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RESEARCH ARTICLE

Spectroscopic Investigation of New Schiff Base Metal Complexes

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Abstract

New transition metal complexes of Ni(II), Cu(II), Zn(II), and Ce(IV) with tetradentate (N_2O_2) Schiff base, CIP-o-phdn, (N,N'-o-phenylene (bis 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazine-1-yl)-quinoline-3-carboxylic acid) have been prepared. Characterization of the ligand and its complexes is also reported. Their bonding and structures of the newly prepared were identified by elemental analysis, IR, UV-Vis, ^{1}H NMR, mass spectra, magnetic moment measurements, conductivity as well as thermal analysis. The metal ions complete their six coordination with two coordinated water molecules forming a distorted octahedral geometry. The prepared compounds have antibacterial activity against two gram-negative bacteria; Escherichia coli and Pseudomonas aeruginosa and also against two gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis*. The activity data showed that the complexes are more potent antibacterial than the parent Schiff base and also the Schiff base more active than free ciprofloxacin
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INTRODUCTION

Schiff bases have been studied extensively because of their high-potential chemical permutation. Schiff bases represent a class of important compounds in a medicinal and pharmaceutical field. They have biological activities such as antibacterial, [1–4] anticancer, [5–7] antifungal [8,9] and herbicidal activities [10]. Furthermore, Schiff bases offer opportunities for inducing substrate chirality; tuning metal centred electronic factors, enhancing solubility and stability of either homogeneous or heterogeneous catalyst [11–16]. Schiff base ligands are able to coordinate many different metals [17-19] and to stabilize them in various oxidation states. In this context, we report the synthesis of novel tetradentate mononuclear Schiff base complexes. The ligand was prepared by the condensation of ciprofloxacin hydrochloride with o-phenylenediamine to afford the corresponding Schiff base, CIP-o-phdn, ligand. The reaction of this ligand with Ni(II), Cu(II), Zn(II) and Ce(IV) ions, in the 1:1 molar ratio (ligand: metal ion) was studied. The ligand and newly prepared metal complexes were characterized by different physicochemical and spectroscopic techniques. The antibacterial activity of Schiff base ligand and its metal chelates are reported against; Staphylococcus aureus and Bacillus subtilis as gram positive and Escherichia coli and Pseudomonas aeruginosa as gram negative.

Experimental

Chemicals

All commercially available reagents for synthesis and analyses were of analytical grade and used as received. Ciprofloxacin hydrochloride used in this study was purchased from the Egyptian International Pharmaceutical Industrial Company (EIPICO). o-phenylenediamine, glacial acetic acid, acetone, ethanol, methanol, NaOH, $FeCl_3.6H_2O$, $BaCl_2$ and $FeSO_4$ were purchased from Fluka Chemical Co. $NiSO_4.6H_2O$, $Zn(NO_3)_2.6H_2O$, $Cu(OCOCH_3)_2.H_2O$ and $Ce(SO_4)_2$ from Aldrich Chemical Co.

A- Synthesis of ligand(CIP-o-phdn) ($C_{40}H_{42}N_8O_4F_2Cl_2$)

An ethanolic solution of ciprofloxacin (2mmol, 0.734 g) with o- phenylenediamine (1mmol, 0.108 g) was boiled under reflux in the presence of glacial acetic acid separately for 4 hr. The resulting solution was concentrated to 8 mL on a water bath and allowed to cool at 0 °C. Yellowish white precipitate was filtered off, washed several times by ethanol and dried under vacuum over $CaCl_2$ in a dissecator. The proposed formula of the ligand ($C_{40}H_{42}N_8O_4F_2Cl_2$, M.Wt.=807) is in good agreement with mass spectrum ($M^{·+}$) at m/z=806.2 (68.91%) and confirmed by IR spectral data. The ^1H NMR spectrum of the ligand in DMSO-d_6 showed signals atδ 11.0 ppm assigned to the proton of carboxylic (COOH).

B- Synthesis of metal complexes

The light yellowish solid complex $[Ni(CIP\text{-}o\text{-}phdn)(H_2O)_2](SO_4).8H_2O$ was prepared by adding 0.5 mmol (0.131 g) of nickel sulphate $NiSO_4.6H_2O$ in 20 mL methanol drop-wisely to a stirred suspended solution 0.5 mmol (0.403 g) of CIP-o-phdn and 1mmol (0.04 g) NaOH in 50 mL methanol. The reaction mixture was stirred for 15 hr at 35 °C in water bath. The light yellowish precipitate was filtered off and dried under vacuum over anhydrous $CaCl_2$. The dark green and yellowish-white solid complexes of $[Cu(CIP\text{-}o\text{-}phdn)(H_2O)_2](CH_3COO)_2.3H_2O$ and $[Zn(CIP\text{-}o\text{-}phdn)(H_2O)_2](NO_3)_2.5H_2O$, $[Ce(CIP\text{-}o\text{-}phdn)(H_2O)_2](SO_4)_2.3H_2O$ were prepared in a similar manner described above by using acetone as a solvent and using $Cu(OCOCH_3)_2.H_2O$, $Zn(NO_3)_2.6H_2O$ and $Ce(SO_4)_2$, respectively, in 1:1 molar ratio. All compounds were characterized by their elemental analysis, molar conductance, magnetic moment, infrared, ^1H NMR, electronic, mass spectra as well as thermal analysis. For the isolated complexes, in order to verify that the sulphate, acetate and nitrate groups are ionic and not coordinate, the complexes solutions were tested with aqueous solutions of barium chloride, ferric chloride and freshly prepared ferrous sulphate a white precipitate for Ni(II) and Ce(IV), red-brown and black-ring ($FeSO_4.NO$) were formed. This indicates that sulphate, acetate and nitrate groups are found as counter ions (outside the complexes sphere).

We did not manage to obtain a crystal of the complexes suitable for the structure determination with X-ray crystallography, although diverse crystallization techniques were used.

Elemental C, H, N and halogen analysis was carried out on a Perkin Elmer CHN 2400. The percentage of the metal ions were determined gravimetrically by transforming the solid products into 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 purposed. 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 under N_2 atmosphere within the temperature range from room temperature to 800 °C 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 from 0-1090. Magnetic measurements were carried out on a Sherwood scientific magnetic balance using Gouy method using $Hg[Co(SCN)_4]$ as calibrant. Molar conductivities of the solution of the ligand and metal complexes in DMF at 1×10^{-3} M were measured on CONSORT K410. All measurements were carried out at ambient temperature with freshly prepared solution.

C- Antimicrobial Investigation

Antibacterial activity of the ligand, metal salts and its metal complexes was investigated by a previously reported modified method of Beecher and Wong [20] against different bacterial species, such as *Staphylococcus aureus* (*S. aureus*), *Bacillus subtilis* (*B. subtilis*), *Escherichia coli* (*E. coli*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) and antifungal screening was studied against two species, *Candida Albicans* (*C. albicans*) and *Aspergillus fumigatus* (*A. fumigatus*). The tested microorganisms isolates were isolated from Egyptian soil and identified according to the standard mycological and bacteriological keys for identification of fungi and bacteria as stock cultures in the microbiology laboratory, Faculty of Science, Zagazig University. The nutrient agar medium for antibacterial was (0.5% Peptone, 0.1% Beef extract, 0.2% Yeast extract, 0.5% NaCl and 1.5% Agar-Agar) czapeks Dox medium for antifungal (3% Sucrose, 0.3% $NaNO_3$, 0.1% K_2HPO_4, 0.05% KCl, 0.001% $FeSO_4$, 2% Agar-Agar) was prepared [21] and then cooled to 47 °C and seeded with tested microorganisms. Sterile water agar layer was poured, solidified then pour, the prepared growth medium for fungi and bacteria (plate of 12 cm diameter, 15 ml medium plate). After solidification 5 mm diameter holes were punched by a sterile cork-borer. The investigated compounds, ligand, metal salts and their complexes, were introduced in Petri-dishes (only 0.1 ml) after dissolving in DMF at 1.0×10^{-3} mol L^{-1}. These culture plates were then incubated at 37 °C for 20 hr for bacteria and for seven days at 30 °C for fungi. The activity was determined by measuring the diameter of the inhibition zone (in mm). Growth inhibition was calculated with reference to the positive control, i.e., (Ampicilin, Amoxycillin and Cefaloxin).

Results and Discussion

Ciprofloxacin Schiff base (CIP-o-phdn) of Ni(II), Cu(II), Zn(II) and Ce(IV) were synthesized as solids of color characteristics of the metal ion. The formulae of the complexes, together with the physical properties, elemental analyses, melting points, molar conductivities and magnetic properties obtained for complexes are listed in Table 1. The isolated solid complexes are stable at room temperature (25 °C) and almost insoluble in water and in most organic solvents but are easily soluble in DMF and DMSO-d_6. The results obtained indicate that all the isolated complexes are formed from the reaction of the metal salts with ciprofloxacin Schiff base at 1:1 molar ratio for all the elements. All the complexes reported here in are hydrates with various degrees of hydration and air stable solids at room temperature. The structures of the complexes suggested from the elemental analysis agree quite well with their proposed formulae. The found values of elemental analysis and metal content are in a well agreement with the calculate percentage and proves the molecular formulae of the prepared complexes. The molar conductance values of CIP-o-phdn and their metal complexes were found to be in the range from 113.1 to 275.8 S cm^2 mol^{-1} at room temperature (Table 1). Conductance data showed that the metal complexes are electrolyte compared with ciprofloxacin Schiff base alone these data confirmed with qualitative reactions for identification of counter ions in experimental section. The magnetic moments (as B.M.) of the complexes were measured at room temperature. The Zn(II) and Ce(IV) complexes are found in diamagnetic character and octahedral geometry around the metal ion but Ni(II) and Cu(II) complexes are found in paramagnetism with measured magnetic moment values at 3.01 and 1.97 B.M., respectively [22]. The biological activity of Schiff base and their metal chelates are studied against some selected Gram-positive and Gram-negative bacteria and two species fungi.

Table (1): Elemental analysis and physico-analytical data for ciprofloxacin Schiff base (CIP-o-phdn) and its metal complexes.

Compounds M.Wt. (M.F.)	Yield%	Mp/ °C	Color	Found (Calcd.) (%)						μ_{eff} (B.M.)	Λ S cm^2 mol^{-1}
				C	H	N	M	Cl	S		
(CIP-o-phdn) 807 ($C_{40}H_{42}N_8O_4F_2Cl_2$)	80.0	308	Yellowish white	(59.48) 59.47	(5.20) 5.17	(13.88) 13.87	-	(8.80) 8.79	-	Diamagnetic	113.1
[Ni(CIP-o-phdn)$(H_2O)_2$]SO_4.8H_2O 1068.8 ($NiC_{40}H_{60}N_8O_{18}F_2S$)	75.51	>360	Light yellow	(44.91) 44.87	(5.61) 5.56	(10.48) 10.44	(5.49) 5.46	-	(3.00) 3.00	3.01	195.8
[Cu(CIP-o-phdn)$(H_2O)_2$]$(CH_3COO)_2$.3H_2O 1005.5 ($CuC_{44}H_{56}N_8O_{13}F_2$)	80.26	284	Dark green	(52.51) 52.49	(5.57) 5.56	(11.14) 11.11	(6.32) 6.30	-	-	1.97	179.8
[Zn(CIP-o-phdn)$(H_2O)_2$]$(NO_3)_2$.5H_2O 1049.4 ($ZnC_{40}H_{54}N_{10}O_{17}F_2$)	76.90	310	Yellowish white	(45.74) 45.73	(5.15) 5.12	(13.34) 13.32	(6.23) 6.21	-	-	Diamagnetic	169.5
[Ce(CIP-o-phdn)$(H_2O)_2$]$(SO_4)_2$.3H_2O 1156.2 ($CeC_{40}H_{50}N_8O_{17}F_2S$)	69.80	330	Yellowish white	(41.52) 41.50	(4.32) 4.30	(9.69) 9.66	(12.11) 12.09	-	(2.78) 2.78	Diamagnetic	275.8

A- IR absorption spectra

The infrared spectra [Ni(CIP-o-phdn)$(H_2O)_2$]SO_4.8H_2O, [Cu(CIP-o-phdn)$(H_2O)_2$]$(CH_3COO)_2$.3H_2O, [Zn(CIP-o-phdn)$(H_2O)_2$]$(NO_3)_2$.5H_2O and [Ce(CIP-o-phdn)$(H_2O)_2$]$(SO_4)_2$.3H_2O and ciprofloxacin Schiff base free were measured as KBr discs. These spectra are shown in fig. 1 and the assignments are given in table 2. The infrared spectra of the four complexes are compared with these of the free ciprofloxacin Schiff base in order to determine the site of coordination that may be involved in chelation. The position or the intensities of the peaks are expected to be changed upon complexation. The proposed structure for all complexes is represented by Scheme (1), the four donor atoms of CIP-o-phdn coordinated to central metal ions in a plane forming tetragon with two oxygen atoms of two coordinated water molecules axial [23]. According to the proposed structure for the complexes under investigation, the complexes possess a two-fold axis and two plane of symmetry and hence they are C_{2v} symmetry. The C_{2v} complexes, $[M(CIP\text{-}o\text{-}phdn)(H_2O)_2]^{n+}$ are expected to display 297 vibrational fundamentals which are all monodegenerate. These are distributed between A_1, A_2, B_1 and B_2 motions; all are IR and Raman active, except for the A_2 modes which are only Raman active.

The infrared spectrum of CIP-o-phdn Schiff base shows the absence of the bands attributable to ν(NH_2) group of o-phenylenediamine and of ν(C=O) of ciprofloxacin. Instead, newly formed very strong band at 1624 cm^{-1} is obtained. This suggests the complete condensation of the amino groups with keto group [24] indicating the formation of the Schiff base linkage [25]. The IR spectra of the complexes revealed characteristic changes (as compared with the spectrum of the ligand) confirming complexation. The IR spectra of all complexes containing hydration and or coordination water molecules display bands at 3467-3344 cm^{-1} due to ν(O-H) vibration mode of the water molecules [26] and this was confirmed by the results of thermal analysis, mass spectra as well as ^{1}H NMR. The stretching vibrations ν(C-H) of phenyl groups and the corresponding vibrations ν(C-H) of $-CH_2$ and $-CH_3$ units in these complexes are assigned as a number of bands in the region 3089–2711 cm^{-1}. The assignments of all C–H stretching vibrations agree quite well with the expected in the literature [27,28]

The presence of a group of bands with different intensities in the range 2654–2465 cm^{-1}, which assigned to vibration of the quaternized nitrogen of the piperazine group, indicates the zwitterionic form of ciprofloxacin Schiff base is involved in the coordination to the investigated metal ions [29]. The two bands observed at 1732 and 1624 cm^{-1} in the spectrum of the free ciprofloxacin Schiff base have been assigned to the stretching vibration of carboxylic ν(COOH) and the azomethine group ν(C=N), respectively [27,29-38]. Upon comparison of the IR spectra of the complexes with that of free CIP-o-phdn, the absent of the band at 1732 cm^{-1} in all complexes and the shift of the characteristic band of azomethine group ν(C=N) to a lower value around 50 cm^{-1} (from 1624 to 1578 or 1574 cm^{-1}) confirming the Schiff base molecule coordinated to metal ions by nitrogen and oxygen atoms and the carboxylic group is deprotonated [39].

In the case of monodentate carboxylate ligand, the antisymmetric and symmetric COO^- stretches will be shifted to higher and lower frequencies, respectively, with an average $\Delta\nu>200$ cm^{-1} [40-42]. For our complexes the presence of $\nu_{as}(COO^-)$ in the region 1624-1620 cm^{-1} and the $\nu_s(COO^-)$ in the region 1396–1385 cm^{-1} [27,39,43,44] and with $\Delta\nu>200$ cm^{-1} confirming that the carboxylato group react as monodentate through one of oxygen atoms.

The spectra of the isolated solid complexes show a group of bands which characteristics for ν(M-O) and (M-N) of the ligand. The ν(M-O) and (M-N) bands observed at 625, 578, 544 and 502 cm^{-1} for Ni(II), at 625, 578, 544 and 505 $cm^{-1}$for Cu(II), at 629 and 559 $cm^{-1}$for Zn(II), also at 617and 567 $cm^{-1}$for Ce(IV) (Table 2) which are absent in the spectrum of ciprofloxacin Schiff base. This indicates the coordination of (CIP-o-phdn) through both C=N and carboxylic groups [27,29].

Figure 1: Infrared spectra for (A) (CIP-o-phdn), (B) [Ni(CIP-o-phdn)$(H_2O)_2$](SO_4).$8H_2O$, (C) [Cu(CIP-o-phdn)$(H_2O)_2$]$(CH_3COO)_2$.$3H_2O$, (D) [Zn(CIP-o-phdn)$(H_2O)_2$]$(NO_3)_2$.$5H_2O$ and (E) [Ce(CIP-o-phdn)$(H_2O)_2$]$(SO_4)_2$.$3H_2O$.

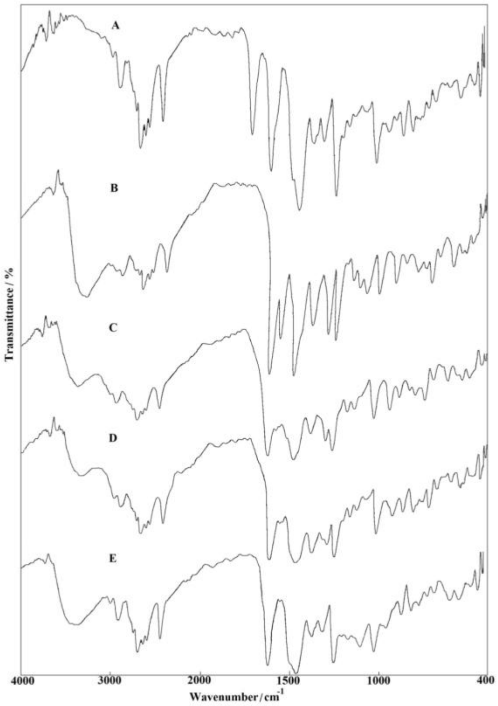


Table (2): Infrared frequencies (cm^{-1}) and tentative assignments for (A) (CIP-o-phdn), (B) [Ni(CIP-o-phdn)(H_2O)$_2$](SO_4).8H_2O, (C) [Cu(CIP-o-phdn)(H_2O)$_2$](CH_3COO)$_2$.3H_2O, (D) [Zn(CIP-o-phdn)(H_2O)$_2$](NO_3)$_2$.5H_2O and (E) [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O.

A	B	C	D	E	Assignments
3533w	3344mbr	3379mbr	3402mbr	3467w	ν(O-H); H_2O; COOH
				3391mbr	
3156w	3089vw	3022w	3022w	3089w	ν(C-H); aromatic
3044w	3022w			3011m	
2943s	2955m	2947ms	2951m	2936ms	ν(C-H); aliphatic
2867vw	2844w	2844vw	2867vw	2867vw	
2778m	2756w	2744w	2756w	2756w	
2712ms	2716ms	2712ms	2712ms	2711ms	
2650m	2650m	2650m	2650m	2654m	ν($-NH_2^+$)
2611m	2611w	2611w	2611m	2611m	
2465s	2465ms	2465ms	2465s	2465s	
1732vs	-	-	-	-	ν(C=O); COOH
-	1620vs	1624vs	1624vs	1624vs	$\nu_{as}(COO^-)$
1624vs	1574s	1578m	1578w	1578w	ν(C=N)
			1556w	1500sh	
1466vs	1485vs	1481vs	1477s	1466vs	-CH; deformations of CH_2
1385m	1396s	1385ms	1389s	1385ms	$\nu_s(COO^-)$
1367sh					
1331ms	1308vs	1304ms	1350vw	1327ms	$\delta_b(-CH_2)$,ν (NO_3^-)
			1304m		
1261vs	1265vs	1265vs	1261s	1258vs	ν(C-O),
1223w	1222w	1184m	1222vw	1222w	ν(C-N) and
1188m	1184m	1145m	1184m	1178m	ν(C-C)
1156m	1161m	1122sh	1150m	1111ms	
1089m	1103ms	1034s	1103m	1034s	$\delta_r(-CH_2)$
1034s	1034ms		1034s		ν(SO_4^{-2})
989vw	945ms	945s	949ms	972m	-CH-bend; phenyl
968m	895m	895m	891ms	933sh	
933m	829m	833w	833ms	887ms	
887ms		806m	822sh	833m	ν(NO_3^{-2})
833ms					
822vw					
795m	772m	752ms	791vw	791m	$\delta_b(COO^-)$
767vw	748ms	706m	778vw	745m	
748m	710m		748s	706m	
710m			711m		
656w	625ms	644vw	629m	617m	ν(M-N), ν(M-O), ring deformation
622m	578m	625m	571m	567m	
571ms	544m	578m	559vw	511vw	
550vw	502m	544m	486w	486m	
486m	432m	505m	436s	436s	
478vw	405m	489sh	403ms	406m	
436s		432m			
406 s		409m			

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

B- Electronic spectra

The use of visible and ultraviolet spectroscopy to explain the structural aspects of chelates is a rather simple but powerful tool. The application of ultraviolet spectroscopy is more universal and can be useful in structural determinations of all chelates since they all absorb in this region [45]. The formation of the metal ciprofloxacin Schiff base complexes was also confirmed by the electronic solid reflection spectra. The electronic solid reflection spectra of (CIP-o-phdn) along with the Ni(II), Cu(II), Zn(II) and Ce(IV) complexes in the wavelength interval from 200 to 800 nm range are shown in fig. 2. It can be seen that free ciprofloxacin Schiff base reflected at 209, 229 and 321 nm (Table 3).The first two bands at 209 and 229 nm may be attributed to π-π^*transition and the second band observed at 321 nm is assigned to n-π^*transitions, these transitions occur in case of unsaturated hydrocarbons which contain ketone groups or azomethine group [39]. The shift of the reflection bands to higher values (bathochromic shift) and the absent of the band at 321 nm and presence of new bands in the reflection spectra of complexes indicate that the formation of their metal complexes [34-36]. The four complexes have bands in the range from 410 to 560 nm which may be assigned to the ligand to metal charge-transfer [37,38,46]. The electronic spectrum of the Ni(II) and Cu(II) complexes show bands at 560, 600, 623 and 614 nm, respectively. These bands were assigned to d-d transition in the octahedral complexes. The octahedral structures of these complexes were confirmed by the obtained magnetic moment data (3.01 and 1.97 B.M.) [22,47]. The Schiff base Ni(II) complex absorption spectrum show three absorption bands at 560, 600 and 623 nm which are assigned to ${}^3A_{2g}(F)\longrightarrow{}^3T_{2g}$, ${}^3A_{2g}(F)\longrightarrow{}^3T_{1g}(F)$ and ${}^3A_{2g}(P)\longrightarrow{}^3T_{1g}(P)$ transitions, respectively, in favor of octahedral geometry.

Finally, the results presented here, clearly indicate that the metal ions form stable solid complexes with the Schiff base, CIP-o-phdn and monodentate ligand such as H_2O where metal ions are six coordinate.

Figure 2: Electronic reflection spectra for (A) (CIP-o-phdn), (B) [Ni(CIP-o-phdn)(H_2O)$_2$](SO_4).8H_2O,(C) [Cu(CIP-o-phdn)(H_2O)$_2$](CH_3COO)$_2$.3H_2O, (D) [Zn(CIP-o-phdn)(H_2O)$_2$](NO_3)$_2$.5H_2O and (E) [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O.

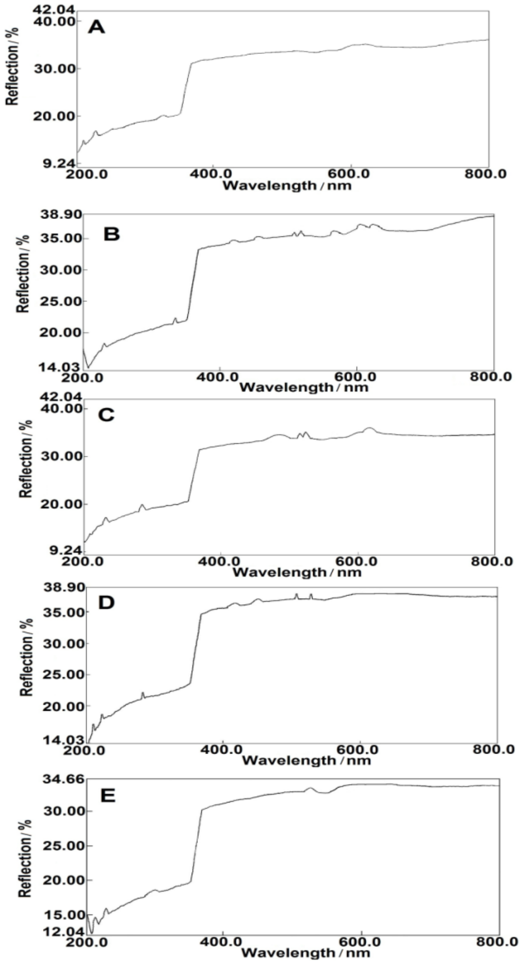


Table (3): UV-Vis. spectra of (CIP-o-phdn), Ni(II), Cu(II), Zn(II) and Ce(IV).

Assignments (nm)	(CIP-o-phdn)	(CIP) Schiff base complex with			
		Ni(II)	Cu(II)	Zn(II)	Ce(IV)
π-π^* transitions	209, 229	231	230	210, 224	212, 229
n-π^* transitions	321	331,	281	279	293
Ligand-metal charge transfer	-	419,452, 502,512	476, 507, 517	410, 445, 498, 514	517
d-d transition	-	560, 600,623	614	-	-

C- ^{1}H NMR spectra

To confirm the proposed structure of the isolated metal complexes [Ni(CIP-o-phdn)(H_2O)$_2$]SO_4.8H_2O, [Cu(CIP-o-phdn)(H_2O)$_2$](CH_3COO)$_2$.3H_2O, [Zn(CIP-o-phdn)(H_2O)$_2$](NO_3)$_2$.5H_2O and [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O. ^{1}H NMR spectra in DMSO-d$_6$ were carried out (Fig. 3). The ^{1}H NMR spectrum of ciprofloxacin Schiff base (CIP-o-phdn), (Table 4) shows the characteristic singlet at δ:11 ppm to the proton of carboxylic (COOH). The resonance of the carboxylic proton (COOH) is not detected in the spectra of the isolated solid complexes that suggest the coordination of ciprofloxacin Schiff base through its carboxylato oxygen atoms [36-38,48]. Also, the ^{1}H NMR spectra for complexes exhibit a new peak in the range 4.20-4.55 ppm, due to the presence of water molecules in the complexes. On comparing main peaks of ciprofloxacin Schiff base with its complexes, it is observed that all the peaks of the free ligand are present in the spectra of the complexes with the chemical shift upon binding of Schiff base to the metal ion [49].

Figure 3: ^{1}H NMR spectra for (A) (CIP-o-phdn), (B)[Ni(CIP-o-phdn)(H_2O)$_2$](SO_4).8H_2O, (C) [Cu(CIP-o-phdn)(H_2O)$_2$](CH_3COO)$_2$.3H_2O, (D) [Zn(CIP-o-phdn)(H_2O)$_2$](NO_3)$_2$.5H_2O and (E) [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O.

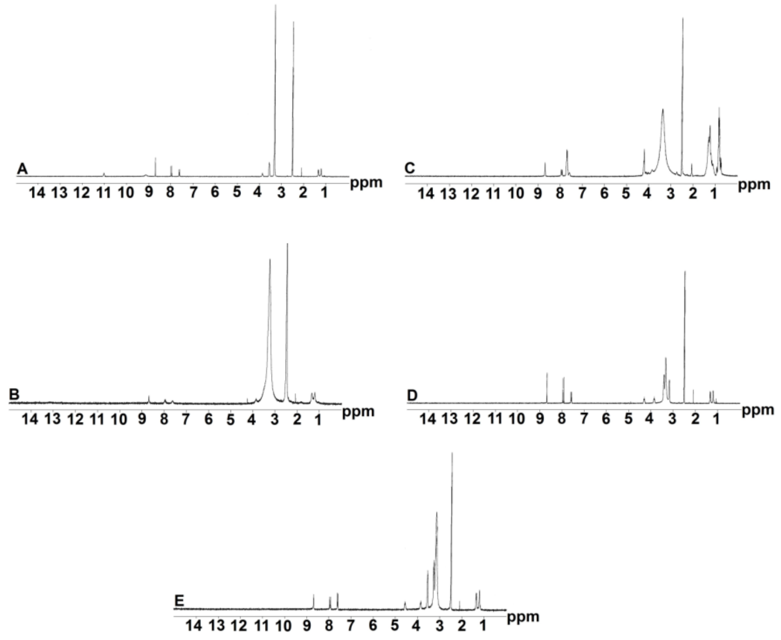


Table (4): ^1H NMR values (ppm) and tentative assignments for (A) (CIP-o-phdn), (B) [Ni(CIP-o-phdn)(H_2O)$_2$]SO_4.8H_2O, (C) [Cu(CIP-o-phdn)(H_2O)$_2$](CH_3COO)$_2$.3H_2O, (D) [Zn(CIP-o-phdn)(H_2O)$_2$](NO_3)$_2$.5H_2O and (E) [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O.

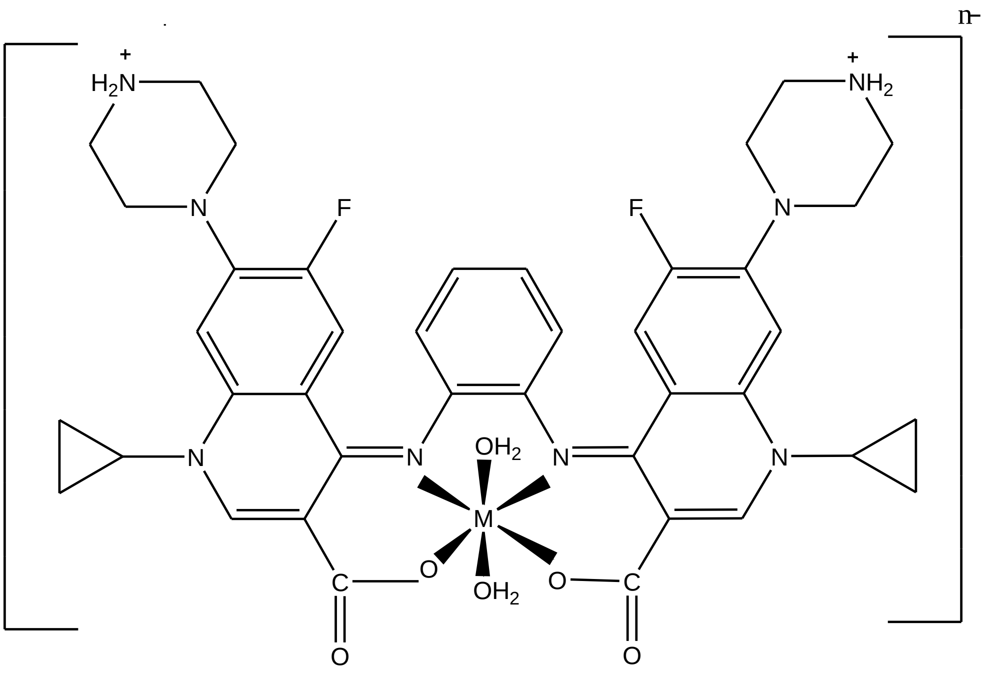
A	B	C	D	E	Assignments
1.21-1.34	1.20-1.33	0.71-1.30	1.03-1.30	1.20-1.35	δH, -CH_2 and -CH cyclopropane
2.09	2.09	2.08	2.09	2.09	δH, -NH; piperazine
2.49	2.50	2.50-2.73	2.49	2.49	δH, -$^+NH_2$
3.32-3.86	3.28-3.86	3.37	3.16-3.84	3.18-3.86	δH, -CH_2 aliphatic δH,
-	4.25	4.20	4.30	4.55	H_2O
7.60- 9.11	7.63- 8.69	7.57-8.68	7.57- 8.68	7.60- 8.70	δH, -CH aromatic
11	-	-	-	-	δH, -COOH

D- Thermal studies

Thermal behavior of the title compounds was followed up to 800 °C under nitrogen atmosphere with heating rates controlled at 10°C min^{-1}. Fig. 4 represents the TGA and DrTG curves and Table 5 gives the maximum temperature values for decomposition along with the corresponding weight loss values for each step of the decomposition reaction. These data support the proposed complexes chemical formulae. Ciprofloxacin Schiff base (CIP-o-phdn) is thermally stable at room temperature. The TG curve shows decomposition of the ciprofloxacin Schiff base started at 35 °C and finished at 715 °C with one stage at three maxima 200, 311 and 630 °C and is accompanied by a weight loss of 99.82%.

The TG thermograms of all complexes are characterized by two degradation steps. Therefore we take the TG thermogram of [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O as a representative example for the decomposition of these complexes. The first stage of decomposition occurs at temperature maxima of 68 and 140 °C. The found weight loss associated with step is 4.29% and may be attributed to the loss of three lattic water molecules which is in good agreement with the calculated value of 4.67%. The second stage of decomposition occurs at three maxima 321, 392 and 782 °C .This step is reasonably accounted for the organic CIP-o-phdn ligand [50,51] and the weight loss found at this stage equals to 66.71% corresponds to loss $20C_2H_2+5NO+2HF+H_2O+1.5N_2$. The proposed structure formula on the basis of the results discussed in our paper located as follows (Scheme 1).

Scheme 1: The coordination mode of M with ciprofloxacin Schiff base (CIP-o-phdn).



M= Ni(II), Cu(II), Zn(II) and Ce(IV)
n=2 for Ni(II), Cu(II), Zn(II) and 4 for Ce(IV)

According to these conculsions, the decomposition mechansims proposed forCIP-o-phdn and [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O are summarized as follows:

$$(1)\ C_{40}H_{42}N_8O_4F_2Cl_2 \xrightarrow{200,\ 311,\ 630\ ^{\circ}C} 18C_2H_2+4CO+2HF+H_2+4N_2+2HCl$$

$$(2)\ [Ce(C_{40}H_{40}N_8O_4F_2)(H_2O)_2](SO_4)_2.3H_2O \xrightarrow{68,\ 140\ ^{\circ}C} [Ce(C_{40}H_{40}N_8O_4F_2)(H_2O)_2](SO_4)_2+3H_2O$$

$$[Ce(C_{40}H_{40}N_8O_4F_2)(H_2O)_2](SO_4)_2 \xrightarrow{321,\ 392,\ 782\ ^{\circ}C} Ce(SO_4)_2+20C_2H_2+5NO+2HF+H_2O+1.5N_2$$

Figure 4: TGA and DTG diagrams for (A) (CIP-o-phdn), (B)[Ni(CIP-o-phdn)(H_2O)$_2$](SO_4).8H_2O, (C) [Cu(CIP-o-phdn)(H_2O)$_2$](CH_3COO)$_2$.3H_2O, (D) [Zn(CIP-o-phdn)(H_2O)$_2$](NO_3)$_2$.5H_2O and (E) [Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O.

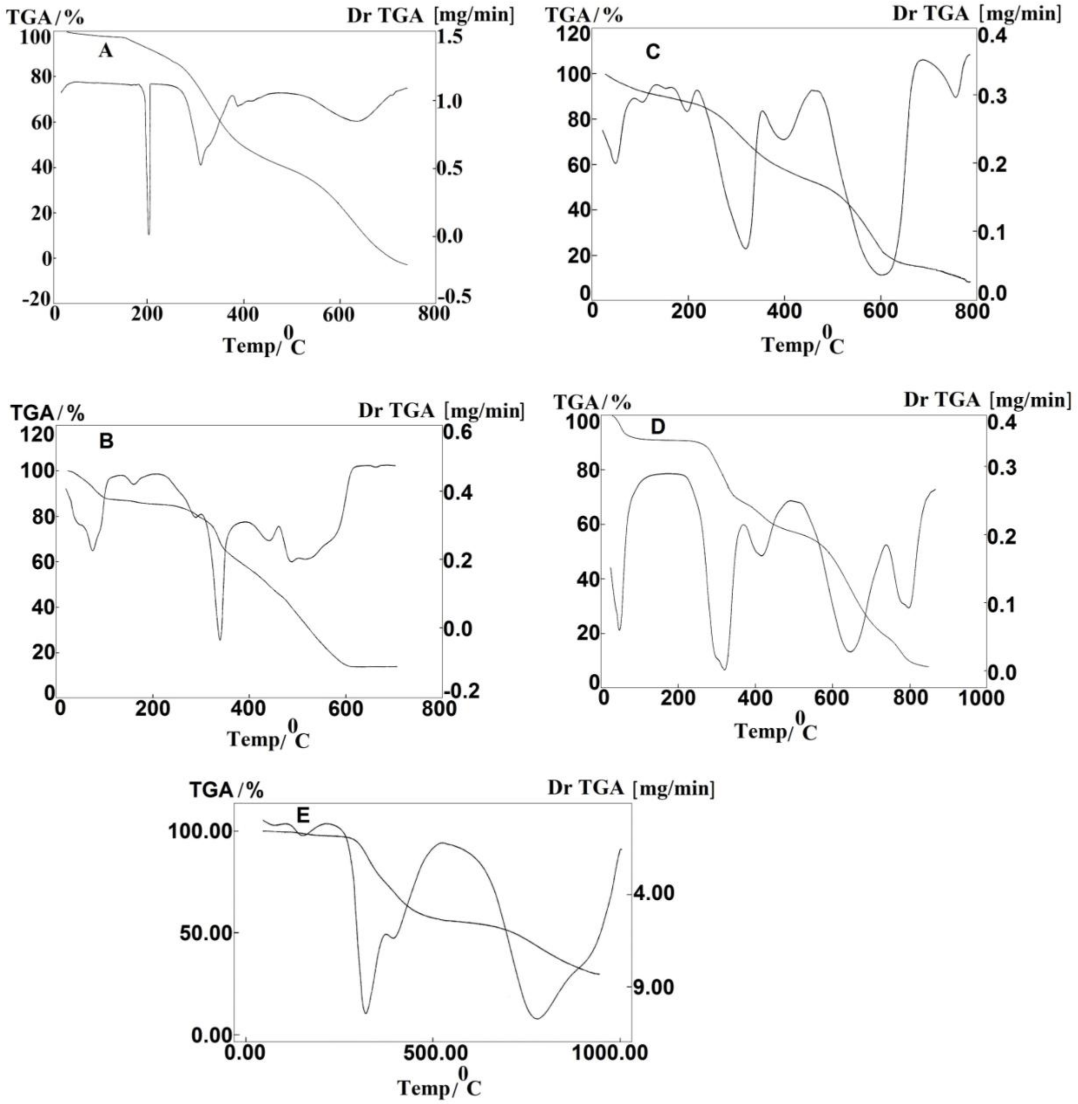


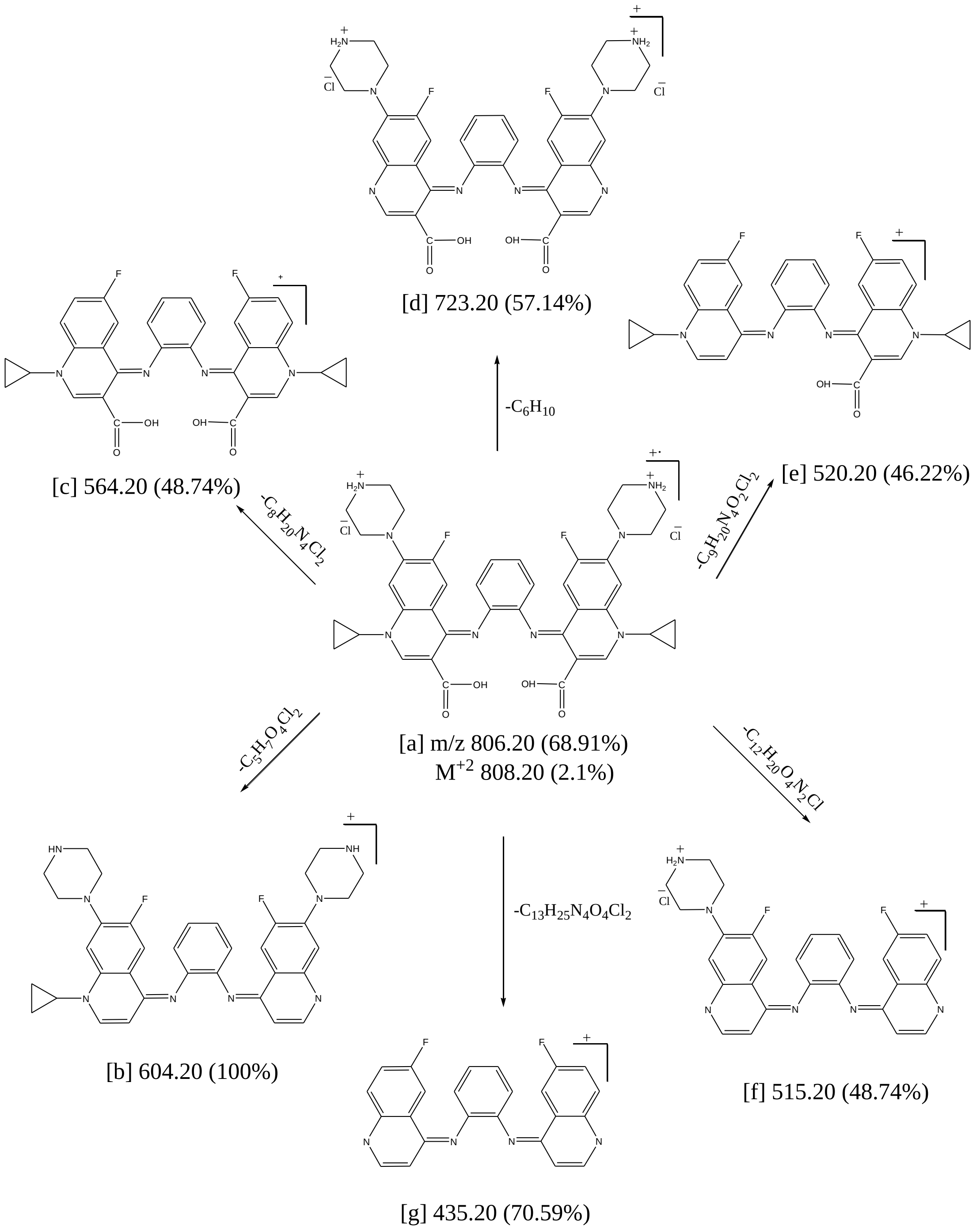
Table (5): The maximum temperature T_{max} (°C) and weight loss values of the decomposition stages for (CIP-o-phdn), Ni(II), Cu(II), Zn(II) and Ce(IV).

Compounds	Decomposition	T_{max}(°C)	Weight loss (%)		Lost species
			Calc.	Found	
(CIP-o-phdn) ($C_{40}H_{42}N_8O_4F_2Cl_2$)	First step	200,311, 630	100	99.82	$18C_2H_2+4CO+2HCL+2HF+H_2+4N_2$
	Total loss		100	99.82	
	Residue				
[Ni(CIP-o-phdn)(H_2O)$_2$]SO_4.8H_2O ($C_{40}H_{60}N_8O_{18}F_2SNi$)	First step	77	13.47	13.80	$8H_2O$
	Second step	335,438, 523	72.04	72.26	$19C_2H_2+2NO+2HF+3N_2+2H_2O+2CO$
	Total loss		85.51	86.06	
	Residue		14.49	13.94	
[Cu(CIP-o-phdn)(H_2O)$_2$](CH_3COO)$_2$.3H_2O ($C_{44}H_{56}N_8O_{13}F_2Cu$)	First step	65, 111	5.37	5.70	$3H_2O$
	Second step	200,307, 394,583, 761	86.72	86.30	$21C_2H_2+4NO+2HF+2CO+3H_2O+2N_2$
	Total loss		92.09	92.00	
	Residue		7.91	8.00	
[Zn(CIP-o-phdn)(H_2O)$_2$](NO_3)$_2$.5H_2O ($C_{40}H_{54}N_{10}O_{17}F_2Zn$)	First step	60	8.58	8.57	$5H_2O$
	Second step	318,409, 641, 786	83.66	84.03	$19C_2H_2+7NO+2HF+2CO+2H_2O+1.5N_2$
	Total loss		92.24	92.60	
	Residue		7.76	7.40	
[Ce(CIP-o-phdn)(H_2O)$_2$](SO_4)$_2$.3H_2O ($C_{40}H_{50}N_8O_{17}F_2SCe$)	First step	68, 140	4.67	4.29	$3H_2O$
	Second step	321,392, 782	66.60	66.71	$20C_2H_2+5NO+2HF+H_2O+1.5N_2$
	Total loss		71.27	71.00	
	Residue		28.73	29.00	

E- Mass spectra

The recorded mass spectra and the molecular ion peaks for the compounds have been used to confirm the molecular formulae. The mass spectrum of the synthesized free Schiff base (CIP-o-phdn) (Fig. 5) is in a good agreement with the suggested structure (Scheme 2). The Schiff base showed molecular ion peak ($M^{\cdot+}$) at m/z=806.2 (68.91%), and M^{+2}at m/z=808 (2.1%). The molecular ion peak [a] gave fragment which refers to sharp peak (base peak) [b] with m/z=604.20 (100%). The molecular ion peak [a] losses $C_8H_{20}N_4Cl_2$ to give fragment [c] with m/z=564.20 (48.74%) and it losses C_6H_{10} to give fragment [d] with m/z=723.20 (57.14%). It loses $C_9H_{20}N_4O_2Cl_2$ to give [e] with m/z=520.20 (46.22%).The molecular ion peak [a] gave fragment [f] with m/z=515.20 (48.74%) and also [g] with m/z=435.20 (70.59%). The fragmentation patterns of our studied complexes were obtained from the mass spectra (Fig. 5). The mass spectrum of Ni(II) complex displayed molecular peak at m/z (%) 1068 (52.31%) suggesting that the molecular weight of the assigned product matching with elemental analysis calculated. Fragmentation pattern of the complex [Ni(CIP-o-phdn)(H_2O)$_2$]SO_4.8H_2O is given as an example in Scheme 3. The molecular ion peak [a] appeared at m/z=1068 (52.31%) losses two molecules of water to give [b] with m/z=1032.10 (16.41%) and it also loses $C_8H_{20}N_4$ to give [c] with m/z=895.10 (45.64%). The molecular ion peak [a] losses C_6H_{10} to give [d] with m/z=987.10 (45.64%) and it losses $C_{14}H_{30}N_4$ to give [e] with m/z=816.10 (49.74%). The molecular ion peak also losses SO_4.7H_2O to give [f] with m/z=846.10 (35.90%). The mass spectra of Cu(II) and Zn(II) complexes displayed molecular peak at 1005.5 and 1049 which refer to M.Wt. of the complexes with the abundance 6% and 90%.For the other complex Ce(IV) with the calculated molecular weight 1156.2 according to the elemental analysis and thermogravimetric analysis, the molecular peaks are found outside the scale of the instrument.

Scheme 2: Fragmentation pattern of free Schiff base (CIP-o-phdn).



Scheme 3: Fragmentation pattern of $[Ni(CIP\text{-}o\text{-}phdn)(H_2O)_2]SO_4.8H_2O$.

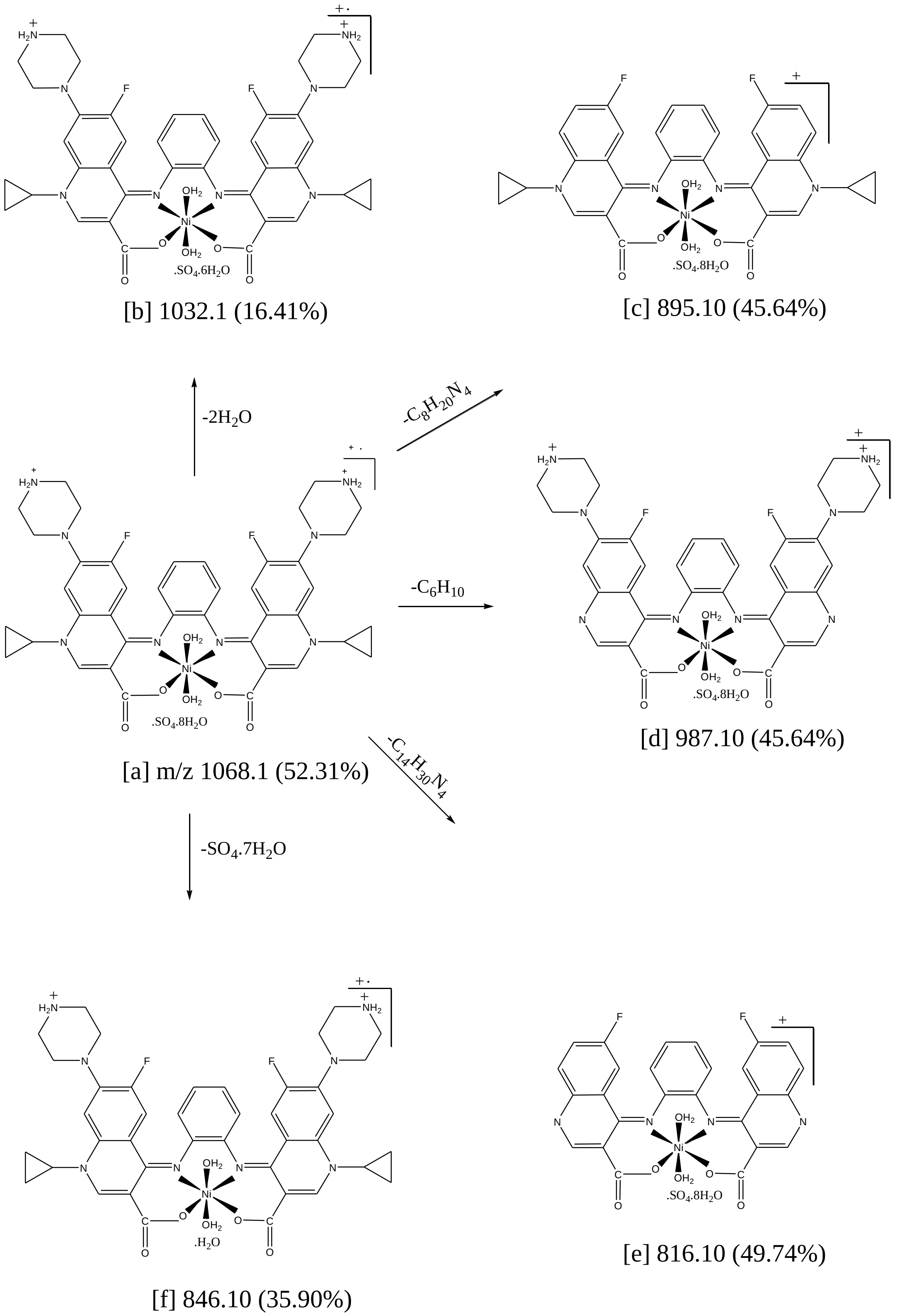
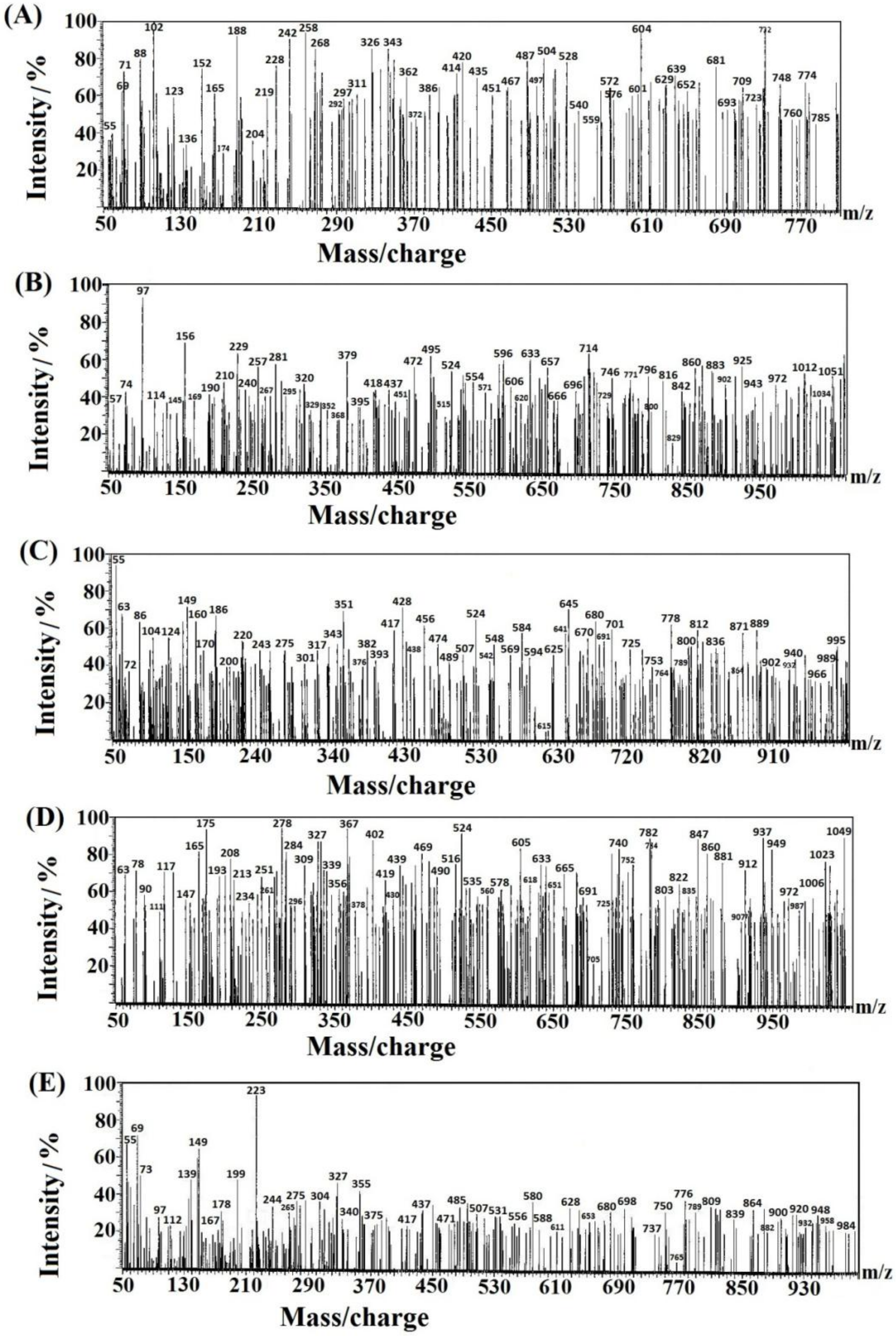


Figure 5: Mass spectra diagrams for (A) (CIP-o-phdn), (B)$[Ni(CIP\text{-}o\text{-}phdn)(H_2O)_2](SO_4).8H_2O$, (C) $[Cu(CIP\text{-}o\text{-}phdn)(H_2O)_2](CH_3COO)_2.3H_2O$, (D) $[Zn(CIP\text{-}o\text{-}phdn)(H_2O)_2](NO_3)_2.5H_2O$ and (E) $[Ce(CIP\text{-}o\text{-}phdn)(H_2O)_2](SO_4)_2.3H_2O$.



F- Biological activity

The susceptibility of certain strains of bacterium, such as *Staphylococcus aureus* (*S. aureus*), *Bacillus subtilis* (*B. subtilis*), *Escherichia coli* (*E. coli*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) and antifungal screening was studied against two species *Candida albicans* (*C. albicans*) and *Aspergillus fumigatus* (*A. Fumigatus*) towards ciprofloxacin schiff base (CIP-o-phdn) and its complexes was judged by measuring size of the inhibition diameter. As assessed by color, the complexes remain intact during biological testing (Table 6 and Fig. 6). A comparative study of ligand and their metal complexes showed that the Zn(II) complex showed highly significant for Gram-negative and significant for Gram-positive bacteria. For Cu(II) is antibacterial activity against *Escherichia coli* (*E. coli*) and no antifungal activity observed for ligand and their metal complexes (Table 6). The results are promising compared with the previous studies [52,53]. Such increased activity of metal chelate can be explained on the basis of the oxidation state of the metal ion, overtone concept and chelation theory. According to the overtone concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid-soluble materials in which lipo solubility is an important factor that controls the antimicrobial activity. On chelation the polarity of the metal ion will be reduced to a greater extent due to overlap of ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further it increases the delocalization of π-electrons over the whole chelate ring and enhances the lipophilicity of the complexes [54]. This increased lipophilicity enhances the penetration of complexes into the lipid membranes and blocks the metal binding sites in enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the microorganisms. Finally, we study the effect of condensation of o-phenylenediamine with ciprofloxacin on the antibacterial activity compared with free ciprofloxacin the data indicate that CIP-o-phdn Schiff base exhibits much higher than ciprofloxacin alone [55].

Figure 6: Statistical representation for biological activity of (CIP-o-phdn) and its metal complexes.

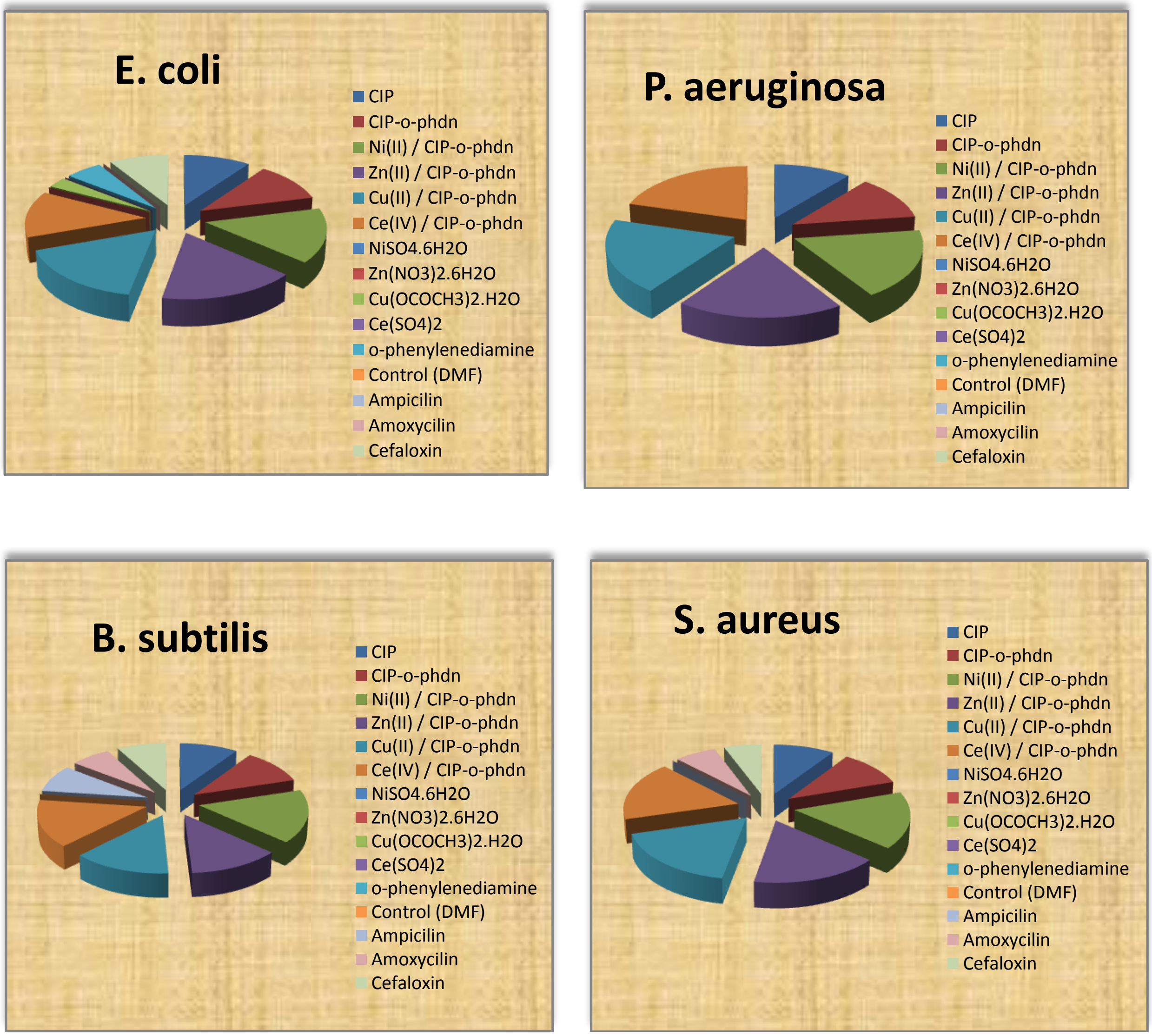


Table (6): The inhibition diameter zone values (mm) for (CIP-o-phdn) and its metal complexes.

Tested compounds		Microbial species					
		Bacteria				Fungi	
		E. coli	P. aeruginosa	B. subtilis	S. aureus	C. albicans	A. fumigatus
CIP		27 ±0.35	23 ±0.11	32 ±0.22	26 ±0.40	0	0
CIP-o-phdn		30 ±0.33	25 ±0.11	36 ±0.22	29 ±0.90	0	0
$[Ni(CIP\text{-}o\text{-}phdn)(H_2O)_2]SO_4.8H_2O$		41^{+1} ±0.13	38^{+2} ±0.06	55^{+3} ±0.09	46^{+1} ±0.01	0	0
$[Cu(CIP\text{-}o\text{-}phdn)(H_2O)_2](CH_3COO)_2.3H_2O$		45^{+2} ±0.16	40^{+2} ±0.08	42^{+1} ±0.51	46^{+1} ±0.12	0	0
$[Zn(CIP\text{-}o\text{-}phdn)(H_2O)_2](NO_3)_2.5H_2O$		45^{+2} ±0.12	41^{+3} ±0.07	45^{+1} ±0.60	49^{+2} ±0.14	0	0
$[Ce(CIP\text{-}o\text{-}phdn)(H_2O)_2](SO_4)_2.3H_2O$		35^{NS} ±0.19	43^{+3} ±0.09	49^{+1} ±0.22	48^{+2} ±0.18	0	0
$NiSO_4.6H_2O$		0	0	0	0	0	0
$Zn(NO_3)_2.6H_2O$		0	0	0	0	0	0
$Cu(OCOCH_3)_2.H_2O$		8 ±0.33	0	0	0	0	0
$Ce(SO_4)_2$		0	0	0	0	0	0
Control (DMF)		0	0	0	0	0	0
o-phenylenediamine		15 ±0.33	12 ±0.11	0	0	0	0
Standard	Ampicilin	0	0	28 ±0.40	0	0	0
	Amoxycilin	0	0	22 ±0.11	18 ±1.73	0	0
	Cefaloxin	24 ±0.34	0	27 ±1.15	16 ±0.52	0	0

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).

Conclusion:

The four new metal complexes of new tetradentate Schiff base (CIP-o-phdn), (N,N'-o-phenylene (bis 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazine-1-yl)-quinoline-3-carboxylic acid) with Ni(II), Cu(II), Zn(II) and Ce(IV) complexes were prepared and isolated as solids and formulated as $[Ni(CIP\text{-}o\text{-}phdn)(H_2O)_2]SO_4.8H_2O$, $[Cu(CIP\text{-}o\text{-}phdn)(H_2O)_2](CH_3COO)_2.3H_2O$, $[Zn(CIP\text{-}o\text{-}phdn)(H_2O)_2](NO_3)_2.5H_2O$ and $[Ce(CIP\text{-}o\text{-}phdn)(H_2O)_2](SO_4)_2.3H_2O$. The new compounds have been characterized using molar conductance, melting point, magnetic moment, elemental analysis, IR, UV-Vis, ^{1}H NMR, mass spectra as well as thermal analysis (TGA and DrTG). From these tools, it may observe that the azomethine and carboxylic groups coordinated with metal ions and the metal ions complete their coordination number with two coordinated water molecules forming a distorted octahedral geometry. All the tested complexes have greater activity than the Schiff base ligand in addition; the prepared complexes may become clinically relevant for new drug candidates for future antibiotic agent development

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