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Copper(II) complexes based on levofloxacin and 2N-donor ligands: synthesis, crystal structures and *in vitro* biological evaluation

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Supplementary material file

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Crystallographic data

Table S1. Crystallographic data collection and structural refinement parameters for complexes **1** and **2**.

	(1)	**(2)**
Formula	$C_{28}H_{29}Cl_3CuFN_6O_4$	$C_{42}H_{36}Cl_3CuFN_5O_4$
M_w	702.46	863.65
T (K)	298	293 (2)
Crystal system	monoclinic	triclinic
Space group	P 21/n	P -1
a, Å	15.1992 (16)	12.5234(11)
b, Å	13.4765 (11)	13.0688(14)
c, Å	15.5358 (17)	13.2794(12)
α (°)	90	101.577 (8)
β (°)	103.078 (11)	108.055 (8)
γ (°)	90	94.122 (8)
Volume Å^3	3099.7 (6)	2003.2 (3)
Z	4	2
Z`	1	1
$D_{calc.}$/g cm^{-3}	1.505	1.432
μ/mm^{-1}	1.013	0.799
Crystal size/mm^3	0.09×0.08×0.07	0.09×0.07×0.06
Colour	Blue	Light green
Wavelength/Å	0.71073	0.71073
Radiation type	MoKα	MoKα
Θ_{min}/°	3.310	3.425
Θ_{max}/°	26.369	25.681
Measured Refl	41879	25765
Independent Refl.	6335	7589
Reflections with I >2(I)	4140	4868
R_{int}	0.0773	0.0919
Parameters	431	534
Restraints	109	24
Largest Peak	0.483	1.399
Deepest Hole	-0.408	-0.895
GooF	1.049	1.069
wR_2 (all data)	0.1828	0.3031
wR_2	0.1625	0.2669
R_1 (all data)	0.1073	0.1410
R_1	0.0696	0.1014

Table S2. Hydrogen bonding interactions in the structures of the complexes **1** and **2**.

D−*H*·····A	*D*(*D*·····*H*) (Å)	*d*(*H*·····*A*) (Å)	*d*(*D*·····*A*) (Å)	<(*DHA*) (º)
[Cu(*lvx*)(bipyam)Cl]$^{+}$, **(1)**				
C(27)−H(27B)·····O(4)	0.971	2.346	2.841	110.91
C(3)−H(3A)·····O(3)	0.930	2.313	3.114	144.09
N(3)−H(3)·····Cl(0A)	0.931	2.356	3.231	156.23
C(28)−H(28B)·····Cl(1)	0.959	3.196	3.443	96.67
[Cu(*lvx*)(BPhen)Cl]$^{+}$, **(2)**				
C(32)−H(32B)·····Cl(1)	0.970	2.006	3.397	132.52
C(2)−H(2)·····O(3)	0.929	2.461	3.217	136.31
C(41)−H(41B)·····O(4)	0.970	2.419	2.871	108.00
N(5)−H(5)·····Cl(2)	0.980	2.004	2.995	163.09
C(7)−H(7)·····Cl(3)	0.930	2.617	3.349	136.00

Table S3. The BSA and HSA binding parameters (Ksv, kq, K, *n*) derived for Cu(II) complexes at two different temperature 30 and 35ºC.

Complexes	**T (ºC)**	**$K_{SV} \times 10^5$ (M^{-1})**	**$kq \times 10^{13}$ ($M^{-1}s^{-1}$)**	**$K \times 10^5$ (M^{-1})**	***n***
		BSA			
1	30	4.31±0.01	4.31±0.01	2.88±0.02	1.05±0.03
	35	3.36±0.01	3.36±0.01	2.42±0.01	0.69±0.04
2	30	10.58±0.02	10.58±0.02	6.43±0.03	1.21±0.02
	35	5.37±0.02	5.37±0.02	5.82±0.06	1.35±0.03
		HSA			
1	30	7.89±0.01	7.89±0.01	1.2±0.04	0.82±0.05
	35	7.42±0.02	7.42±0.02	1.1±0.02	1.13±0.03
2	30	1.12±0.01	1.12±0.01	0.69±0.01	1.45±0.01
	35	1.09±0.01	1.09±0.01	0.41±0.02	1.56±0.02

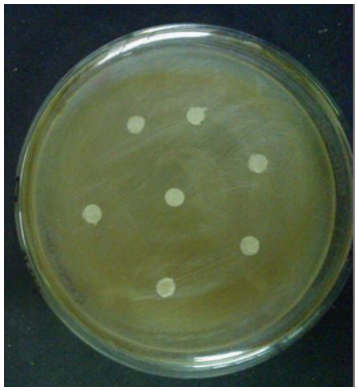
Table S4. Antibacterial assay of the compounds (*lvx* and complexes **1** and **2**) against *Gram*(+) positive bacterial pathogens.

Test pathogens	Concentration (μg/disc)	Compounds			Standard drug	Control DMSO (10μL/disc)
		lvx	*Complex **1***	*Complex **2***	*Neomycin sulfate*	
Staphylococcus aureus	10	0.7	1.0	1.2	1.4	–
	20	1.1	1.6	1.7	1.9	
	30	1.3	1.9	2.1	2.3	
	40	1.7	2.6	2.9	3.2	
	50	2.5	3.2	3.3	3.5	
	60	3.0	3.4	3.6	3.9	
Bacillus subtilis	10	0.5	1.2	1.0	1.4	–
	20	1.0	1.5	1.5	1.8	
	30	1.4	1.9	1.9	2.1	
	40	1.8	2.4	2.3	2.5	
	50	2.0	3.0	2.8	3.2	
	60	2.5	3.3	3.1	3.5	
Enterococcus faecalis	10	0.9	1.3	1.2	1.5	–
	20	1.2	1.6	1.5	1.8	
	30	1.4	2.0	1.8	2.2	
	40	2.0	2.3	2.2	2.4	
	50	2.6	2.8	2.5	2.9	
	60	2.8	3.0	2.8	3.2	
Streptococcus pneumonia	10	1.2	1.5	1.7	1.8	–
	20	1.5	2.1	2.2	2.3	
	30	1.8	2.6	2.8	3.0	
	40	2.3	2.9	3.1	3.3	
	50	2.8	3.2	3.5	3.6	
	60	3.0	3.6	3.7	4.0	

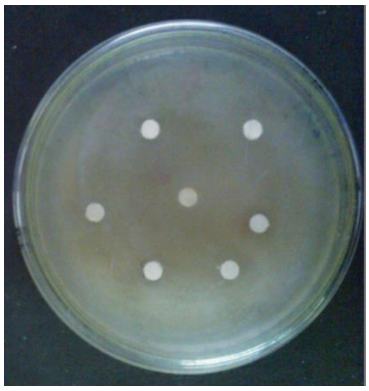
Table S5. Antibacterial assay of the compounds (*lvx* and complexes **1** and **2**) against *Gram*(−) bacterial pathogens.

Test pathogens	Concentration (μg/disc)	Compounds			Standard drug	Control DMSO (10 μL/disc)
		lvx	*Complex **1***	*Complex **2***	Neomycin sulfate	
Proteus mirabilis	10	1.1	1.4	1.3	1.5	–
	20	1.4	2.0	1.5	2.1	
	30	1.6	2.1	1.8	2.3	
	40	2.0	2.3	2.5	2.7	
	50	2.1	2.3	2.5	2.9	
	60	2.6	2.8	3.0	3.2	
Shigella flexneri	10	0.8	1.1	1.3	1.4	–
	20	1.2	1.4	1.5	1.7	
	30	1.7	1.8	1.9	2.1	
	40	2.0	2.3	2.2	2.5	
	50	2.4	2.5	2.9	3.1	
	60	2.7	2.8	3.2	3.4	
Escherichia coli	10	1.3	1.6	1.7	1.9	–
	20	1.6	1.8	1.8	2.1	
	30	2.1	2.3	2.5	2.7	
	40	2.5	3.1	3.2	3.3	
	50	3.4	3.7	3.8	4.0	
	60	3.6	4.0	4.1	4.2	
Citrobacter species	10	1.4	1.6	1.6	1.9	–
	20	1.7	2.0	1.9	2.5	
	30	2.4	2.5	2.6	3.0	
	40	2.6	2.8	2.9	3.8	
	50	3.3	3.4	3.6	3.9	
	60	3.5	3.7	3.8	4.1	
Salmonella typhi	10	1.2	1.3	1.4	1.5	–
	20	1.6	1.8	1.9	2.2	
	30	2.0	2.2	2.4	2.6	
	40	2.6	2.9	2.8	3.0	
	50	3.2	3.4	3.5	3.6	
	60	3.4	3.7	3.6	3.9	

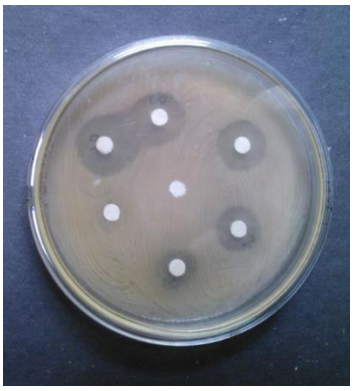
Antibacterial Activity



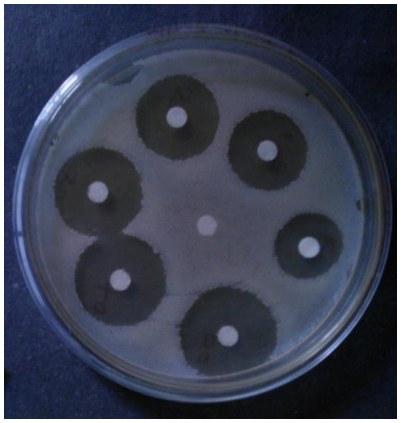
Metal salts ($CuCl_2.2H_2O$)



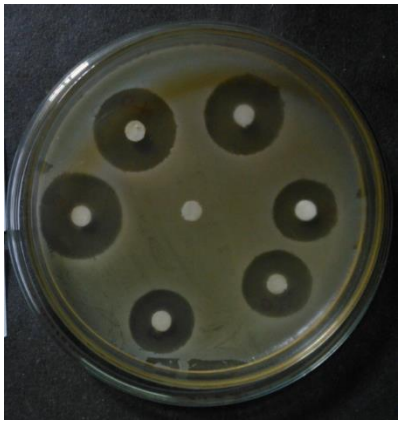
DMSO as control (No effect)



Effect of *lvx* on *S. flexneri*



Complex **1** over *E.Coli*



Complex **2** over *E.Coli*

Scheme 2. The *in vitro* antibacterial screening of metal salts ($CuCl_2.2H_2O$), *lvx* and copper (II) complexes against *Gram*(+) and *Gram*(−) microorganisms.

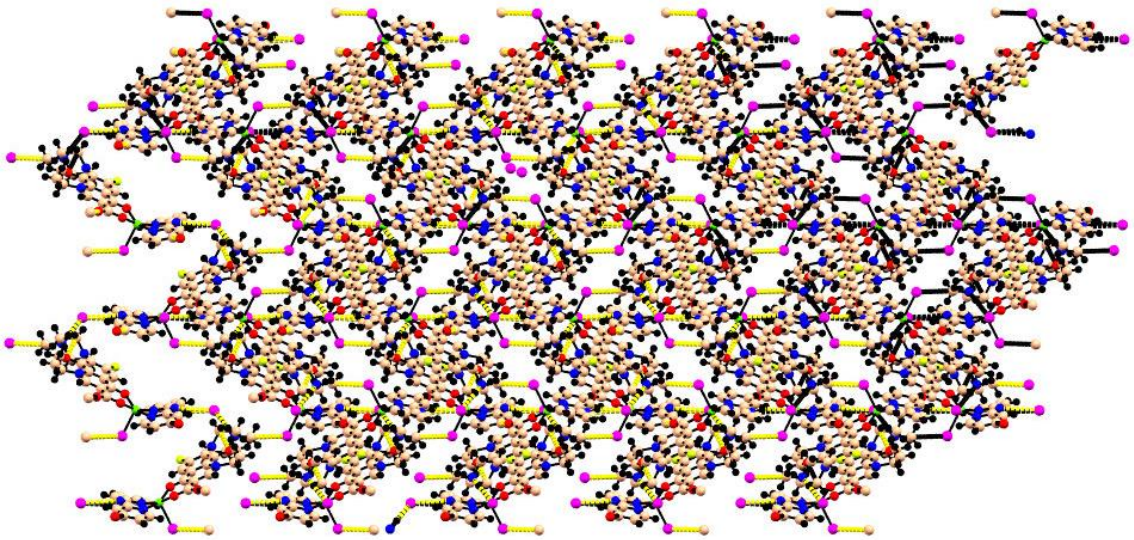


Fig. S1. Intermolecular hydrogen bonding interactions in complex **(1)** leading to the formation of cage-like structure.

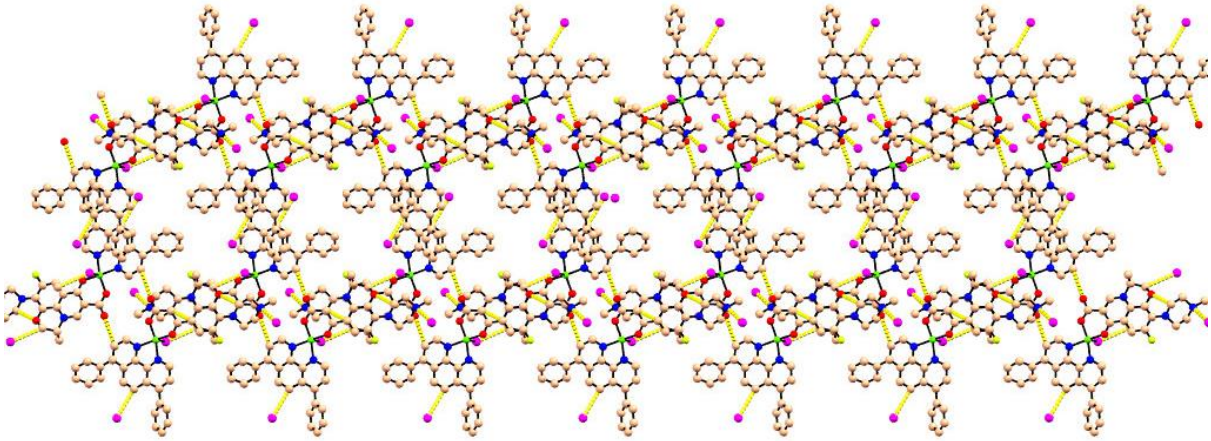


Fig. S2. Intermolecular hydrogen bonding interactions in complex **(2)** leading to the formation of sheet-like structure.

1. Mass Spectrum analysis

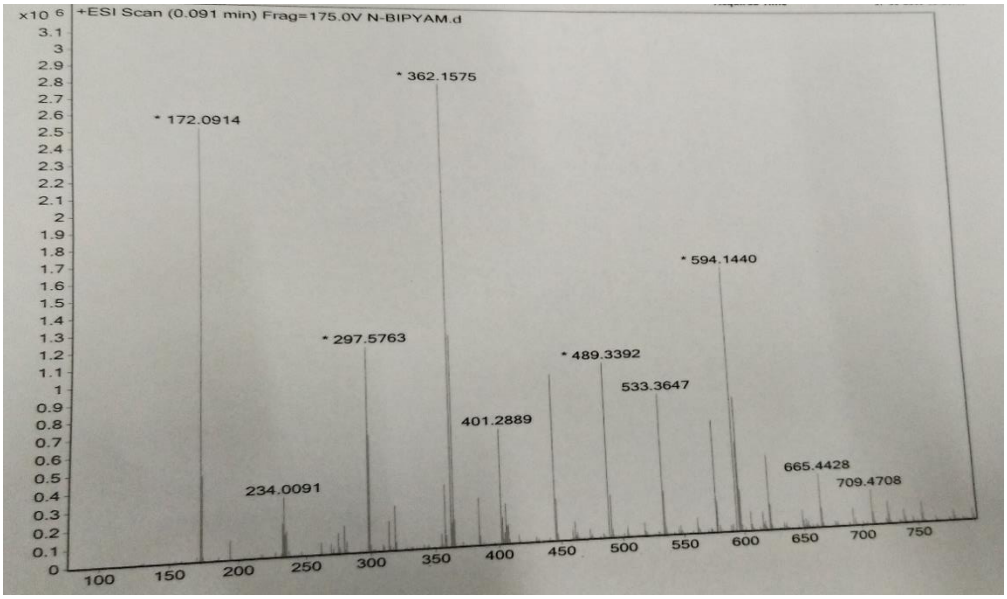


Fig. S3. ESI-MS spectrum of complex **1**.

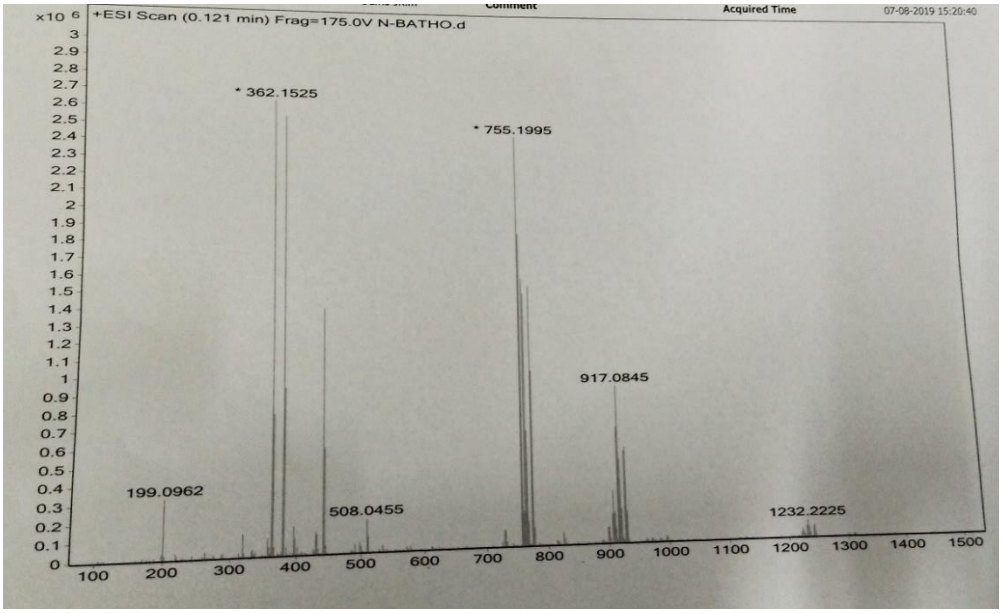


Fig. S4. ESI-MS spectrum of complex **2**.

2. LC-MS analysis

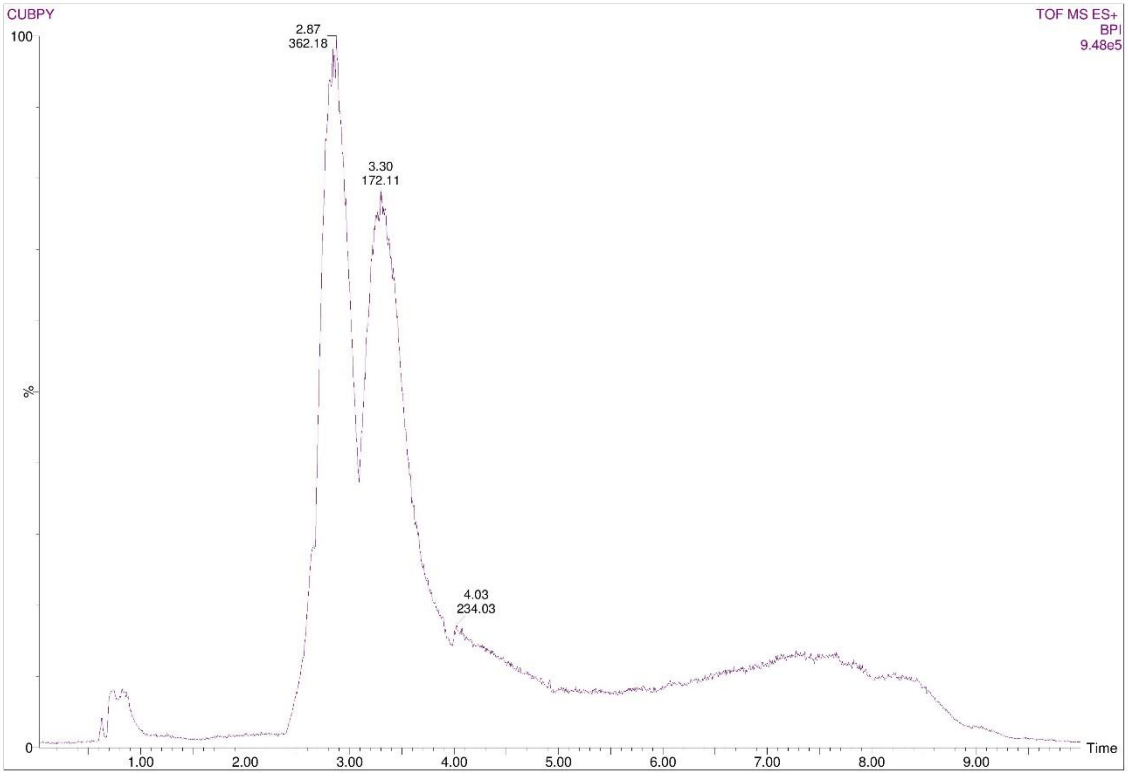


Fig. S5. LC-MS chromatography of the complex **1**.

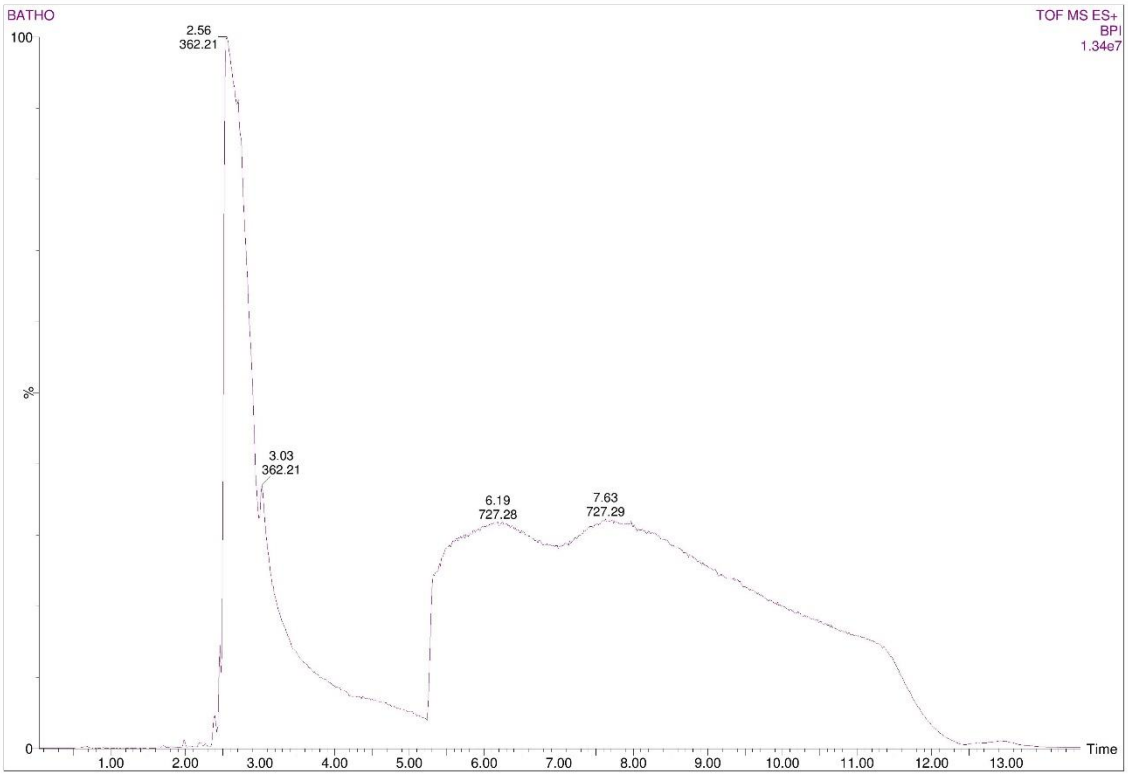


Fig. S6. LC-MS chromatography of the complex **2**.

3. Stabiity and solubiliy

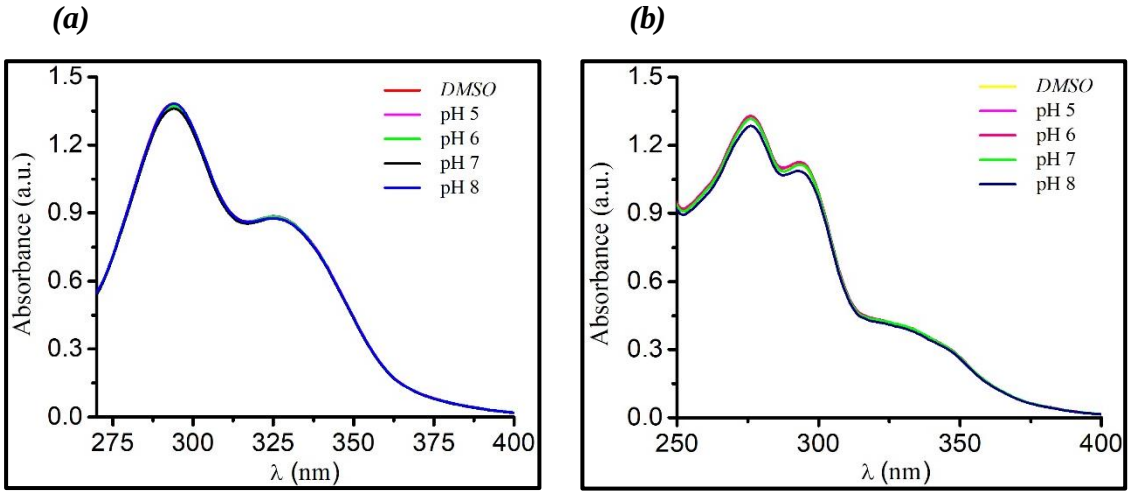


Fig. S7. The stability plots of complexes **(a)** [Cu(*lvx*)(bipyam)Cl]$^{+}$, **(1)** and **(b)** [Cu(*lvx*)BPhen)Cl]$^{+}$, **(2)** in DMSO and different pH range (5-8).

4. DNA binding studies

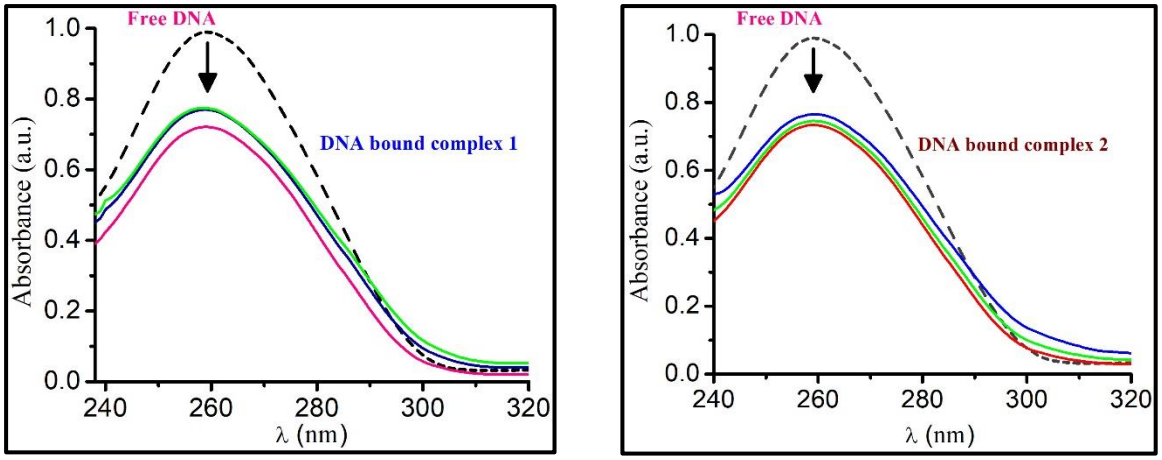


Fig. S8. UV spectra of CT DNA solution (90 μM) in buffer solution (150 mM NaCl and 15mM trisodium citrate at pH 7.2) were recorded in the absence as well presence of the increasing concentrations of the complexes ***(a)*** [Cu(*lvx*)(bipyam)Cl]$^{+}$, **(1)** and ***(b)*** [Cu(*lvx*)(BPhen)Cl]$^{+}$, **(2)**. The arrows represents the changes occurs during the addition of the complexes.

5. Cyclic voltammetry

(a) ***(b)***

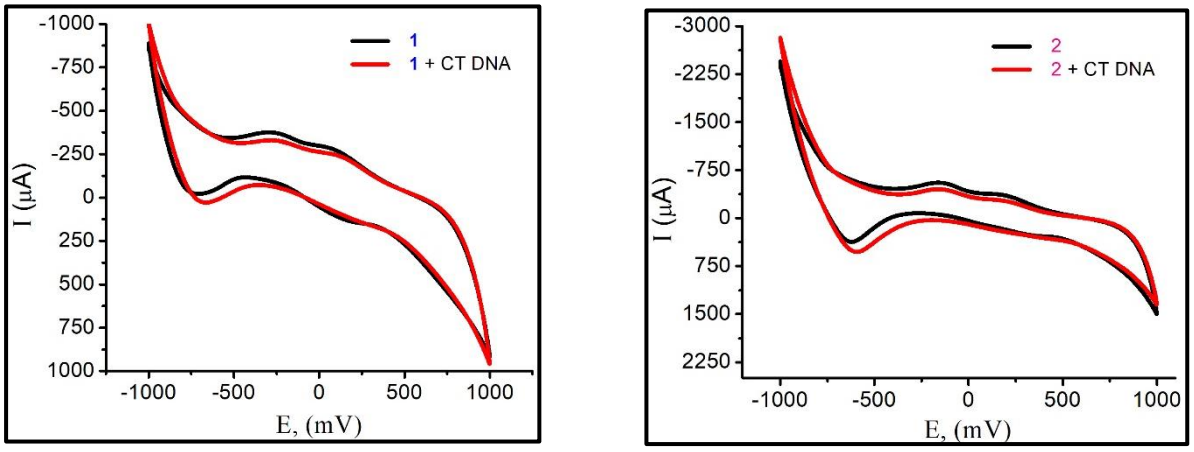


Fig. S9. Cyclic voltammogram of 0.5 mM 1:2 dmso:buffer solution of ***(a)*** [Cu(*lvx*)(bipyam)Cl]$^{+}$, **(1)** and ***(b)*** [Cu(*lvx*)(BPhen)Cl]$^{+}$, **(2)** in the absence as well as in the presence of CT DNA. Scan rate = 100 mV s-1. Supporting electrolyte = buffer solution.

6. *Ethidium Bromide*

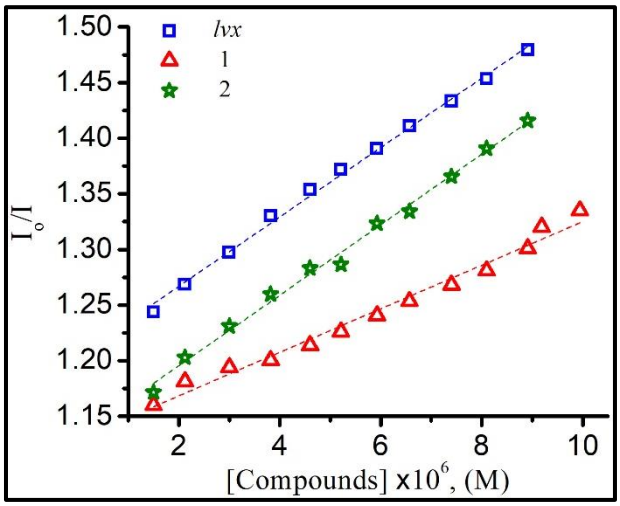


Fig. S10. *Stern-Volmer* quenching plots of EB bound to CT DNA for *lvx* and complexes **(1)** or **(2)**.

7. *Proteins binding studies*

a. *Stern-Volmer quenching plots at 25 ºC*

(a) **(b)**

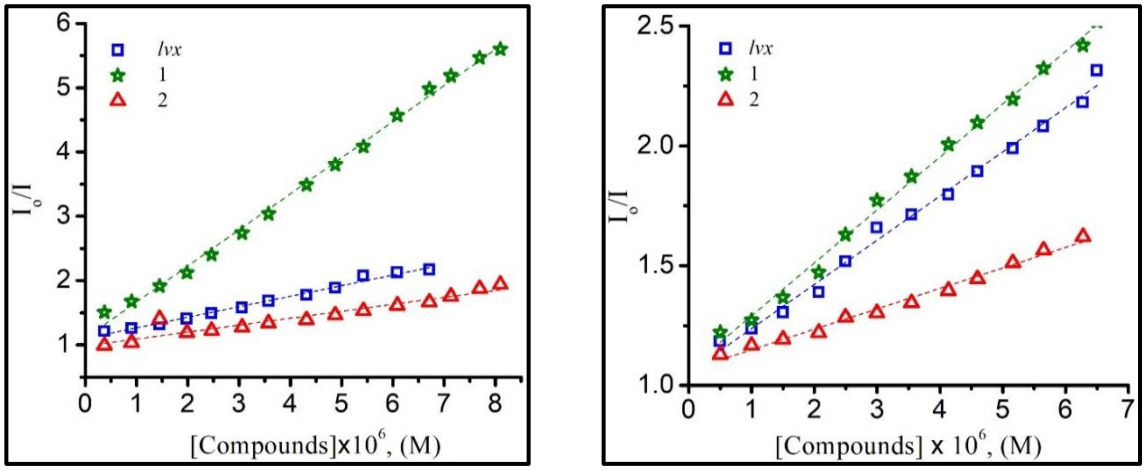


Fig. S11. *Stern-Volmer* quenching plots of **(a)** BSA **(b)** HSA for *lvx* and complexes **(1)** or **(2)** at 25 ºC.

b. *Scatchard plots at 25 ºC*

(a) **(b)**

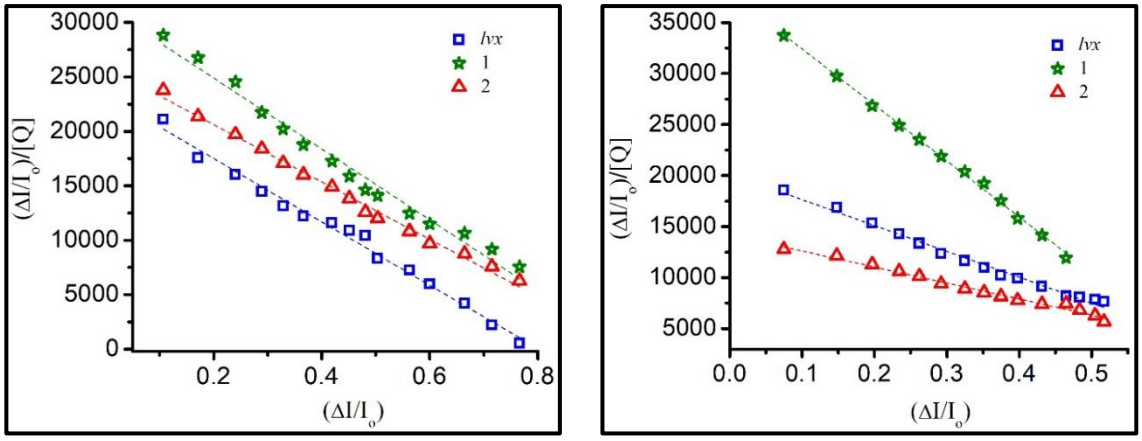


Fig. S12. *Scatchard* plots of **(a)** BSA **(b)** HSA for *lvx* and complexes **(1)** and **(2)** at 25 ºC.

c. Scatchard plots at two different temperatures at 30 and 35 ºC

(a) **(b)**

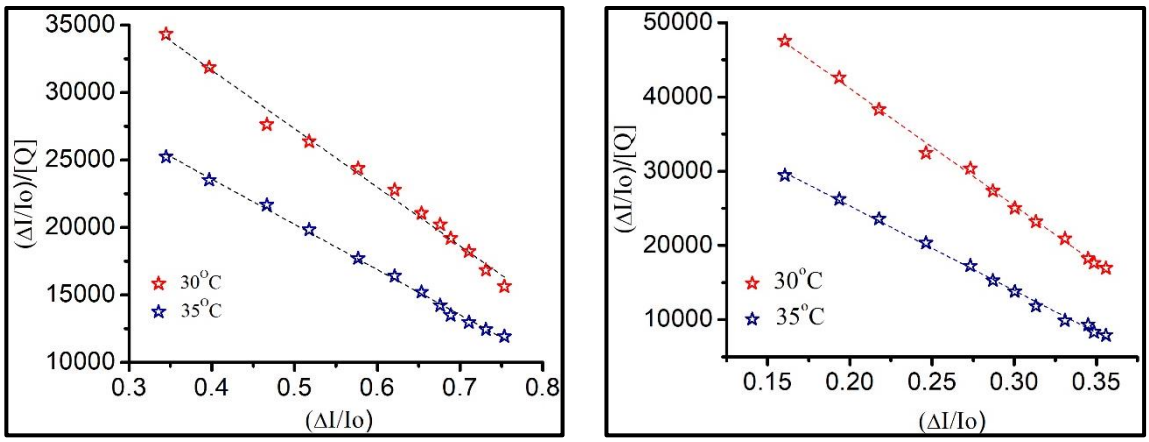


Fig. S13. *Scatchard* plots of BSA for **(a)** complex **(1)** and **(b)** complex **(2)** at two different temperature 30 and 35ºC.

(a) **(b)**

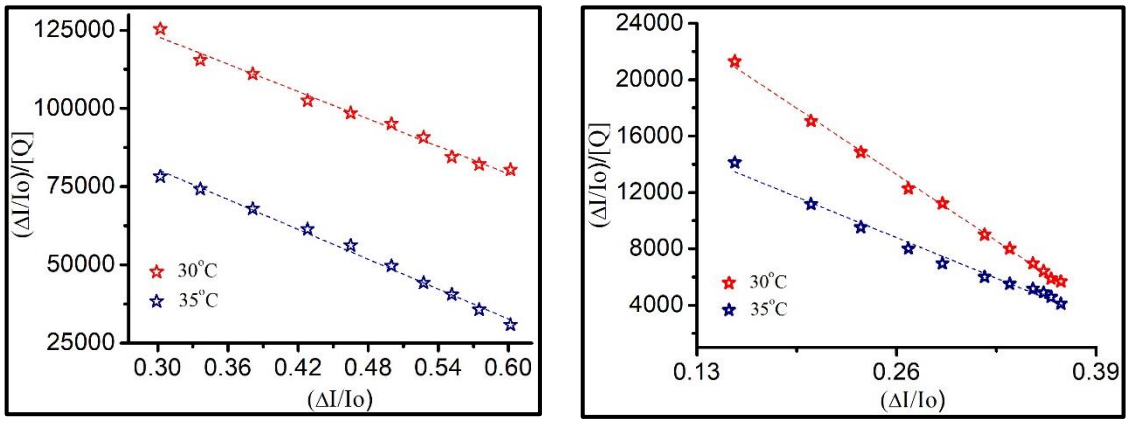


Fig. S14. *Scatchard* plots of HSA for **(a)** complex **(1)** and **(b)** complex **(2)** at two different temperature 30 and 35ºC.

8. *van't Hoff plots*

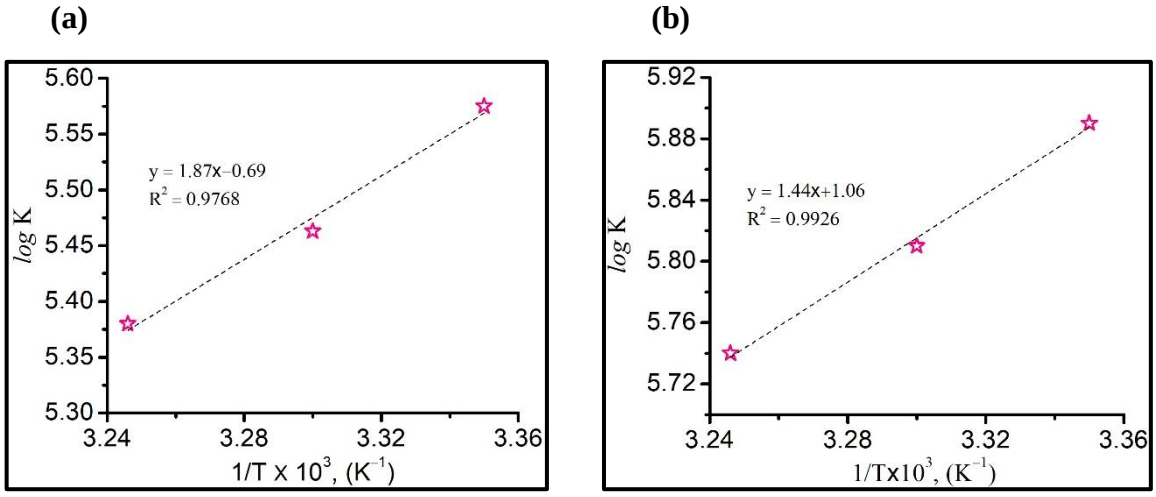


Fig. S15. The van't Hoff plots for the binding of BSA to the **(a)** complex **(1)** and **(b)** complex **(2)** at 298, 303, and 308 K (25, 30 and 35 ºC).

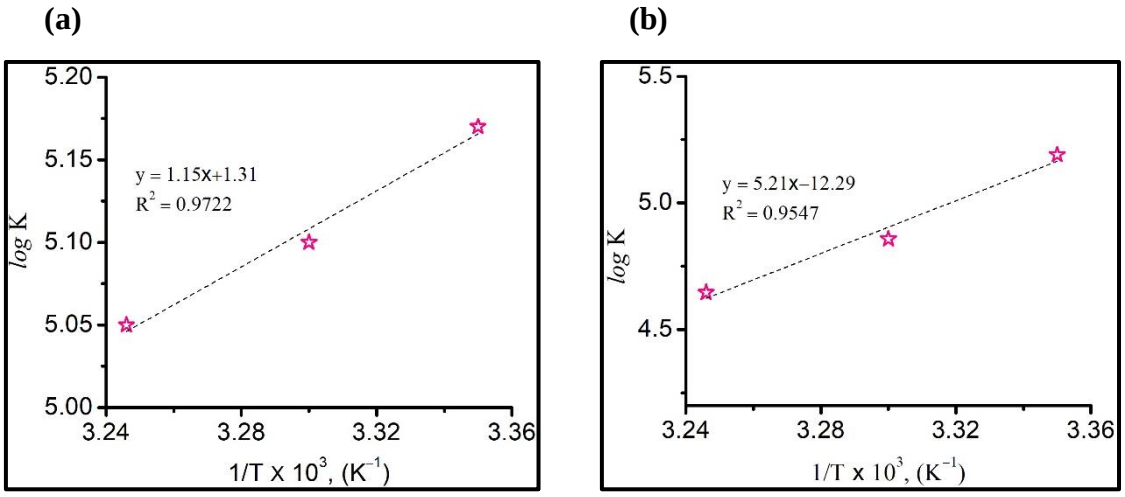


Fig. S16. The van't Hoff plots for the binding of HSA to the **(a)** complex **(1)** and **(b)** complex **(2)** at 298, 303, and 308 K (25, 30 and 35 ºC).