Benha Journal of Applied Sciences (BJAS) **print: ISSN 2356–9751**
Vol. (9) Issue (3) (2024), (161-172) **online: ISSN 2356–976x**
http://bjas.journals.ekb.eg

Synthesis, Characterization and Modelling Studies of Some Transition Metal Complexes with Mixed Chelating Drugs

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Abstract

The solid complexes formed between Mn^{2+}. Fe^{3+}, Ni^{2+}, Cu^{2+}, Zn^{2+} and VO_2^{3+} with Enrofloxacine-L-Ascorbic acid (Enro-Asc) and Levofloxacine-L-Ascorbic acid (Levo-Asc) as mixed drugs were prepared in the solid state. The chemical structure of the synthesised complexes were elucidated using different chemical and physical techniques which proved the formation of complexes with stoichiometric ratios Enro:Asc:M and Levo:Asc:M (1:1:1). Elemental analysis and molar conductivity showed satisfactory agreement between the proposed and found formulae, while IR and electronic absorption spectra proved the mode of bonding and the expected *d-d* transitions within the metal ions. Using the DMOL3 program, which is designed for wide-scale density function theory (DFT), several quantum chemical and energetic characteristics of the free drug and their metal complexes were computed. The existence of high or low electron density in a certain molecular site was represented graphically by electron charge density using molecular modeling software. For both free medicines and their mixed complexes, the DFT approach was used to determine the total density, the deformation density, and the frontier orbital energies in 3D plots.

Keywords: mixed chelating drug metal complexes, Levofloxacine, Enrofloxacine, L-Ascorbic acid

Introduction

In many biological activities and metallo-enzymes, the coordination chemistry of mixed-chelating drugs with transition metal ions is crucial. These complexes typically exhibit higher bioactivities than the free drugs, and the complexation process may lessen some side effects and drug resistance [1,2]. The fact that many antibiotics have metal-binding sites—where transition metal ions are firmly bound and form stable coordination connections—was made evident [3]. These sites either serve a structural role or are in charge of the antibiotics' potent action. Several antibiotics are dependent on metal ions for optimal performance, and these compounds' complexes frequently exhibit superior physicochemical characteristics and significant efficacy compared to the parent medications [4]. The likelihood of a complex's expected attributes changing increases when many drug types are present. .. The biological activities of a large number of mixed ligand transition metal complexes were investigated using a variety of techniques. It was discovered that these complexes exhibit a wide range of neurophysiological and neuro pharmacological effects, including antimicrobial, antiviral, anticonvulsant, anticancer, anti-mycobacterial, antimalarial, cysticidal, herbicidal, and anti-inflammatory activity [4–10]. Levofloxacin is a synthetic antibacterial drug with a 4-oxo-1,4-dihydroquinoline structure that belongs to the third generation of fluoroquinolones [11]. Fluoroquinolones' antibacterial activity is dependent on the tangential substituents' type and their spatial connection in addition to the bicyclic heteroaromatic pharmacophore [12]. By increasing the bacterial enzymes' affinity and boosting cell penetrations, these substituents have an impact on the antibacterial action [13]. Herein The solid complexes formed between Mn^{2+}. Fe^{3+}, Ni^{2+}, Cu^{2+}, Zn^{2+} and VO_2^{3+} with Enrofloxacine-L-Ascorbic acid (Enro-Asc) and Levofloxacine-L-Ascorbic acid (Levo-Asc) as mixed drugs were prepared in the solid state. The chemical structure of the synthesised complexes were elucidated using different chemical and physical techniques which proved the formation of complexes with stoichiometric ratios Enro:Asc:M and Levo:Asc:M (1:1:1). Using the DMOL3 program, which is designed for wide-scale density function theory (DFT), several quantum chemical and energetic characteristics of the free drug and their metal complexes were computed.

Experimental

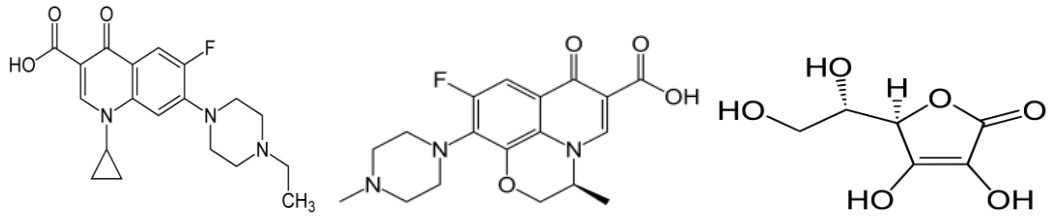
All chemicals utilized in this work were extremely pure that didn't require any additional purification. L-ascorbic acid, enrofloxacine, levofloxacine, and metal salts were purchased from Sigma, Aldrich Chemical Company, and were used as received. The solvent used comes from the Merck Company and is extremely pure. A Japanese spectrophotometer; Jasco V-530 (UV-VIS), was used to measure the electronic spectra while the IR spectra were measured using KBr disk technique using a Beckmann IR 4220 spectrophotometer.

Results and discussion

1- Studies on the metal complexes in solid state.

i. Clarification of structure.

The following stoichiometric ratios were used to produce the solid complexes of Mn^{2+}, Fe^{3+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, and VO_2^{3+} with the mixed chelating medicines under study: mixed Enrofloxacine - L-ascorbic acid; [Enro :Asc: M [1:1:1:] and mixed levofloxacine - ascorbic acid; [Levo : Asc.M [1:1:1:]. The chelating drugs under study have the following structural formula:



Enrofloxacine Levofloxacine L-Ascorbic acid

1- Elemental analysis

Each complex has a distinct color, is air-stabilized, and has a high decomposition point (> 350oC). They are only marginally soluble in other widely used organic solvents, however they are modestly soluble in dimethylsulphoxide (DMSO) and dimethylformamide (DMF). The elemental analysis, molar conductivities, thermal analysis, IR, and UV-Vis spectra in Nujol Mull were used to characterize the metal complexes. The suggested formula was first verified using FTIR spectroscopy and elemental analysis. A fair agreement is observed between the calculated and found values of C, H, N, and M percentages in the elemental analysis (Table 1).

Molar conductivity

The complexes under study had their molar conductance (Λm) measured in DMF solutions (ohm-1cm2mol-1). Fe3+ and VO23+ complexes are ionic in nature, but the numbers in Table (1) show that the complexes formed with divalent metal ions are non-ionic. By adding AgNO3 solution to the solubilized chelates in DMF, the counter anion (Cl-) precipitates as AgCl, confirming the presence of Cl- outside the coordination sphere.

Table (1): Elemental analysis and molar conductivities of Mn^{2+}. Fe^{3+}, Ni^{2+}, Cu^{2+}, Zn^{2+} and VO_2^{3+} complexes with **Enrofloxacin -** acorbic acid and **levofloxacin -** acorbic acid (1:1:1) mixed complexes

Complex	Tentative formula	M.Wt.	Elemental analysis*				Λ_m*
			%C	%H	%N	%M	
Enrofloxacin - acorbic acid mixed complexes							
Enro – Asc. -Ni^{2+}	$[C_{25}H_{27}N_3O_9FNi]$,	591.19	50.79	4.60	7.11	9.93	7.4
Enro – Asc. -Mn^{2+}	$[C_{25}H_{27}N_3O_9FMn]$,	587.44	51.12	4.63	7.15	9.35	7.9
Enro – Asc. -Fe^{3+}	$[C_{25}H_{27}N_3O_9FFe]Cl$	630.8	48.14 (48.44)	4.36 (4.54)	6.74 (7.11)	8.95	32.4
Enro – Asc. -Cu^{2+}	$[C_{25}H_{27}N_3O_9FCu]$,	596.05	50.38 (51.03)	4.57 (4.68)	7.05 (7.22)	10.66	9.1
Enro – Asc. -Zn^{2+}	$[C_{25}H_{27}N_3O_9FZn]$			4.55 (4.37)	7.03 (7.53)	10.94	7.6
Enro–Asc. -VO_2^{3+}	$[C_{25}H_{27}N_3O_9FVO_2]$	615.44	48.79 (49.11)	4.42 (4.76)	6.83 (6.64)	8.28	28.6
levofloxacin - acorbic acid mixed complexes							
Lev-Asc – asc.--Ni^{2}	$[C_{24}H_{25}N_3O_{10}FNi]$	593.17	48.60	4.25	7.08	9.89	8.9
Lev-Asc – asc.--Mn^{2}	$[C_{24}H_{25}N_3O_{10}FMn]$	589.41	48.91	4.28	7.13	9.32	7.4
Lev-Asc – asc.-Fe^{3+}	$[C_{24}H_{25}N_3O_{10}FFe]Cl$	625.78	46.07	4.03	6.71	8.92	36.4
Lev-Asc – asc.--Cu^{2}	$[C_{24}H_{25}N_3O_{10}FCu]$	598.02	48.20 (48.66)	4.21	7.03	10.63	7.8
Lev-Asc – asc.-Zn^{2+}	$[C_{24}H_{25}N_3O_{10}FZn]$	599.86	48.06	4.20	7.01	10.90	8.3
Lev-Asc – asc.-VO_2	$[C_{24}H_{25}N_3O_{12}FV]$	617.42	46.69	4.08	6.81	8.25	33.8

* $ohm^{-1}cm^2mol^{-1}$ *values between parentheses are found values

3- Thermal analysis

Some chosen solid complexes are explored for their thermogravimetrical behavior; example thermograms are provided in Figs. (1-3), and Table (2) provides a numerical representation of the degradation events. In TGA technique, each inflection on the TG curves is accompanied by either exo – or endothermic peak on the DT curves corresponding to the phase transformation of the degradation step. In general, thermogravimetric analysis show that the complexes degrade, more or less, by means of three primary steps:

i-Physically adsorbed and coordinated water molecules are dehydrated from the coordination sphere.

ii- Decomposition of the unhydrated complexes and iii- finally full thermal decomposition through the third step leading to the metal oxides as final products.

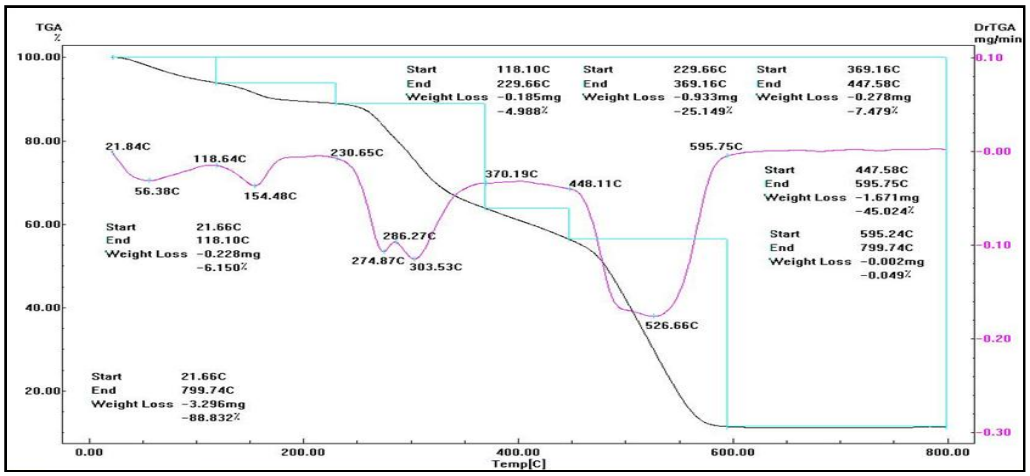


Fig (1): TGA and DTA curves of the complex Enrofloxacine - Fe – Ascorbic acid

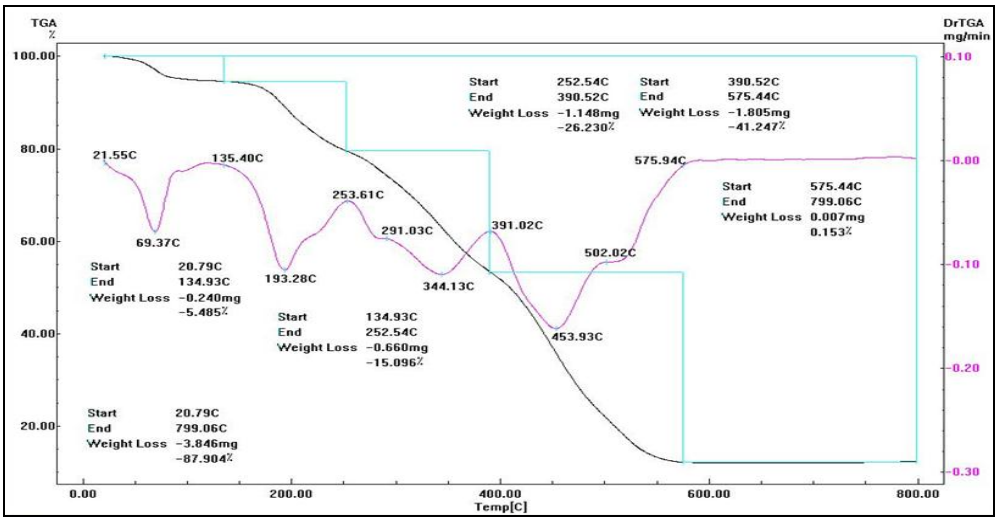


Fig (2): TGA and DTA curves of the complexe Levofloxacine - Fe – Asc.

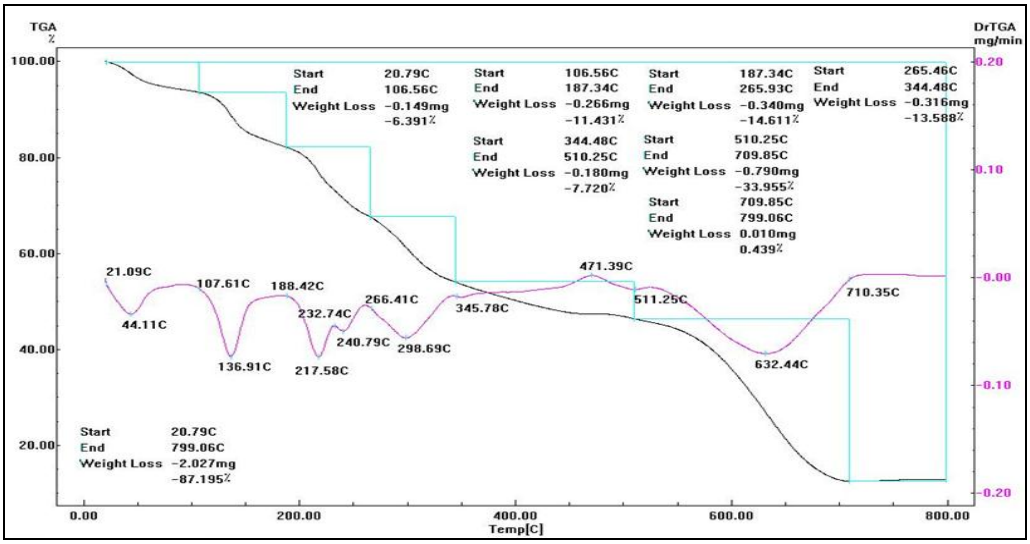


Fig (3): TGA and DTA curves of the complexes Enrofloxacine - Cu – Asc

Table (2): Thermogravimetric data of the degradation steps of selected complexes

complex	Peak Temp.(C)	Weight loss%	Assignment
Enro- Fe - Asc	69.88 - 173.88	6.150 - 4.99	elimination of coordinated and physically adsorbed water molecules
	299.41 - 408.37	25.15 - 7.48	beginning of the unhydrous complex's
	521.67 - 697.49	45.02 - 0.05	breakdown
			Complete complex breakdown yielding FeO:11.17% and Fe%=8.68(9.38)
Enro- Cu - Asc	77.86 -193.74	5.49(6.66) - 15.09	elimination of coordinated and physically adsorbed water molecules
	321.53	26.23 - 41.25	beginning of the unhydrous complex's
	482.98 - 687.25	0.153	breakdown
			Complete complicated breakdown yielding CuO:11.17% and Fe%=8.68(9.38)
Levo-Cu - Asc	63.68 - 146.95	6.39(5.97) - 11.43	elimination of coordinated and physically adsorbed water molecules
	226.64 - 304.97	14.61 - 13.59 - 7.72	beginning of the unhydrous complex's
	427.37 - 610.05	33.96 - 0.439	breakdown
	754.46		Whole complex breakdown yielding CuO:12.81%,Cu%=10.23(10.54)
levo- Fe - Asc	64.97 - 156.68	5.21 - 21.43	elimination of coordinated and physically adsorbed water molecules
	230.53 - 365.45	9.74 - 16.82	beginning of the unhydrous complex's
	581.06 - 744.99	35.51 - 0.24	breakdown
			Whole complex breakdown yielding FeO:12.81%, Cu%=10.23(10.54)

FTIR spectroscopic spectroscopy

Complete understanding of the mode of bonding in the studied metal chelates is gained from IR spectral data in absorption arrangements. The spectrum was divided into the following sections in order to allocate the infrared bands: *i- Absorption in the 4000 – 1500 cm^{-1} regions:*

The OH and C=O stretching vibration bands are visible in this area. The spectra of the free medicines show the VC=O band at 1680 - 1627 cm^{-1} and the VOH band between 3465 - 3231 cm^{-1}. The delocalization of the electron cloud towards the metal ion during complex formation caused this band in the spectra of metal complexes to noticeably shift to a lower frequency, which is interpreted as evidence for the center's role in complex formation.

ii- Absorption spectra in the 1500 – 1000 cm^{-1} region:

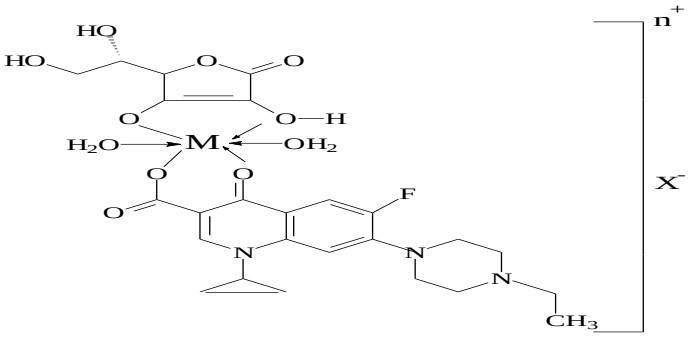
Due to the bands caused by the C-H in-plane deformation and several skeletal vibrations,

including the bending deformation of OH and C-O groups, this region is of importance. The free drugs' OH in-plane deformation results in a band at 1121–1067 cm^{-1}, which is shifted to a lower frequency during complex development.

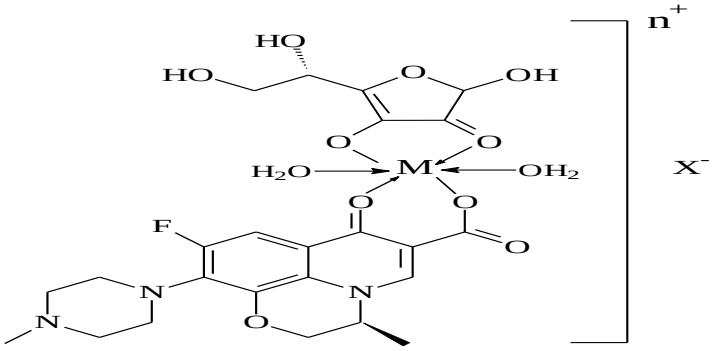
iii- Absorption spectra in the 1000 – 400 cm^{-1} region:

In addition to the stretching vibrations of the M-O and M-N bonds, the out-of-plane deformation vibrations of the hydrogen atoms within the ring are responsible for the majority of the strong bands that are visible in this region. Due to the stretching vibrations of the M–O bonds, two new sets of bands occur in the spectra of the Enro–Asc–M and Levo–Asc–M complexes, ranging from 520–455 cm^{-1}.

The development of mixed drug-metal complexes with a stoichiometric ratio of 1:1:1 was thus validated by elemental analysis and FTIR spectra; as a result, the mode of bonding of such complexes may be depicted as follows:



Enrofloxacine – M- ascorbic acid,



Levofloxacine-M- ascorbic acid

Table (3) Infrared vibrational frequencies (cm-1) of some combined ascorbic acid function groups, including M-Enrofloxacine and Levoofloxacine M-Metal complexes of ascorbic acid, Ni^{2+}, Mn^{2+}, Fe^{3+}, Cu^{2+}, Zn^{2+}, and VO_2

Compound	ν_{OH}	$\nu_{C=O}$	$\nu_{C=C}$	δ_{OH}	ν_{M-O}
Ascorbic acid	3465	1627	1415	1121	---
Enrofloxacine	3418	1322	1403	1126	500
Enro – Asc. -Ni $^{2+}$(1:1:1)	3419	1623	1402	1101	455
Enro – Asc. -Mn $^{2+}$(1:1:1)	3450	1574	1493	1115	505
Enro – Asc. -Fe^{3+}(1:1:1)	3333	1621	1414	1105	504
Enro – Asc. -Cu $^{2+}$(1:1:1)	3267	1665	1439	1107	---
Enro – Asc. -Zn^{2+}(1:1:1)	3362	1629	1432	1098	520
Enro–Asc. VO_2^{3+}(1:1:1)	3448	1625	1390	1130	514
Lev-Asc – Ni $^{2+}$(1:1:1)	3419	1623	1402	1101	455
Lev-Asc – Mn^{2+}(1:1:1)	3450	1574	1493	1115	505
Lev-Asc – Fe $^{3+}$(1:1:1)	3333	1621	1414	1105	504
Lev-Asc – Cu $^{2+}$(1:1:1)	3267	1665	1439	1107	---
Lev-Asc – Zn $^{2+}$(1:1:1)	3362	1629	1432	1098	520
Lev-Asc – VO_2 $^{2+}$(1:1:1)	3448	1625	1390	1130	514

5- Magnetic susceptibility and electronic absorption spectra

1- Paramagnetism is seen in magnetic susceptibility studies conducted at room temperature for Fe(III), Mn(II), Co(II), and Cu(II) complexes, as anticipated based on their electronic structure. Table (4) lists the ground state symbols, term symbols, and μeff values for a few selected complexes.Magnetic susceptibility

Table (4): Magnetic properties of some selected complexes

Complex	d^n	Electronic Configuration	Term Symbol	Ground State	μ_{eff} (BM)	
					Found	Theor.
Asc. - Mn^{2+}	d^5	$t_{2g}^3e_g^2$	$^6S_{5/2}$	$^6A_{1g}(S)$	6.05	5.916
Levo - Mn^{2+}	d^5	$t_{2g}^3e_g^2$	$^6S_{5/2}$	$^6A_{1g}(S)$	5.91	5.916
Enro- Mn^{2+}	d^5	$t_{2g}^3e_g^2$	$^6S_{5/2}$	$^6A_{1g}(S)$	5.90	5.916
Asc - Fe^{3+}	d^5	$t_{2g}^3e_g^2$	$^5D_4$	$^6A_{1g}(S)$	5.55	5.916
Levo - Fe^{3+}	d^5	$t_{2g}^3e_g^2$	$^5D_4$	$^6A_{1g}(S)$	5.14	5.916
Enro- Fe^{3+}	d^5	$t_{2g}^3e_g^2$	$^5D_4$	$^6A_{1g}(S)$	5.72	5.916
Asc. - Co^{2+}	d^7	$t_{2g}^5e_g^2$	$^4F_{9/2}$	$^4T_1$	5.22	3.873
Levo. - Co^{2+}	d^7	$t_{2g}^5e_g^2$	$^4F_{9/2}$	$^4T_1$	4.77	3.873
Enro.- Co^{2+}	d^7	$t_{2g}^5e_g^2$	$^4F_{9/2}$	$^4T_1$	5.07	3.873
Asc. - Cu^{2+}	d^9	$t_{2g}^6e_g^3$	$^2D_{5/2}$	^2E_g	1.77	1.732
Levo. - Cu^{2+}	d^9	$t_{2g}^6e_g^3$	$^2D_{5/2}$	^2E_g	1.90	1.732
Enro - Cu^{2+}	d^9	$t_{2g}^6e_g^3$	$^2D_{5/2}$	^2E_g	1.85	1.732

Electronic absorption spectra

The electronic absorption spectra of the complexes are studied in solid state (using Nujol mull technique) with special interest to the ligand – spectrala region in which absorption bands arise from electronic transition within the d-orbitals of the metal that have been splitted in a ligand field [d→d transition taking place between the two sets of the d orbital (t_{2g}→e_g) splitted under the impact of the ligand's electrostatic field] Examining the acquired data reveals that:

1. The ground state for Mn(II) and other d5 instances is 6S, and higher states include 4G, 4D, 4P, 4F, etc. It is anticipated that the electronic spectrum will only comprise extremely weak bands since spin-allowed transitions are not conceivable.

2- Every d-d transition in the high spin Fe (III) complexes with d5 configuration is spin and laporte forbidden, and the ground state is 6A1g. The Fe(III) – Levo complex's electronic spectra show three bands at 91138.1, 22780.8, and 10161.8 cm-1 that correspond to the 6A1g(S) → 4T1g(G), 6A1g(S) → 4T2g(G), and 6A1g(S) → 4Eg, 4A1g(G) transitions, respectively [18]. This suggests that the complex has an octahedral structure with a high spin.

3-In the NIR–VIS range (ν 1: 8811–11,635 cm−1; ν 2: 13,550–16,447 cm−1; ν 3: 18,553–19,260 cm−1), the electronic spectra of the octahedral Co(II) complexes show absorption bands corresponding to 4T1g(F) → 4T2g(F) (ν 1), 4T1g → 4A2g (ν 2), and 4T1g(F) → 4T1g(P) (ν 3) transitions [18].

4-Two spin allowed transition bands are visible in copper (II) complexes at 30303 cm-1 and 33333.3 cm-1, respectively, because of the 2a1g(D) → 2b1g(D) and 2eg(D) → 2b1g(D) transitions. Cu (II) complexes were reported to have a broad asymmetric band in the area 20576 cm-1, which is expected for an octahedral Cu(II) complex's d-d transition [80]. The band's broadness may be explained by many bands overlapping as a result of the substantial Jahn-Teller distortion that is anticipated in a d9 ion [18].

Theoretical studies

MOLECULAR MODELLING

Geometry Optimization: A set of measurements using the Materials Studio package's DMOL3 tool, which is designed for large-scale Density Function Theory (DFT), were used.

Total charge density:

It is typically located around the atom and its bonds and is a measurement of the likelihood that an electron will be present at a particular site. In contrast, it encompasses a whole region in delocalized or conjugated systems; in benzene, for example, they are present both above and below the planar ring. Chemical reactivity is directly correlated with total density. It is discovered that the unbound drug's nitrogen and oxygen atoms have a larger negative charge surface surrounding them, which may make them more vulnerable to an electrophilic attack. The complexation process is favored by the metal ion's surrounding larger positive charge. Molecular modeling software frequently generates graphical representations

of electron charge density by indicating whether molecules are in a position with a high or low electron density. For free medicines and their mixed complexes, the DFT approach was used to obtain the total density, deformation density, and 3D plots frontier orbital energies; representative examples are displayed in Figs. (4–13).

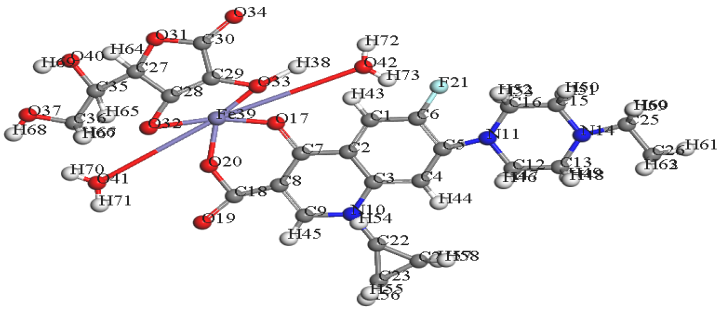


Fig. (4): Molecular modelling of Enrofloxacine

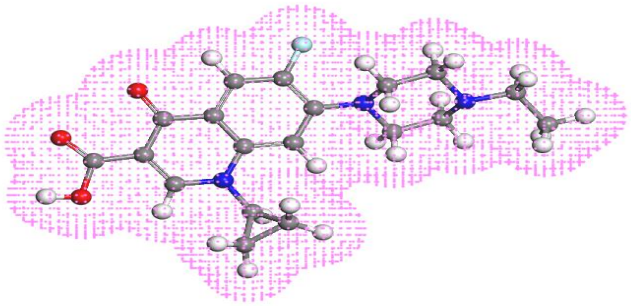


Fig. (5): Total density using DFT method for ligand Enrofloxacin

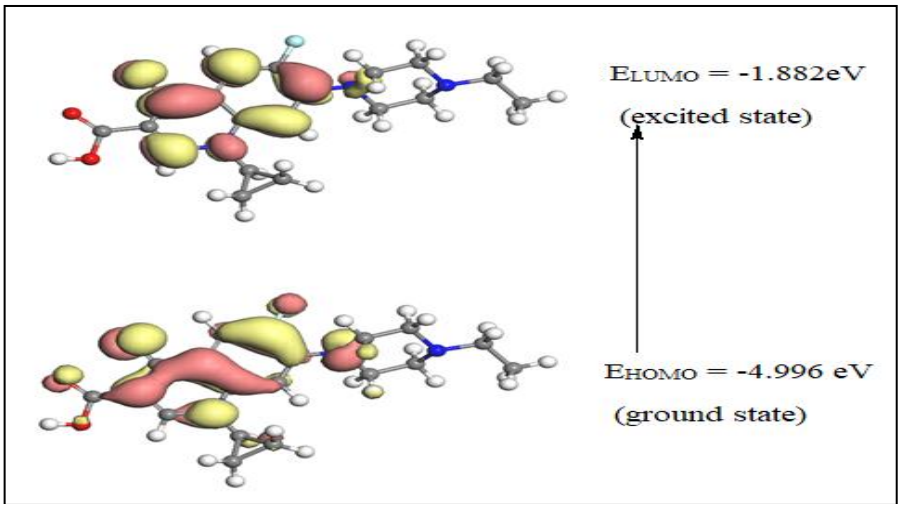


Fig. (6): 3D plots frontier orbital energies using DFT method for ligand Enrofloxacin

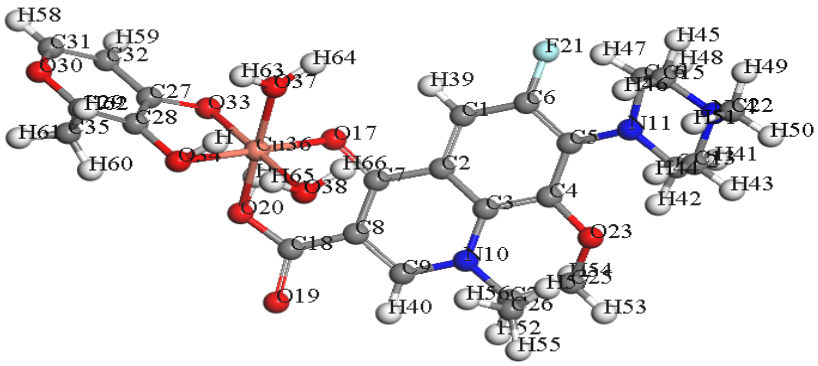


Fig. (7): Molecular modelling of Levo: Asc: Cu complex

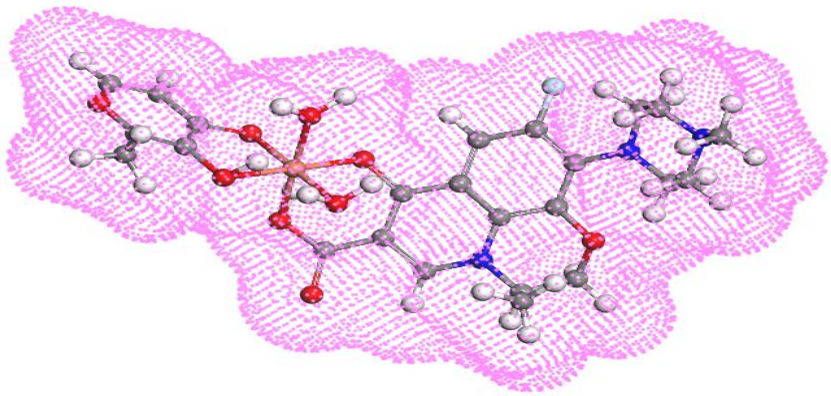


Fig. (8): Total density using DFT method of Levo: Asc: Cu complex

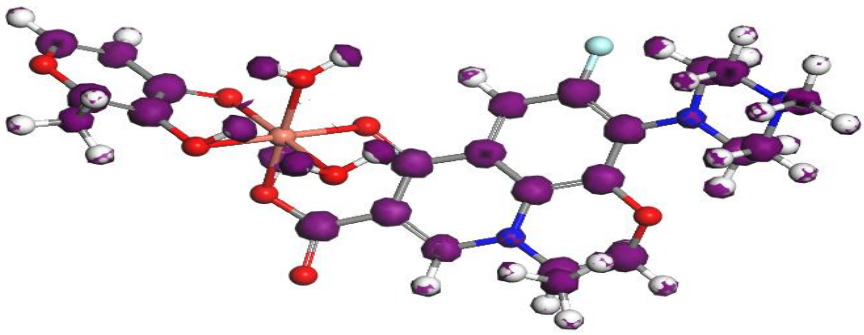


Fig. (9): Deformation density using DFT method of Levo: Asc: Cu complex

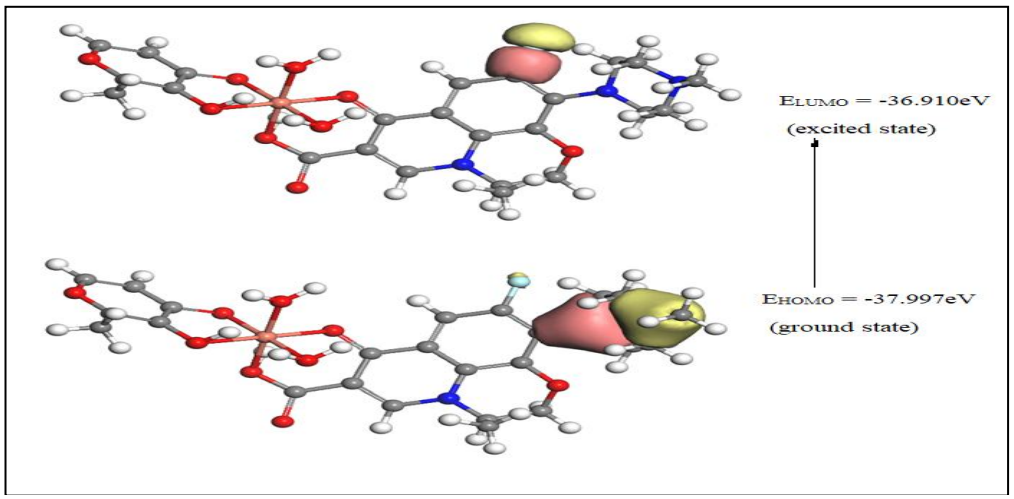


Fig. (10): 3D plots frontier orbital energies using DFT method of Levo: Asc: Cu complex

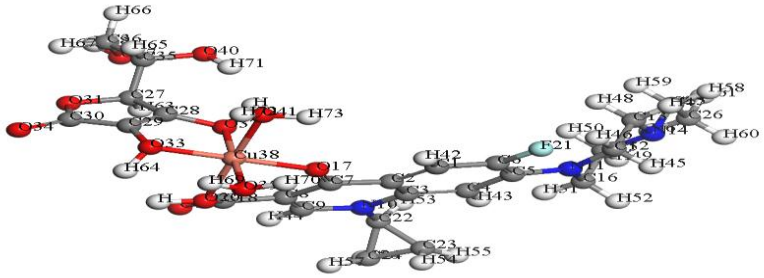


Fig. (11): Molecular modelling of Enro: Asc: Cu complex

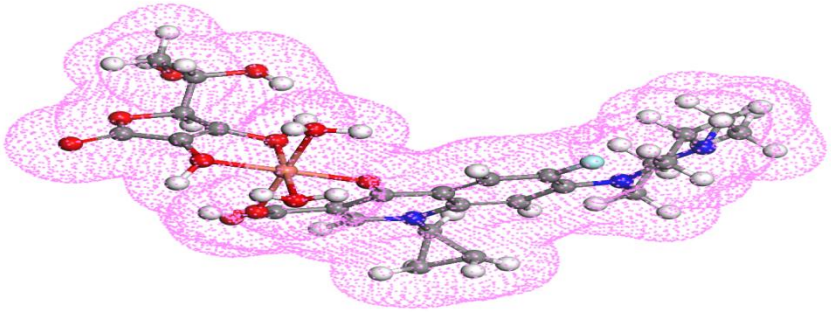


Fig. (12): Total density using DFT method of Enro: Asc: Cu complex

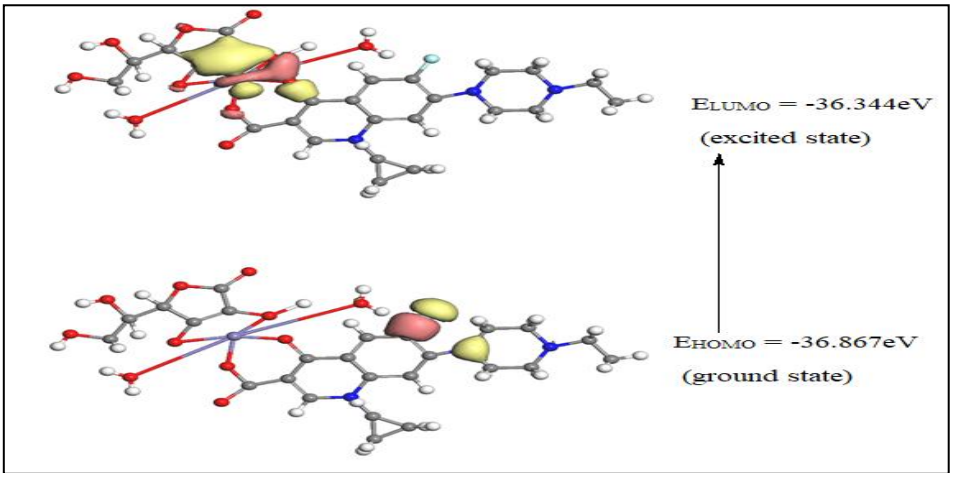


Fig. (13) 3D plots frontier orbital energies using DFT method of Enro: Asc: Fe complex

Molecular orbitals at the frontier

Frontier molecular orbitals (FMOs), which are made up of the HOMOs and LUMOs, are crucial for assessing the chemical stability, chemical reactivity, and hardness/softness of molecules. Whereas the LUMO is an electron acceptor, the HOMO serves as an electron donor. The electron density primarily delocalized across the OH and COOH groups on quinolone rings in the HOMO of the unbound drug molecule. This density is delocalized on every phenyl ring while in the LUMO orbital. A compound's chemical reactivity is represented by its energy gap (ΔE); a smaller value of ΔE indicates a more reactive or less stable system. The energy gap of the free drug compounds is the highest and diminishes with complex formation, as seen in Tables 5 and 7. Similar to hardness and chemical potential, the electron-accepting capacity of the systems is described by the electrophilicity index (ω), another global reactivity descriptor. The ability of molecules to take electrons is increased by high values of the electrophilicity index. An electrophile is a chemical species that can accept electrons from the environment; upon accepting electronic charge, its energy must decrease. This is why the electrophilicity index (ω) is a positive, definite quantity and the direction of the charge transfer is entirely determined by the electronic chemical potential (μ) of the molecule. As a result, the numbers in Tables 6 and 9 absolutely support the requirement that the electronic chemical potential be negative. Tables 5 and 7 list the calculated values of the following: global hardness (η), global softness (σ), additional electronic charge (ΔNmax), electronegativity (χ), chemical potential (μ), global hardness (η), global softness (σ), global electrophilicity index (ω), and energy band gap (which explains the final charge transfer interaction inside the molecule):

EH + EH = -1/2 (χ) + μ = - χ = 1/2 (ELUMO + EHOMO) + η = 1/2 (ELUMO-EHOMO)

ω = μ2/2 η, ΔNmax = -μ / η The softness (σ), which is equal to 1/η, is the inverse value of the global hardness. Tables 6 and 8 provide the computed energy parameters of the free ligands and their complexes.

Table (5): The calculated quantum chemical parameters of Levofloxacin and some Levo:Asc: M complexes

Comp.	HOMO	LUMO	ΔE	H	Σ	X	M	Ω	ΔN_{max}
Levofloxacin	-4.385	-2.132	2.253	1.1265	0.887705282	-3.2585	3.2585	4.712748447	2.892587661
Levo:Asc:Mn^{2+}	-37.997	-36.91	1.087	0.5435	1.839926403	-37.4535	37.4535	1290.49187	68.91168353
Levo:Asc:Fe^{3+}	-38.174	-37.066	1.108	0.554	1.805054152	-37.62	37.62	1277.31444	67.90613718
Levo:Asc:Cu^{2+}	-38.002	-36.957	1.045	0.5225	1.913875598	-37.4795	37.4795	1344.22289	71.73110048
Levo:Asc:Ni^{2+}	-38.513	-23.38	15.133	7.5665	0.132161501	-30.9465	30.9465	63.28460069	4.089935902

Table (6) Some energetic properties of Levofloxacin and some Levo:Asc: M complexes

Comp.	Eenergy components (Kcal/mol)						Binding energy (Kcal/mol)	Dipole moment (debye)
	Sum of atomic energies	Kinetic energy	Electrostatic energy	Exchange-correlation energy	Spin polarization energy	Total energy		
Levofloxacin	-7.88 $X10^6$	-9.04$X10^3$	7.11$X10^3$	1.67 $X10^3$	1.76 $X10^3$	-792.5 $X10^3$	-4.90 $X10^3$	15.2421
Levo:Asc:Mn^{2+}	-1.31 $X10^6$	-328.4$X10^3$	108.76$X10^3$	5.07$X10^3$	2.25 $X10^3$	-131.5 $X10^3$	-216.92 $X10^3$	2.0359
Levo:Asc:Fe^{3+}	-1.26 $X10^6$	-319.41$X10^3$	100.09$X10^3$	7.01$X10^3$	2.29 $X10^3$	-126.44 $X10^3$	-218.22 $X10^3$	-3.9522
Levo:Asc:Cu^{2+}	-1.329 $X10^6$	-329.13$X10^3$	109.21$X10^3$	4.65$X10^3$	2.24 $X10^3$	-133.16 $X10^3$	-217.22 $X10^3$	1.7648
Levo:Asc:Ni^{2+}	-1.23 $X10^6$	-316.32$X10^3$	95.34$X10^3$	7.98$X10^3$	2.19 $X10^3$	-122.93 $X10^3$	-217.99 $X10^3$	4.0829

Table (7) Quantum chemical characteristics of enrofloxacin and various enrocalculatedAsc: M-complexes

Comp.	HOMO	LUMO	ΔE	H	Σ	X	M	Ω	ΔN_{max}
Enrofloxacin	-4.996	-1.882	3.114	1.557	0.642260758	-3.439	3.439	3.797919396	2.208734746
Enro:Asc: Mn^{2+}	-5.148	-2.91	2.238	1.119	0.893655049	-4.029	4.029	7.253280161	3.600536193
Enro:Asc:Fe^{3+}	-36.867	-36.344	0.523	0.2615	3.824091778	-36.6055	36.6055	2562.070039	139.9827916
Enro:Asc: Cu^{2+}	-5.304	-2.836	2.468	1.234	0.810372771	-4.07	4.07	6.711871961	3.29821718
Enro:Asc: Ni^{2+}	-5.204	-3.165	2.039	1.0195	0.980872977	-4.1845	4.1845	8.587562653	4.104462972

Table (8) Some energetic properties of Enrofloxacin and some Enro:Asc: M complexes

Comp.	Eenergy components (Kcal/mol)						Binding energy (Kcal/mol)	Dipole moment (debye)
	Sum of atomic energies	Kinetic energy	Electrostatic energy	Exchange-correlation energy	Spin polarization energy	Total energy		
Enrofloxacin	-7.65 $X10^6$	-9.33$X10^3$	40.98	1.99 $X10^3$	1.81 $X10^3$	-770.4 $X10^3$	-5.48 $X10^3$	10.2708
Enro:Asc: Mn^{2+}	-1.42 $X10^6$	-12.89$X10^3$	-2.68$X10^3$	2.72$X10^3$	2.47 $X10^3$	-143.58 $X10^3$	-7.98 $X10^3$	9.3803
Enro:Asc:Fe^{3+}	-1.37 $X10^6$	-343.529$X10^3$	109.36$X10^3$	9.41$X10^3$	2.46 $X10^3$	-160.82 $X10^3$	-230.76 $X10^3$	12.8012
Enro:Asc: Cu^{2+}	-1./45 $X10^6$	-11.99$X10^3$	-9.32$X10^3$	2.69$X10^3$	2.41 $X10^3$	-145.39 $X10^3$	-7.83 $X10^3$	8.7812
Enro:Asc: Ni^{2+}	-1.88 $X10^6$	-10.49$X10^3$	-2.84$X10^3$	2.84$X10^3$	2.21 $X10^3$	-188.84 $X10^3$	-8.28 $X10^3$	2.339

Conclusion

The solid complexes formed between Mn^{2+}. Fe^{3+}, Ni^{2+}, Cu^{2+}, Zn^{2+} and VO_2^{3+} with Enrofloxacine-L-Ascorbic acid (Enro-Asc) and Levofloxacine-L-Ascorbic acid (Levo-Asc) as mixed drugs were prepared in the solid state. The chemical structure of the synthesised complexes were elucidated using different chemical and physical techniques which proved the formation of complexes with stoichiometric ratios Enro:Asc:M and Levo:Asc:M (1:1:1). Using the DMOL3 program, which is designed for wide-scale density function theory (DFT), several quantum chemical and energetic characteristics of the free drug and their metal complexes were computed.

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