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Structural, spectral and thermal analysis of some metallocephradines

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ABSTRACT

A series of cephradine metal complexes were prepared and investigated by elemental analysis, IR, electronic spectra, magnetic susceptibility, ESR spectra, ^{1}HNMR spectral studies and mass spectra. EDX patterns were carried out to emphasis the nature of the particles and the purity of products, while SEM is a sensitive tool used to justify on the microstructure and surface morphology. Thermal behavior of the synthesized complexes was illustrated by different techniques (TGA, DTA and DSC). The thermal decomposition of all the complexes ended with the formation of metal oxides and carbon residue as a final product. Also, the thermodynamic parameters and thermal transitions, such as glass transitions, crystallization and melting temperatures for cephradine and its metal complexes were evaluated and discussed. The entropy change values, $\Delta S^{\#}$, showed that the transition states are more ordered than the reacting complexes.

1. Introduction

Cephalosporins are β-lactam antibiotics differ from the penicillins in that the B ring is a 6- membered dihydrothiazine ring [1–3]. Cephalosporins are classified into five generations, cephradine is the first generation cephalosporins, which are most active against aerobic gram-positive cocci and they are often used for skin infections caused by *S. aureus, Streptococcus*, *E. coli* and some activity against *H. influenzae* and *Klebsiella* species [4,5]. Fig. 1.

The synthesis and spectral characterization of cephradine–tin (II) complex of general formula [Sn(L)Cl] (L = cephradine) characterized by physicochemical and spectroscopic methods. The spectra of the formed tin complex indicated that cephradine act as multidentate ligand via the amide and lactam carbonyl and carboxylate which, probably have a polymeric structure and showed an enhancement of the antibacterial activity [6]. Also, cytotoxicity and antibacterial activities of cephradine-tin complex was investigated against *Artemia salina* and four bacterial strains which gave an increase in antibacterial activity compared to the parent cephradine [7]. Also, cephradine reacts with $VOSO_4.3H_2O$ in 1:1, 1:2 and 1:3 molar ratios in methanol at three different temperatures 20 °C, 0 °C and −10 °C, respectively. Three complexes formulated as $VO(H_2O)_3\,L^{2-}$, $VO(H_2O)L_2^{2-}$ and VL_3^- were formed. Biological screening tests showed significant antibacterial and antifungal activities against various bacterial and fungal strains [8]. It was reported that metals were proved to be a good chelating agents and antibiotics were considered as useful ligands in the formation of metalloantibiotics. Physical, chemical and biological changes in cephradine antibiotic were seen after combining with metals as metallocephradine, which act as therapeutic approach for halting AD pathogenesis in comparison with cephradine only. Thus, metal chelators make improvement in the parent to act as an inhibitor. It was found that Mn and Cu (3:1) cephradine complexes can act as AChE inhibitors and the mixed metal (Fe–Cu) cephradine complex can act as MAO-B inhibitor [9].

2. Experimental

2.1. Synthesis of metallocephradine

Metal complexes of cephradine were previously prepared [9] by mixing the molar amount of the metal salts Cr (III), Mn (II), Fe (III), Co (II), Ni (II), Cu (II), Zn (II), Cd (II) and Hg (II) as chloride dissolved in 10 ml water with the calculated amount of cephradine, while the mixed metal Fe(III) M(II) complexes, where [M (II) = Cu (II) or Co (II)] were prepared by dissolving 1 mmol of Fe (III) and 1 mmol Cu

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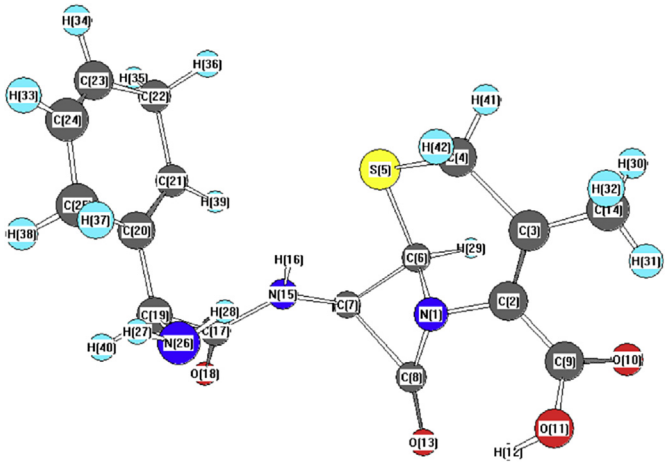

Fig. 1. Structure of cephradine.

(II) chloride or Co (II) in 10 ml, the resulting solution was then added to cephradine (1 mmol in 10 ml). The mixture was refluxed for about 5 min. The complexes were precipitated and were filtered, then washed several times with a mixture of EtOH–H_2O and dried in a desiccator over anhydrous $CaCl_2$. The metal ion contents were determined by complexmetric titration procedures [10]. The halogen content was determined by titration with standard Hg $(NO_3)_2$ solution using diphenyl carbazone indicator [11]. The analytical data of metallocephradine were presented in Table 1 and the proposed structures of synthesized metal complexes were illustrated in Fig. 2.

2.2. Instruments and working procedures

2.2.1. Infrared spectra

The KBr disk infrared spectra were recorded on Perkin–Elmer 1430 spectrophotometer.

2.2.2. Electronic absorption spectra

The electronic spectra were measured by using Perkin Elmer spectrophotometer, model Lambda 4B, covering the range 200–900 nm.

2.2.3. Magnetic susceptibility measurements

Molar magnetic susceptibilities, corrected for diamagnetism using Pascal's constants, were determined at room temperature (298 K) using faraday's method. The apparatus was calibrated with Hg [Co $(SCN)_4$].

2.2.4. ESR spectra

The ESR spectra of the copper complexes were recorded with a reflection spectrometer operating at 9.75 GHz (X-Band) in a cylindrical resonance cavity with 100 kHz modulation. The g-values were determined by comparison with DPPH signal (g = 2.0037).

2.2.5. Mass sprctra

Mass spectra were recorded on MS reflactor positive ion mode 4700, the device is located at Memorial university of Newfoundland, Canada.

2.2.6. HNMR spectra

HNMR spectra were recorded in CD_3OH and $(CD_3)_2SO$, respectively on Varian FT-200 MHz spectrometer.

2.2.7. Scanning electron microscope and EDX

Scanning electron microscope using a JEOL instrument (Japan) model JSM-5410 was used to determine the microstructure of the obtained materials, the samples were sputter coated with gold. However, EDX (TESCAN) X-max version 4.1.17. D/Mi 152. The instrument is located in the Faculty of Science, Cairo University, Giza, Egypt.

2.2.8. Thermal analysis

Thermal analysis (TGA, DTA and DSC) were carried out in the temperature range 25–600 °C, and the rate of heating was 10 °C/min.

Table 1
Analytical data and physical properties of metallocephradine.

Complex	M. wt	Color	Formula	Calculated/(found)%				
				M	C	H	N	Cl
[Cr_2 (Cephradine)$_3$ (OH)$_3$ H_2O]3H_2O (2: 3)	1272.27	Violet	Cr_2 C_{48} H_{65} N_9 O_{19} S_3	8.17 (8.00)	45.31 (45.40)	5.15 (5.00)	9.91 (9.85)	–
[Mn (Cephradine) Cl (H_2O)$_3$] HCl. 2H_2O (1: 1)	565.33	Brown	Mn C_{16} H_{29} N_3 O_9 S Cl_2	9.72 (9.76)	33.99 (34.35)	5.17 (5.42)	7.43 (7.82)	12.54 (12.10)
[Fe_2 (Cephradine) Cl_5 (H_2O)$_3$]H_2O (2:1)	709.41	Brown	Fe_2 C_{32} H_{46} N_6 O_{12} S_2 Cl_3	15.74 (15.98)	27.09 (27.22)	3.69 (3.78)	5.92 (8.33)	24.99 (24.38)
[Co (Cephradine)$_3$] 2HCl. H_2O (1:3)	1196.07	brown	Co C_{48} H_{59} N_9 O_{13} S_3 Cl_2	4.93 (4.99)	48.20 (48.50)	4.97 (5.11)	10.54 (10.91)	5.93 (5.99)
[Ni (Cephradine) Cl H_2O] HCl. 3H_2O (1: 1)	551.07	Pale green	Ni C_{16} H_{27} N_3 O_8 S Cl_2	10.65 (10.64)	34.87 (35.12)	4.94 (5.11)	7.63 (7.84)	12.87 (12.95)
[Ni (Cephradine)$_2$]2HCl (1: 2)	882.41	Gray	Ni C_{32} H_{38} N_6 O_8 S_2 Cl_2	6.64 (6.30)	43.51 (43.55)	4.30 (4.38)	9.51 (9.60)	7.93 (8.0)
[Cu (Cephradine)$_2$] 2HCl. 6H_2O (1: 2)	941.35	Dark green	Cu C_{32} H_{50} N_6 O_{14} S_2 Cl_2	6.75 (6.33)	40.83 (40.11)	5.35 (5.64)	8.93 (9.12)	7.53 (7.66)
[Cu_3 (Cephradine) Cl_5 H_2O] HCl (3:1)	770.78	Dark brown	Cu_3 C_{16} H_{21} N_3 O_5 S Cl_6	24.73 (24.89)	24.93 (25.1)	2.75 (2.88)	5.45 (5.60)	27.60 (27.75)
[Zn_2 (Cephradine) Cl_3 H_2O] HCl. H_2O (2: 1)	658.03	Yellow	Zn_2 C_{16} H_{23} N_3 O_6 S Cl_4	19.87 (19.80)	29.20 (29.64)	3.52 (4.11)	6.39 (6.82)	21.55 (21.61)
[Cd_2 (Cephradine) Cl_3 H_2O] HCl. H_2O (2: 1)	751.21	Yellow	Cd_2 C_{16} H_{29} N_3 O_{10} S Cl_2	29.93 (29.80)	25.58 (25.62)	3.89 (4.10)	5.59 (5.55)	9.44 (9.58)
[Hg (Cephradine)$_3$] 2HCl. 6H_2O (1:3)	1427.80	Beige	Hg C_{48} H_{69} N_9 O_{18} S_3 Cl_2	14.05 (14.00)	40.38 (40.33)	4.87 (4.82)	8.83 (8.79)	4.97 (5.1)
[Fe Cu_2 (Cephradine)$_2$ Cl_5 H_2O] 2HCl. 3H_2O (1:2:2)	1201.98	Brown	Fe Cu_2 C_{32} H_{46} N_7 O_{12} S_2 Cl_7	Fe 4.65 (4.47) Cu 10.57(11.1)	31.98 (32.10)	3.86 (3.89)	6.99 (7.10)	20.65 (20.71)
[Fe Co (Cephradine)$_2$ Cl_3 H_2O] 2HCl. 3H_2O (1:1:2)	1062.91	Brown	Fe Co C_{32} H_{49} N_6 O_{12} S_2 Cl_5	Fe 5.25 (5.7) Co 5.5 (5.05)	36.16 (36.20)	4.36 (4.40)	7.91 (7.98)	16.68 (16.85)
[Fe Ni (Cephradine) Cl_4 (H_2O)$_2$] HCl. 4H_2O (1:1:1)	749.30	Brown	Fe Ni C_{16} H_{31} N_3 O_{10} S Cl_5	Fe 7.45 (7.30) Ni 7.83 (7.79)	25.65 (25.69)	4.17 (4.20)	5.61 (5.65)	23.66 (23.69)

* All complexes have m.p ≥ 300 °C.