

Physicochemical Studies of the Interaction of an Antimalarial Drug Amodiaquine Hydrochloride with Metal Ions of Biological Importance

PRAMILA SINGH* and M.S. KACHHAWAHA

Department of Chemistry

Doctor Hari Singh Gour Vishwavidyalaya, Sagar-470 003, India

Octahedral complexes of Fe(III), Co(II) and Ni(II) with an antimalarial drug amodiaquine hydrochloride have been prepared. The complexes contain two molecules of the amodiaquine, which functions as a tridentate monoprotic ligand coordinating through quinoline nitrogen, tertiary nitrogen of diethyl moiety and by deprotonation of hydroxyl group. The drug precipitates quantitatively in a particular pH range which provides a new method for the microestimation of the drug as its complex.

INTRODUCTION

The present paper deals with the isolation and characterization of amodiaquine HCl (ADQ·HCl) complexes of the Fe(III), Co(II), Ni(II). The complexes of the composition $[\text{Fe}(\text{ADQ})_2]\text{Cl}$, $[\text{Co}(\text{ADQ})_2]$ and $[\text{Ni}(\text{ADQ})_2]$ were prepared and characterised by analytical data, molar conductance, magnetic moment, electronic spectra and IR.

EXPERIMENTAL

Metal salts used were of AnalaR/BDH grade. Amodiaquine HCl was obtained by the courtesy of Park-Davis, Bombay, India and was used as such. Metal complexes were isolated using the following general method.

A concentrated aqueous solution of the ligand in slight excess over the stoichiometric M : L : 1 : 2 ratio was added slowly with constant stirring to an acidic aqueous metal ion solution. To the clear solution dilute (1 : 10) ammonia was added dropwise to adjust the pH to about 6. The mixture was refluxed for 1 hr on a water bath, then kept at 5–15°C overnight. The precipitate so obtained was dried in an oven at about 110°C, after filtration and repeated washing with warm distilled water.

RESULTS AND DISCUSSION

The molecular formulae of the complexes have been obtained from the analytical data (Table 1). The molar conductance value of Fe(III) complex

indicates that the complex behaves as an electrolyte (1 : 1) breaking up into two ions. The Fe(III) complex is thus assigned the formula $[\text{Fe}(\text{ADQ})_2]\text{Cl}$. The molar conductance values of Co(II) and Ni(II) complexes were found very low which indicates that these complexes are non-electrolytes. The Co(II) and Ni(II) complexes are thus assigned the formulae $[\text{Co}(\text{ADQ})_2]$ and $[\text{Ni}(\text{ADQ})_2]$. Magnetic data indicate (Table 1) octahedral geometry for Fe(III), Co(II) and Ni(II) complexes. Magnetic moment value of Fe(III) complexes has been found to be 5.95 BM suggesting spin free complex with octahedral structure (ground state ${}^6\text{A}_{1g}$). Electronic spectra of all the complexes show two bands. The first band present near 24691–24096 cm^{-1} has been assigned to ligand metal charge transfer origin. The second broad and asymmetric band between 20000–10752 cm^{-1} is indicative of an octahedral stereochemistry for Fe(III), Co(II) and Ni(II) complexes.

TABLE 1

Complex	Analytical data %, Found (Calcd)					Molar conductance $\text{ohm}^{-1} \text{cm}^2$ mol^{-1}	Magnetic moment μ_{eff} B.M.
	C	H	N	Cl	M		
$[\text{Fe}(\text{C}_{20}\text{H}_{21}\text{ClN}_3\text{O})_2]\text{Cl}$ Reddish brown (Decomp. temp. 285°C)	59.99 (59.91)	5.32 (5.24)	10.55 (10.49)	13.50 (13.30)	7.11 (6.97)	60.58	5.95
$[\text{Co}(\text{C}_{20}\text{H}_{21}\text{ClN}_3\text{O})_2]$ Bluish green (Decomp. temp. 190°C)	62.40 (62.50)	5.58 (5.46)	10.81 (10.93)	9.33 (9.24)	7.81 (7.67)	10.5	4.82
$[\text{Ni}(\text{C}_{20}\text{H}_{21}\text{ClN}_3\text{O})_2]$ Green (Decomp temp. 246°C)	62.66 (62.52)	5.61 (5.47)	10.81 (10.94)	9.44 (9.24)	7.80 (7.64)	6.46	2.92

The assignment of the IR bands (ν_{max} in cm^{-1}) in the complexes has been carried out by the comparison with the spectrum of the free ligand. The band observed in the ligand at 3410 was due to $\nu(\text{OH})$. In complexes this band was shifted to 3450 which is indicative of involvement of OH group in chelation¹. The bands found near 1310 and 1287 have been assigned to phenolic² mode C–O (ligand). These bands were observed at 1320 and 1320, 1325 and 1280, and 1260 and 1275 in the spectra of Fe(III), Co(II) and Ni(II) complexes respectively. The shifting of tertiary amino group³ from 1160 (ligand) to 1165, 1182 and 1170 in Fe(III), Co(II) and Ni(II) complexes respectively suggests the involvement of this group in chelation. The bands in the region 3160 and 1335 in the ligand are assignable to $\nu(\text{N–H})$ and aromatic carbon aliphatic nitrogen stretching vibrations⁴. In complexes these bands remain almost unchanged indicating non-involvement of amino group in metal binding. Nitrogen atom of quinoline ring appears to participate in chelation as bands observed at 1660 and 1590 assignable to

$\nu(\text{C}=\text{C})$ and $\nu(\text{C}=\text{N})^5$ were shifted in the complexes to near 1600 and 1550 respectively. It was reported⁶ that some bands observed in the region 1200–1000 are due to quinoline ring vibration. In the present case similar bands were observed in the spectra of ligand and complexes in the region 1150–1040 but they were of quite weak intensity. Strong bands at 540, 552 and 550 in the spectra of Fe(II), Co(II) and Ni(II) have been assigned to $\nu(\text{M}-\text{N})$ which indicate complexation of metal ion with the drug molecule⁷. The bands in the region 470–450 in the spectra of complexes may be due to coordination of oxygen atom of OH group with metal by replacement of hydrogen atoms^{8–13}. The weak bands at 390, 375 and 370 in Fe(III), Co(II), Ni(II) complexes respectively may be assigned to coordinate nitrogen of quinoline ring^{14–16}.

It has been found that the precipitation of the drug amodiaquine 2HCl as Ni(II) and Co(II) complexes was quantitative; therefore a method has been developed for the micro estimation of drug as metal chelate. Co(II) and Ni(II) react with the drug at pH 4.5 and 5.7 quantitatively resulting in the formation of coloured, insoluble, well defined and thermally stable complexes.

- (1) Amodiaquine dihydrochloride as Co(II) complex
wt. of ADQ·2HCl = 0.5580 × wt. of Co(II) complex
- (2) Amodiaquine dihydrochloride as Ni(II) complex
wt. of ADQ·2HCl = 0.5572 × wt of Ni(II) complex.

ACKNOWLEDGEMENT

One of the authors (P.S.) is grateful to ICMR, New Delhi for the award of a Junior Research Fellowship. She is also grateful to Prof. S.P. Banerjee, Head, Department of Chemistry, University of Sagar, for providing laboratory facilities. Thanks are also due to Park-Davis, Bombay for providing free gift sample of Amodiaquine hydrochloride.

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(Received: 15 September 1991; Accepted: 1 July 1992)

AJC-443

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