

**Metal–Antibiotic Chelation: Synthesis, Characterization, DNA Binding,
Molecular Docking and Cytotoxicity Study of Zn(II), Cu(II), Ni(II), Co(II) and
Fe(II) Complexes with Thiamphenicol**

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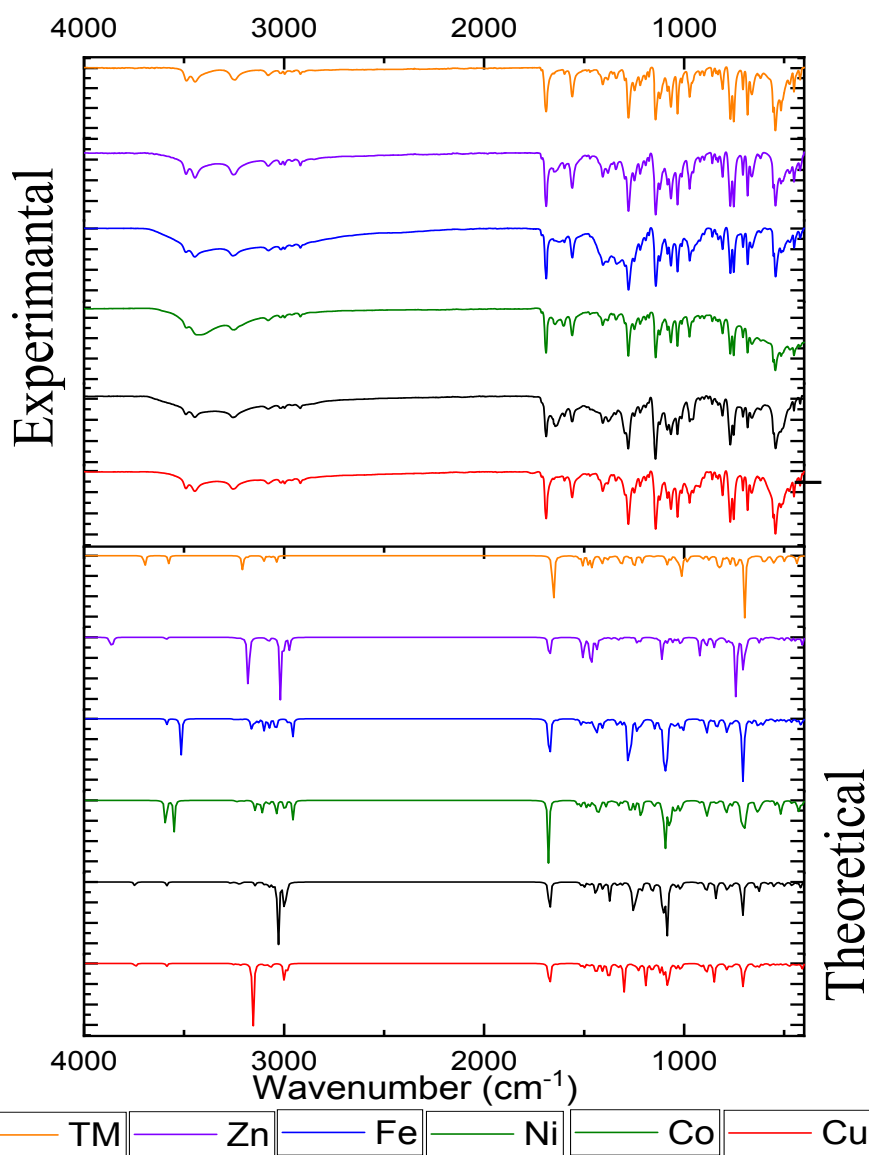


Figure 1S. Infrared spectrum of the free TM ligand and the metal complexes.

Table 1S. Thermodynamic activation parameters of decomposition processes of the TM complexes.

Complex	Temp. range C	Method	Parameter					Correlation coefficient (r)
			E_a (kJmol ⁻¹)	A (s ⁻¹)	$-\Delta S$ (J mol ⁻¹ K ⁻¹)	ΔH (kJmol ⁻¹)	ΔG (kJ mol ⁻¹)	
	166-187	CR	2.20×10^4	2.65×10^4	1.64×10^2	1.82×10^4	9.21×10^4	0.9924
		HM	4.75×10^4	1.50×10^3	1.88×10^2	4.38×10^4	1.28×10^5	0.9644
		Average	3.48×10^4	1.40×10^4	1.76×10^2	3.10×10^4	1.10×10^5	0.9784

	212-265	CR	3.82×10^4	2.39×10^2	2.04×10^2	3.39×10^4	1.38×10^5	0.9845
		HM	9.33×10^4	2.35×10^7	1.08×10^2	8.91×10^4	1.45×10^5	0.9591
		Average	6.57×10^4	1.17×10^7	1.56×10^2	6.15×10^4	1.41×10^5	0.9718
	390-454	CR	2.79×10^4	7.41×10^3	1.78×10^2	2.22×10^4	1.45×10^5	0.9973
		HM	1.36×10^5	1.07×10^8	9.82×10	1.30×10^5	1.98×10^5	0.9839
		Average	8.18×10^4	5.33×10^7	1.38×10^2	7.61×10^4	1.71×10^5	0.9906
Fe-TM	119-142	CR	3.27×10^4	1.30×10^3	1.88×10^2	2.94×10^4	1.05×10^5	0.9905
		HM	4.99×10^4	1.66×10^4	1.67×10^2	4.65×10^4	1.14×10^5	0.9965
		Average	4.13×10^4	8.95×10^3	1.77×10^2	3.80×10^4	1.10×10^5	0.9935
	207-242	CR	3.09×10^4	1.83×10^3	1.87×10^2	2.66×10^4	1.23×10^5	0.9919
		HM	8.54×10^4	2.92×10^6	1.26×10^2	8.11×10^4	1.46×10^5	0.9755
		Average	5.81×10^4	1.46×10^6	1.56×10^2	5.38×10^4	1.34×10^5	0.9837
	352-390	CR	2.89×10^4	3.64×10^3	1.83×10^2	2.36×10^4	1.39×10^5	0.9895
		HM	1.24×10^5	9.69×10^7	9.83×10	1.18×10^5	1.81×10^5	0.9826
		Average	7.62×10^4	4.85×10^7	1.41×10^2	7.10×10^4	1.60×10^5	0.9860
Ni-TM	70-164	CR	3.62×10^3	2.05×10^6	1.26×10^2	3.89×10^2	4.94×10^4	0.9633
		HM	1.07×10^4	3.88×10^2	2.74×10^2	7.45×10^3	1.14×10^5	0.9851
		Average	7.15×10^3	1.03×10^6	2.00×10^2	3.92×10^3	8.16×10^4	0.9742
	227-281	CR	3.47×10^4	9.73×10^2	1.93×10^2	3.03×10^4	1.32×10^5	0.9771
		HM	9.96×10^4	4.58×10^7	1.03×10^2	9.52×10^4	1.50×10^5	0.9636
		Average	6.71×10^4	2.29×10^5	1.48×10^2	6.27×10^4	1.41×10^5	0.9704
	374-494	CR	1.76×10^4	2.05×10^5	1.50×10^2	1.17×10^4	1.18×10^5	0.9749
		HM	1.13×10^5	1.03×10^6	1.37×10^2	1.07×10^5	2.03×10^5	0.9624
		Average	6.51×10^4	6.15×10^5	1.44×10^2	5.92×10^4	1.60×10^5	0.9686
Co-TM	147-174	CR	2.15×10^4	3.74×10^4	1.64×10^2	1.63×10^4	1.18×10^5	0.9908
		HM	8.62×10^4	7.06×10^4	1.58×10^2	8.10×10^4	1.80×10^5	0.9973
		Average	5.38×10^4	5.40×10^4	1.61×10^2	4.86×10^4	1.49×10^5	0.9940
	327-436	CR	1.54×10^4	4.29×10^5	1.43×10^2	1.02×10^4	9.98×10^4	0.9818
		HM	7.77×10^4	1.23×10^4	1.73×10^2	7.25×10^4	1.80×10^5	0.9679
		Average	4.65×10^4	2.21×10^5	1.58×10^2	4.14×10^4	1.40×10^5	0.9749
Zn-TM	259-302	CR	2.64×10^4	7.77×10^3	1.75×10^2	2.19×10^4	1.16×10^5	0.9950
		HM	7.97×10^4	3.09×10^5	1.45×10^2	7.52×10^4	1.53×10^5	0.9955

		Average	5.30×10^4	1.58×10^5	1.60×10^2	4.85×10^4	1.35×10^5	0.9953
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Table 3S. Horowitz–Metzger (HM) and Coats–Redfern (CR) plots of metal complexes

Complex	Temp. range C	Horowitz–Metzger (HM)	Coats–Redfern (CR)
Cu-TM	166-187		
	212-265		
	390-454		
Fe-TM	119-142		
	207-242		
	352-390		

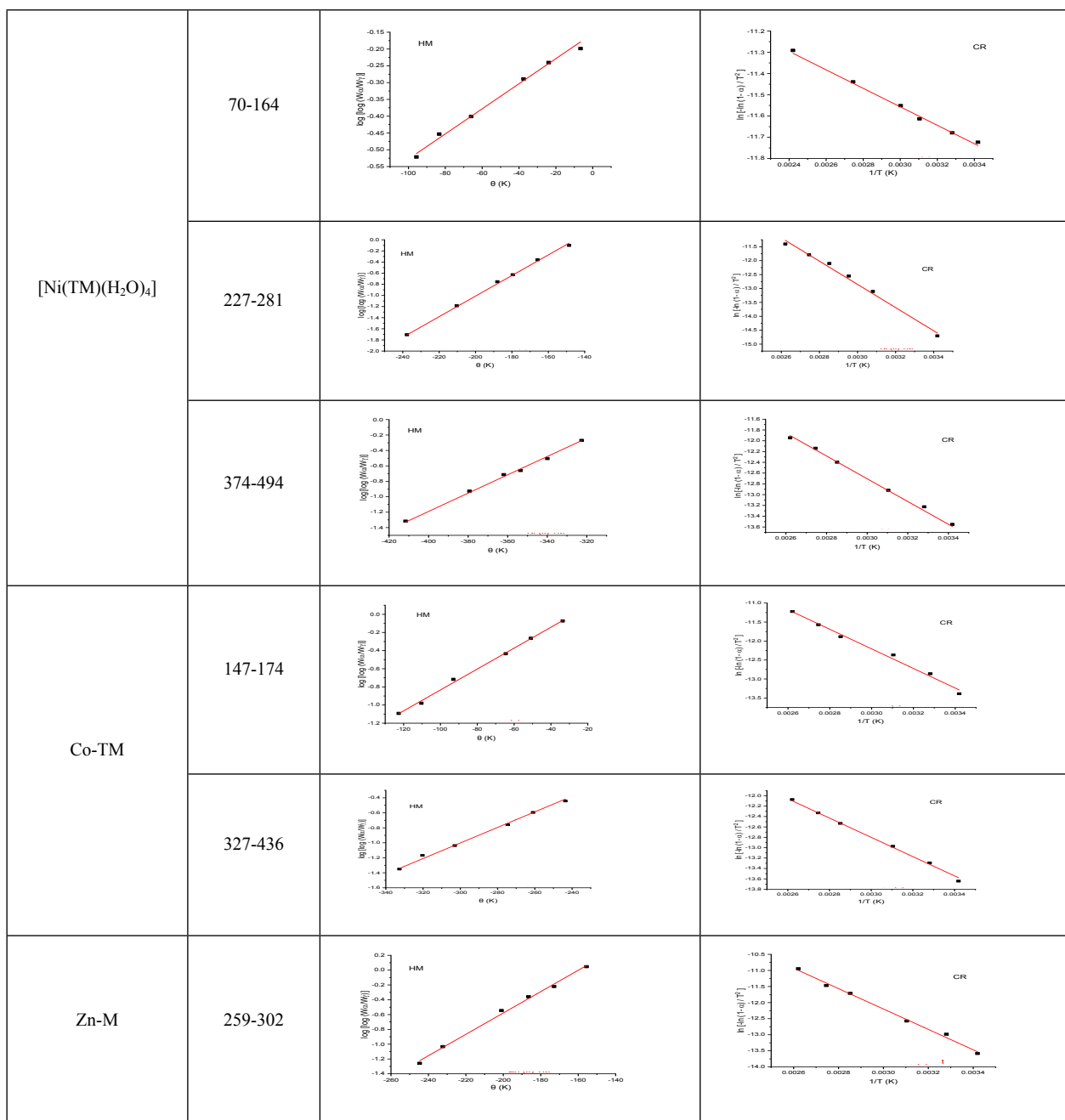


Table 4S. Binding parameters for free TM ligand and the metal–TM complexes from spectrophotometric analysis.

Complex	K_b (M^{-1})	ΔG (kJ mol)	Chromism (%) ^a	λ_{max} Free (nm)	λ_{max} Bound (nm)	Type of chromism
TM Ligand	3×10^5	-3.15×10^4	8.78	265	242 Blue shift	hypochromic
Cu-TM	5×10^5	-3.25×10^4	1.2	266	265 Red	hyperchromic

					shift	
Co-TM	4×10^5	-3.20×10^4	1.64	244	266 Red shift	hyperchromic
Ni-TM	5×10^5	-3.25×10^4	2.09	234	244 Red shift	hyperchromic
Fe-TM	3.5×10^5	-3.16×10^4	6.42	265	248 Blue shift	hypochromic
Zn-TM	6.67×10^5	-3.32×10^4	2.29	262	268	hyperchromic

a Chromism (%) = $[(Abs_{free} - Abs_{bound})/Abs_{free}]$.

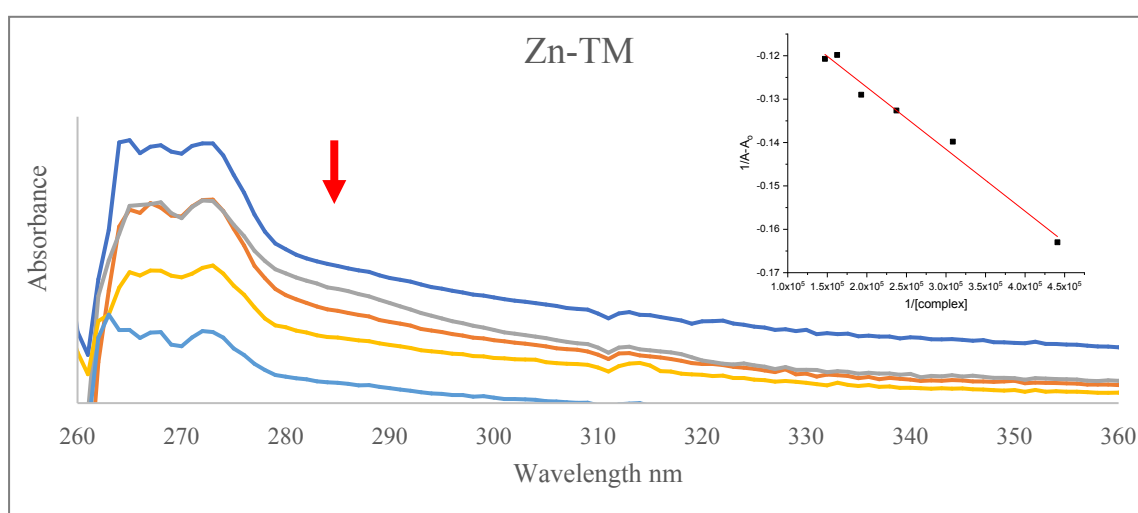


Table 5S. Docking scores and the rmsd-refine for TM and metal complexes for both proteins.

Protein	Compound	S	rmsd_refine
Breast protein (1hk7)	Cu-TM	-7.08812	2.199025
	Zn-TM	-6.17182	2.005747
	Ni-TM	-6.81586	3.273783
	Co-TM	-6.48474	2.742117
	Fe-TM	-6.30869	4.132316
	TM	-6.70443	1.678414
Colon protein (4fm9)	Cu-TM	-8.17851	2.792402
	Ni-TM	-7.85882	3.607329
	Co-TM	-7.51551	3.01175
	Fe-TM	-7.1406	4.59102
	Zn-TM	-9.2232	3.34493
	TM	-6.13445	1.760381

Table 6S. interaction types with the receptors and ligand atoms with their distance and energies for TM, Cu(II) and Zn(II) complexes for both proteins.

Breast protein (3eqm)	Ligand	Receptor	Interaction	Distance	E (kcal/mol)
[Cu(TM)(H ₂ O) ₄]	O 32	SG CYS 437 (A)	H-donor	3.15	-3.6
	O 13	NH2 ARG 115 (A)	H-acceptor	2.89	-3.8
[Zn(TM)(H ₂ O) ₄]	C 14	SD MET 364 (A)	H-donor	4.04	-0.6
	CL 34	SD MET 303 (A)	H-donor	3.71	-0.5
	O 45	SG CYS 437 (A)	H-donor	4.34	-0.7
	O 22	CB ALA 306 (A)	H-acceptor	3.14	-0.7
	O 28	CA GLY 439 (A)	H-acceptor	3.24	-1.2
TM	O 34	SG CYS 437 (A)	H-donor	3.28	-0.9
	O 34	N GLY 439 (A)	H-acceptor	3.37	-0.5
colon protein (4fm9)	Ligand	Receptor	Interaction	Distance	E (kcal/mol)
[Cu(TM)(H ₂ O) ₄]	O 35	OD2 ASP 831 (A)	H-donor	2.74	-4.9
	O 11	OH TYR 612 (A)	H-acceptor	2.91	-1.6
	O 25	NE2 GLN 544 (A)	H-acceptor	3.31	-1.7
	CL 26	NZ LYS 614 (A)	H-acceptor	3.16	-0.7
	CL 27	NZ LYS 614 (A)	H-acceptor	3.51	-1.3
	O 33	NZ LYS 728 (A)	H-acceptor	3.09	-14.0
	Cu 32	NZ LYS 728 (A)	Ionic	3.82	-0.9
	C 6	5-ring HIS 758 (A)	H-pi	4.48	-0.7
	6-ring	NZ LYS 614 (A)	pi-cation	4.76	-1.1
	6-ring	CB ASP 831 (A)	pi-H	4.45	-0.7
[Zn(TM)(H ₂ O) ₄]	O 11	SG CYS 1008 (A)	H-donor	3.64	-0.6
	O 33	OE1 GLU 712 (A)	H-donor	2.63	-5.4
	O 40	OE1 GLU 712 (A)	H-donor	2.81	-2.7
	O 11	NH2 ARG 673 (A)	H-acceptor	2.99	-4.8
TM	C 14	OE1 GLN 544 (A)	H-donor	3.49	-0.5
	O 13	NZ LYS 614 (A)	H-acceptor	2.83	-9.4

