

COMPLEXATION STUDIES OF COBALT AND MANGANESE WITH ISONIAZID, AN ANTITUBERCULAR DRUG

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ABSTRACT

Isoniazid, an antitubercular drug forms 2:1 complexes with Co and Mn as indicated by conductometric titrations and further verified by Job's method of continuous variation as modified by Turner and Anderson. Analytical results are also in favour of 2:1 ratio between ligand and metal. Complexes of isoniazid were synthesized with Co and Mn, isolated in pure form, dried and weighed. The general structure assigned to these complexes is supported by I. R. spectral bands.

INTRODUCTION

Isoniazid (Chemical name : 4-Pyridine carboxylic acid hydrazide, trade name : INH) is a well known antitubercular drug. Looking to the use of metals in chemotherapy¹⁻² and the wide applications of schiff bases³⁻⁵ derived from drugs, the schiff base of drug was complexed with different metals (Mn and Co) to form a new compound, which could be more potent than the parent drug.

MATERIALS AND METHOD

Pure sample of isoniazid molecular formula $C_6H_7N_3O$, molecular wt. 137.14 was obtained from Dr. Reddy's Laboratory, Hyderabad. Its m.p. is 171.4 °C, soluble in 50% alcohol.

Metal salts used like $CoCl_2 \cdot 6H_2O$ and $MnCl_2 \cdot 4H_2O$ were of Qualigens chemicals. Solvents used were ethanol and acetone of A R Grade and distilled water.

Synthesis of schiff base of drug- Equimolar solutions of pure drug and salicylaldehyde were taken in alcohol-water mixture in the ratio 1:1. The solutions were mixed in a round bottom flask of 500 ml capacity and refluxed for 3 hrs. The solution was cooled which gave white crystalline precipitate, which was filtered, dried and weighed.

Ligand metal ratio and stoichiometry- 20 ml of ligand solution (schiff base of INH) was diluted to

200 ml (using 70% acetone) and titrated against 0.02 M solution of Co and Mn respectively indicate 2:1 (L:M) ratio in the complex formation which was further verified by Job's method of continuous variation as modified by Turner and Anderson. Stability constant and Free energy change were also calculated (Table 1).

Synthesis of complexes- Complexes of isoniazid were synthesized with Co and Mn respectively by way of refluxing in 2:1 (L:M) molar solution in 70% acetone. After refluxing for 3½ hrs. the resultant solution was cooled and dried. Solid crystalline complexes of Co and Mn were isolated. The complexes formed were washed with 70% acetone and dried. Finally, the wt. was taken and m.p. were recorded.

RESULTS AND DISCUSSION

Conductivity measurements⁶⁷ Job's method of continuous variation as modified by Turner and Anderson indicate the formation of 2:1(L:M) complexes for schiff base of the drug with cobalt and manganese. Analytical data of these complexes are in agreement with the composition $(C_{13}H_{10}N_3O_2)_2M \cdot 2H_2O$.

Infra red spectral frequencies⁸⁻¹¹ like pyridine, free carbonyl, azomethine, phenolic group and aromatic ring for the schiff base of the drug (INH), on complexation gets modified and new frequencies appeared like M-O (682.7 and 650.0

Table-1: Analytical data and other properties of complexes

Composition of the complexes (Moi.wt.)	Colour (%) Yield)	m.p. °C	% Analysis found (Calculated)					Stability constant Log K.	Free energy change ΔF (K cal/mole)	Magnetic moment (B.M.)
			M	C	H	N	H ₂ O			
(C ₁₃ H ₁₀ N ₃ O ₂) ₂ Co.2H ₂ O (575.41)	Reddish brown (50.8)	205	10.28 (10.24)	53.40 (54.27)	4.01 (3.50)	15.20 (14.60)	6.08 (6.25)	11.19	-15.680	4.87
(C ₁₃ H ₁₀ N ₃ O ₂) ₂ Mn.2H ₂ O (571.42)	Light green (54.0)	215	9.38 (9.61)	53.91 (54.65)	4.08 (3.52)	15.47 (14.70)	6.30 (6.30)	11.35	-15.996	5.92

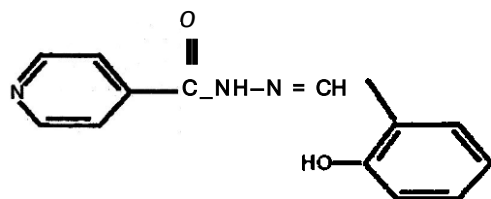


Fig. 1. Structure of Schiff base of INH

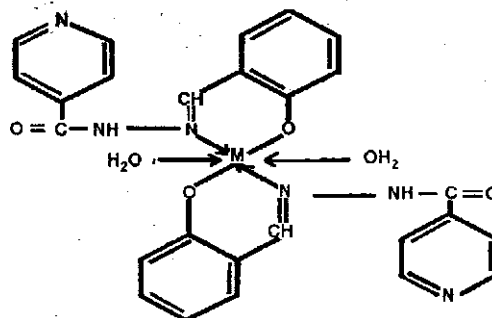


Fig. 2. Structure of complex (M = Mn or Co)

cm^{-1}), M-N (830.0 and 820.0 cm^{-1}). Co-ordinate water (3328.0 and 3360.0), chelate ring (1380.0 and 1400.0). Frequency of phenolic -OH group in the schiff base indicates the participation of this group in complexation. The frequencies of the co-ordinated water supports the six co-ordination number of the metals and its octahedral symmetry which is also supported by the magnetic moment data for Mn and Co complexes respectively.

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