www.sphinxsai.com

ChemTech

International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.1, pp 286-288, Jan-Mar 2010

SYNTHESIS AND CHARACTERIZATION OF METAL COMPLEXES OF SOME ANTIBACTERIAL DRUGS

B. S. Sekhon* and Leena Gandhi

Department of Biochemistry and Chemistry, Punjab Agricultural University,

Ludhiana.-141004, India.

E-mail:sekhon224@yahoo.com

Abstract: Synthesis and characterization of metal complexes of succinylsulfathiazole, sulfisoxazole, nalidixic acid and norfloxacin were carried by elemental analyses and IR spectral studies. Spectral data suggest that succinylsulfathiazole coordinates through O & N atom of sulfonamide as well as O atom of carboxylate while O and N atom of sulfonamide, N of aniline NH_2 and N of isoxozole ring in case of sulfisoxazole. Nalidixic acid and norfloxacin behave as bidentate ligands coordinating through 4-carbonyl oxygen and 3-carboxylate group.

Keywords: succinylsulfathiazole, sulfisoxazole, nalidixic acid , norfloxacin, metal complexes.

INTRODUCTION

Succinylsulfathiazole [2-{N (4)-succinylsulfaniliamido}thiazole] (SSTZ) is an antibacterial drug use in the prevention and treatment of gastrointestinal infections. SSTZ was employed in some dietary treatments to further enhance the level of folate depletion both before cancer initiation and during promotional/progressions phase of carcinogenesis[1]. Sulfisoxazole [4-amino-N-(3, 4-dimethyl-5-isoxazolyl) benzenesulfonamide] (SUL) is used to treat urinary tract infections[2]. Nalidixic acid (NAL) and norfloxacin (NOR) are synthetic antibacterial agents and have been extensively used in the treatment of gram –ve urinary tract infections[3] and are the most potent DNA gyrase inhibitors[4]. Many drugs possess modified pharmacological and toxicological properties when administered in the form of metallic complexes. Few reports on complexes of SSTZ have been reported[5] and some metal complexes of quinolones and sulpha drugs are cytotoxic[6]. Divalent metal complexes of norfloxacin exert antimicrobial activity[7]. The present investigations have been carried out to synthesize and characterize the solid complexes of succinylsulfathiazole, sulfisoxazole, nalidixic acid and norfloxacin with some metal ions viz., Ni(II), Mn(II), Cu(II), Zn(II), Co(II), VO(II), UO_2(II) and Ru(III).

EXPERIMENTAL

The ligands namely succinylsulfathiazole, sulfisoxazole, nalidixic acid and norfloxacin were of Sigma grade. All other chemicals used for the preparation of complexes were Analar grade quality and were used without further purification.

Synthesis of metal complexes

The complexes were prepared by mixing the molar solutions of metal ions dissolved in distilled water and ligands (dissolved in aqueous NaOH) in 1:2 ratios. However, M: L ratio was 1:3 in Ru(III). The pH of the reaction mixture was adjusted to about 8. The compounds were filtered off, washed with aqueous ethanol and dried over calcium chloride. The complexes were analyzed for metal by standard procedures. IR spectra of ligands and their metal complexes were recorded in KBr matrix on Perkin-Elmer Spectrophotometer and elemental analysis of C, H, and N were carried out at RSIC, Chandigarh. Molar conductivity measurements were carried out on bridge type CM 82 T Conductometer.

RESULTS AND DISCUSSION

Physical parameters of the ligands and their metal complexes are given in Table 1. Molar conductance of SSTZ-complexes lies between 8.8-11.3 ohm^{-1} cm^{2} mol^{-1} indicating their non-electrolyte nature. IR spectral data revealed that strong band at 1701.4 cm^{-1} (ν_{COOH}) and ν_{N-H} of sulfonamide at 3319.8 cm^{-1} for SSTZ disappeared for each metal complex. Further, new bands appeared in the range 1675-1685 cm^{-1} ($\nu_{asym\ (coo-)}$) and 1429-1449 cm^{-1} ($\nu_{sym\ (coo-)}$) as well as in the range 3200-3540 cm^{-1} ($\nu_{O-H\ (H2O)}$). In each complex , ν_{C-N} of sulfonamide[8] observed at 1251.4 cm^{-1} for SSTZ showed a +ve shift of 3-23 cm^{-1} .The changes in position and intensity were observed in the SSTZ band at 1300.7 cm^{-1} ($\nu_{asym\ (SO2)}$) ,1145.3 cm^{-1} ($\nu_{sym\ (SO2)}$) in spectra of Cd (II), Zn (II), Ru(III) and UO$_2$(II) complexes. The band observed at 694.1 cm^{-1} (ν_{N-H} of sulfonamide) for SSTZ showed a –ve or +ve shift of 5-10 cm^{-1} in spectra of metal complexes. These observations suggested that O atom (except Cu complex) and N atom of sulfonamide and O atom of carboxylate are involved in coordination to metal in each complex. In addition, -ve shift of 4-8 cm^{-1} (ν_{C-N})[9] observed in the spectra of metal complex suggested that N atom of thiazole ring participated in coordination to metal. In all the SSTZ complexes, $\Delta\nu$ is greater than 229.8 cm^{-1} indicating monodentate coordination of carboxylate group in its metal complexes [10].

The SUL complexes are non-electrolytic in nature as their molar conductance values are 40.2 and 50.9 ohm^{-1} cm^{2} mol^{-1}. The disappearance of peaks at 3485.5 cm^{-1} ($\nu NH_{2\ (asym)}$, 3381.1 cm^{-1}, 1647.5 cm^{-1} (δ_{NH2}+ $\nu_{C=N}$), and (1324.4, 1300.2 cm^{-1} due to ν_{C-N} of sulphonamide and aniline) suggested the participation of N of NH$_2$ group in coordination. Further, the absence of peak at 1345.6 cm^{-1} [$\nu_{SO2\ (asym)}$] along with negative shift of 35 cm^{-1} w.r.t peak at 1163.9 cm^{-1} [$\nu_{SO2\ (sym)}$] in spectra of SUL complexes indicated participation of metal ion through sulfonyl oxygen. Two strong bands at 1438 and 1392 cm^{-1} due to isoxazole ring[11] stretching vibrations for SUL showed a negative shift of 12-16 cm^{-1} in Cd-SUL complex. A broad band in region 3313- 3335 cm^{-1} in SUL complexes corresponded to ν_{O-H}.

Metal-NAL complexes are insoluble in water and common organic solvents like chloroform, benzene, ether, carbon tetrachloride and ethanol. The molar conductance of the complexes in DMF has been found to lie in the range 4.75 – 8.37 ohm^{-1} cm^{2} mol^{-1} indicating their non- electrolytic nature. IR spectra of metal-NAL complexes revealed that the strong absorption band of NAL at 1713.6 cm^{-1} due to $\nu_{c=o}$ of COOH disappeared giving place to ν_{COO}^{-} in 1622-1624 cm^{-1}(asym) and 1447-1449 cm^{-1} (sym). The ring $\nu_{c=o}$ observed at 1617 cm^{-1} for NAL showed negative shift of 42-54 cm^{-1} in spectra of complexes. This observation substantiated the participation of oxygen atom of 4-carbonyl and 3-carboxylate groups.

Metal-NOR complexes are sparingly soluble in N, N′-dimethylformamide and insoluble in most of the common solvents, viz, ethanol, acetonitrile, benzene, ether and methanol. The molar conductance of complexes in DMF have been found to be 56.8, 6.2 and 6.8 ohm^{-1} cm^{2} mol^{-1} for UO$_2$(II), Cu(II) and Ru(III) respectively, indicating their non-electrolytic nature. The $\nu_{(COOH)}$ peak[12] of NOR observed at 1731.6 cm^{-1} disappeared in the spectra of the complexes. The observed ($\Delta\nu$ = [$\nu_{(COO-)\ asym}$ - $\nu_{(COO-)\ sym}$] 134.1, 140.1 and 139.8 cm^{-1} for UO$_2$(II), Cu(II) and Ru(III) complexes respectively suggested bridging complexes[9]. In the spectra of the complexes two new bands appeared in the range 1626-1628 cm^{-1} ($\nu_{(COO-)asym}$) and 1486-1492 cm^{-1} ($\nu_{(COO-)sym}$). The observed changes in position and intensity of IR bands of the metal complexes corresponding to the ketone deformation region (1200 – 1350 cm^{-1}) suggested the participation of 4-oxo-group in complexation with metal ions. Inspection of the spectral data also revealed that the intensity and frequency of the band ($\nu_{c=o}$ ring) at 1620.3 cm^{-1} in NOR decreases on complexation. They appeared at 1562.2, 1583.3 and 1580.3 cm^{-1} in UO$_2$(II), Cu(II) and Ru(III) and complexes. Ru(III) complex has a peak at 3409.9 cm^{-1} corresponding to hydroxo complex, while 3404.6, 980.3 and 754.1 cm^{-1} absorption bands corresponding to O-H stretching rocking and wagging vibrations[11] in Cu(II) complex indicated the presence of coordinated water molecule.

Table 1: Analytical and physical characteristics of ligands and metal complexes

Compound	T_M (°C)	Elemental Analysis (%)			
		M	C	H	N
Succinylsulfathiazole (SSTZ)					
SSTZ (White) $C_{13}H_{13}N_3O_5S_2$	195	-	43.93 (43.99)	3.68 (3.74)	11.82 (11.88)
Cd(SSTZ) (White)	252	24.13 (22.34)	33.52 (33.45)	2.38 (2.12)	9.02 (8.71)
Cu(SSTZ)$(H_2O)_2$ (Pale Pink)	248	14.03 (15.11)	34.47 (35.34)	3.31 (3.42)	9.27 (9.26)
Ru(SSTZ)OH (Black)	>260	21.43 21.31	33.12 (34.25)	2.56 (2.53)	8.91 (8.92)
UO_2(SSTZ)$(H_2O)_6$ (Lemon Yellow)	>260	32.54 (37.25)	21.34 (20.44)	3.16 (3.17)	5.74 (5.68)
VO$(SSTZ)_2$ (Green)	>260	6.58 (6.45)	40.36 (40.39)	2.86 (2.53)	10.86 (10.77)
Sulfisoxazole (SUL)					
SUL(White) $C_{11}H_{13}N_3O_3S$	196	-	49.42 (49.48)	4.90 (4.91)	15.72 (15.64)
Cd(SUL)$(H_2O)_2$ OH (White)	258	26.03 (26.31)	30.60 (30.36)	3.03 (2.97)	9.73 (8.97)
Co(SUL)$(H_2O)_2$ OH (Purple)	230	14.85 (14.57)	33.30 (33.38)	4.06 (3.47)	10.59 (10.66)
Nalidixic acid (NAL)					
NAL(White) $C_{12}H_{12}N_2O_3$	230	-	62.06 (61.89)	5.20 (4.98)	12.06 (11.86)
Co(NAL)OH(Peach)	242	19.18 (18.04	46.92 (46.39)	3.94 (3.85)	9.12 (9.53)
Mn(NAL)OH(Mustard)	>250	18.12 (17.94)	47.54 (47.04)	3.99 (3.81)	9.24 (9.57)
Zn(NAL)OH(White)	>250	20.85 (20.01)	45.96 (46.16)	3.85 (4.06)	8.93 (8.35)
Ni(NAL)(OH) H_2O(Bluish Green)	>250	18.06 (17.85)	44.35 (44.59)	4.34 (4.01)	8.62 (8.12)
Cd$(NAL)_2H_2O$(White)	>250	18.96 (18.25)	48.62 (48.72)	4.08 (3.95)	9.45 (9.15)
Cu$(NAL)_2H_2O$(Sky blue)	>250	11.68 (11.07)	52.98 (52.84	4.44 (4.55)	10.30 (10.15)
VO$(NAL)_2(H_2O)_3$(Sap Green)	>250	8.73 (11.58)	49.40 (49.97)	4.84 (4.83)	9.60 (9.37)
$UO_2(NAL)_2(H_2O)_2$(Lemon Yellow)	>250	30.97 (30.85)	37.51 (37.39)	3.41 (2.68)	7.29 (7.35)
Ru$(NAL)_2ClH_2O$(Black)	>250	16.38 (16.25)	46.72 (47.72)	3.92 (4.07)	9.08 (9.19)
Norfloxacin (NOR)					
NOR(White) $C_{16}H_{18}FN_3O_3$	221	-	60.18 (60.15)	5.68 (4.60)	13.16 (13.18)
UO_2(NOR)NO_3(Yellow)	238	36.60 (40.89)	29.55 (30.05	2.63 (2.67)	8.61 (8.19)
Cu(NOR)OH$(H_2O)_3$(Sky Blue)	252	14.03 (13.09)	42.43 (42.44)	5.34 (4.51)	9.28 (9.17)
Ru(NOR)ClOH(Black)	>260	21.42 (21.32)	40.73 (40.39)	3.63 (3.58)	8.90 (8.80)

REFERENCES

1. R. K. Le Leu, G. P. Young and G. H. Mc Infosh, *Carcinogenesis* , 2000, **21**, 2261.
2. G. Kanagaraj and G. N. Rao, *Indian J. Chem*., 1993, **32,**594.
3. R. Gleckman, S. Alvarez, W. Joubert and S. J. Mathews, *Am. J. Hosp. Pharm*., 1979, **36**, 1071.
4. L. L. Shen and A. G. Pernet, Proc. *Natl. Acad. Sci. USA*, 1985, **82**, 307.
5. Torre M H, Kremer E, Estevez E and Baran E J (1999) *9th International Conference on Biological Inorganic Chemistry*. Department of Chemistry, University of Minnisota. Minneapolis. p100052; Gupta, J K and Jha, N K (1987) *Croat Chem Acta*, **60**, 303-308.
6. L. Ming, Med. Res. Rev., 2003, **23**, 697.
7. V. Uivarosi, S.Neagoe, V. Aldea and A. Nitulescu, *Roum. Arch. Microbiol. Immunol.* , 2001, **60**, 267
8. H. K. Sahai, B. S. Sekhon and H. S. Randhawa, *S. Afr. J. Chem.*, 1999, 52, 20.
9. K. K. Narang and J. K. Gupta, *J. Inorg. Nucl. Chem.,*1976, **38**, 589.
10. N. B. Behrens, G. Mendoza-Diaz and D. M. L.Goodgame, (1986) *Inorg. Chim. Acta,*1986, **125 ,** 21.
11. G. Kanagaraj and G. N. Rao, (1992) *Synth. React. Inorg. Met. Org. Chem*., 1992, **22**, 559.
12. K. Nakamoto, *Infrared Spectra of Inorganic and Coordination Compounds.* John Wiley and Sons INC, New York, 1978.

*****