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Norfloxacin La(III)-based complex: synthesis, characterization, and DNA-binding studies

SHABAN Y. SHABAN†*, MAGED A. EL-KEMARY†, GEHAN SAMIR†, HOSNY EL-BARADEI† and RALPH PUCHTA‡

†Faculty of Science, Department of Chemistry, Kafrelsheikh University, Kafrelsheikh, Egypt
‡Inorganic Chemistry, Department of Chemistry and Pharmacy, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany

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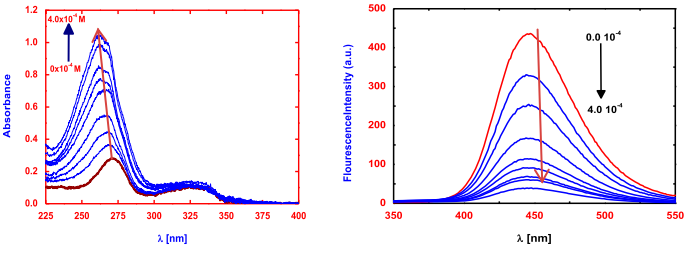


A La(III) complex, $[La^{III}Cl_2(NOR)_2]Cl$ (**2**), containing norfloxacin (NOR) (**1**), a synthetic fluoroquinolone antibacterial agent, has been synthesized and characterized by elemental analysis, IR, UV–vis spectra and ^1H NMR spectroscopy, and molar conductance measurements. The interaction between **2** and CT-DNA was investigated by steady-state absorption and fluorescence techniques in different pH media, and showed that **2** could bind to CT-DNA presumably via non-intercalative mode and the La(III) complex showed moderate ability to bind CT-DNA compared to other La(III) complexes. The binding site number n, and apparent binding constant K_A, corresponding thermodynamic parameters $\Delta G^{\#}$, $\Delta H^{\#}$, $\Delta S^{\#}$ at different temperatures were calculated. The binding constant (K_A) values are 0.23 ± 0.05, 0.56 ± 0.05, and 0.18 ± 0.08 × 10^5 L mol^{-1} for pH 4, 7, and 11, respectively. It was also found that the fluorescence quenching mechanism of CT-DNA by La(III) complex was a static quenching process.

Keywords: La(III) complexes; Norfloxacin; DNA-binding; Fluorescence spectra; Excitations

1. Introduction

Norfloxacin (**1**) is a synthetic fluoroquinolone antibacterial agent addressing a variety of aerobic gram-negative and gram-positive bacteria [1]. Its activity is directly related to

*Corresponding author. Email: shaban.shaban@sci.kfs.edu.eg
Dedicated to Professor Rudi van Eldik on the occasion of his 70th birthday.

the pH values, as the presence of charged groups is required for biological activity. It has two functional groups, the first is a carboxylic group and the other is an amino group. In aqueous solution, it exhibits cationic, zwitterionic, and anionic species. At a physiological pH (7.4), the fluoroquinolone is totally or partially ionized and the predominant species is the zwitterionic form, whereas, the cationic and the anionic forms predominate in acid and basic solutions, respectively [1(c), 2, 3]. The 4′-N of the piperazine ring and the carboxylate are the most significant proton-binding sites from the biological point of view (pK in the 5–9 pH range) [3(a)]. The biological activity of NOR is directly related to its ability to cross cell membranes, to bind to cytoplasmic proteins and/or inhibit the replication of DNA of the microorganism. The formation of complexes may increase the bioavailability of the metal ion or the drug, or both. In this sense, the coordination of metal ions to fluoroquinolones can influence the ligand's physicochemical properties, and thus facilitate and improve their mechanism of action [1(c), 4]. Fluoroquinolones generally form complexes with several metal ions, which greatly influence their antibacterial activity [5]. Usually, the binding sites of metal ions with quinolones involve the 4-oxo and 3-carboxyl oxygens, but Ag^{+}, Au^{3+}, and Pt^{2+} ions coordinate with the norfloxacin ligand through the N atom of the piperazinyl ring [6]. Recently, Luiz *et al.* [2] studied the interaction of norfloxacin with gold(III) and observed that Au^{3+} produces pH-dependent spectral modifications, attributed to different interactions with the distinct ionic species. Very recently, Zn(II) complexes with NOR were synthesized and the biological activity of these complexes was directly related to the acid ionization constant (pK) [4]. Spectrophotometric studies showed that the complexes interact with DNA with moderate affinity. It was reported also that the efficacy of the Zn(II) complexes with NOR showed a considerable increase in the levels of parasite lyses. Bailly and co-workers [7] proposed intercalative binding of norfloxacin. In the presence of Mg^{2+} ions, a Mg^{2+}-bridged model is proposed, in which carbonyl and carboxylic groups of norfloxacin and two phosphate groups of the scDNA are coordinated to Mg^{2+} ion. The effect of Mg^{2+} ion, which is a required cofactor for the enzymatic process, on norfloxacin–scDNA binding was also investigated. As an extension of a previous study in this area [8], we report herein the synthesis of a lanthanum complex with norfloxacin. The aim for using lanthanum was because rare earth metals have been widely used for their coordination properties and special chemical characteristics arising from 4f electrons and the properties to form isostructural complexes [9]. While working in this project, Refat *et al.* reviewed a chemical and biological impact resulting from the interaction between norfloxacin (NOR) and lanthanum(III) metal ions in normal and nano-features. La(III) complexes were synthesized with chemical formulas $[La(NOR)_3]$ with a hexadentate geometry [10]. In this study, we synthesized La(III) complex containing norfloxacin with a hexadentate geometry but in a different form $[La(NOR)_2Cl_2]Cl$. Little is known about the interaction of lanthanum(III) complexes to DNA [11] and a survey of the literature reveals that no work has been done on the interaction of lanthanum(III) complexes containing NOR with DNA. It was, therefore, considered worthwhile to study the interaction of La(III) complex with DNA, as DNA is one of the possible targets of anti-T. cruzi chemicals, which may include the parasite's mitochondrial or nuclear DNA [12]. In order to investigate the binding properties of the complex with calf-thymus DNA (CT-DNA), UV–vis spectroscopy was used. The affinity between La(III) complex and DNA was investigated using UV–vis absorption spectroscopy as well as time-resolved fluorescence spectroscopy.

2. Experimental

2.1. *Materials*

Norfloxacin (Nor) was purchased from Eipico Cairo, Egypt and lanthanum chloride was purchased from Fluka. Calf-thymus DNA (CT-DNA) was obtained from Sigma Chemicals Co. (USA) and used as received. Reagents and solvents purchased were of reagent grade and used without purification.

2.2. *Synthesis*

$[La^{III}Cl_2(NOR)_2]Cl$ (**2**): In a round-bottomed flask, Norfloxacin (0.50 mmol) and $LaCl_3$ (0.25 mmol) were suspended in methanol (30 ml). This suspension was stirred gently for 10 h and allowed to reflex for 8 h. The product was isolated by filtration, washed with a small amount of cold methanol, and dried to give a brown solid of **2**. M.p. over 350 °C; IR (KBr, cm^{-1}): 3383 [m, C–H], 1628 [s, ν_{as}(COO) ester], 1590 [s, C=O Keton], and 1390 [s, ν_{sym}(COO) ester]. Elemental analysis: calcd. for $[La^{III}Cl_2(NOR)_2]Cl{\cdot}H_2O$ (**2**); $C_{32}H_{44}Cl_3F_2LaN_6O_{10}$ (Mol. Wt.: 955.99); C 40.20, H 4.64, N 8.79; Found C 40.55, H 5.95, N 8.49. ^{1}H NMR (DMSO-d_6): 1.32 (t, 6H, $2CH_3$); 3.23–3.76 (m, 16H, Pip); 4.69 (q, 4H, $2CH_2$); 7.58–8.62 (m, 6H, Ar).

2.3. *Instrumentation and measurements*

Spectra were recorded on the following instruments: IR (KBr disks, solvent bands were compensated): Mattson Infinity instrument (60 AR) at 4 cm^{-1} resolution from 400 to 4000 cm^{-1}; Elemental analyses: Carlo Erba EA 1106 or 1108 analyzer; NMR: Jeol-JNM-GX 270, EX 270, and Lambda LA 400 with the protio-solvent signals used as an internal reference. Spectra were recorded at 25 °C. Steady-state absorption spectra were measured on Shimadzu 2450 spectrophotometer and *KinetAsyst* SF-61DX2 stopped-flow instrument coupled to an online data acquisition system. Fluorescence measurements were carried out on a Shimadzu RF-5301pc fluorescence spectrophotometer in a 1-cm path-length quartz cell.

2.4. *DNA-binding experiments*

Experimental work was carried out to investigate the interaction of drugs with DNA.

2.4.1. Electronic absorption spectra. Concentrated stock solutions of the complex were prepared by dissolving it in tris-HCl buffer (pH 4, 7, and 11) and carried out using a UV–visible Shimadzu 2450 spectrophotometer. A solution of calf-thymus DNA (CT-DNA) in the buffer gave an UV absorbance at 260 nm, indicating that the DNA was sufficiently free of protein [13]. The concentration of the DNA was determined by absorption spectroscopy using the molar absorption coefficient (6600 M^{-1} cm^{-1}) at 260 nm [14].

The interactions of **2** with CT-DNA were studied using UV spectroscopy in order to investigate the possible binding modes to CT-DNA and to calculate the binding constant (K_b). Binding constant, K_b, was determined using a constant concentration of the complex recorded in the absence or presence of increasing CT-DNA amounts. K_b values were

obtained by monitoring the changes in the absorbance of the complexes at 270 nm. K_b was given according to the method reported by Benesi and Hildebrand [14] as expressed by equation (1):

$$\frac{1}{A_{obs} - A_0} = \frac{1}{A_c - A_0} + \frac{1}{K_b(A_c - A_0)[DNA]} \quad (1)$$

The relationship between $1/(A_{obs} - A_0)$ *versus* reciprocal concentration of the DNA afforded a slope equal to $1/K_b(A_C - A_0)$ and an intercept equal to $1/(A_C - A_0)$, from which the binding constant, K_b, can be calculated.

2.4.2. Fluorescence quenching spectra. The interaction of **2** (1×10^{-4} M) with different concentrations of CT-DNA, with the excitation and emission wavelength set at 285 nm, was studied. The intrinsic equilibrium binding constant (K_{sv}) was obtained by the linear Stern–Volmer equation (2) [15]:

$$I_0/I = 1 + K_q\tau_0[Q] = 1 + K_{sv}[Q] \quad (2)$$

where I_0 and I represent the fluorescence intensities in the absence and presence of quencher, respectively, K_q is the quenching rate constant of the biomolecule, K_{sv} is the dynamic quenching constant, τ_0 is the average lifetime of the biomolecule without quencher, and [Q] is the concentration of quencher. The set of data fitted to equation (2) gives a slope K_{sv}.

3. Results and discussion

The reaction of Norfloxacin, NOR (**1**) with $LaCl_3$ in methanol in the mole ratio of 1 : 2 leads to the formation of lanthanum(III) complex $[La^{III}Cl_2(NOR)_2]Cl$ (**2**) in 65% yield (scheme 1). The formation of **2** was confirmed by elemental analysis, spectroscopic and analytical methods. The elemental analysis confirmed the structure which contains one mole of $La(III)Cl_3$ to two moles of the ligand. The conductivity measurement of the complex was taken in DMF and the obtained value, 60 Ω^{-1} cm^2 mol^{-1}, is in the conductivity level generally associated with a 1 : 1 electrolyte in DMF according to the literature [16].

The IR spectrum of free NOR exhibited one band at 1617 cm^{-1}, which was assigned to the stretching vibration of ν(C=O) ketonic. In the spectra of La(III) complex, the ν(CO) was affected by interaction with the lanthanum(III) ion and appeared as a shoulder at 1590 cm^{-1}. Such behavior has been observed in several quinolone metal ion complexes [4, 17]. The band at 1628 cm^{-1} in spectra of the complex was assigned to the asymmetric stretch (ν_{as}) of the coordinated carboxylate group. A strong and intense band at 1390 cm^{-1} for **2**, absent in the NOR spectrum, was assigned to the symmetric vibration (ν_s) of the coordinated COO^- group. This band appeared after ionization of the carboxyl group and was characterized by the formation of a resonance structure. This occurrence suggested the involvement of this group in interaction with the metal ion [4, 17, 18]. **2** shows no bands around 3500 cm^{-1} for the O–H stretching frequency indicating that O–H has been deprotonated via complex formation, further supporting the interaction of the carboxylate with lanthanum. The carboxylate can be unidentate, bidentate, or bridging, and the frequency separation [$\Delta\nu = \nu_{as}(COO^-) - \nu_s(COO^-)$] between the asymmetric and symmetric

stretch of this group distinguishes between these binding states [18]. Unidentate carboxylate complexes exhibit $\Delta\nu > 200\ cm^{-1}$ [19]. Complex **2** shows $\Delta\nu$ value of $238\ cm^{-1}$, which suggested a unidentate interaction of carboxylate to La.

The ^1H NMR spectrum of the free NOR has a triplet at $\delta = 1.41$ ppm attributed to CH_3 and two multiplets at $\delta = 2.89$ and 3.23 ppm corresponding to the piperazine ring's hydrogens are shifted in **2** to 1.23, 3.23, and 3.76 ppm, respectively. The quartet corresponding to the non-aromatic CH_2 at $\delta = 4.56$ in free NOR was observed at $\delta = 4.69$ ppm in **2**. The signals of the aromatic hydrogens at $\delta = 7.13$, 7.88, and 8.92 in free NOR was observed in **2** at $\delta = 7.58$, 7.48, and 8.62 ppm, respectively. The chemical shift values of **2** were only slightly changed, on the order of 0.4 ppm. This small shift was expected as there was no hydrogen near the coordination sites. Refat [10, 20] and Teixeira [4] assigned a signal at $\delta = 5.78$ ppm to the NOR zwitterionic form and can be observed only when the metal is coordinated to the ketonic and the carboxylic carbons. In our case, we could not observe any signals probably due to low solubility of **2**.

Thus, the metal ion is six-coordinate, the ligand is bidentate, and the metal : ligand ratio is 1 : 2, as the experimental results showed. Six-coordinate lanthanum complexes coordinating via oxygen donors are reported [10, 21].

3.1. *UV–vis absorption measurements*

UV–vis spectroscopy of the drug and its lanthanum(III) complex has been investigated under neutral, acidic, and basic media (figure 1; left). Absorption spectra of NOR displayed an absorption with maximum at 271 nm in the neutral medium assigned for the ($S_0 \rightarrow S_2$) $\pi - \pi^*$ transition. Under basic conditions, the drug NOR shows shift to shorter wavelength and exhibits a maxima at 260 nm, whereas, in acidic medium it shifts to longer wavelength and shows a maxima at 278 nm. The absorption spectra are pH dependent and this can be explained via the zwitterion equilibrium. In spectra of **2**, the effect of pH is very small and this can be traced to the absence of zwitter ion via complex formation with lanthanum ion (figure 1; right). The bands also showed less hypochromism, indicating that the carboxylic and the ketone groups were involved in complexation [4, 10, 20].

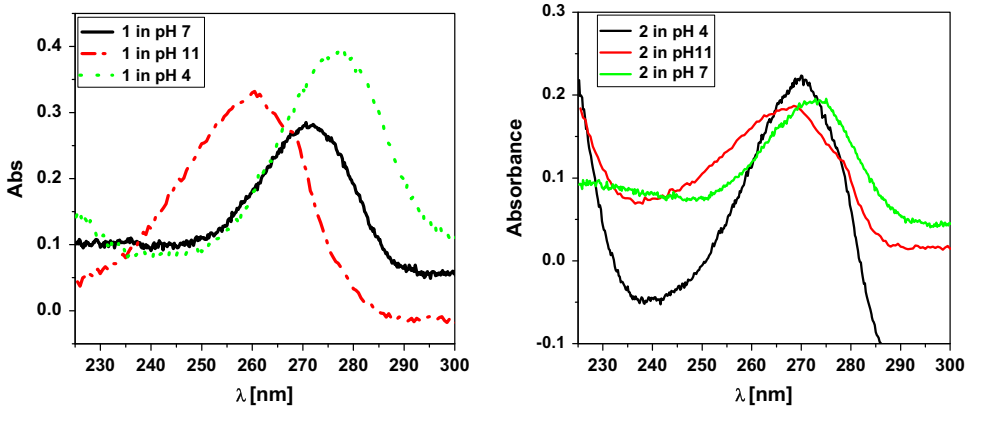


Figure 1. Absorption spectra of norfloxacin **1** and its La(III) complex **2** in aqueous buffered solutions at different pH at $T = 298$ K.

DNA is the primary intracellular target of anticancer drugs and consequently the interaction studies of complexes with DNA are very important in the development of new therapeutic reagents. For this reason, the binding abilities and modes of **2** to CT-DNA were investigated using UV–visible spectrophotometry (figure 2) in different pH media. In all investigated pH media, as the DNA concentration increased, the absorption spectra of **2** showed clear hyperchromicity at 270 nm, together with a blue shift of about 15 nm, suggesting existence of ground-state interaction between La(III) complex and CT-DNA. The hyperchromicity in the absorption spectra of the complex is indicative of partial or non-intercalative binding modes, such as electrostatic interaction among the $[La^{III}L_2Cl_2]^{1+}$ cationic species and the negatively charged phosphate groups on DNA, van der Waals interaction, dative bonds, hydrogen bonds of the –NH groups, and the oxygens on the ligand with DNA nucleobases or hydrophobic interaction [22]. The binding constants, K_b, of La(III) complex to DNA were calculated from equation (4) and the values listed in table 1 suggest a low affinity of the La(III) complex to CT-DNA compared to that reported for Zn(II) complexes containing NOR as ligands [4]. The K_b value in neutral medium is lower than in both acidic and basic media.

3.2. *Fluorescence measurements of 2 in the absence and presence of DNA*

The steady-state fluorescence spectra of La(III) complex in aqueous solutions were obtained and compared with that in a pH range of 4–11 (figure 3). At pH 11, **2** showed very low fluorescence intensity, indicating that for high pH values, it had become a low fluorescent molecular species with peak at 435 nm. When the pH decreased, the fluorescence increased, and at pH 7.4, the maximum intensity at 412 nm was registered. Such dependence of fluorescence with the change in pH values agrees with the reported work of NOR [2]. This transition between pH 11 and 7 is due to the protonation of the distal amine of the piperazine group. In the pH range of 7.6–4.0, there was a transition between two fluorescent species. The fluorescence peak at 412 nm decreased and that at 450 nm increased with the decrease in pH in this range. This transition refers to the protonation of the carboxylate group (figure 3) and similar results were reported for Zn(II) complexes containing NOR [4].

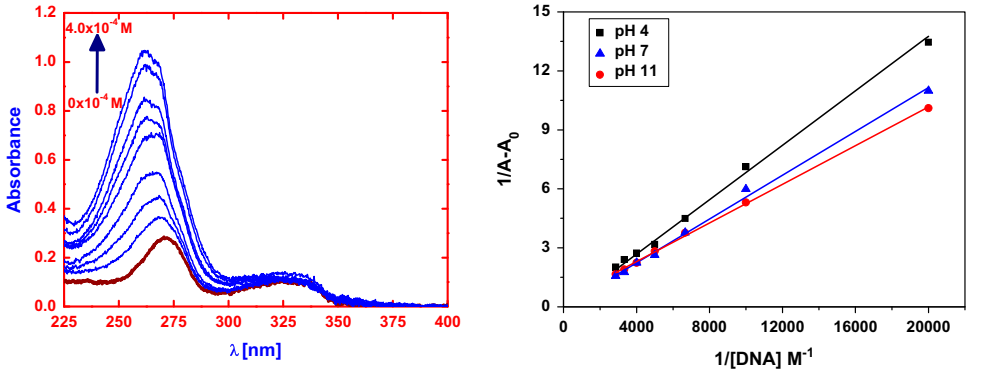


Figure 2. (Left figure) Absorption spectra of **2** (1.0×10^{-4} M) recorded in the absence (red) and presence (violet) of different concentrations of DNA as monitored by ultraviolet/visible spectroscopy. (Right figure) plot of $\frac{1}{A-A_0}$ *vs.* $\frac{1}{[DNA]}$ at 270 nm in different pH media (4, 7, and 11) at 298 K (see http://dx.doi.org/10.1080/00958972.2015.1065320 for color version).

Table 1. The DNA-binding constants (K_b) obtained for the La(III) complex in different pH media.

pH	**4**	**7**	**11**
$K_b \pm$ SD (10^3 L mol^{-1})	0.58 ± 0.03	0.13 ± 0.02	0.63 ± 0.06
R	0.9963	0.9973	0.9968

Note: R is the correlation coefficient, SD is the standard deviation.

As seen in figure 4 (left), the fluorescence intensity of **2** was significantly quenched by the addition of DNA; such decrease in the intensity can be rationalized by decrease in the binding sites of DNA [23]. Fluorescent quenching can occur in two different mechanisms, static quenching and dynamic quenching. For dynamic quenching, the mechanism can be described by the Stern–Volmer equation (2). In order to confirm the quenching mechanism, the fluorescence quenching was first assumed to be a dynamic quenching process.

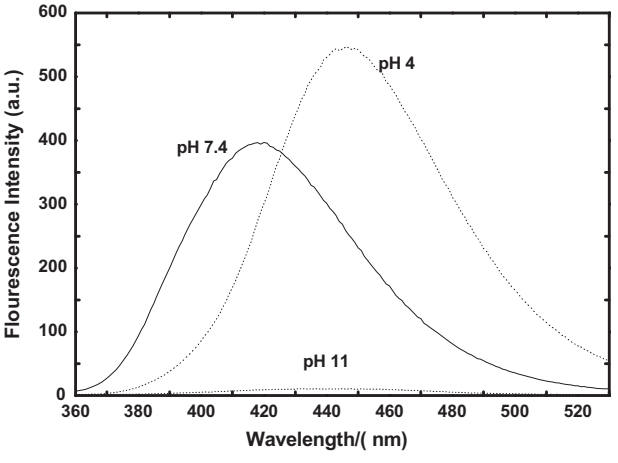


Figure 3. Steady-state fluorescence spectra of **2** (1.0×10^{-4} M) in pH = 4, 7, and 11; λ_{ex} = 285 nm.

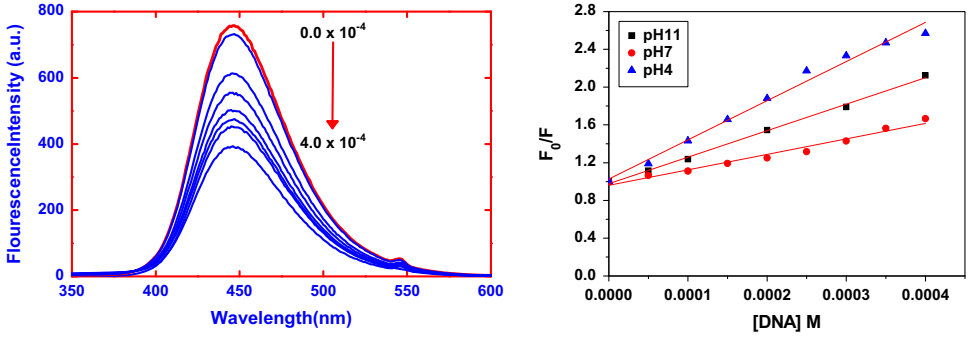


Figure 4. (Left figure) Fluorescence quenching of **2** (1×10^{-4} M) with DNA (0–4.0×10^{-4} M) in different concentrations at pH 4 and at T = 298 K. (Right figure) Stern–Volmer plots for the fluorescence quenching of **2** by DNA in different pH (▲ pH 4; ● pH 7; ■ pH 11).

The Stern–Volmer plots of F_0/F *versus* [Q] in different pH media and temperatures are presented in figures 4 and 5. The values of K_{sv} and K_q are listed in table 2. The K_q values were much larger than the limiting diffusion constant of the biomacromolecules (2.0×10^{10} L mol^{-1}s^{-1}) [24, 25]. The results suggested the quenching mechanism of the system was a static quenching process and is confirmed by the following: (i) the ground-state interaction between **2** and DNA forming **2**···DNA complex (figure 2) and (ii) the decrease in the K_{sv} value with increase in the temperature (figure 4 and table 2). Compared to reported lanthanum complexes, **2** showed moderate interaction to CT-DNA in all pH media [11].

3.3. *Binding constant and binding sites of DNA with 2 at different temperatures*

In order to obtain more detailed information on the mechanism of quenching and to further support the static quenching mechanism, a static quenching model was studied. For static quenching, the relationship between fluorescence quenching intensity and concentration of quencher can be described by equation (3) [26]:

$$\log\left[\frac{F_0 - F}{F}\right] = \log K_A + n\log[Q] \tag{3}$$

where K_A and n are the binding constant and the number of binding sites in base pairs, respectively. After the fluorescence quenching intensities on DNA at 285 nm were measured, the double-logarithm algorithm was assessed by equation (3). The plots of log

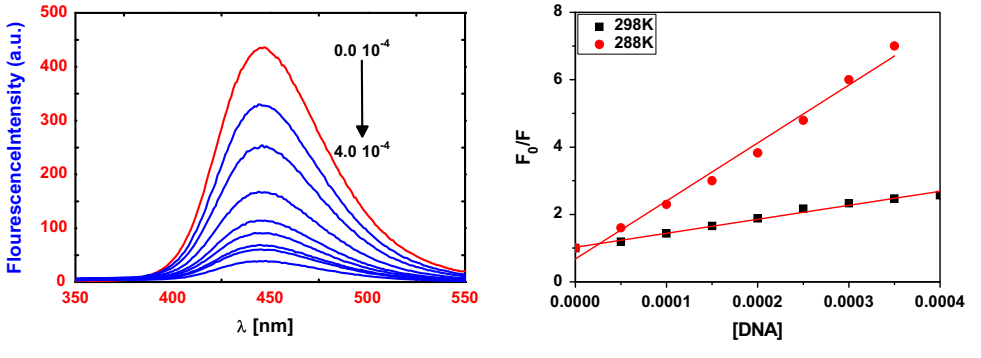


Figure 5. (Left figure) Fluorescence quenching of **2** (1×10^{-4} M) in the presence of DNA (0–4.0×10^{-4} M) in different concentrations at pH 4 and at $T = 288$ K. (Right figure) Stern–Volmer plots for the quenching of La(III) complex **2** by DNA at pH 4 (■ 298 K; ● 288 K).

Table 2. The Stern–Volmer quenching constants of system in different pH media and temperatures.

pH	T (K)	$K_{SV} \pm$ SD (10^4 L mol^{-1})	$K_q \pm$ SD (10^{12} L mol^{-1} s^{-1})	R
4	288	1.72 ± 0.02	1.72 ± 0.02	0.9940
	298	0.42 ± 0.02	0.42 ± 0.02	0.9950
7	298	0.28 ± 0.01	0.28 ± 0.01	0.9973
11	298	0.16 ± 0.01	0.16 ± 0.01	0.9984

Note: R is the correlation coefficient, SD is the standard deviation.

$[(F_0 - F)/F]$ *versus* log[Q] are shown in figure 6 and the values of K_A and n are listed in table 3. The correlation coefficients are larger than 0.94, indicating that the interaction between DNA and **2** agrees well with the site-binding model underlined by equation (3) and support the static quenching mechanism. The results suggest that there is a moderate binding force between DNA and **2** and the binding constant K_A is decreased with increase in the temperature, which may indicate forming an unstable compound [25(a)]. The unstable compound would be partly decomposed when the temperature increases. The values of n approximately equal to 1 indicate the existence of just a single binding site in DNA. Compared to the binding constant of La(III) complex reported by Huang *et al.* (1.71×10^5 L mol^{-1}) [11], **2** is about three times weaker.

3.4. *Thermodynamic parameters and nature of the binding forces*

The interaction forces between drug molecules and DNA may involve hydrophobic force, electrostatic interactions, van der Waals interactions, hydrogen bonds, etc. [24(b)]. The thermodynamic parameters were calculated from equations (4)–(6) to elucidate the interaction of DNA with **2**. Based on the binding constants at different temperatures, the free energy change, ΔG, can be estimated from the following equation:

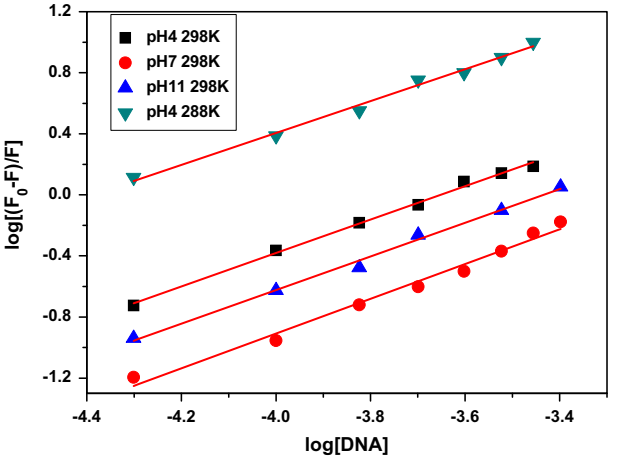
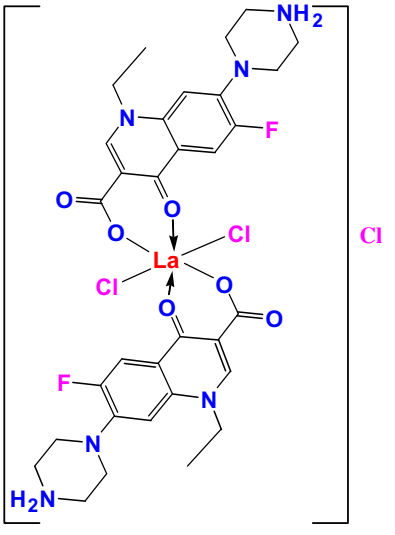


Figure 6. Plot of $\log[\frac{F_0-F}{F}]$ *vs.* log [DNA] in different pH media (■ pH 4; ● pH 7; ▲ pH 11) and different temperatures (■ 288 K; ● 298 K) for pH 4; [**2**] = 5×10^{-4} M.

Table 3. The binding constants and binding sites at different temperatures as well as the thermodynamic constants for the binding of DNA with La(III) complex at different temperatures in different pH media.

pH	T (K)	$K_A \pm$ SD (10^5 L mol^{-1})	n	R	$\Delta G \pm$ SD (kJ mol^{-1})	$\Delta S \pm$ SD (J mol^{-1} K^{-1})	$\Delta H \pm$ SD (kJ mol^{-1})
4	288	0.30 ± 0.08	1.3	0.997	−24.68 ± 0.006	19.1 ± 0.5	−19.2 ± 0.4
	298	0.23 ± 0.05	1.1	0.996	−23.38 ± 0.002	14.9 ± 0.3	
7	298	0.56 ± 0.05	1.4	0.997	−26.7 ± 0.003		
11	298	0.18 ± 0.08	1.2	0.997	−24.3 ± 0.006		

Note: R is the correlation coefficient, SD is the standard deviation.



Scheme 1. Suggested metal–ligand coordination in the investigated La(III) complex $[La^{III}Cl_2(NOR)_2]Cl$ (**2**).

$$\Delta G = -RT\mathrm{Ln}K_A \tag{4}$$

where R is the gas constant, T is the experimental temperature, and K_A is the binding constant at corresponding T. The enthalpy change (ΔH) and entropy change (ΔS) can be calculated from the following equations:

$$\ln\frac{K_2}{K_1} = \frac{\Delta H}{R}\left(\frac{T_2 - T_1}{T_2 T_1}\right) \tag{5}$$

$$\Delta G = \Delta H - T\Delta S \tag{6}$$

The negative sign for ΔG (table 3) indicates spontaneity of binding of La(III) complex with DNA. ΔH is a negative value and ΔS is a positive value. A positive ΔS is frequently taken as evidence for hydrophobic interaction. Furthermore, specific electrostatic interactions between ionic species in aqueous solution are characterized by a positive value of ΔS and a negative ΔH. Accordingly, the thermodynamic parameters indicate that hydrophobic force plays a major role in the binding between DNA and La(III) complex [27].

4. Conclusion

The synthesis, characterization, and pH-dependent UV–vis spectra of $[La^{III}Cl_2(NOR)_2]Cl$ (**2**) are reported. Fluorescence and absorption spectroscopy methods for determination of the interaction between **2** and DNA were used. The results revealed the presence of a single binding site on DNA and its binding constants, K_A, are 0.23 ± 0.05, 0.56 ± 0.05, and $0.18 \pm 0.08 \times 10^5$ L mol^{-1} for pH 4, 7, and 11, respectively. In addition, the thermodynamic functions, standard enthalpy ($\Delta H°$), and standard entropy ($\Delta S°$), for the reaction were

calculated to be -19.2 ± 0.4 kJ mol^{-1} and 14.9 ± 0.3 J mol^{-1} K^{-1}. According to Van't Hoff equation, these data indicated that hydrophobic and electrostatic interactions play a major role in stabilizing the complex. The results obtained give preliminary information on the binding of **2** to DNA and static quenching mechanism is confirmed by the following: (i) the ground-state interaction between **2** and DNA forming **2**···DNA complex; and (ii) the decrease in K_{sv} value with increase in the temperature. Work now is underway with La(III) complexes containing other drugs in order to investigate and correlate the ligand effect on the DNA-binding.

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Disclosure statement

No potential conflict of interest were reported by the authors.

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