

Synthesis and Characterization of Two Novel Zinc(II) Complexes with Ciprofloxacin. Crystal Structure of $[C_{17}H_{19}N_3O_3F]_2 \cdot [ZnCl_4] \cdot 2H_2O$

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The complexation of Zn^{II} ions with quinolone in aqueous solution depends mainly upon pH. To investigate the pH dependence of the complexation between Zn^{II} and the quinolone derivative ciprofloxacin (abbreviation cfH), UV-Vis spectroscopy was used. The crystal structure of the compound $[C_{17}H_{19}N_3O_3F]_2 \cdot [ZnCl_4] \cdot 2H_2O$ (compound **I**) was determined by X-ray diffraction, which showed the structure to be ionic, consisting of a tetrachlorozincate(II) dianion and two protonated, monocationic ciprofloxacin molecules. Compound **II** ($[Zn(cf)_2] \cdot 3H_2O$) was obtained as microcrystals from an aqueous solution of ciprofloxacin hydrochloride and zinc sulphate adjusted to pH = 8 by the addition of sodium hydroxide. Both complexes were characterized by elemental analysis, mass spectrometry, TG analysis and IR spectroscopy. From the analysis of these results we have proposed a probable mode of bonding for the complexation of Zn^{II} to ciprofloxacin in compound **II**.

Key words: fluoroquinolone, metal-ion complexation, ciprofloxacin, zinc.

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INTRODUCTION

Ciprofloxacin (1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid) is a synthetic fluoroquinolone antibacterial agent with a broad spectrum of activity.¹ It is active against a wide variety of aerobic gram-negative and gram-positive bacteria. The mechanism of ciprofloxacin action involves inhibition of bacterial DNA gyrase, which is essential for DNA replication, and it has been proposed that metal complex intermediates are involved in this process.²⁻³ In contrast, the application of quinolones in the presence of antacids or other drugs which contain metal ions, especially when administered simultaneously or within a short period of time, reduced their bioavailability significantly.⁴⁻⁶ Polk *et al.* conducted a four-way crossover study in 12 healthy men to investigate the effects of multivitamins with zinc on the absorption of ciprofloxacin and found that »Multivitamins Stress tabs 600« with zinc reduced bioavailability by an average of 24%.⁷ It has been proposed that this reduction in bioavailability is a consequence of metal complex formation in the gastric system.⁴

The protonation constants of ciprofloxacin and the formation constants of its complexes with copper(II) were determined by potentiometric titration.⁸⁻⁹ These studies proposed the presence of numerous species in solution, though only one complex could be isolated as a solid.

Our aim was to use UV-Vis spectroscopy to determine the pH dependence of the complexation of Zn^{II} with ciprofloxacin in aqueous solution, and to isolate and characterize the complexes formed.

EXPERIMENTAL

Synthesis

All chemicals and reagents were used as received from commercial sources. The solutions were prepared with twice-distilled water.

 $[cfH_2]_2 \cdot [ZnCl_4] \cdot 2H_2O$ (Compound I)

Ciprofloxacin (0.270 g) was dissolved in 10 ml of 0.10 M HCl and 0.050 g of ZnCl₂ was added. The solution was stirred and a white precipitate appeared after one day. The precipitate was filtered and washed with ethanol. A saturated aqueous solution of the compound was then prepared and kept in an ethanol chamber. After a few weeks, transparent colourless needle shaped crystals appeared and were analyzed by X-ray diffraction.

Anal. Calcd. for C₃₄H₄₂N₆Cl₄F₂O₈Zn (*M_r* = 907.98): C 44.97, H 4.67, N 9.26%; found: C 44.83, H 4.31, N 9.18%.

The same product was obtained from a saturated aqueous solution of ciprofloxacin hydrochloride at pH = 6 when ZnSO₄ · 7H₂O was added (mole ratio cfH : Zn = 2 : 1).

$[Zn(cf)_2] \cdot 3H_2O$ (Compound II)

A saturated aqueous solution of ciprofloxacin hydrochloride, pH = 8, was prepared (the pH was adjusted with 0.10 M NaOH). $ZnSO_4 \cdot 7H_2O$ was added and the pH was adjusted back to pH = 8 (mole ratio cfH : Zn = 2 : 1). The solution was stirred for one day, though a white precipitate appeared after just half an hour. The precipitate was filtered, washed with ethanol and dried at 60 °C for 5 hours.

Anal. Calcd. for $C_{34}H_{40}N_6F_2O_9Zn$ ($M_r = 780.17$): C 52.34, H 5.18, N 10.78%; found: C 52.76, H 5.34, N 10.77%.

The product was insoluble in water, ethanol, methanol, chloroform, acetone, ether, ethylene glycol, 2-propanol, carbon tetrachloride, cyclohexanone, dichloromethane and dimethyl sulfoxide. It decomposed in diluted solutions of all strong acids. All attempts to prepare single crystals were unsuccessful.

Measurements

Spectrometric measurements were performed on a Perkin-Elmer UV-Vis-NIR Lambda 19 instrument equipped with 10-mm quartz cuvettes. Aqueous solutions of ciprofloxacin hydrochloride (1.0×10^{-4} mol L⁻¹) and ciprofloxacin hydrochloride/zinc sulphate (1.0×10^{-4} mol L⁻¹ ciprofloxacin, 1.0×10^{-2} mol L⁻¹ zinc sulphate) were prepared for all integer values of pH from 2–10. In each case the pH was adjusted by the addition of either 0.10 mol L⁻¹ NaOH or 0.10 mol L⁻¹ HCl, as appropriate. UV-Vis spectra were recorded for all of these solutions in the range 220 to 400 nm.

The elemental analyses were carried out on a Heraeus CHNO Rapid Element Analyser at the University of Hamburg.

Infrared spectra (IR) were recorded on a Perkin-Elmer 1720 IR Fourier Transform Spectrophotometer in poly-(chlorotrifluoroethylene) oil mulls (4000–1300 cm⁻¹) and nujol (1300–400 cm⁻¹) between CsI windows, resolution 2 cm⁻¹, 10 scans.

Thermogravimetric (TG) data were recorded on a Mettler TA 3000 system with platinum crucibles at a heating rate of 5 K min⁻¹ and dry airflow rate of 20 mL min⁻¹. The samples weighed approximately 10 mg.

Mass spectrometry was performed on a VG-Analytical AutospecEQ instrument. Ionization was accelerated with Cs⁺ ions with energies of 20–30 keV (Fast Atom Bombardment, FAB); *m*-nitrobenzyl alcohol (NBA) was used as matrix.

Powder diffraction analyses were performed on a Guinier Camera 620 with a Guinier Monochromator 615 using Cu-K α radiation. Powder Diffraction File PDF-2 was used for data matching.¹⁰

Decomposition of complexes was performed in an autoclave, specially designed by Viktor d.o.o., Radomlje at Ljubljana, at 150 °C for 5 h.

The pH's of the solutions were determined using a pH 540 GLP WTW (Wissenschaftlich-Technische Werkstätten) pH-meter equipped with a WTW SenTix pH electrode.

RESULTS AND DISCUSSION

UV Spectroscopy

UV-Vis spectroscopy was used to investigate the pH dependence of the complexation of Zn^{II} with ciprofloxacin in aqueous solution.

The absorption maxima for an aqueous solution of ciprofloxacin hydrochloride, at pH = 2, appeared at 277, 316 and 328 nm. On increasing the pH, the maximum at 277 nm shifted to lower values and the maxima at 316 and 328 nm shifted to higher values. These changes can be attributed to the extent of ionization of the carboxylic group as a consequence of the removal of a proton.¹¹ At pH = 7, the absorption maxima appeared at 272, 322 and 333 nm.

These spectra were compared with those of a solution of zinc sulphate and ciprofloxacin hydrochloride at the same pH values. At pH = 2–6, no significant differences were observed between the spectra of the two solutions, indicating no interaction between the Zn^{II} ions and the ciprofloxacin. At pH ≥ 7 (Figure 1), both bathochromic and hypsochromic shifts were found in the spectra with the bands of ciprofloxacin at 322 and 333 nm shifted to 318 and 330 nm, respectively, in the presence of Zn^{II} ions, and the band at 272 nm shifted to 275 nm. Thus we propose that, at pH ≥ 7 , there is complexation between Zn^{II} ions and ciprofloxacin. On reaching pH = 9, a copious quantity of a white precipitate was seen to form. This precipitate was filtered off and analyzed using X-ray powder diffraction. Data matching with Powder Diffraction File PDF-2 confirmed the precipitate to be $Zn_5(OH)_8Cl_2 \cdot H_2O$.¹⁰

Transport of quinolone across the bacterial cytoplasmic membrane is strongly pH dependent, peaking at neutral pH.¹² Y. Kawai *et al.*¹³ have proposed that zwitterionic and uncharged quinolone species are responsible for diffusion through cytoplasmic membranes. In the stomach the pH range is between 2–5, whilst in the intestines the pH varies from 6–8. The results of our UV-Vis spectroscopic studies show that quinolones interact extensively with Zn^{II} ions only at pH = 7 and higher. Thus, in the stomach, where there is no metal-quinolone complexation due to acidic pH's, the absorption of quinolone is very low. Intensive transport of quinolone across the bacterial cytoplasmic membrane probably occurs extensively in the intestines, where the pH is high enough. Additionally, the metal-quinolone complexation probably occurs initially in the intestines. H. H. M. Ma *et al.*¹⁴ have investigated the mechanism of the reduction in antimicrobial activity of ciprofloxacin caused by metal cations. They have reported that the presence of metal ions results in a higher ciprofloxacin uptake by bacterial cells compared to that of the drug alone. The reason for the reduced bioavailability of the drug is the loss

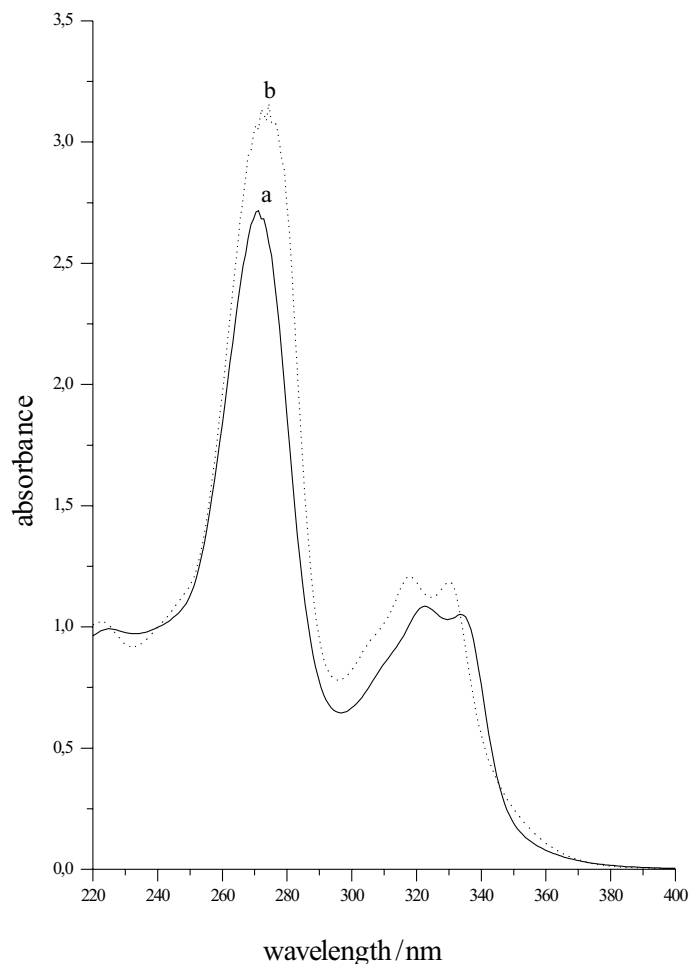


Figure 1. UV-Vis spectra of the solutions of (a) ciprofloxacin and (b) ciprofloxacin and zinc sulphate at pH = 8.

of ciprofloxacin activity that occurs when the cation chelates the carbonyl and the carboxylate functional groups of the molecule. The exact mechanisms of these processes have not yet been fully elucidated.

Determination of the Presence of Cl^- and SO_4^{2-} Ions in the Samples

Decomposition of complexes was performed in concentrated HNO_3 in an autoclave. After decomposition, the samples were diluted with water to 100 mL, and the qualitative presence of Cl^- and SO_4^{2-} ions in the samples was

determined by means of AgNO_3 and BaCl_2 respectively. The decomposition product of compound **I** was found to contain Cl^- ions, and their concentration was determined with an ion selective electrode.

Anal. Calcd. for $\text{C}_{34}\text{H}_{42}\text{N}_6\text{Cl}_4\text{F}_2\text{O}_8\text{Zn}$: 15.6%; found: 15.2%.

The decomposition product of compound **II** contained neither Cl^- nor SO_4^{2-} ions.

IR Spectroscopy

The IR spectra of quinolones are most indicative in the region 1800–1300 cm^{-1} . The IR spectra of ciprofloxacin, ciprofloxacin hydrochloride hydrate and ciprofloxacin hexahydrate have been assigned.^{15–16} The characteristic band for the $\nu(\text{C}=\text{O})$ vibration of the carboxylic group in ciprofloxacin hydrochloride hydrate is at 1707 cm^{-1} .¹⁵ In the IR spectra of ciprofloxacin and ciprofloxacin hexahydrate, there are no analogous peaks due to the deprotonation of COOH group.¹⁶ Some authors have pointed out that ionic carboxylates show no carbonyl band around 1700 cm^{-1} , but instead have two absorption bands due to the asymmetric ($\nu_{\text{as}}(\text{O}-\text{C}-\text{O})$) and symmetric ($\nu_{\text{s}}(\text{O}-\text{C}-\text{O})$) stretching vibrations that occur in the ranges 1610–1550 cm^{-1} and 1400–1280 cm^{-1} , respectively.¹⁷ It is difficult, however, to assign unambiguously these vibrations in the spectra of quinolones on account of the numerous other bands present in these regions, so only the region from 1800–1500 cm^{-1} is reported here. The band at 1618 cm^{-1} in the IR spectrum of ciprofloxacin (Figure 2, spectrum a) was ascribed to the stretching vibration of the pyridone ($\text{C}=\text{O}$) group.

As can be seen from the IR spectrum of compound **I** (Figure 2, spectrum b), both of the $\nu(\text{C}=\text{O})$ absorption bands are shifted to slightly higher wavenumbers (1718 cm^{-1} and 1629 cm^{-1}). Similar shifts were observed in the IR spectra of the norfloxacin complex $(\text{nfH}_2)(\text{nfH})[\text{ZnCl}_4]\text{Cl} \cdot 2\text{H}_2\text{O}$.¹⁸

The IR spectrum of compound **II** (Figure 2, spectrum c) shows no band for the $\nu(\text{C}=\text{O})$ vibration of the carboxylic group in the region 1800–1500 cm^{-1} , indicating that the $-\text{COOH}$ group has been deprotonated. The spectrum is generally very similar to that of the copper complex $[\text{Cu}(\text{cfH})_2]\text{Cl}_2 \cdot 6\text{H}_2\text{O}$, where the copper ion is coordinated with the pyridone oxygen atom and one of the carboxylic oxygens of the quinolone molecule.¹⁹

Thermogravimetric Analysis

The product of the thermal decomposition of both complexes is ZnO (as confirmed by X-ray powder diffraction). The weight loss of compound **I** from 25 °C to 90 °C corresponds to dehydration. The experimental value (4.40%)

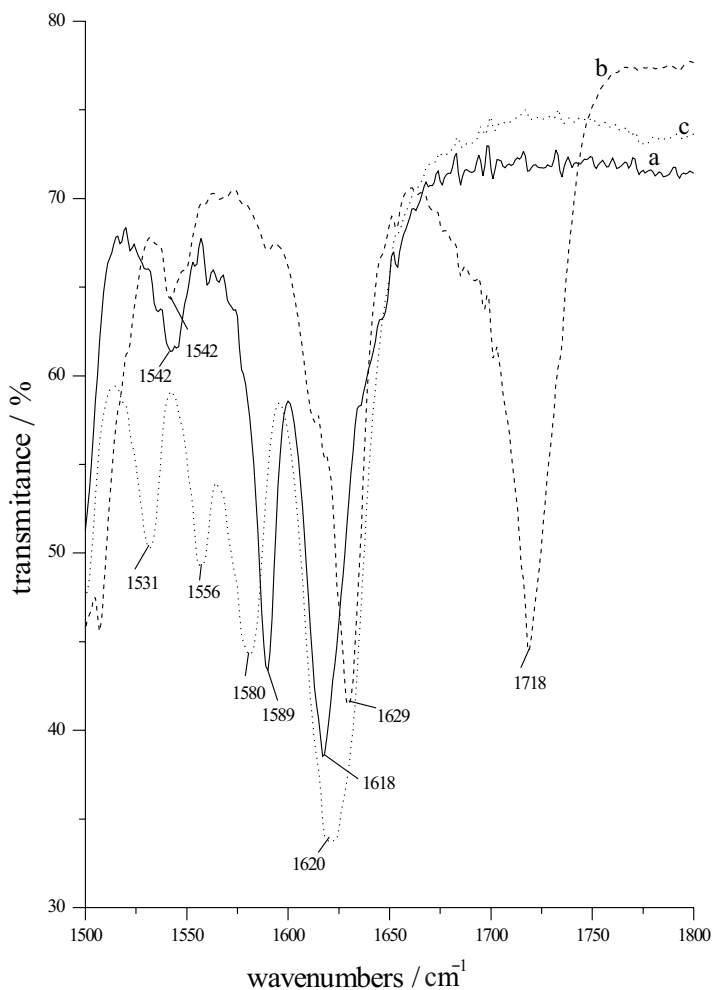


Figure 2. IR spectra of (a) ciprofloxacin, (b) $[cfH_2]_2[ZnCl_4] \cdot 2H_2O$ and (c) $[Zn(cf)_2] \cdot 3H_2O$.

is in fair agreement with the calculated value for the loss of two water molecules per molecule of substance (3.97%). The reason for the slight discrepancy is probably the hygroscopicity of the complex, a difficulty that has been reported for other metal-quinolone complexes.²⁰ The shape of the DTG curve of the dehydration reaction shows the presence of moisture. The pyrolysis of compound **I** begins at 220 °C and ends at 645 °C. From the mass of the residue of the thermal decomposition it was calculated that the sample contains 4.88% of zinc (*cf.* calculated value of 7.20%). However, it is known that zinc oxide sublimates at elevated temperatures.²¹ After the decomposition of the

compound in the autoclave, zinc concentration was determined by titration with EDTA. The solution was found to contain 6.97% of zinc, suggesting that the earlier zinc assay (determined by TGA) was low due to sublimation during the thermal decomposition.

Dehydration of compound **II** ends at 110 °C and the weight loss corresponds to 7.12% water (calculated value for three water molecules is 6.93%). The DTG curve of the dehydration process is not split, suggesting that all water molecules are equally strongly held within the solid, in contrast to the related magnesium complex with ciprofloxacin.²² The pyrolysis begins at 234 °C and ends at 593 °C with a total weight loss of 92.4%, corresponding to 5.13% of zinc (*cf.* a calculated value of 8.38%). The reason for this discrepancy is probably the sublimation of zinc oxide again.

Mass Spectrometry

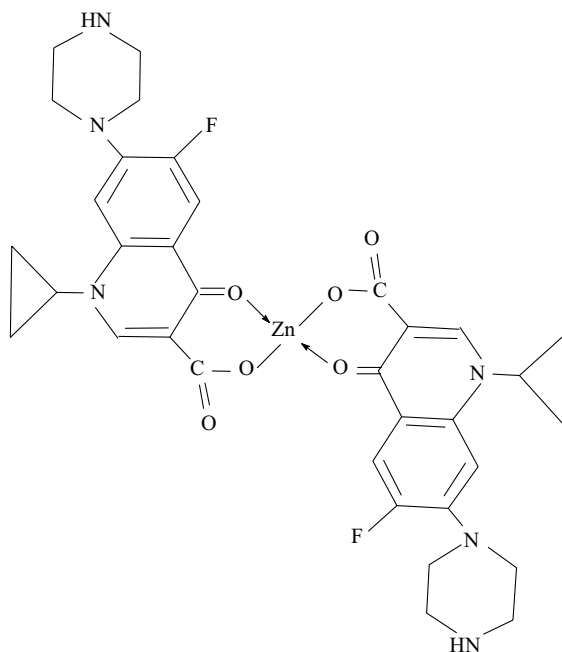
In the mass spectra of compounds **I** and **II**, intense mass peaks at m/z 332 and 663 were observed. The first mass peak corresponds to the $[\text{cfH}_2]^+$ ion and the second one to the $[(\text{cfH})(\text{cfH}_2)]^+$ ion. Intense peaks at m/z 725, 727 and 729 were observed in the mass spectra of compound **II**, corresponding to the $[\text{Zn}(\text{cf})(\text{cfH}_2)]^+$ ion considering all three isotopes of zinc. No such peaks appeared in the mass spectrum of compound **I**. These results are again consistent with the presence of direct metal-ligand bonding in compound **II**.

Thus, on the basis of all these results, we propose that in compound **II** the zinc binds to the quinolone ligand in the fashion depicted in the Scheme 1.

X-ray Structure Analysis of Compound **I**

Crystal Structure Determination

Crystal data for I. – $[\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_3\text{F}]_2 \cdot [\text{ZnCl}_4] \cdot 2\text{H}_2\text{O}$, $M = 907.9$, triclinic, space group $P\bar{1}(\text{no. } 2)$, $a = 9.872(1)$, $b = 13.863(1)$, $c = 16.593(1)$ Å, $\alpha = 70.40(1)$, $\beta = 76.78(1)$, $\gamma = 69.50(1)^\circ$, $V = 1987.9(3)$ Å³, $Z = 2$, $D_c = 1.517$ g cm⁻³, $\mu(\text{Cu-K}\alpha) = 39.0$ cm⁻¹, $F(000) = 936$, $T = 293$ K; clear platy needles, $0.73 \times 0.23 \times 0.10$ mm, Siemens P4/PC diffractometer, ω -scans, 5554 independent reflections. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically using full matrix least-squares based on F^2 to give $R_1 = 0.068$, $wR_2 = 0.178$ for 4246 independent observed absorption corrected (ψ -scans) reflections $[|F_o| > 4\sigma(|F_o|), 2\theta \leq 120^\circ]$ and 505 parameters. The N–H and O–H hydrogen atoms were located from ΔF maps and refined isotropically subject to an X–H distance constraint (0.90 Å). Refinements were carried out using the SHELXTL program system.²³



Scheme 1.

Description of the Structure

The X-ray analysis of the salt formed between ciprofloxacin and ZnCl_2 in hydrochloric acid showed the crystals to contain two crystallographically independent ciprofloxacinium cations **A** and **B** (Figure 3 depicts molecule **A**), a single tetrachlorozincate(II) dianion and two water molecules. The two independent ciprofloxacinium cations have very similar conformations, the only major difference being in the relative orientations of the piperazinium rings (the torsional twists about the C(7)–N(21) bond differ by *ca.* 110°). In both molecules, protonation is on the terminal nitrogen atom [N(24)] of the piperazine ring and not at the substituted N(21) position. In each case there is an intramolecular O–H...O hydrogen bond between the terminal carboxylic oxygen O(11) and the quinolone carbonyl oxygen O(1) (the O...O, H...O distances / Å and the O–H...O angles / ° are 2.55, 1.70, 156 for molecule **A** and 2.52, 1.76, 139 for molecule **B**). In both molecules, the carbonyl character of the quinolone C(4)–O(1) bond is retained (1.251(7) and 1.258(6) Å in molecules **A** and **B**, respectively, Table I). There is, however, a distinct pattern of delocalization within this ring, a pattern of bonding directly analogous to that observed in the copper and zinc salts of the related norfloxacin.¹⁸

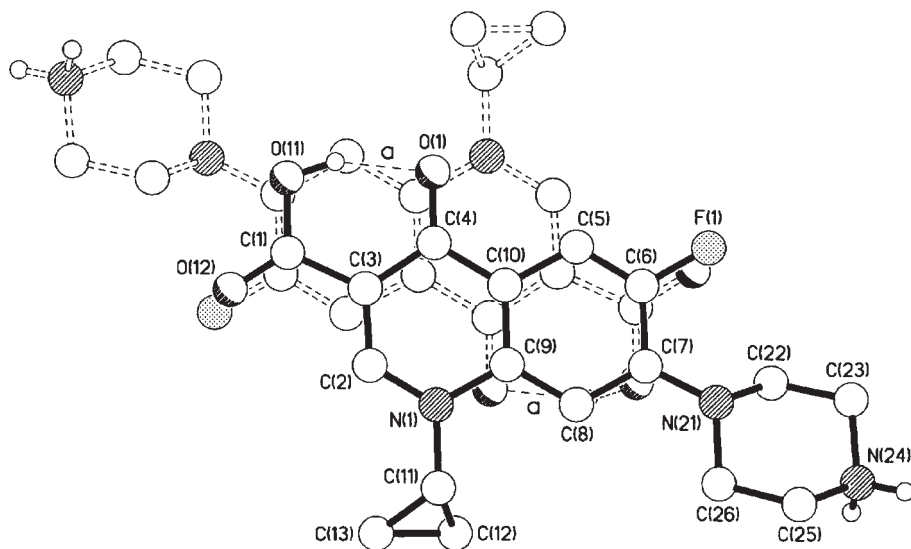


Figure 3. The π - π stacking of one of the two crystallographically independent ciprofloxacinium cations (type **A**) present in the crystals of **I**. The O-H...O hydrogen bonding geometry is (O...O and H...O distances / Å, O-H...O angles / °): a) 2.55, 1.70, 156.

TABLE I

Bond lengths / Å for the two independent ciprofloxacin molecules **A** and **B** present in the structure of **I**

	A	B		A	B
N(1)–C(2)	1.338(8)	1.336(7)	N(1)–C(9)	1.418(7)	1.402(6)
N(1)–C(11)	1.456(8)	1.461(7)	F(1)–C(6)	1.358(6)	1.363(6)
O(1)–C(4)	1.251(7)	1.258(6)	C(1)–O(12)	1.207(9)	1.204(7)
C(1)–O(11)	1.318(10)	1.333(7)	C(1)–C(3)	1.500(9)	1.481(8)
C(2)–C(3)	1.354(9)	1.378(8)	C(3)–C(4)	1.432(8)	1.428(7)
C(4)–C(10)	1.439(8)	1.441(8)	C(5)–C(6)	1.344(8)	1.358(8)
C(5)–C(10)	1.414(7)	1.400(7)	C(6)–C(7)	1.413(8)	1.413(8)
C(7)–C(8)	1.384(7)	1.378(8)	C(7)–N(21)	1.395(7)	1.388(7)
C(8)–C(9)	1.392(8)	1.400(8)	C(9)–C(10)	1.393(8)	1.406(7)
C(11)–C(12)	1.473(9)	1.493(9)	C(11)–C(13)	1.487(8)	1.478(8)
C(12)–C(13)	1.487(10)	1.496(10)	N(21)–C(26)	1.455(7)	1.462(7)
N(21)–C(22)	1.475(7)	1.474(8)	C(22)–C(23)	1.489(8)	1.495(9)
C(23)–N(24)	1.497(8)	1.489(9)	N(24)–C(25)	1.487(8)	1.477(10)
C(25)–C(26)	1.512(8)	1.503(9)			

The two independent molecules **A** and **B** each stack with their centrosymmetrically related counterparts. In molecules of type **A** the ring systems are offset, the centres of the two quinolone rings being separated by 3.92 Å whilst the mean interplanar separation is 3.48 Å (Figure 3). The mode of stacking of molecules of type **B** is similar (Figure 4) but with a greater overlap of the two quinolone rings (centroid...centroid separation: 3.49 Å, mean interplanar separation: 3.47 Å). The π - π stacking interaction between molecules of type **B** is supplemented by N-H...O and O-H...O hydrogen bonding to, and including, the solvent water molecules to produce an H-bonded macrocyclic dimer. Type **A** and type **B** molecules are also π -stacked, the planes of the ring systems being inclined by only 3° and separated by *ca.* 3.4 Å (Figure 5). There are secondary weak N-H...Cl and O-H...Cl interactions together with stronger O-H...O hydrogen bonds linking these two types of molecule. The total assembly of type **A** and type **B** molecules is thus a continuous π -stack in the sequence ...**AABBAA**... with adjacent stacks being cross-linked by a combination of N-H...Cl and O-H...Cl hydrogen bonding interactions (Figure 6). This mode of packing is very similar to that observed in the solid state for the copper and zinc norfloxacin species.¹⁸

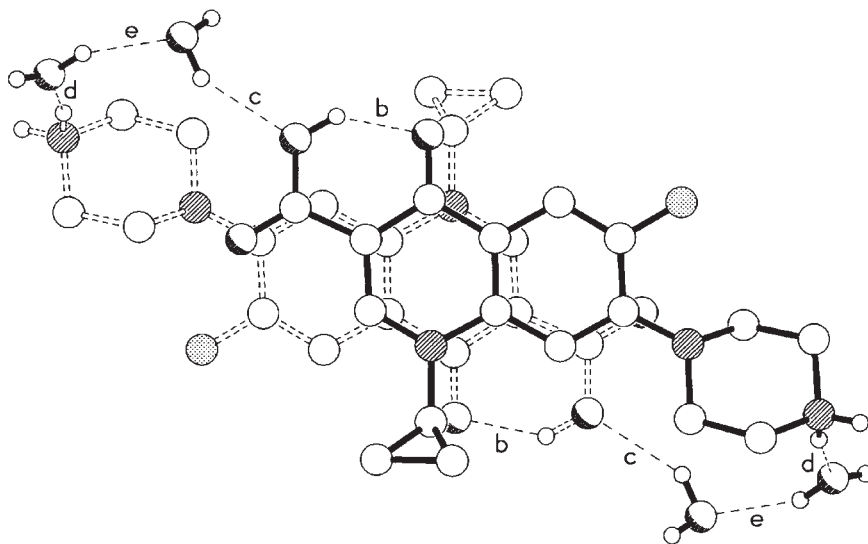


Figure 4. The π - π stacking of type **B** molecules showing also the supplementary linking by N-H...O and O-H...O hydrogen bonding involving hydrate molecules. The N-H...O and O-H...O hydrogen bonding geometries are (X...O and H...O distances / Å, and X-H...O angles / °): b) 2.52, 1.76, 139; c) 2.93, 2.15, 144; d) 2.74, 1.85, 168; e) 2.74, 1.94, 147.

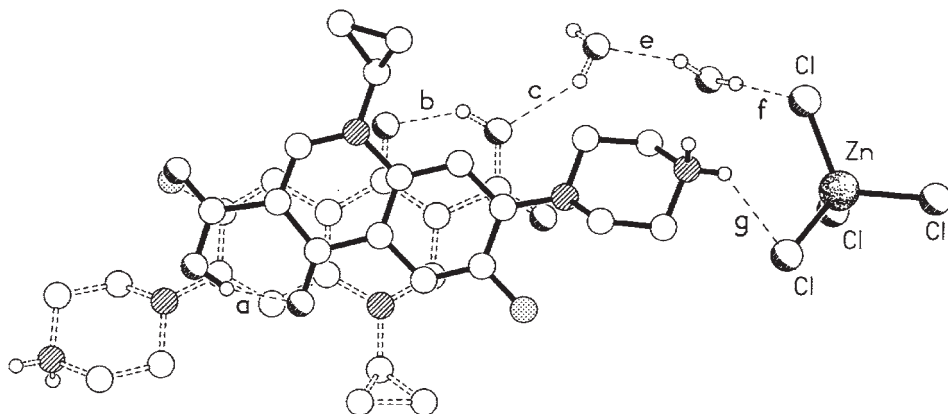


Figure 5. The π - π stacking between a molecule of type **A** and a molecule of type **B**, showing also the weak N-H...Cl and O-H...Cl interactions and the strong O-H...O hydrogen bonding. The N-H...Cl, O-H...Cl and O-H...O hydrogen bonding geometries are (X...O and H...O distances / Å and X-H...O angles / °): a) 2.55, 1.70, 156; b) 2.52, 1.76, 139; c) 2.93, 2.15, 144; e) 2.74, 1.94, 147; f) 3.32, 2.42, 177; g) 3.25, 2.52, 138. The Zn-Cl distances are in the range 2.231(2)–2.274(2) Å.

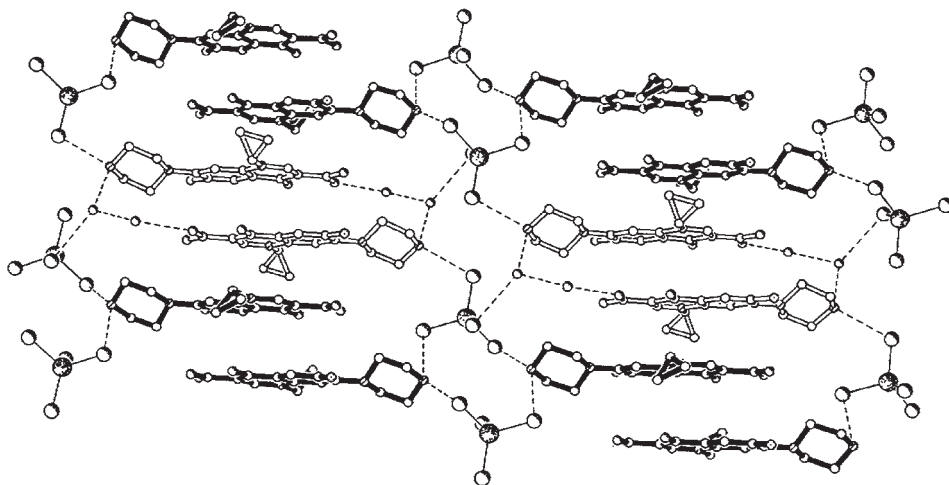


Figure 6. The cross-linked continuous ...AABBAA... π - π stacks present in the crystals of compound **I**.

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Supplementary materials. – Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) and can be obtained on request, free of charge, by quoting the publication citation and the deposition number 135043.

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SAŽETAK

Sinteza i karakterizacija dvaju novih kompleksa cinka(II) s ciprofloksacinom. Kristalna struktura $[\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_3\text{F}]_2 \cdot [\text{ZnCl}_4] \cdot 2\text{H}_2\text{O}$

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Nastajanje kompleksa iona Zn^{II} s kinolonom, u vodenoj otopini, ovisi uglavnom o pH. Da bi se proučavala pH-ovisnost kompleksiranja Zn^{II} i kinolonskog derivata ciprofloksacina (skraćeno cfH) primjenjena je UV-Vis spektroskopija. Difrakcijom X-zraka određena je kristalna struktura $[\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_3\text{F}]_2 \cdot [\text{ZnCl}_4] \cdot 2\text{H}_2\text{O}$ (spoj **I**) koja je pokazala da je spoj ionski i sastoji se od dianinona tetraklorocinkata(II) i dvije protonirane, monokationske molekule ciprofloksacina. Spoj **II** ($[\text{Zn}(\text{cf})_2] \cdot 3\text{H}_2\text{O}$) dobiven je u obliku mikrokristala iz vodene otopine ciprofloksacin-hidroklorida i cinkova sulfata podešene na pH = 8 dodavanjem natrijeva hidroksida. Oba kompleksa okarakterizirana su elementnom analizom, masenom spektroskopijom, TG analizom i IR spektroskopijom. Nakon analize tih rezultata, predložen je vjerojatni način vezanja Zn^{II} na ciprofloksacin u spoju **II**.