Complexation and Antimicrobial Studies of Some Divalent Metal Chelates

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Abstract: Metal chelates of Ni(II) and Cu(II) with the ligand 5-acetamido-1,3,4-thiadiazole-2-sulphonamide have been synthesized. The isolated compounds have been characterized by elemental analysis, molar conductivity, magnetic moment, electronic and IR spectral studies. The analytical data reflects the metal to ligand stoichiometry to be 1: 2. The conductivity data of the complexes also suggests their non-electrolytic nature. The stability constants and free energy change for the complexes have been calculated. Ligand and their complexes have been screened for their biological activity and the data show good activity of these complexes and ligands.

Keywords: Schiff base, Conductivity, Stoichiometry, Non-electrolytic, Stability constant.

Introduction

Schiff base metal chelates are widely applicable because of their industrial and biological importance and hence have well been studied in the past^{1,2}. A detailed survey of literature reveals that very little work has been done on metal complexes of diuretic drugs. Nickel and copper salts have been reported to have therapeutic value³⁻⁵. Therefore, in the present communication, synthesis and characterization of metal complexes of Ni(II) and Cu(II) with 5-acetamido -1,3,4 - thiadiazole - 2 - sulphonamide (acetazolamide) has been done.

Experimental

All the chemicals used were of AR/GR grade. Pure sample of acetazolamide (AZM), molecular formula $C_4H_6N_4O_3S_2$, molecular weight 222.24, was obtained from Shalak's Pharmaceuticals. Metal salts $NiCl_2$ and $CuCl_2$ used were of Merck. Solvents used were methanol, acetone and deionized double distilled water.

Preparation of Schiff base

Equimolar solutions of pure drug and salicylaldehyde were separately dissolved in methanol-water mixture (1:1) and refluxed for four hours and kept for a day. Pale yellow crystals of acetazolamide Schiff base were formed in the reaction mixture which were filtered and washed thoroughly with 50% methanol, dried over vacuum and weighed. Melting point of Schiff base was recorded.

Figure 1. Structure of Schiff base.

Synthesis of complex

For the synthesis of complex, ligand-metal ratio was confirmed by conductometric titrations using monovariation method on Systronics conductivity meter using dip type electrode. Conductometric titrations supported 2:1 (L:M) ratio in the complex which was further supported by Job's method⁶ of continuous variation as modified by Turner & Anderson⁷. The stability constants and free energy change values were also calculated.

For the synthesis of complex of AZM-SA-Ni and AZM-SA-Cu, 0.006 M ligand solution (AZM- SA) was prepared in 60% acetone and refluxed for four hours with 0.003 M solution of NiCl₂ and CoCl₂ separately. The refluxed solutions were kept for some days. Solid crystalline compounds appeared in the solution, which were filtered, washed with 60% acetone, dried and weighed, Melting point of the complexes were recorded.

Analytical procedure

The magnetic moments were obtained by vibrating sample magnetometer (model 7304 Lakeshore with a 735 Controller and 450 Gauss meter). Elemental analysis were carried out on model 240 Perkin elemental analyzer. Metal contents were determined gravimetrically. The electronic spectra of the metal complexes in DMF were recorded on JASCO 7800 Elico SL-159 and Shimadzu UV-160A UV-VIS spectrophotometers. The infrared spectra were measured on a Nicolet 400 D FT- IR spectrophotometer in KBr pellets. The melting points of the ligand and complexes were recorded in open capillaries on a capillary melting point apparatus.

Antibacterial activity

Above synthesized compounds and the ligand (Schiff base) were screened against bacteria *Escherichia coli* by filter paper disc method at various concentrations using nutrient agar as medium. Sterilized filter papers of 5 mm diameter were soaked in solutions of different concentrations of test samples and introduced on nutrient agar plates. These plates were incubated for 48 h at 35 °C.

Results and Discussion

On the basis of physicochemical characteristics (Table 1) it has been found that both the complexes are non- hygroscopic, stable at room temperature, insoluble in water but fairly soluble in DMSO. The magnetic moment data indicate that Ni(II) and the Cu(II) complexes to be paramagnetic in nature. The molar conductance values for both the complexes were found between 10-17 Ω⁻¹ cm² mol⁻¹ in DMSO, which indicate their non-electrolytic nature. Elemental analysis data, formula weights and melting points are given in Table 2.

Table 1. Synthesis and physicochemical characteristics of complexes

	Ligand-Metal ratio	Colour	Yield, %	Stability constant log K, L/mole	ΔF K cal/mole	Molar Conductance $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$	μ_{eff} (BM)
AZM-SA	-	Pale yellow	54.5	-	-	-	-
(AZM) ₂ Ni	2:1	Pale Green	65	10.84	-15.580	13.0	3.18
(AZM) ₂ Cu	2:1	Dark Green	42.5	12.08	-17.056	14.6	1.83

Table 2. Analytical data of complexes

Complex	Elemental analysis % found (calculated)					Melting point, °C
	C	H	N	S	Metal	
(C ₁₁ H ₉ N ₄ O ₄ S ₂) ₂ Ni	35.00 (35.45)	2.80 (2.41)	14.93 (15.03)	17.14 (17.18)	7.96 (7.91)	260
(C ₁₁ H ₉ N ₄ O ₄ S ₂) ₂ Cu	36.98 (36.00)	2.50 (2.91)	15.69 (16.67)	17.93 (17.50)	8.86 (8.91)	199

Electronic spectra

The electronic spectra provide the detailed information about the electronic structure of the metal complexes. The electronic spectra of the complexes were recorded in solution state. The energies of the observed spin allowed bands in both the complexes agree with the octahedral geometry. The electronic spectrum of the Ni(II) complex displays three bands at 12500 cm⁻¹, 18900 cm⁻¹ and 26400 cm⁻¹ assigned due to ³A_{2g}(F) → ³T_{2g}(F), ³T_{1g}(F) and ³T_{1g}(P) transitions respectively, which indicate octahedral geometry⁸ of Ni(II) complex which is also supported by the μ_{eff} value⁹ (3.18 B.M.). The electronic spectra of Cu(II) complex shows two ligand field bands at 13700 cm⁻¹ and 18000 cm⁻¹ assigned to the transitions ²E_g → ²T_{2g} and charge transfer band respectively. The electronic spectra of Cu(II) complex suggests an octahedral geometry¹⁰, which is further supported by the μ_{eff} value⁹ (1.83 B.M.).

Infrared spectra

The IR spectra^{11,12} of Schiff base shows a sharp band near 1680 cm⁻¹ which may be due to azomethine linkage and shows lowering in frequency in metal complexes indicating the coordination of metal ions through azomethine linkage. Strong bands observed at 1580 cm⁻¹ and 1590 cm⁻¹ indicate the presence of (CH=N) bonds in complexes. Bands observed at 1176 cm⁻¹, 1175 cm⁻¹ and 1173.5 cm⁻¹ are characteristics of SO₂-N linkages in Schiff base, Ni and Cu complexes respectively. Absorption bands at 1435.4 cm⁻¹ and 1440 cm⁻¹ show the presence of chelate ring in complexes. The appearance of the M-O bands at 670 cm⁻¹ and 680 cm⁻¹ and M-N bands at 511 cm⁻¹ and 550 cm⁻¹ in both the complexes indicates that AZM-SA is coordinated through O & N atom. Absorption band appearing at 700 cm⁻¹, 706 cm⁻¹ and 709 cm⁻¹ show the presence of S in the heterocyclic ring. Absorption band at 818 cm⁻¹, 815 cm⁻¹ and 838 cm⁻¹ indicate the S-N linkage. The disappearance of phenolic-OH group in complex supports its involvement in complexation. IR spectral data and their tentative assignments are shown in Table 3.

Table 3. Infrared spectral data (cm⁻¹) and their tentative assignments

Ligand/ Complex	ν (HC=N)	ν (SO ₂ N)	Chelate Ring	ν M-N	ν M-O	ν (Ar-S)	ν (S-N)
AZM-SA	1680 vs	1176 vs	-	-	-	700 m	818 m
(AZM-SA) ₂ Ni	1590 s	1175 vs	1435.4 m	590 m	670 s	706 s	815 m
(AZM-SA) ₂ Cu	1599 s	1173.5 s	1440 m	550 s	680 w	709 s	838 w

(vs = very strong, s = strong, m = medium, w = weak).

Hence, on the basis of elemental analysis, IR spectra, electronic spectra, magnetic moment data and conductivity measurement, following structure is proposed for complexes (Figure 2).

Figure 2

Antibacterial activity

The zone of inhibition based upon size around the disc was measured. Inhibition zone percentages are recorded in Table 4. From the results it is observed that Ni(II) and Cu(II) complexes show greater activity against *Escherichia coli* as compared to the Schiff base. This indicates that chelation increases the antibacterial activity¹³.

Table 4. Antibacterial activity of Schiff base and complexes

Compounds	% of inhibition zone	
	<i>Escherichia coli</i>	
	Concentration in ppm	
	500	1000
AZM-SA	-	40
(AZM) ₂ Ni	86	92
(AZM) ₂ Cu	56	87

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