Hybrid thiazolyl-benzylidene-phenol metal complexes as novel chemotherapeutic agents with anti-topoisomerase 1 activity in human breast carcinoma: Synthesis, *in vitro* and *in silico* studies

Ahmed Z. Alharbi[1], Mona Katary[2], Khulud M. Alshehri[3], Basim H. Asghar[4], Mohmed M. Omran[5], Reda F. M. Elshaarawy[6,7], Amira Mili[8], Hani S. Hafez[9*], Rozan Zakrya[10]

[1] Department of Biology, Faculty of Science, University College of Taymaa, University of Tabuk, Tabuk 71491, Saudi Arabia; aawaji@ut.edu.sa

[2] Biology Department, Faculty of Science, King Khalid University, 9004 Abha, Saudi Arabia; hebaalhamdi@yahoo.com

[3] Chemistry department, Faculty of Science, Port-Said University, Port-Said, Egypt; monakatary@gmail.com, rzakrya@yahoo.com

[4] Department of Biology, Al-Baha University, Saudi Arabia; kalshehri@bu.edu.sa

[5] Chemistry department, Faculty of Science, Helwan University, Helwan, Egypt. Mohmed.Omran@gmail.com

[6] Chemistry Department, Faculty of Science, Alexandria University, Alexandria, Egypt. amanyassem111@gmail.com

[7] Zoology Department, Faculty of Science, Suez University 43533 Suez, Egypt. hani.hafez@suezuniv.edu.eg.

[8] Department of Chemistry, Faculty of Science, Suez University, 43533 Suez, Egypt. reda.elshaarawy@suezuniv.edu.eg.

[9] Institut für Anorganische Chemie und Strukturchemie, Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany.

***** Correspondence: Hani S. Hafez, hani.hafez@suezuniv.edu.eg.

1. Experimental Section

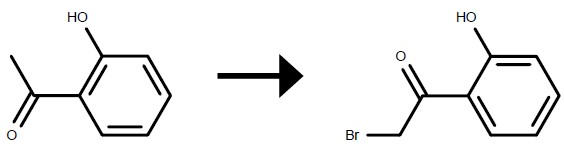
1.1. Materials

Chemicals were obtained from the following suppliers and used without further purification: o-hydroxyacetophenone (98%), thiosemicarbazide (99%), bromine (≥99.5%), p-chloroaniline (98%) (Sigma–Aldrich), sodium acetate anhydrous (CH_3COONa) (99%), Na_2CO_{3b}(99%), $ZnCl_2.2H_2O$ (98%), $NiCl_2.6H_2O$ (98%), $CoCl_2.2H_2O$ (98%), and $CuCl_2.2H_2O$ (98%) (GRÜSSING GmbH).

1.2. Instrumentation

Elemental analyses for C, H, N and S were performed with a Perkin–Elmer 263 elemental analyzer. FT-IR spectra were recorded on a BRUKER Tensor-37 FT-IR spectrophotometer in the range 400–4000 cm^{-1} as KBr discs or in the 4000-550 cm^{-1} region with 2 cm^{-1} resolution. For signal intensities the following abbreviations were used: br (broad), sh (sharp), w (weak), m (medium), s (strong), vs (very strong). NMR-spectra were obtained with a Bruker Avance DRX200 (200 MHz for ^1H) or Bruker Avance DRX500 (500 MHz for ^{13}C) spectrometer with calibration to the residual proton solvent signal in DMSO-d_6 (^1H NMR: 2.52 ppm, ^{13}C NMR: 39.5 ppm), $CDCl_3$ (^1H NMR: 7.26 ppm, ^{13}C NMR: 77.16 ppm) against TMS with δ = 0.00 ppm. Multiplicities of the signals were specified s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet).

1.3. Synthesis of 2-hydroxy phenacyl bromide (2):



A solution of bromine (0.27 mL, 5 mmol) in acetic acid (10 mL) is added stepwise to a solution of o-hydroxyacetophenone 1 (0.84 g, 5 mmol) in acetic acid (20 mL). After a reflux of 2h, the reaction mixture was poured into water (100 mL) and ice (50 g). The obtained solid was filtered-off andrecrystallized from a 1:1 mixture of hexane-chloroform, being compound 2c obtained as yellow crystals (0.75 g, 61%): mp 45-46 °C. **FTIR** (KBr, cm^{-1}): 3329 (OH), 3075 (C-H arom.), 2958 (C-H aliph.), 1681 (C=O ceto), 1600, 1568, 1511 (C=C), 1268, 1177 (C-O), 687 (C-Br). **^{1}H NMR** ($CDCl_3$, δ, ppm, J, Hz): 4.89 (s, 2H: H2), 6.96 (dt, *J*= 7.2, *J*= 8.0, 1H: H5'), 7.01 (dd, *J*= 8.4, *J*= 0.8, 1H: H3'), 7.52 (dt, *J*= 8.4, *J*= 7.2, 1H: H4'), 7.82 (dd, *J*= 8.0, *J*= 1.6, 1H: H6'), 11.22 (s, 1H: OH). **^{13}C NMR** (TMS, CDCl3, δ, ppm): 36.12 (C2), 117.54 (C3'), 119.30 (C5'), 119.91 (C1'), 130.86 (C6'), 135.93 (C4'), 159.53 (C2'), 194.55 (C1: C=O).

1.4. Structural characterization of HBHTP:

FTIR (KBr, cm^{-1}): 3435 (m, sh), 3280 (m, sh), 3163 (m, sh), 2993 (m, br), 1634 (s, sh), 1601 (vs, sh), 1525 (s, sh), 1466 (s, sh), 1366 (s, sh), 1287 (m, sh), 1088 (s, sh), 924 (m, sh), 872 (m, sh), 818 (s, sh), 753 (m, sh), 615 (m, sh), 511 (m, sh). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) (**Figure S1**, **ESM†**): 11.51 (s, 1H, NH), 8.26 (d, *J* = 7.8 Hz, 1H, Ar–H), 8.07 (s, 1H, H–C=N), 7.96 – 7.66 (m, 4H, Ar–H), 7.47 (m, 1H, Ar–H), 7.17 (s, 1H, Ar-OH), 6.97-6.86 (m, 2H, Ar–H). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) (**Figure S2**, **ESM†**): 167.88, 162.80, 155.60, 141.11, 138.60, 136.77, 134.31, 133.61, 131.77, 130.23, 128.42, 127.67, 120.49, 118.31, 117.18, 107.17. Anal. Calcd for $C_{16}H_{12}ClN_3OS$ (M = 329.80 g/mol): C, 58.27; H, 3.67; N, 12.74; S, 9.72%. Found: C, 58.19; H, 3.71; N, 12.58; S, 9.63.

2. Computational analysis

Computational analysis has been conducted to study the structural properties of the benzylidene-phenol-thiazole (HBHTP) ligand and its cupper complex (CuBHTP). Avogadro [S1] program was used to draw and initially minimize the energy of the compounds under study. Based on density functional theory (DFT), these calculations were carried out using gaussian W09 software [S2]. The selected computational method is Becke's three-parameter exchange function from the Lee Yang Parr, B3LYP [S3, S4] with mixed basis set SDD with a regular level for the Cu metal and 6-311G++ (d,p) for C,H,O,N and Cl of the benzylidene-phenol-thiazole ligand [S5, S6]. Such combination is used with systems containing hydrogen bonds. Significant geometrical parameters obtained from the full optimization of the compounds under study indicate the actual structure of the synthesized compounds. Many parameters were calculated, including optimization energy, bond lengths, bond angles, reactivity parameters, and quantum parameters such as HOMO and LUMO energies. GaussView [S7] program was utilized to visualize the optimized structures and produce calculations relying on the Frontier Molecular Orbitals (FMOs). Natural Bond Orbital (NBO) analysis and Molecular Electrostatic Potential (MEP) studies were performed on the optimized structures at the DFT/B3LYP level [S3, S4].

2. Tables Captions

Table S1: Structures of some literature complex

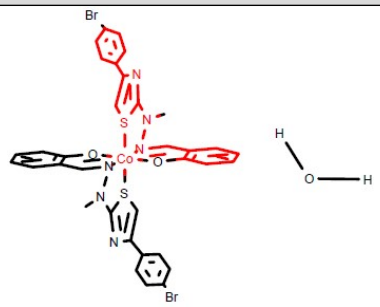
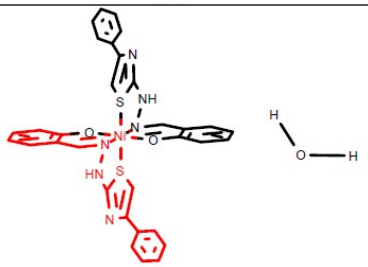
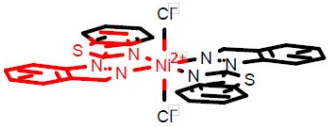
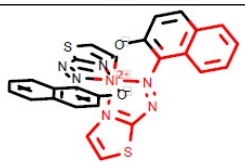
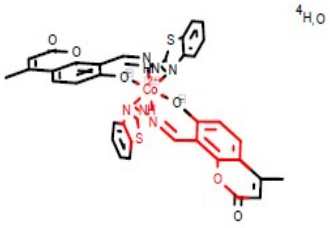
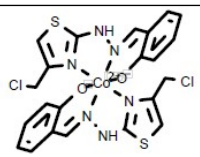
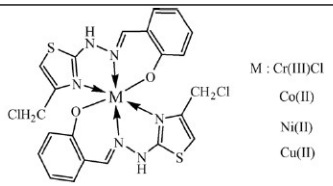
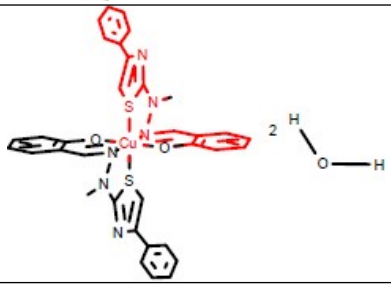
Entry	Structure	Reference
1		[S8]
2		[S9]
3		[S10]
4		[S11]
5		[S12]
6		[S13]
7		[S13]
8		[S9]

Table S2: 50 conformations resulted from the molecular docking process of staurosporine, HBHTP, and CuBHTP against IT8I receptor

Conformer No.	staurosporine		HBHTP		CuBHTP	
	Binding energy (Kcal/mol)	Inhibition constant Ki	Binding energy (Kcal/mol)	Inhibition constant Ki	Binding energy (Kcal/mol)	Inhibition constant Ki
1	-5.01	214.05 uM	-6.61	14.24 uM	-5.28	135.37 uM
2	-4.99	219.73 uM	-6.11	33.48 uM	-5.05	198.45 uM
3	-5.87	50.11 uM	-4.33	671.67 uM	-4.68	368.27 uM
4	-5.63	74.50 uM	-5.62	75.81 uM	-4.51	495.02 uM
5	-4.66	380.88 uM	-4.77	318.31 uM	-4.11	970.23 uM
6	-4.95	234.15 uM	-4.11	971.44 uM	-5.44	103.27 uM
7	-5.12	177.53 uM	-4.01	1.14 mM	-5.09	184.35 uM
8	-6.63	13.78 uM	-4.11	964.94 uM	-4.51	497.58 uM
9	-5.93	45.23 uM	-4.57	450.16 uM	-4.48	523.70 uM
10	-4.35	646.88 uM	-5.38	113.92 uM	-4.93	243.19 uM
11	-5.76	60.44 uM	-4.72	349.67 uM	-9.64	85.82 nM
12	-4.27	737.93 uM	-5.42	106.79 uM	-5.52	89.66 uM
13	-4.86	274.89 uM	-5.47	97.03 uM	-5.11	179.17 uM
14	-5.14	171.50 uM	-5.31	127.55 uM	-4.74	335.64 uM
15	-5.11	179.08 uM	-5.33	124.80 uM	-5.24	144.01 uM
16	-6.50	17.31 uM	-4.59	431.51 uM	-5.39	111.17 uM
17	-5.52	90.46 uM	-4.19	848.53 uM	-4.84	282.40 uM
18	-5.01	212.02 uM	-6.23	26.93 uM	-4.86	275.95 uM
19	-4.74	334.93 uM	-4.80	304.57 uM	-4.75	331.89 uM
20	-5.03	203.94 uM	-3.80	1.63 mM	-5.37	115.64 uM
21	-4.87	268.56 uM	-5.34	121.91 uM	-5.47	98.65 uM
22	-5.13	172.81 uM	-5.22	149.08 uM	-4.40	598.75 uM
23	-5.39	111.13 uM	-5.66	70.92 uM	-4.86	273.32 uM
24	-4.74	333.01 uM	-4.96	232.17 uM	-4.89	259.58 uM
25	-4.99	219.55 uM	-4.38	620.38 uM	-7.19	5.37 uM
26	-5.18	158.94 uM	-3.94	1.29 mM	-4.99	220.24 uM
27	-5.36	117.21 uM	-5.54	87.40 uM	-5.41	108.70 uM
28	-4.77	321.02 uM	-4.60	422.95 uM	-5.57	82.00 uM
29	-4.66	385.47 uM	-5.31	128.04 uM	-9.27	161.56 nM
30	-5.44	103.09 uM	-4.21	817.24 uM	-6.06	36.43 uM
31	-5.16	164.40 uM	-4.94	240.84 uM	-4.75	331.91 uM
32	-4.60	426.32 uM	-4.32	686.19 uM	-4.28	724.82 uM
33	-5.18	158.65 uM	-4.44	553.48 uM	-5.26	139.18 uM
34	-4.63	400.52 uM	-4.29	719.74 uM	-4.94	239.37 uM
35	-5.38	114.07 uM	-5.49	94.83 uM	-5.54	87.27 uM
36	-4.57	447.66 uM	-4.35	644.27 uM	-5.45	101.08 uM
37	-4.73	339.84 uM	-5.08	187.66 uM	-5.21	151.55 uM
38	-5.24	145.30 uM	-5.10	181.27 uM	-5.05	198.39 uM
39	-4.71	355.31 uM	-4.10	990.33 uM	-5.29	133.58 uM
40	-5.53	88.81 uM	-4.75	329.42 uM	-5.52	89.35 uM
41	-4.76	323.46 uM	-4.87	270.87 uM	-4.21	822.15 uM
42	-4.61	418.57 uM	-4.09	999.95 uM	-9.57	96.05 nM
43	-6.26	25.90 uM	-5.82	54.60 uM	-5.07	190.54 uM
44	-5.35	118.79 uM	-5.62	75.36 uM	-5.64	72.97 uM
45	-5.03	207.02 uM	-5.27	137.94 uM	-4.96	231.21 uM
46	-5.67	69.74 uM	-4.71	350.02 uM	-5.28	134.04 uM
47	-6.06	36.40 uM	-4.34	662.16 uM	-5.23	146.45 uM
48	-5.54	87.50 uM	-5.17	161.29 uM	-5.44	102.99 uM
49	-5.11	179.00 uM	-5.21	150.88 uM	-7.51	3.13 uM
50	-4.48	519.21 uM	-5.66	70.56 uM	-4.68	368.41 uM

Table S3: the geometrical bond lengths and bond angels of the benzylidene-phenol-thiazole ligand (HBHTP) and the cupper complex (CuBHTP).

HBHTP ligand		**CuBHTP complex**	
Important bond lengths			
N8-C10	1.289	Cu45-O1	1.895
C10-N12	1.379	Cu45-O23	1.923
N12-N13	1.348	Cu45-N16	3.575
N12-H28	1.016	Cu45-N21	2.374
N13-C14	1.283	Cu45-N38	2.133
C10-S11	1.769	Cu45-N43	1.977
S11-C9	1.743	O1-C2	1.347
C9-C7	1.368	C2-C7	1.436
C4-O22	1.373	C7-C20	1.479
O22-H34	0.963	C20-N21	1.427
C19-Cl21	1.758	N21-C22	1.309
Important bond angels		C22-N17	1.389
C4-O22-H34	109.211	N17-N16	1.377
O22-C4-C5	118.780	C22-S18	1.827
C9-S11-C10	87.871	S18-C19	1.797
S11-C10-N8	115.133	O23-C24	1.341
C10-N8-C7	111.538	C24-C29	1.444
N8-C7-C9	114.720	C29-C42	1.467
N8-C10-N12	126.207	C42-N43	1.415
C10-N12-N13	121.695	N43-C44	1.316
N12-N13-C14	117.733	C44-N39	1.379
C20-C19-Cl21	119.407	N39-N38	1.397
C18-C19-Cl21	119.511	C41-S40	1.819
Important dihedrals		S40-C44	1.791
H34-O22-C4-C5	-179.993	Important bond angels	
C9-C7-N8-C10	0.005	O1-Cu45-O23	100.205
N8-C10-S11-C9	-0.002	O1-Cu45-N21	85.676
N8-C10-N12-N13	-0.123	O1-Cu45-N38	87.204
C10-N12-N13-C14	-179.934	O23-Cu45-N43	90.014
C20-C19-Cl21-C18	180.00	O23-Cu45-N21	90.150
		O23-Cu45-N16	115.114
		N38-Cu45-N43	78.888
		N21-Cu45-N16	54.410
		N16-Cu45-N43	63.491
		N16-Cu45-N38	71.629
		N21-Cu45-N43	110.568
		N21-Cu45-N38	105.937
		Important dihedrals	
		O1-Cu45-N21-C20	-45.614
		O23-Cu45-N43-C42	-172.286
		N39-N38-Cu45-N43	0.478
		N21-Cu45-N16-N17	-37.906

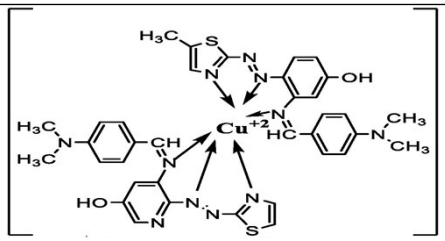
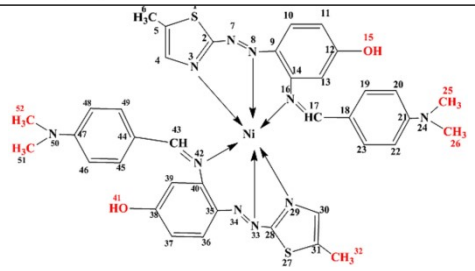
Table S4: NBO charges of HBHTP and CuBHTP.

HBHTP		**CuBHTP**			
Atom No.	Natural charge	Atom No.	Natural charge	Atom No.	Natural charge
C1	-0.19342	O1	-0.34328	C35	-0.0819
C2	-0.15491	C2	0.19816	C36	-0.05613
C3	-0.26742	C3	-0.12628	C37	0.06105
C4	0.34558	C4	-0.10419	N38	-0.11998
C5	-0.12352	C5	-0.12457	N39	-0.22546
C6	-0.22675	C6	-0.09618	S40	0.13712
C7	0.12144	C7	-0.069	C41	-0.18477
N8	-0.51326	Cl8	-0.02914	C42	0.09243
C9	-0.39524	C9	-0.10853	N43	-0.26456
C10	0.27498	C10	-0.11009	C44	0.18072
-S11	0.33099	C11	0.01217	Cu45	0.80391
N12	-0.40898	C12	-0.11166	H46	0.1088
N13	-0.21448	C13	-0.08931	H47	0.10656
C14	0.05002	C14	-0.0565	H48	0.10613
C15	-0.10344	C15	0.0151	H49	0.10299
C16	-0.15217	N16	-0.12603	H50	0.11577
C17	-0.16807	N17	-0.22821	H51	0.12231
C18	-0.22414	S18	0.11396	H52	0.1215
C19	-0.03406	C19	-0.18079	H53	0.11417
C20	-0.21736	C20	0.08873	H54	0.10586
Cl21	0.00394	N21	-0.27684	H55	0.2033
O22	-0.68268	C22	0.18414	H56	0.12241
H23	0.20432	O23	-0.31399	H57	0.11478
H 24	0.23192	C24	0.20072	H58	0.10827
H25	0.19592	C25	-0.12295	H59	0.10698
H26	0.2059	C26	-0.09957	H60	0.10108
H27	0.25238	C27	-0.1278	H61	0.11371
H28	0.36299	C28	-0.09434	H62	0.12208
H29	0.14934	C29	-0.0865	H63	0.12344
H30	0.23043	Cl30	-0.02525	H64	0.11898
H31	0.20527	C31	-0.10739	H65	0.13386
H32	0.22181	C32	-0.11012	H66	0.21296
H33	0.22232	C33	0.01358	H67	0.12327
H34	0.47043	C34	-0.10971		

Table S5: Comparison between the best conformers of staurosporine, HBHTP, and CuBHTP with IT8I receptor

Parameter	**Staurosporine**	**HBHTP**	**CuBHTP**
Binding energy (Kcal/mol)	-6.63	-6.61	-9.64
Inhibition constant Ki	13.78 μM	14.24 μM	85.82 nM
Reference RMSD	34.45	43.35	27.06
H-binding	Conventional H-bonding LIG H: ASN352(A)O LIG O: DA113(D)H Carbon H-bonding LIG O: DA113(D)C LIG C: DT10(B)O Pi-donor H-bonding LIG benzene ring: DA113(D)N 3.43 A°. LIG benzene ring: DA113(D)N 3.86 Ao. LIG benzene ring: DC112(D)N	None.	None.

Table S6: comparison between the anticancer activity of new complexes with reported ones

4	Structure	Cancer cell	IC_{50} (µg/mL)	Reference
1		PA-I	> 50	[S13]
2		HepG2, MCF-7	21.70, 60.35	[S14]
3		HepG2, MCF-7	73.48, 82.02	[S14]
4	CoBHTP	MCF-7	253.57	This work
5	NiBHTP	MCF-7	68.93	This work
6	CuBHTP	MCF-7	13.311	This work
7	ZnBHTP	MCF-7	78.57	This work

3. Figure Captions

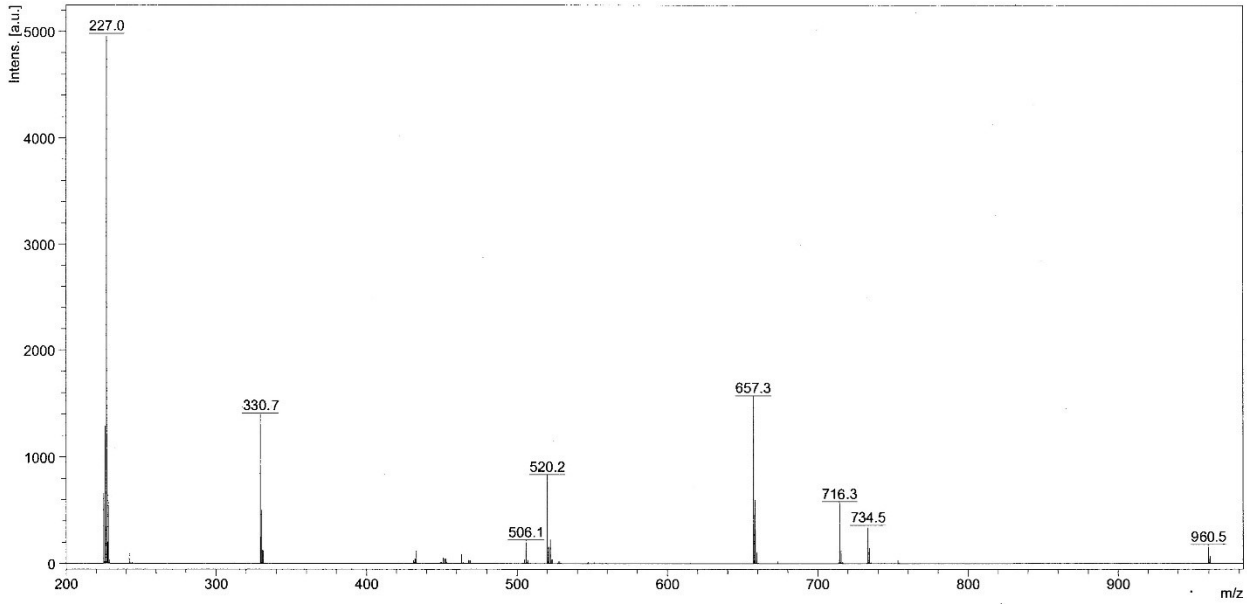


Figure S1: MALDI-TOF-MS spectra of CoBHTP using dithranol as MALDI matrix

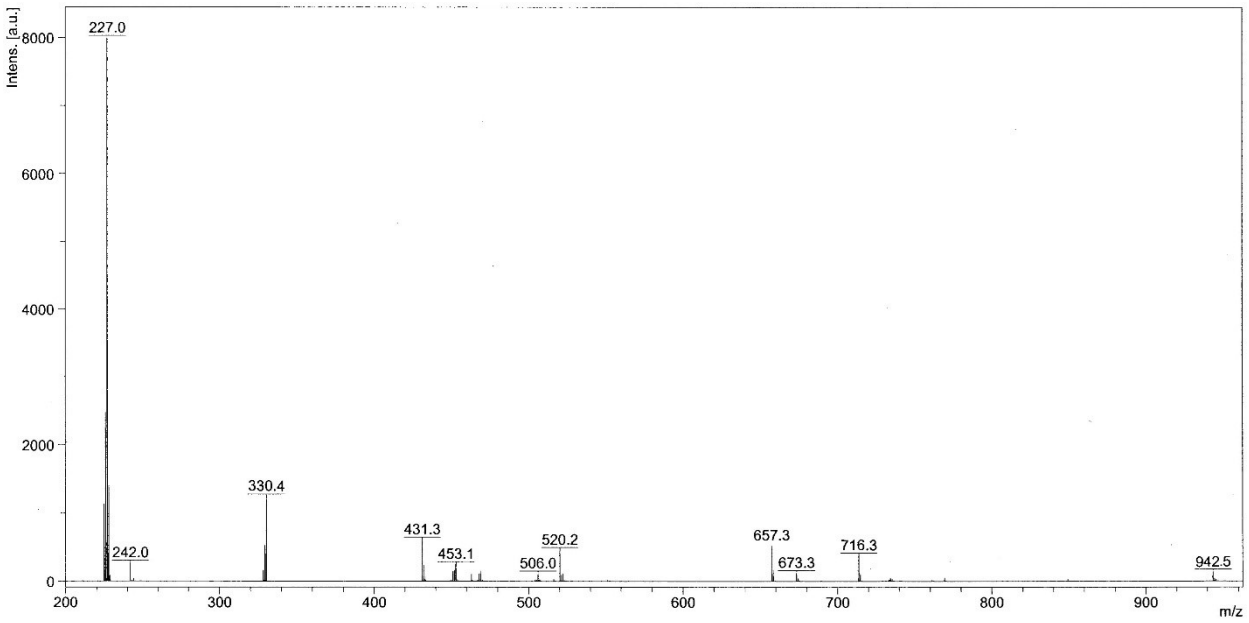


Figure S2: MALDI-TOF-MS spectra of NiBHTP using dithranol as MALDI matrix

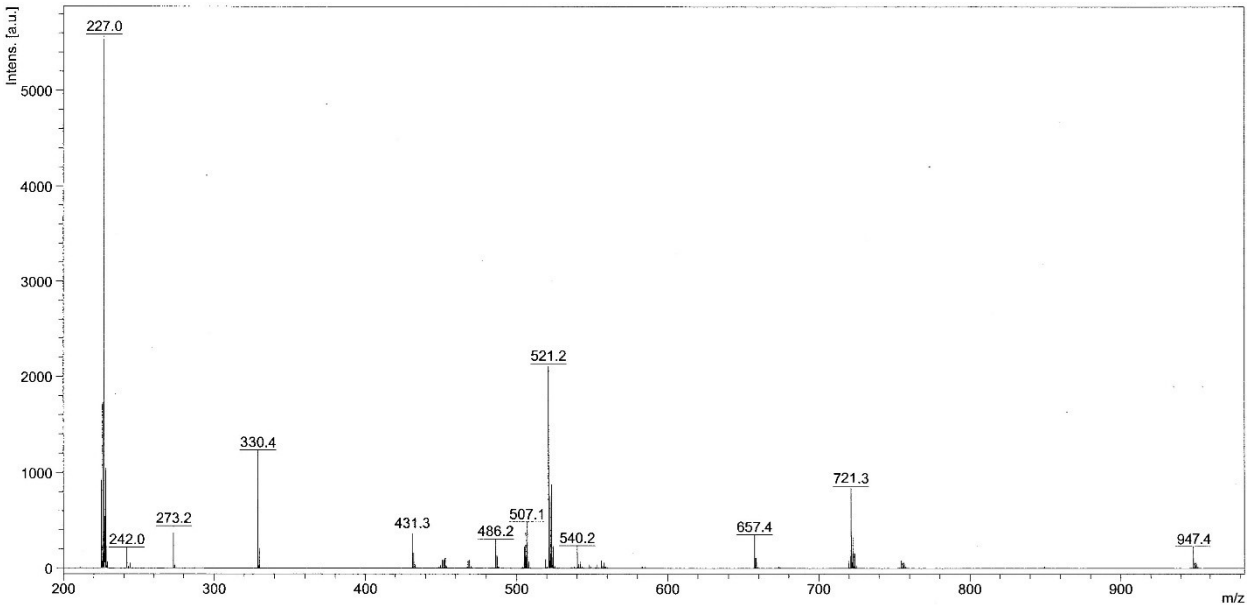


Figure S3: MALDI-TOF-MS spectra of CuBHTP using dithranol as MALDI matrix

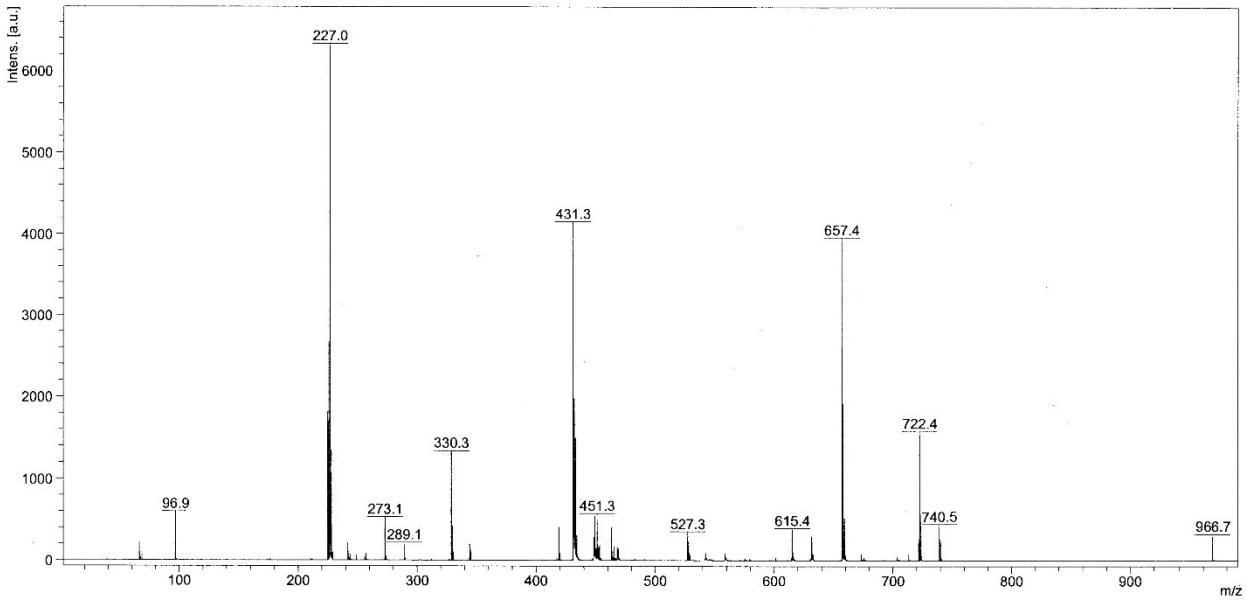


Figure S4: MALDI-TOF-MS spectra of ZnBHTP using dithranol as MALDI matrix

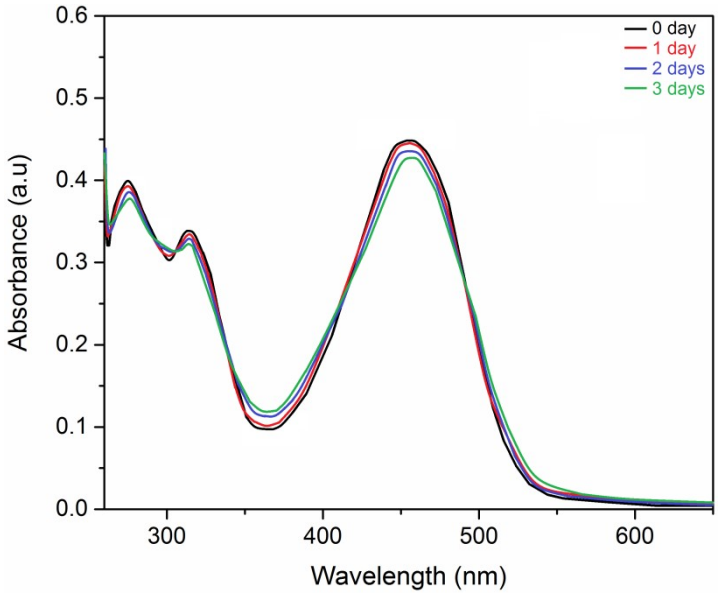


Figure S5: Monitoring the storage stability of the solution of CuBHTP complex under physiological conditions (T = 298 k, pH =7.4) using UV-vis spectroscopy

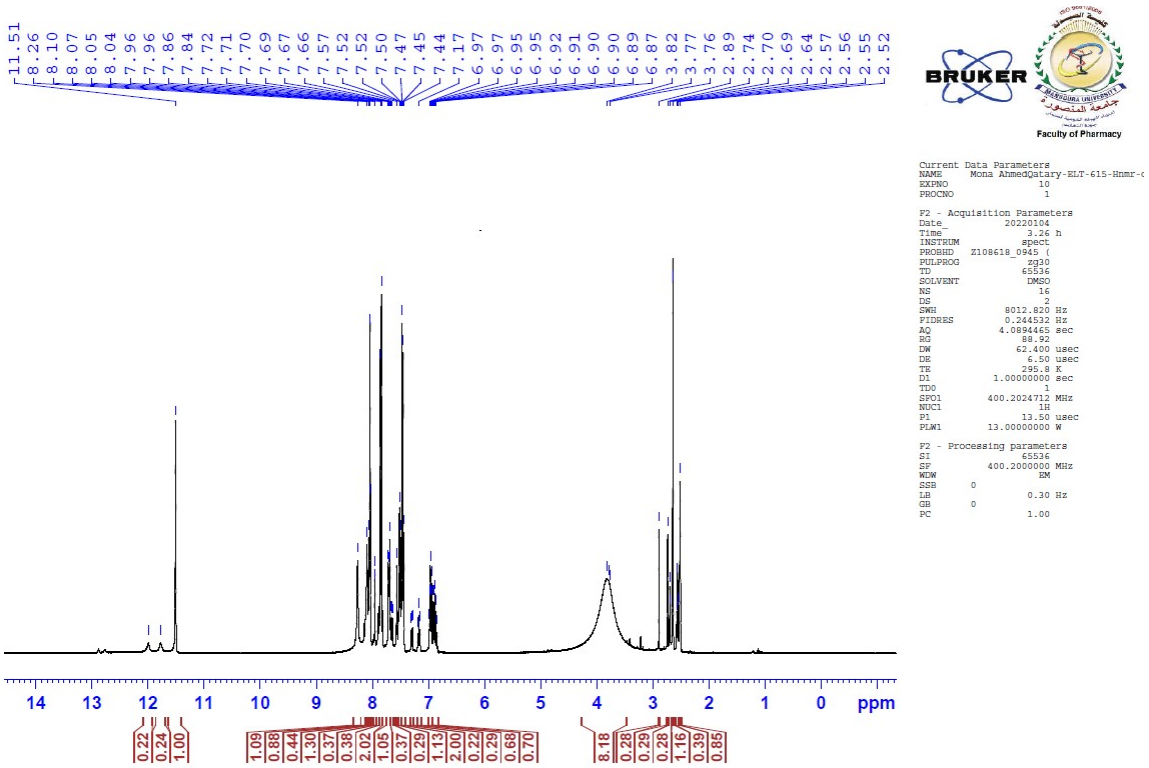
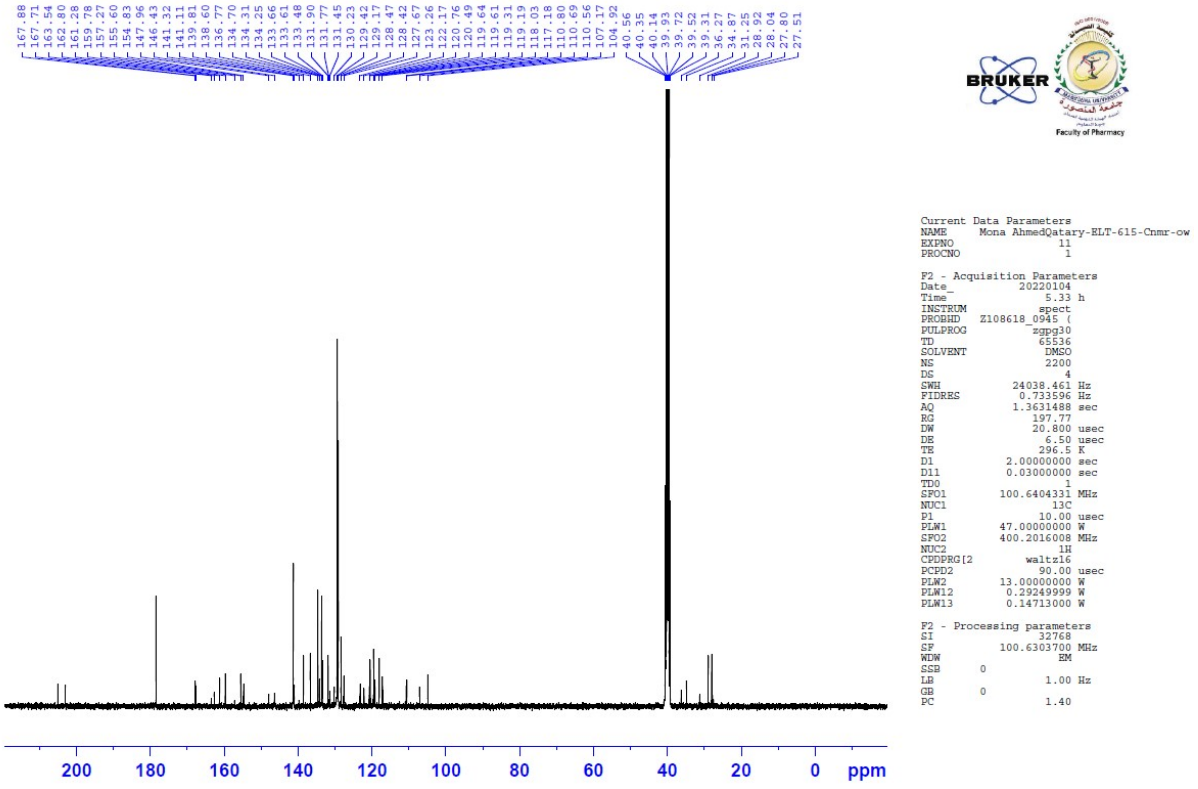


Figure S6: ^{1}H spectrum of HBHTP ligand (300 MHz, DMSO-d_6)




```
Current Data Parameters
NAME      Mona AhmedQatary-ELT-615-Cnmr-ow
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220104
Time               5.33 h
INSTRUM           spect
PROBHD    Z108618_0945 (
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                  2200
DS                     4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ              1.3631488 sec
RG                 197.77
DW                 20.800 usec
DE                  6.50 usec
TE                 296.5 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1          100.6404331 MHz
NUC1                 13C
P1                  10.00 usec
PLW1          47.00000000 W
SFO2          400.2016008 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2               90.00 usec
PLW2          13.00000000 W
PLW12          0.29249999 W
PLW13          0.14713000 W

F2 - Processing parameters
SI                 32768
SF            100.6303700 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

Figure S7: ^{13}C NMR spectra of HBHTP ligand (100 MHz, DMSO-d_6).

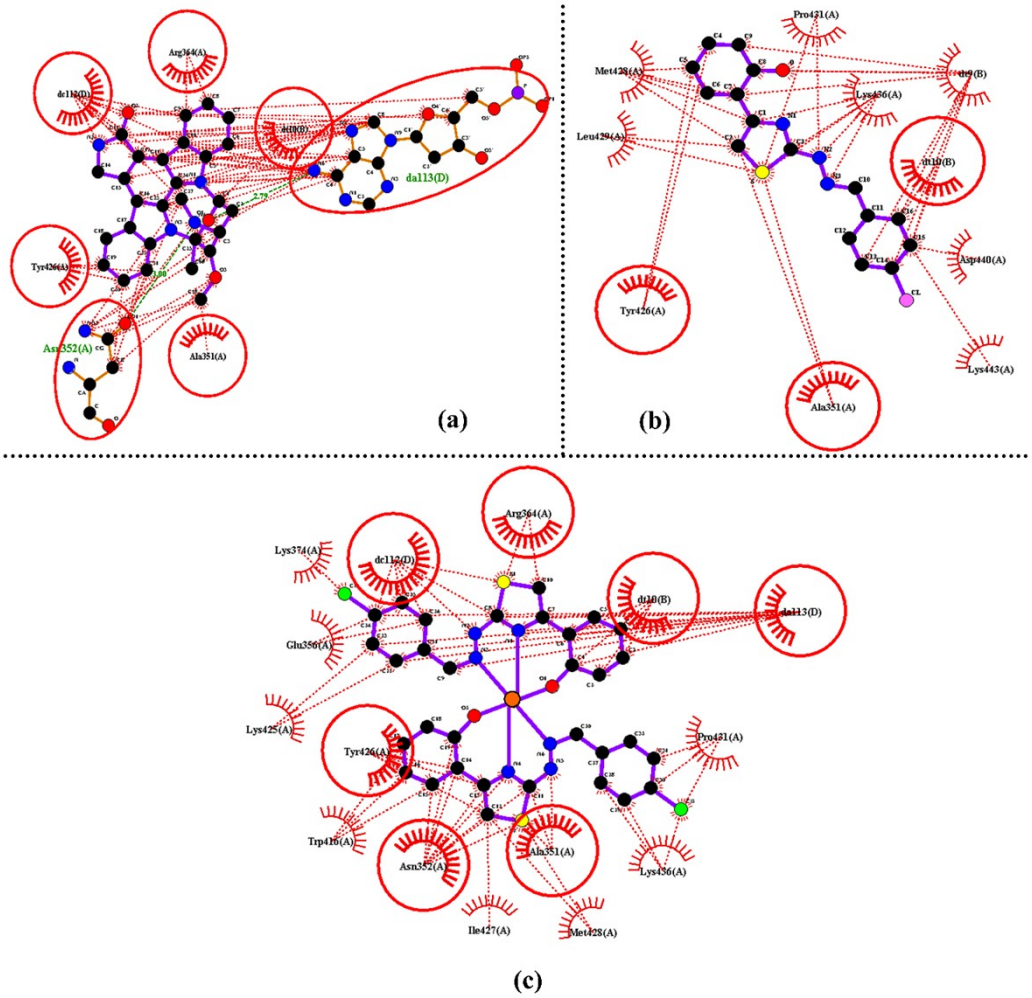


Figure S8: Hydrophobic interactions between (a: staurosporine), (b: HBHTP), (c: CuBHTP) and different amino acids of 1T8I receptor

References

[S1] Hanwell, M.D., Curtis, D.E., Lonie, D.C. et al. Avogadro: an advanced semantic chemical editor, visualization, and analysis platform. J Cheminform 4, 17 (2012).

[S2] Frisch M. J. et al, Gaussian 09, Revision A.02, Gaussian, Inc., Wallingford CT, 2016.

[S3] Parr RG, Yang W. Density-functional theory of atoms and molecules. New York: Oxford University Press; 1989.

[S4] Fayed TA, Gaber M, Abu El-Reash GM, El-Gamil MM. Structural, DFT/B3LYP and molecular docking studies of binuclear thiosemicarbazide Copper (II) complexes and their biological investigations. Appl Organomet Chem. 2020;34:e5800.

[S5] Becke AD. Density-functional thermochemistry. III. The role of exact exchange. J Chem Phys. 1993; 98: 5648–52.

[S6] López JB, González JC, Holguín NF, Mitnik DG. Quantum chemical study of a new class of sensitisers: influence of the substitution of aromatic rings on the properties of copper complexes. Mol Phys. 2014; 112(7): 987– 94.

[S7] Dennington R., Keith T.A., Millam J.M., GaussView, Version 6.1, Semichem Inc., Shawnee Mission, KS, 2016.

[S8] Dash, D.C., et al. "SYNTHESIS AND CHARACTERIZATION OF SOME TRANSITION METAL COMPLEXES OF 4-SUBSTITUTED-2-THIAZOLYLHYDRAZONES OF SALICYL ALDEHYDE AND 2-HYDROXYACETOPHENONE." *Journal of the Indian Chemical Society* 68.12 (1991): 663-664.

[S9] Khan, Tabrez A., and Shahjahan. "Biheterocyclic Ligands: Synthesis and Coordinating Properties of 2-(1-Indazolyl)benzothiazole Towards Some Transition Metal Ions." *Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry* 31.6 (2001): 1023-1030.

[S10] Omar, M. M., and Gehad G. Mohamed. "Potentiometric, spectroscopic and thermal studies on the metal chelates of 1-(2-thiazolylazo)-2-naphthalenol." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 61.5 (2005): 929-936.

[S11] Jawoor, Shailaja S., Sangamesh A. Patil, and Shivakumar S. Toragalmath. "Synthesis and characterization of heteroleptic Schiff base transition metal complexes: a study of anticancer, antimicrobial, DNA cleavage and anti-TB activity." *Journal of Coordination Chemistry* 71.2 (2018): 271-283.

[S12] Saydam, S., and E. Yilmaz. "Synthesis, characterization and thermal behavior of 4-chloromethyl-2-(2-hydroxybenzilidenehydrazino) thiazole and its complexes with Cr (III), Co (II), Ni (II) and Cu (II)." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 63.2 (2006): 506-510.

[S13] Al-Adilee, KJ, Hasan, SR, Waheeb, AS, Kadhim, MM, & Khadom, AA (2023). Synthesis, characterization, medical activity, and docking prediction of new heterocyclic Azo-Schiff base ligand derived from 2-Amino-5-methyl thiazole and Cr (III), Ni (II), and Cu (II) metal ions. *Inorganic Chemistry Communications* , 111954.