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Physicochemical Characterization of Solid Norfloxacin and Ciprofloxacin Metal Complexes: Spectroscopic and Thermal Studies

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SPECTROSCOPIC methods such as mass, infrared, nuclear magnetic resonance and X-ray diffraction in combination with thermal measurements are used to monitor and describe the physicochemical properties of the solid drug substances; the novel nor- and ciprofloxacin chromium(III) and zirconium (IV) metal complexes. The results support the formation of complexes with the formula $[Cr(Nor)_2](NO_3)_3.4\ H_2O$, $[Cr\ (Cip)_2].7H_2O$, $[Zr\ (Nor)_2].3.5\ H_2O$ and $[Zr\ (Cip)_2].5H_2O$. The FT/IR spectra of the isolated complexes suggest that norfloxacin and ciprofloxacin act as bidentate ligands through the ring carbonyl oxygen atom and one of the oxygen atoms of the carboxylic group. Thermal studies indicate that the complexes dehydrate at lower temperatures followed by pyrolytic decomposition at higher temperatures and the results show that zirconium complexes are more stable than chromium complexes.

Keywords: Ciprofloxacin, Norfloxacin, Spectroscopy and Thermal analysis .

Solid-state chemistry research plays a central role in the pharmaceutical industry. Solid pharmaceuticals exist as polymorphs, solvates, or amorphous forms, which collectively are described as solid forms. Most drugs are used in a crystalline form; the arrangement of molecules in a crystal determines its physical properties which can affect its performance. Quinolone antibiotics are complexing agents for a variety of metal ions[(1)]. Norfloxacin (Nor) is a synthetic, broad-spectrum antibacterial agent for oral administration. It is used to treat various bacterial infections such as urinary tract infections, gonorrhea and prostate infections. Ciprofloxacin (Cip) is another synthetic, broad-spectrum antibacterial drug used to treat pneumonia, bronchitis and some types of gonorrhea, diarrhea caused by bacteria, typhoid fever, prostate, sinus, and urinary tract infections.

Both Nor- and Ciprofloxacin are quinolone antibacterial agents, with 4-oxo-3-carboxylic acid groups that are essential for their bactericidal activity [(1,2)] . The design of metal–drug complexes is of particular interest in the pharmacological research.

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Metal combinations with pharmaceutical agents are known to improve the drugs activity and to decrease their toxicity. The coordinated metal ions in these antibiotics play an important role in maintaining proper structure and/or function.

The neutral quinolones in the zwitterionic state are potentially capable of forming simple complexes. In these complexes the quinolone coordinate to metal ions as a bidentate ligand via the ring carbonyl group at position 4 and through one of the oxygen atoms of the carboxylate group at position 3[3–7] .

Many authors studied the interactions of metal ions with quinolones[1, 2] . They found that the absorption of the quinolone drugs is lowered when they are adminstered simultaneously with magnesium, aluminum, calcium, and zinc. The proposed reason for such behavior could be the chelate bonding of the quinolone to the metal. This was one of the reasons that many authors started to study the interactions of metal ions and quinolones[8-10] .

Therefore, the present investigation was designed to explore the physiochemical characteristics of four solid quinolone complexes. Up to the best of our knowledge, the synthesis and physicochemical properties of quinolones of Nor- and Ciprofloxacin with chromium (III) and zirconium (IV) metals have not been reported yet. To accomplish the present research objectives: (i) thermal events involved in the decomposition course were revealed by thermogravimetry and differential thermal analysis, (ii) chelation, proposed structure and crystallinity of the metal complexes were identified by Fourier-transform infrared spectroscopy, mass spectrometry, ^{1}H-NMR spectroscopy and X-ray powder diffractometry.

Experimental

Materials

Norfloxacin and Ciprofloxacin used in this study were purchased from the (Medical Union Pharmaceuticals, Abu-Sultan, Ismailia, Egypt) and (Egyptian International Pharmaceutical Industrial Company EIPICO), respectively. All chemicals used for the preparation of the complexes were of analytical reagent grade, commercially available from different sources. $Cr(NO_3)_3.\ 9H_2O$ and $Zr(NO_3)_4$ are: 99% (BDH laboratory reagents, England). Norfloxacin and Ciprofloxacin are indicated throughout the text by the abbreviations (Nor) and (Cip), respectively.

Synthesis

Method 1: Preparation of solid chromium complex of norfloxacin

A solution of (1.0 mmol. 0.40 g) of $Cr(NO_3)_3.9H_2O$ in 5 ml of distilled water was added to a solution of (1.0 mmol. 0.319g) of norfloxacin ligand in 25 ml acetone. The resulting mixture was heated at 50 °C under reflux on a water bath for about 12 hr and then cooled. The precipitate formed was filtered off under vacuum, washed with boiling water then acetone and dried over $CaCl_2$. The complex prepared is indicated throughout the text by the abbreviation (CrNor).

Method 2: Preparation of chromium ciprofloxacin complex and zirconium complexes of norfloxacin and ciprofloxacin

Appropriate quantity of ciprofloxacin (0.5 mmol, 0.165 g) or norfloxacin (0.5 mmol. 0.159 g) ligands was suspended in distilled water (5ml) which were then added to the solution of $Cr(NO_3)_3.9H_2O$ (0.5 mmol, 0.2 g) or $Zr(NO_3)_4$ (0.5 mmol, 0.169 g) in distilled water (5ml). Triethylamine solution (1mol/l) was added dropwise , maintaining the pH between 7.5 and 8.0. The reaction mixture was stirred at room temperature for two days. The solid precipitate obtained was filtered off under vacuum, washed with distilled water and methanol, and dried. The prepared complexes are indicated throughout the text by the abbreviations (ZrNor), (CrCip) and (ZrCip).

Apparatus and techniques

Ex-situ FTIR spectra were taken of lightly loaded (<1%) thin discs of KBr-supported test materials at 4000 to 400 cm^{-1} with the resolution of 4 cm^{-1}, using a model 410 Jasco FT-IR spectrophotometer (Japan).

The ^{1}H-NMR spectra were determined on a GEMINI- (200 MHz) spectrometer, Micro analytical Center, Cairo University and on JEOL- (500 MHz) spectrometer, Faculty of Science, Alexandria University, using TMS as internal standard.

Mass spectra (MS) were taken on AEI MS 30 mass spectrometer at 70 eV.

Thermal analysis was performed by 30H Shimadzu analyzer (JAPAN). TG and DTA curves were recorded while heating a small portion (10- 15 mg) of the drug compound up to 800 °C at 10 °C/ min in a N_2 atmosphere (20 cm^3/ min) of the test gas. A highly sintered α-Al_2O_3 (Shimadzu Corp.) was the thermally inert reference material for the DTA. The abbreviation ML stands for mass loss.

X-ray powder diffraction patterns were obtained with a JSX-60 PA JEOL diffractometer (JAPAN) equipped with Ni-filtered CuKα radiation (λ =1.5416 Å). Based on scans in the range $4° \leq 2\theta \leq 60°$, the d-spacings and relative intensities (I/I°) were obtained.

Results and Discussion

The physical properties of (Nor) and (Cip) ligands and complexes are listed in Table 1. The melting points of the complexes are higher than that of the ligand revealing that the complexes are much more stable than ligands. All complexes are stable in air, and their solubility is much better than (Nor) and (Cip) itself, in water, methanol, chloroform, acetone, cyclohexane and 2- propanol.

TABLE 1. Physical properties of the compounds of norfloxacin, ciprofloxacxin and their complexes.

Molecular formula	Molecular weight	Yield (%)	Color	mp (°C)
(Nor) $C_{16}H_{18}FN_3O_3$	319	-	yellow	233-34
$C_{32}H_{44}F_2N_9O_{19}Cr$	772.63	77	Dark green	<300
$C_{32}H_{41}F_2N_6O_{9.5}Zr$	789.15	60	yellow	293-95
(Cip)$C_{17}H_{18}FN_3O_3$	331.34	-	White	
$C_{34}H_{50}F_2N_6O_{13}Cr$	745.3	73	Pale green	287-89
$C_{34}H_{46}F_2N_6O_{11}Zr$	767.42	57	Pale yellow	292-94

FT/ IR spectra taken for the parents nor- and ciprofloxacin and their complexes with chromium and zirconium metals are compared in Fig. 1. TG and DTA curves of nor- and cipro -complexes obtained on heating (in nitrogen atmosphere) at (10°C / min) up to 800°C are given in Fig. 2 and 3, respectively. Table 2 summarizes the characteristics of thermal events encountered throughout during the decomposition courses of the four complexes under investigation. X-ray diffraction pattern obtained for (CrCip) complex is given in Fig. 4.

^{1}H-NMR assignment for the parent (Nor) and Nor- metals complexes are listed in Table 3, whereas that for (Cip) and Cip- metals complexes are listed in (Table 4). The proposed structure of norfloxacin and its complex with chromium (III) (CrNor) and Zirconium (IV) (ZrNor) are shown in Scheme 1. The proposed structure of ciprofloxacin and its complex with Chromium (III) (CrCip) and Zirconium (IV) (ZrCip) are shown in Scheme 2.

Characterization of the Cr- norfloxacin and Cr- ciprofloxacin complexes

The IR spectra of quinolones are quite complex due to the presence of numerous functional groups in the molecules. The IR spectra of quinolones are most representative in the region 1800-1300 cm^{-1}[11] . Comparing the main IR frequencies of metal complexes with that of norfloxacin (Fig. 1A), the following was found (i) In the spectrum of the ligand (Nor), the two strong absorption peaks at 1727 and 1617 cm^{-1} are characteristic to (υCOOH) and (υCO), respectively[12] (ii) Different from the spectrum of the ligand (Nor), the band at 1727 cm^{-1} for the two complexes completely vanished due to deprotonation of –COOH group and formation of Cr–O and Zr- O bond (Scheme 1). The peak at 1617 cm^{-1} was retained in the IR spectrum of CrNor and ZrNor but shifted to 1633 and 1635 cm^{-1}, respectively. (iii) For the complexes, the bands positioned at the ranges of 1585-1500 cm^{-1} and 1480-1460 cm^{-1} may be attributed to the asymmetric and symmetric vibrations of the –COO group. So we proposed that the ligand norfloxacin interacted with the metal ions through bidentate chelating[11] . This is consistent with the disappearance of the strong absorption at 1727 cm^{-1} in the spectra of complexes. The averaging effect took place between the single and double bonds on the carbonyl group owing to the coordination. (iv) New vibrating absorptions were observed in the range of 550-620 cm^{-1}, which were characterized as the absorption of M-O bonds[13] .

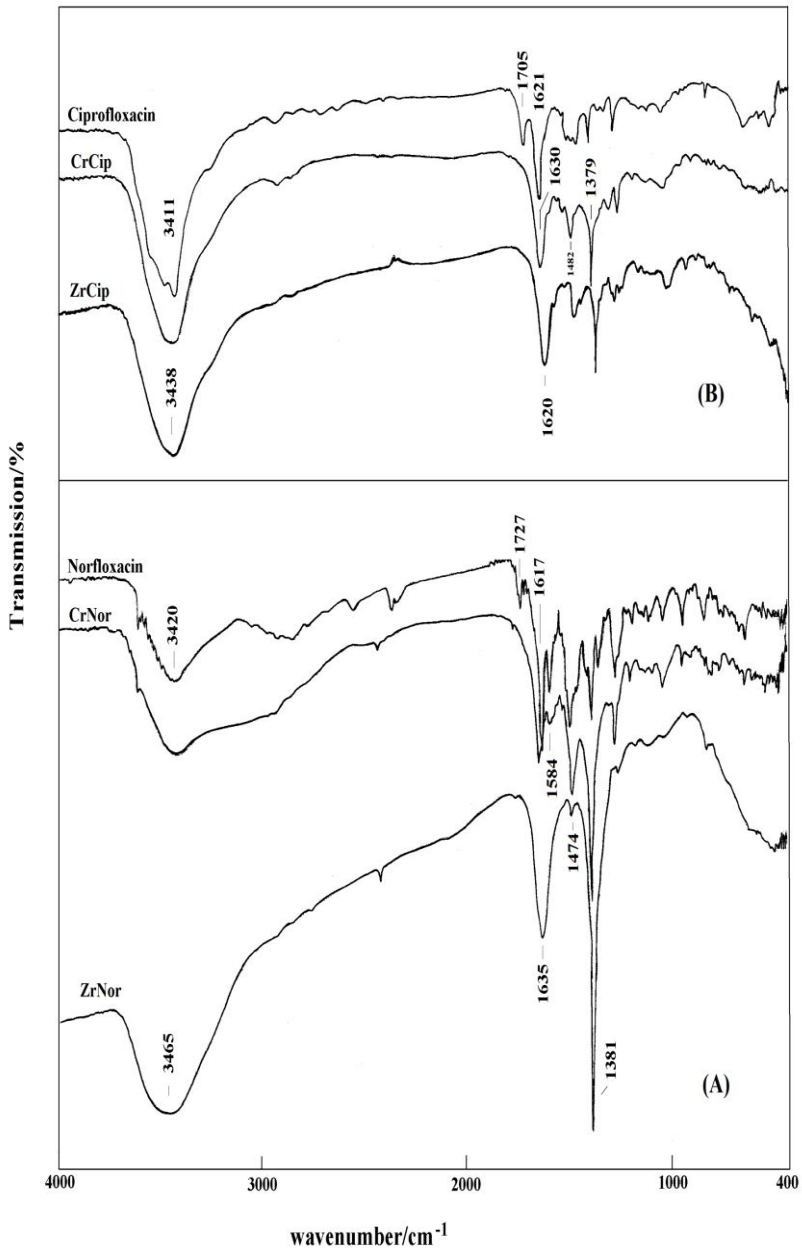


Fig. 1. FT/ IR spectra taken from (A) norfloxacin and its complexes with Cr and Zr metals and (B) ciprofloxacin and its complexes with Cr and Zr metals.

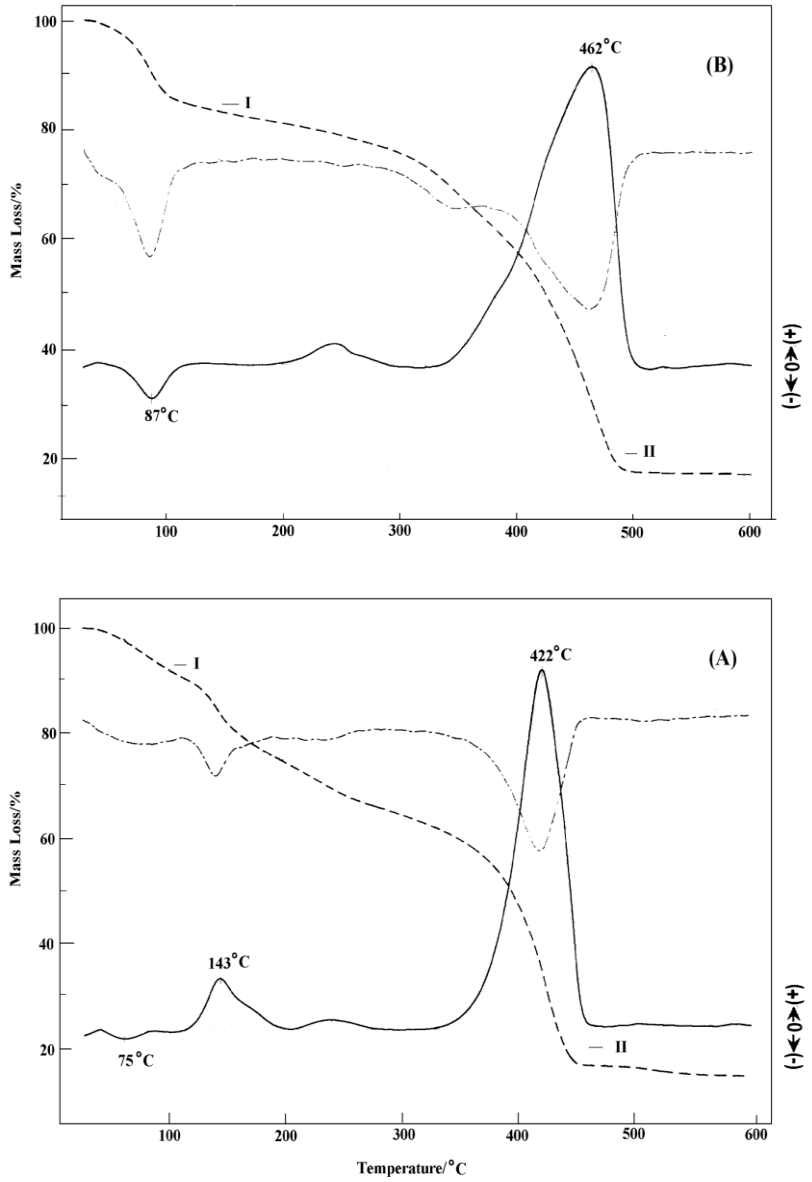


Fig. 2. TG(---), DTG(-·-) and DTA(—) curves obtained (at 10 °C/min) for (A) CrNor complex (B) CrCip complex in a dynamic atmosphere of N_2 (20 cm^3/min). The Roman numerals (I-II) indicate locations where the thermal stages encountered are terminated, as further cited in Table 1.

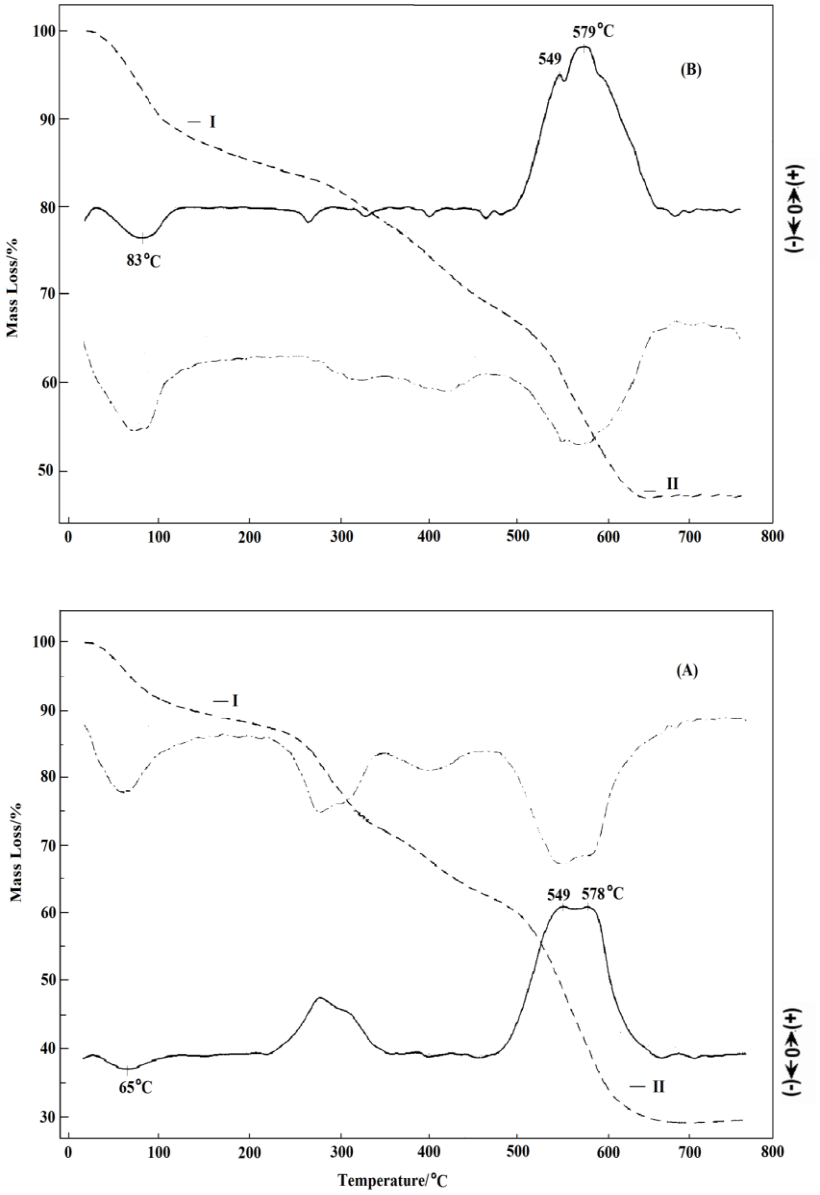


Fig. 3. TG(---), DTG(-··-) and DTA(—) curves obtained (at 10 °C/min) for (A) ZrNor complex (B) ZrCip complex in a dynamic atmosphere of air (20 cm^3/min). The Roman numerals (I-II) indicate locations where the thermal stages encountered are terminated, as further cited in Table 1.

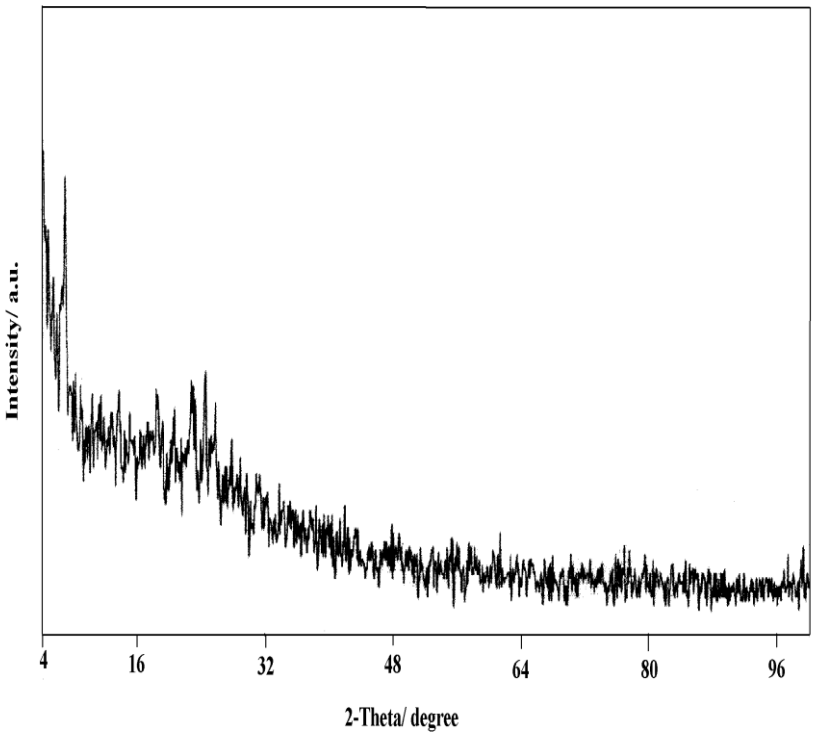
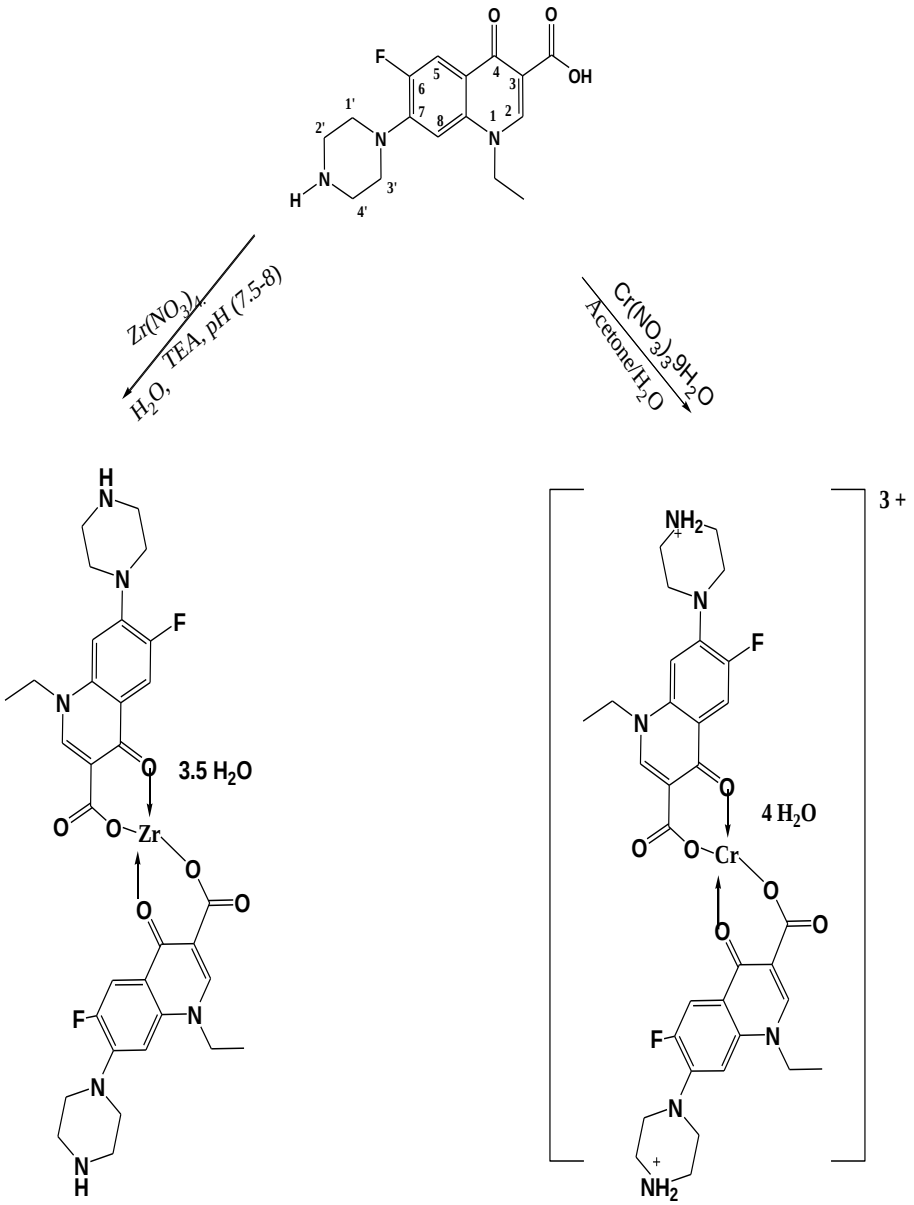


Fig. 4. X- ray diffraction pattern of chromium- ciprofloxacin complex (CrCip).

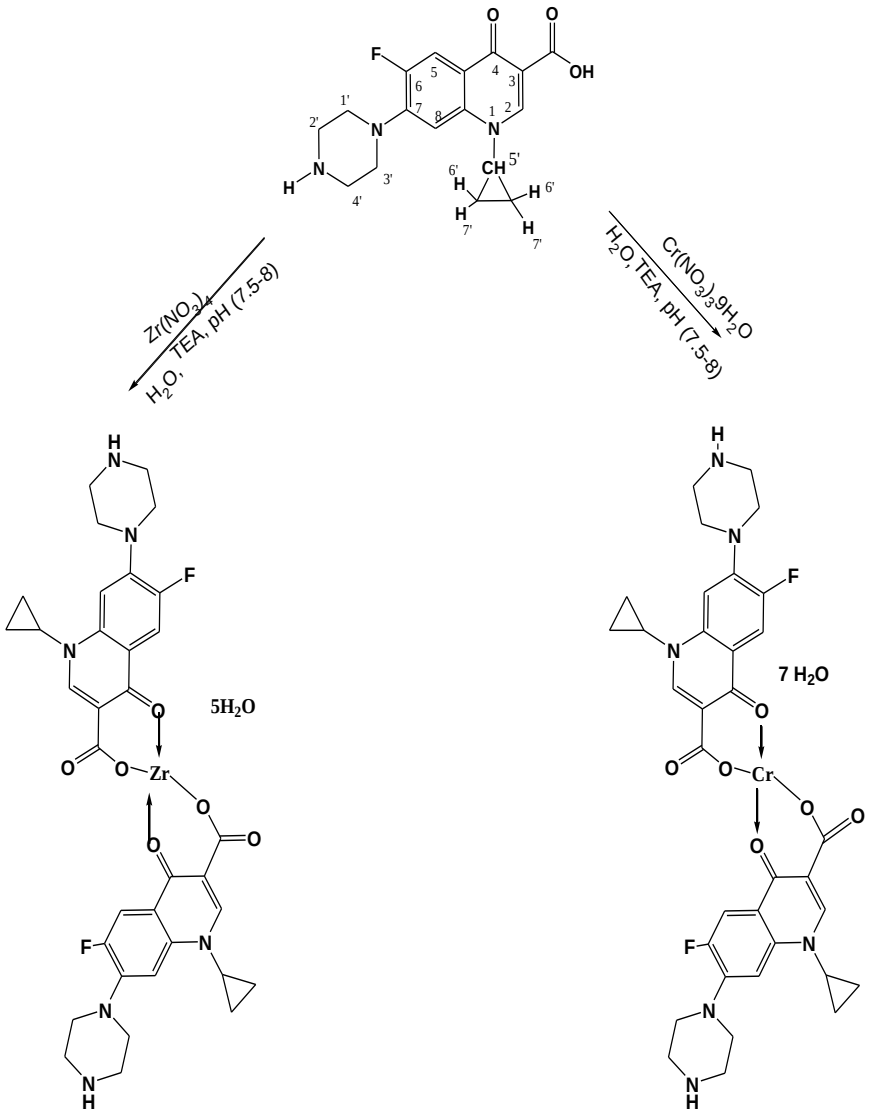
TABLE 2. Characteristics of thermal events encountered (Fig. 1) and (Fig. 2) throughout the decomposition course of Nor-and Cipro-metal complexes (at 10 ^{o}C/min) in N_2.

Complex	Dehydration temperature/ °C	Mass loss/ %	Decomposition temperature/ °C	Total Mass loss/ %
[Cr $(Nor)_2$ $(NO_3)_3$].4 H_2O	50 - 110	7.8	200 - 480	83.7
[Cr $(Cip)_2$].7H_2O	50 - 110	15	140- 520	82
[Zr $(Nor)_2$].3.5H_2O	45 - 120	8	200 - 800	72
[Zr $(Cip)_2$]. 5H_2O	50 - 120	10.7	150 - 800	52



$[Zr\ (Nor)_2]3.5\ H_2O$ $[Cr\ (Nor)_2](NO_3)_3.4H_2O$

Scheme 1



[Zr (Cip)$_2$].5H$_2$O [Cr (Cip)$_2$].7H$_2$O

Scheme 2

TABLE 3. Assignment of ^{1}H-NMR spectral data of norfloxacin, Cr- norfloxacin and Zr-norfloxacin complexes in DMSO.

Assignment	(Nor)	(CrNor)	(ZrNor)
CH3	1.41	1.25	1.44
CH2	4.59	5.18	5.18
1', 3'	2.80- 3.00	2.90-3.80	2.90-3.80
2', 4'	3.10-3.30	2.90-3.80	2.90- 4.40
H-2	8.92	8.49	8.99
H-5	7.94	8.00	7.98
H-8	7.12	7.25	7.32
COOH	15.00	-----	------

Acin and Zr-norfloxacin complexes in DMSO.

TABLE 4. Assignment of ^{1}H-NMR spectral data of free ciprofloxacin, Cr-ciprofloxacin and Zr- ciprofloxacin complexes in DMSO.

Assignment	(cip)	(Crcip)	(Zrcip)
1', 3'	3.56	2.70-3.00	2.90- 3.00
2', 4'	3.66	3.30- 3.50	3.20- 3.40
H-2	8.63	8.63	8.65
H-5	7.49	7.85	7.89
H-8	7.22	7.50	7.53
5'	3.80	3.80	3.85
6'	1.47	1.25- 1.40	1.29- 1.35
7	1.22	1.00- 1.20	1.18- 1.19
COOH	15.00	-----	------

Assignment of ^{1}H-NMR spectral data of free ciprofloxacin, Cr- ciprofloxacin and Zr-ciprofloxacin complexes in DMSO .

Although the IR spectrum of Ciprofloxacin is different from that of norfloxacin, the spectra of their complexes are remarkably similar. The measured spectrum of the free (Cip) is similar to that reported by Turel *et al.*[14]. The ketone C=O of (Cip) was observed at 1705 cm^{-1}, the C=C bands in the region of 1600 and 1495 cm^{-1}. The main feature of the (Cip) spectrum is the absence of the (υCOOH) vibration, a behavior that is consistent with zwitterionic nature of ciprofloxacin established by x-ray diffraction. Two bands at 1452 and 1384 cm^{-1} in the spectrum of (Cip) for the asymmetric and symmetric stretching of the deprotonated carboxylate group, respectively. The shift observed of these bands to 1482 and 1379 cm^{-1}, respectively, would be explained due to the coordination of Chromium metal to (Cip) ligand.

Thermal analysis results of the parent drugs norfloxacin[15] show that norfloxacin is thermally stable in the temperature range 25–55ºC. Decomposition of the (Nor) started at 59 ºC and finished at 726 ºC with two stages. The first stage of decomposition occurs at maximum temperature of 116ºC and is accompanied by ML of 8.75%. The second stage of decomposition occur at three

maxima 330, 423 and 654 ºC and is accompanied by a ML of 83.73%. The total ML from these two stages is equal to 92.46%. Thermal analysis results of the parent drug ciprofloxacin[16] show that its decomposition started at 104 ºC and ended at ~ 500 ºC. The first stage of decomposition occurs in the temperature range 104- 140 ºC, due to sample dehydration, which was confirmed by a ML of 4.5%. The second stage of decomposition occurs beyond 299 ºC and is accompanied by a ML of ~ 62%.

Thermal analysis results (Fig. 2 and 3) reveal that the decomposition course of (CrNor) and (CrCip) commences near 50 °C and terminates at ≥ 480 °C and ≥ 520 °C, respectively, encompassing poorly resolved exothermic events.

Dehydration reactions

TG and DTA results of (CrNor) and (CrCip) (Fig. 2) show broad endothermic events in the temperature range 50- 110 °C, characteristic to the removal of hydrated water. The ML accompanying event I in (CrNor) (7.4- 7.8%) is rather close to that expected (7.5%) for the release of four molecules of water (Table 2). Whereas, in the case of (CrCip) the ML at the end of event I is in the range (14.8 – 15.3 %) as that expected (15%) for the removal of seven moles of water (Table 2).

Decomposition reactions

(CrNor) complex begins to decompose at ~ (110- 115 °C) through overlapped exothermic events bringing the total ML for (CrNor) (83- 84 %) and the total ML for (CrCip) (82.5- 83 %) are close to that (83.9%) and (81.8 %), respectively, calculated for the formation of the final decomposition product of the green colored Cr_2O_3. The thermal events are resolved on the temperature scale of the DTA curve, but strongly overlapped on the temperature scale of the TG curve. It is worth mentioning that the decomposition course of these complexes is carried out in air atmosphere (results are not shown) to detect the impacts of different atmosphere (other than the inert N_2) that may affect the kinetics of the decomposition reaction. The result revealed beyond doubt that there is no detectable difference between the thermal analysis results accompanying changing the applied atmosphere except that the decomposition events are kinetically enhanced in air atmosphere. It is almost completed in a narrower range of temperature (110- 430 °C) for (CrNor) and (110- 470 °C) for (CrCip).

Characterization of the Zr- norfloxacin and Zr- ciprofloxacin complexes

In all spectra represented in Fig. 1A and B, the absorption bands in the region 3450- 3200 could be assigned to the symmetric and asymmetric stretching vibrations of water molecules. The IR spectra of (ZrNor) and (ZrCip) complexes are compared in (Fig. 1A and B). The spectra show clearly the characteristic peaks of the complexes at frequencies similar as in case of Cr- complexes but shifted to higher or lower few wavenumbers due to coordination of Zirconium metal to (Nor) and (Cip) via the ring carbonyl group at position 4 and through one of the oxygen atoms of the carboxylate group at position 3.

Thermal analysis results of (ZrNor) and (ZrCip) compounds (Fig. 3) indicate that the decomposition course of both complexes takes place in a wider temperature range than chromium complexes. The decomposition course commences near 40 °C and terminates at ~ 700 °C.

Dehydration reactions

The dehydration stage begins at low temperature < 40 °C, not all water molecules are equivalently bonded. The weaker bonded water molecules in metal quinolones could be lost at very low temperature. This may be observed from the DTG curve, where the endothermic effect corresponding to the dehydration stage is poorly resolved into two peaks maximized at 35 and 59 °C in (ZrNor) and at 35 and 76 °C in (ZrCip), indicating the presence of two types of bonded water molecules. The ML accompanying the dehydration processes in (ZrNor) and (ZrCip) are (7.5- 8%) and (10-10.7%), respectively. The experimental ML indicates that (ZrNor) contains 3.5 molecules of hydrated water, whereas, (ZrCip) has 5 molecules of water.

Decomposition reactions

Decomposition reactions immediately commence occurring following the dehydration reactions at ~ 150 °C involving overlapped exothermic events. The mass losses at the end of this stage in (ZrNor) and (ZrCip) complexes are (71 and 52%) indicate that zirconium complexes are stable.

X- ray diffraction

X-ray diffraction patterns recorded at 2θ = 0- 90 range for all complexes show that all complexes are amorphous solids (results are not shown), except (CrCip) complex, has a poorly crystalline nature (Fig. 4).

Mass spectrometry

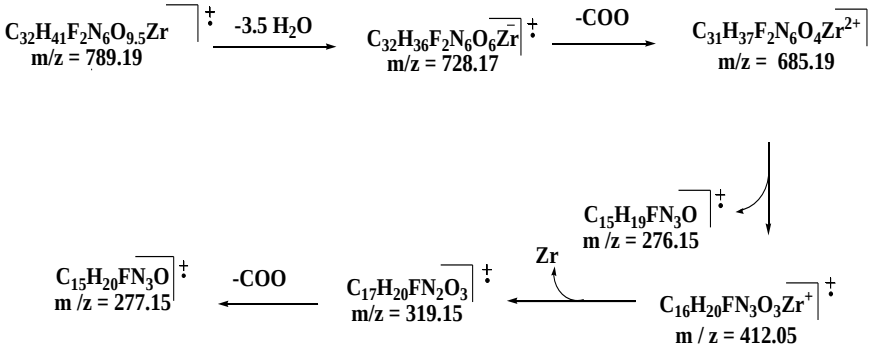
In the mass spectrometer, the sample is ionized to produce a charged molecule and a series of ionic fragments. The assortment of charged particles is then separated according to their mass to charge ratios (m/z) and displayed as a mass spectrum. Mass spectral data provide information about molecular mass if the molecular ion is identified whereas the fragmentation patterns give identification of unknowns and structural features.

The mass spectra detect the mass ions corresponds to the parent ligand drug (nor and cip ligands) at m/z = 320 and 331, respectively. The appearance of nor and cip ligand as a fragment in mass spectroscopy of the prepared complexes is consistent with that was found in a previously prepared Ag-Nor complex[15] . The molecular ion peaks which correspond to metal- ligand fragments are also detected in various abundances as well as that corresponds to variable molecules of water ranging from 0.5 to 4.0, some expected ions are not detected or present in very low intensity. In the mass spectrum of (CrNor) with the formula $C_{32}H_{44}F_2N_9O_{19}Cr$, the following mass peaks are detected at m/z = 922 (10 %), 320 (12%), whereas in (CrCip) with the formula $C_{34}H_{50}F_2N_6O_{13}Cr$, mass peaks at 838.7 (5 %), 349.3 (20 %), 332.0 (7 %).

Similar fragments appeared in case of zirconium complexes. The mass spectrum of (ZrNor) with the formula $C_{32}H_{41}F_2N_6O_{9.5}Zr$, mass peaks at 789.4 (20%), 319.15 (100 %), whereas the mass peaks of (ZrCip) with the formula $C_{34}H_{46}F_2N_6O_{11}Zr$, mass peaks at m/z 840 (5 %), 332 (100 %), 288 (6 %).

These results are consistent with the presence of direct metal- ligand bonding in chromium and zirconium complexes as well as the formation of a bidentate complex of the type of (2 ligand:1 metal).

In general, the fragmentation patterns give identification of unknowns and structural features. It is believed that the fragmentation pattern of the complexes occurs through stepwise removal of water, a ligand in addition to the metal leaving the fragment corresponding to the other ligand as the base peak (100 % intensity) in case of zirconium complexes of norfloxacin and ciprofloxacin. The following is a proposed fragmentation pattern for (ZrNor) complex:



Nuclear magnetic resonance

Nuclear magnetic resonance (^{1}H- NMR) spectroscopy is used to determine the structures of materials such as new drugs. NMR spectroscopy gives information about the environment in which the nuclei of atoms are found in molecules.

The ^{1}H-NMR chemical shifts of the parent quinolones and the corresponding metal complexes are listed in Tables 3 and 4. The spectra of the complexes of (nor) and (cip) with both zirconium and chromium metals showed broad signals that were attributed to what is known as paramagnetic characters[17] . Generally, minor changes had been demonstrated in the chemical shifts of the prepared complexes on comparison with their corresponding signals in the parent quinolones. This was explained previously[17] by the change in the counteranion or to a different association of the quinolone molecules. The ^{1}H-NMR spectra of all the studied complexes showed lack of the characteristic -COOH signal at about δ=15 ppm, indicating that complexation occurs through the carboxylate and the C_4 carbonyl group. The doublet characteristic for H-8 in the complexes appeared at δ= 7.25, 7.31 ppm for (CrNor) and (ZrNor), respectively (Table 3).

Whereas in (CrCip) and (ZrCip) complexes, the signals appeared at about δ= 7.5 ppm (Table 4). The characteristic signal for H-5 appeared at about δ = 8 ppm for both (CrNor) and (ZrNor), while appeared at δ 7.85-7.90 ppm in case of (CrCip) and (ZrCip) complexes, respectively. The singlet signal characteristic for H-2 appeared at δ= 9.0 ppm, that is downfield shifted by δ =0.2 ppm than the corresponding proton in case of (CrNor) and (ZrNor), it appeared at about δ= 8.65 for the corresponding proton in both complexes of (Cip) that is downfield shifted about δ =0.15 ppm from the parent ciprofloxacin H-2 proton. There was found a downfield shift for the multiplet corresponding to the piperazine protons H-8, where it appeared at δ= 2.9 - 4 ppm for the complexes (CrNor) and (ZrNor), and δ =3.2 – 3.6 ppm for the corresponding ciprofloxacine complexes. Also, the ^{1}H-NMR spectra showed the characteristic signals for both the *N*-CH_2CH_3 and *N*-cyclopropyl groups, but unfortunately, multiplicity could not be distinguished due to broadness of the signals.

Conclusion

Four new Cr(III) and Zr(IV) complexes of norfloxacin and ciprofloxacin have been synthesized. Spectroscopic and thermal analysis measurements help in drawing the following conclusions:

1. The interaction of Cr(III) or Zr(IV) with norfloxacin resulted in the formation of the complexes with the formulas $C_{32}H_{44}F_2N_9O_{19}Cr$ and $C_{32}H_{41}F_2N_6O_{9.5}Zr$.
2. The interaction of Cr(III) or Zr(IV) with ciprofloxacin resulted in the formation of the complexes with the formulas $C_{34}H_{50}F_2N_6O_{13}$ Cr and $C_{34}H_{44}F_2N_6O_{11}Zr$.
3. All complexes formed involve direct coordination of the metal ion to quinolones in the ratio of 1: 2.
4. ^{1}H- NMR have been used to study the behavior of quinolones and their metal complexes in solution. The spectra of free quinolones were assigned and the chemical shift changes have confirmed the chelate bonding of metal ions to quinolone ring carbonyl and carboxylic oxygens.
5. The decomposition of all complexes proceeds in two steps; the first is the dehydration at low temperatures, which is followed by pyrolytic decomposition at higher temperatures.
6. The zirconium metal complexes decompose over a wider temperature range than the chromium metal complexes.

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توصيف فـيزيـوكيميائى ودراسة طيفية وحراريـــة لمتراكبـــات النورفلوكساسين والسيبروفلوكساسين الصلبة

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تم استخدام الطرق الطيفيه مثل الاشعه تحت الحمراء و الرنين النووى المغناطيسى و الاشعه السينيه ومطياف الكتله بالاضافه الى قياسات التحليل الحرارى لتحديد الخـــواص الفـــزيوكيميائيه للمتراكبـــات الجديـــدة مـــن عقار السيبروفلوكساسين و النورفلوكساسين مع كل من معدنى الكروميوم (III) و الزركونيوم (IV). و قد اثبتت النتائج تكوين متراكبات لها الصيغه البنائيه التاليه :

$[Cr(Nor)_2](NO_3)_3. 4H_2O$, $[Cr(Cip)_2]. 7H_2O$ [$Zr(Nor)_2]. 3.5H_2O$, and $[Zr(Cip)_2] 5H_2O$.

واوضحت نتائج تحليل الاشعه تحت الحمراء للمتراكبات الناتجه ان كل من النورفلوكساسين والسيبروفلوكساسين ثنائى الارتبـــاط عبر مجموعة الكربونيـــل و اكسجين من مجموعة الكربوكسيل و اثبتت الدراسات الحراريه ان المتراكبات المتكونه تفقد جزيئات الماء فى درجات الحراره المنخفضة و يتبعه انحلال عند درجات الحراره الأعلى و قد اثبتت النتائج ايضا ان متراكبات الزركونيوم اكثر ثباتا من متراكبات الكروميوم.