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RESEARCH ARTICLE

Metal Complexes of Mixed Ligands (Quinolone Antibiotics and α-Aminonitrile Derivatives) Their Applications: An Update with Fe (III), Co (II) and Ni (II) Ions and Study the Biological Activity

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Abstract

Quinolones (ciprofloxacin) have abroad- antibiotics spectrum with best oral absorbing. Consequent to the biological action located on nucleus of CH_3COOH which works in the 3-location and in best state a piperazinyl base circle (or any type of N-heterocycle) at 7- positron and an oxygen carbonyl atom at 4-position). Quinolones (L1) and 2-phenyl-2-(1-Naphthylamitie) acetonitrile (L2) can bind to the ions for metal return making complexes which acting as binary ligand. The complexes and ligands which diagnosed by Micro element analysis chloride container, FTIR, UV-Vis spectra, conductivity in addition to measurement of magnetic susceptibility. Under this act founding the likely geometries shapes were proposed as octahedral complexes, several of them were classified as non-electrolyte the rest consider as weak electrolyte. The $L_1$and L_2 with [Fe(III),Co(II) and Ni(II)] respectively provided the formulae: $[ML_1L_2Cl]Cl.2H_2O$ and $[FeL_1L_2Cl]2H_2O$ Were M:{ Co^{2+} and Ni^{2+}}

Keywords: *Quinolones (ciprofloxacin), 2-phenyl-2- (1-Naphthylamine) acetonitrile.*

Introduction

The derivatives of quinolone have many benefits in the medication aspect, food, help factors, pigments, tools, plants and electron is created as a product, the basic of synthesis quinolone with yields gave a good-looking aim in the synthetic organic chemist. Formation of metal complexes for quinolones as a result of their ability to bind metal ions [1].The quinolones in their metal complexes, represent as bidentate ligand, unidentate ligand and also abridging ligand.

"Commonly, quinolones in a bidentate manner wear coordinated, by oxygen atoms of deprotonated carboxylic group and by oxygen atom of the carbonyl ring. The word generic “quinolone antibiotics” due to a group of manufactured antibiotics which have a special things of bacterial, in the 1960 [2] the series of first compound, was presented in analysis. The nalidixic acid in the clinical used was limited because of its activity have a narrow spectrum. Modifications which made on the nucleus were completed to increase the spectrum of antibacterial and development properties of the pharmacokinetics [3, 4].

Preparation of the Ligand

The following procedure was used to prepared ligand (L_2). KCN (0.130 g, 0.0020mol) was melted in (4mL) of purified H_2O in less 5°C cooled. To the above solution, benzaldehyde (0.2120 g, 0.0020mol) in (25mL of 95 percent of ethyl alcohol) was additional.

This mixture moved maintains temperature under 5°C. snowy CH_3COOH (0.120 g, 0.0020mol) was adding with moving, the heat less 5°C, following the addition of primary amine 1-Naphthylamine(0.286g 0.0020mol) in (10mL of 95% CH_3CH_2OH) and (5mL) of Icy CH_3COOH (temperature under 5°C) with constant movement at a good aired hood. The heat keeping in (15°C) during addition. The mix wear keeping moved for tow hours and saved at room heat for twenty four hours. Coolers needles (Marron) was obtained splashed with diluted

HCl (0.2M) to take away any extra of KCN. Re-crystallized was mad to the compound with 95% ethyl alcohol [5, 6]. The yield was (72.9%). Reaction below gave synthesis method of the ligand:-

Benzaldehyde 1-Naphthylamine 2-phenyl-2-(1-Naphthylamine) acetonitrile (L_2)

Preparation of Complexes

Preparation of Complexes (C_1-C_3)

A mixture of (0.386g, 1mmol) of ligand L_1(ciprofloxacin) in (12mL) of absolute ethyl alcohol and (0.257g ,1mmol) of L_2 in (12mL) of free C_2H_5OH additional gradually to a metal chloride of (1mmol) from (0.238g, 0.270g and 0.237g from ($FeCl_3.6H_2O$ $CoCl_2.6H_2O$, and $NiCl_2.6H_2O$, in that order) was melted in (23mL) of ethyl alcohol and escalation with moving by using in absence of water conditions Na_2SO_4 (anhydrous) for twenty four hours. The complexes produce was collected after vaporization and left in the desiccators to become dry under P_2O_5 [7] (Yield% = 81.5).

Results and Discussion

The interesting of making (C≡N) groups related to their flexibility as major article for preparation of various compounds [8]. The certain form of α-aminonitriles which was record can diagnose by C.H.N (Table1), FTIR (Table2), UV-Visible (Table3) techniques.

Table 1: Some physical properties with elemental micro analysis of (L_1, L_2) with their complexes

COMP.	FORMULA M.W.T (GM/MOL)	YIELD %	COLOR	M.P (°C)	C% CAL (FOUND)	H% CAL (FOUND)	N% CAL (FOUND)	M% CAL (FOUND)	CHLORINE %
L_1	$C_{17}H_{21}FClN_3O_4$ (385.82)	-----	Off-White	254-256	52.77 (52.30)	5.42 (5.12)	10.85 (10,60)	------	9.17 (8.68)
L_2	$C_{18}H_{14}N_2$ (258,12)	70,90	Marron	152-155	83.72 (82.33)	5.,42 (5.17)	10.85 (10.00)	------	------
C_1	$[FeL_1L_2Cl(H_2O)]Cl.2H_2O$ (787,0)	72,70	Dark yellow	306 Dec.	53.36 (52.12)	5.08 (3.98)	8.90 (8.00)	7.07 (6.10)	9.02 (8.09)
C_2	$[CoL_1L_2Cl(H_2O)].2H_2O$ (754.4)	80,50	Green	380-383	55.67 (53.26)	5.30 (4.76)	9.27 (8.16)	7.80 (6.63)	4.69 (4.04)
C_3	$[NiL_1L_2Cl(H_2O)].2(H_2O$ 718.3)	83,70	Dark gray	325 Dec.	55.64 (54.75)	5.43 (4.08)	9.27 (8.83)	7.68 (6.78)	4.63 (3.11)

FTIR Spectra

A-Aminonitrile and ciprofloxacin ligands

The characteristic bands in the spectra of the complexes was presented as coordinated H_2O looked at (3452-3533) cm^{-1} related to υ(OH) [9, 10] as shown in C_1 and C_3 or lattice water looked at (747 cm^{-1}) back to to ρw(H-OH) in (C_1,C_2 and C_3) complexes [11, 12].In this area (419-568) cm^{-1} anew band observed to υ (M-N) [13]. The beams which looked at (3350 cm^{-1}) which is related to the vibrations of the (N-H) bond in (L_2) was removed as shown in the following spectra of complex (C_1, C_2 and C_3) to (3339, 3358 and 3382) cm^{-1} in that order [14, 15]. This provided a hint that the coordination of ligand with ions of the metal with α-amino group by nitrogen atom.

This band (2162cm^{-1}) that come back to the nitrile group of the second ligand was lifted in the complexes spectrum of (C_1, C_2 and C_3), the frequencies became higher (2164, 2170 and 2189) cm^{-1} in this way, this gave a guide for bonding of nitrile group from atomic nitrogen [16, 17], the increasing in shifting of υ(C≡N) band to greater frequencies give more indication for linking of metal ion from the paired electrons of atomic nitrogen [18].

The (N-H) band which was back to the second ligand was removed in the (C_1,C_2andC_3) from (1631 cm^{-1}) to (1629,1631and 1616) cm^{-1} respectively, this gave more indication about contact of metal from the N_2 atom of α-amino group and this provided more indication to formation of complexes [19]. The carboxylic group appear at (1708 cm^{-1}) was due to the υ(c=o) of the first ligand, also, ionic carboxylic gives two interesting bands in the regain 1602-1512 $cm^{-1}$and 1402-1255 cm^{-1} [20], which due to υ(c-o-c) asymmetric and symmetric was also moved in the respectively

[21].The quinolone ring C-C and C-N bond appear around 1494cm^{-1}. Organized by two O_2 from quinolone molecules (first O_2 from pyridine and other from carboxylic group) [22], as shown in Table (2) and in Figures (3, 4 and 5).

Table 2: Specific infrared absorption bands of ligands ($L_1$and L_2) with their complexes

Comp.	υN−H cm^{-1}	υC≡N cm^{-1}	υ(C=O) cm^{-1}	δN−H cm^{-1}	υ(C-O-C) (asy)	υ(C-O-C) (sy)	υC-N cm^{-1}
L_1	3377 w.sh	-------	1708 v.sh	1625 s.sh	------	-------	1143 w.sh
L_2	3350 m.sh	2162 v.sh	-------	1631 m.pr	------	-------	1006 w.sh
C_1	3339 w.pr	2164 m.sh	-------	1629 v.sh	1519 m.sh	1299 m.sh	1186 w.sh
C_2	3358 w.sh	2170 v.s.sh	-------	1631 m.sh	1568 m.sh	1300 s.sh	1190 w.sh
C_3	3382 s.pr	2189 m.sh	------	1616 s.sh	1568 s.sh	1309 s.sh	1182 m.sh

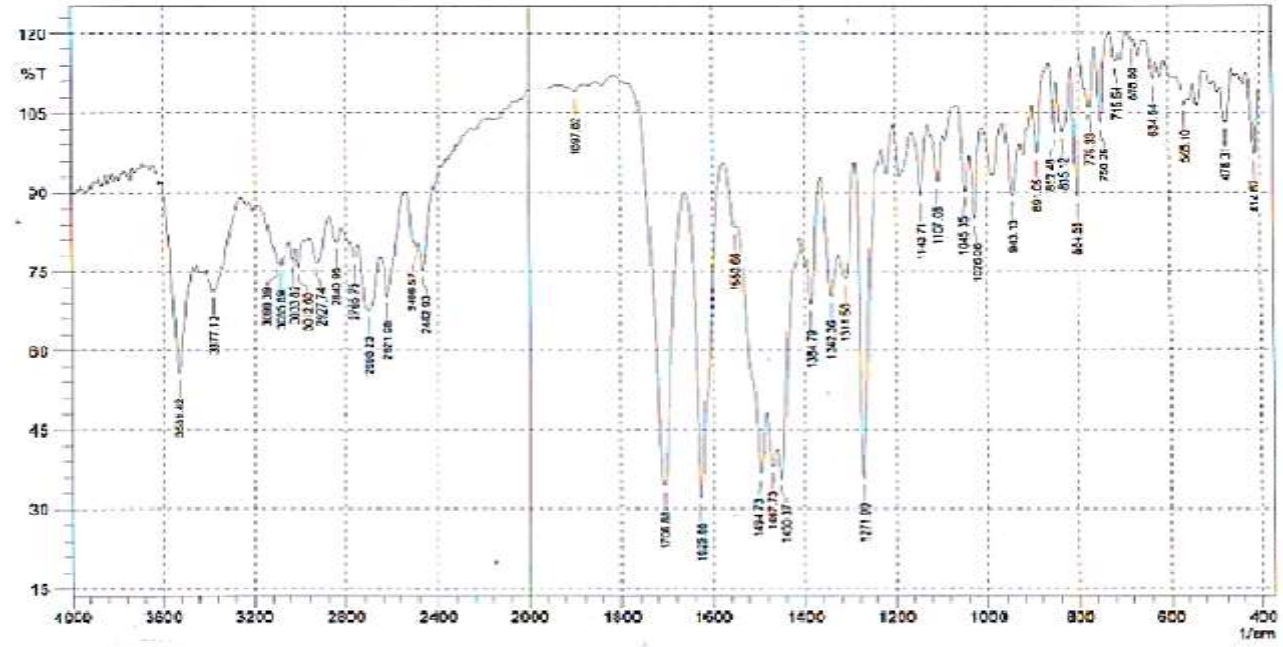


Fig.1: FTIR spectrum of L_1

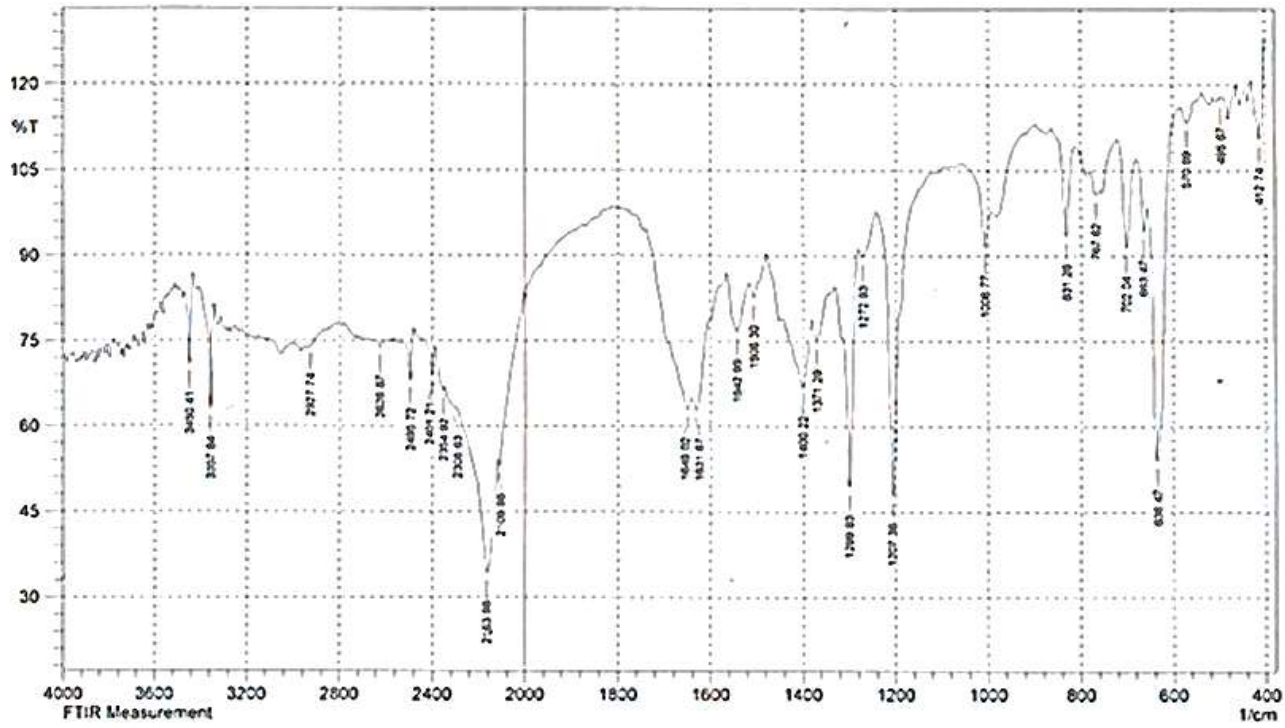


Fig.2: FTIR spectrum of L_2

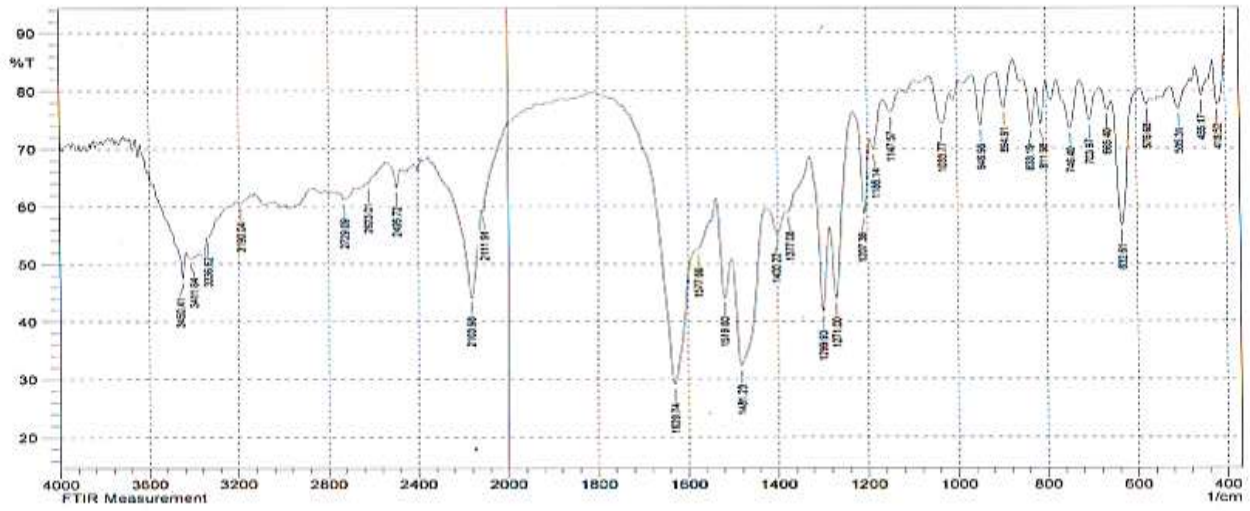


Fig.3: FTIR spectrum of C_1

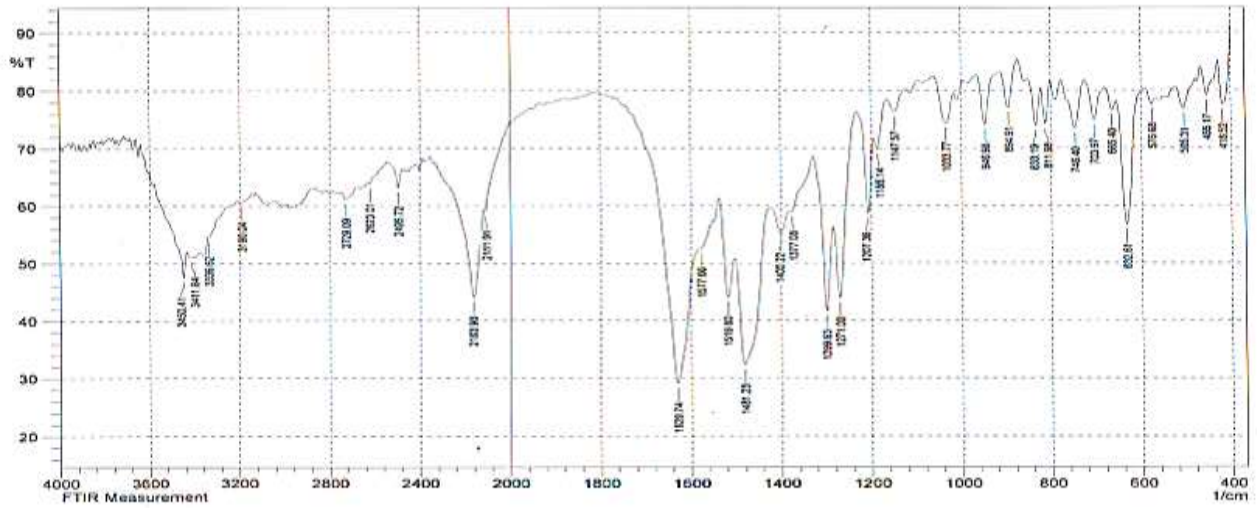


Fig.4: FTIR spectrum of C_2

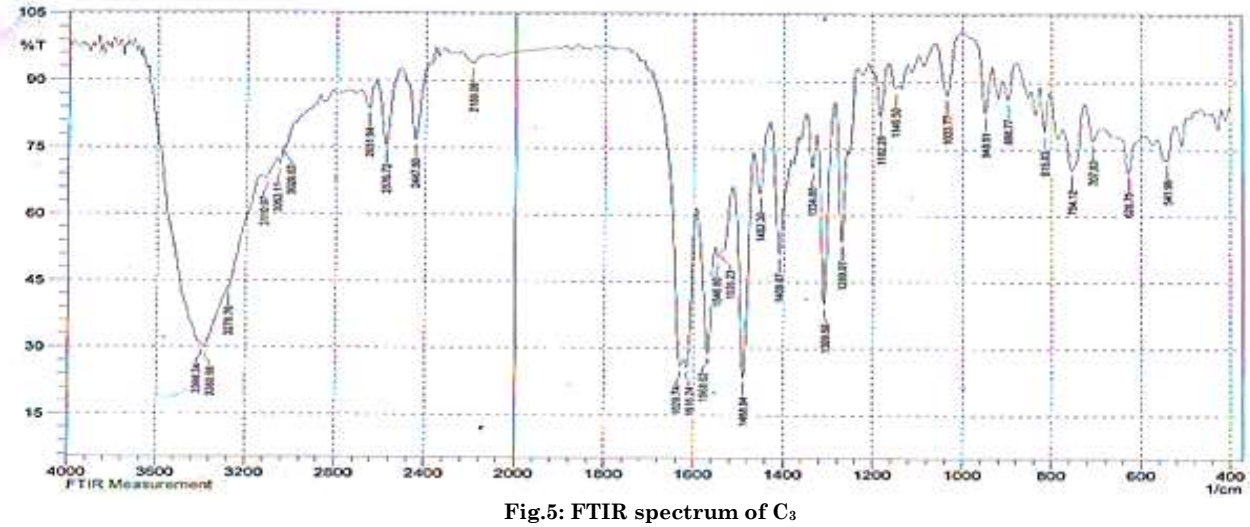


Fig.5: FTIR spectrum of C_3

Electronic Spectra (UV-Visible)

The ligends (L_1andL_2) and their complexes, electronic absorption data of (10^{-4}M) were noted in C_2H_5OH was given in Table (3) at thermal room, while their spectrum were displayed in forms (6-10) The spectrum of three ligands shown a great intensity package looked in the area (48543 and 38461) cm^{-1}, related to π→π* of relay system [23].Another bands have low intensity showed in the close place of U.V. (31645 and 24691) cm^{-1} separately, were due to n→π* shift, the practical shape and the properties of the solvent is very important things to determine intensity and positions of these bands [24] in addition to that special effects of ligand area [25].

Table3: Electronic spectrum, molar conductivity, magnetic susceptibility and proposed chemical structures of ligand with complexes

Comp.	Assignments	wave no (cm)ύ	Wavelength λ (nm)	Geometry Suggested	(B.M)	Molar Cond. Ω cm^2 moL^{-1}
L_1	n→π π→π*	31645 48543	316 206	---------	----	-------
L_2	n→π π→π*	24691 38461	405 260	---------	----	-------
C_1	$^6A_1$ g→$^6t_1$g(G) $^6A_1$ g→$^4A_1$ g +^{4}E g	20491 36490	488 273	Octahedral	5.19	11.92
C_2	$^4t_1$g(F)→$^4t_2$g(F) $^4t_1$g(F)→$^4A_2$ g(F) $^4t_1$g(F)→$^4t_1$g(P)	15267 30769 31055	655 325 270	Octahedral	4.03	12.44
C_3	$^3A_2$ g→$^3t_1$g $^3A_2$ g→$^3t_1$g(F) $^3A_2$ g→$^3t_1$g(p)	13071 16915 31055	765 590 322	Octahedral	2.81	13.19

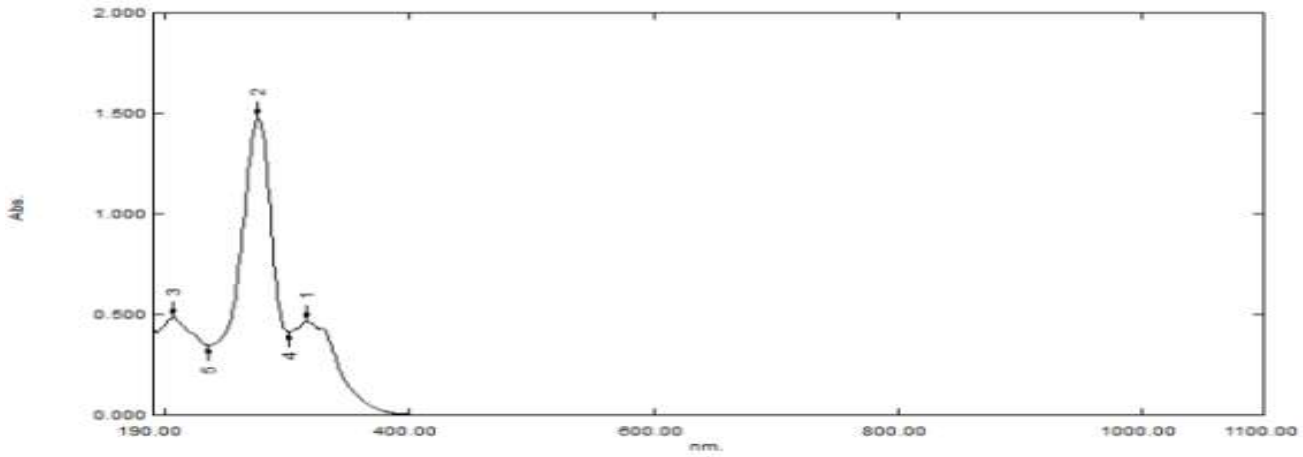


Fig 6: UV-Visible Spectrum of L_1

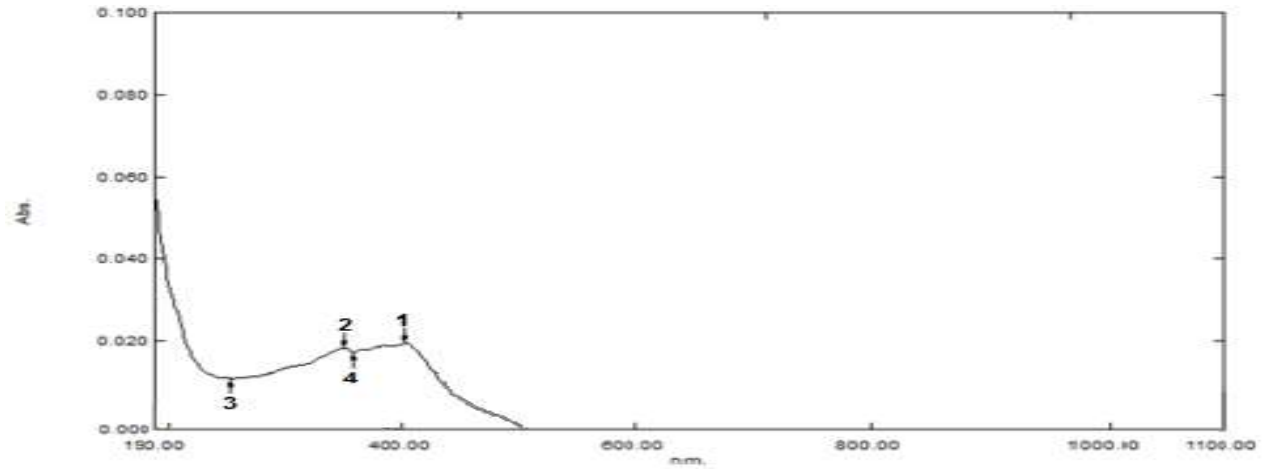


Fig.7: UV-Visible Spectrum of L_2

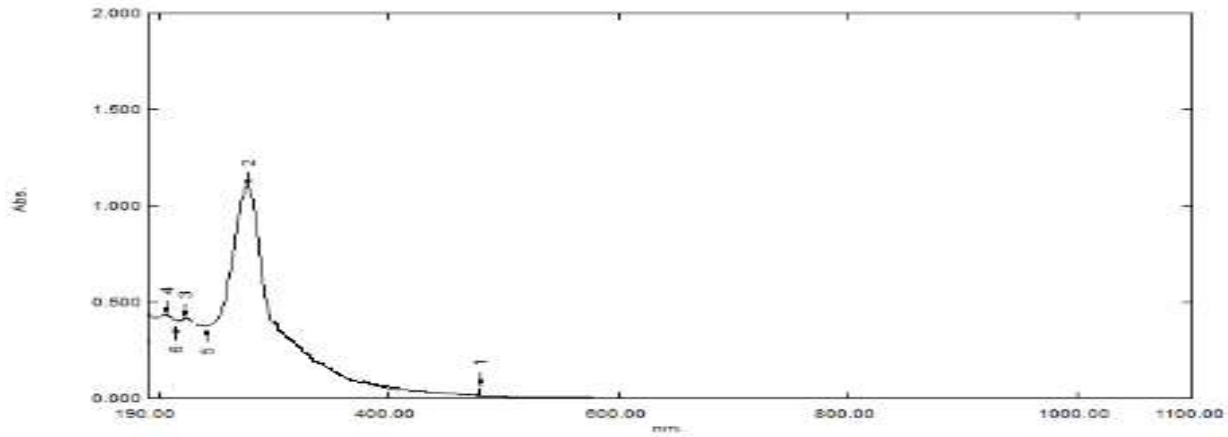


Fig.8: UV-Visible Spectrum of C_1

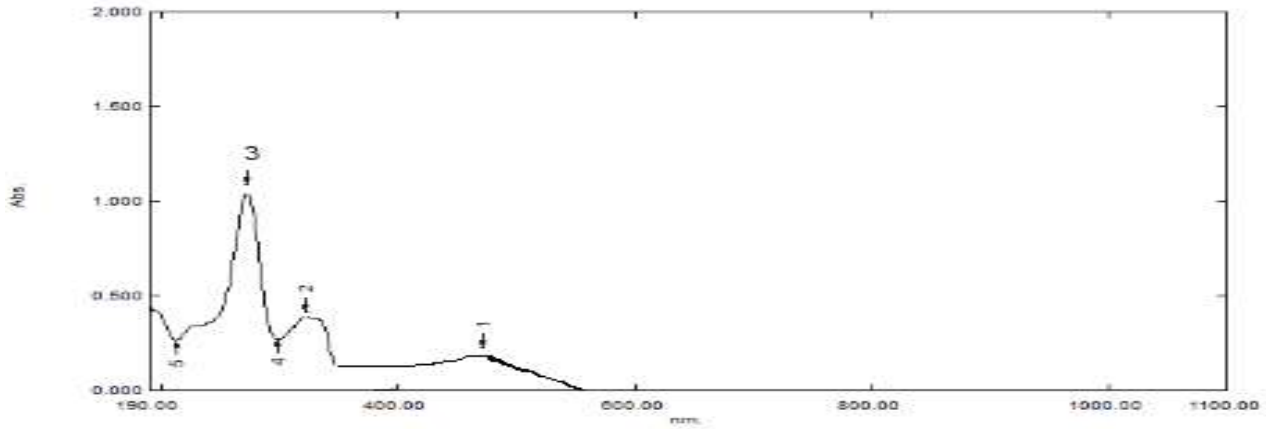


Fig 9: UV-Visible Spectrum of C_2

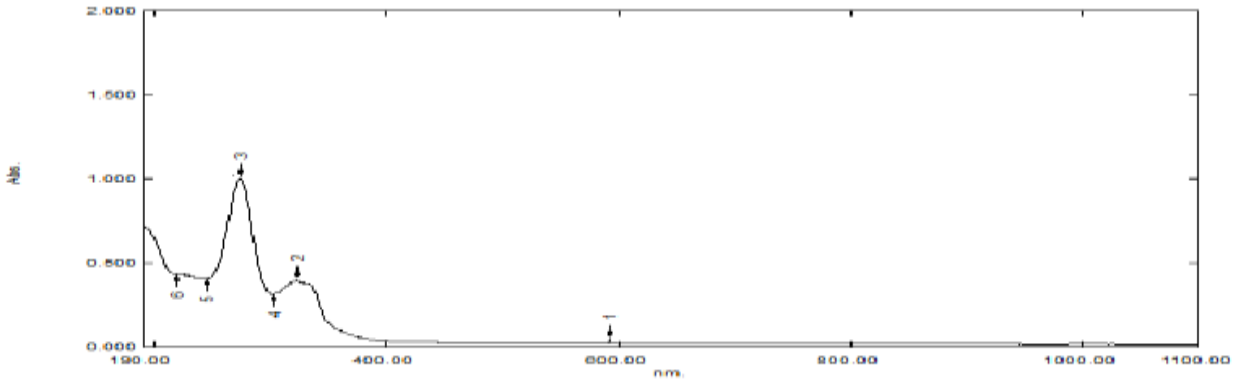
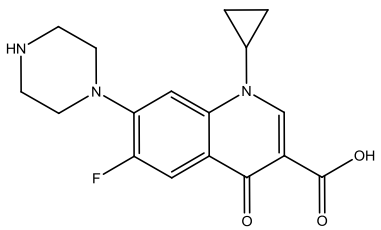


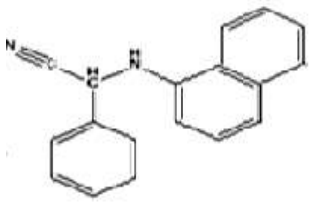
Fig 10: UV-Visible Spectrum of C_3

^{1}H-NMR and ^{13}C-NMR Spectra

The ligands (L_1 and L_2) were described by ^{1}H-NMR and ^{13}C-NMR spectroscopic methods, using dimethyl sulfoxide (**d6**) as solvent given in Table (4), The ^{1}H-NMR spectra of the (L_1) seen five peaks; first appeared at δ(1.41) ppm was related to the (-CH_2-), second founded at δ(2.23) ppm assigned to the (=NH), the third seemed at δ(3.45) ppm which belong to the (-CH_2-N=) [26], and forth peak at δ(7.44-7.56) ppm was returned to the aromatic protons , the last one in the regent δ(8.90) ppm went to the (-COOH) [27]. The ^{1}H-NMR spectra of (L_2) gave many peaks; the first one at δ (2.77) ppm peak solvent (DMSO, δ (3.77) ppm (-N-H) proton peak but the third in that δ (5.47) ppm return to (-CHC≡N). The last back to aromatic protons [28] at δ(6.75-7.98) ppm.^{13}C-NMR spectrum of the ligand (L_1) showed seven peaks; related to the (-CH_2-CH_2-), (=CH-N=), (-CH_2-NH-), (-CH_2-N=), (-COOH), (=C=O) carbon, and the last peak back to aromatic carbon atoms [31] as explain in table(4) respectively. The ^{13}C-NMR for (L_2) gave three character bands; appeared at δ (38.86), δ (53.21) and δ (115.36)ppm which was corresponded to the solvent (DMSO), (-CH-C≡N) and (-CH-C≡N) carbon atom [27] in this order as appear in the Table (4) below.

Table4: ^{1}H-NMR and ^{13}C-NMR Spectra of the L1 and L2

Comp.	Formula	Groups	Chemical Shifts δ(ppm)	Groups	Chemical Shifts δ(ppm)
L_1	$C_{17}H_{21}FClN_3O_4$	(-C**H**$_2$-)	1.41	(-CH_2-**C**H_2-)	7.71
		(=N**H**)	2.23	(=**C**H-N=)	35.81
		(-C**H**$_2$-N=)	3.45	(-**C**H_2-NH-)	45.83
		(Ar-**H**)	7.44-7.56	(-**C**H_2-N=)	51.30
		(-COO**H**)	8.90	(-**C**OOH)	166.23
				(=**C**=O)	176.41
				Ar-H	115-102

L_2	$C_{18}H_{14}N_2$ 	(=N<u>H</u>) (=C<u>H</u>-C≡N) (Ar-<u>H</u>)	3.77 5.47 6.75-7.98	(-<u>C</u>H-C≡N) (-CH-<u>C</u>≡N)	53.21 115.36

In vitro Antibacterial Activity

All checking complexes against test bacteria that hold a name; Staphylococcuaurouss, Bacillus subtilize (Gram+), Escherichia and Pseudomonas aerugin (Gram-).Agar, (distribution way method) which is using to assign the action [29, 30]. Borer diameter of 0.6 mm was using in all complexes which prepared at (10^{-3}M) in the presence of a solvent (dimethylsulphoxide), as well as also taken on a controller negative Gram while Ciprofloxacin it was consider to be controlling of Gram positive. The (DMSO) shown no action compared to the tested bacteria, while several complexes given very best effects. The Figures in Table (5) gave an indications data to the inhibition zones of the prepared complexes and solvent. The measuring zones inhibition data in (mm) in comparison with inhibition zone of antibiotic broad spectrum. All complexes obtained not effective compared with the negative bacterium (Escherichia coli), was causes sickness, like, enterotoxigenic strains products a toxin in the gut, causing naturally in diarrhea [31].The (C_3) gave effective against the plus bacterium (Staphylococcus aureus), (Bacillus subtilis) .The bacterium are famous and fight to the antibiotics development and it is consider as a big state of various health problem and infections [32], while the gram negative (Escherichia coli. Pseudomonas aeruginosa) presented good activity. Complexes (C_1andC_2) wear observed very good activity towards both positive gram and negative gram bacterium. To control on biological activities of metal complexes a lot of reasons were mentioned [33]. Such as ligand formation, type of metal, charged complex, the series of transition metal, geometrical arrangement of the metal complex and ion.

Table 5: Measuring inhibition zones (mm) in DMSO, for Ciprofloxacin with their complexes

	Inhibition-zone (mm) Escherichia coli	Inhibition -zone (mm) Pseudomonas aeruginosa	Inhibition zone(mm) Staphylococcus aureus	Inhibition zone (mm) Bacillus subtilis
DMSO	----	----	----	----
L_1(cip)	18.5	23.7	18.15	12.23
C_1	28.5	27.8	29.7	26.9
C_2	31.1	28.7	22.3	21.6
C_3	----	----	31.6	35

The Nomenclature and Suggested Structures of the Complexes

The expected shapesand properties of complexes were preparimg provided by their (C.H.N.), infrared radiation, ultra-voilet spectroscopy, as well as the values of molar conductivity. The opration result found of analysis of element compatible with the values wich have been calculated, IR, UV-Visible spectroscopy, of the complexes which prepared proven their creation and their figures, the values of conductivity provide us with facts about the complexes ionic behaver that will be prepared and their configuration. Elemental analyses of the L_1 ,L_2 with Fe(III) Co(II) and Ni(II) indicate that can be expressed as (1:2) (M:L).The nitrile group are removed approximately(30-53) cm^{-1} in comparison with ligands which was free, and υ(N-H) bands are stirred by (20-50) cm^{-1} if we comparative with the freely ligand. The IR resulting gave aprove that linking of the ligands with Co^{+2} Ni^{+2}, and Fe^{+3} through tow N_2 atoms of (N-H) and (C≡N). The band which appeared at (1707 cm^{-1}) retuned to the carbonyl of the COOH(L_1) in adding to that ,ionic carboxylic that own two bands within area of 1400-1257 cm^{-1}, 1600-1510 cm^{-1} and that will be related to υ(c-o-c) asymmetric and symmetric was moved in the spectrume of the complexes. The IR results give an indication to that the ligands are linked to

Co^{+2}, Ni^{+2} and Fe^{+3} by both O_2 atoms of carbonyl.Add to that U-V spectra, the magnetic susceptibility and molar conductivity provided us many facts related to the coordination and geometry of the complexes. According to the above information the shap of complexes are proposed are octahedral as explain in Fig below:

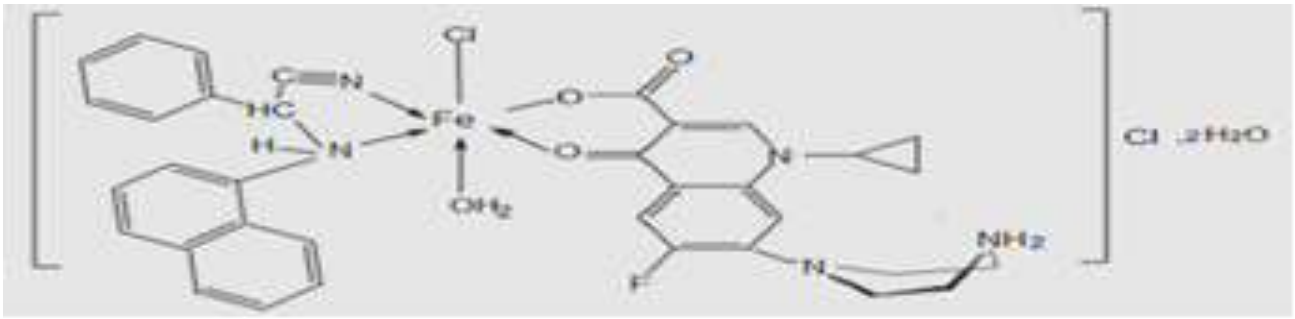


Fig. 11: Suggested structure of C_1 [Fe $L_1L_2Cl(H_2O)$]Cl.$2H_2O$ [chloro mono aqua {2-phenyl-2-(1-Naphthylamine) acetonitrile} ciprofloxacin} Irone (III)] chloride dehydrate

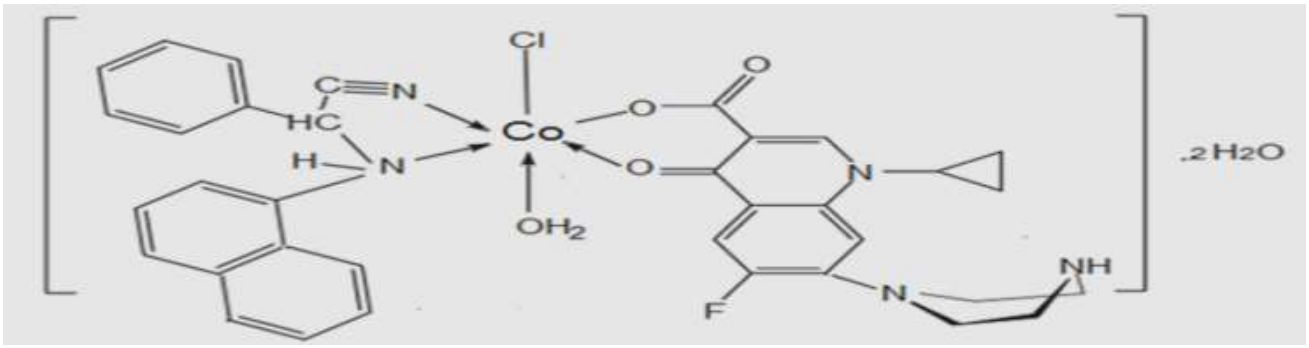


Fig.12: Suggested structure of C_2 [Co L_1 L_2 $Cl(H_2O)$].$2H_2O$ [chloro mono aqua {2-phenyl-2-(1-Naphthylamine) acetonitrile ciprofloxacin} cobalt (II)] dehydrate

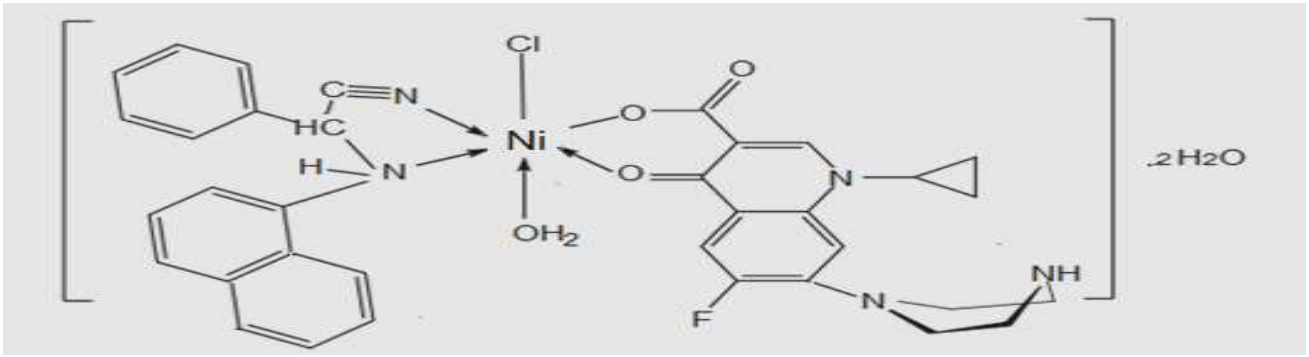


Fig. 13: Suggested structure of C_3 [Ni L_1 L_2 $Cl(H_2O)$].$2H_2O$ [chloro mono aqua {2-phenyl-2-(1-Naphthylamine) acetonitrile ciprofloxacin} nickel (II)] dihydrate

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