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Synthesis, Spectral and Chemotherapeutic Potentials of some Metal(II) Difluoromethylorthine Complexes

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Abstract

Six new complexes(C1-C6):Co(II), Fe(II), Zn(II), VO(II) and Cd(II) ions bearing difluoromethylornithine hydrochloride hydrate (DMH) have been synthesized and characterized using EA, FTIR, ESI-MS,NMR, magnetic susceptibility measurements etc. From FTIR spectra, shift on ligand's carboxylate and amino group around central metal ions depicts either octahedral or tetrahedral geometries. All other measures support the expected molecular for the complexes. The results of conductivity measurements showed that the ligand and its metal complexes are electrolytes. Except oxovanadium (IV) complex which showed decreased activity against all the test microorganisms, Co(II) and Fe(II) complexes showed higher activities than the parent antibiotic (streptomycin) used. Thus, metal based drugs stand tall for recommendation in pharmacy among chemotherapeutic agents.

Keywords: Difluoromethylornithine hydrochloride hydrate, Novel metal complexes, Spectral characterization, Antibacterial studies, N-,O- donor ligand.

1.0. Introduction

In recent times, several metal complexes having ligands with N, O donors have been synthesized and studied [1, 2]. A literature survey has revealed the synthesis and characterization of complexes with ligand in which carboxylate anion and nitrogen or both are involved in coordination with

metal ions, some of these complexes have been found to possess good antimicrobial activities [3, 4]. The presence of nitrogen and oxygen donor atoms in the complexes makes these compounds effective and stereospecific catalysts for oxidation, reduction hydrolysis and they also show biological activity and other transformations of organic and inorganic chemistry [2, 5]. Also metal complexes having N, O donor atoms have been found to be very important because of their significant biological properties such as antibacterial [6, 7], antifungal [8], anticancer [9], and herbicidal [10] activity. Transition metals such as copper, cobalt, zinc and iron show enhanced property of antimalarial, antiparasitic, antimicrobial, electron transfer or any type of oxygen transport reaction when bounded to ligand containing Oxygen, Nitrogen or Sulphur [10]. The choice cobalt, iron and zinc in this study is as a result of their importance in biological and physiological activities that facilitate a variety of chemical reaction needed for life. They are essential in fundamental biological processes, required for the growth and differentiation of all types of life, play a catalytic, co-catalytic, or structural role in many metabolic enzymes and regulatory proteins [11-14]. İt is well known that some drugs have higher activity when administered as metal complexes than as free ligand [2].

According to the survey of literature review, little is known about the coordination of 3d metal ions with difluoromethylornithine hydrochloride hydrate. Therefore in continuation of our studies of chelation of transition metals with biologically importance ligand, we report the synthesis, characterization and antibacterial studies of new transition metals Co(II), Zn(II), Fe(II), VO(II) and Cd(II)) complexes with difluoromethylornithine hydrochloride hydrate asligand (DMH) (Fig. 1).

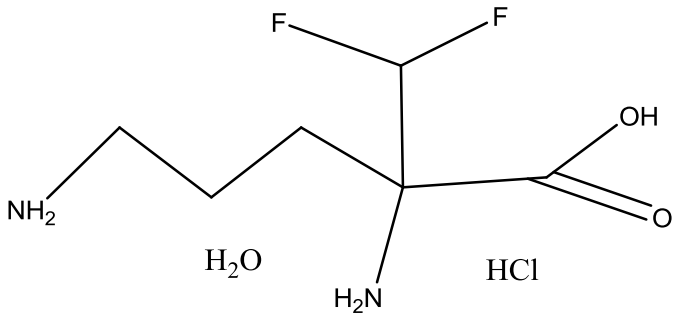


Fig. 1: Molecular Structure of Ligand (DMH)

2. Experimental

2.1 Materials

The ligand, difluoromethylornithine hydrochloride hydrate was commercially obtained and used without further purification. All hydrated metal salts used for complexation were obtained from British Drug House (BDH) Chemical Limited Co. Isolates of *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeroginosa* and *Bacillus substilis* were obtained from University of Ilorin Teaching Hospital through Microbiology Department, University of Ilorin, Nigeria.

2.2 Instrumentation

The elemental (CHN) analysis were performed on Thermo Flask 112 CHNSO elemental analyzer from Micro analytical Laboratory at Medac Limited, Surrey, United Kingdom. The FTIR spectra were collected on FTIR-8501 Shimadzu spectrophotometer over 4000-400cm^{-1} using KBR pellets. Melting points were determined using MPA100 OptiMelt Automated Melting Point system. Solution electronic absorption spectra of the ligand and complexes were ran in the range of 180-400 nm and 180-1100 nm respectively on Jenway 6405uv/vis. The conductivity of the ligand and their complexes were

determined in distilled water using EC214 conductivity meter Hanna instrument with cell constant of 1.013. The electrospray ionization mass spectra were recorded on Micromass Autoseptic Premier/Agilent HP6890GC at Medac Limited, UK. The magnetic susceptibility measurements (X_mT) for the transition metal complexes between 5 and 400 K were measured with a superconducting quantum interference device (SQUID) magnetometer (Quantum Design MPMS – 5S) available at Chemistry department, Kumamoto University, Japan .

2.3 Synthesis of the Complexes

2.3.1[Co(DMH)(NH_3)$_3$(Cl]H_2O.HCl(C1)

The addition of (0.2379 g, 1 mmol) $CoCl_2 \cdot 6H_2O$ dissolved in 20 ml of acetone to a stirring solution of (0.2367 g, 1 mmol) of the ligand in 10ml of concentrated ammonia resulted into darkish brown solution which was heated under refluxed for 2h. The reddish brown solution formed was cooled

and allowed to evaporate slowly at room temperature. Reddish brown micro-crystal obtained was washed several times with methanol and dried over silica gel.

M.wt 382.12 $gmol^{-1}$; Colour purple; Yield 0.341 g (89.08%); M.pt: 186-188 ^{0}C, Anal Calc for $C_6H_{24}F_2N_5O_3Cl_2Co$ (%) : C, 18.86; H, 6.33; N, 18.33. Found (%) C, 19.14; H, 5.92; N, 17.98.FTIR data (KBr, cm^{-1}): 3524, 3447, 3200, 3102, 1661, 1437, 1163, 976, 788, 580, 455, UV-vis (H_2O λ_{max}nm), 299,494, 550, 750

2.3.2 [Cd(DMH)(CH_3COO)(H_2O)]H_2O. HCl (C2)

$Cd(CH_3COO)_2 \cdot 2H_2O$ (0.2665 g, 1 mmol) in 20 ml methanol was added to a stirring solution of the ligand (0.2367 g, 1 mmol) in 10 ml distilled water. The resulting colourless solution was refluxed for 3h. The white precipitate obtained was recrystallized in a mixture of water and methanol, allowed to evaporate slowly at room temperature and dried over silica gel.

M.wt 426.12 $gmol^{-1}$; Colour white; Yield 0.398 g (93.46%); M.pt: 275-277 ^{0}C, Anal Calc for $C_8H_{20}F_2N_2O_6ClCd$ (%) : C, 22.55; H, 4.73; N, 6.57. Found (%) C, 22.50; H, 4.17; N, 6.63. IR data (KBr, cm^{-1}): 3353, 3455, 3255, 3159, 1600, 1392, 1199, 941, 766, 561, 465. UV-vis (H_2O, λ_{max} nm) : 232, 297, 355.

2.3.3[Cd(DMH)(Cl_2)]H_2O.HCl (C3)

The colourless solution obtained by mixing the aqueous solutions of (0.2367 g, 1 mmol) ligand and (0.2283 g, 1 mmol) $CdCl_2 \cdot 2½H_2O$ was refluxed for 3h. The white precipitate formed was cooled, separated out by filtration, washed with hot methanol and dried over silica gel.

M.wt 419.96 $gmol^{-1}$; Colour white; Yield 0.223 g (63.10%); M.pt: 256-258 ^{0}C, Anal Calc for $C_6H_{15}F_2N_2O_3Cl_3Cd$ (%) : C, 17.16; H, 3.60; N, 6.67. Found (%) C, 17.58; H, 3.54; N, 6.67. IR data (KBr, cm^{-1}): 3471, 3149, 3061, 1630, 1368, 1130, 972, 792, 522, 464, UV-Vis (H_2O, λ_{max} nm) : 238, 296, 333.

2.3.4 [Zn(DMH)(CH_3COO)(H_2O)]H_2O. HCl(C4)

The complex was prepared by slow addition of 1mmol of Zinc acetate dihydrate $Zn(CH_3COO)_2 \cdot 2H_2O$ (0.2195 g) in 15 ml methanol to a stirring solution containing 0.2367 g (1 mmol) of the ligand in 10 ml distilled water. The colourless solution was then heated under

refluxed for 5h. The off-white slate-like crystal obtained was re-dissolved in methanol, filtered and allow to evaporate slowly at room temperature. The off-white product formed was then dried over silica gel in a desiccator.

M.wt 379.11 $gmol^{-1}$; Colour off-white; Yield 0.270 g (71.17%); M.pt: 190-192 ^{0}C, Anal Calc for $C_8H_{20}F_2N_2O_6ClZn$ (%) : C, 25.34; H, 5.32; N, 7.39. Found (%) C, 25.22; H, 4.66; N, 7.66. IR data (KBr, cm^{-1}): 3447, 3345, 3246, 3126, 3041, 1604, 1344, 1117, 768, 565, 499. UV-vis (H_2O, λ_{max} nm) : 229, 271, 386.

2.3.5 $[VO(DMH)(SO_4)(H_2O)_2]2H_2O.HCl$ (C5)

(0.1184 g, 0.5 mmol) DMH was dissolved in 10 ml of methanol (warm) followed by slow addition of (0.1269 g, 0.5 mmol) $VOSO_4 \cdot 5H_2O$ dissolved in 5 ml of distilled water while stirring. The blue colour solution formed was refluxed for 4h. The dark green precipitate formed was filtered hot to remove unreacted reactants, washed thrice with methanol and dried over silica gel.

M.wt 453.69 $gmol^{-1}$; Colour green; Yield 0.132 g (68.80%); M.pt: 203-205 ^{0}C, Anal Calc for $C_6H_{21}F_2N_2O_{11}SClV$ (%) : C, 15.88; H, 4.67; N, 6.17. Found (%) C, 15.79; H, 4.62; N, 5.92. . IR data (KBr, cm^{-1}): 3423, 3404, 3244, 3039, 1659, 1385, 1120, 978, 746, 486. UV-vis (H_2O, λ_{max} nm) : 268, 334, 661.

2.3.6 $[Fe(DMH)(Cl)(H_2O)]H_2O.HCl$ (C6)

$FeCl_2 \cdot 4H_2O$ (0.1968 g, 1 mmol) dissolved in 10 ml of methanol was slowly added to aqueous solution of (0.2367 g, 1 mmol) of DMH. The brownish mixture solution was stirred at 45 ^{0}C for 2h and kept to evaporate slowly at room temperature. The ligand (DMH) crystallized out from the solution after 3 days. The mixture was thenheated under refluxed for 3h. The yellowish solution was cooled and allowed to undergo slow evaporation at room temperature. The light brown precipitate obtained was re-dissolved in methanol, found to dissolve completely, and was allowed to evaporate slowly at room temperature, product obtained dried over silica gel.

M.wt 345.96 $gmol^{-1}$; Colour light brown; Yield 0.184 g (73.31%); M.pt: 217-219 ^{0}C, Anal Calc for $C_6H_{17}F_2N_2O_4Cl_2Fe$ (%) : C, 20.83; H, 4.95; N, 8.10. Found (%) C, 20.76; H, 5.14; N, 8.54. . IR data (KBr, cm^{-1}): 3383, 3374, 3122, 3022, 1653, 1375, 1120, 937, 779, 584, 440. UV-vis (H_2O, λ_{max} nm): 299, 345, 407.

3.0 Results and Discussion

The preparation of DMH-metal complexes can be represented by the general formula thus:

$$\mathbf{(DMH).H_2O.HCl + MX_2.nH_2O \xrightarrow[MeOH/H_2O/NH_3]{stirred/refluxed} [M(DMH)X_2].H_2O.HCl}$$

All the complexes conform to the general formular $[M(DMH)X_2].H_2O.HCl$ where X – Cl, CH_3COO, or H_2O except C1and C5 which conform to $[M(DMH)X_4].H_2O.HCl$ where X is NH_3, Cl, SO_4 or H_2O. The molecular compositions are formulated on the basis of elemental analysis as shown in the Table 1. The complexes are formed by 1:1 molar condensation of the ligand to transition metals with appreciable yield. Different in melting point of the products (complexes) from the ligand (236 - 237 ^{0}C) gives an insight into the formation of the coordination compound and the high purity of the complexes can be predicted from the sharp melting point. The presence of uncoordinated water molecules in all the complexes was confirmed by the use of cobalt chloride paper. The complexes were heated gently in dry test tubes, droplets of colourless liquid found on the sides of test tubes turned cobalt chloride paper from blue to pink. The colours of cobalt (purple), iron (light brown) and oxovanadium (green) complexes are distinctly different from that of the ligand (white). Thus, it can be inferred that the colour displayed by the metal complexes is regulated by the metal ion, a possible indication to the formation of coordination compounds. The metal complexes were completely soluble in polar solvents such as water and methanol and also in DMF and DMSO but, practically insoluble in non-polar solvents indicating that the complexes are electrolytes. This is evidenced from the conductivity values as contained in Table 3.

Two amino groups are present in the ligand (DMH), the terminal one is protonated to form NH_3^+ while the second one is involved in coordination with metal ionsthrough nitrogen atom. The carboxylic moiety is deprotonated leading to the formation of zwitterionic structure of metal complexes in agreement with earlier similar work [15].This may be due to the strong hydrogen bonding between water molecules and amino group [16]. This has also been confirmed by our earlier work on the same ligand where X-ray structure was obtained [17]

3.1 Fourier Transform Infrared Spectra (FTIR)

Vibration frequency in the range of 4000-400 cm^{-1} was employed to predict the expected functional groups or bonds in the ligands and their metal complexes (Figure 2). The bands in the

region 3254 and 3173 cm^{-1} which could be attributed to asymmetric and symmetric stretching frequencies of primary amine(NH_2) in the spectrum of the ligand undergone a red shift in the spectra of complexes, indicating involvement of NH_2 in the chelation [21,22]The observation was further strengthened by the sharp absorption band at 754 cm^{-1} in the spectrum of the ligand, due to NH_2 deformation (out-of-plane band) which shifted to higher frequencies after coordination through nitrogen with metal ions

A strong bands observed in the range of (3383 – 3524)cm^{-1} in the spectra of ligand and metal complexes are assignable to υ(H_2O/HCl). The spectra of Oxovanadium(IV) complex show a characteristic non-ligand sharp band at 978 cm^{-1} attributed to stretching frequencies of V=O. The value is in the range observed for monomeric VO (II) complexes [23]. New bands with medium to weak intensities which provide direct evidence for the complexation (Metal – Ligand bond) were observed in the spectra of the complexes hence bands in the range of 584 –440 cm^{-1} in the spectra of complexes are assigned to **υ**(M – N/M-O/M-Cl) stretching frequencies [24].

The characteristics FTIR bands of the ligands and metal complexes are shown in Table 1 and the principal bands attributed to asymmetric (υ_{asy}) and symmetric (υ_{sym}) stretching frequencies of (COO) groups are reported in Table 2. The characteristic FTIR bands of the complexes differed from the free ligand and showed either a shift or disappearance of some characteristics frequencies and appearance of some new frequencies as a proof of coordination.

The IR spectrum of the ligand shows a medium intensity band at 3048cm^{-1} which is attributable to **υ**(OH) of carboxylic acid group. The hypsochromic/bathochromic shift on complexation with metal ions suggesting possible coordination through carboxylate oxygen atom through deprotonation [18]. This is further supported by out-of plane bending (OPB) frequencies of δOH(carboxylic acid) as contained in Table 1.

The coordination through the OH of carboxylic acid is further confirmed by asymmetric **υ**asy(OCO) and symmetric **υ**sym(OCO) stretching frequencies of carboxylate group as contained in Table 2. For metal complexes that contain carboxylate groups directly coordinated to metal, the magnitude of the separation between asymmetric and symmetric bands (COO^-) cm^{-1} has been used as spectroscopic criterion in determination of the carboxylate coordination mode. The separation (Δ**υ**) of all the metal complexes are greater than 200 cm^{-1} and also greater than that of ligand

($\Delta\upsilon_{ligand} > \Delta_{complexes}$) which indicates that carboxylate groups coordinated to the metal ion in a monodentate mode [19-21].

Table 1: Major IR (cm^{-1}) data of the ligand and the metal complexes

Compound	L(DMH)	C1	C2	C3	C4	C5	C6
$\upsilon(NH_3^+)$	-----	-----	3353	----	3345	----	3373
$\upsilon(H_2O)/(HCl)$	3493	3524,3447	3455	3471	3447	3423,3404	3383
$\upsilon(NH_2)$ (asy/sym)	3254 3173	3200 3102	3255 3159	---- 3149	3246 3126	3244 ----	---- 3122
υ(OH) carboxylic	3048	-----	-----	3061	3041	3039	3022
υ((COO) (asy/sym)	1647 1499	1661 1437	1600 1392	1630 1368	1604 1344	1659 1385	1653 1375
υ(C-N)	1138	1163	1199	1130	1117	1120	1120
δ(OH)carboxylic acid OPB	947	976	941	972	----	----	937
$\delta(NH_2)$ OPB	754	788	766	792	768	746	779
υ(M-O/(M-Cl/M-N)	-----	580,455,424	561, 465	522,464	565,499	486	584, 440

Table 2: Principal IR bands (cm^{-1}) for (COO) groups in ligand and Metal Complexes

	L(DMH)	C1	C2	C3	C4	C5	C6
υ_{asy} (COO)	1647	1661	1600	1630	1604	1659	1653
υ_{sym} (COO)	1499	1437	1392	1368	1344	1385	1375
$\Delta\upsilon = \upsilon_{asy} - \upsilon_{sym}$	148	224	208	262	260	274	278

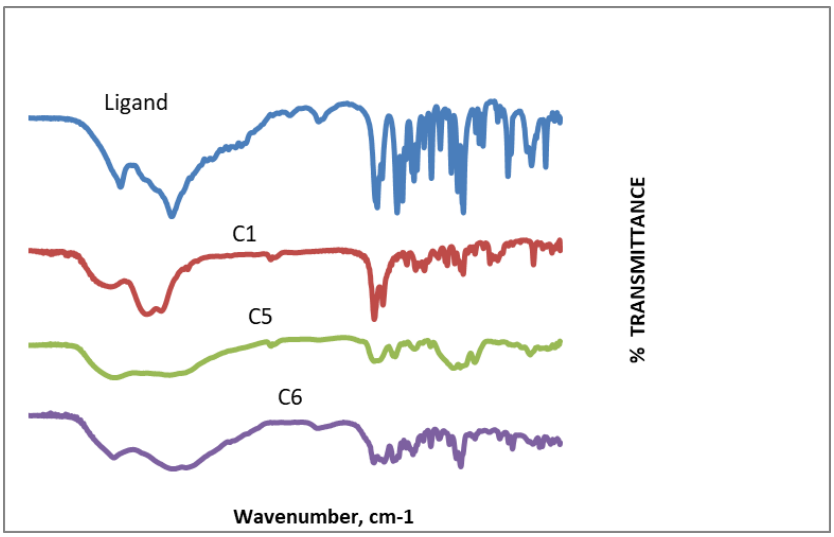


Fig. 2: Comparative FTIR Spectra of the Ligand and some Metal complexes

3.2 Electronic Spectroscopy: Conductance and Magnetic Susceptibility

The electronic spectra, conductance and magnetic properties of the ligand and their metal complexes are contained in Table 3. The temperature dependences of the magnetic susceptibilities for the complex were measured in the form of the χmT vs T curve, where χm is the molar magnetic susceptibility and T is the temperature (Fig 3). The metal complexes were completely soluble in polar solvents such as water and methanol and also in DMF and DMSO but, practically insoluble in non-polar solvents indicating that the complexes are electrolytes. This is evidenced from the conductivity values (Table 3). The electronic spectrum of the aqueous solution of free ligand showed absorption bands in the UV-region at 228nm (43,860 cm^{-1}), 240nm (41,667 cm^{-1}) and 307nm (32,573 cm^{-1}) (Table 3). These bands are assigned to intra-ligand transition due to n-π* transition of the non-bonding electrons present on the oxygen of (C=O) group and nitrogen of the amine groups. The slight bathochromic shift and disappearance of the bands in the complexes relative to the ligand is attributable to coordination [25].

The electronic spectrum of the Co(II) complex exhibited absorption bands 494nm, 550nm, 750nm which may be assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions respectively [20,26]. The magnetic measurements gave an idea about the electronic state of the metal ion in the complex. The magnetic moment for Co(II) complex has a magnetic moment of 4.30B.M. which is typical of Co(II) ion in an octahedral environment(with three unpaired electrons) [20, 27].

The two band observed for the VO(II) of DMH complex in the region of 661nm and 334 nm assignable to $b_2 \longrightarrow b_1^*$(band II) and $b_2 \longrightarrow a_1^*$ (band III) respectively is an indicative that the complex is octahedral. This fact is supported by the magnetic moment of 1.74 B.M which equally revealed that it is monomeric compounds [28].

Four coordinated iron(II) complex show bands as a result of charge transfer (CT) at 28,986 cm^{-1} and 24,570 cm^{-1} which is similar earlier reported spectra for square planar iron (II) complexes. The magnetic moment value of 4.92 B.M. also suggest a square planar stereochemistry for the Fe (II) complex. [29]

The electronic configuration of Zn (II) and Cd (II) complexes are (d^{10}) which confirms the absence of any d-d transitions. The maximum absorptions were similar to those of free parent ligands, except a small shift in the maxima as a result of their coordination to the zinc and cadmium metal ions [14]

Table 3: Magnetic Moment, Conductance and Electronic Spectra of Ligand and Metal Complexes

	Magnetic Moment μ_{eff}(B.M.)	Molar conductance (Scm^2mol^{-1})	λ_{max} (nm)	λ_{max} (cm^{-1})	λ_{max} Energy ($KJmol^{-1}$)	Assignment
L (DMH)	-	115	228 240 307	43, 860 41, 667 32, 573	525 499 390	$n-\pi^*$ $n-\pi^*$ $n-\pi^*$
C1	4.30	124	299 494 550 750	33, 445 20, 243 18, 182 13, 333	400 242 218 160	$n-\pi^*$ $^4T_{1g}(F) \longrightarrow {}^4T_{1g}(P)$ $^4T_{1g}(F) \longrightarrow {}^4A_{2g}(F)$ $^4T_{1g}(F) \longrightarrow {}^4T_{2g}(F)$
C2	-	154	232 279 355	43, 103 35, 842 28, 169	576 429 337	$n-\pi^*$ $n-\pi^*$ Charge Transfer (CT)
C3	-	145	238 296 333	42, 017 33, 784 30, 030	503 404 359	$n-\pi^*$ $n-\pi^*$ CT
C4	-	123	229 271 386	43, 668 36, 900 25, 907	523 442 310	$n-\pi^*$ $n-\pi^*$ CT
C5	1.74	292	268 334 661	37, 313 29, 940 15, 129	447 358 181	$n-\pi^*$ $b_2 \longrightarrow a_1^*$ $b_2 \longrightarrow b_1^*$
C6	4.92	148	299 345 407	33, 445 28, 986 24, 570	400 347 294	$n-\pi^*$ CT

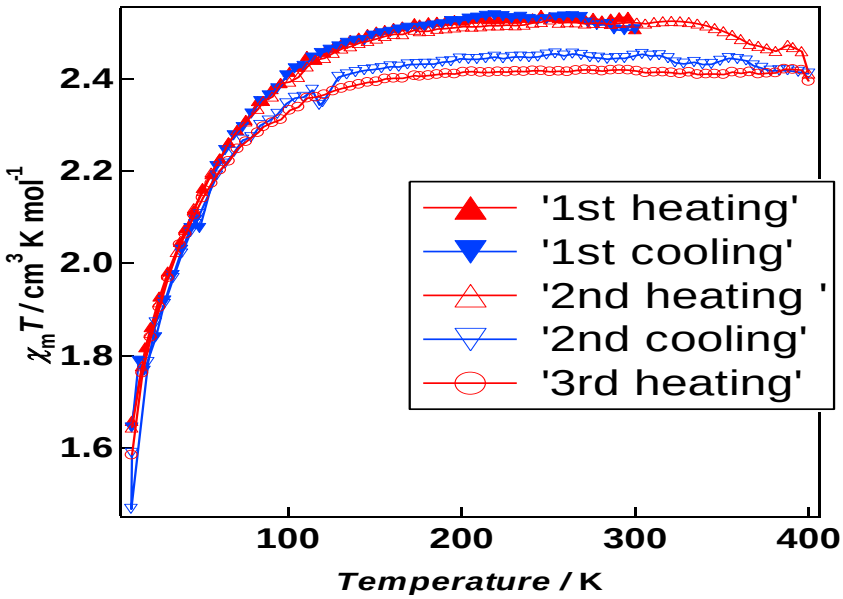


Fig. 3: Magnetic susceptibility (χ_mT) versus Temperature (T)plots for complex 1: $C_6H_{24}F_2N_5O_3Cl_2Co$. The sample was warmed from 5 to 400K and then cooled from 400 to 5K in the first cycle, and then the sample was warmed from 5 to 400K second and third cycles at a rate of 2 K min^{-1}

3.3 Electrospray Ionization Mass Spectrometry (ESI-MS) Results

The ESI mass studies of complexes 1 and 4 have shown the presence of two types of species, namely, molecular ions and dimeric species. The major fragments ions, peak assignment (theoretical and found) mass per charge ratio (m/z) values and relative abundance of complexes were shown in Tables 4-5. The m/z values observed in each case compete very favourably well with the theoretical values; an evidence which further support the stoichiometric formulation (1:1 metal-ligand chelates). The peak noticed at

m/z = 183.10 in all the spectra due to $[DMH + H]^+$ signified the presence of DMH in the coordination sphere hence proof for coordination.

Table 4: ESI-MS data for $[Co(DMH)(NH_3)_3Cl]H_2O.HCl$ [Cplx 1]

Compound	Major Fragment ions	Peak assignment (m/z)		Relative intensity (%)
		Found	Theoretical	
C1	$[2M + 2K]^{2+}$	421.10	421.22	6.67
	$[2M - H_2O - HCl + Na]^+$	338.60	338.00	100.00
m/z = 382.12	$[2M - H_2O - HCl + 2H]^{2+}$	328.08	329.90	10.00
	$[2(Co(DMH)(NH_3)_3Cl) + 2H]^{2+}$	327.90	327.07	15.00
	$[2(Co(DMH) + NH_4]^+$	500.10	500.10	36.67
	$[DMH + H]^+$	183.10	183.20	13.33
	$[Co + DMH + NH_4 + H]^+$	261.10	260.20	33.33

Table 5: ESI-MS data for $[Zn(DMH)(CH_3COO)(H_2O)]H_2O.HCl$ [Cplx 4]

Compound	Major Fragment ions	Peak assignment (m/z)		Relative intensity (%)
		Found	Theoretical	
C4	$[2M + Na + Li]^+$	789.10	788.20	0.14
	$[2Zn(DMH)(CH_3COO)(H_2O) +$			
m/z = 379.11	$Na + K]^+$	709.10	710.40	35.33
	$[M+Na+K]^+$	441.00	441.20	20.00
	$[M + K + NH_4 + H]^+$	437.00	437.30	26.67
	$[2(Zn(DMH)(CH_3COO) + H]^+$	613.20	613.06	16.00
	$[Zn(DMH)_2 + 2H_2O + K + H)^+$	505.10	505.10	100.00
	$[DMH + H]^+$	183.10	183.18	13.33

3.4 Antibacterial Screening Results

The in-vitro antibacterial activity of the ligand (DMH) and four (4) metal complexes were evaluated using agar well diffusion technique [30,31] against Gram-positive bacteria, *Staphylococcus aureus* and *Bacillus substilis*, Gram-negative bacteria, *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. The activity was carried out at concentration of 100ppm, 200ppm and 300ppm using distilled water as a solvent. A known antibiotics, streptomycin was used as a standard. The susceptibility of these bacteria strains towards the metal complexes was estimated by measuring the zone or size of inhibition diameter. The results of antimicrobial evaluation of the metal complexes and ligand are presented in Table

6 while the graphical representation of effect of the ligands and their metal complexes on different organism at 300 ppm was revealed (Figure 4).

The solvent (distilled water) showed no zone of inhibition confirming non-involvement of solvent on the activity of the metal complexes and the DMH. Generally, the results of the antibacterial screening show appreciable activity of the drug-metal complexes against some test pathogens (Figure 4). The inhibitions are much larger by metal complexes when compared to the free ligand [11,32]. C1 and C6 showed higher antibacterial activities than the parent ligand and compete favourably well with antibiotic used; C4complex displayed an enhanced activity than the ligand but lower activity than the antibiotics while C5 showed decreased activity against all the test microorganisms when compared to the ligand and antibiotic employed. It is equally established from the results that the antibacterial potency is concentration dependent which generally agrees with the finding of other researchers who asserted that antimicrobial potency is usually concentration dependent [27, 31, 33]. It was also observed that the most resistant pathogens to the metal complexes were *Staphylococcus aureus*, *Bacillus substilis* and *Pseudomonas aeruginosa* while the most susceptible were *Klebsiella pneumoniae* and *Escherichia coli*.

Table 6: Zone of Inhibition (ppm) of the Ligand and Metal Complexes on Test Organisms

	Gram (-)			Gram(-)			Gram(-)				Gram (+)		Gram (+)		
Compounds	**E. coli**			**P. aeruginosa**			**K. pneumonia**				**S. aureus**		**B. substilis**		
	100	**200**	**300**	**100**	**200**	**300**	**100**	**200**	**300**	**100**	**200**	**300**	**100**	**200**	**300**
Distilled Water (Solvent)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ligand	NA	8.5	12.5	NA	NA	5.0	2.0	9.0	15.6	NA	6.0	8.1	NA	2.0	6.1
C1	6.2	14.2	20.5	2.0	6.0	11.7	10.0	15.6	24.3	4.0	9.5	17.0	3.0	6.6	10.3
C4	2.0	8.8	15.2	1.0	3.2	6.8	4.0	10.0	17.1	1.5	7.0	11.2	NA	3.0	8.0
C5	NA	7.3	11.3	NA	NA	4.6	1.2	7.5	12.6	NA	5.6	7.1	NA	1.6	5.4
C6	4.0	12.1	19.0	1.9	5.0	9.0	8.0	14.0	23.2	3.0	8.0	15.0	2.0	5.0	8.5
Standard (Streptomycin)	10.0	16.0	22.5	4.5	8.0	12.5	12.4	18.6	25.2	6.0	12.0	18.0	4.0	8.5	12.0

NA- Not Active

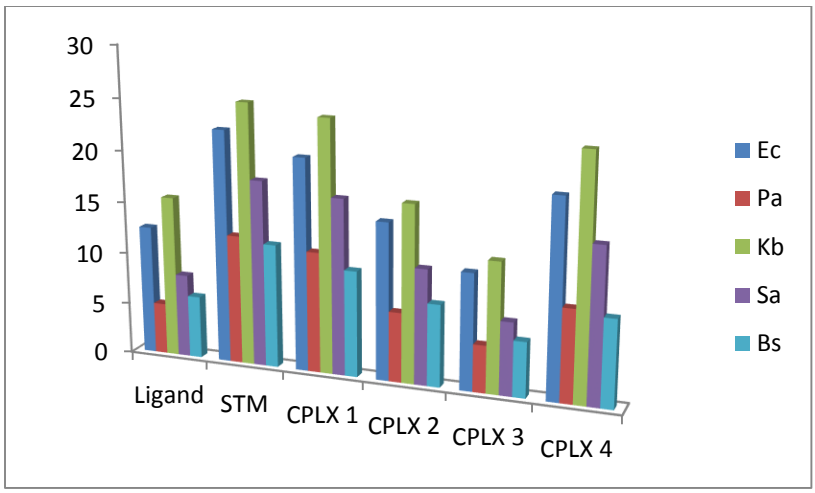
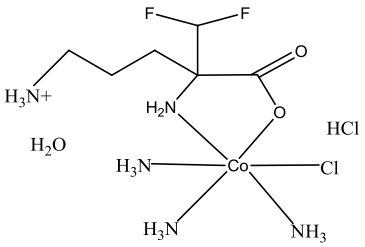


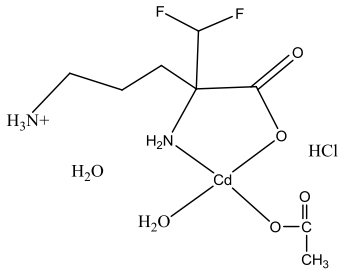
Fig. 4: Graphical representation of effect of ligand and metal complexes on different organisms at 300 ppm

*Ec : Escherichia coli**;** Pa : Pseudomonas aeruginosa **;** Kb : Klebsiella pneumonia*

*Sa : Staphylococcus aureus ; Bs : Bacillus substilis **;*** STM : Streptomycin

Based on electronic spectra and magnetic data, proposed structures of metal complexes are contained in Figure 5 which depict Co(II) and VO(IV) complexes as having octahedral geomtry, Zn(II) and Cd(II) complexes have tetrahedral geometries while Fe(II) complex is square planar.





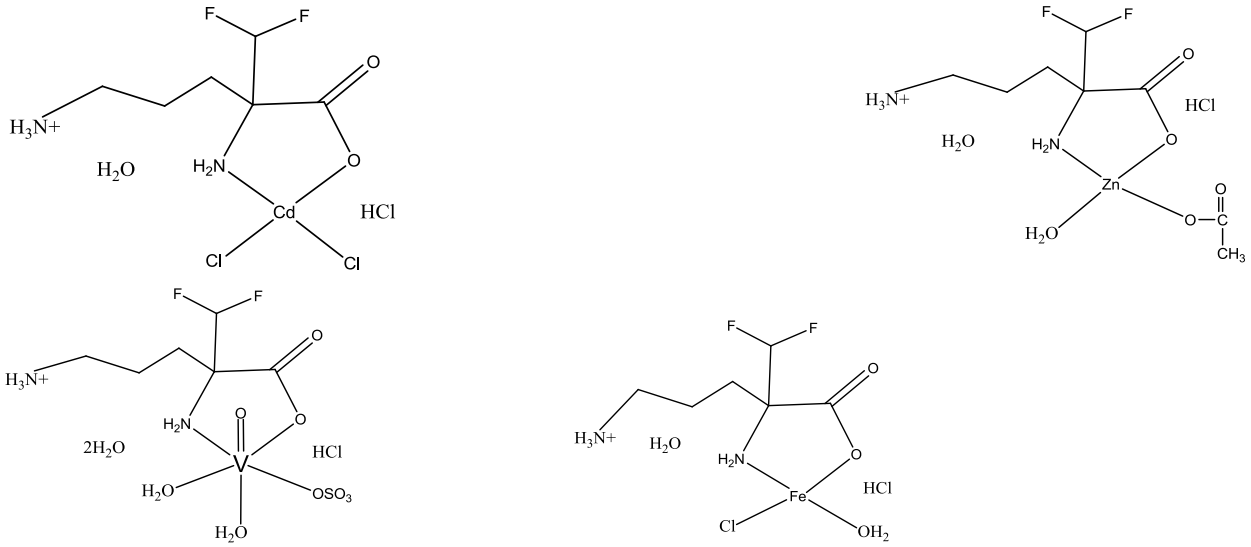


Fig 5: Proposed Structure of Metal Complexes

Conclusion

New transition metal (Co(II), Cd(II) Fe(II), Zn(II) and VO(II)) complexes of difluoromethylornithine hydrochloride hydrate (DMH) were synthesized and characterized using melting point, conductivity, elemental analysis, FTIR spectroscopy, electronic spectroscopy, magnetic susceptibility measurements and Electrospray Ionization Mass Spectrometry (ESI-MS). Spectra data confirmed that the ligand coordinated to the metal ion in a bidentate mode through an oxygen atom of the carboxylate and a nitrogen atom of amino group. Octahedral geometryis suggested for cobalt(II) and oxovanadium(IV) complexes while tetrahedral geometry is proposed for Zn(II), Cd(II) complexes and square planar for Fe(II) complex (Figure 5). The results of the antibacterial screening show appreciable activity of the metal complexes when challenged with the test pathogens. The inhibitions are much larger by metal complexes when compared to the free ligand.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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