

SYNTHESIS, CHARACTERIZATION & ANTIMICROBIAL STUDIES OF COMPLEXES OF TRANSITION METAL CHELATES OF SOME ORGANIC ACIDS WITH CLOXACILLIN

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A number of mixed ligand complexes of transition metal chelates of some organic acids with cloxacillin of the type $[ML_n.antb.]$ have been synthesized. These complexes have been characterized by elemental analysis, spectral data, conductance and magnetic moment measurements. Antimicrobial efficiency of the compounds has been screened against five different micro-organism. Interestingly all complexes demonstrated potent in vitro antibacterial/antifungal activity against Gram +ve bacteria (*S.aureus*), Gram -ve bacteria (*E.coli*) and fungi (*C.albicans*).

Key word : Mixed ligand complexes, Transition metal chelates, Cloxacillin, Organic acids, Spectral data & Antimicrobial activity.

INTRODUCTION

Cloxacillin belongs to quinolones class of antibiotics. It behaves as a monoprotic bidentate ligand coordinating through oxygen atoms of $>C=O$ and $-COOH$ groups of the drug. Many drugs possess modified toxicological and pharmacological properties when they are complexed with metals [1–3]. Metal complexes of the quinolone antibacterial agent ciprofloxacin with Mn(II), Fe(III), Co(II) and Ni(II) are reported [4-5]. The literature survey has indicated that two kinds of mixed ligand fluoroquinolones complexes with transition metal adducts of neutral bidentate ligands have been isolated by several workers. These are of types : $[ML_n.antb.]$ and $[M(antb)L_n]$ where M = Mn(II), Fe(III), Cu(II), Ni(II) etc., L = bidentate neutral ligand, antb. = antibiotics. Recently, we have reported a number of complexes of transition metal chelates of some organic acids with Norfloxacin [6]. In continuation, we have synthesized and characterized several mixed ligand transition metal complexes with well

known antibiotic cloxacillin to study the relative bioactivity and stereochemistry of the complexes.

EXPERIMENTAL :

1. Synthesis of transition metal chelates of organic acids, ML_n : 95% Ethanolic solution of organic acid (DNP or 1N2N) and suspension/solution of metal acetate in 95% ethanol were mixed together in 2 : 1 molar proportion. The mixture was refluxed on magnetic hot plate at 80°C for nearly one and half hours with continuous stirring. The colour of the contents changed and a clear solution was obtained, on adding ammonia solution, the adduct got separated. It was filtered and washed with the solvent and dried in an electric oven at 100°C.

2. Synthesis of mixed ligand complexes of transition metal chelates of some organic acids with Ciprofloxacin : To the suspension of transition metal chelate 2, 4-dinitrophenol or 1-nitroso-2-naphthol in ethanol, cloxacillin was added in 1 : 1 molar proportion till the colour changed/precipitate formed. The mixture was refluxed on magnetic hot plate with constant stirring at 80°C for 1-2 hours. On cooling the solution, characteristic colour precipitate got separated. It was filtered, washed with absolute ethanol and finally dried in an electric oven at 100°C

RESULT & DISCUSSION :

Colours, decomposition temperatures, molar conductances, magnetic moment values and analytical data of the prepared complexes are given in Table - 1. Molar conductance values of the complexes were measured in DMF at 30°C at a concentration of 10^{-3} M. The low values (9.6 - 14.5 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$) of molar conductances, indicate that they are non-electrolyte in nature [7].

TABLE -1

Compound	Colour	Deco mp. temp. (°C)	Condu-ctivity	Magnetic moment	% Analysis Found/(Calc.)				
					C	H	N	Cl	M
[Fe(DNP) ₂ .Norf]	Light brown	226	10.2	5.4	45.34 (45.21)	3.24 (3.16)	13.22 (13.04)	2.56 (2.47)	7.56 (7.40)
[Ni(DNP) ₂ .Norf]	Dark brown	285	11.5	3.1	45.18 (45.01)	3.23 (3.15)	13.18 (13.05)	2.55 (2.45)	7.89 (7.75)
[Cu(DNP) ₂ .Norf]	Brown	230	14.1	1.9	44.89 (44.75)	3.21 (3.11)	13.09 (12.80)	2.54 (2.44)	8.48 (8.35)
[Fe(1N2N) ₂ .Norf]	Brown	245	12.2	5.6	60.08 (59.95)	4.17 (4.05)	9.73 (9.62)	2.64 (2.55)	7.79 (7.54)
[Ni(1N2N) ₂ .Norf]	Yellowish brown	290	10.5	3.2	59.85 (59.71)	4.15 (4.03)	6.70 (6.52)	2.63 (2.51)	8.10 (7.95)
[Cu(1N2N) ₂ .Norf]	Golden brown	235	15.0	1.8	59.46 (59.31)	4.13 (4.05)	9.63 (9.51)	2.61 (2.48)	8.74 (8.61)

Infrared spectra : The assignment of the infrared bands in the complexes have been carried out by comparison with the spectrum of pure drug (Table - 2). In the infrared spectra of mixed ligand complexes of Fe(II), Ni(II), Cu(II), bands only appeared in the region 3649 - 3444 cm^{-1} assignable to O-H(free) stretching. The band $\nu_{\text{C=O}}$ which is present in the ligand at 1600 cm^{-1} shifted by 25 cm^{-1} in the complexes indicating the coordination through this group [8]. Presence of -OH group has been supported by a sharp medium bands present in the region 1112 - 1127 cm^{-1} in the mixed ligand transition metal complexes which indicates M-OH bonding. All the complexes show new medium intensity bands ~ 586 and ~ 462 cm^{-1} may be due to $\nu_{\text{M-N}}$ and $\nu_{\text{M-O}}$ [9-10] respectively.

TABLE - 2

Assignments	Norfloxacin	[Fe(DNP) ₂ . Nor]	[Cu(DNP) ₂ . Nor]	[Fe(1N2N) ₂ . Nor]	[Cu(1N2N) ₂ . Nor]	[Ni(1N2N) ₂ . Nor]
$\nu_{\text{O-H}}$	----	3805	3885, 3750	3800	3880, 3750	3830, 3740
$\nu_{\text{N-H}}$	3400	3300, 3205	3380, 3000	3305, 3210	3360, 3010	3415, 3075
$\nu_{\text{C=O}}$	1620	1630	1625	1625	1620	1630
$\nu_{\text{COO}^-/\text{COOH}}$	1470	1440	1465	1445	1470	1565, 1495,
$\nu_{\text{C=N}}$	1350	1335	1338	1330	1335	1340
$\nu_{\text{C-N}}$ (ring vibration)	1255, 1190, 1130	1270, 1190, 1110	1260, 1190	1265, 1195, 1115	1250, 1190, 1110	1265, 1190
$\nu_{\text{C-F}}$	1375	1370	1380	1365	1385	1385
$\nu_{\text{M-OH}}$ (bending)	----	1128	1110	1130	1115	1120
Out of plane deformation benzenoid ring	745, 625	750, 620	750, 625	755, 610	760, 535	625
C-N-C (bending)	525	515	515	510	522	520
$\nu_{\text{M-O}}$	----	485, 415	485	480, 420	476	475

Magnetic and electronic spectra : The electronic spectra of all the complexes of cloxacillin shows broad a broad band in the region ~ 40000 cm^{-1} which is due to $\pi_2 \rightarrow \pi_4$ transition.

The Fe(II) complex showed bands at 13774, 17513 and 23980 cm^{-1} corresponding to ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{1\text{g}}$, ${}^6\text{A}_{2\text{g}} \rightarrow {}^4\text{T}_{2\text{g}}$ and ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{E}_{\text{g}}$ transitions respectively, characteristic of octahedral stereochemistry around metal ion. Magnetic moment of Fe(II) complex was found to be 4.1BM indicating the presence of four unpaired electrons, *i.e.* paramagnetic in nature. This value is well within the range of octahedral Fe(II) (ground state ${}^6\text{A}_{1\text{g}}$) complexes [11]. The ligand field parameters Dq, B and β values were found to be 630.3 cm^{-1} , 573 cm^{-1} and 0.5645 respectively.

