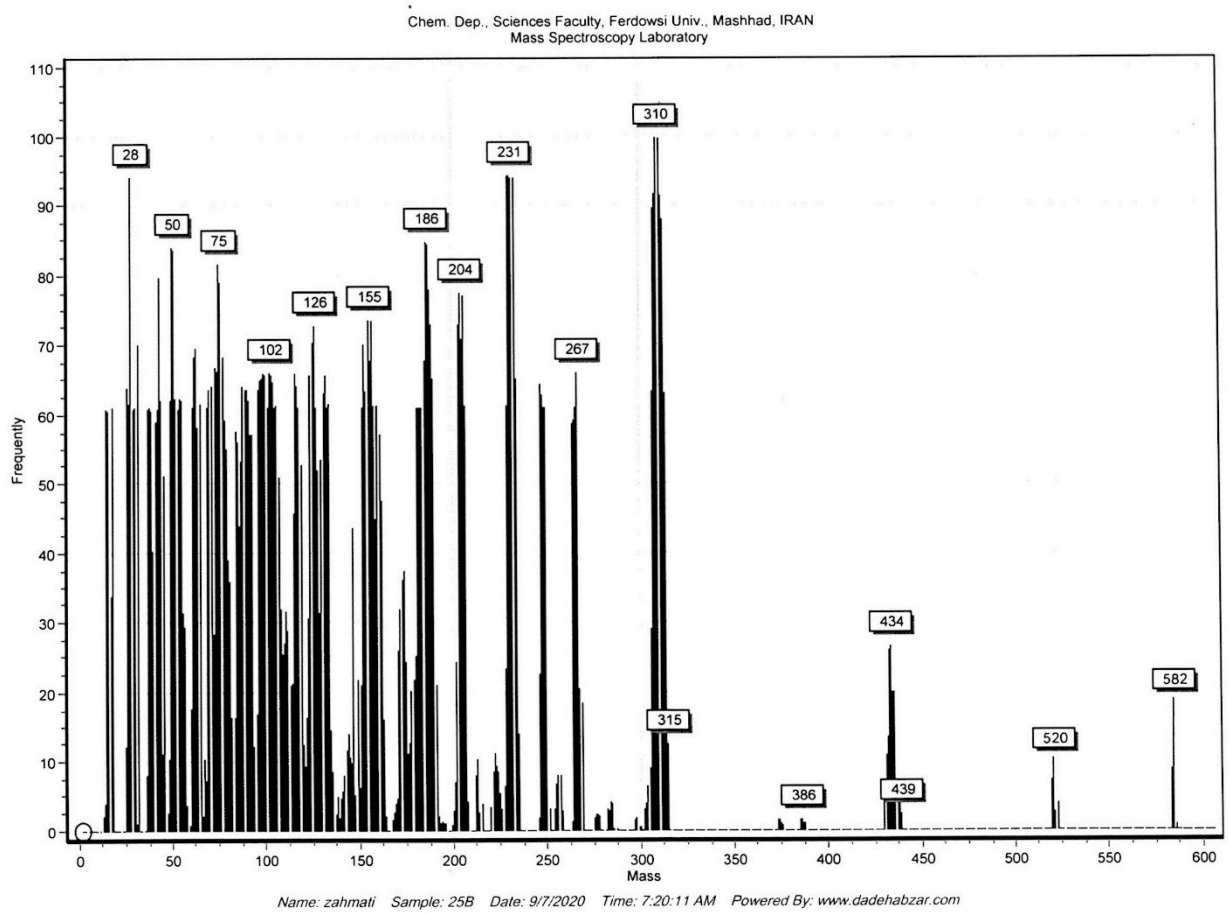


Figure S1. Mass spectrum of [Cu(mal)(4,4-dibromo-2,2-bpy)(H_2O)]·NO_3(1)

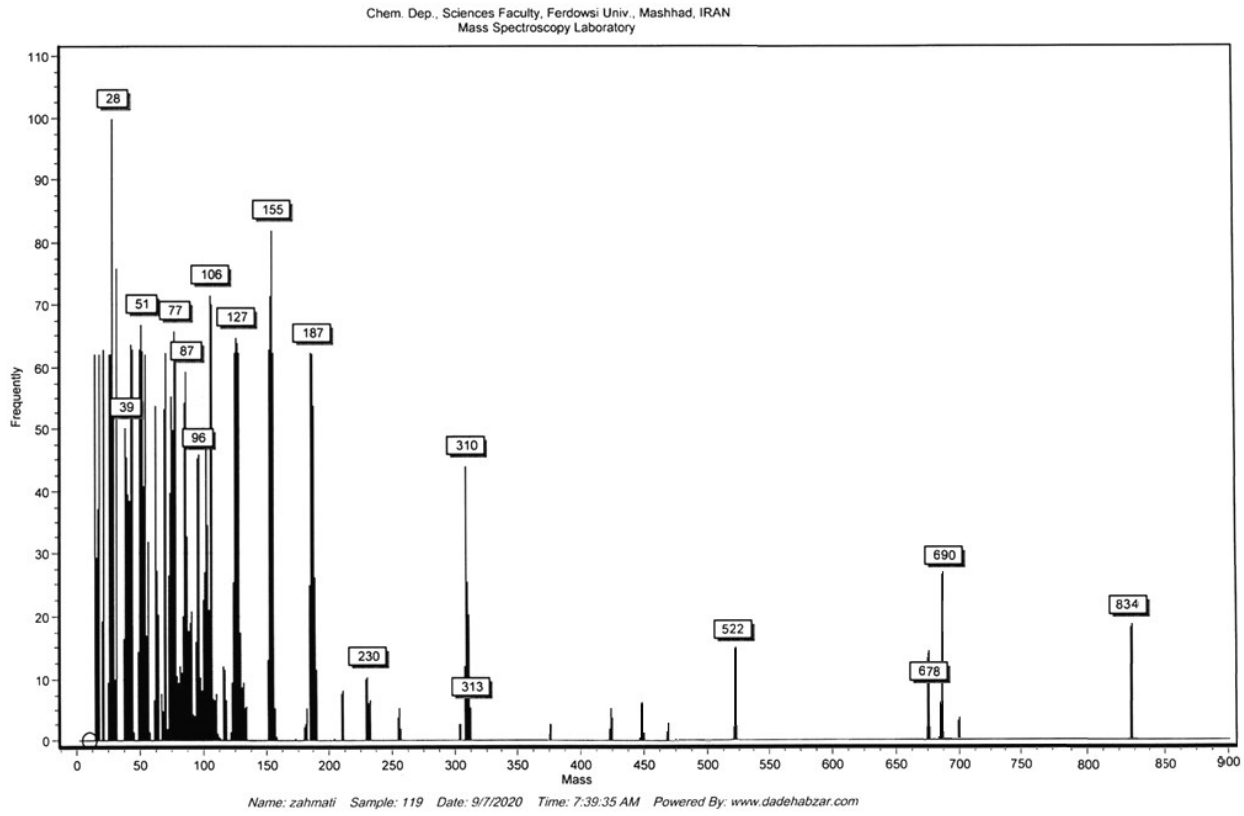


Figure S2. Mass spectrum of $[Cu(mal)(bpy)]_2PF_6$ (2)

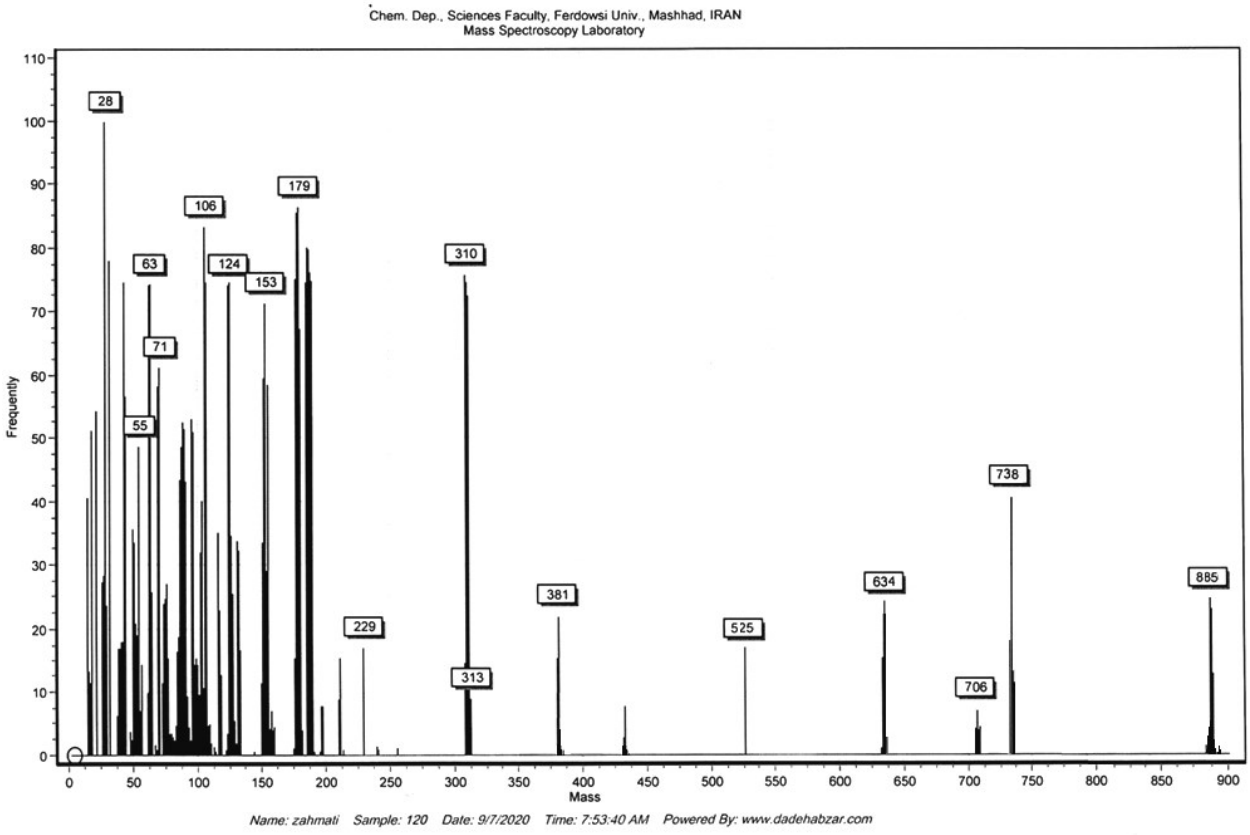


Figure S3. Mass spectrum of $[Cu(mal)(1,10\ phen)]_2PF_6$ (3)

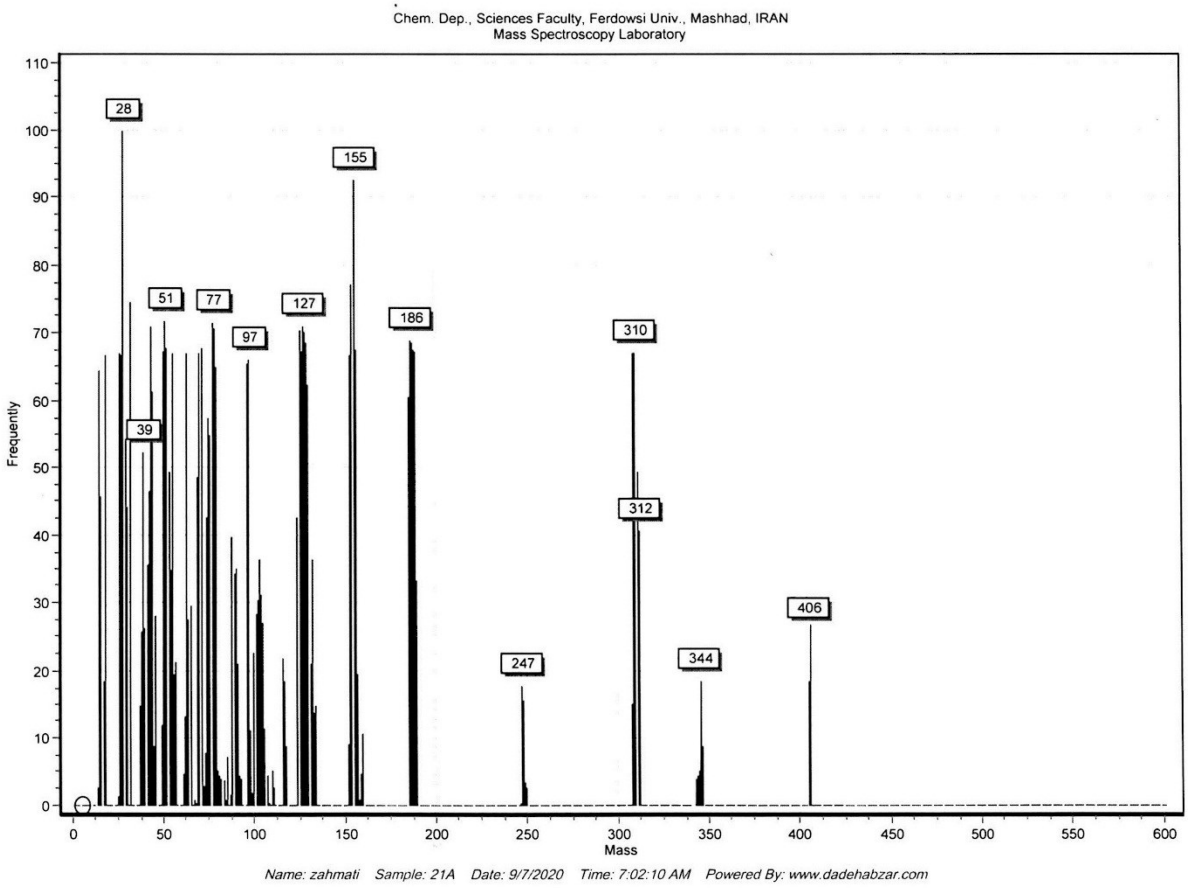
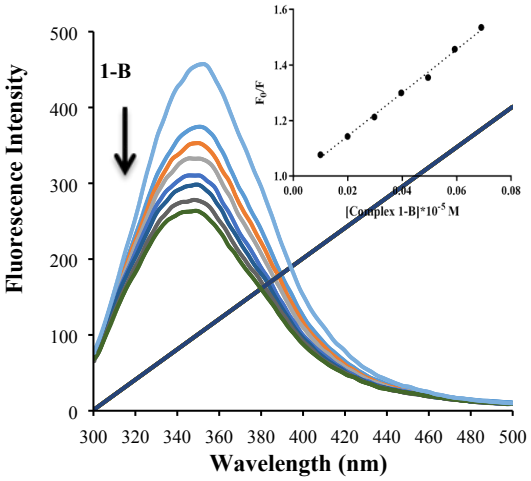
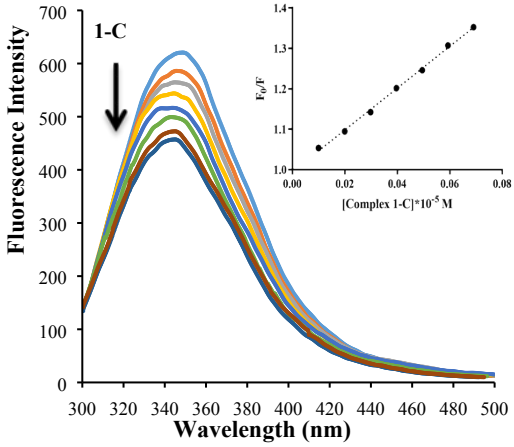
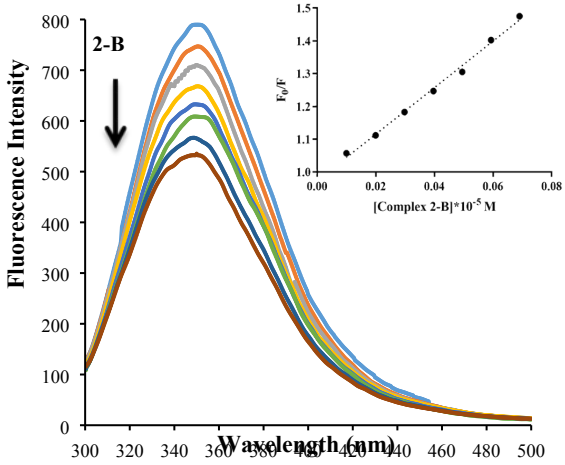
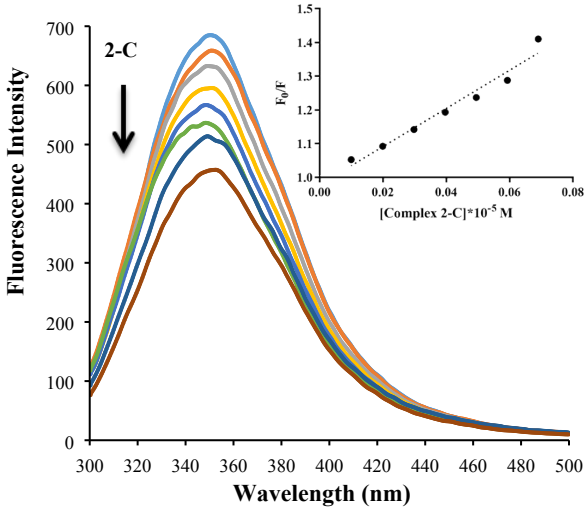


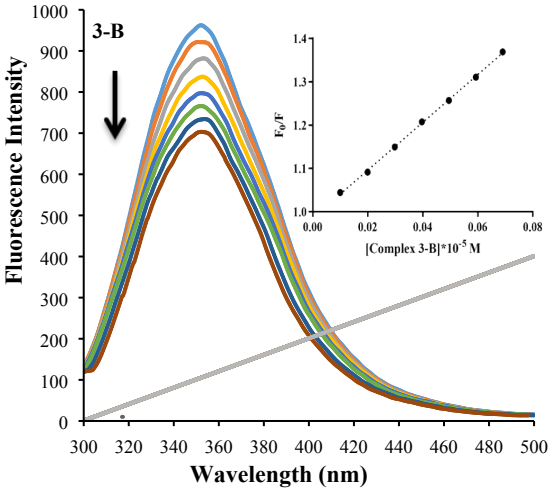
Figure S4. Mass spectrum of [Cu(bpy)(mal)(NO_3)] (4)

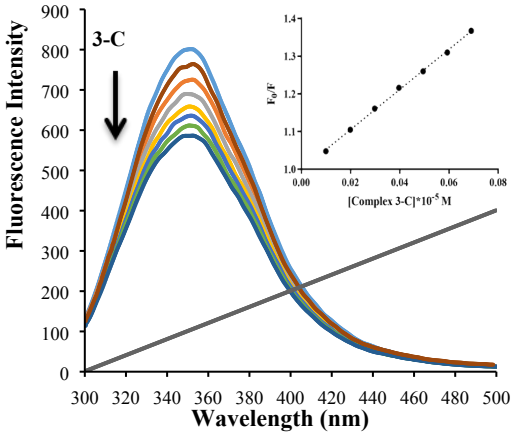

1-B
Fluorescence Intensity
Wavelength (nm)
F0/F
[Complex 1-B]*10-5 M


1-C
Fluorescence Intensity
Wavelength (nm)
F0/F
[Complex 1-C]*10-5 M


2-B
Fluorescence Intensity
Wavelength (nm)
F0/F
[Complex 2-B]*10-5 M


2-C
Fluorescence Intensity
Wavelength (nm)
F0/F
[Complex 2-C]*10-5 M


3-B
Fluorescence Intensity
Wavelength (nm)
F0/F
[Complex 3-B]*10-5 M


3-C
Fluorescence Intensity
Wavelength (nm)
F0/F
[Complex 3-C]*10-5 M

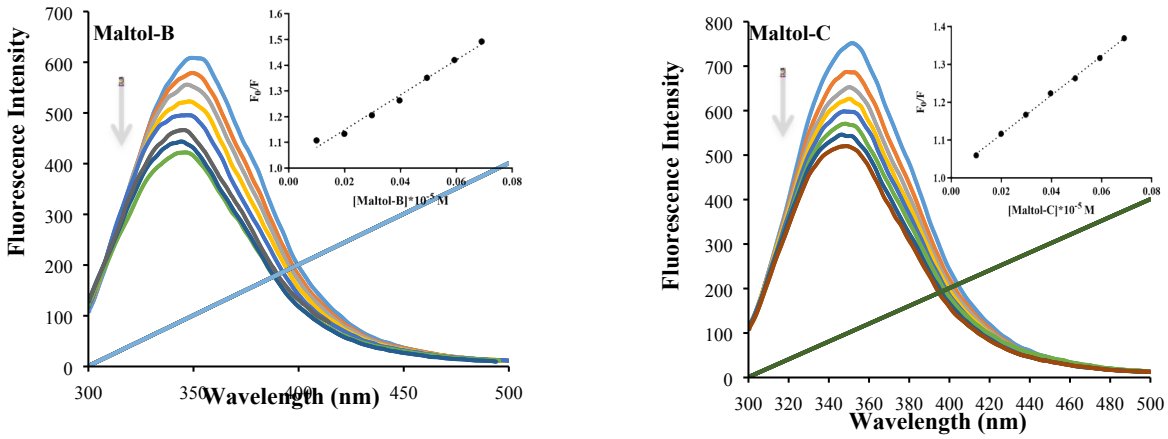
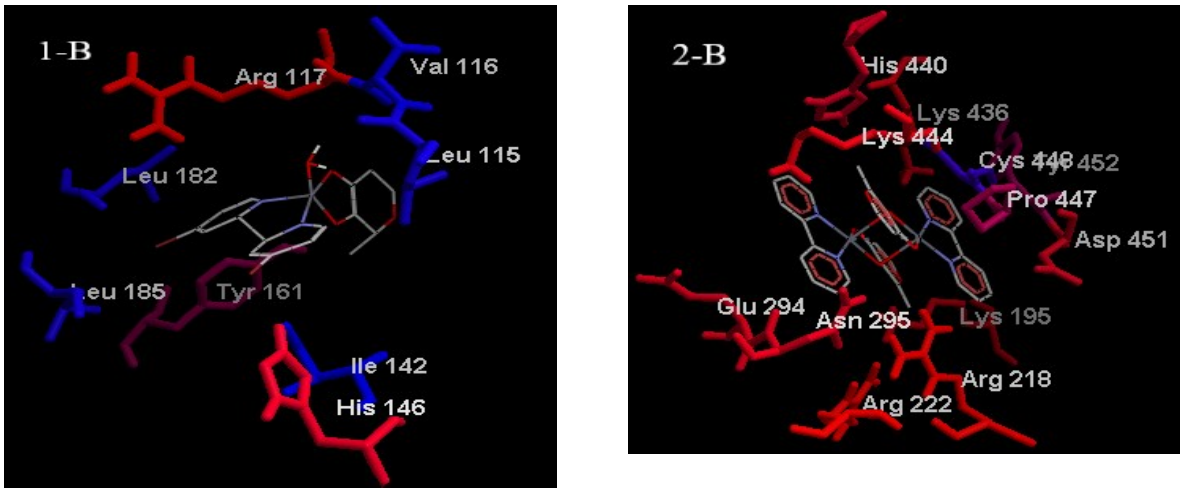
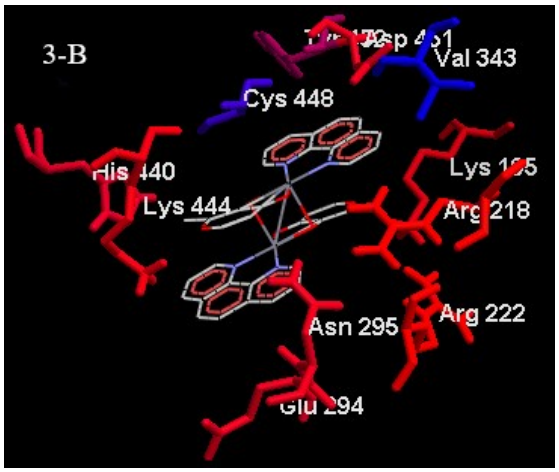
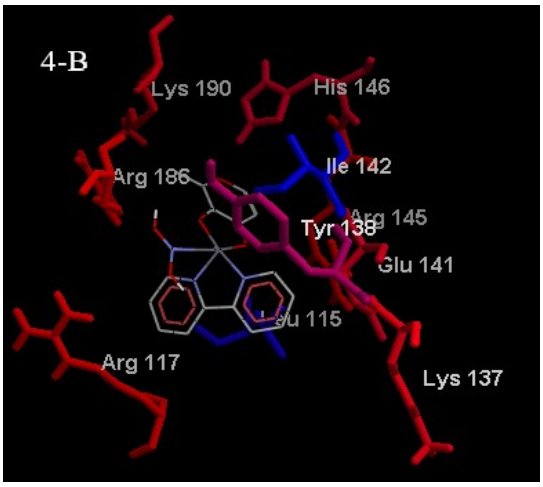


Figure S5. Fluorescence emission spectra of HSA (1.0 *10^{-6} M) in different concentrations of complexes 1, 2, 3, 4 and maltol corresponding to (0.00, 0.09, 0.19, 0.29, 0.39, 0.49, 0.59 and 0.69 µm) with the excitation wavelength at 280 nm in 5 mM Tris_HCl/50 mM NaCl buffer, pH 7.4, at temperatures (B: 296 and C: 310). The Arrow shows the intensity changes upon increasing the concentration of the quencher. Inset: The Stern–Volmer plots F_0/F versus [complex] for fluorescence quenching of HSA by the complexes at three different temperatures.







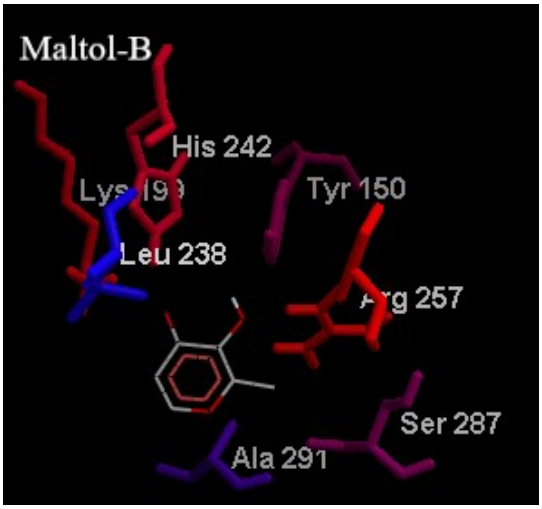


Figure S6. Molecular docking studies of complexes 1, 2, 3, 4 and maltol ligand with HSA. B: Hydrophobic interactions exist between the compound and HSA.