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RESEARCH ARTICLE

Spectroscopic, structural and antibacterial evaluation of some lomefloxacin metal complexes

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Abstract

A new metal complexes of the second-generation quinolone antimicrobial agent lomefloxacin hydrochloride (LFX) with Ti(IV), V(IV), Pd(II) and Ce(IV) have been prepared and characterized by physicochemical, spectroscopic and thermal analyses techniques. In all complexes lomefloxacin reacts as a bidentate deprotonated ligand bound to the metal through the pyridone oxygen and a carboxylate oxygen. The central metal ion in each complex is six-coordinate and a slightly distorted octahedral geometry is proposed. The decomposition mechanisms proposed for lomefloxacin hydrochloride and their metal complexes were discussed. The activation energies, E^*, enthalpies, ΔH^*, entropies, ΔS^* and Gibbs free energies, ΔG^*, of the thermal decomposition reactions have been derived from thermogravimetric (TG) and differential thermogravimetric (DTG) curves, using Coats-Redfern (CR) and Horowitz-Metzeger (HM) methods. The lowest energy model structure of Ti(IV), V(IV), Pd(II) and Ce(IV) complexes were detected by using the density functional theory (DFT) at the B3LYP/CEP-31G level of theory. The antimicrobial activity of the free lomefloxacin hydrochloride, metal salts and their metal complexes have been tested against some Gram-positive and Gram-negative microorganisms.
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INTRODUCTION

Fluoroquinolones belong to a group of synthetic antibacterial agents derived from basic structure of naldixic acid and have substituents at N-1, C-5, C-7; position 8 and a fluorine atom at position 6. Lomefloxacin hydrochloride is one of the second generation drugs of the quinolone antibiotics. Lomefloxacin hydrochloride sold under name maxaquin is a fluoroquinolone antibiotic, used to treat bacterial infections including bronchitis and urinary tract infections. It is also used to prevent urinary tract infections prior to surgery. Maxaquin, a difluoroquinolone, is the monohydrochloride salt of 1-ethyl-6,8-difluoro-1,4-dihydro-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid and its structural formula is:

Lomefloxacin hydrochloride is unique in that it forms a magnesium chelate. The chelate is formed between the 2-carbonyl groups of two separate lomefloxacin molecules. Crystal structures of several free quinolone molecules have been determined [1-9]. It is interesting to note that in some cases the carboxylic group is protonated and the molecule thus exists in a zwitterionic form with protonated terminal nitrogen of the piperazine ring in a solid state and in other cases the carboxylic group is not deprotonated and the hydrogen atom of this group forming hydrogen bond to an adjacent 4-oxo atom.

The crystal structure and infrared spectroscopic studies of various fluoroquinolones complexes suggest that the fluoroquinolones are reacted with the metal ions through ring carbonyl and carboxylate oxygen atoms [9-20]. The coordination of the fluoroquinolones with metallic ions by piperazine nitrogen is much less common [20-27]. Discussion of the structures of lomefloxacin (LFX) complexes in the literature is rare and the available publications

suggested that the lomefloxacin molecule coordinated to metal ions through carboxylic oxygen and 4-keto oxygen [28-30].

In connection with our studies in the trend of fluoroquinolones metal complexes [31,32], we report in the present article, the isolation and characterization of new metal complexes formed from the interaction of lomefloxacin with Ti(IV), V(IV), Pd(II) and Ce(IV) in ethanol. The prepared solid complexes were confirmed by using elemental analysis, melting points, spectroscopic, thermal analyses and biological studies. Density functional theory (DFT) was used to compute the cation influence on theoretical parameters of the Ti(IV), V(IV), Pd(II) and Ce(IV) complexes of lomfloxacin. Profiles of the optimal set and geometry of these complexes were simulated by applying the GAUSSIAN 98W package of programs [33] at B3LYP/CEP-31G [34] level of theory

2. Materials and methods

2.1. Chemicals

Lomefloxacin hydrochloride was purchased from Sigma, $Ti(SO_4)_2$ and $VOSO_4.H_2O$ were from Aldrich Chemical Co., $PdCl_2$, $Ce(SO_4)_2$ and all solvents were from Fluka Chemical Co. All the chemicals and solvents were analytical reagent grade and were used as purchased without further purification.

2.2. Synthesis

The buff solid complex $[Ce(LFX)_3](SO_4)_2.4H_2O$ was prepared by adding 0.33mmol (0.077 g) of cerium(IV) sulphate $Ce(SO_4)_2$ in 20 ml ethanol drop wisely to a stirred solution of 1mmol (0.38 g) of LFX and NaOH (1mmol, 0.04 g) in 50 ml ethanol. The reaction mixture was stirred for two days at 50 ^oC in water bath. The buff precipitate was filtered off and dried under vacuum over $CaCl_2$.

The faint-orange, faint-green and brown solid complexes of $[Ti(LFX)_3](SO_4)_2.2H_2O$, $[VO(LFX)_2H_2O]SO_4.9H_2O$ and $[Pd(LFX)_2Cl_2].4H_2O$ were prepared in a similar manner described above by using ethanol as a solvent and using $Ti(SO_4)_2$, $VOSO_4.H_2O$ and $PdCl_2$ in 1:3 for Ti(IV) and 1:2 for V(IV) and Pd(II) molar ratio, respectively. We did not manage to obtain a crystal of the complexes suitable for the structure determination with X-ray crystallography. To verify that the sulphate and chloride are ionic or coordinated, the complex solutions were tested with an aqueous solution of $BaCl_2$ and silver chloride (white precipitate from $BaSO_4$ was formed). The four complexes were characterized by their elemental analysis, molar conductivities, magnetic measurements, infrared, electronic, ^1H NMR, mass spectra and thermal analyses.

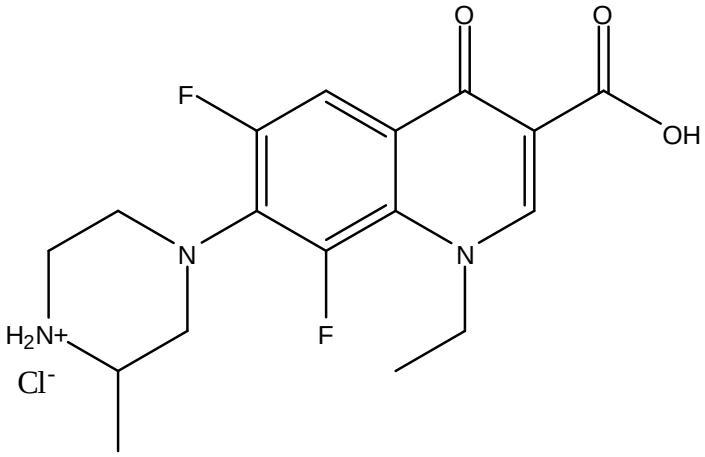
2.3. Instruments

C, H and N 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 metal oxide or sulphate and also determined by using atomic absorption method. Spectrometer model PYE-UNICAM SP 1900 fitted with the corresponding lamp was used for this purpose. IR spectra were recorded on FTIR 460 PLUS (KBr discs) in the range from 4000-400 cm^{-1}, ^1H NMR spectra were recorded on Varian Mercury VX-300 NMR Spectrometer using DMSO-d_6 as solvent. TGA-DTG measurements were carried out with heating rate being controlled at 10^oC min^{-1} under N_2 atmosphere from room temperature to 800 ^oC 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 solid reflection spectra were recorded with KBr pellets. Mass spectra were recorded on GCMS-QP-1000EX Shimadzu (ESI-70ev) in the range of 0-1090. Magnetic measurements were carried out on a Sherwood scientific magnetic balance using Gouy method using $Hg[Co(SCN)_4]$ as calibrant. Melting points were determined on an Electrothermal-9100 apparatus. Molar conductivities of the solution of the ligand and metal complexes in DMSO at 1×10^{-3} M were measured on CONSORT K410.

2.4. Antimicrobial investigation

Antibacterial activity of the ligand and its metal complexes was investigated by modified method of Beecher and Wong [35], against different bacterial species, such as S. aureus K1, B. subtilis K22, Br. Otitidis K76, E. coli K32, P. aeruginosa SW1 and K. oxytoca K42. The Müller-Hington agar (30.0% Beef extract, 1.75% Casein hydrolysate, 0.15% Starch and 1.7% Agar) was prepared and then cooled to 47 ^oC and seeded with tested microorganisms. After solidification 5mm diameter holes were punched by a sterile cork-borer. The investigated compounds, i.e., ligand, metal salts and their complexes, were introduced in holes (only 100 μL) after being dissolved in DMSO at 10^{-3} M. These culture plates were then incubated at 37 ^oC for 20 h. The activity was determined by measuring the diameter of the inhibition zones (in mm). Growth inhibition was calculated with reference to the positive control, i.e., lomefloxacin.

3. Results and discussion



1-ethyl-6,8-difluoro-1,4-dihydro-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid

Ti(IV), V(IV), Pd(II) and Ce(IV) complexes of lomefloxacin (LFX) were synthesized (Table 1). The found and the calculated percentages of C, H and N data agree well with each other and these prove the suggested molecular formula. The molar ratio for all synthesized complexes is LFX: M=2:1 for V(IV), Pd(II) and 3:1 for Ti(IV) and Ce(IV).

Conductance, magnetic moments and melting points of the complexes were given in Table 1. The molar conductance values of the lomefloxacin hydrochloride and their metal complexes in DMSO with standard reference, using 10^{-3} M solutions at room temperature were found to be in the range 19.31 to 290.39 S cm^2 mol^{-1}. The data indicated that the complexes of Ti(IV), V(IV) and Ce(IV) were electrolyte and the sulphate ion was found as counter ions at all three complexes, while the Pd(II) complex is non-electrolyte and the chloride ion was found inside the complex sphere [36]. The complexes of Ti(IV) and Ce(IV) are found in diamagnetic character [37] with molecular geometries octahedral but the complexes of V(IV) and Pd(II) were susceptible and their magnetic moments are 1.73 and 2.91 B.M.

Table1: Elemental analysis and physico-analytical data for lomefloxacin and its metal complexes:

Compounds M.Wt. (M.F.)	Yield%	Mp/ ^{o}C	Color	Found (Calcd.) (%)						μ_{eff} (B.M)	Λ (S cm^2 mol^{-1})
				C	H	N	M	Cl	S		
LFX	-	110	White	(52.60)	(5.16)	(10.83)	-	(9.14)		Diamagnetic	56.18
387.801 ($C_{17}H_{20}N_3O_3F_2Cl$)				52.59	5.13	10.82		9.11			
$[Ti(LFX)_3](SO_4)_2.2H_2O$	83	270	Faint-orange	(46.05)	(4.59)	(9.48)	(3.60)	-	(4.82)	Diamagnetic	290.4
1328.9 ($TiC_{51}H_{61}N_9O_{19}F_6S_2$)				46.00	4.51	9.38	3.60		4.80		
$[VO(LFX)_2H_2O]SO_4.9H_2O$	79	>360	Faint-green	(39.04)	(5.55)	(8.04)	(4.87)	-	(3.06)	1.73	185.58
1044.94 ($VC_{34}H_{58}N_6O_{21}F_4S$)				38.95	5.45	8.00	4.78		2.96		
$[Pd(LFX)_2Cl_2].4H_2O$	90	280	Brown	(42.86)	(4.83)	(8.83)	(11.23)	(7.35)	-	2.91	19.31
951.9 ($PdC_{34}H_{46}N_6O_{10}F_4Cl_2$)				42.76	4.80	8.80	11.20	7.30			
$[Ce(LFX)_3](SO_4)_2.4H_2O$	95	290	Buff	(42.00)	(4.46)	(8.65)	(9.62)	-	(4.39)	Diamagnetic	282.39
1457.12 ($CeC_{51}H_{65}N_9O_{21}F_6S_2$)				41.91	4.39	8.61	9.60		4.31		

3.1. IR data and bonding

The IR spectra of lomefloxacin and its metal complexes are shown in Fig. 1 and listed in Table 2. The IR spectra of the complexes were used with free ligand LFX for the determination of coordinating sites that may involved in complexation. All lomefloxacin complexes showed abroad band in the 3320-3438 cm^{-1} zone, the presence of these bands confirms the presence of water molecules.

The infrared spectrum of lomefloxacin showed a very strong band at 1725 cm^{-1} which attributed to the stretching vibration of $\nu(C=O)_{carboxyl}$ of its carboxylic group (-COOH) [38] this band has been replaced, in the spectra of the four complexes, with two characteristic bands in the range of 1615-1624 cm^{-1} and around 1392 cm^{-1}, which assigned to $\nu(COO^-)$ antisymetric and symetric stretching vibrations, respectively, of the carboxylato group of lomefloxacin ligand. The values of $[\Delta\nu=\nu_{as}(COO^-)-\nu_s(COO^-)]$ a useful tool for determining the coordination mode of the carboxylate group of the ligands, are for the complexes in the range 200-232 cm^{-1} indicating a monodentate coordination mode of the carboxylato group [15,39-41]. These changes of the IR spectra suggest that LFX is bound to the four metal ions via the carboxylato oxygen atom [39-41]. Also, the shift of the carbonyl group to a lower value, table 2, from 1618 cm^{-1} to 1580 cm^{-1} for Ti(IV), 1585 cm^{-1} for V(IV), 1554 cm^{-1} for Pd(II) and 1558 cm^{-1} for Ce(IV) indicating the bonding of lomefloxacin through oxygen atom of the carbonyl group [21,42-44]. Also, the data given in table 2, showed the $\nu(V=O)$ in $[VO(LFX)_2H_2O]SO_4.9H_2O$ complex observed at 929 cm^{-1} [45]. The appearance of the $\nu(V=O)$ frequency in V(IV) complex at 929 cm^{-1} suggests that a monoanionic ligand lies in trans position to O_V ($O_{vanadyl}$) [46]. This acceptance is indicative of the arrangement of one O_{Car} or O_{pyr} atom in the axial position of the octahedron around vanadium atom and excludes the O_W (O_{water}) [47].

The IR spectra of the metal complexes also showed some new bands in the region 600-451 cm^{-1} which confirmed the coordination of the metal ions via oxygen atoms [31,32]. The infrared spectra of the synthised complexes display changes in the aromatic ring vibrations in comparison to the corresponding absorption bands for free ligand (Table 2).

Table 2:

Infrared frequencies (cm^{-1}) and tentative assignments for (A) lomefloxacin, (B) $[Ti(LFX)_3](SO_4)_2.2H_2O$, (C) $[VO(LFX)_2H_2O]SO_4.9H_2O$, (D) $[Pd(LFX)_2Cl_2].4H_2O$, (E) $[Ce(LFX)_3](SO_4)_2.4H_2O$.

A	B	C	D	E	Assignments
3438m,br	3400m,br	3400m,br	3430m,br	3320m,br	ν(O-H); H_2O; COOH
3056m	3055m	3055m	3040vs	3059vs	ν(C-H); aromatic
2966vw	2978vw	2945w	2856vw	2978w	ν(C-H); aliphatic
2933m	2936m	2878m	2839ms	2936w	
2890w	2889vw			2839w	
2845m	2867vw				
	2800w				
2757m	2704m	2640vw	2743w	2762w	$\nu(-NH_2^+)$
2701ms	2665vw	2604w	2461m	2704m	
2661w	2457ms	2426m		2457ms	
2635vw					
2455s					
1725vs	-	-	-	-	ν(C=O); COOH
-	1620s	1615ms	1624vs	1620vs	$\nu_{as}(COO^-)$
1618vs	1580sh	1585m	1554ms	1558s	ν(C=O)and phenyl breathing modes
1526ms	1551sh	1535m	1524vs		
1497s	1528ms				
1471w	1470ms	1474s	1477w	1485vs	-CH; deformations of CH_2
1456vw			1462vs		
1413w			1412ms		
			1444sh		
-	1400w	1378vw	1385ms	1404ms	$\nu_s(COO^-)$
1331s	1331vs	1335ms	1377vw	1345s	$\delta_b(-CH_2)$
1298vw		1289w	1327s	1289w	
			1311w		
			1281s		
1257ms	1254m	1250s	1254s	1250vw	ν(C-O),
1208s	1211ms	1200vw	1204s	1254m	ν(C-N),
1166s	1134s	1189vw	1190w	1200sh	ν(C-C)

				1211w 1122vs	
1116m 1093ms 1043s 1014m	1096w 1045ms 1003m	1139vw 1126ms 1088s 1049s 1011w	1176w 1150m 1119ms 1096ms 1049vs 1038s 999vs	1049s 980vw	$\delta_r(-CH_2)$ $\nu(SO_4^{-2})$
978w 930s 889s 850m 806ms	940sh 930s 887m 868shs 810s	891s 840vw 814vs	990w 941vw 934vs 900sh 891m 861w 853ms 806vs	930s 900vw 878w 811ms	-CH-bend; phenyl
- 739ms	- 741vs	929s 780vw 745m 725m 700vw	- 741s 720w 710m	- 744ms	ν (V=O) $\delta_b(COO^-)$
650m 550w 514m 480w	664m 602vs 550sh 530vw 485sh 451vs	652vs 620vw 583m 552m 517s 482m	652ms 544ms 490ms 462m 432m	667vw 617m 556w 520vw 480vw	ν(M-O), ring deformation and $\delta(SO_4^{-2})$

Keys: s=strong, w=weak, v=very, m=medium, br=broad, sh=shoulder, ν=stretching, δ_b=bending

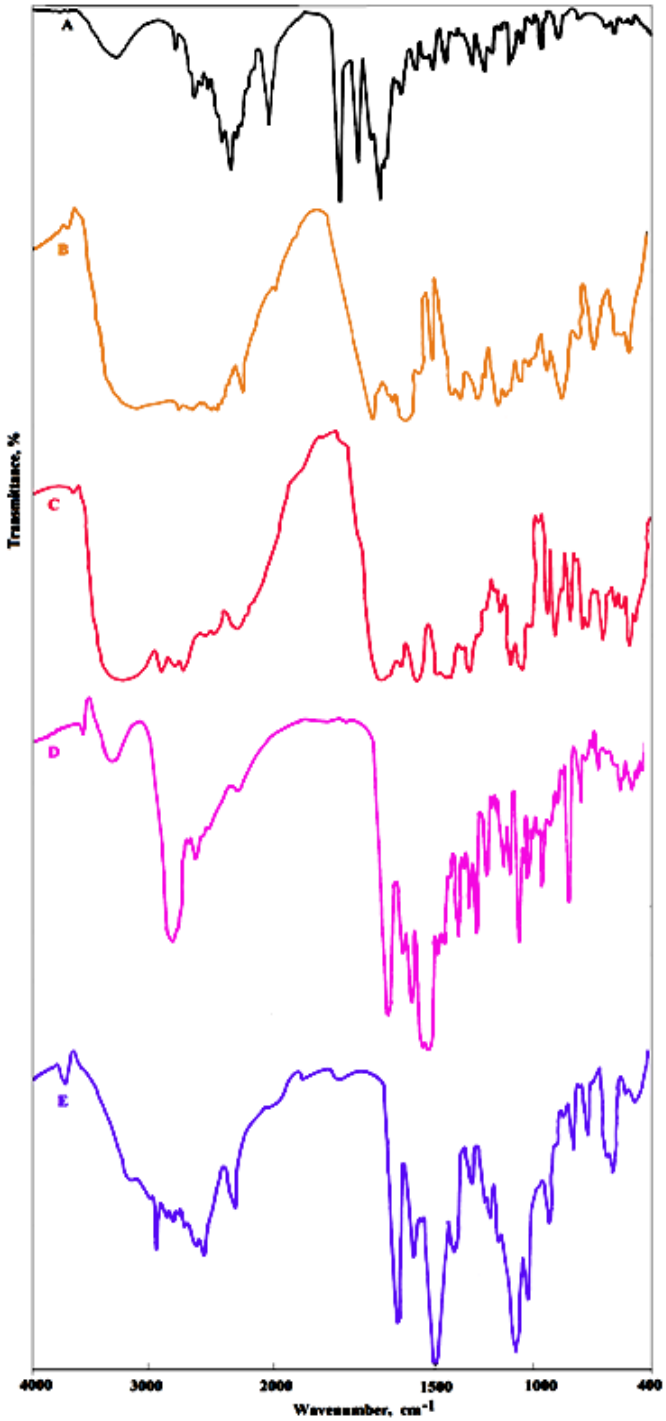


Fig. 1: Infrared spectra of for (A) lomefloxacin; (B) $[Ti(LFX)_3](SO_4)_2.2H_2O$, (C) $[VO(LFX)_2H_2O]SO_4.9H_2O$, (D) $[Pd(LFX)_2Cl_2].4H_2O$ and (E) $[Ce(LFX)_3](SO_4)_2.4H_2O$.

3.2. UV-Vis. Spectra

The electronic solid reflection spectra of lomefloxacin and the resulted solid complexes were recorded (Fig. 2 and Table 3). The reflection spectrum of free lomefloxacin showed bands at 214, 298 and 304 nm which is assigned to π-π^* and n-π^* transitions. For the our complexes the absent of the reflection band at 298 nm and the shift of the other two reflectance bands 214 and 304 nm to higher and lower values and the presence of new bands attributed to complexation behavior of lomefloxacin towards metal ions. The new bands at 417-658 nm assigned to the ligand to metal charge-transfer and d-d transition for V(IV) and Pd(II) complexes [21,31,32,47].

Table 3:

UV-Vis. spectra of lomefloxacin (LFX) and its metal complexes.

Assignments (nm)	LFX	LFX complex with			
		Ti(IV)	V(IV)	Pd(II)	Ce(IV)
π-π^* transitions	214, 298	221, 261	220, 242	211, 241, 249	-
n-π^* transitions	304	305, 318	312, 335, 353	331	303, 317, 359, 379, 390
Ligand-metal charge transfer	-	460	420	417, 484	462, 480
d-d transition	-	-	511, 542, 568	581	-

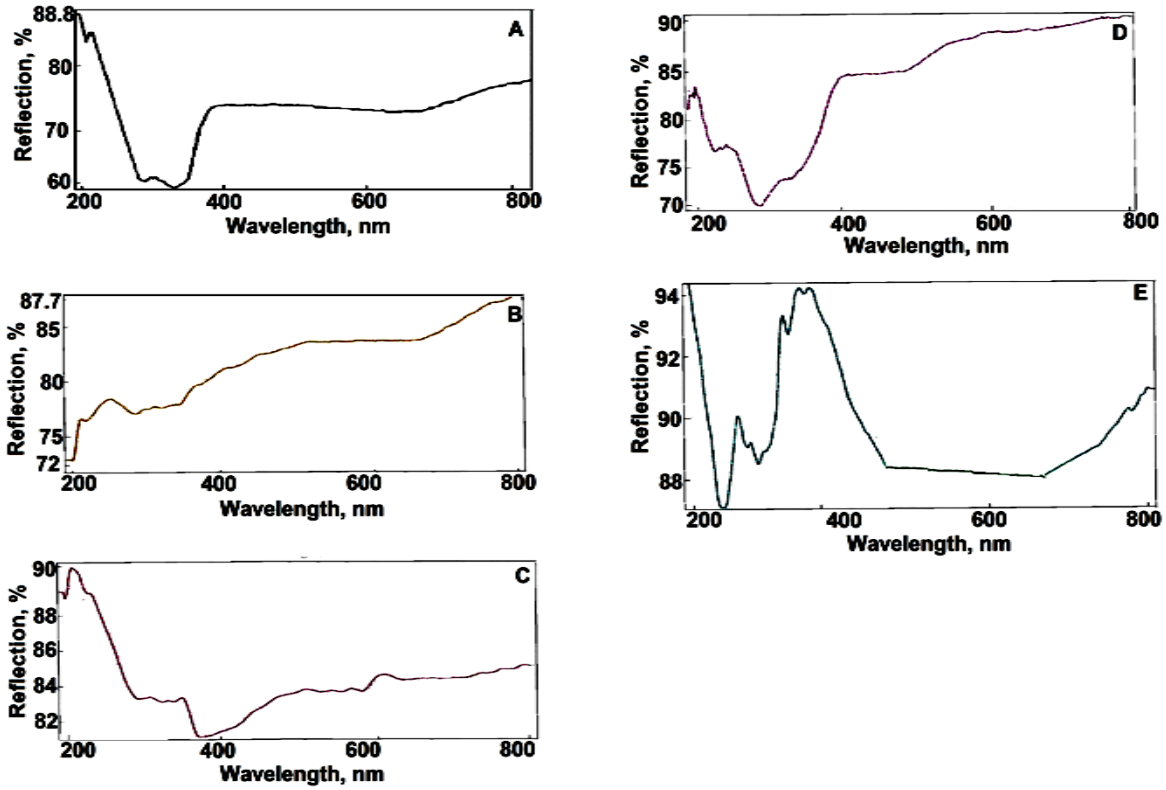


Fig. 2: Electronic reflection spectra of for (A) lomefloxacin; (B) $[Ti(LFX)_3](SO_4)_2.2H_2O$, (C) $[VO(LFX)_2H_2O]SO_4.9H_2O$, (D) $[Pd(LFX)_2Cl_2].4H_2O$ and (E) $[Ce(LFX)_3](SO_4)_2.4H_2O$.

3.3. The ^{1}H NMR spectra

The suggested molecular structures of complexes also proved by nulear magnetic resonance (NMR) spectrocopy. The ^{1}H NMR spectra of lomefloxacin and its complexes in DMSO-d_6 (Fig. 3) displayed distinct signals with appropriate multiplets while their signals assignments are given in Table 4. Results of ^{1}H NMR spectrum of LFX showed singlet at 7.57 and 8.95 ppm for the protons of aromatic ring, and singlet at 11.0 ppm for the proton of carboxylic acid. Comparing the main signals of complexes with that of LFX, proton NMR spectrum shows almost identical signals to these of LFX with small shifts for all signals except carboxylic acid proton signals, the resonance of the carboxylic proton (COOH) is not detected in the spectra of all complexes that suggest the coordination of LFX through its carboxylato oxygen atoms [31,32,48,49]. Also, according to the ^{1}H NMR data for $[Ti(LFX)_3](SO_4)_2.2H_2O$; δH, H_2O: 4.60 ppm and for $[Pd(LFX)_2Cl_2].4H_2O$; δH, H_2O; 4.57 ppm which is absent in the free lomefloxacin, indicated the presence of water molecules.

Table 4:

^{1}H NMR values (ppm) and tentative assignments for (A) LFX, (B) $[Ti(LFX)_3](SO_4)_2.2H_2O$ and (C) $[Pd(LFX)_2Cl_2].4H_2O$.

A	B	C	Assignments
1.31	1.05-1.47	0.99-1.44	δH, -CH_3
3.51-3.61	2.44-3.38	2.49-3.38	δH, -NH; piperazine
3.98	3.55, 3.58, 3.62	3.44, 3.50	δH, -N-CH_2
-	4.60	4.57	δH, H_2O

7.00	7.90, 7.94	7.80, 7.84	δH, -$^{+}NH_2$
7.57, 8.95	8.96, 9.2	8.90	δH, -CH_2 aromatic
11.00	-	-	δH, -COOH

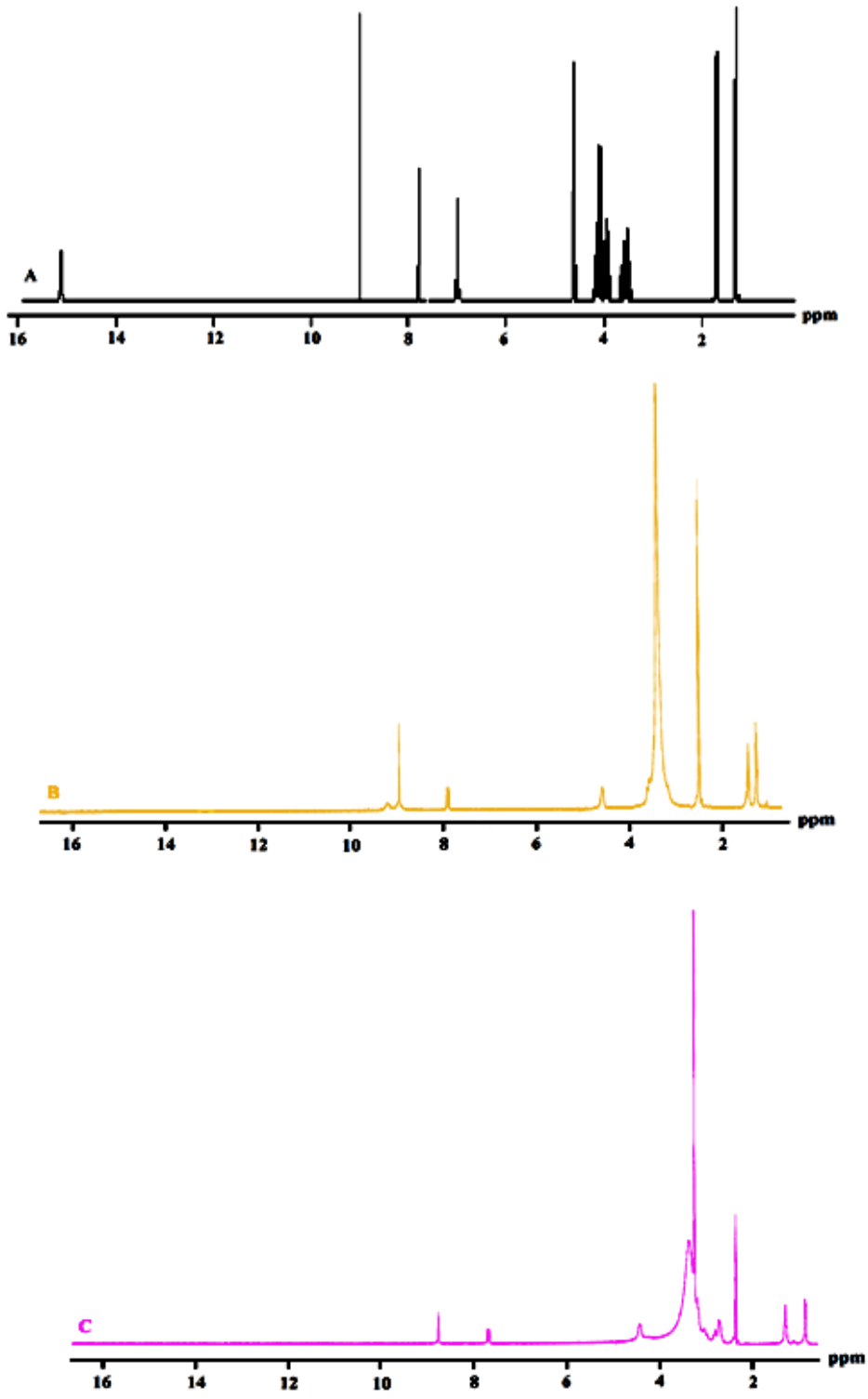


Fig. 4: ^{1}HNMR spectra for (A) LFX, (B) $[Ti(LFX)_3](SO_4)_2.2H_2O$ and (C) $[Pd(LFX)_2Cl_2].4H_2O$ in DMSO, δ_{TMS}.

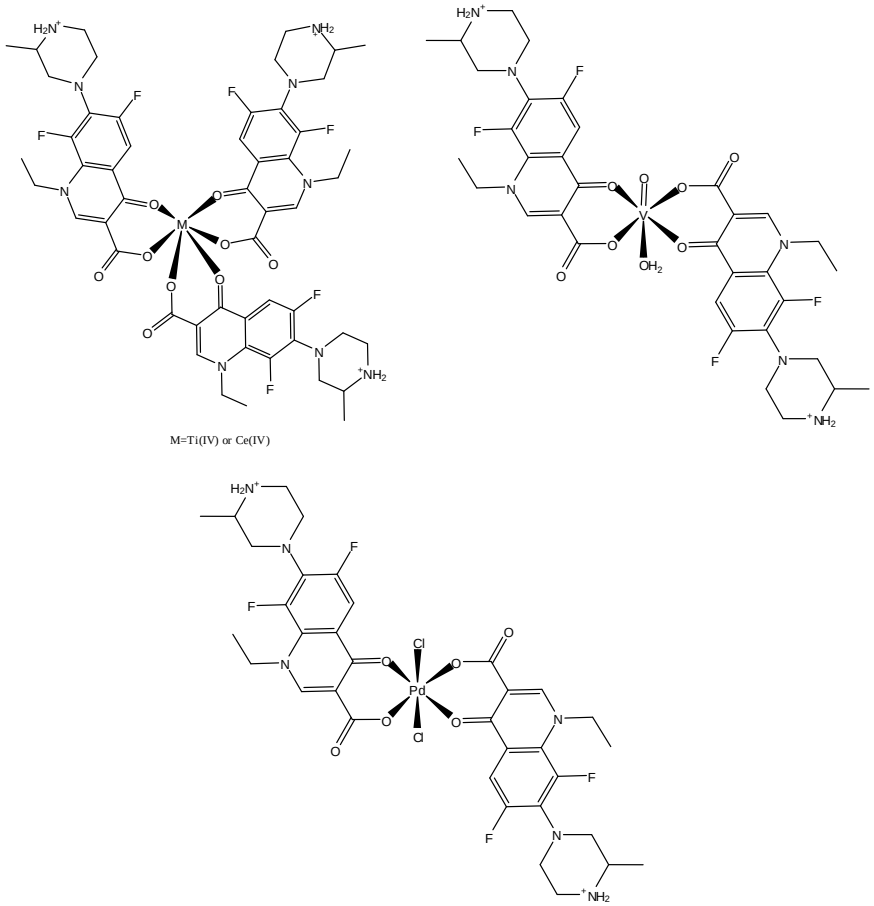
3.4. Thermal studies

To establish the proposed formula and structure for each of the complexes under investigation, TGA and DTG for the ligand and its solid complexes were carried out. Table 5 gives the maximum temperature values for decomposition along with the corresponding weight loss values for each step of the decomposition reaction. The LFX was thermally stable in the temperature range 25–250 ^{o}C. Decomposition of the lomefloxacin started at 250^{o}C and finished at 600 ^{o}C with one stage at two maxima 319 and 553 ^{o}C and is accompanied by a weight loss of 99.95% ((Fig. 4(A)).

The thermal degradation of $[Ti(LFX)_3](SO_4)_2.2H_2O$ complex take place in two degradation stages, the first stage of decomposition occurs at maximum 138 ^{o}C and is accompained by a weight loss of 2.69% corresponding to the loss of two crystallization water molecules. The dehydrated complex is simultaneous decomposed to $Ti(SO_4)_2$ as a final product at three maxima 302, 410 and 501 ^{o}C with intermediate formation of very unstable products which were not identified [31,32,50].

The hydrated complex of V(IV) loss upon heating nine crystallization water molecules in the first step of decomposition within the temperature range of 25-189 ^{o}C. The second step of decomposition occurs at three maxima at 288, 450 and 499 ^{o}C. This step is associated with the loss of coordinated water molecule and the lomefloxacin forming VSO_4 as a final product. The weight for the residue after decomposition is 14.10% giving an actual total weight loss of 85.87% in agreement with our calculated total weight loss values of 85.94%.

The hydrated complexes of Pd(II) and Ce(IV) loss upon heating all crystallization water molecules at 198 ^{o}C for Pd(II) and at 123 ^{o}C for Ce(IV). The dehydrated Pd(II) and Ce(IV) lomefloxacin complexes are simultaneously decomposed to Pd metal and $Ce(SO_4)_2$ at 296, 363, 466 and 291, 315, 540 ^{o}C maximum temperatures (table 5) with intermediate formation of very unstable products which were not identified [49]. The infrared spectra of the final decomposition products of four complexes obtained at 800 ^{o}C, showed a group of bands characteristic of ionic sulphate for complexes of Ti(IV), V(IV) and Ce(IV).



Formula I: The coordination mode of Ti(IV), V(IV), Pd(II) and Ce(IV) with LFX.

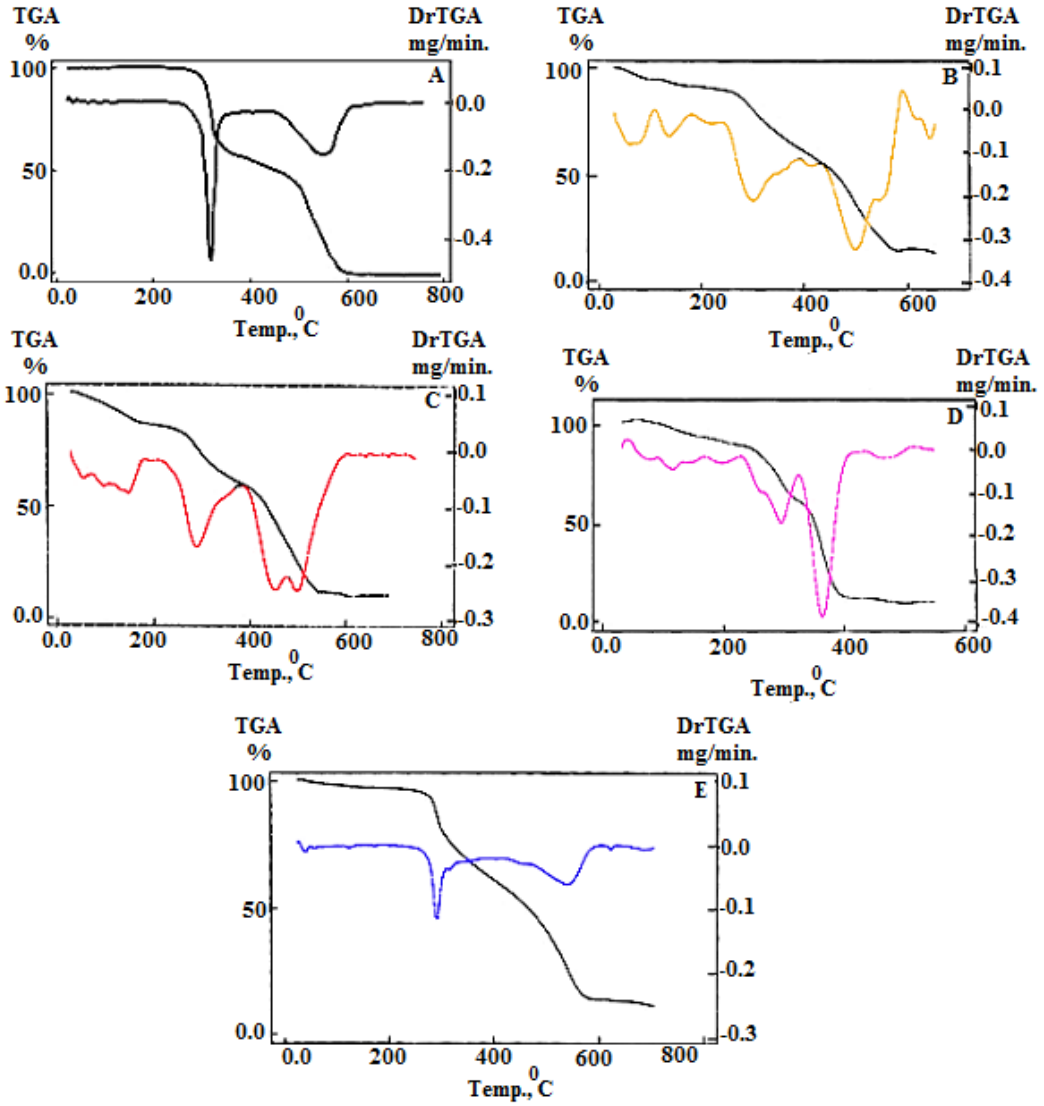


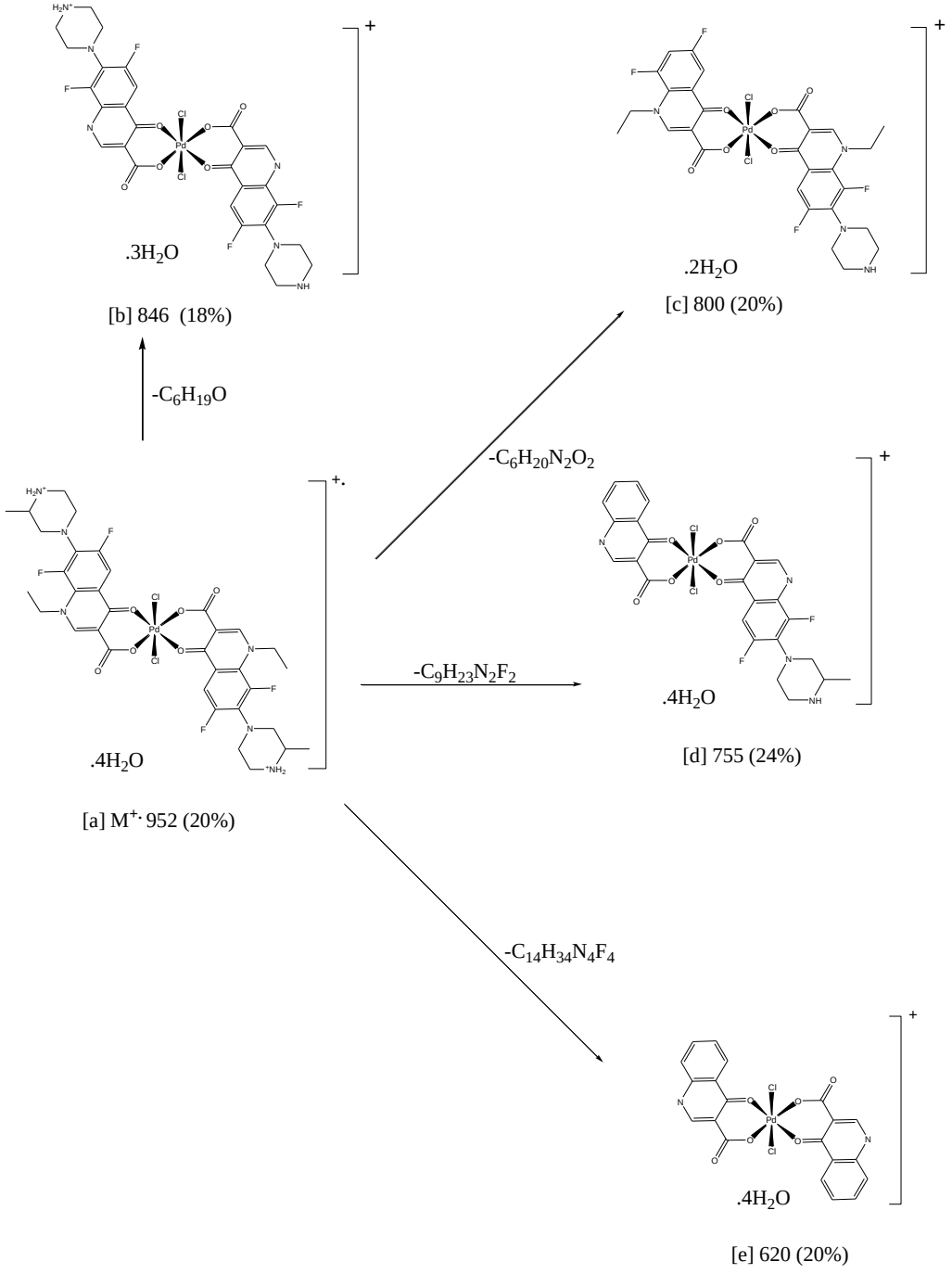
Fig. 4: TGA and DTG diagrams of for (A) LFX, (B) $[Ti(LFX)_3](SO_4)_2.2H_2O$, (C) $[VO(LFX)_2H_2O]SO_4.9H_2O$, (D) $[Pd(LFX)_2Cl_2].4H_2O$ and (E) $[Ce(LFX)_3](SO_4)_2.4H_2O$.

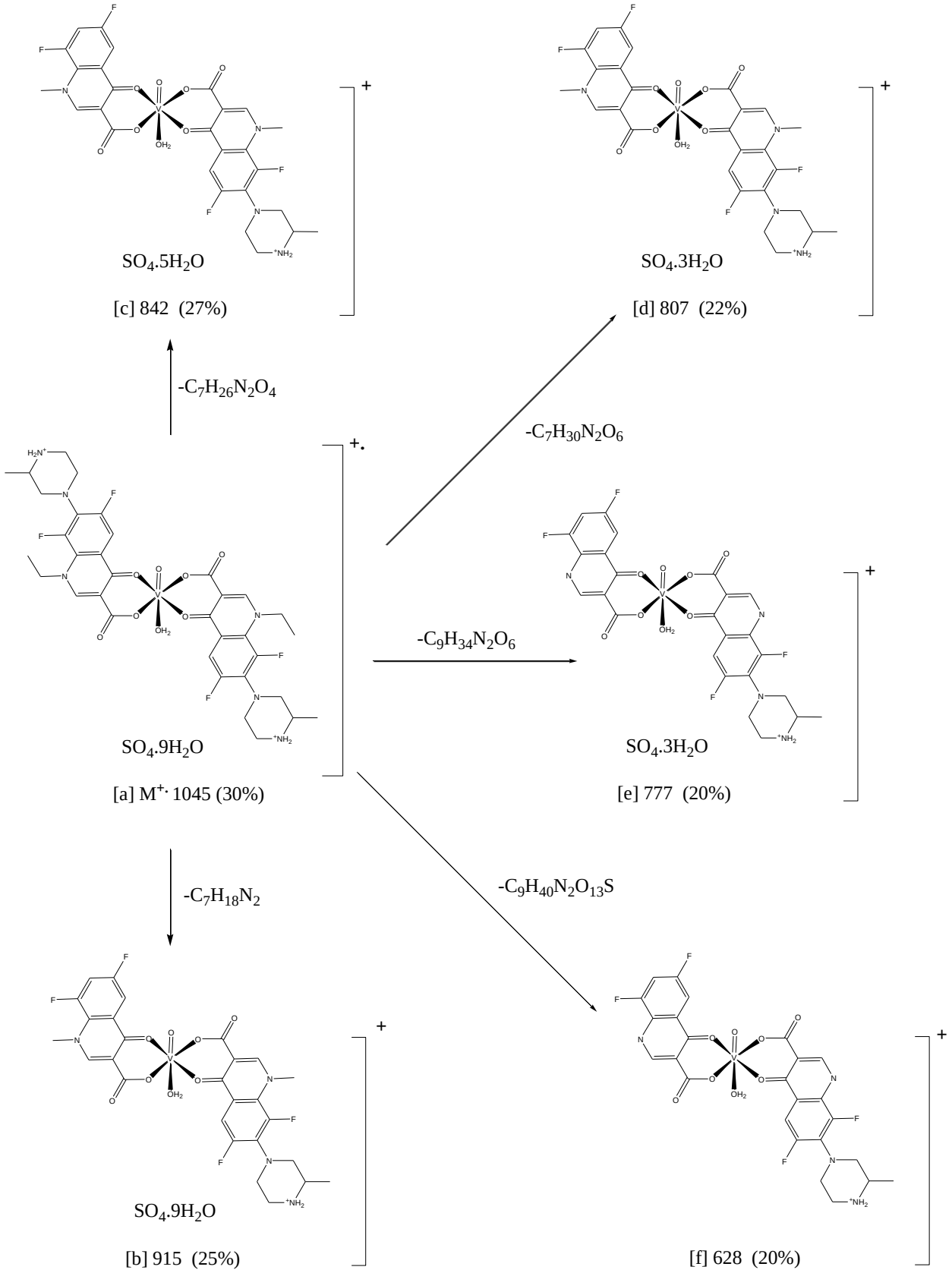
Table 5:
The maximum temperature T_{max} (^{o}C) and weight loss values of the decomposition stages for LFX, Ti(IV), V(IV), Pd(II) and Ce(IV) Lomefloxacins.

Compounds	Decomposition	T_{max}(^{o}C)	Weight loss (%)	
			Calc.	Found
LFX ($C_{17}H_{20}N_3O_3F_2Cl$)	First step	319, 553	100	99.99
	Total loss, Residue		100, 0.0	100, 0.0
$[Ti(LFX)_3](SO_4)_2.2H_2O$	First step	138	2.71	2.69
($TiC_{51}H_{61}N_9O_{19}F_6S_2$)	Second step	302, 410, 501	79.24	79.19
	Total loss, Residue		81.95, 18.05	81.88, 18.12
$[VO(LFX)_2H_2O]SO_4.9H_2O$	First step	145	15.50	15.45
($VC_{34}H_{58}N_6O_{21}F_4S$)	Second step	288, 450, 499	70.44	70.42
	Total loss, Residue		85.94, 14.06	85.87, 14.10
$[Pd(LFX)_2Cl_2].4H_2O$	First step	198	7.56	7.53
($PdC_{34}H_{46}N_6O_{10}F_4Cl_2$)	Second step	296, 363, 466	81.21	81.11
	Total loss, Residue		88.77, 11.23	88.64, 11.36
$[Ce(LFX)_3](SO_4)_2.4H_2O$	First step	123	4.94	4.91
($CeC_{51}H_{65}N_9O_{21}F_6S_2$)	Second step	291, 315, 540	72.27	72.85
	Total loss, Residue		77.21, 22.79	77.76, 22.24

3.5. Mass spectra

The idea of mass spectrometer builds up on the separation of fragments ions dependent to the variation of these ions with the ratio of mass to charge (m/z). The fragmentation patterns of our studied complexes were obtained from the mass spectra. The mass spectrum of Pd(II) complex displayed molecular peak ($M^{\cdot+}$) at m/z (%) 951 (20%) and M^{+2} at m/z (%) 953 (2.1%) suggesting that the molecular weight of the assigned product matching with elemental analysis calculated. Also, the mass spectrum of V(IV) complex displayed molecular peak ($M^{\cdot+}$) at m/z (%) 1045 (30%) and M^{+1} at m/z (%) 1046 (1.9%) which refer to M.Wt. of the complex. The following fragments observed in the mass spectra of the two complexes confirms the assigned structure for the complexes (Scheme 1). For the other two complexes Ti(IV) and Ce(IV) with the calculated molecular weights 1328.9 and 1457.12, respectively, according to the elemental analysis and thermogravimetric analysis, the molecular peaks are found outside the scale of the instrument.





Scheme 1: Fragmentation pattern of V(IV) and Pd(II) complexes

3.6. Antibacterial activity

The antibacterial activity data of free lomefloxacin and their metal complexes as diameter of growth inhibition zone against three Gram-positive bacteria such as S. aureus K1, B. subtilis K22, Br. Otitidis K76 and three Gram-negative species E. coli K32, P. aeruginosa SW1 and K. oxytoca K42 are summarized in Table 6 and Fig. 5.

The newly synthesized complex $[VO(LFX)_2H_2O]SO_4.9H_2O$ posses very highly significant against E. coli K32 and higly significant against K. oxytoca K42, P. aeruginosa SW1, Br. Otitidis K76 and B. subtilis K22. Also, the two complexes $[Ti(LFX)_3](SO_4)_2.2H_2O$ and $[Pd(LFX)_2Cl_2].4H_2O$ are more activity than lomefloxacin against E. coli K32, K. oxytoca K42, P. aeruginosa SW1, Br. Otitidis K76 and B. subtilis K22. For $[Ce(LFX)_3](SO_4)_2.4H_2O$ showed significant and highly significant against B. subtilis K22 and S. aureus K1 compared with lomefloxacin. The specific biological activities of Ce(IV) complex is highly significant against S. aureus K1 and significant against B. subtilis K22 and nonsignificant against E. coli K32 and Br. otitidisK76. The non regularity of Ce(IV) complex with the other complexes may be regarded to the high atomic volume of the Ce(IV) complex with the other metal ions.

In general, the increasing of biological activity of metal complexes compared with free ligand can be explained according to the following five principal factors [12,51-53]: (i) the chelate effect. i.e, bidentate ligands, such as the fluoroquinolones, show higher antimicrobial efficiency towards complexes with monodentate ligands; (ii) the nature of the ligands; (iii) the total charge of the complex; (iv) the nature of the counter ion in the case of the ionic complex; (v) the nuclearity of the metal center in the complex. Also, the chelation reduces the polarity of the metal ions, mainly because of the partial sharing of its positive charge with the donor groups and possibly the π-electron delocalization within the whole chelate ring system thus formed during coordination. This process of chelating increases the lipophilic nature of the metal ion, which in turn favors its permeation through the lipid layer of the membrane and this is also increasing the hydrophobic character and liposolubility of the molecule in crossing the cell membrane of the microorganism and hence enhances the biological utilization ratio and activity of the testing antibiotic compounds [54,55].

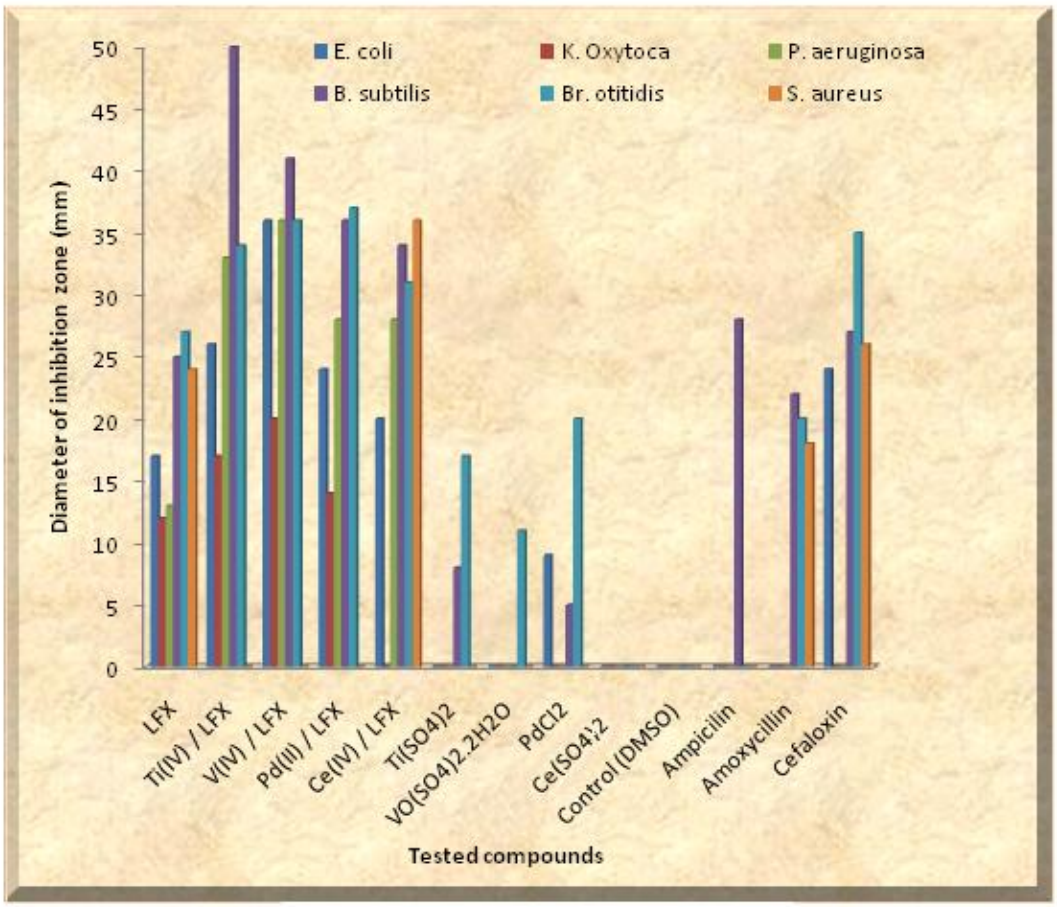


Fig. 6: Statistical representation for biological activity of lomefloxacin and its metal complexes.

Table 6:The inhibitation diameter zone values (mm) for LFX and their complexes.

compounds		Microbial Bacteria species					
		E. coli	K. oxytoca	P. aeruginosa	B. subtilis	Br. otitidis	S. aureus
LFX		17 ±0.12	12 ±0.08	13 ±0.29	25 ±0.54	27 ±0.11	24 ±0.23
Ti(IV) / LFX		26^{+2} ±0.12	17^{+1} ±0.88	33^{+3} ±0.69	50^{+3} ±0.85	34^{+1} ±0.52	ND
V(IV) / LFX		36^{+3} ±0.06	20^{+2} ±0.87	28^{+2} ±0.19	41^{+2} ±0.45	36^{+2} ±0.64	ND
Pd(II) / LFX		24^{+2} ±0.58	14^{+1} ±0.44	28^{+2} ±0.28	36^{+1} ±0.42	37^{+2} ±0.51	ND
Ce(IV) / LFX		20^{NS} ±0.88	-	-	34^{+1} ±0.60	31^{NS} ±0.98	36^{+2} ±0.19
$Ti(SO_4)_2$		-	-	-	8 ±0.15	17 ±1.51	-
$VO(SO_4)_2.2H_2O$		-	-	-	0	11 ±0.23	-
$PdCl_2$		9 ±0.73	-	-	5 ±0.52	20 ±1.15	-
$NH_4Ce(SO_4)_4$		-	-	-	-	-	-
Control (DMSO)		-	-	-	-	-	-
standard	Ampicilin	-	-	-	28 ±0.40	-	-
	Amoxycillin	-	-	-	22 ±0.11	20 ±0.10	18 ±1.73
	Cefaloxin	24 ±0.34	-	-	27 ±1.15	35 ± 0.27	16 ±0.52

ND: non-detectable. i.e., the inhibition zones exceeds the plate diameter

(-): no activity observed aginst microbial bacteria species

Statistical significance P^{NS} P not significant, P >0.05; P^{+1} P significant, P<0.05; P^{+2} P highly significant, P <0.01; P^{+3} P very highly significant, P <0.001; student's t-test (Paired).

3.7. Computational details

3.7.1. Computational method

The geometric parameters and energies were computed by density functional theory at the B3LYP/CEP-31G level of theory, using the GAUSSIAN 98W package of the programs, on geometries that were optimized at CEP-31G basis set. The high basis set was chosen to detect the energies at a highly accurate level. The atomic charges were computed using the natural atomic orbital populations. The B3LYP is the key word for the hybrid functional [56], which is a linear combination of the gradient functionals proposed by Becke [57] and Lee, Yang and Parr [58], together with the Hartree-Fock local exchange function [59].

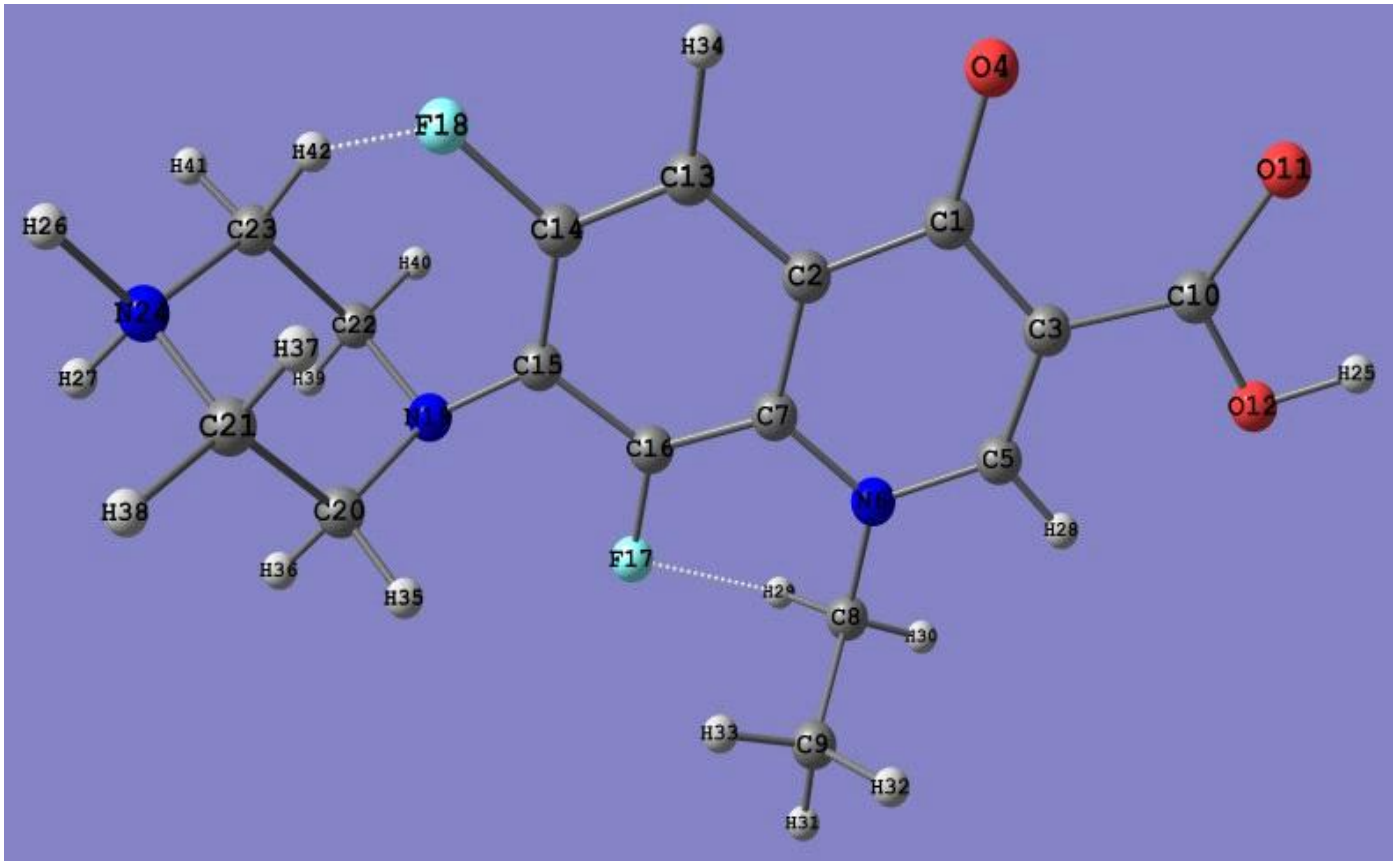
3.7.2. Structural parameters and models

3.7.2.1. Lomfloxacin(LFX)

A role of the quinolone molecule in the structure is similar to the ionic compounds reported [60-62], it is protonated at a terminal nitrogen atom of piperazine ring N24. The bond lengths for C1-O4, C10-O11 and C10-O12 are 1.30, 1.28 and 1.36Å, respectively, there is a double bond between C10 and O11 atoms 1.28Å and C10-O11 is a single bond 1.36Å [63]. Detailed analysis of corresponding bond lengths in various quinolone molecules was given elsewhere [64]. All these distances as well as the angles between the atoms of the rigid quinolone ring system and those of the piperazine ring are similar appearance described earlier [60-62].

The biological activity of quinolones (lomfloxacin) is mainly determined by its fine structure, the lomfloxacin has many characteristic structural features. The molecule is a highly sterically-hindered, the ethyl group not located in the same plane of quinolone ring the dihedral angles C3C5N6C8 and C7N6C8C9 are 178.87˚ and -77.98˚, also, the piperazine ring out of plane of the molecule. This observation is supported by the values of calculated dihedral angles: C20N19C15C16 and C20N19C15C14 are 87.71˚ and -88.63˚, where the values are neither zero nor 180˚. Scheme 2 shows the optimized geometrical of lomfloxacin molecule, the dihedral angles C5C3C10O11 and C1C3C10O11 are -179.92 and 0.85˚ also, C1C3C10O12 and C5C3C1O12 are -178.74˚ and 0.46˚ which confirms that the O4 and O11 located in the same direction. The plane of C1-O4 bond located in the same plane of C10-O11 bond while O4 and O12 are located in the opposite direction to each other so, the plane of C1-O4 is not found in the same plane of C10-O12. The ionized bond lengths of C-H of piperazine and benzoxazine rings are calculated to range from 1.09 to 1.12 and from 1.102 to 1.104 as compared to the observed values of 1.422 and 1.440, respectively.

Table 7 gives the optimized geometry of lomfloxacin as obtained from B3LYP/CEP-31G calculations. These data are drowning to give the optimized geometry of molecule. The bond lengths of C10-O12, C10-O11 and C1-O4 are 1.36, 1.28 and 1.30Å. The value of bond angle C1C3C10 is 124.22˚ reflects on sp^2 hybridization of C3, the same result is obtained with C1 and C10. These values of bond distances agree well with the obtained from X-ray data [63]. From the theoretical investigation of the free drug lomfloxacin there is strong interaction between F18 and H42 of piprazine ring the distance between these two atoms is 1.54 Å, also this behavior exists between F17 and H29 with distance 1.68 Å. Comparisons of the performance of different DFT methods allow outlining the main trends of these theoretical approaches which are necessary to better understand the properties and biological reaction mechanisms of lomfloxacin. However, till now, no attempt has been made to analyze the application of various DFT methods and different basis sets for accurate calculations of structure of lomfloxacin [65-68].



Scheme 2: Optimized geometrical structure of Lomfloxacin by using B3LYP/CEP-31G.

Table 7: Equilibrium geometric parameters bond lengths (Å), bond angles (˚), dihedral angles (˚) and charge density of LFX by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
C10-O11	1.28 (1.30)	C1-C3	1.45 (1.47)
C10-O12	1.36 (1.41)	C3-C5	1.43 (1.48)
C3-C10	1.44 (1.46)	C1-O4	1.30 (1.22)
N6-C8	1.43 (1.49)]	C8-C9	1.48 (1.52)
C20-N19	1.44 (1.45)	C22-N19	1.47 (1.48)
C15-N19	1.42 (1.45)]		
Bond angle (˚)			
C3C10O12	114.75	C2C1O4	121.94
C3C10O11	130.69	C15N19C22	118.01
O11C10O12	114.56	C15N19C20	112.64
C1C3C10	124.22	C8N6C7	121.64
O4C1C3	121.64	C8N6C5	119.19
N6C8C9	113.48	C21N24C23	110.99
		C13C14F18	116.55
Dihedral angles (˚)			
C20N19C15C16	87.71	C9C8N6C5	103.71
C20N19C15C14	-88.63	C7N6C8C9	-77.98
C16C15N19C22	-143.32	C3C5N6C8	178.87
C14C15N19C22	40.34	C2C7N6C8	178.80
C5C3C10O12	0.46	C1C3C10O11	0.85
C5C3C10O11	-179.92	C1C3C10O12	-178.74
Charges			
C1	0.249	F17	-0.267
O4	-0.485	F18	-0.285
C10	0.468	N6	-0.103
O11	-0.421	N19	-0.134
O12	-0.387	N24	0.013
Total energy/au		-250.611	
Total dipole moment/D		24.839	
HOMO		-4.717	
LUMO		3.722	

3.7.2.2. The Ti(IV) lomfloxacin complexes

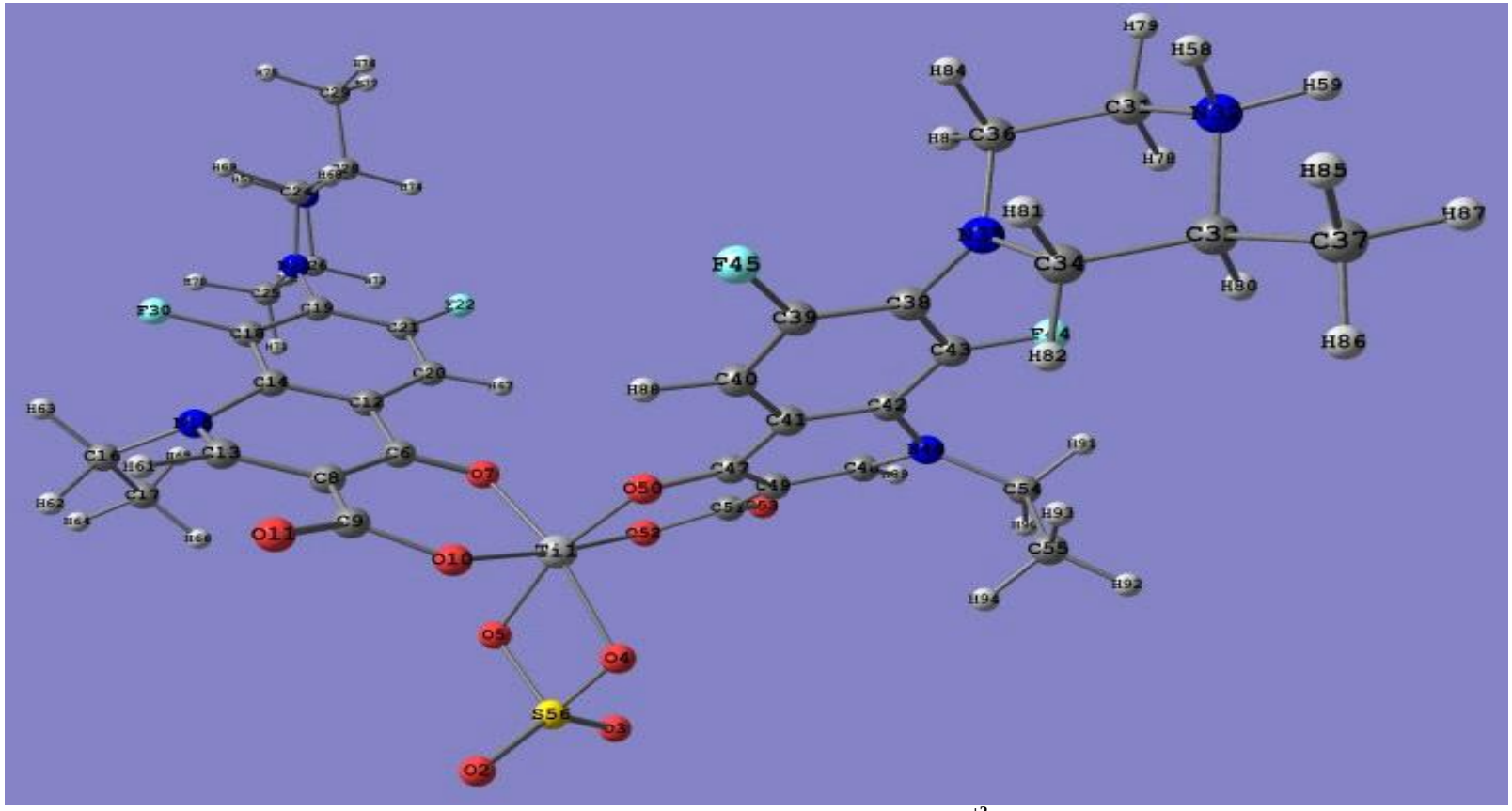
The Ti(IV) chelated with three molecules of lomfloxacin through two coordinate bonds (O_{pyr} and O_{car} atoms) from each molecule. The experimental data set that the result complex is six-coordinate so, the complex consists of six coordinate bonds with three lomfloxacin molecules. In this part we study theoretically the three structures of $[Ti(LFX)_3]^{+4}$, $[Ti\ (LFX)_2(SO_4)]^{+2}$ and $[Ti(LFX)_2(H_2O)_2]^{+4}$ to detect which of them is more stable.

3.7.2.2.1. Description of the structure of $[Ti(LFX)_2(SO_4)]^{+2}$

Scheme 3 shows the optimized geometrical structure of the complex with the atomic numbering scheme selected bond distances and angles are given in Table 8. The suggested complex is composed of $[Ti(lFX)_2(SO_4)]^{+2}$.

The Ti(IV) at a crystallographic inversion center, is in a distorted octahedral environment. In the equatorial plane the metal ion is coordinated by four oxygen atoms (O_{pyr} and O_{car}) of two lomfloxacin ligands at the distances vary from 1.937Å to 1.938Å, these bond lengths are similar to those observed in related compounds [69-73]. The difference in the carboxylate bond length O10-C9 and O11-C9 (1.348Å and 1.211Å) [9], confirms the formation of bond between the ionic carboxylate oxygen atom and titanium ion. The octahedral coordination environment is completed by two oxygen atoms of sulfato group. The bond distance between Ti-O10 and Ti-O7 are1.937Å and 1.938Å, respectively, [69-73] while the distance between Ti-O of sulfato group is 1.883-1.892Å [69,75]. The bond angles around the central Ti(IV) vary from 72.18˚ to 173.62˚; these values differ significantly from these expected for a regular octahedron.

In the equatorial plane the Ti(IV) bonded with two oxygen atoms (O7 and O10) of lomfloxacin molecule in the same plane which perpendicular to the other plane occupied by other two oxygen atom (O50 and O52) of other lomfloxacin molecule. The bond angles O52 Ti O7 and O50 Ti O7 are 85.17˚ and 104.62˚. The sulphato group not lying in the same plane but out of plane in twisting form, the bond angle O10-Ti-O4 is 90.23˚, so the oxygen atom of sulphato group lying trans respect to one oxygen atom (O_{pyr}) of one lomfloxacin molecule, while the angle O5-Ti-O50 is163.82˚, so the other oxygen atom of sulphato group lying trans respect to the oxygen atom (O_{car}) of other lomfloxacin molecule. The dihedral angles O2S56O5Ti and O3S56O4Ti are 107.84˚ and -107.49˚, which means that the two oxygen atoms of sulphato group (O2 and O3) lying in opposite direction to each other and out of plane occupied by other atoms. The energy of this complex is -554.60 au and the dipole moment is weak 22.523D.



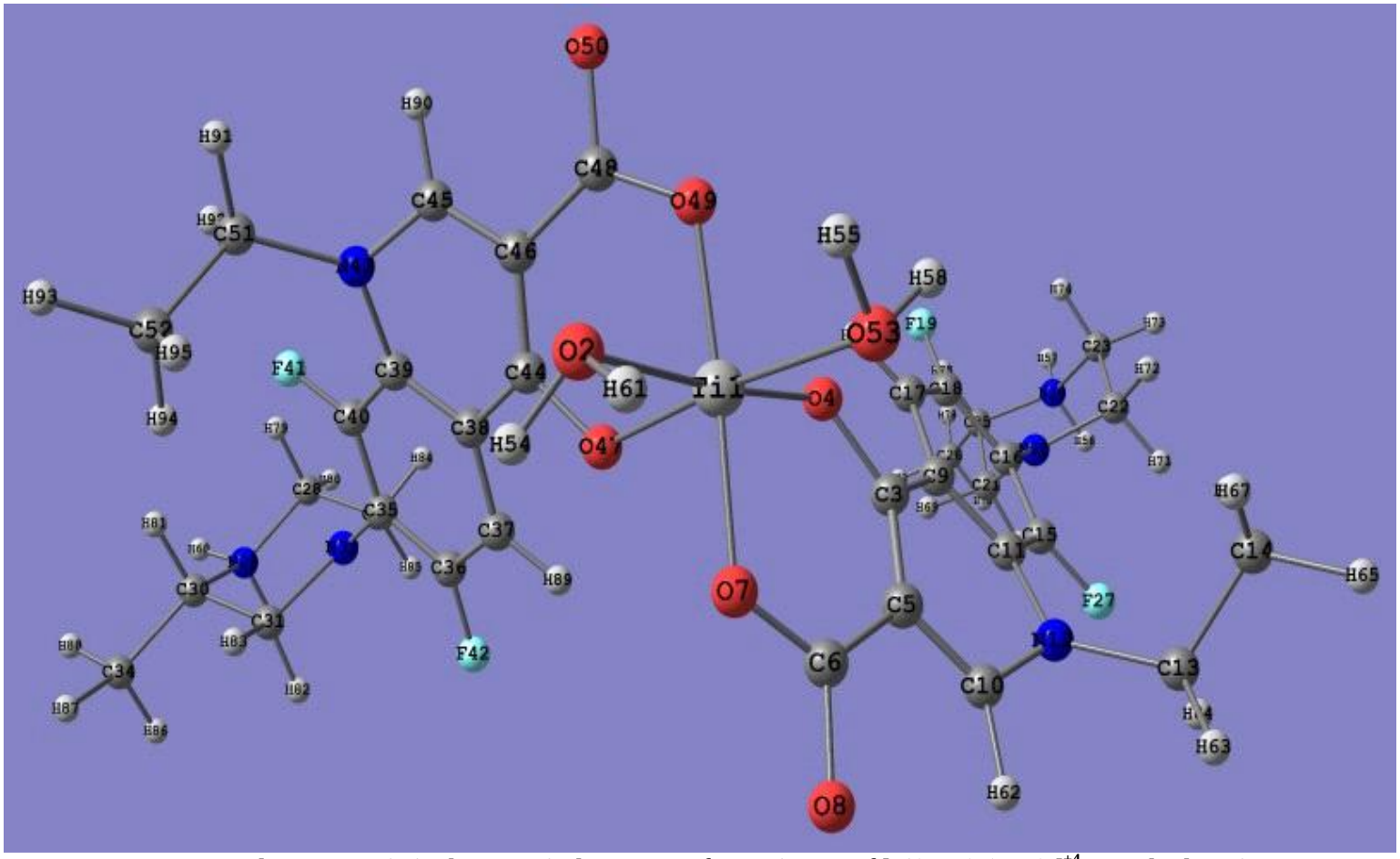
Scheme 3: Optimized geometrical structure of trans-isomer of $[Ti(lFX)_2(SO_4)]^{+2}$ complex by using B3LYP/CEP-31G.

Table 8: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[Ti(lFX)_2(SO_4)]^{+2}$ by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
Ti –O10	1.937	C6-O7	1.210
Ti –O7	1.938	C51-O52	1.348
Ti –O50	1.938	C51-O53	1.211
Ti –O52	1.937	C47-O50	1.211
Ti –O4	1.883	C9-O11	1.211
Ti -O5	1.892	C9-O10	1.348
C6-C8	1.364	C47-C49	1.363
C8-C9	1.364	C49-C51	1.364
Bond angle (˚)			
O10 Ti O7	91.51	O7 Ti O4	163.72
O10 Ti O4	90.23	O5 Ti O4	72.18
O52 Ti O7	85.17	O50 Ti O52	91.23
O5 Ti O52	90.64	O52 Ti O10	173.62
O52 Ti O4	94.46	O5 Ti O7	91.54
O5 Ti O10	94.89	O50 Ti O7	104.62
O50 TiO10	84.32	O5 TiO50	163.82
O4TiO50	91.65		
Charges			
Ti	0.888	O53	-0.467
O7	-0.374	O4	-0.533
O10	-0.451	O5	-0.531
O11	-0.470	S56	1.383
O50	-0.373	O2	-0.639
O52	-0.454	O3	-0.640
C9	0.500	C47	0.247
C51	0.498		
Total energy/au		-554.600	
Total dipole moment/D		22.523	
HOMO		-0.336	
LUMO		4.588	

3.7.2.2.2. Description of the structure of $[Ti(LFX)_2(H_2O)_2]^{+4}$

Table 9 lists selected inter atomic distances and angles. The structure of complex with atomic numbering scheme is shown in Scheme 4. The complex consists of two units of lomfloxacin molecule and two water molecules with Ti(IV) ion. The complex is six-coordinate with octahedral environment around the metal ion. The Ti(IV) is coordinated to O_{pyr} and O_{car} atoms of each lomfloxacin ligand and two O_{H2O} atoms for water. The Ti-O49 and Ti-O7 bond lengths are 1.936Å and 1.932Å, respectively and longer than that Ti-O47 and Ti-O4 (1.893Å and 1.8891Å, respectively). Also, the angles around Ti(IV) with surrounding oxygen atoms vary from 84.97˚ to 176.23˚; these values agree with octahedron. The two lomfloxacin molecules are perpendicular to each other they are not lying in the same plane the bond angle O4TiO47 is 91.21˚ and O4TiO49 is 88.45˚, which confirm that the two lomfloxacin molecules not exist in the same plane. The two water molecules bonded with Ti(IV) not exist in trans position to each other but exist as cis to each other, the bond angle O2TiO53 is 88.23˚. The energy of this complex is -595.661au and highly dipole 29.864D.



Scheme 4: Optimized geometrical structure of trans-isomer of $[Ti(LFX)_2(H_2O)_2]^{+4}$ complex by using B3LYP/CEP-31G.

Table 9: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[Ti(LFX)_2(H_2O)_2]^{+4}$ by using DFT/B3LYP/CEP-31G.

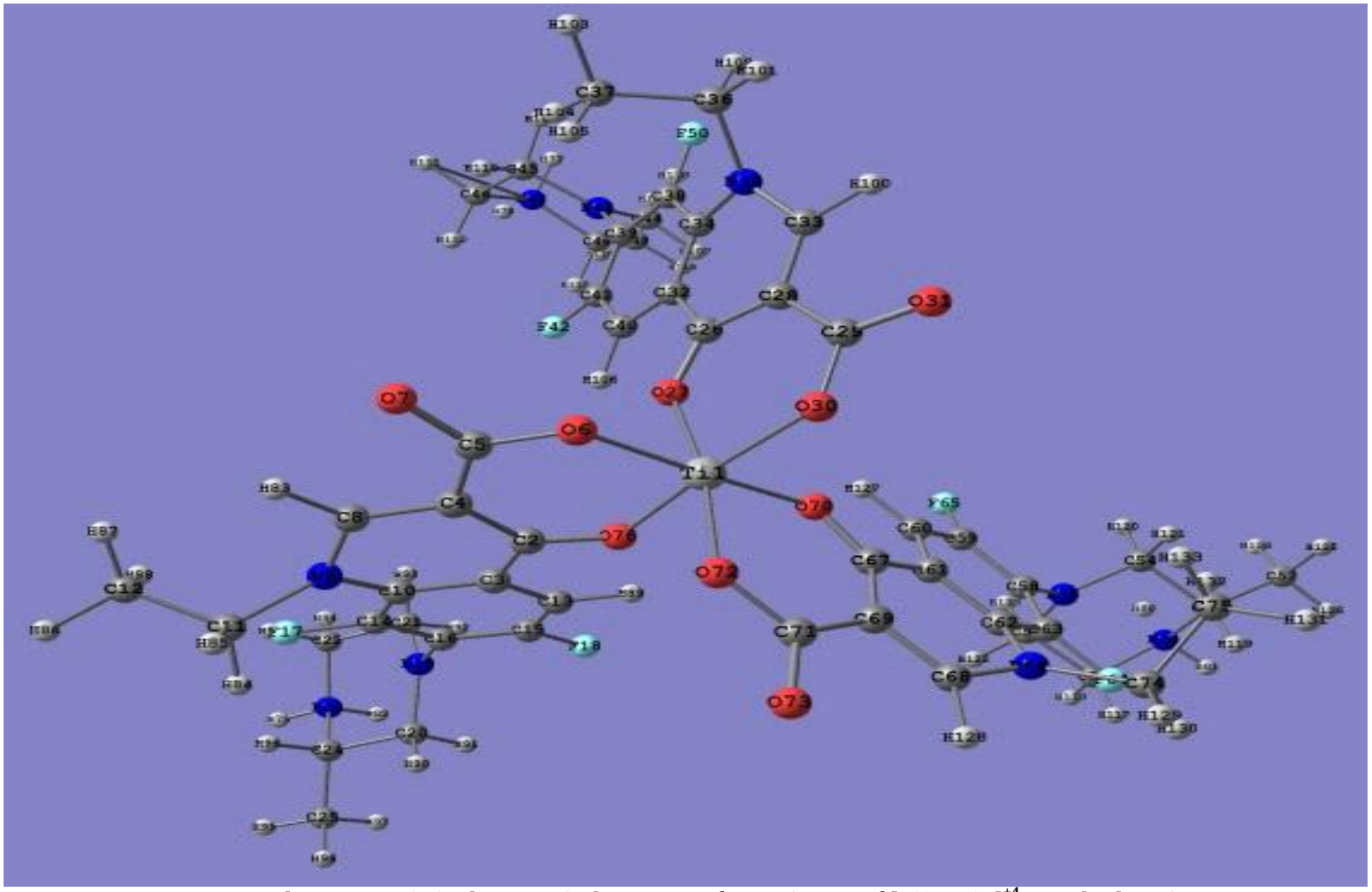
Bond length (Å)			
Ti –O7	1.932	C6-O8	1.219
Ti –O4	1.889	C6-O7	1.321
Ti –O49	1.936	C3-O4	1.360
Ti –O47	1.893	C48-O50	1.291
Ti –O2	2.005	C48-O49	1.320
Ti -O53	2.003	C44-O47	1.358
C3-C5	1.319	C44-C46	1.321
C5-C6	1.382	C46-C48	1.382
Bond angle (˚)			
O4 Ti O7	95.22	O2 Ti O53	88.23
O2 Ti O7	89.83	O47 Ti O49	94.13
O4 Ti O49	88.45	O7 Ti O49	176.23
O53 Ti O49	91.57	O4 Ti O53	89.57
O2 Ti O49	86.53	O4 Ti O4	91.21
O7 Ti O53	89.29	O53 Ti O47	174.26
O7 TiO47	84.97	O2 TiO47	91.49
O4TiO2	174.46		
Charges			
Ti	0.911	O49	-0.406
O7	-0.408	O47	-0.386
O4	-0.389	O50	-0.389
O8	-0.389	C44	0.346
O2	-0.312	C48	0.474
O53	-0.314	C6	0.475
C3	0.344		
Total energy/au		-595.661	
Total dipole moment/D		29.864	
HOMO		-0.311	
LUMO		0.007	

3.7.2.2.3. Description of the structure of $[Ti(LFX)_3]^{+4}$

Table 10 lists selected inter atomic distances and angles. The structure of complex with atomic numbering scheme is shown in Scheme 5. The complex consists of three units of lomfloxacin molecule with Ti(IV) ion. The complex is six-coordinate with octahedral environment around the metal ion. The Ti(IV) is coordinated to one O_{pyr} atom and one O_{car} atom of lomfloxacin ligand. The Ti-O72, Ti-O60 and Ti-O30 bond lengths (1.935Å, 1.931 Å and 1.936Å respectively) are shorter than that Ti-O70, Ti-O76 and Ti-O27 (1.943Å, 1.945 Å and 1.942Å, respectively). Also the angles around the central metal ion Ti(IV) with surrounding oxygen atoms vary from 83.04˚ to 175.37˚; these values agree with octahedron. The two lomfloxacin molecules are perpendicular on the plan occupied by the two oxygen atoms of the third molecule of lomfloxacin and central metal ion so the lomfloxacin molecules are not lying in the same plane. The bond angle O27TiO76, O27TiO60, O27TiO72, O27TiO70 and O30TiO72 are 86.09˚, 83.04˚, 170.83˚, 92.37˚and 96.20˚, which confirm that the three lomfloxacin molecules not exist in the same plane.

The Ti(IV) is bonded strongly with surrounded oxygen atoms of lomfloxacin more than that in sulfate and water complexes. Also, the charge accumulated on O_{car} (-0.450) and O_{pyr} (-0.337), in case of three molecules of lomfloxacin while, O_{car} (-0.451) and O_{pyr} (-0.374), in sulphate complex and O_{car} (-0.408), O_{pyr} (-0.389), in water complex. There is a strong interaction between central metal ion Ti(IV) and three lomfloxacin which become has charge equal +0.985 and more negative oxygen atoms in this complex greater than that in sulphate and water complexes, at which Ti(IV) becomes has less positively charge (+0.888) in sulphate complex and (+0.911) in water complex. The energy of this complex is -776.017 au and highly dipole 41.813D. For all these reasons the complex is more stable than sulphate and water complexes and Ti(IV) favor coordinated with three molecules of lomfloxacin more than two molecules of lomfloxacin with water or sulphate group to complete the octahedron structure. The net result is the Ti(IV) favor reacts with lomefloxacin by molar ratio 1:3 more than 1:2

and produced complex is treated as octahedral structure at which the angles around the central metal ion vary between 83.04˚ to 175.37˚ these result agree nicely with regular octahedron structure.



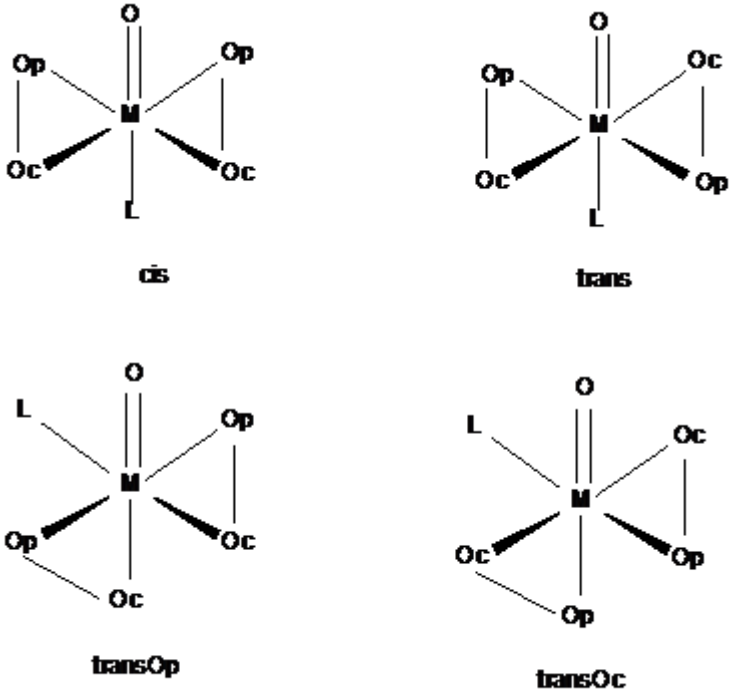
Scheme 5: Optimized geometrical structure of trans-isomer of $[Ti(LFX)_3]^{+4}$ complex by using B3LYP/CEP-31G.

Table 10: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[Ti(LFX)_3]^{+4}$ by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
Ti –O27	1.942	C2-O76	1.211
Ti –O30	1.926	C5-O60	1.349
Ti –O70	1.943	C5-O70	1.210
Ti –O72	1.935	C29-O30	1.349
Ti –O76	1.945	C29-O31	1.211
Ti –O60	1.931	C26-O27	1.210
C67-O70	1.211	C26-C28	1.362
C71-O72	1.348	C28-C29	1.364
C71-C73	1.211	C67-C69	1.364
C2-C4	1.362	C69-C71	1.364
C4-C5	1.364		
Bond angle (˚)			
O30 Ti O27	92.10	O6 Ti O72	92.12
O30 Ti O27	96.20	O76 Ti O70	86.91
O27 Ti O76	86.09	O30 Ti O76	170.71
O60 Ti O76	92.17	O27 Ti O60	83.04
O76 Ti O72	86.31	O27 Ti O70	92.37
O30 Ti O60	96.66	O6 Ti O70	175.37
O30 TiO70	84.06	O72 TiO70	92.34
O27TiO72	170.83		
Charges			
Ti	0.985	O76	-0.339
O30	-0.450	O70	-0.396
O31	-0.451	O73	-0.439
O27	-0.337	O72	-0.438
O60	-0.427	C71	0.499
O70	-0.429	C67	0.221
C2	0.404	C29	0.504
C5	0.505	C26	0.405
Total energy/au		-776.017	
Total dipole moment/D		41.813	
HOMO		-1.465	
LUMO		1.461	

3.7.2.3. The V(IV) lomfloxacin complex

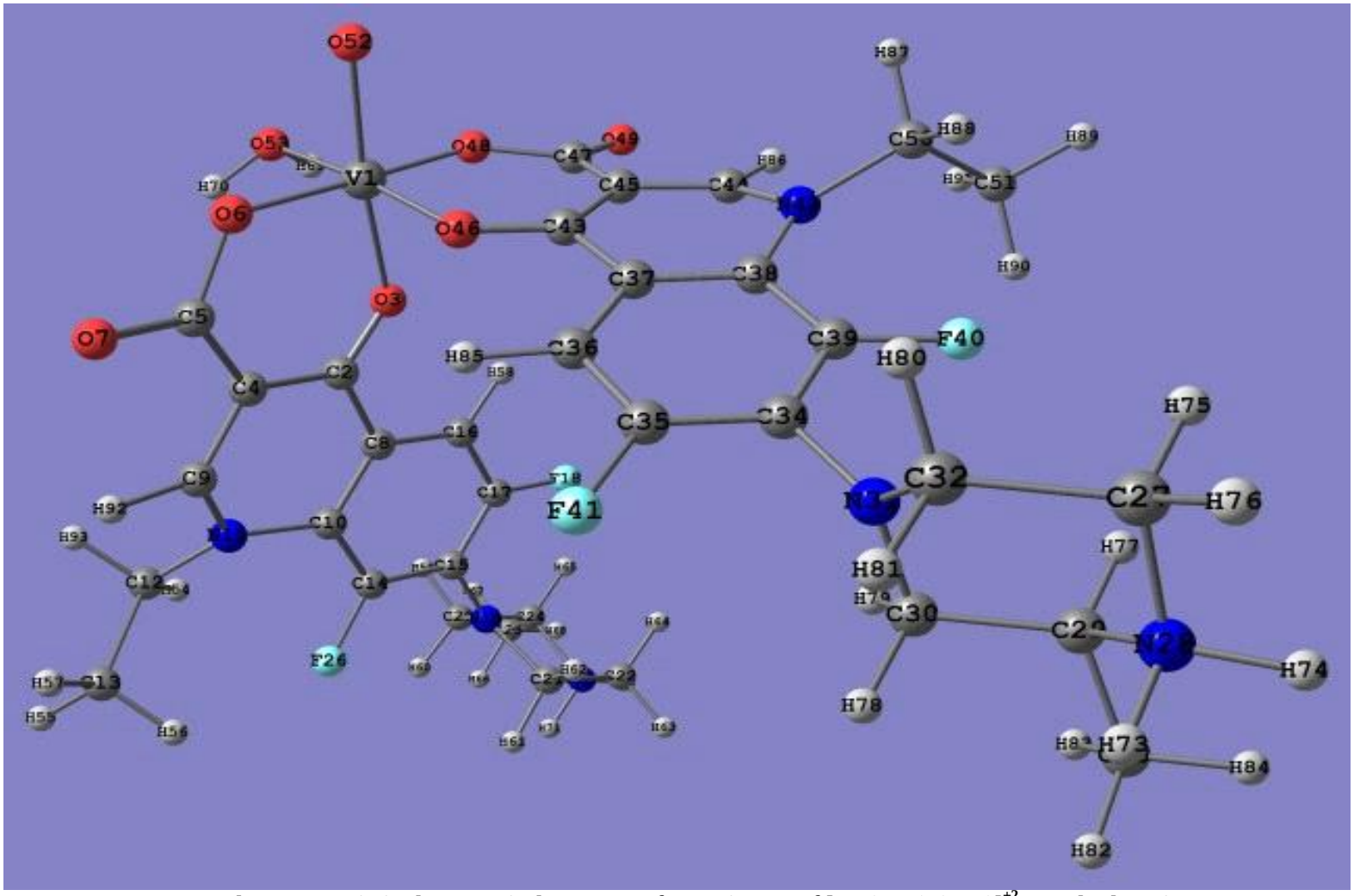
The structure of this complex did not determine by X-ray crystallography. In order to present a model for the complex, only the enantiomers having the two oxygen atoms can lie either at trans [76,77] or at cis [78,79] positions as shown in Scheme 6. The total energy for the two enantiomers were calculated theoretically by using DFT method combine with B3LYP/CEP-31G as basis set to determine the most stable isomer.



Scheme 6: The diastereoisomers of $[VO(LFX)_2(L)]$ complexes employed in theoretical calculations. Oc and Op are the carboxylate and the pyridone oxygen atoms, respectively of the lomfloxacin ligands, M is V(IV) in VO and L is H_2O molecule.

The V(IV) may be chelated with two molecules of lomfloxacin through O_{pyr} and O_{car} atoms from each molecule. The experimental data set that the result complex is six-coordinate so, the complex consists of four coordinate bonds with two lomfloxacin molecules and one coordinated bond with water theoretically the molecule beside oxygen atom of VO ion. In this part we study structure parameters of $[VO(LFX)_2(H_2O)]^{+2}$ complex. The energy of the isomers is almost equal as expected [80], it is difficult to distinguish between trans-isomer or cis isomers. Nevertheless, the trans Oc-isomer exhibit the lowest energy value and the lowest energy model structure is present in Scheme 7.

Table 11 lists selected inter atomic distances and angles. The structure of complex with atomic numbering scheme are shown in Scheme 7. The complex consists of two units of lomfloxacin molecule and one water molecule with V(IV) ion. The complex is six-coordinate with distorted octahedral environment around the metal ion. The V(IV) of VO ion is coordinated to one O_{pyr} atom and one O_{car} atom of lomfloxacin ligand and oxygen atom of water molecule. The V-O46 and V-O3 bond lengths are 1.851Å and 1.854Å, respectively, are longer than that V-O48 and V-O6 1.845Å and 1.842Å, respectively, and the bond distance between V-O_{H2O} is 1.892 Å [81]. Also the angles around the central metal ion V(IV)with surrounding oxygen atoms vary from 74.21 to 105.28˚; these values agree with these expected for octahedron[82].



Scheme 7: Optimized geometrical structure of trans-isomer of $[VO(LFX)_2(H_2O)]^{+2}$ complex by using B3LYP/CCEP-31G.

Table11: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[VO(LFX)_2(H_2O)]^{+2}$ by using DFT/B3LYP/CEP-31G.

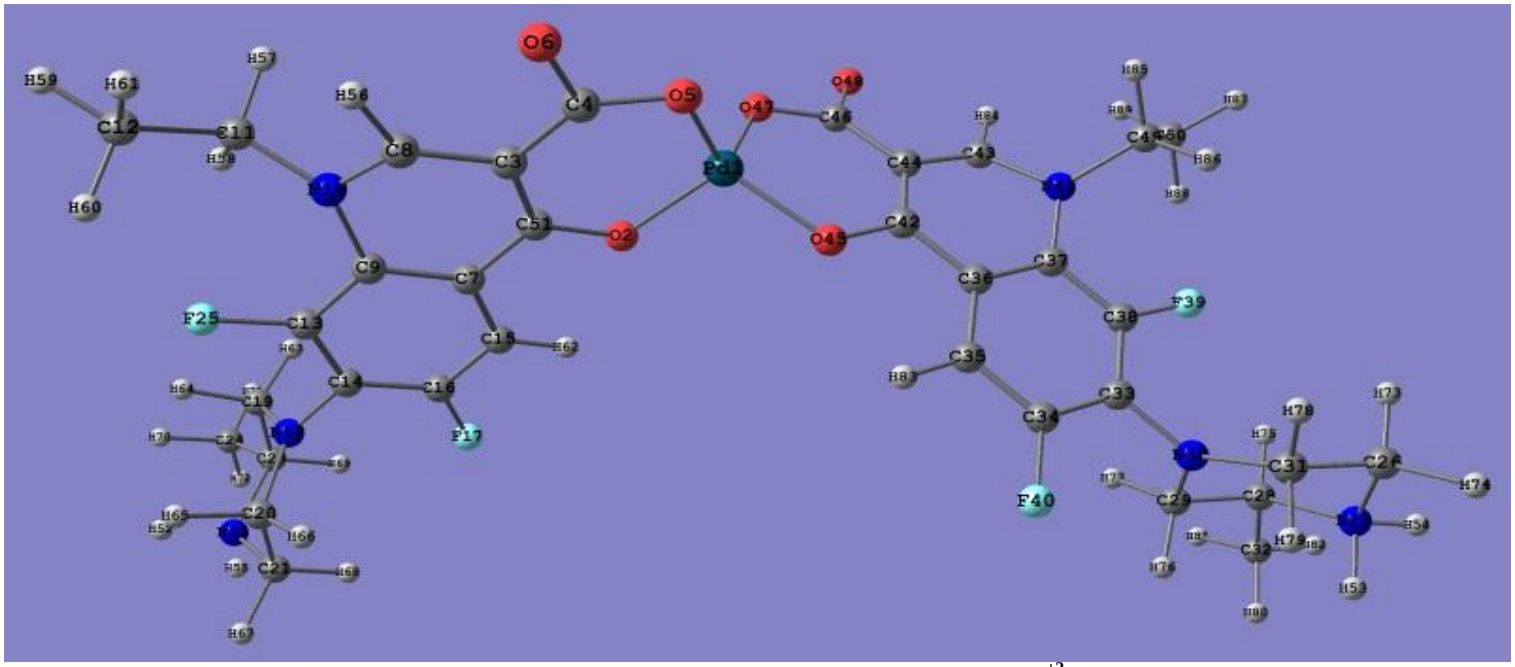
Bond length (Å)			
V-O3	1.854	C47-O48	1.345
V –O6	1.842	C47-O49	1.210
V –O46	1.851	C43-O46	1.211
V –O48	1.854	C5-O6	1.348
V –O52	1.787	C5-O7	1.211
V- O_{H2O}	1.892	C2-O3	1.211
C2-C4	1.362	C43-C45	1.362
C4-C5	1.364	C45-C47	1.364
Bond angle (˚)			
O3 V O6	95.55	O46 V O53	174.63
O46 V O48	95.58	O46 V O6	86.02
O46 V O52	93.43	O6 V O48	178.33
O48 V O3	85.07	O3VO52	174.31
O52 V O53	90.45	O53VO6	90.32
O53VO3	91.87	O46VO3	84.58
O48VO53	88.11	O52VO6	89.62
O48VO52	89.82		
Charges			
V	0.781	O6	-0.408
O46	-0.338	O7	-0.503
O48	-0.409	O52	-0.496
O49	-0.519	O53	-0.288
O3	-0.419	C43	0.283
C2	0.109	C47	0.484
C5	0.451		
Total energy/au		-555.798	
Total dipole moment/D		40.257	
HOMO		-1.225	
LUMO		1.976	

3.7.2.4. The Pd(II) Lomfloxacin complexes

The Pd(II) chelated with two molecules of lomfloxacin through four coordinate bonds via oxygen atom of carboxylic group and oxygen atom of pyridone group (O_{pyr} and O_{car} atoms). The experimental data set that the result complex is six-coordinate and consists of four coordinate bonds with two lomfloxacin molecules and two coordinated bonds with two chloride ions. In this part we study theoretically the two proposed structures of $[Pd(LFX)_2]^{+2}$ and $[Pd(LFX)_2(Cl)_2]$.

3.7.2.4.1. Description of the structure of $[Pd(LFX)_2]^{+2}$

Table 12 lists selected inter atomic distances and angles. The structure of complex with atomic numbering scheme are shown in Scheme 8. The Pd(II) is coordinated with two unites of lomfloxacin molecules through four coordinate bonds (O_{pyr} and O_{car} atoms) forming tetrahedral structure. The Pd-O_{pyr} bond lengths (1.83Å and 1.84Å) are shorter than the Pd-O_{car} (1.84Å and 1.85Å). Both are similar to these observed in related quinolone Pd(II) complex [83,84]. The angles around central metal ion with surrounded four oxygen atoms of lomfloxacin vary from 103.29˚ to 115.77˚, these values not deviated largely from these expected for square planar and agree nicely with tetrahedral structure. The distances between Pd-O_{car} are 1.84Å and 1.85Å and Pd-O_{pyr} are 1.83Å and 1.84Å [83], these values are agreement nicely with experimental data [83, 84]. The energy of this complex is -545.77 au and dipole moment is 24.56D.



Scheme 8: Optimized geometrical structure of $[Pd(LFX)_2]^{+2}$ complex by using B3LYP/CEP-31G.

Table 12: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[Pd(LFX)_2]^{+2}$ by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
Pd-O2	1.83 (1.990)	C46-O48	1.32 (1.245)
Pd –O5	1.85 (2.009)	C42-O45	1.33 (1.275)
Pd –O45	1.84 (2.006)	C4-O5	1.31 (1.278)
Pd –O47	1.84 (2.009)	C4-O6	1.32 (1.245)
C46-O47	1.31 (1.278)	C51-O2	1.34 (1.275)
Bond angle (˚)			
O2 Pd O5	103.29(95.76)	O2Pd O47	112.29
O2 Pd O45	109.97	O5 Pd O47	115.77(95.76)
O5PdO45	112.37	O45PdO47	103.30
Charges			
Pd	0.058	O47	-0.251
O2	-0.250	O48	-0.482
O5	-0.225	O45	-0.118
O6	-0.453	C4	0.490
C51	0.364	C46	-0.132
		C42	-0.223
Total energy/au		-545.77	
Total dipole moment/D		24.56	
HOMO		-8.858	
LUMO		0.161	

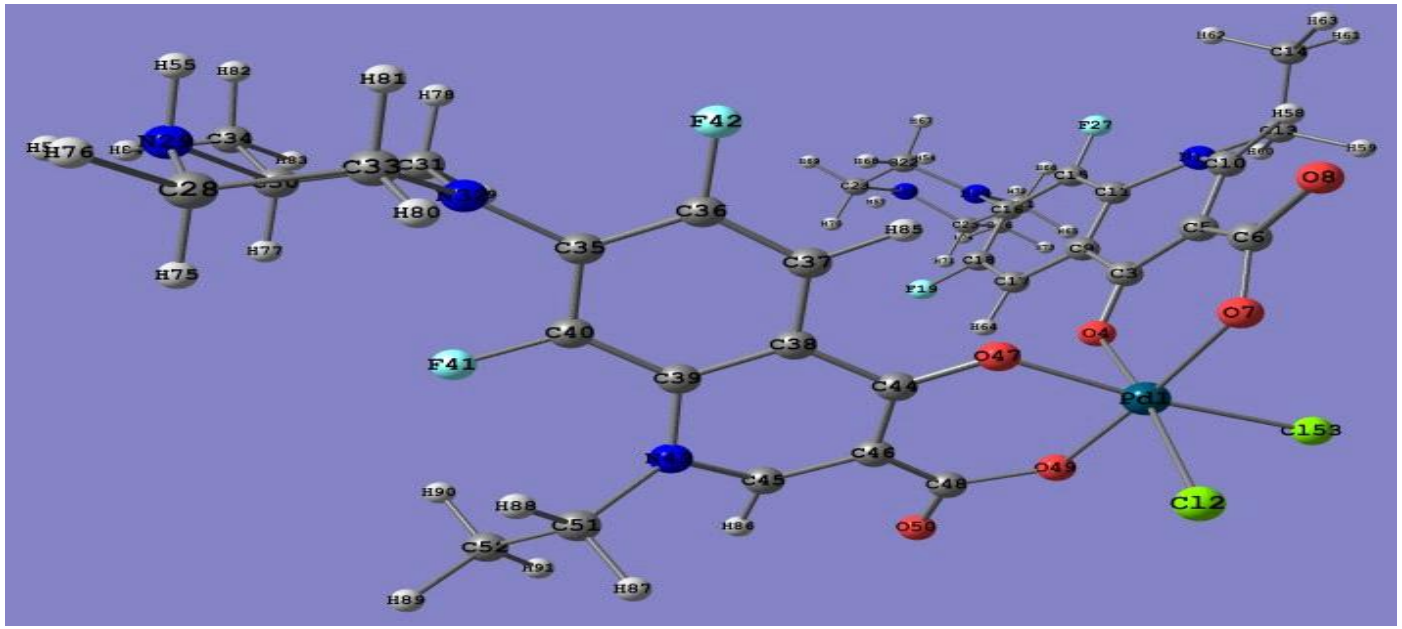
3.7.2.4.2. Description of the structure of $[Pd(LFX)_2(Cl)_2]$

Scheme 9 shows the optimized geometrical structure of the complex with the atomic numbering scheme selected bond distances and angles are given in Table 13.

The Pd(II) at a crystallographic inversion center, is in a distorted octahedral environment. In the axial plane the metal ion is coordinated by four oxygen atoms (O_{pyr} and O_{car}) of two lomfloxacin at the distances vary from 1.9Å to 1.91Å, these bond lengths are similar to those observed in related compounds [83,84]. The difference in the carboxylate O7-C6 and O8-C6 (1.35Å and 1.21Å) [85], confirms the formation of bond between the ionic carboxylate oxygen atom and Pd(II) these bond lengths are virtually identical in uncomplexed lomfloxacin ligand. The octahedral coordination environment is completed by two chloride ions. The bond distance between Pd-O4 and Pd-O7 are 1.91Å and 1.9Å [83,84] while the distance between Pd-Cl is 2.28Å [88]. The Pd-O4 and Pd-O47 bond lengths (1.91Å and 1.92Å, respectively,) are longer than that Pd-O7 and Pd-O49 (1.9Å and 1.89Å, respectively,). Both are similar to these observed in related quinolone Pd(II) compounds [83,84]. The bond angles around the central Pd(II) vary from 83.47˚ to 174.47˚; these values not differ significantly from these expected for octahedron.

The distances and angles within the ligand moiety are similar to those described for free lomfloxacin [60-63]. It is important to note that, in the complex, the C6-O7 and C48-O48 bond lengths become and slightly longer than those found in free ligand of lomfloxacin.

The bond distances between Pd(II) and surrounded oxygen atoms of lomfloxacin in tetrahedral complex are shorter than that in octahedral complex as shown in Tables (11 and 12). Also the charge accumulated on O_{car} (-0.361 and -0.314) and O_{pyr} (-0.335 and -0.172), in octahedral complex while, O_{car} (-0.225 and -0.251) and O_{pyr} (-0.25 and -0.118), in tetrahedral complex. There is a strong interaction between Pd(II) which become has charge equal +0.175 and more negative oxygen atoms in octahedral complex greater than that in tetrahedral complex, at which Pd(II) becomes has less positively charge (+0.058) in tetrahedral complex. The energy of the octahedral complex is -575.781 au and the dipole moment is very high 45.77D. For all these reasons the octahedral complex is more stable than tetrahedral complex and Pd(II) favor coordinated with two molecules of lomfloxacin with four coordinated bonds and completes the octahedron structure by bonding with two chloride ions more than bonding with two molecules of lomfloxacin to form tetrahedron structure.



Scheme 9: Optimized geometrical structure of $[Pd(LFX)_2(Cl)_2]$ complex by using B3LYP/CEP-31G.

Table 13: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[Pd(LFX)_2Cl_2]$ by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
Pd-O4	1.92 (1.990)	C6-O8	1.21 (1.245)
Pd –O47	1.91 (2.009)	C6-O7	1.35 (1.275)
Pd –O7	1.90 (2.006)	C44-O47	1.21 (1.278)
Pd –O49	1.89 (2.009)	C48-O50	1.21 (1.245)
C3-O4	1.21 (1.278)	C48-O49	1.34 (1.275)
Pd-Cl	2.28 (2.314)		
Bond angle (˚)			
O47 Pd O49	92.86(95.76)	O4Pd O49	84.98
O4 Pd O7	93.48	O7 Pd O47	83.47
O4PdO47	84.61	O49PdO7	176.15
O4PdCl2	174.47	O47PdCl2	91.08 (95.76)
Cl2PdO49	91.79	O49PdCl53	90.99
O4PdCl53	90.25	O7PdCl53	92.54
O7PdCl2	89.45	O47PdCl53	173.27
		Cl2PdCl53	94.29
Charges			
Pd	0.175	O47	-0.172
O4	-0.335	O49	-0.314
O7	-0.361	O50	-0.507
O8	-0.498	C44	-0.249
C3	0.066	C48	-0.144
C6	0.505	Cl2	-0.665
		Cl53	0.062
Total energy/au		-575.781	
Total dipole moment/D		45.77	
HOMO		-0.664	
LUMO		0.062	

3.7.2.5. The Ce(IV) lomfloxacin complexes

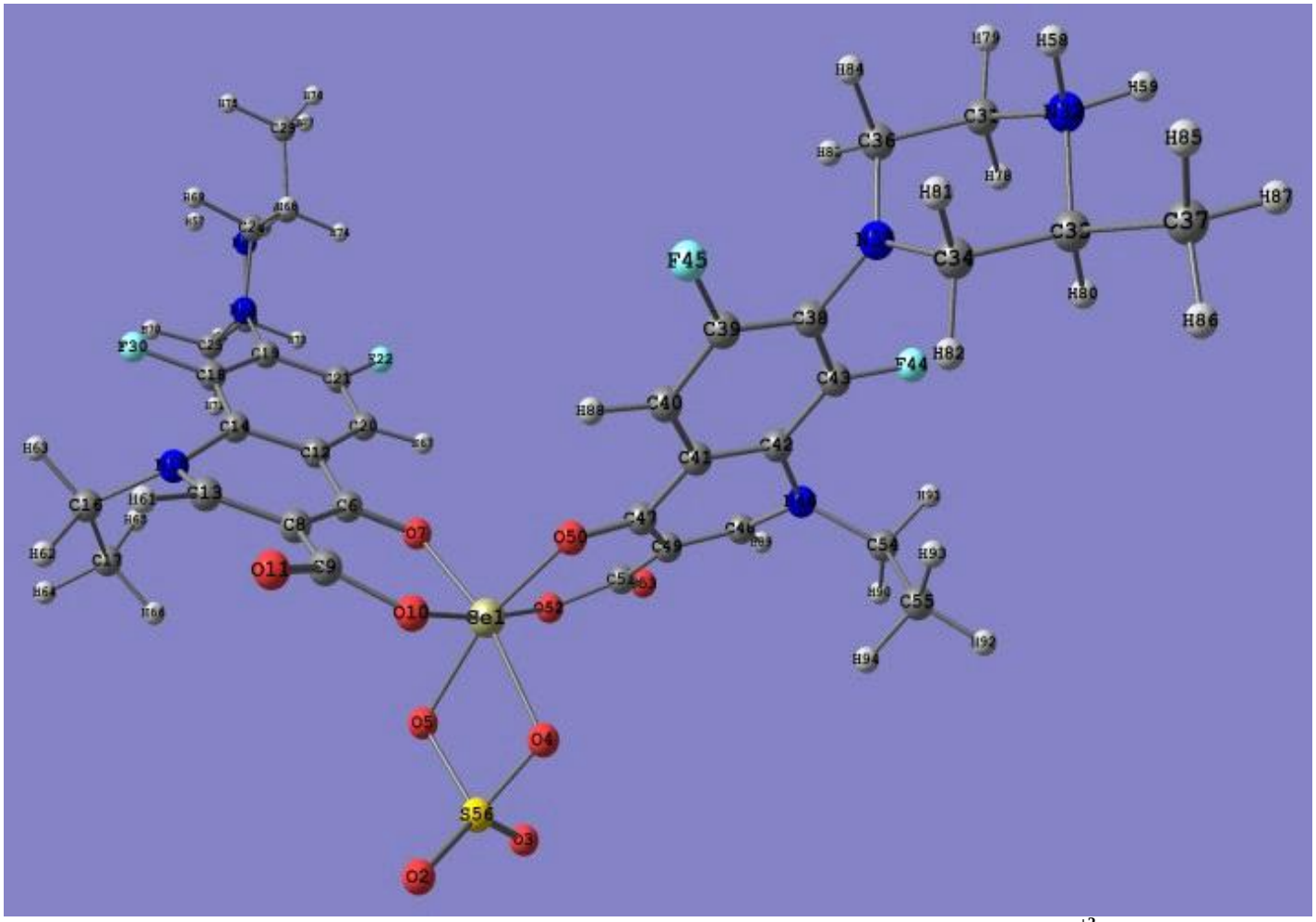
The Ce(IV) chelated with two or three molecules of lomfloxacin through four or six coordinate bonds (O_{pyr} and O_{car} atoms). The experimental data set that the result complex is six-coordinate so, the complex consists of four coordinate bonds with two lomfloxacin molecules and two coordinated bonds with water molecules or with two oxygen atoms of sulfato group mr six coordinate bond with three lomfloxacin molecules. In this part we study theoretically the two structures of $[Ce(LFX)_2(SO_4)]^{+2}$, $[Ce(LFX)_2(H_2O)_2]^{+4}$ and $[Ce(LFX)_3]^{+4}$ to detect which of them is more stable than other.

3.7.2.5.1. Description of the structure of $[Ce(LFX)_2(SO_4)]^{+2}$

Scheme 10 shows the optimized geometrical structure of the complex with the atomic numbering scheme selected bond distances and angles are given in Table 14. The suggested complex is composed of $[Ce(LFX)_2(SO_4)]^{+2}$.The Ce(IV) , at a crystallographic inversion center, is in a distorted octahedral environment. In the equatorial plane the metal ion is coordinated by four oxygen atoms (O_{pyr} and O_{car}) of two lomfloxacin at the distances vary from 1.930Å to 1.943Å, these bond lengths are similar to those observed in related compounds [87-89]. The difference in the carboxylate O10-C9 and O11-C9 (1.348Å and 1.211Å) [64], confirms the formation of bond between the ionic carboxylate oxygen atom and Ce(IV). The octahedral coordination environment is completed by two oxygen atoms of sulfato group. The bond distance between Ce-O10 is [92,93] and Ce-O7 are 1.930Å and 1.943Å [87,89-91] while the distance between Ce-O of sulphato group are 1.992-1.993Å [94,95]. The bond angles around the central metal ion Ce vary from 72.18˚ to 173.62˚; these values differ significantly from these expected for a regular octahedron.

In the equatorial plane the Ce(IV) bonded with two oxygen atoms (O7 and O10) of lomfloxacin molecule in the same plane which perpendicular to the other plane occupied by other two oxygen atom (O50 and O52) of other lomfloxacin molecule. The bond angle O7CeO52 and O7CeO50 are 85.17˚ and

104.62˚. The sulfato group not lying in the same plane but out of plane in twisting form, the bond angle O50CeO5 is 163.82˚, so the oxygen atom of sulphato group lying trans respect to one oxygen atom (O_{pyr}) of one lomfloxacin molecule, while the angle O4CeO10 is 90.23˚, so the other oxygen atom of sulphato group lying trans respect to the oxygen atom (O_{car}) of other lomfloxacin mol and ecule. The dihedral angle O3S56O5Ce and O2S56O4Ce are -107.43˚ and 107.49˚, which means that the two oxygen atoms of sulphato group (O2 and O3) lying in opposite direction to each other and out of plane occupied by other atoms. The energy of this complex is -538.504 au and the dipole moment is weak 7.54D, so this complex is less stable.



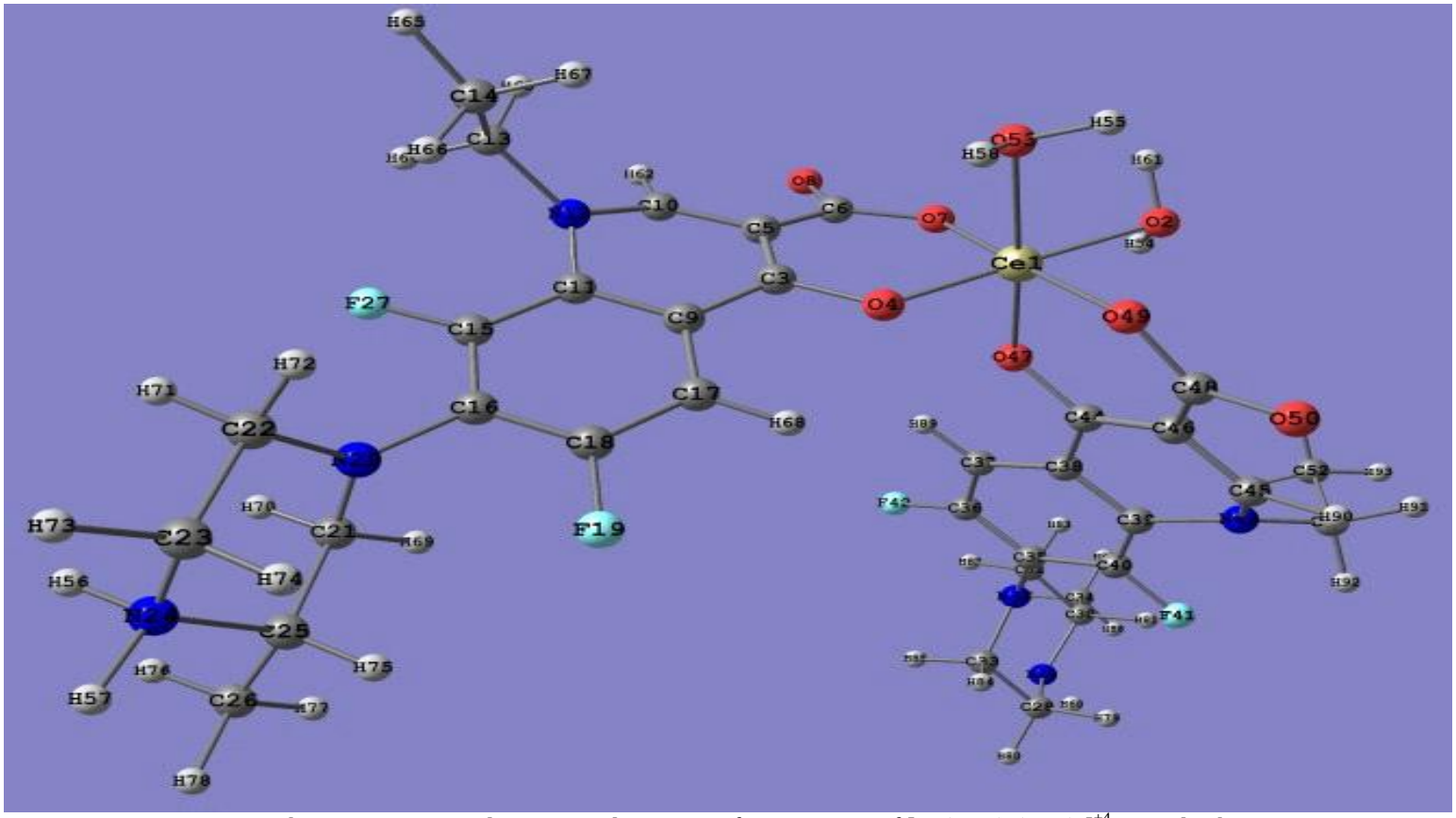
Scheme 10: optimized geometrical structure of trans-isomer of $[Ce(LFX)_2(SO_4)]^{+2}$ complex by using B3LYP/CEP-31G.

Table 14: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[Ce(LFX)_2(SO_4)]^{+2}$ by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
Ce-O7	1.943	C9-O11	1.21 1
Ce –O10	1.931	C9-O10	1.348
Ce –O50	1.943	C6-O7	1.211
Ce –O52	1.932	C47-O50	1.211
Ce –O4	1.993	C51-O52	1.348
Ce -O5	1.992	C51O53	1.211
C6-C8	1.363	C47-C49	1.363
C8-C9	1.364	C49-C51	1.364
Bond angle (˚)			
O7CeO10	91.52	O10CeO50	84.32
O5CeO10	94.89	O7CeO5	91.54
O52CeO10	173.62	O7CeO52	85.17
O10CeO4	90.23	O7CeO4	163.72
O52CeO50	91.23	O52CeO4	94.46
O5CeO52	90.64	O7CeO50	104.62
O4CeO5	72.18	O5CeO50	163.82
		O4CeO50	91.65
Charges			
Ce	0.713	O53	-0.413
O10	-0.413	O4	-0.502
O7	-0.314	O5	-0.529
O11	-0.407	S56	1.318
O50	-0.311	O2	-0.613
O52	-0.412	O3	-0.621
Total energy/au		-538.504	
Total dipole moment/D		7.54	
HOMO		-0.365	
LUMO		3.151	

3.7.2.5.2. Description of the structure of $[Ce(LFX)_2(H_2O)_2]^{+4}$

Table 15 lists selected inter atomic distances and angles. The structure of complex with atomic numbering scheme are shown in Scheme 11. The complex consists of two lomfloxacin molecules and two water molecules with Ce(IV). The complex is six-coordinate with distorted octahedral environment around the metal ion. The Ce(IV) is coordinated with (O_{pyr} and O_{car} atoms) lomfloxacin and two O_{H2O} atoms for water. The Ce-O49 and Ce-O7 bond lengths (1.935Å and 1.936Å, respectively) are longer than that Ce-O47 and Ce-O4 (1.89Å and 1.889Å, respectively). Also, the angles around the central metal ion Ce(IV) with surrounding oxygen atoms vary from 84.97˚ to 176.24˚; these values agree nicely with octahedron. The two lomfloxacin molecules are perpendicular to each other they are not lying in the same plane the bond angle O4CeO49 is and O7CeO47 are 88.45˚ and 84.97˚, which confirm that the two lomfloxacin molecules not exist in the same plane. The two water molecules bonded with Ce(IV) not exist in trans position to each other but exist as cis to each other, the bond angle O2CeO53 is 88.23˚. The energy of this complex is -596.512 au and highly dipole 25.345D.



Scheme 11: Optimized geometrical structure of trans-isomer of $[Ce(LFX)_2(H_2O)_2]^{+4}$ complex by using B3LYP/CEP-31G.

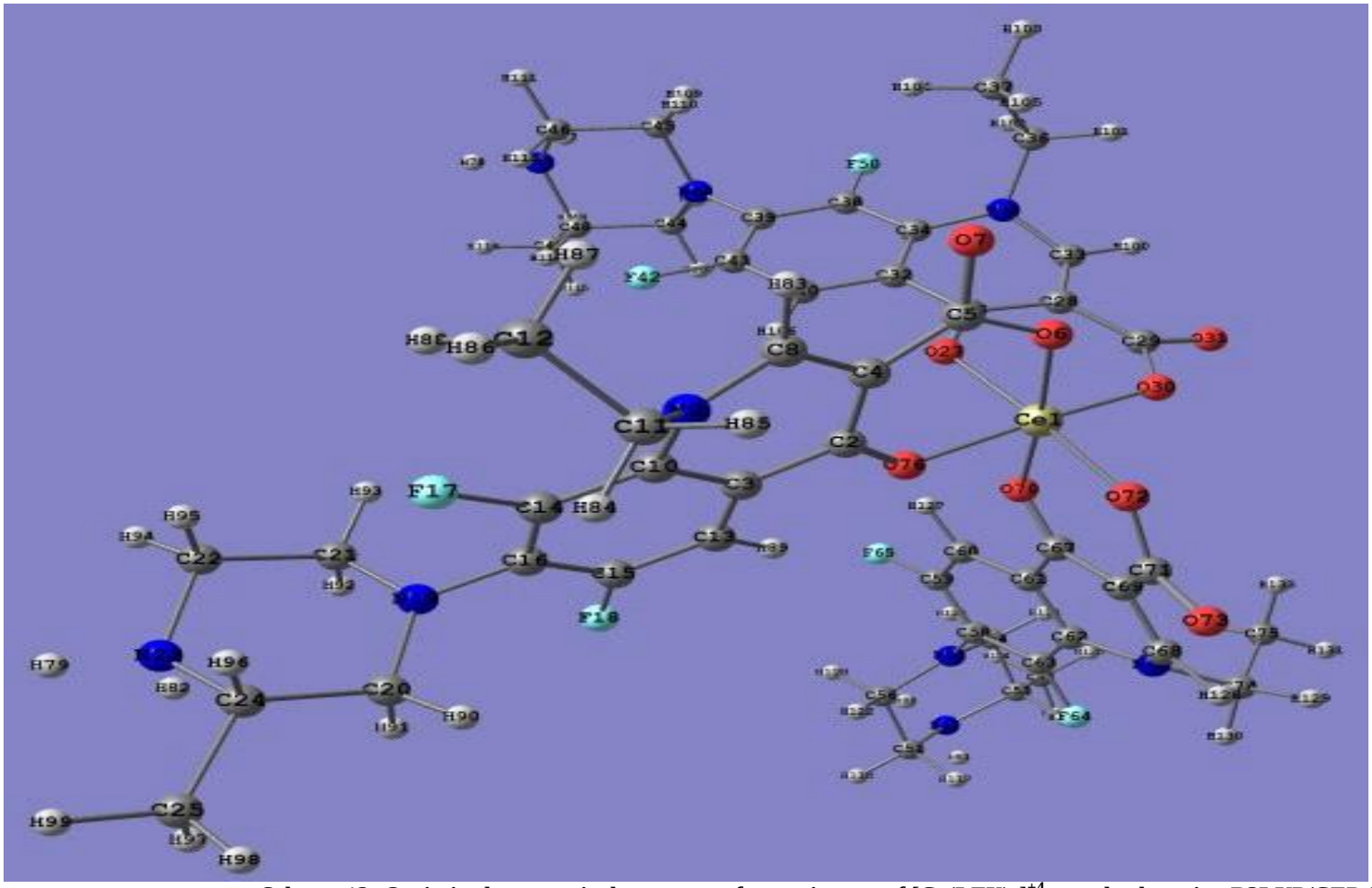
Table 15: Equilibrium geometric parameters bond lengths (Å), bond angles (˚) and charge density of $[Ce(LFX)_2(H_2O)_2]^{+4}$ by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
Ce-O2	2.005	C6-O8	1.291
Ce –O53	2.003	C3-O4	1.361
Ce –O7	1.936	C48-O50	1.291
Ce –O4	1.889	C44-O47	1.358
Ce –O47	1.890	C48-O49	1.321
Ce –O49	1.935	C46-C48	1.382
C6-C7	1.320	C44-C46	1.320
C5-C6	1.382		
Bond angle (˚)			
O4CeO7	95.22	O47CeO4	91.21
O2CeO7	89.83	O2CeO4	174.46
O7CeO47	84.97	O53CeO47	174.26
O49CeO7	176.24	O53CeO4	89.57
O2CeO47	91.48	O47CeO49	94.13
O53CeO7	89.29	O2CeO49	86.53
O49CeO4	88.45	O53CeO49	91.57
		O53CeO2	88.23
Charges			
Ce	0.899	O49	-0.461
O7	-0.449	O2	-0.281
O4	-0.379	O53	-0.282
O8	-0.469	O47	-0.365
		O50	-0.493
Total energy/au		-596.512	
Total dipole moment/D		25.345	
HOMO		-0.251	
LUMO		0.013	

3.7.2.5.3. Description of the structure of $[Ce(LFX)_3]^{+4}$

Table 16 lists selected inter atomic distances and angles. The structure of complex with atomic numbering scheme are shown in Scheme 12. The complex consists of three units of lomfloxacin molecule with Ce(IV). The complex is six-coordinate with regulare octahedral environment around the metal ion. The Ce(IV) is coordinated with O_{pyr} and O_{car} atoms of lomfloxacin ligand. The Ce-O27, Ce-O76 and Ce-O70 bond lengths (1.942Å, 1.942Å and 1.943Å, respectively,) are longer than that Ce-O30, Ce-O72 and Ce-O6 (1.934Å, 1.935Å and 1.936Å, respectively. Also the angles around Ce(IV) with surrounding oxygen atoms vary from 84.06˚ to 175.38˚; these values agree nicely with a regular octahedron. The one molecule of lomfloxacin and metal ion lying in one plane while the other two lomfloxacin molecules are perpendicular to each other they are not lying in the same plane the bond angle O76CeO30 and O76CeO72 are 170.71˚ and 86.31˚, which confirm that the two lomfloxacin molecules not exist in the same plane occupied by third molecule of lomfloxacin.

The Ce(IV) is bonded strongly with surrounded oxygen atoms of lomfloxacin in this case more than that in sulfate and water complexes. Also, the charge accumulated on O_{car} (-0.471) and O_{pyr} (-0.393), so there is a strong interaction between central Ce(IV) which become has charge equal +0.983 and more negative oxygen atoms in this complex greater than that in sulphate and water complexes, at which Ce(IV) becomes has less positively charge (+0.713 and +0.899) in sulphate and water complexes, respectively. The energy of this complex is -685.71 au and highly dipole 32.753D. For all these reasons the $[Ce(LFX)_3]^{+4}$ complex is more stable than sulphate and water complexes and Ce(IV) favor coordinated with three molecules of lomfloxacin more than two molecules of lomfloxacin with water or sulphate group to complete the octahedron structure. The net result indicated that the Ce(IV) favor reaction with lomfloxacin by molar ratio 1:3 more than 1:2 and the produced complex is treated as octahedral structure at which the angles around the central metal ion vary between 84.06˚ to 175.38˚ these result agree nicely with regular octahedron structure.



Scheme 12: Optimized geometrical structure of trans-isomer of $[Ce(LFX)_3]^{+4}$ complex by using B3LYP/CEP-31G.

Table 16: Equilibrium geometric parameters bond lengths (Å), bond angles (°) and charge density of $[Ce(LFX)_3]^{+4}$ by using DFT/B3LYP/CEP-31G.

Bond length (Å)			
Ce-O30	1.934	C5-O7	1.210
Ce –O27	1.943	C5-O6	1.349
Ce –O6	1.936	C2-O76	1.212
Ce –O76	1.942	C29-O31	1.211
Ce –O70	1.942	C29-O30	1.349
Ce –O72	1.935	C26-O27	1.210
C2-C4	1.362	C28-C29	1.364
C4-C5	1.364	C26-C28	1.362
C67-C69	1.363	C67-O70	1.211
C69-C71	1.364	C71-O72	1.348
		C71-O73	1.213
Bond angle (°)			
O30CeO2	92.10	O30CeO76	170.71
O70CeO72	92.34	O6CeO70	175.38
O76CeO6	92.17	O30CeO60	96.66
O70CeO76	86.91	O27CeO70	92.37
O72CeO6	92.13	O70CeO72	170.84
O30CeO70	84.06	O72CeO76	86.31
O30CeO72	94.20		
Charges			
Ce	0.984	O70	-0.391
O6	-0.463	O72	-0.468
O7	-0.475	O73	-0.479
O76	-0.381	O30	-0.471
O31	-0.481	O27	-0.393
Total energy/au		-685.710	
Total dipole moment/D		32.753	
HOMO		-0.958	
LUMO		1.151	

Supplementary materials

1. The kinetics data

The kinetic thermodynamic parameters such as energy of activation (E^*), enthalpy (ΔH^*), entropy (ΔS^*) and free energy change (Gibbs free energy) of the decomposition (ΔG^*), were evaluated graphically by empolying the Coats-Redfern (CR) [1] and Horowitz-Metzger (HM) [2]

$$\ln\left[\frac{-\ln(1-\alpha)}{T^2}\right] = \frac{-E^*}{RT} + \ln\left[\frac{AR}{\varphi E^*}\right]$$

$$\log\left[\log\left(\frac{w_\alpha}{w_\gamma}\right)\right] = \frac{E^*\theta}{2.303RT_s^2} - \log 2.303$$

Where α and φ are the fraction of the sample decomposed at time t and the linear heating rate, respectively. R is the gas constant and $\theta = T - T_s$, $w_\gamma = w_\alpha - w$, w_α=mass loss at the completion of the reaction; w=mass loss up to time t. A plot of $\ln\left[\frac{-\ln(1-\alpha)}{T^2}\right]$ against 1/T or $\log\left[\log\left(\frac{w_\alpha}{w_\gamma}\right)\right]$ versus θ was found to be linear and the energy of activation in kJ mol^{-1} was calculated from the slope (Fig. S1). The entropy of activation ΔS^* in $Jmol^{-1}K^{-1}$ was calculated by using equation, $\Delta S^* = R[\ln(Ah/KT_s)]$. The enthalpy of activation, ΔH^*, and Gibbs free energy, ΔG^*, were calculated from:
$\Delta H^* = E^* - RT$ and $\Delta G^* = \Delta H^* - T\Delta S^*$

The data were summarized in table 1and the activation energies of decomposition were found to be in the range 11.9-137.97 kJ mol^{-1}. The greater positive values of E^* indicate that the processes involving in translational, vibrational, rotational states and a changes in mechanical potential energy for complexes. The high values of the activation energies reflect the thermal stability of the four complexes. The entropy of activation was found to have negative values in all the complexes which indicate that decomposition reactions proceeded with a lower rate than the normal ones. Also, according to the kinetic data obtained, all of the complexes have negative entropy, which indicate that activated complexes have more ordered systems than reactants [2,3].

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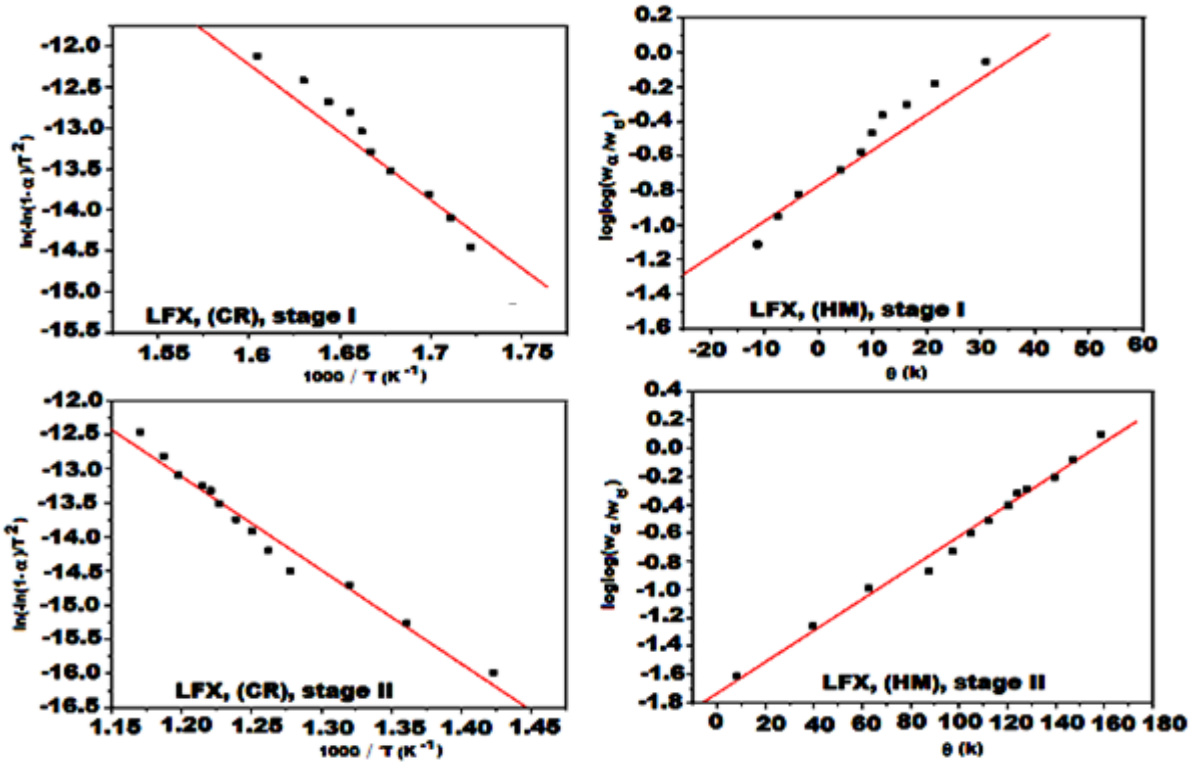
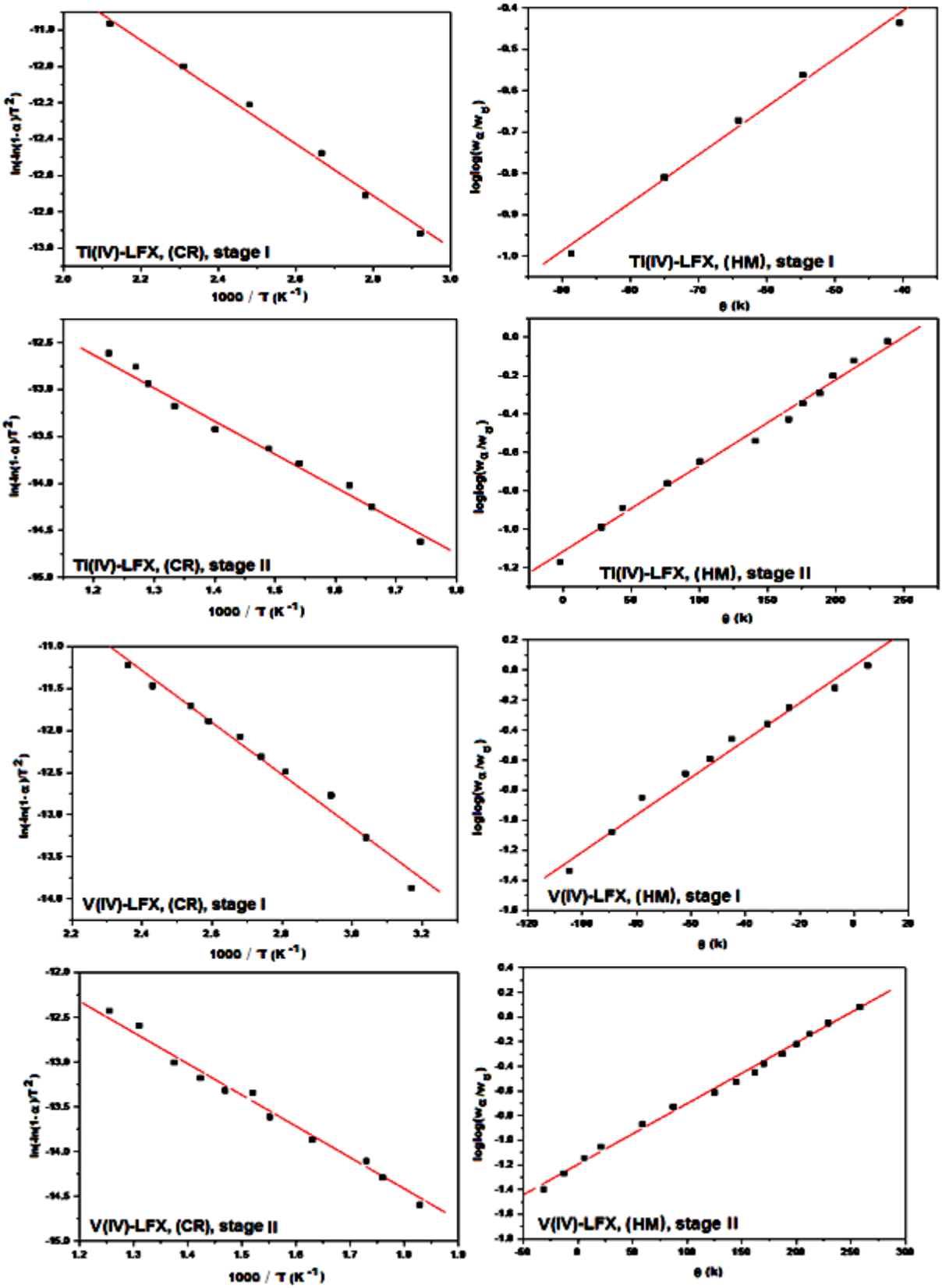
Table S1:

Thermal behavior and kinetic parameters determined using the Coats–Redfern (CR) and Horowitz–Metzger (HM) operated for Lomefloxacin and their complexes.

Compounds	Decomposition Range (K)	T_s (K)	Method	Parameter					R^a	SD^b
				E^* (kJ mol^{-1})	A (s^{-1})	ΔS^* (J mol^{-1} K^{-1})	ΔH^* (kJ mol^{-1})	ΔG^* (kJ $mol^{-1)}$		
LFX	523-673	592	CR	137.71	1.24210^{11}	-38.23	132.79	155.42	0.8885	0.33
			HM	137.97	3.33×10^{11}	-30.03	133.04	150.82	0.8781	0.16
	703-873	695	CR	114.12	6.73×10^{4}	-159.52	108.34	219.21	0.9749	0.17
			HM	102.66	6.27×10^{6}	-121.82	96.88	181.55	0.9886	0.05
$[Ti(LFX)_3](SO_4)_2.2H_2O$	290-523	411	CR	11.9	1.10	-247	8.5	110	0.92	0.13
			HM	32.3	1.63	-247	28.9	130	0.96	0.05
	523-853	575	CR	29.3	3.74	-239	24.5	162	0.94	0.16
			HM	28.5	18.99	-226	23.7	154	0.98	0.06
$[VO(LFX)_2H_2O]SO_4.9H_2O$	298-462	418	CR	25.7	3.07×10^{2}	-2.0	22.2	106	0.98	0.11
			HM	40.2	1.38×10^{4}	-168	36.7	37	0.98	0.08
	462-873	561	CR	29.0	4.85	-237	24.3	157	0.90	0.29
			HM	29.5	0.10	-269	24.8	176	0.94	0.12
$[Pd(LFX)_2Cl_2].4H_2O$	308-503	471	CR	30.9	9.65×10^{3}	-172.4	35.1	116	0.94	0.2
			HM	59.5	6.04×10^{5}	-138	55.6	121	0.94	012
	503-823	636	CR	55.6	2.78×10^{3}	-185	50.3	168	0.98	0.14
			HM	69.7	5.19×10^{4}	-161	64.4	167	0.98	0.06
$[Ce(LFX)_3](SO_4)_2.4H_2O$	523-823	564	CR	22.0	0.94	-251	17.3	159	0.92	0.17
			HM	24.4	7.9	-233	19.7	151	0.96	0.08

a=correlation coefficients of the Arrhenius plots and b=standard deviation


LFX, (CR), stage I
1000 / T (K^{-1})
LFX, (HM), stage I
θ (k)
LFX, (CR), stage II
1000 / T (K^{-1})
LFX, (HM), stage II
θ (k)


Ti(IV)-LFX, (CR), stage I
1000 / T (K-1)
Ti(IV)-LFX, (HM), stage I
θ (k)
Ti(IV)-LFX, (CR), stage II
1000 / T (K-1)
Ti(IV)-LFX, (HM), stage II
θ (k)
V(IV)-LFX, (CR), stage I
1000 / T (K-1)
V(IV)-LFX, (HM), stage I
θ (k)
V(IV)-LFX, (CR), stage II
1000 / T (K-1)
V(IV)-LFX, (HM), stage II
θ (k)

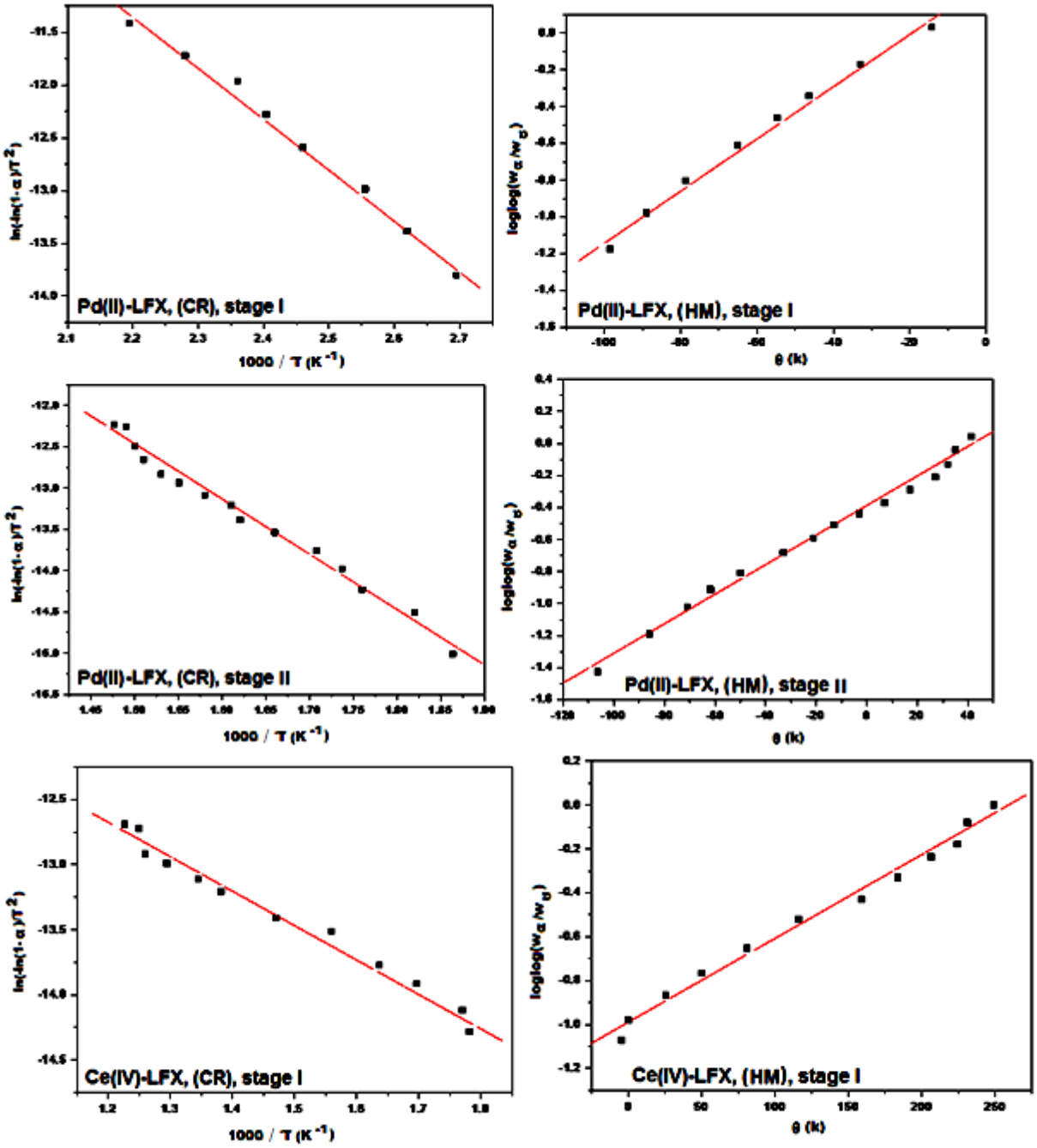
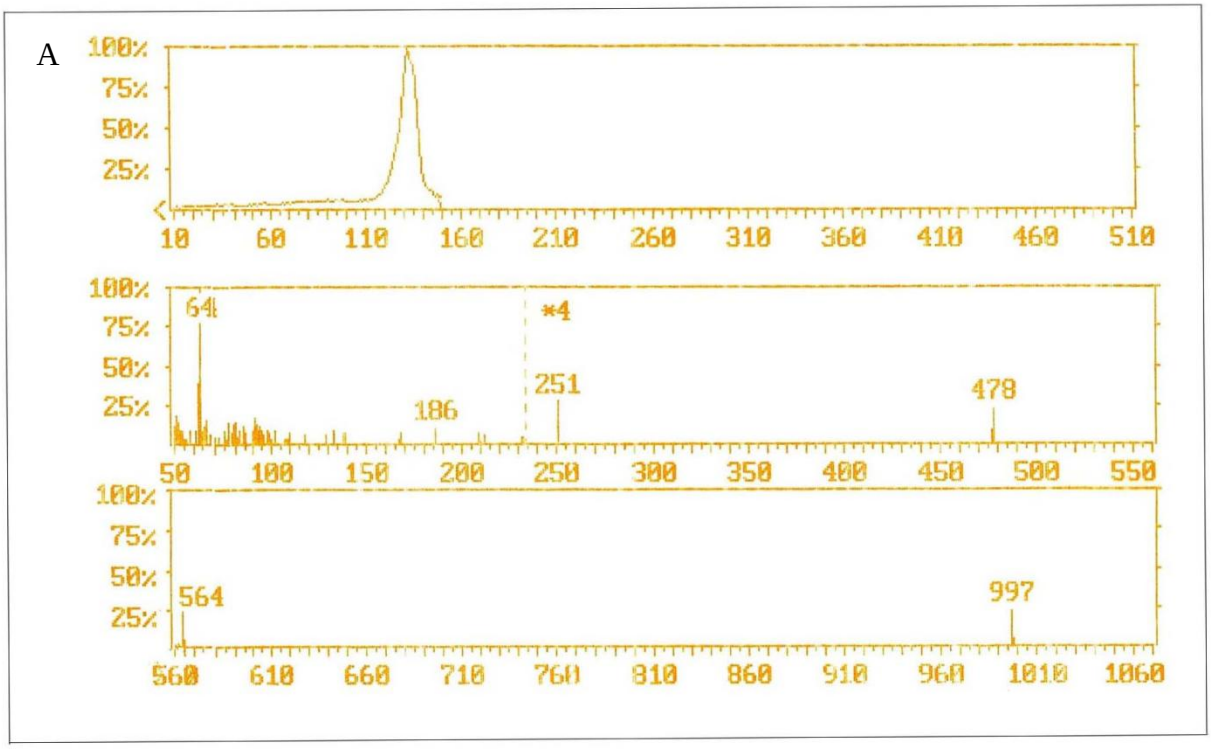
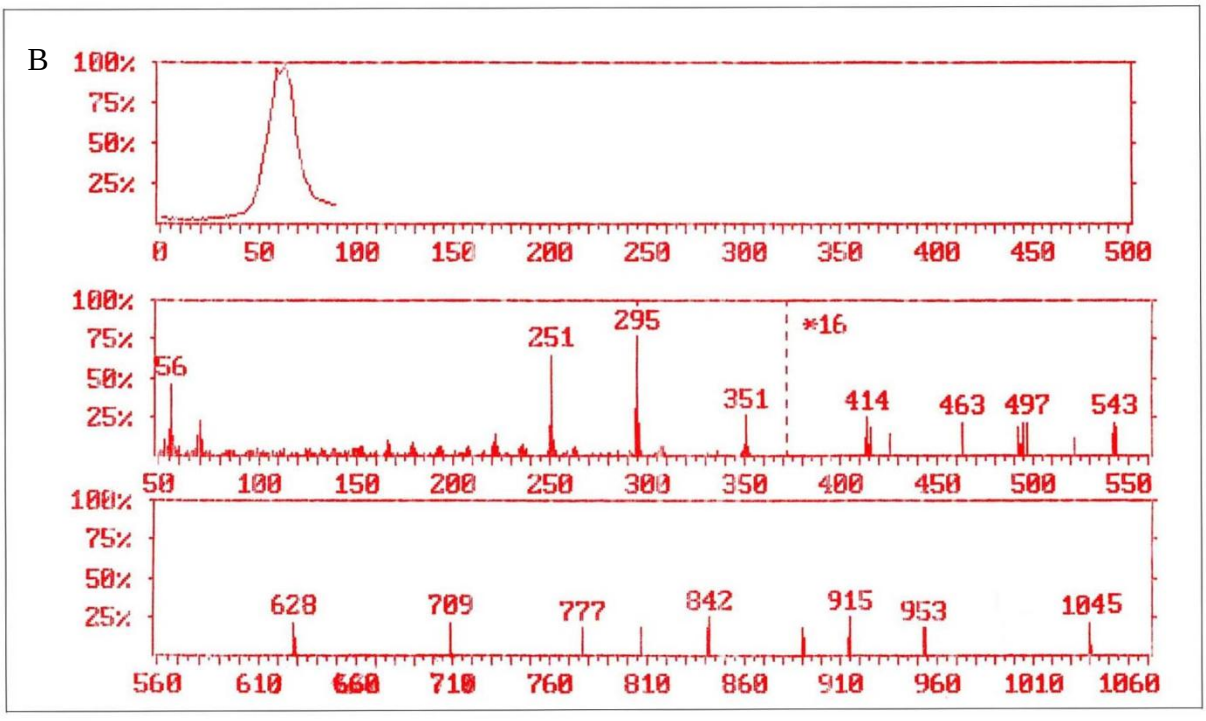


Fig. S1. The diagrams of kinetic parameters of lomefloxacin and their complexes using Coats-Redfern (CR) and Horowitz-Metzger (HM) equations.

A


100%
75%
50%
25%
10 60 110 160 210 260 310 360 410 460 510
64
*4
186
251
478
50 100 150 200 250 300 350 400 450 500 550
564
997
560 610 660 710 760 810 860 910 960 1010 1060

B


100%
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0 50 100 150 200 250 300 350 400 450 500
56
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*16
351
414
463
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50 100 150 200 250 300 350 400 450 500 550
628
709
777
842
915
953
1045
560 610 660 710 760 810 860 910 960 1010 1060

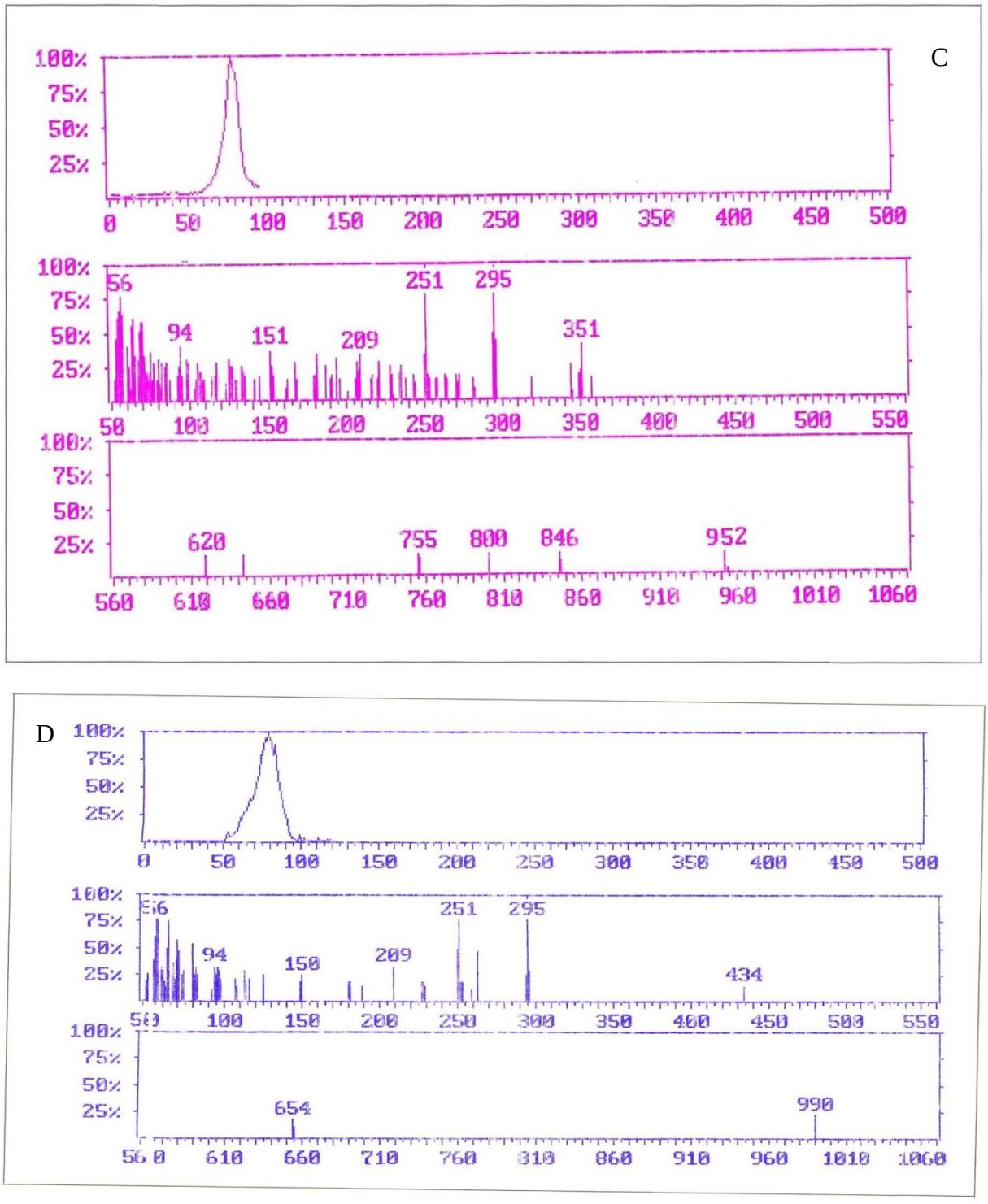

Fig. S2: Mass spectra diagrams of (A) $[Ti(LFX)_3](SO_4)_2.2H_2O$, (B) $[VO(LFX)_2H_2O]SO_4.9H_2O$, (C) $[Pd(LFX)_2Cl_2].4H_2O$ and (D) $[Ce(LFX)_3](SO_4)_2.4H_2O$ complexes.

Conclusion

The four new metal complexes of lomefloxacin with Ti(IV), V(IV), Pd(II) and Ce(IV) were prepared and isolated as solids and formulated as $[Ti(LFX)_3](SO_4)_2.2H_2O$, $[VO(LFX)_2H_2O]SO_4.9H_2O$, $[Pd(LFX)_2Cl_2].4H_2O$ and $[Ce(LFX)_3](SO_4)_2.4H_2O$. The four complexes have been characterized using melting point, molar conductance,

magnetic properties, elemental analysis, IR, UV-Vis., ^{1}H NMR, mass spectra and thermal analyses. From these techniques, it may observed that the carbonyl and carboxylic groups in all complexes shifted to lower values in IR spectra support the chelation effect via carboxylic oxygen and pyridone oxygen and also the non detectable of signals for carboxylic acid proton in the ^{1}H NMR spectra of complexes support the chelation of carboxylic oxygen. The complexes generated are effective antibacterial agents compared with free lomefloxacin against most of used bacterial strain (table 6). This study displays very interesting group of potential antibacterial agents, which may further expand their uses as potential broad spectrum therapeutic antibacterial drugs and pave the way to prepared useful compounds with specific biomedical applications.

The lomfloxacin has two donating centers O_{pyr} and O_{car}, when chelated with palladium ion Pd(II) there are six-coordinated bonds are formed four with two lomfloxacin molecules and other two with two chloride ions the product complex is treated as distorted octahedral complex . The six-coordinated complex of palladium is more stable than four-coordinated complex . The Ce(IV) and Ti(IV) ions favor coordinated with three lomfloxacin molecules according to molar ratio 1:3 more than ratio 1:2. In case of V(IV) in VO unite the energy difference between two enantiomers cis and trans is very low, it is difficult to distinguish between trans or cis isomers. Nevertheless, the trans-isomer exhibits the lowest energy value.

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