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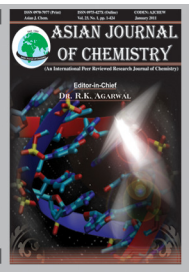

Synthesis and Characterization of Zinc(II) Complex of Schiff Base of Cefadroxil

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Zinc(II) complex with Schiff base of cefadroxil (salicylidene cefadroxil) of the type ZnL_2, (L = deprotonated Schiff base of cefadroxil) have been prepared. The Schiff base obtained by the condensation of cefadroxil with salicylaldehyde. They form 2:1 ligand to metal complexes with Zn(II) as indicated by conductometric titrations. The general structure assigned to these complexes is supported by mass, UV, IR spectral bands.

Key Words: Cefadroxil, Schiff base, Complex, Conductometry, Spectra.

INTRODUCTION

Cefadroxil belongs to the first generation cephalosporins and resistance to it may be related to the extensive use of these drugs causing resistance to cephalosporins[1-3].

Many drugs possess modified toxicological and pharmacological properties when they are complexed with metal[4-6]. The most widely studied metal is zinc(II) which were proved beneficial in diseases such as tuberculosis, cancers[7-9] *etc*. This work involves the synthesis and characterization of zinc complex of Schiff base derived from cefadroxil.

EXPERIMENTAL

Pure sample of cefadroxil (Lupin Ltd., Bhopal), salicylaldehyde (SA) (Merck, 99 %), zinc(II) acetate monohydrate (Merck 98 %) and all other solvents used were of Analar grade or Merck products, which were available commercially.

Synthesis of Schiff base of cefadroxil (SACFDX): Methanolic solution of cefadroxil (0.01 M, 25 mL) was added to methanolic solution of salicylaldehyde (0.01 M, 25 mL) and refluxed for 3 h. The reaction mixture was allowed to cool to room temperature. On cooling, reddish yellow precipitate was isolated. It was washed with methanol-water (1:1) mixture and dried under vacuum.

Synthesis of SACFDX-zinc(II) complex: Methanolic solution of zinc(II) acetate monohydrate (0.01 M, 25 mL) was added to methanolic solution of SACFDX (0.02 M, 25 mL) with constant stirring. The pH was adjusted between 7-8. The mixture was refluxed for 2-3 h and cooled to room temperature. On cooling, brown precipitate was formed, which was filtered, washed with methanol and dried by vacuum suction. Dark brown crystals of SACFDX-zinc(II) complex were obtained.

RESULTS AND DISCUSSION

The condensation of cefadroxil with salicylaldehyde results in the formation of salicylidene cefadroxil (Schiff base)[10]. The complexes was synthesized by reacting Schiff base ligand with zinc(II) acetate in the ratio 2:1 in the methanolic medium. The physico-chemical data of Schiff base and Zn(II) complex was studied and are listed in Table-1. The complex was found to be sparingly soluble in distilled water and acetone. However, it is soluble in hot methanol and ethanol. The conductivity values of the SACFDX and its Zn(II) complex in 50 % methanol were 3.9×10^{-6} and 6.2×10^{-5} Ω^{-1} cm^{-1} dm^{-3}, respectively, showing their non-electrolytic behaviour[11]. The magnetic moment data indicate that Zn(II) complex is diamagnetic in nature.

The IR spectra of the pure drug, ligand and its metal complex were recorded in KBr pellets in the 4000-400 cm^{-1} range with a Spectrum BX Series spectrophotometer and compared[12-15]. Some important characteristic IR frequencies of Schiff base ligand and its complex are recorded in Table-2.

The spectra of the complex showed most of the absorption bands of ligand and some new bands due to the co-ordination of ligand with zinc ion with N and O as donors. The spectra of the Schiff base ligand showed a broad vibration band at 3242 cm^{-1}. This can be assigned to phenolic OH group of the salicylaldehydic moiety. The disappearance of this peak in the spectra of complex derived from Schiff base of cefadroxil indicates the deprotonation of phenolic proton of salicylaldehydic moiety prior to coordination[16,17]. The band assigned to the azomethine group in the free Schiff base ligand of cefadroxil (SACFDX) was observed at 1493 cm^{-1} has almost

TABLE-1
PHYSICO-CHEMICAL CHARACTERISTICS OF SCHIFF BASE (SACFDX) AND ITS Zn(II) COMPLEX

Compound/m.f./m.w.	Colour and decomp. temp. (ºC)	Yield (%)	Composition (%) found (calcd.)					Conductivity (Ω^{-1} cm^{-1} dm^{-3})
			C	H	N	S	Zn	
Schiff base ligand (SACFDX)-$C_{23}H_{21}N_3O_6S$/467	Reddish yellow, 195-198	75.45	59.04 (59.10)	4.27 (4.49)	8.74 (8.99)	6.58 (6.85)	–	3.9×10^{-6}
Salicylidene cefadroxil-Ca(II) complex/$(SACFDX)_2ZnC_{46}H_{40}N_6O_{10}S_2Zn$/997	Brown, 205-207	69.86	55.12 (55.35)	3.91 (4.01)	8.20 (8.42)	6.36 (6.42)	6.47 (6.56)	6.2×10^{-5}

TABLE-2
PRINCIPAL IR SPECTRAL DATA OF THE SACFDX AND ITS Zn(II) COMPLEX

Assignments for	Salicylidene cefadroxil (SACFDX) (cm^{-1})	Salicylidene cefadroxil-Zn(II) complex (cm^{-1})
Free NH_2	–	–
-CH=N-	1674	1628
ν(OH)	3242	–
Aldehydic C-H stretching attached to benzene ring	2770	2800
ν(Zn-N)	–	490
ν(Zn-O)	–	701
Chelation	–	1384
Lattice water	–	3379

disappeared in its complex. This indicates the participation of nitrogen atom of azomethine group[18,19] in coordination. The IR spectra of the complex show new bands at 496 and 705 cm^{-1} assigned to ν(Zn-N) and ν(Zn-O), respectively[20,21]. Also, there is no much difference in the bands at 1675-1670 cm^{-1}, assigned to the carbonyl frequency, indicating its non participation in complexation. The presence of a broad band at 3393 and 3379 cm^{-1} in the spectra of complex is associated with coordinated and/or lattice water molecules, as supported from thermal analysis[22,23] in the complexes.

Thermal analysis: The results of DTA-TG analysis show the elimination of two water molecules at the temperature of 66 ºC, as shown in Fig. 1, confirms that the water molecule is present as lattice one[24].

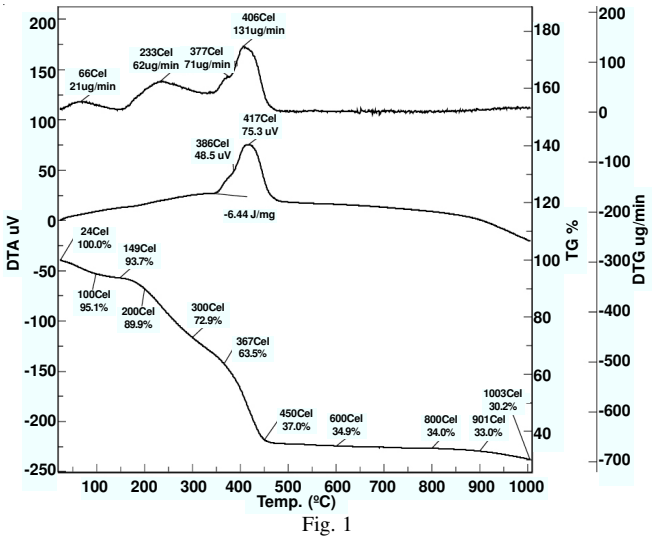

Fig. 1

Mass spectra: The mass spectrum of the Schiff base ligand shows a weak molecular ion peak (M^+) peak[14] at m/z = 466 amu, corresponding to $[C_{23}H_{20}N_3O_5S]^+$. This confirms the proposed molecular formula for Schiff base. The other peaks with m/z values of 424, 406, 345, 328, 317, 277, 231, 210, 192,154, 136, 124 and 131 amu corresponds to various fragments of Schiff base ligand. Also, the spectra shows that the fragments corresponding to m/z values of 192 is the stablest fragment, the ones at 154, 136, 124, 113 and 210 are less stable while the other fragments are not stable.

Electronic spectra: The electronic spectral bands[25,26] (Table-4) of the free Schiff base of cefadroxil studied in methanol exhibited two main peaks. The first absorption band observed at 255 nm for the Schiff base of cefadroxil can be assigned to the π→π* transition originating in the phenyl ring. This first band was not significantly affected by chelation. The second band in the spectra of Schiff base of cefadroxil at 300 nm may be assigned to the π→π* transition originating in the azomethine (CH=N) chromophore. This band undergoes a bathochromic shift to 315 nm. This may be attributed to the charge transfer from nitrogen atom of Schiff base ligand to the metal ion (N→M)[27].

The physical, analytical and spectral study of the Schiff base and its complex discussed above confirms the coordination of metal to the Schiff base *via* phenolic deprotonated oxygen and the imino nitrogen, thus agreeing well with the proposed structure of SACFDX-Zn(II) complex as presented in Fig. 2.

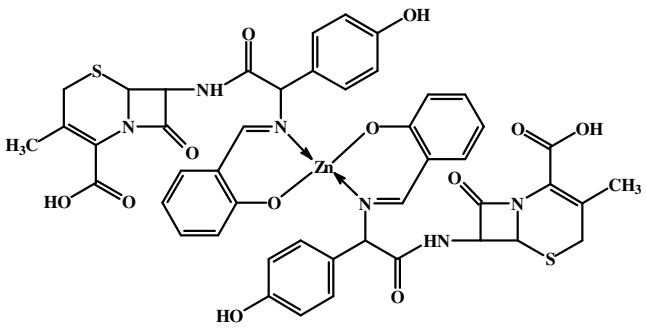

Fig. 2. Structure of Schiff base (SACFDX)-Zn(II) complex

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