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Synthesis, characterization, cytotoxicity, DFT calculations, and DNA interaction studies of new Schiff base metal (II) complexes

SUPPLEMENTARY MATERIAL

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Content:

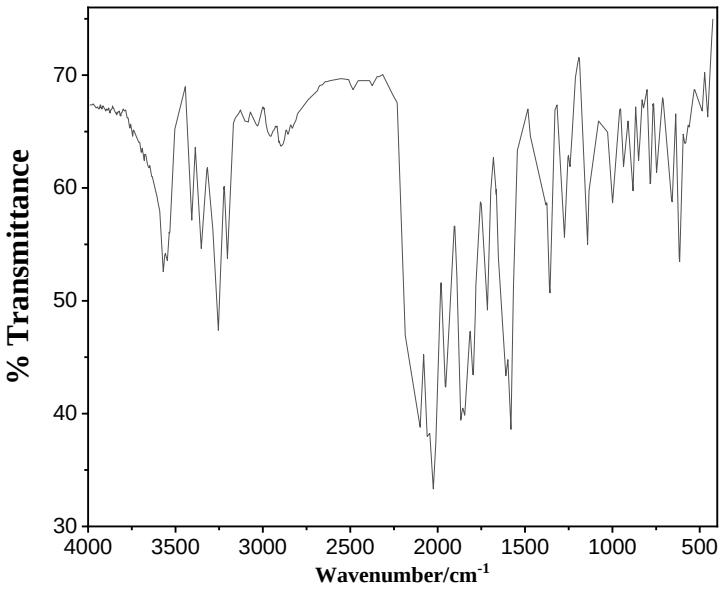

Fig. SI-1. FTIR spectrum of the ligands of L1 ligand.

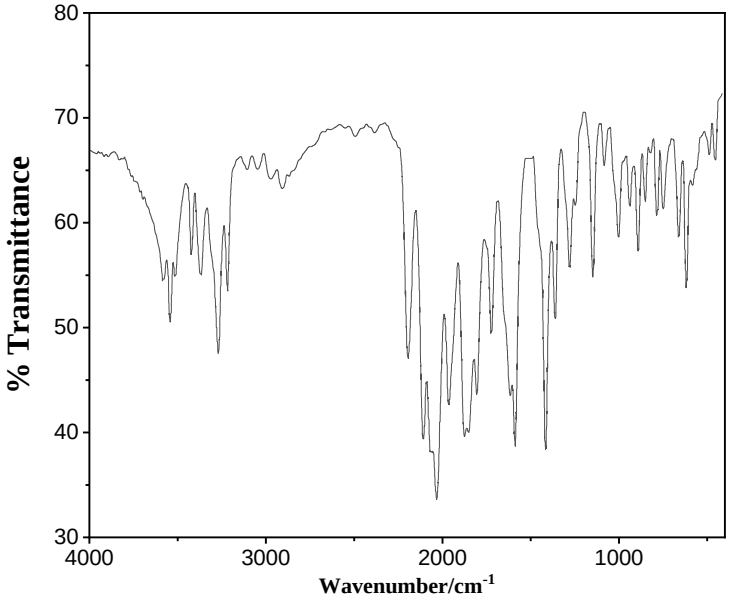

Fig. SI-2. FTIR spectrum of the ligands of L2 ligand.

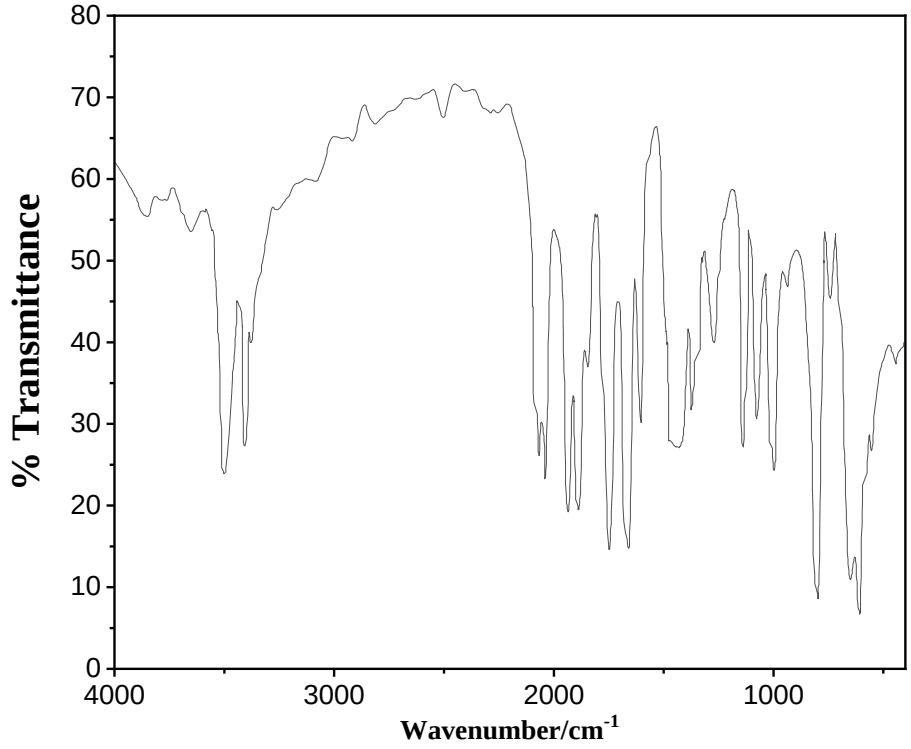

Fig. SI-3. FTIR spectrum of the ligands of Z1 complex.

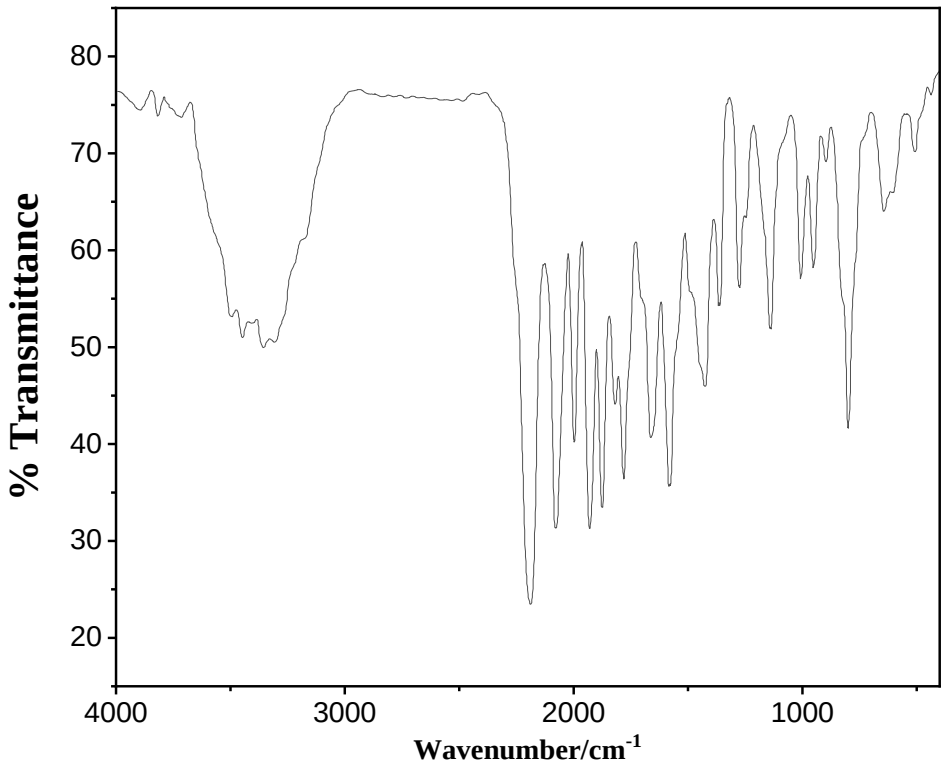

Fig. SI-4. FTIR spectrum of the ligands of Z4 complex.

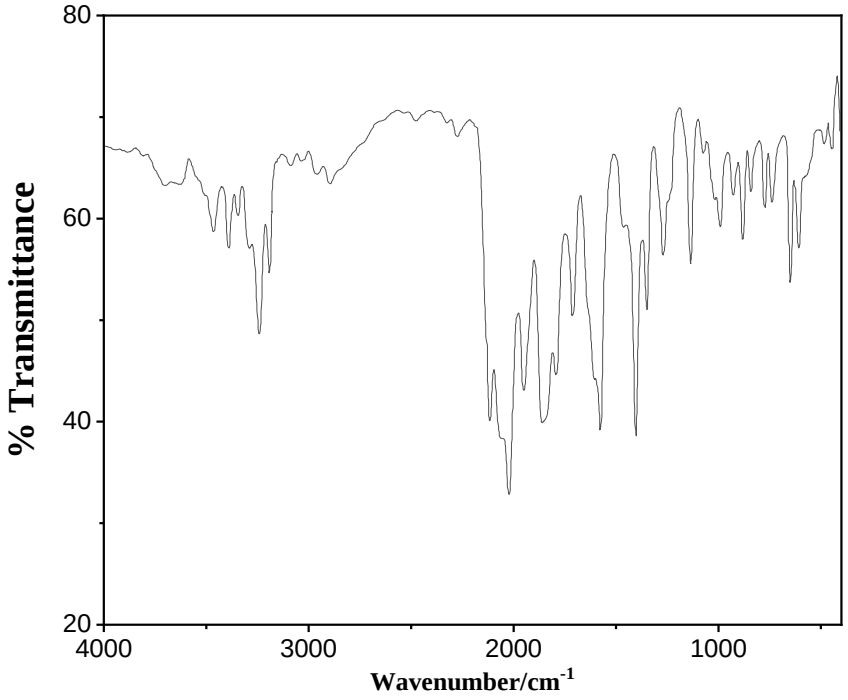

Fig. SI-5. FTIR spectrum of the ligands of Z7 complex.

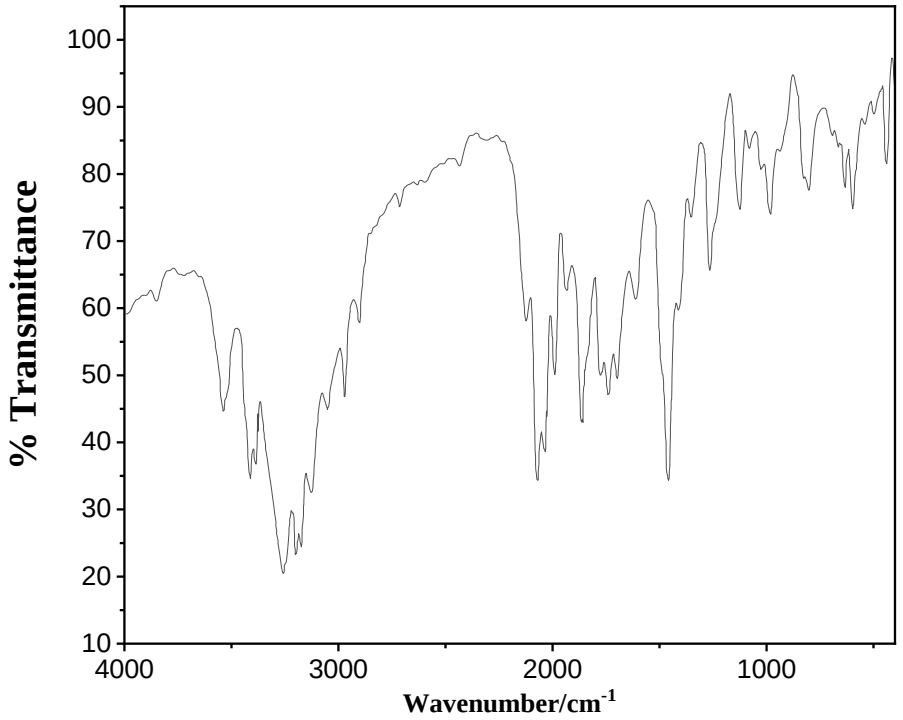

Fig. SI-6. FTIR spectrum of the ligands of Z2 complex.

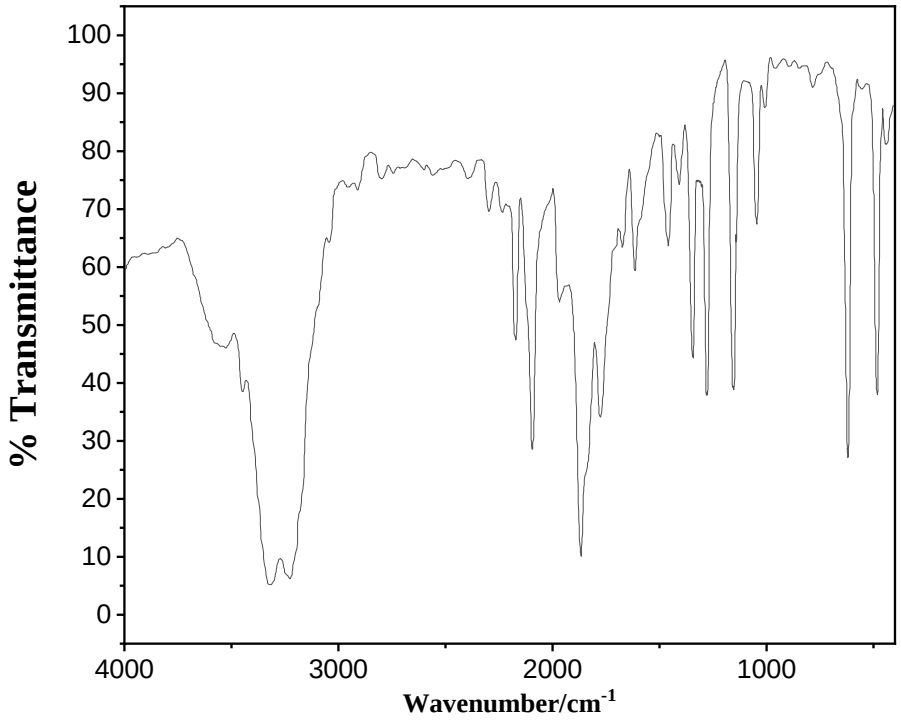

Fig. SI-7. FTIR spectrum of the ligands of Z5 complex.

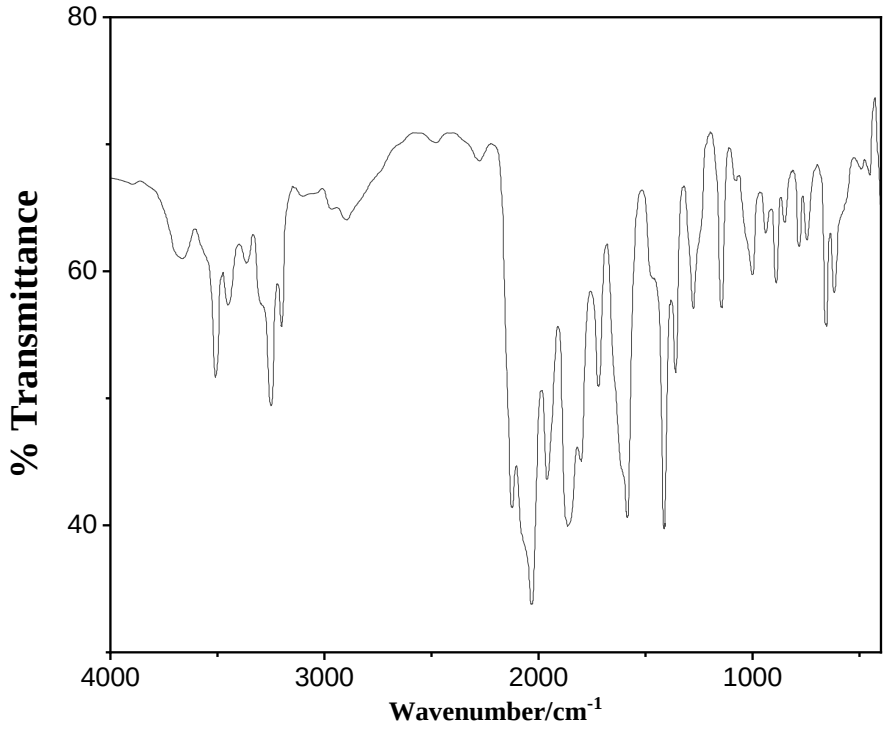

Fig. SI-8. FTIR spectrum of the ligands of Z8 complex.

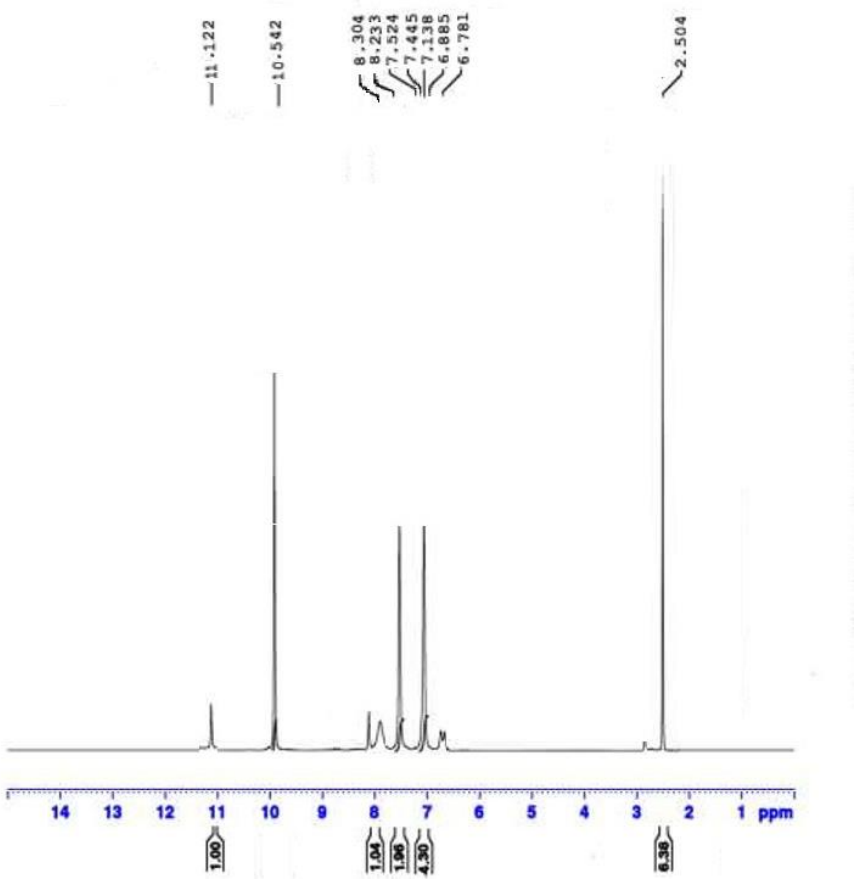

Fig. SI-9. ^{1}H NMR spectrum of L1 in DMSO-d6.

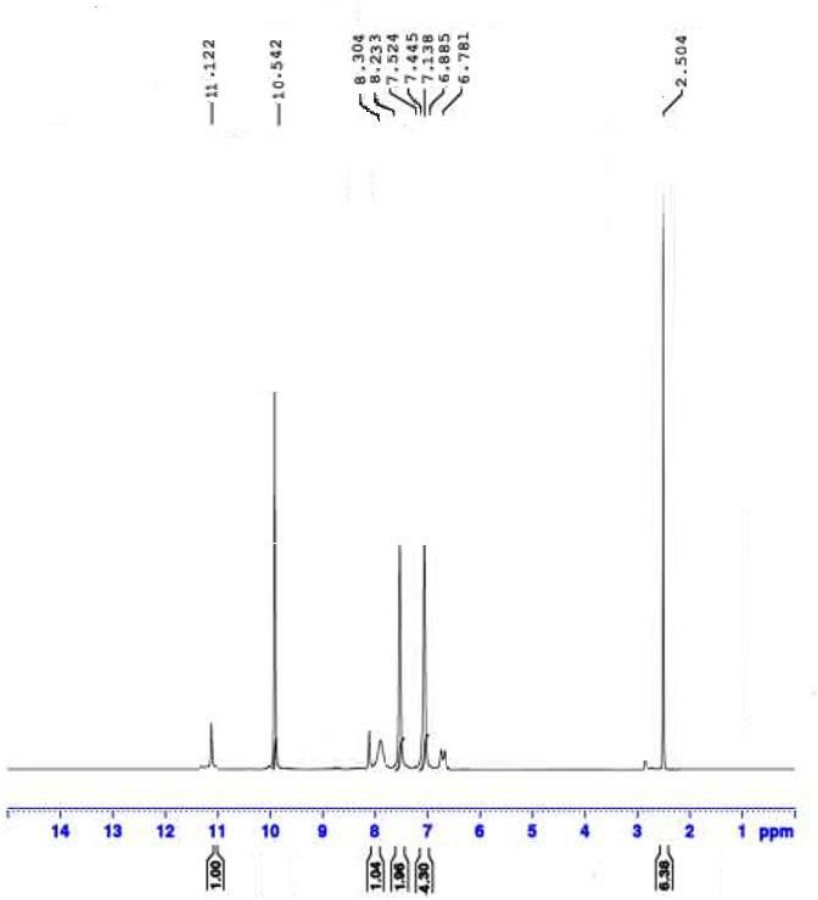

Fig. SI-10. ^{1}H NMR spectrum of L2 in DMSO-d6.

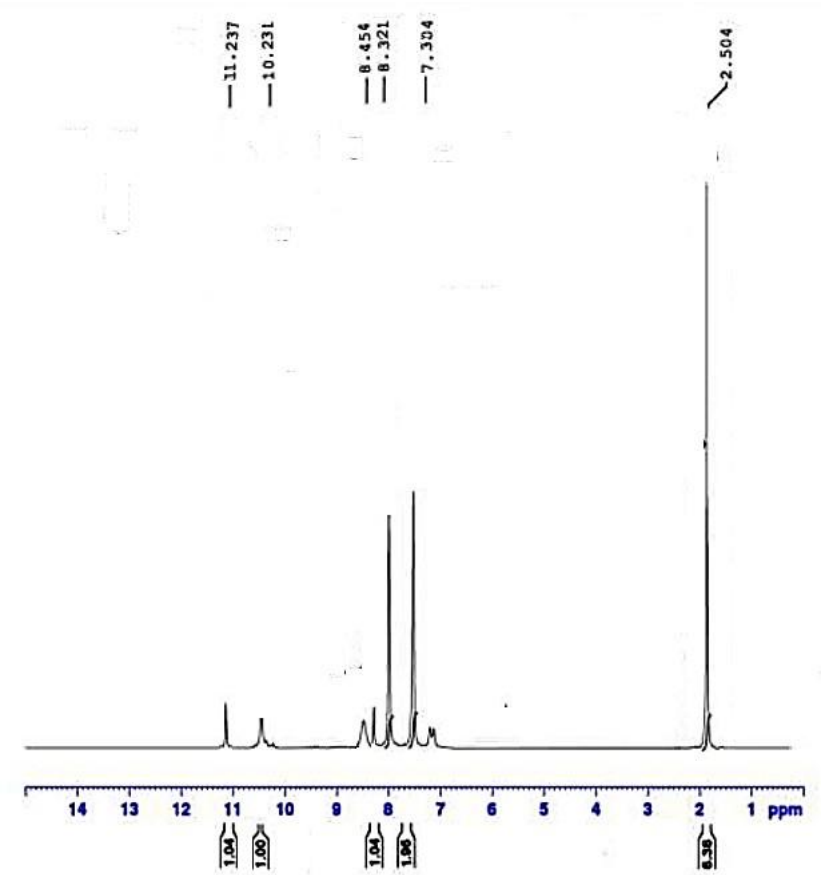

Fig. SI-11. ^{1}H NMR spectrum of L3 in DMSO-d6.

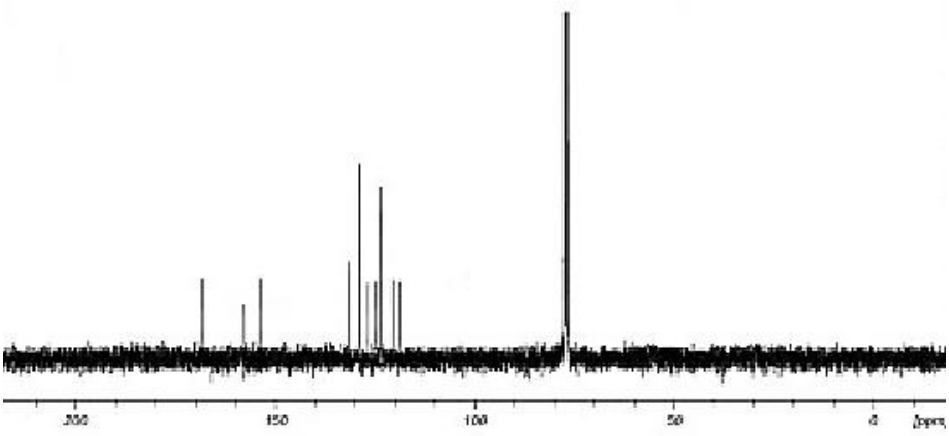

Fig. SI-12. ^{13}C NMR spectrum of L2 in DMSO-d6.

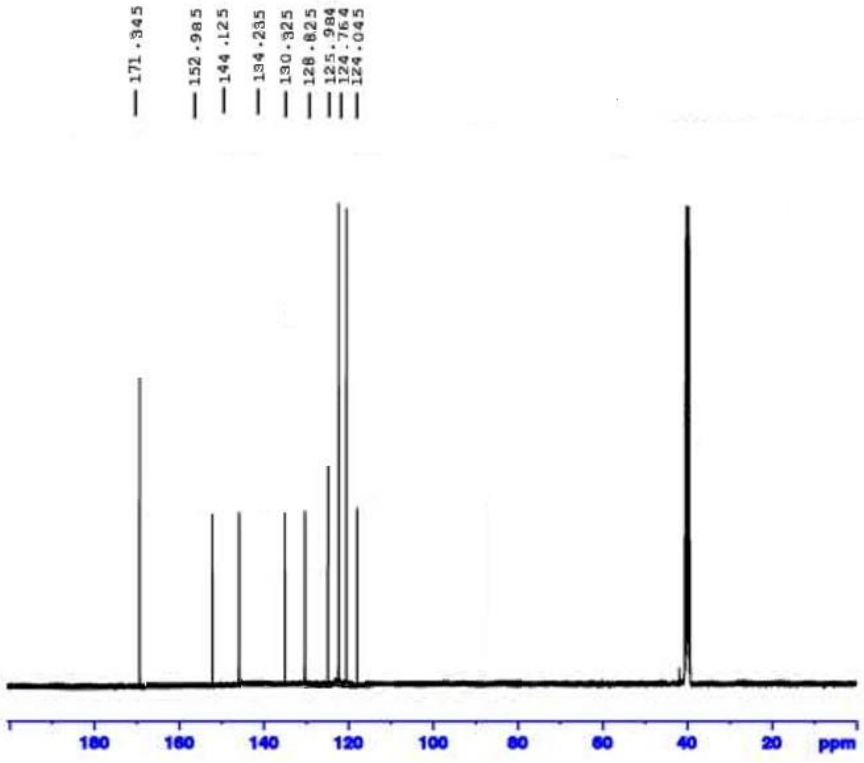

Fig. SI-13. ^{13}C NMR spectrum of L3 in DMSO-d6.

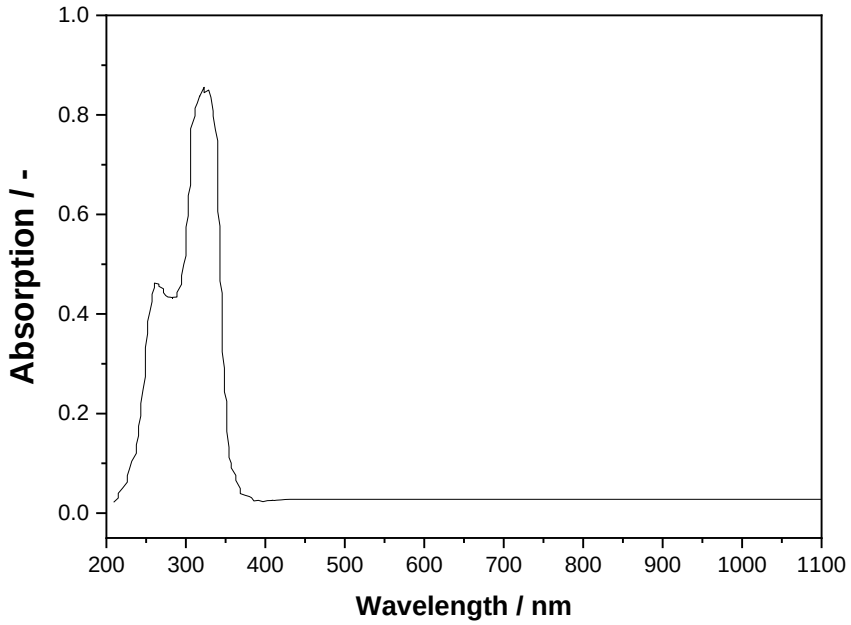

Fig. SI-14. UV-Vis absorption spectrum of L1 in DMSO solvent.

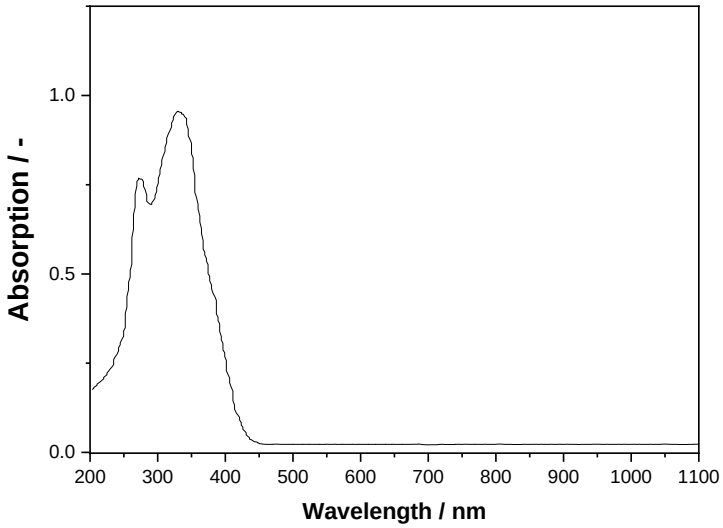

Fig. SI-15. UV-Vis absorption spectrum of L2 in DMSO solvent.

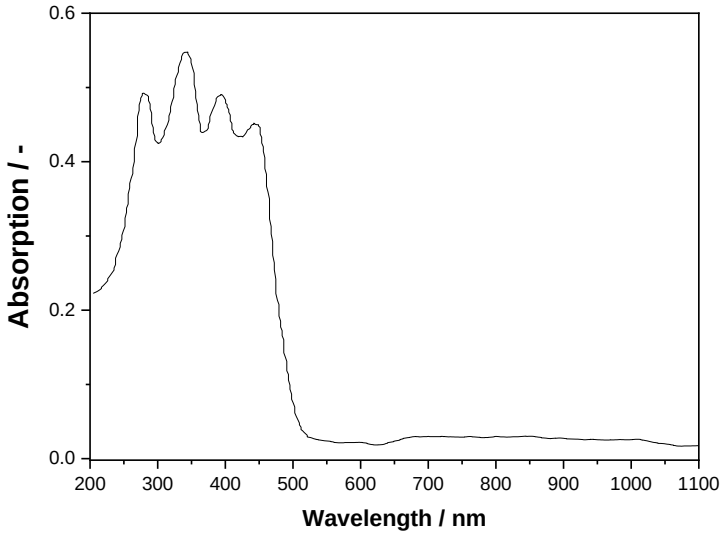

Fig. SI-16. UV-Vis absorption spectrum of Z1 in DMSO solvent.

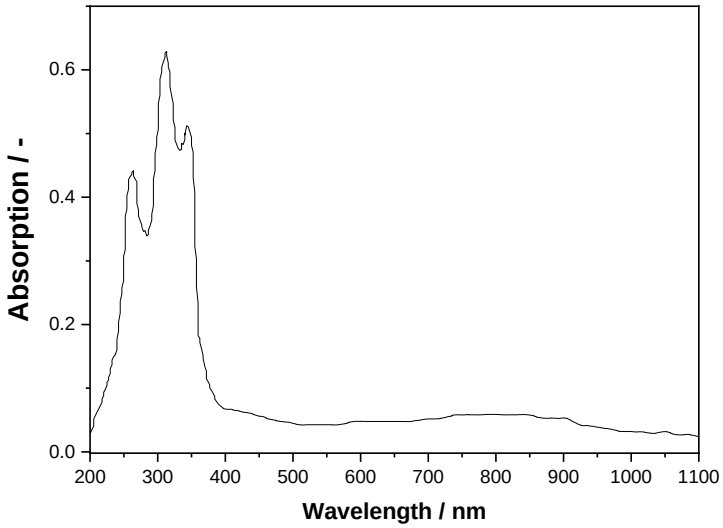

Fig. SI-17. UV-Vis absorption spectrum of Z2 in DMSO solvent.

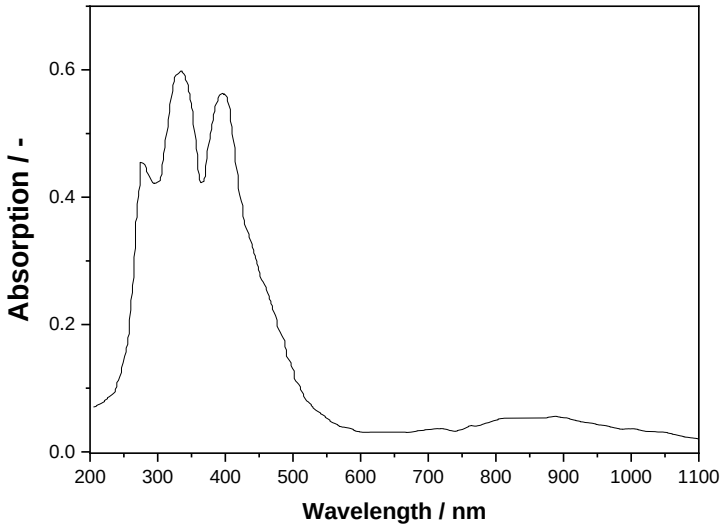

Fig. SI-18. UV-Vis absorption spectrum of Z4 in DMSO solvent.

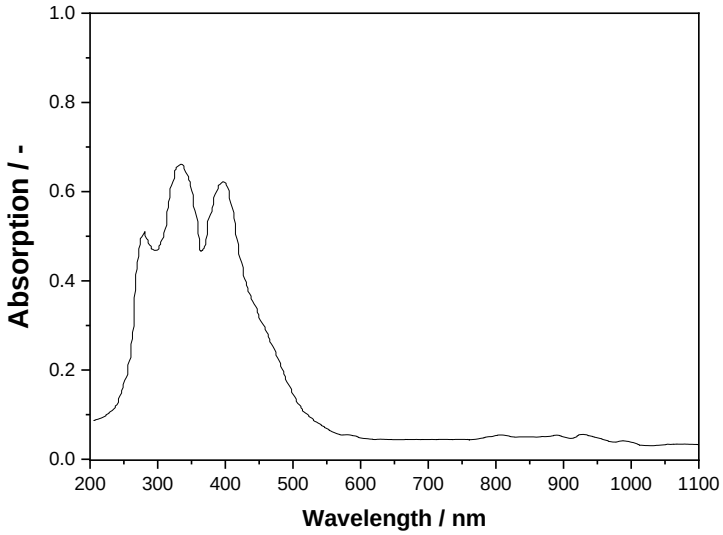

Fig. SI-19. UV-Vis absorption spectrum of Z6 in DMSO solvent.

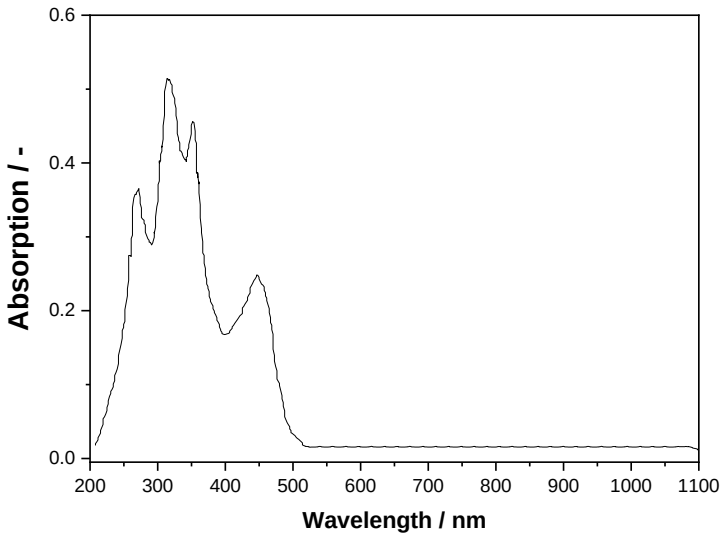

Fig. SI-20. UV-Vis absorption spectrum of Z7 in DMSO solvent.

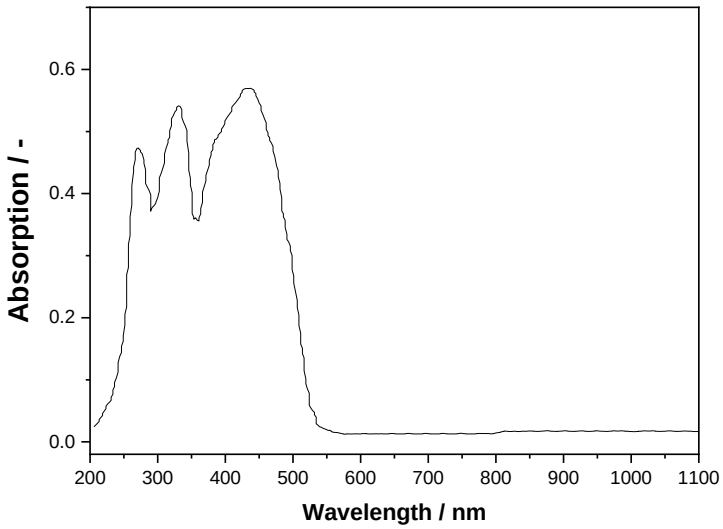

Fig. SI-21. UV-Vis absorption spectrum of Z8 in DMSO solvent.

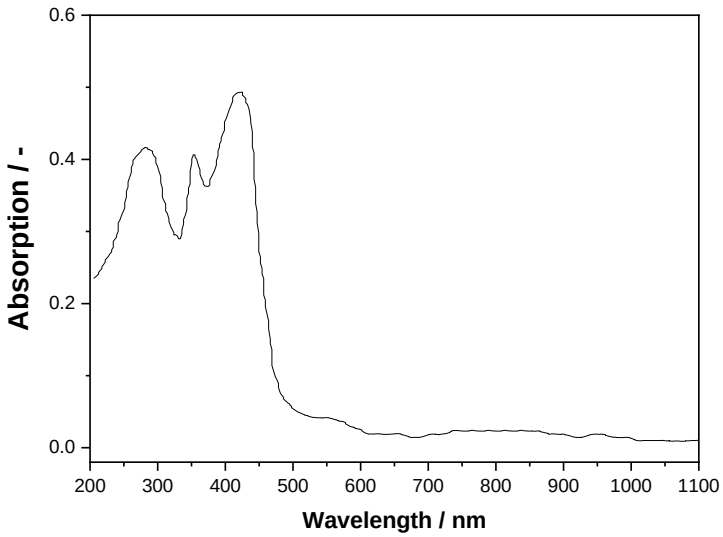

Fig. SI-22. UV-Vis absorption spectrum of Z9 in DMSO solvent.

Table SI-1. The docking interaction data calculations of the ligands L1, L2 and L3 with the active sites of the receptor of Human DNA Topoisomerase I (70 Kda) (PDB ID: 1SC7).

Compound	Binding Energy (kcal/mol)	Inhibition Constant (Ki)	Receptor site	Compound site	Interaction	Distance (Å)
L1	-8.13	1.09 μM	C:TGP11:H22	N	H-Bond	2.87
			A:ARG364:HH12	O	H-Bond	2.83
			A:ARG364:HH22	O	H-Bond	2.02
			A:ARG364:HH21	O	H-Bond	1.94
			D:DA113:O4'	H	H-Bond	2.38
			D:DC112:O2	H	H-Bond	2.20
			B:DT10	Phenyl ring	Pi-Pi Stacked[a]	4.42
			C:TGP11	Phenyl ring	Pi-Pi Stacked[a]	4.00
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.57
			D:DA113	Phenyl ring	Pi-Pi Stacked[a]	4.40
			C:TGP11	Diazole ring	Pi-Pi Stacked[a]	4.05
			D:DC112	Diazole ring	Pi-Pi Stacked[a]	4.88
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.53
L2	-7.45	3.46 μM	A:LYS425:HZ3	O	H-Bond	1.71
			A:GLU356:OE1	H	H-Bond	1.86
			B:DT10	p-disubstituted benzene ring	Pi-Pi Stacked[a]	3.92
			C:TGP11	p-disubstituted benzene ring	Pi-Pi Stacked[a]	4.30
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	4.22
			D:DA113	p-disubstituted benzene ring	Pi-Pi Stacked[a]	5.26
			C:TGP11	Diazole ring	Pi-Pi Stacked[a]	3.36
			D:DC112	Diazole ring	Pi-Pi Stacked[a]	5.42
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.66
L3	-8.37	731.62 nM	A:ARG364:HH12	N	H-Bond	2.60
			A:LYS425:HZ3	O	H-Bond	1.66

			A:GLU356:OE1	H	H-Bond	1.97
			B:DT10	Chloro-benzene ring	Pi-Pi Stacked[a]	3.98
			C:TGP11	Chloro-benzene ring	Pi-Pi Stacked[a]	4.13
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.84
			D:DA113	Chloro-benzene ring	Pi-Pi Stacked[a]	4.47
			C:TGP11	Diazole ring	Pi-Pi Stacked[a]	3.79
			D:DC112	Diazole ring[b]	Pi-Pi Stacked[a]	4.96
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.66
			B:DT10	Cl (Chloro-benzene ring)	Pi-halaid[a]	3.45

a: Hydrophobic

Table SI-2. The docking interaction data calculations of the complexes Z4, Z5 and Z6 with the active sites of the receptor of Human DNA Topoisomerase I (70 Kda) (PDB ID: 1SC7).

Complex	Binding Energy (kcal/mol)	Inhibition Constant (Ki)	Receptor site	Compound site	Interaction	Distance (Å)
Z4	-8.66	446.42 nM	A:LYS425:NZ	o-disubstituted benzene ring	Pi-cation[b]	4.38
			B:DT10	Phenyl ring	Pi-Pi Stacked[a]	3.72
			C:TGP11	Phenyl ring	Pi-Pi Stacked[a]	4.59
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.97
			D:DA113	Phenyl ring	Pi-Pi Stacked[a]	4.85
			C:TGP11	Diazole ring	Pi-Pi Stacked[a]	3.62
			D:DC112	Diazole ring	Pi-Pi Stacked[a]	5.48
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.45
			C:TGP11	Cl	Pi-halaid[a]	5.15
			A:LYS425	o-disubstituted benzene ring	Pi-alkyl[a]	5.02
Z5	-8.74	392.11 nM	A:ARG364:HH12	N	H-Bond	3.04
			A:ARG364:HH22	N	H-Bond	1.86
			C:TGP11:O4'	H	H-Bond	2.29
			A:LYS425:NZ	o-disubstituted benzene ring	Pi-cation[b]	4.15
			B:DT10	p-disubstituted benzene ring	Pi-Pi Stacked[a]	4.30
			C:TGP11	p-disubstituted benzene ring	Pi-Pi Stacked[a]	3.95
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.76
			D:DA113	p-disubstituted benzene ring	Pi-Pi Stacked[a]	4.42
			C:TGP11	Diazole ring	Pi-Pi Stacked[a]	3.90

			D:DC112	Diazole ring	Pi-Pi Stacked[a]	4.78
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.72
			C:TGP11	Cl	Pi-halaid[a]	5.27
			A:LYS425	o-disubstituted benzene ring	Pi-alkyl[a]	4.491
Z6	-9.22	173.08 nM	A:ARG364:HH12	N	H-Bond	3.00
			A:ARG364:HH22	N	H-Bond	1.85
			A:LYS425:NZ	o-disubstituted benzene ring	Pi-cation[b]	4.13
			B:DT10	p-disubstituted benzene ring	Pi-Pi Stacked[a]	4.21
			C:TGP11	p-disubstituted benzene ring	Pi-Pi Stacked[a]	4.10
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.73
			D:DA113	p-disubstituted benzene ring	Pi-Pi Stacked[a]	4.33
			C:TGP11	Diazole ring	Pi-Pi Stacked[a]	3.92
			D:DC112	Diazole ring	Pi-Pi Stacked[a]	4.83
			D:DA113	Diazole ring	Pi-Pi Stacked[a]	3.66
			B:DT10	Cl (Chloro-benzene ring)	Pi-halaid[a]	3.69
			A:LYS425	o-disubstituted benzene ring	Pi-alkyl[a]	4.47

a: Hydrophobic, b: Electrostatic

Table SI-3. Infrared absorption (cm^{-1}) data observed and calculated for the ligands (L1-L3) and complexes (Z1-Z9).

Compound	ν(C=N) imine	ν(C-O) oxadiazole	ν(OH)	ν(M-N)	ν(M-O)
L1	1678 (1668)[a]	1262 (1269)[a]	3325 (3540)[a]	-	-
L2	1674 (1672)[a]	1268 (1269)[a]	3330 (3539)[a]	-	-
L3	1677 (1668)[a]	1270 (1269)[a]	3347 (3540)[a]	-	-
Z1	1658 (1638)[a]	1260 (1241)[a]	-	465 (445)[a]	554 (553)[a]
Z2	1656 (1639)[a]	1249 (1244)[a]	3340 (3562)[a]	445 (456)[a]	521 (538)[a]
Z3	1660 (1637)[a]	1259 (1243)[a]	-	456 (448)[a]	567 (562)[a]
Z4	1656 (1635)[a]	1261 (1257)[a]	-	462 (459)[a]	550 (544)[a]
Z5	1661 (1631)[a]	1255 (1258)[a]	3337 (3563)[a]	432 (427)[a]	543 (543)[a]
Z6	1658 (1646)[a]	1250 (1247)[a]	-	456 (460)[a]	563 (557)[a]
Z7	1657 (1655)[a]	1252 (1246)[a]	-	466 (463)[a]	560 (556)[a]
Z8	1655 (1631)[a]	1251 (1259)[a]	3335 (3563)[a]	476 (475)[a]	567 (554)[a]
Z9	1659 (1647)[a]	1256 (1260)[a]	-	467 (469)[a]	564 (564)[a]

[a]: Calculated value, ν: stretching; M: the corresponding metal.

Table SI-4. Values of DNA linking constant for (Z1–Z9) complexes.

Complexes	$K_b \times 10^3 (M^{-1})$	$K_{sv} \times 10^2 (M^{-1})$
Z1	*0.85*	*0.44*
Z2	*0.98*	*1.08*
Z3	*1.88*	*0.79*
Z4	*2.12*	*1.54*
Z5	*2.82*	*1.76*
Z6	*1.91*	*1.31*
Z7	*1.78*	*1.10*
Z8	*1.48*	*0.57*
Z9	*1.24*	*0.65*

Table SI-5. IC50 data of compounds with cancer cells of (A549), (HCT-15), and (HeLa)

IC_{50} values (nM)			
Compounds	Cervical (HeLa)	Colon (HCT-15)	Lung (A549)
L1	-	-	-
L2	-	-	-
L3	-	-	-
Z1	>900	854.1	>900
Z2	876.4	6873	794
Z3	456.3	709	847.5
Z4	>1000	543.3	432.4
Z5	987.4	456.1	854.5
Z6	>900	678.0	954.3
Z7	796.4	343.2	>900
Z8	890.4	765.6	865.5
Z9	>800	830.1	992.7
Cisplatin	421.4	512.3	355

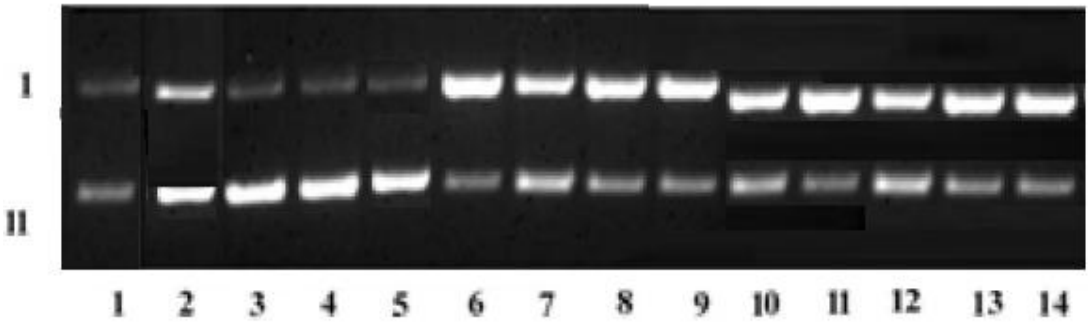

Fig. S23. Changes pattern in the electrophoretic of C-T DNA and complexes. Lane 1, DNA alone; lane 2, DNA + control ; lane 3, DNA + L1; lane 3, DNA + L2; lane 4, DNA + L3; lane 5, DNA + Z1; lane 6, DNA + Z2; lane 7, DNA + Z3; lane 8, DNA + Z4; lane 9, DNA + Z5; lane 10, DNA + Z6; lane 11, DNA + Z7; lane 12, DNA + Z8; lane 13, DNA + Z9.

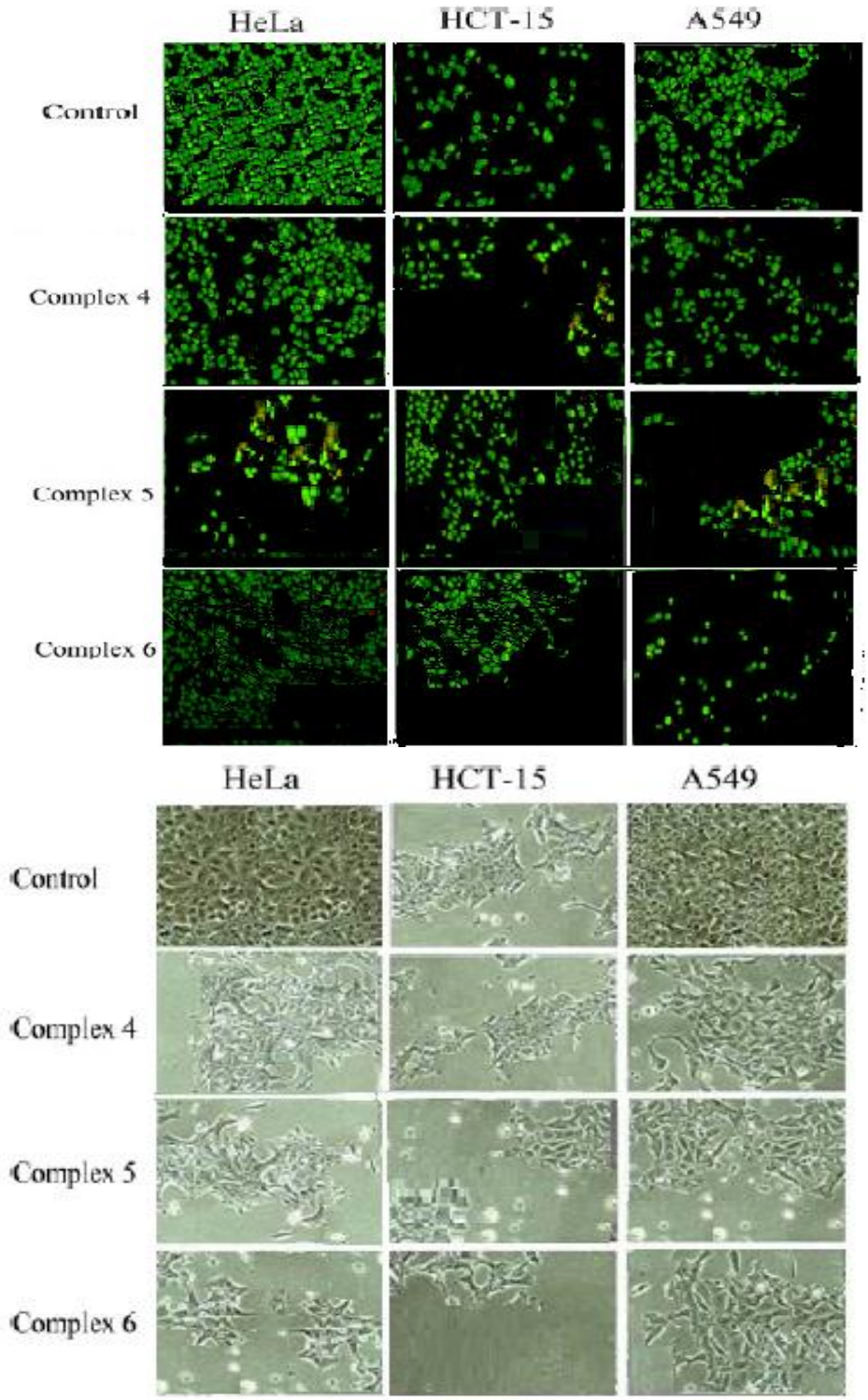

Fig. S24. (a) The morphological changes for cancer cells remedied with IC50 concentrations of (Z4-Z6). **(b)** Image of Live cell of cancer cells remedied with the same complexes.