Interaction of Benzimidazole Metal Derivatives with DNA and Micellar Media

Sadia Noor[1,*], Muhammad Babar Taj[2]
[1]Department of Chemistry Govt. College Women University Faisalabad, 3800, Pakistan
[2]Department of Chemistry, Islamia University Bahawalpur 63100, Pakistan
*Email: sadianoor@gcwuf.edu.pk

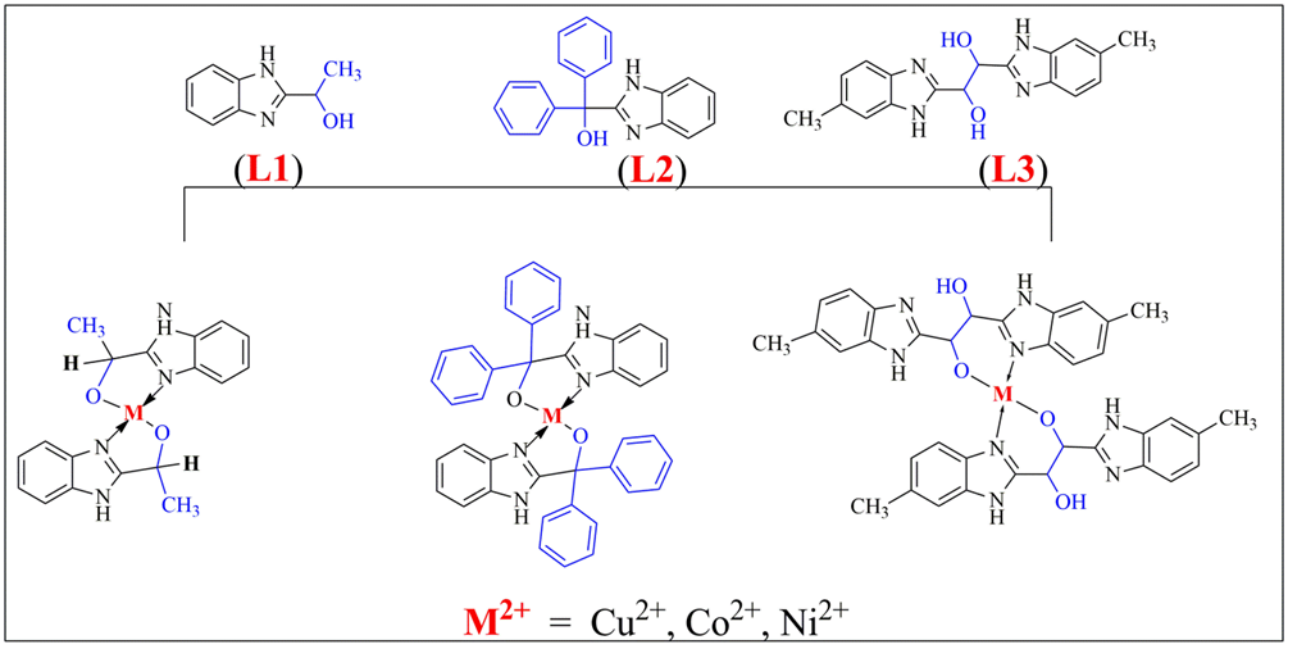
ABSTRACT

Metal complexes of copper, cobalt and nickel with three benzimidazole derivatives (1-(1H-benzimidazol-2-yl)ethanol (L1); 1H-benzimidazol-2-yl(diphenyl)methanol (L2) and 1,2-bis(1H-benzimidazol-2-yl)ethane-1,2-diol (L3) were investigated for their interaction with anionic, cationic and non-ionic micellar media. These compounds showed greater interaction with ionic surfactants and lesser interaction was observed with non-ionic surfactant. The synthesized metal complexes were investigated for their binding with DNA to estimate their binding constants and Gibbs free energy from electronic absorbance analyses. The micellar interaction in terms of binding was measured for anionic (sodium stearate SS), cationic (cetyltrimethylammonium bromide CTAB) and non-ionic surfactant (Triton X-100) by UV-Visible spectroscopy.

Keywords: 3d metal complexation; Benzimidazole derivatives; DNA binding; Micellar solubilization; UV-Visible spectroscopy

INTRODUCTION

Benzimidazoles are heterocyclic compounds with a wide range of applications in pharmaceutics and biological science to design interesting moieties [1]. These diverse compounds have numerous therapeutic uses viz. anti-ulcer, anti-cancer, anti-hypertensive, anti-fungal, anti-viral, and anti-histaminic agents [2]. The compounds under study are presented in Scheme **1**.



Scheme 1. Benzimidazole Derivatives and their corresponding metal complexes

Solubilization of sparingly soluble compounds in aqueous media is possible with the help of surfactants. The colloidal sized micelles of surfactants facilitate in unveiling drug/biomembrane type interaction due to the hydrophilic and hydrophobic components. The micelles have resemblance with biomembranes which make the ideal substitute for *in-vitro* investigation of drug/biomembrane interactions. The present study encompasses the solubilization of Benzimidazole derivatives of transition metals in the presence of surfactants [3-4].

OBJECTIVES

- Investigation of solubilization of Benzimidazole derivatives in the presence of surfactants.
- Determination of binding parameters with differential UV-Vis spectroscopy.
- DNA binding of synthesized compounds by electronic absorbance analyses.

METHODOLOGY

Characterization of synthesized compound:

Ligands and complexes were synthesized from the reported method and the products were characterized through FTIR, FTNIR, multinuclear NMR (^{1}H & ^{13}C), mass spectroscopy and elemental analyses and details are presented in previously published paper [4].

Preparation of solutions: The stock solutions of all compounds were prepared in distilled water and the secondary solutions in the presence of surfactants in pre-micellar to post-micellar concentration (SS: 3-6 mmol). The selected complexes showed greater interaction with anionic surfactant as compared to other participating surfactants and value of critical micellar concentration was also monitored in all cases.

UV-Visible absorbance:

Simple and differential UV-Visible absorbance was measured to determine binding parameters by employing equations 1, 2.

DNA binding:

Interaction with Calf Thymus DNA was investigated, and DNA binding constant was determined by equation 3 and the corresponding Gibb´s free energy was calculated using equation 2.

$$\frac{C_S C_a}{\Delta A} = \frac{C_S}{\Delta \epsilon l} + \frac{1}{K_b \Delta \varepsilon l} \qquad (Eq.1)$$

$$\Delta G_b = -RT\, ln\, K_b \qquad (Eq.2)$$

$$\frac{[DNA]}{(\varepsilon a - \varepsilon f)} = \frac{[\mathrm{DNA}]}{(\varepsilon b - \varepsilon f)} + \frac{1}{\mathrm{K}b\ (\varepsilon b - \varepsilon f)} \qquad (Eq.3)$$

RESULTS

UV-Visible spectroscopy:

UV–Visible spectroscopy provides the most feasible, simple and applicable method to understand the nature of interactions in surfactants and additives. The maximum absorbance of aqueous solution of SS shifted to higher value in the presence of complex molecules due to ionic interactions (Figure **1**). There was no significant interaction of metal complexes with cationic and non-ionic surfactant as proved by initial screening. The binding constants and the change in free energy of binding is presented in Table **1**.

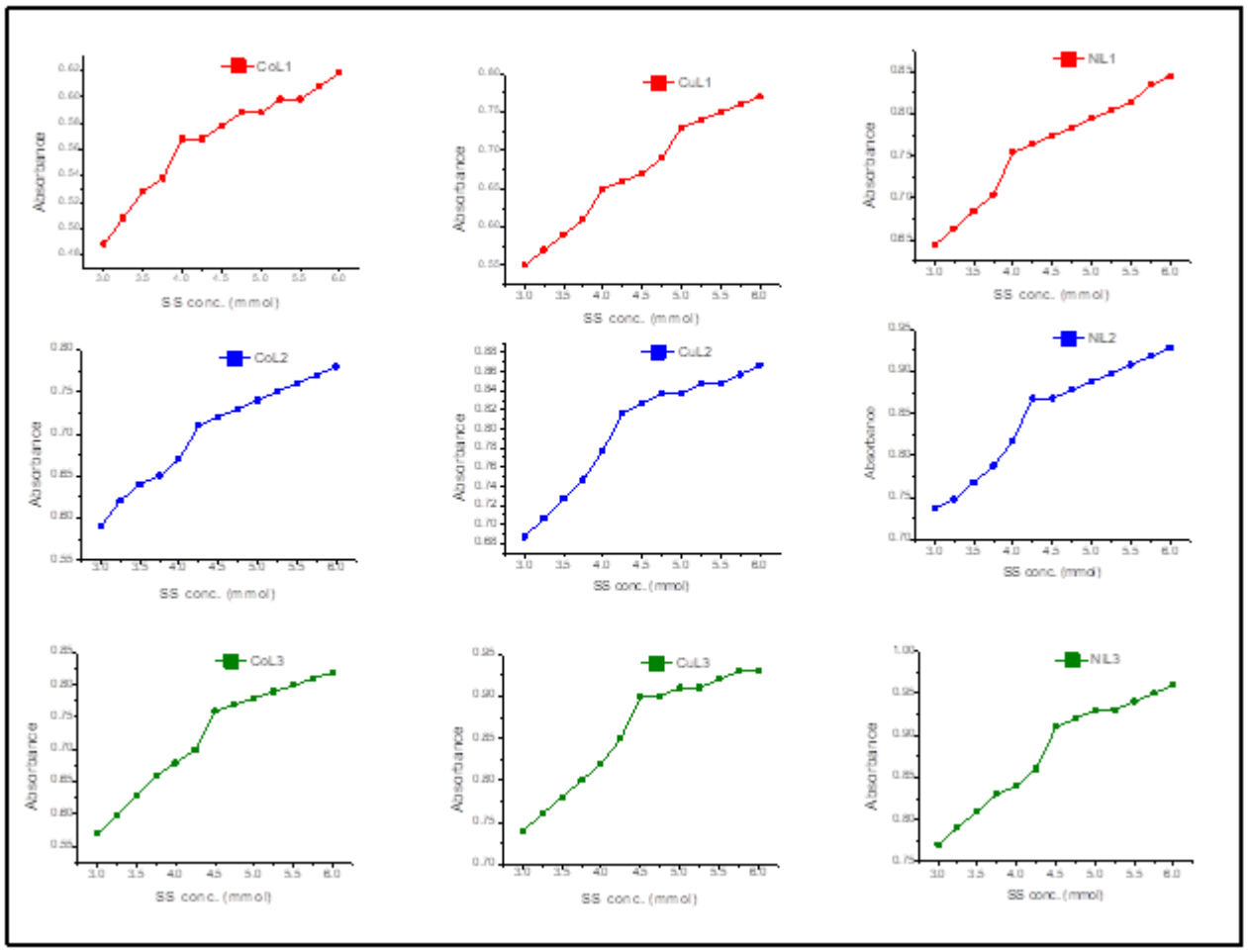


Figure 1. Simple absorbance plots of complexes as function of SS concentration.

Table 1. Binding and free energy of binding determined by UV-Visible spectroscopic analysis.

	K_b × 10^2 (mol.L^{-1})	ΔG_b (kJmol^{-1})		K_b × 10^2 (mol.L^{-1})	ΔG_b (kJmol^{-1})		K_b × 10^2 (mol.L^{-1})	ΔG_b (kJmol^{-1})
CoL1	2.8	-13.96	CoL2	1.8	-12.87	CoL3	1.33	-12.12
CuL1	1.11	-11.64	CuL2	3.6	-14.58	CuL3	3.2	-14.29
NiL1	2.83	-13.99	NiL2	3.4	-14.44	NiL3	1.67	-13.83

DNA binding studies:

The compounds with Ligand L3 and its corresponding complexes showed highest DNA binding as compared to other ligands as presented in Table **2**. The complexes of all metals with L3 showed highest DNA binding.

Table 2. Binding and free energy of binding determined by DNA binding analysis.

	K_b × 10^5 (mol.L^{-1})	ΔG_b (kJmol^{-1})		K_b × 10^5 (mol.L^{-1})	ΔG_b (kJmol^{-1})		K_b × 10^5 (mol.L^{-1})	ΔG_b (kJmol^{-1})
CoL1	4.03	-31.97	CoL2	3.98	-31.95	CoL3	4.44	-31.21
CuL1	4.56	-32.28	CuL2	4.45	-32.22	CuL3	5.05	-32.54
NiL1	4.93	-32.47	NiL2	4.78	-32.4	NiL3	5.22	-32.61

ACKNOWLEDGEMENTS

The authors are thankful to the support provided by Islamia University Bahawalpur, Pakistan.

REFERENCES

1. Shaharyar and Mazumder. Benzimidazoles: A biologically active compounds. Arabian Journal of Chemistry 10 (2017): S157-S173.
2. Bansal, Yogita, and Om Silakari. "The therapeutic journey of benzimidazoles: a review. Bioorganic & medicinal chemistry (2012): 6208-6236.
3. Noor S, *et al*. Spectroscopic, conductometric and biological investigation of [Ni (phen)$_3$]F$_2$. EtOH. MeOH.8H$_2$O complex in anionic micellar media. Colloid and Interface Science Communications. (2018) 1;27:26-34.
4. Taj, M. *et al*. A Swift One-Pot Solvent-Free Synthesis of Benzimidazole Derivatives and Their Metal Complexes: Hydrothermal Treatment, Enzymatic Inhibition, and Solubilization Studies. Russian Journal of General Chemistry (2020), 90, 1533-1543.