



Preparation, characterization and cytotoxicity studies of some transition metal complexes with ofloxacin and 1,10-phenanthroline mixed ligand



S.A. Sadeek*, S.M. Abd El-Hamid

Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, Egypt

ARTICLE INFO

Article history:

Received 24 February 2016

Received in revised form

27 May 2016

Accepted 30 May 2016

Available online 30 May 2016

Keywords:

Fluoroquinolone

1,10-Phenanthroline

IR

¹H NMR

Thermal

Cytotoxicity

ABSTRACT

[Zn(OfI)(Phen)(H₂O)₂](CH₃COO)·2H₂O (1), [ZrO(OfI)(Phen)(H₂O)]NO₃·2H₂O (2) and [UO₂(OfI)(Phen)(H₂O)](CH₃COO)·H₂O (3) complexes of fluoroquinolone antibacterial agent ofloxacin (OfI), containing a nitrogen donor heterocyclic ligand, 1,10-phenanthroline monohydrate (Phen), were prepared and their structures were established with the help of elemental analysis, molar conductance, magnetic properties, thermal studies and different spectroscopic studies like IR, UV-Vis., ¹H NMR and Mass. The IR data of OfI and Phen ligands suggested the existing of a bidentate binding involving carboxylate O and pyridone O for OfI ligand and two pyridine N atoms for Phen ligand. The coordination geometries and electronic structures are determined from electronic absorption spectra and magnetic moment measurements. From molar conductance studies reveals that metal complexes are electrolytes and of 1:1 type. The calculated bond length and force constant, F(U=O), in the uranyl complex are 1.751 Å and 641.04 Nm⁻¹. The thermal properties of the complexes were investigated by thermogravimetry (TGA) technique. The activation thermodynamic parameters are calculated using Coats–Redfern and Horowitz–Metzger methods. Antimicrobial activity of the compounds was evaluated against some bacteria and fungi species. The activity data show that most metal complexes have antibacterial activity than that of the parent OfI drug. The *in vitro* cytotoxicities of ligands and their complexes were also evaluated against human breast and colon carcinoma cells.

© 2016 Elsevier B.V. All rights reserved.

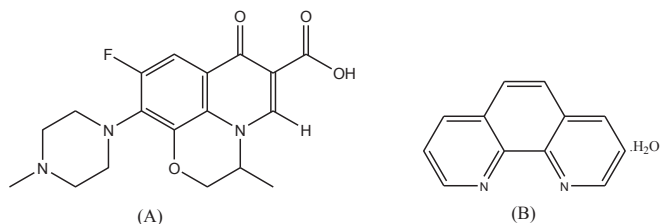
1. Introduction

Fluoroquinolones are a large and constantly expanding group of synthetic antimicrobial agents [1,2]. This class of compounds, when compared to existing bactericidal drugs, shows improved pharmacokinetic properties and a broad spectrum of activity against parasites, bacteria and mycobacteria, including resistant strains; in addition to that they displayed significant *in vitro* antibacterial activity against many bacteria species through inhibition of their DNA gyrase [3]. Ofloxacin (OfI) (Scheme 1A) is one of the most popular members of second-generation quinolone, which characterized by good to excellent activity against Gram-positive and Gram-negative bacteria. It is indicative for many infections such as those of the sinuses, lungs, ears, skin, bones and many others caused by susceptible bacteria, urinary infections and prostatitis [4,5].

Due to their wide use, there has been an increasing menace of bacterial resistance to quinolones [6], which led to the need to improve existing antimicrobial drugs and/or develop new ones, pushing forwards the concept that metal complexes could be an alternative to conventional drugs, as novel derivatives of fluoroquinolones [7,8]. Therefore, numerous studies regarding the interaction between quinolones with several metallic cations have reported in the literature [9–11]. Recently, a relatively new approach to the rational design of antitumor agents has been introduced based on some new fluoroquinolones molecules that display a novel mode of action [12,13]. Metal complexes containing phen and related ligands have been intensively investigated because of their numerous biological activities such as antitumor, antibacterial and antimicrobial [14–16]. Little articles have been reported on the coordination properties of mixed ligand metal complexes of ofloxacin with the hetero ligand 1,10-phenanthroline and the known mixed ligand metal complex has the formula [Cu(oflo)(phen)(H₂O)](NO₃)·2H₂O [17]. The complex shows stronger suppression effects against liver cancer BEL-7402 cell line and

* Corresponding author. Tel.: +20 01220057510; fax: +20 0553208213.

E-mail address: s_sadeek@zu.edu.eg (S.A. Sadeek).



Scheme 1. (A) (RS)-9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-3,7-dihydro-2H-[1,4]oxazino[2,3,4-ij]quinoline-6-carboxylic acid (HOfl), (B) 1,10-phenanthroline monohydrate (Phen).

lung cancer A549 cell line, with suppression ratios reaching approximately 100% for complex concentrations of 10^{-4} – 10^{-5} mol L $^{-1}$ also, the complex shows stronger antibacterial activities against *Staphylococcus enteritidis*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* [17]

Therefore, in this article, synthesis, spectroscopic and thermal characterization of (1), (2) and (3) complexes of ofloxacin in presence of 1,10-phenanthroline monohydrate (Phen, Scheme 1B) are reported using physicochemical techniques such as elemental analysis, molar conductance, magnetic susceptibility, thermal analysis, IR, UV–Vis, ^1H NMR and mass spectral studies. The antimicrobial activity of HOfl, Phen and their metal complexes has been screened against some Gram-positive and Gram negative bacteria. Antifungal activity against three different fungi has been evaluated. Furthermore, the antitumor activities were investigated *in vitro* against human breast carcinoma cell line (MCF-7) and human colon carcinoma cell line (HCT-116).

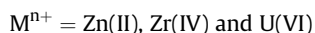
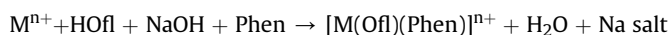
2. Materials and methods

2.1. Materials

All chemicals used for the preparation of the complexes were of analytical reagent grade, commercially available from different sources and used without further purification. Ofloxacin used in this study was purchased from Egyptian Company for Chemicals & Pharmaceuticals (ADWIA). 1,10-phenanthroline, NaOH, acetone, ethanol, FeCl $_3$ ·6H $_2$ O, FeSO $_4$, Zn(CH $_3$ COO) $_2$ ·2H $_2$ O, Zr(NO $_3$) $_2$, and UO $_2$ (CH $_3$ COO) $_2$ ·2H $_2$ O were commercial products (from Fluka and Aldrich Chemical Co.) and were used without further purification.

2.2. Synthesis of mixed ligand metal complexes

The white solid complex (1) was prepared by mixing 1 mmol (0.361 g) of hot saturated ethanolic solution of HOfl with 1 mmol (0.04 g) NaOH and 1 mmol (0.198 g) of Phen with the same ratio 1 mmol (0.219 g) of zinc(II) acetate dihydrate. The mixture was refluxed for 3 h. The white precipitate was filtered off and dried under vacuum over anhydrous CaCl $_2$. The orange and dark yellow solid complexes (2) and (3) were prepared in a similar manner described above by using acetone as a solvent and Zr(NO $_3$) $_2$ and UO $_2$ (CH $_3$ COO) $_2$ ·2H $_2$ O, respectively, in 1:1:1:1 (M $^{n+}$:HOfl:NaOH:Phen) molar ratio. Single crystal suitable for X-ray crystallographic measurements was not obtained.



The chemical Structures of synthesized metal complexes were confirmed as follows:

Complex (1): White; Yield 81.22%; m.p.: 302 °C; **Elemental analysis:** found, C 52.11, H 5.18, N 9.47, M 8.85. Calc. for ZnC $_{32}$ H $_{38}$ FN $_5$ O $_{10}$ (737.1) C 52.14%, H 5.20%, N 9.50%, M 8.87%; $\Lambda_m = 76.6$ S cm 2 mol $^{-1}$; μ_{eff} : diam.; **IR (KBr):** $\nu = 3420$ mbr (O–H, H $_2$ O, COOH), 1622 s (asymmetric COO $^-$), 1581s (C=O, pyridone group), 1525 ms (C=N), 1370w (symmetric COO $^-$), 641 m, 544vw, 504w (M–O) and (M–N). **UV–Vis. (DMSO- d_6):** $\lambda = (274$ nm) (36,496 cm $^{-1}$) (π - π^* transition), (310 nm) (32,258 cm $^{-1}$) (n- π^* transition), $\lambda = (530$ nm) (18,867 cm $^{-1}$) ($\epsilon = 150$ M $^{-1}$ cm $^{-1}$) Ligand-metal charge transfer. **^1H NMR (DMSO- d_6):** $\delta = 1.15$ (2) (d, 3H, –CH $_3$), 2.24 (10) (s, 3H, –CH $_3$), 2.44–2.51 (7,9) (t, 2H, –CH $_2$), 3.33 (3) (m, 1H, –CH), 3.77 (6,8) (t, 2H, –CH $_2$), 4.37 (4) (d, 2H, –CH $_2$), 4.51–4.84 (s, 2H, H $_2$ O), 7.56–8.00 (1,5) (s, 2H, H $_{Ar}$), 8.16–8.91 (1 $^{//}$ -8 $^{//}$) (m, 8H, H $_{py}$). (Scheme 2(A)).

Complex (2): Orange; Yield 92.6%; m.p.: 310 °C; **Elemental analysis:** found, C 47.13, H 4.32, N 11.02, M 11.92. Calc. for ZrC $_{30}$ H $_{33}$ FN $_6$ O $_{11}$ (763.8) C 47.17%, H 4.35%, N 11.00%, M 11.94%; $\Lambda_m = 73.2$ S cm 2 mol $^{-1}$; μ_{eff} : diam.; **IR (KBr):** $\nu = 3430$ mbr (O–H, H $_2$ O, COOH), 1623s (asymmetric COO $^-$), 1576 m (C=O, pyridone group), 1527 ms (C=N), 1381vs (symmetric COO $^-$), 810 m (Zr=O), 688vw, 631w, 544vw, 503w (M–O) and (M–N). **UV–Vis. (DMSO- d_6):** $\lambda = (275$ nm) (36,363 cm $^{-1}$) (π - π^* transition), (352 nm) (28,409 cm $^{-1}$) (n- π^* transition), $\lambda = (541$ nm) (18,484 cm $^{-1}$) ($\epsilon = 76$ M $^{-1}$ cm $^{-1}$) Ligand-metal charge transfer. **^1H NMR (DMSO- d_6):** $\delta = 1.16$ (2) (d, 3H, –CH $_3$), 2.30 (10) (s, 3H, –CH $_3$), 2.41–2.52 (7,9) (t, 2H, –CH $_2$), 3.40 (3) (m, 1H, –CH), 3.64 (6,8) (t, 2H, –CH $_2$), 4.38 (4) (d, 2H, –CH $_2$), 4.57–5.02 (s, 2H, H $_2$ O), 7.02–8.00 (1,5) (s, 2H, H $_{Ar}$), 8.49–8.96 (1 $^{//}$ -8 $^{//}$) (m, 8H, H $_{py}$). (Scheme 2(B)).

Complex (3): Dark yellow; Yield 84.88%; m.p.: 274 °C; **Elemental analysis:** found, C 42.41, H 3.75, N 7.70, M 26.25. Calc. for UC $_{32}$ H $_{34}$ FN $_5$ O $_{10}$ (905.7) C 42.44%, H 3.78%, N 7.73%, M 26.28%; $\Lambda_m = 82.4$ S cm 2 mol $^{-1}$; μ_{eff} : diam.; **IR (KBr):** $\nu = 3424$ mbr (O–H, H $_2$ O, COOH), 1620 m (asymmetric COO $^-$), 1562 m (C=O, pyridone group), 1524 m (C=N), 1369w (symmetric COO $^-$), 916vs (asymmetric U=O), 814 m (symmetric U=O), 674 s, 632vw, 562vw, 504 m (M–O) and (M–N). **UV–Vis. (DMSO- d_6):** $\lambda = (276$ nm) (36,231 cm $^{-1}$) (π - π^* transition), (304 nm) (32,894 cm $^{-1}$) (n- π^* transition), $\lambda = (535$ nm) (18,691 cm $^{-1}$) ($\epsilon = 200$ M $^{-1}$ cm $^{-1}$) Ligand-metal charge transfer. **^1H NMR (DMSO- d_6):** $\delta = 1.15$ (2) (d, 3H, –CH $_3$), 2.28 (10) (s, 3H, –CH $_3$), 2.50–2.52 (7,9) (t, 2H, –CH $_2$), 3.39 (3) (m, 1H, –CH), 3.70 (6,8) (t, 2H, –CH $_2$), 4.35 (4) (d, 2H, –CH $_2$), 4.50–5.09 (s, 2H, H $_2$ O), 7.77–8.01 (1,5) (s, 2H, H $_{Ar}$), 8.19–8.52 (1 $^{//}$ -8 $^{//}$) (m, 8H, H $_{py}$). (Scheme 2(C)).

2.3. Instruments

The elemental analyses were performed using a Perkin Elmer 2400CHN elemental analyzer. The percentage of the metal ions were determined gravimetrically by transforming the solid products into metal oxide and also determined by using atomic absorption method. Spectrometer model PYE-UNICAM SP 1900 fitted with the corresponding lamp was used for this purpose. FT-IR spectra in KBr discs were recorded in the range from 4000 to 400 cm $^{-1}$ with FTIR 460 PLUS Spectrophotometer. ^1H NMR spectra were recorded on Varian Mercury VX-300 NMR Spectrometer using DMSO- d_6 as solvent. TGA-DTG measurements were run under N $_2$ atmosphere within the temperature range from room temperature to 1000 °C using TGA-50H Shimadzu, the mass of sample was accurately weighted out in an aluminum crucible. Electronic spectra were obtained using UV-3101PC Shimadzu. The absorption spectra were recorded as solutions in DMSO- d_6 . Mass spectra were recorded on GCMS-QP-1000EX Shimadzu (ESI-70ev) in the range from 0 to 1090. Room temperature Magnetic susceptibilities of the powdered samples were done on a Sherwood scientific magnetic balance using Gouy balance at room temperature using Hg

Download English Version:

<https://daneshyari.com/en/article/1407681>

Download Persian Version:

<https://daneshyari.com/article/1407681>

[Daneshyari.com](https://daneshyari.com)