Journal of Molecular Structure 1047 (2013) 267–276

Contents lists available at SciVerse ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Spectroscopic, thermal analyses, structural and antibacterial studies on the interaction of some metals with ofloxacin

W.A. Zordok, W.H. El-Shwiniy *, M.S. El-Attar, S.A. Sadeek

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

HIGHLIGHTS

- Three new ofloxacin complexes were synthesized and characterized.
- The metal–ligand binding of V(IV) and Zr(IV) complexes was predicted by using the density functional theory (DFT).
- The antibacterial activity of ofloxacin and their metal complexes were evaluated.

ARTICLE INFO

Article history:
Received 25 March 2013
Received in revised form 23 April 2013
Accepted 29 April 2013
Available online 17 May 2013

Keywords:
HOfl.
Metal ions
^{1}H NMR
Microbial activity

ABSTRACT

Reaction between the fluoroquinolone antibacterial agent ofloxacin and V(IV), Zr(IV) and U(VI) in methanol and acetone was studied. The ability of ofloxacin to form metal complexes is high. The isolated solid complexes were characterized by elemental analysis, magnetic moment, conductance measurements, infrared, electronic, ^{1}H NMR spectra and thermal investigation. In all complexes the ofloxacin ligand is coordinated through the pyridone and carboxylate oxygen forming 1:2 M:HOfl complexes. The calculated bond length and force constant, F(U=O), in the uranyl complex are 1.73 Å and 640.83 N m^{-1}, respectively. The metal–ligand binding of the V(IV) and Zr(IV) complexes was predicted by using the density functional theory (DFT) at the B3LYP-CEP-31G level of theory and total energy, dipole moment estimation of different V(IV) and Zr(IV) ofloxacin structures. All the synthesized complexes exhibited higher biocidal activity against *S. aureus* K1, *Bacillus subtilis* K22, *Br. otitidis* K76, *Escherichia coli* K32, *Pseudomonas aeruginosa* SW1 and *Klebsiella oxytoca* K42. compared to parent compounds and standard drugs.

1. Introduction

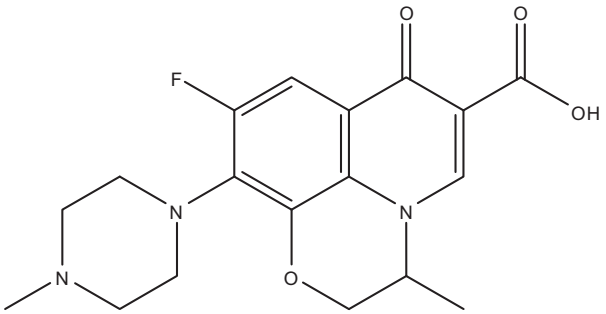
The fluoroquinolone (quinolone) class of chemotherapeutic agents are considered by prudent physicians to be a drug of last resort to treat serious and life threatening bacterial infections[1,2]. Ofloxacin (Scheme 1) is one of fluoroquinolone class and is a synthetic chemotherapeutic antibiotic [3,4] considered to be a second-generation fluoroquinolone. Ofloxacin was first patented in 1982 (European Patent Daiichi) and received approval from the U.S. Food and Drug Administration (FDA) on December 28, 1990. Ofloxacin is sold under a wide variety of brand names as well as generic drug equivalents, for oral and intravenous administration. It exhibits strong activity against Gram-negative and some Gram-positive bacteria, through many anaerobic strains are resistant After oral administration of a single dose of ofloxacin tablet (200 mg) good penetration into body tissues and fluids is observed [5,6].

Studies of interaction between ofloxacin and several metal cations commonly found in several drugs used as antacids have been reported in the literature [7–25]. These studies have been mainly directed towards identifying the groups directly attached to the metal site, and establishing the structure of the coordination compounds thus formed. The crystal structure of ofloxacin [7,8] and its complexes [9,10,26–29] have been very limited studied. From their X-ray crystal data, it was found that the metal ion is coordinate bonded to the ofloxacin in the complexes through ring carbonyl and one of the carboxylic oxygen atoms.

Connecting with our previous studies in the trend of fluoroquinolones metal complexes [30,31], we are reporting in the present article, the isolation and characterization of some new metal complexes formed from the interaction of ofloxacin with V(IV), Zr(IV) and U(VI) in the solvent. Density functional theory (DFT) is used to compute the cation type influence on theoretical parameters of the Zr(IV) and V(IV) complexes of ofloxacin and shows if the two oxygen atoms (O_{pyr} and $O_{carboxilic}$) of ofloxacin lie at *trans* or

* Corresponding author. Tel.: +20 01220057510, +20 01119462284; fax: +20 0553208213.
E-mail addresses: walaa1986@zu.edu.eg (W.H. El-Shwiniy), s_sadeek@zu.edu.eg (S.A. Sadeek).

0022-2860/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.molstruc.2013.04.076



Scheme 1. (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.

at *cis* positions so the two diastereoisomers of the studied complexes are going to be calculated. Such computational characterization reduces time consuming experiments for biomedical and pharmaceutical studies of the drugs and its complexes. Profiles of the optimal set and geometry of these complexes are going to be simulated by applying the GAUSSIAN 98W package of programs [32] at B3LYP/CEP-31G [33] level of theory. The prepared solid complexes will confirmed by using spectroscopic and thermal analyses techniques. The thermal behavior of these complexes is going also to be studied. The antibacterial activity of the investigated complexes, metal salts and free ofloxacin are going to be tested against three Gram-positive bacteria such as *S. aureus* K1, *Bacillus subtilis* K22, *Br. otitidis* K76 and three Gram-negative species *Escherichia coli* K32, *Pseudomonas aeruginosa* SW1 and *Klebsiella oxytoca* K42.

2. Materials and methods

2.1. Chemicals

Ofloxacin was purchased from Egyptian Company for Chemicals & Pharmaceuticals (ADWIA), $VOSO_4{\cdot}H_2O$ was from Aldrich Chemical, $ZrOCl_2{\cdot}8H_2O$, $UO_2(NO_3)_2{\cdot}6H_2O$ and all solvents were purchased from Fluka Chemical Co. All the chemicals and solvents were analytical reagent grade and were used as purchased without further purification.

2.2. Synthesis

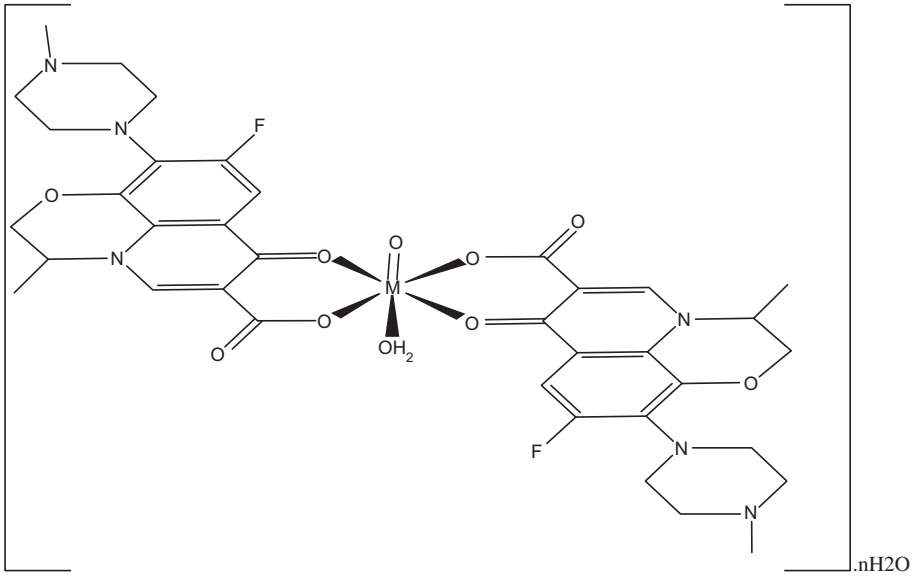
2.2.1. Synthesis of metal complexes

The complexes have been prepared by direct reaction between HOfl with the corresponding metal cations in the form of water-soluble salts, such as sulfate and chloride. NaOH was added to the solution in order to improve solubility of HOfl complex of $[VO(Ofl)_2(H_2O)]{\cdot}5H_2O$ (Scheme 2) was synthesized as follows: 0.5 mmol (0.091 g) of vanadyl sulfate monohydrate dissolved in 5 ml bidistilled water was added to a magnetically stirred solution containing 1 mmol (0.361 g) HOfl and 1 mmol (0.40 g) NaOH in 25 ml methanol. The mixture was stirred at room temperature for 1 day. The mixture was left for slow evaporation to concentrate the reaction mixture; the Olive-green precipitate formed was filtered off, washed several times by bidistilled water, and dried under vacuum over $CaCl_2$ in a desiccator. The yellowish-white and yellow solid complexes of $[ZrO(Ofl)_2(H_2O)]{\cdot}4H_2O$ and $[UO_2(Ofl)_2(H_2O)]{\cdot}2H_2O$ (Schemes 2 and 3) were prepared in a similar manner described above by using methanol and acetone as a solvent and $ZrOCl_2{\cdot}8H_2O$, $UO_2(NO_3)_2{\cdot}6H_2O$ as a metal salts in 1:2 M ratio. We did not manage to obtain a crystal of the complexes suitable for the structure determination with X-ray crystallography.

The complexes are stable in their solid case in room temperature, and their integrity in solution state were good and stable enough within 3 weeks (in DMSO-d_6 and DMF solvents) considering that we have used these solutions during that time to measure Molar conductivity, antibacterial activity and ^{1}H NMR spectra.

2.3. Instruments

Elemental C, H, N and halogen analysis was carried out on a Perkin Elmer CHN 2400. The percentage of the metal ions were determined gravimetrically by transforming the solid products into oxide, and also determined by using atomic absorption method. Spectrometer model PYE-UNICAM SP 1900 fitted with



.nH2O

M=V(IV) or Zr(IV)
n=5 for V(IV) and n=4 for Zr(IV)

Scheme 2. The proposed structure of V(IV) and Zr(IV) with ofloxacin.