

Studies on Interaction of an Antimalarial Drug Pyrimethamine with Co(II), Ni(II) and Cu(II)

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The present communication describes the preparation and characterisation of pyrimethamine (an antimalarial drug) complexes with Co(II), Ni(II) and Cu(II) with the help of elemental analysis, magnetic susceptibility, electronic and infrared spectral studies. 2 : 1 metal to drug stoichiometry for Co(II) and Ni(II) and 1 : 2 metal to drug stoichiometry for Cu(II) complexes have been confirmed by analytical data. From the reflectance spectra octahedral geometry for Co(II), Ni(II) and Cu(II) complexes has been assigned. Ligand field parameters (Dq , B and β) have been calculated for the complexes.

INTRODUCTION

In recent years it has become increasingly apparent that the proper balance of the biologically available metals such as Cu, Ni, Co, Fe, Zn etc. is necessary for the efficient metabolism and growth of human and animal organisms. Study of coordination compounds of the drug led to the investigation directed towards establishing the site(s) of the metal binding in the drug. The study of the stereochemistries and the chemical reactivity of the coordination compounds of the drug will help to determine the relationship which exists between chemical structure and biological activity. It has been reported that in biological activity the metal complex is more potent and less toxic as compared to the free ligand.¹

RESULTS AND DISCUSSION

The molecular formulae of the complexes obtained from the analytical data (Table 1) indicate 2 : 1 (metal to drug) stoichiometry for Co(II) and Ni(II) complexes and 1 : 2 (metal to drug) stoichiometry for Cu(II) complex.

All these complexes are crystalline, stable at room temperature. Cu(II) and Ni(II) complexes are insoluble in water and most of the common organic solvents but Co(II) complex is soluble only in DMF.

Co(II) complex shows magnetic moment 2.06 B.M. which lies between the range of low spin or spin paired octahedral complexes.^{2,3} Diffuse reflectance spectra of Co(II) complex shows bands at 14044, 17241 and 23529 cm^{-1} due to transitions ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ respectively suggesting an octahedral geometry of cobalt(II) complex.⁴ Ligand field parameters $Dq = 770 \text{ cm}^{-1}$, $B = 816 \text{ cm}^{-1}$ and $\beta = 0.80$ further supports octahedral geometry for Co(II) complex.

Magnetic moment of Ni(II) complex is 3.0 B.M. which exists between the range of octahedral Ni(II) complexes. In the reflectance spectra of Ni(II) complex

two bands observed at 13698 and 23584 cm^{-1} correspond to ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ (ν_2) and ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$ (ν_3) transition respectively which supports distorted octahedral geometry. The value of Racah parameter (670 cm^{-1}) is less than the free ion value (1030 cm^{-1}) indicating covalent character of the complex. The ν_3/ν_2 ratio of 1.72 further supports octahedral geometry of Ni(II) complex.⁵

TABLE-I
ANALYTICAL DATA OF THE COMPLEXES

S. No.	Complexes/ (colour)	Analysis %: Found (Calcd.)				Decomp. Temp. °C
		M	C	H	N	
1.	[Co ₂ (C ₁₀ H ₁₃ N ₄ Cl)·Cl ₄ ·6H ₂ O]·2H ₂ O (Pink)	18.96 (18.77)	18.70 (19.02)	3.81 (4.61)	8.12 (8.91)	115
2.	[Ni ₂ (C ₁₀ H ₁₃ N ₄ Cl)·Cl ₄ ·6H ₂ O]·2H ₂ O (Light green)	21.04 (18.69)	18.62 (19.11)	3.87 (4.61)	8.95 (8.91)	245
3.	[Cu ₂ (C ₁₀ H ₁₃ N ₄ Cl) ₂ ·Cl ₂ ·2H ₂ O]	10.85 (10.25)	40.15 (38.73)	4.59 (4.89)	18.13 (18.07)	242

Cu(II) complex has subnormal magnetic moment value⁶ 1.09 B.M. at 300 K compared to the spin only value of 1.73 B.M., which could be attributed to the presence of strong anionic bridges between Cu(II) ions in a dimeric structure and a partial quenching of the unpaired spins on the Cu(II) ions.⁷ Reflectance spectra of Cu(II) complex show a broad band at 13333 cm^{-1} and charge transfer band at 25000 cm^{-1} . The first band is assignable to the ${}^2E_g \rightarrow {}^2T_{2g}$ transition characteristics of a tetragonally distorted octahedral stereochemistry.⁸

The assignment of the IR bands ($\nu_{\text{max}} \text{ cm}^{-1}$) in the complexes has been carried out by the comparison with the spectrum of the free ligand. In the ligand and the spectra of Co(II), Ni(II) and Cu(II) complexes three principal regions of absorption NH₂ group are *ca.* 3180–3160, 1310–1300 and 1120–1100 cm^{-1} . These absorptions have been assigned to the NH stretching mode,⁹ the symmetric deformation and the NH₂ wagging and twisting mode respectively,^{10,11} remain unchanged; C=C, C=N and ring stretching vibrations have been observed in the region 1660 and 1580 cm^{-1} in the free ligand. The band due to C=N has been found to be shifted by *ca.* 30 cm^{-1} to lower side as compared to the free ligand, indicating coordination through the nitrogen atom.¹² Two bands appearing near 3600–3460 cm^{-1} and 870–860 cm^{-1} may be due to $\nu(\text{O—H})$ and rocking vibration of coordinated water molecules in complexes. $\nu(\text{M—N})$ stretching bands lie in the region 530–510 cm^{-1} in the spectra of Co(II) and Ni(II) complexes, while in Cu(II) complexes it appears at 490 cm^{-1} . The band in region 400–395 cm^{-1} is due to $\nu(\text{M—Cl})$ in the complexes of cobalt(II), nickel(II) and copper(II).

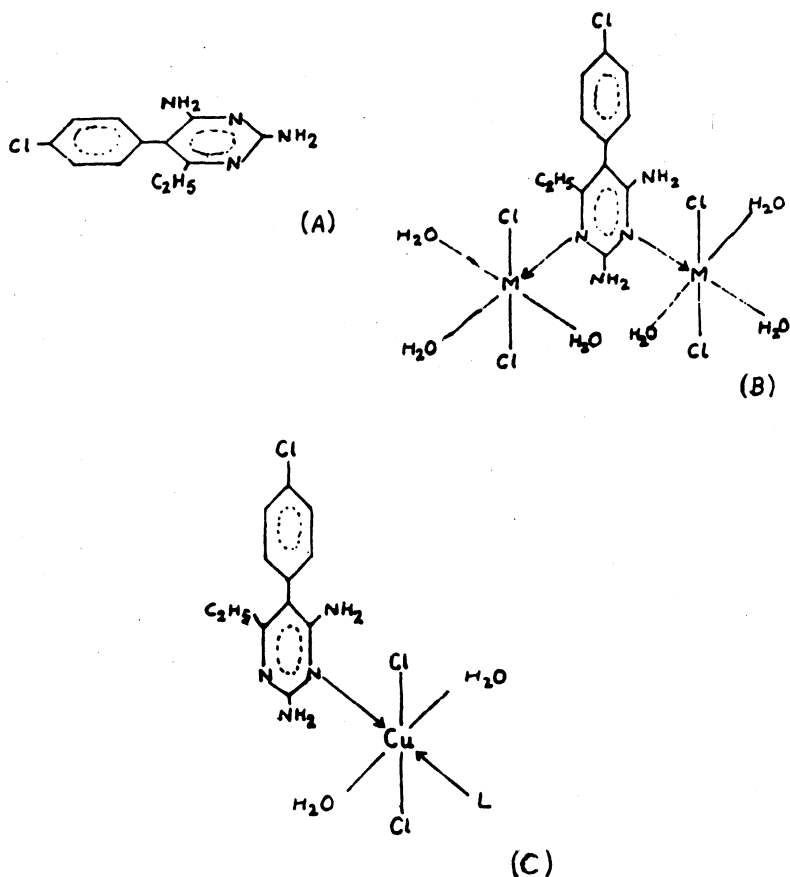


Fig. 1. (A) Pyrimethamine; (B) Pyrimethamine complexes ($M = \text{Co(II)}, \text{Ni(II)}$); (C) Pyrimethamine Cu(II) complex ($L = \text{Ligand (Pyrimethamine)}$).

EXPERIMENTAL

All the reagents used were of AR/BDH grade. Pyrimethamine was obtained by the courtesy of Central Drugs Laboratory, Calcutta, India and was used as such. Metal complexes were isolated using the following general method.

To a hot solution of metal salt in ethanol, solutions of the ligand in the same solvent in ratio 1 : 2 metal to drug for Co(II) and Ni(II) were added. The resulting mixture was refluxed on a water bath for 2 h. The precipitated complex was filtered, washed with ethanol and dried over anhydrous CaCl_2 and then at 110°C for 1 h. The elemental analyses were carried out on a Carlo Ebra analyser at RSIC, CDRI Lucknow. Magnetic measurements were done at room temperature by Gouy's method using $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as calibrant. Reflectance spectra were carried out at RSIC, IIT Bombay between the range 350 to 1100 nm.

The IR spectra were recorded on Shimadzu IR-470 infrared spectrophotometer in KBr medium, between the range $4000\text{--}400\text{ cm}^{-1}$.

ACKNOWLEDGEMENTS

The authors are thankful to the Head, Department of Chemistry for providing the facilities. The authors are also grateful to RSIC, CDRI Lucknow for elemental analysis, RSIC, IIT Bombay for reflectance spectra and gratefully acknowledge their thanks to Central Drug Laboratory, Calcutta for providing pyrimethamine as gift sample.

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(Received: 7 April 1997; Accepted: 2 June 1997)

AJC-1295