



# Structural, chemical and biological aspects of some mix ligand chelates d<sup>10</sup> metal

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## General Note

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## ABSTRACT

The more resourceful d<sup>10</sup>metal chelates in their biological activity were synthesized by using biologically important ligands. Synthesized chelates were characterized by IR, Mass spectra, TGA analysis and Elemental analysis. All the chelates and ligand have been screened for antibacterial and antifungal activities.

**Key words:** ACV, antibacterial, antifungal.

## 1. INTRODUCTION

The study of mixed ligand chelates having two or more different ligands attached to metal ion has received a great importance in recent years because of their wide applications in various fields of chemicals activity and more particularly because of their presence in biological systems. As a matter of fact, many naturally, occurring metal complexes are mixed ligand chelates [1]. Amino acids are highly functional small molecules whose side chain groups are like prototypes of metal coordination and weak interactions in proteins. This perspective focuses on non-covalent or weak interactions of the side chain groups of amino acids, such as the charged

groups of arginine and aspartic acid and the aromatic rings of tyrosine and tryptophan, in metal chelates in solution and in the solid state [2]. Chelation of zinc and cadmium by amino acids, both natural and otherwise, polypeptides, has been the subject of study for many years because of the importance of zinc-protein systems and the physiological effect of cadmium compounds [3]. The importance of Zn(II), Cd(II), and Hg(II) chelates in ternary system is crucial. In the present work, isolation of mixed ligand chelates of Zn(II), Cd(II), and Hg(II) with oxine and acyclovir has been carried out. Their physicochemical properties have been studied using analytical techniques. Structures and composition of the chelates have been established on the basis of their elemental analysis, magnetic measurements, infrared spectra, electronic spectra and thermo gravimetric analysis etc. This study is interesting because biochemical role of many metal ions have been well established [4]. So this study would be important for bio-inorganic chemists and coordination chemists.

## 2. MATERIALS AND METHODS

### Water

Conductivity water was used right through the work. Conductivity water was redistilled over alkaline potassium permanganate. The distilled conductivity water was boiled to expel carbon dioxide and stored in an air-tight Pyrex aspirator. The pH of this water was found to be ~ 6.9. This water was used for preparing solutions of metal perchlorates and reagents.

### Ligand and Other Chemicals

The primary ligand oxine was obtained from Fluka and secondary ligand acyclovir (ACV) was obtained from different pharmaceuticals companies. and their purities were checked by noting their melting point as well as TLC. All metal carbonates used were also A.R. grade. Stock solutions of Zn(II), Cd(II), and Hg(II) perchlorates were prepared and analyzed by complexometric methods. Sodium hydroxide (E.Merk) was used.

### Preparation of Chelates

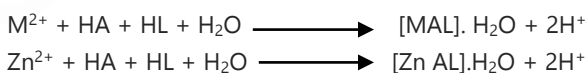
The synthesis of the chelates was carried out by mixing 25ml of a 0.1 M aqueous solutions of Zn(II), Cd(II), and Hg(II) perchlorates with 25ml 0.1 M solution of oxine in water. After stirring this mixture for 40-50 minutes, 25 ml of a 0.1 m ACV were taken in the form of DMSO solutions and was added slowly with constant mechanical stirring for 30 min. It was refluxed with water condenser for 2 hours at 150°C temperature, until the mixture remains ¼ part. There was no immediate precipitation. The pH of the above solutions was then raised to ~6.9 using 0.1 M sodium hydroxide solution which resulted in the precipitation of solids. The chelates thus obtained were washed well with a 1:1 mixture of absolute alcohol and water to remove unreacted metal salt and ligand. All chelates were dried in vacuum at room temperature.

### Analyses and Physical Measurements

Elemental analyses were performed with a Perkin-Elmer model 2400 series-II C, H, N analyzer. The IR spectra were recorded on a Perkin Elmer Impact model 400D FT-IR spectrophotometer. The samples were run as KBr pellets. The mass spectra of some selected compounds were recorded on a JEOL SX 102\ DA-6000 Mass Spectrometer using Argon\xenon (6kv, 10mA) as the FAB gas. The accelerating voltage was 10kV and spectra were recorded at room temperature. Thermal measurements were performed using a Mettler - Toledo model TG-50 thermal analyzer at a 15°C min<sup>-1</sup> heating rate. DSC measurements were also performed using a Mettler - Toledo model DSC-822e.

## 3. RESULTS AND DISCUSSION

The analytical data of the chelates presented in Table 1.0 showed 1:1:1 stoichiometry. The general equation for the formation of the chelate with oxine and acyclovir is as shown below.



Where, HA = Oxine

HL = Conjugated base of acyclovir

M<sup>2+</sup> = Zn<sup>2+</sup>, Cd<sup>2+</sup>, Hg<sup>2+</sup>

The Zn(II), Cd(II), and Hg(II) chelates are coloured, all are crystalline or amorphous and stable in air. The chelates are soluble in DMSO and insoluble in water and other common organic solvents. The melting points of the chelates are higher, which suggest their greater thermal stability. To check the presence of single or more than one chelates, TLC of the solid was carried out using silica gel as the stationary phase and N-amyl alcohol, glacial acetic acid and water (6:1:2) as the solvent system. For all the four chelates only one clear spot was obtained indicating the formation of only a single product.

### Conductance Measurements

Chelates are found to be only slightly soluble in DMSO and insoluble in water and other organic solvents. The conductivities of all the chelates are measured in DMSO at 25°C at a concentration 10<sup>-3</sup> M using systronics conductivity meter. All chelates were found to be nonconducting in nature. The molar conductance values of the chelates are listed in Table 1.

**Table 1** Analytical Data and Some Physical Properties of the Metal Chelates

Compound Molecular Formula	Colour	Molar conductance Mho cm <sup>-1</sup>	Rf value	Yield %	Formula Weight	Analysis (%) Calculated / (Found)			M.P. °C
						C %	H %	N %	
C <sub>8</sub> H <sub>11</sub> N <sub>5</sub> O <sub>3</sub> (L1)	White	-	-	-	225.21	42.67 (42.77)	4.92 (4.99)	31.10 (31.89)	256.5 °C
C <sub>9</sub> H <sub>7</sub> N O (L2)	White	-	-	-	145.15	74.47	4.86	9.65	76 °C
[Zn (L1) (L2)]3H <sub>2</sub> O	Lemon yellow	1.438	0.769	55.15	489	46.86 (47.38)	4.16 (4.26)	19.29 (20.98)	>300°C
[Cd (L1) (L2)]10H <sub>2</sub> O	Lemon yellow	0.931	0.774	56.04	661	42.29 (44.63)	3.76 (4.06)	17.41 (17.75)	>300°C
[Hg (L1) (L2)] 10H <sub>2</sub> O]	Green	5.776	0.745	29.64	749	35.76 (35.08)	3.18 (2.98)	14.72 (14.93)	>300°C

L1 = Acyclovir and L2 = Oxine

**Table 1.1** Infrared Spectra of the Metal Chelates (Cm<sup>-1</sup>)

Compound Molecular Formula	-NH <sub>2</sub>	>NH	-OH	>C=O	C-O-C	C-O Ether	C-O Alcohol	-CH <sub>2</sub>	-C-N	M-N
C <sub>8</sub> H <sub>11</sub> N <sub>5</sub> O <sub>3</sub> (L2)	3471, 3440 1573	3302 1541	3522	1715	1106	1183	1048	3183 2927-2854	1346 1308	-
C <sub>9</sub> H <sub>7</sub> N O (L1)	-	-	3179	-	-	1202	-	-	1381	-
[Zn (L1) (L2)]3H <sub>2</sub> O	-	3344	-	1695	1109	1175	1036	2916	1371 1328	410
[Cd (L1) (L2)]10H <sub>2</sub> O	3406	-	-	1691	1107	-	1018	2293	1390 1364 1323	498
[Hg (L1) (L2)] 10H <sub>2</sub> O]	-	3336	-	1673	1107	1180	1088	2922	1382 1318	493

### Elemental Analyses

Elemental analyses of the ternary chelates isolated in the present study are given in Table: 1.1. They indicate 1:1:1 composition. This is also confirmed by observing their non-conducting nature.

Both, Zn<sup>2+</sup> and Cd<sup>2+</sup> have invariably +2 oxidation state Zn<sup>2+</sup> is spherically symmetric with d<sup>10</sup> configuration and hence no LFSE is present. As a result other factors decide the preference for coordination Zn<sup>2+</sup> is typically tetrahedral or octahedral However trigonalbipyramid and square pyramidal 5 coordinate complexes are also reported. Zn<sup>2+</sup> compounds hydrolyse rapidly in water to

increase their coordination number above 4. For  $\text{Cd}^{2+}$  coordination numbers 3, 4, 5, 6 are known.  $\text{Cd}^{2+}$  and  $\text{Hg}^{2+}$  have a tendency to achieve 5 coordination by dimerizing.  $\text{Hg}^{2+}$  has 2, 3, 4 and 6 coordination number.  $\text{Hg}^{2+}$  has great affinity with sulphur.  $\text{Hg}^{2+}$  has various tendencies to form polymeric compounds, bridged compounds and also  $\text{Hg}^{2+}$  the mercurous state as a result isomeric compounds also may be present.

### Electronic Spectra Study

Synthesis of chelates is analyzed for uv-visible absorption spectra and magnetic moment. These metals belong to II-B (12) group ( $d^{10}$ ). This group has a usual characteristic of absence of d-d transition because no space for excited electron is present in the d orbital which is completely filled in these ions. The results indicate diamagnetic nature of the chelates with ligand to metal charge transfer bands [5]. The elemental analysis and other physical data of chelates are presented in table 1.

### Infrared Spectral Study

Infrared spectra of metal chelate exhibit bands corresponding to oxine, acyclovir and metal chelates. Bands were observed in far IR region. It is known that in the IR spectra of oxine and acyclovir coordinate chelates, there is strong coupling between various vibration modes of the resulting chelate rings and hence, quantitative interpretation of the bands is not possible without the normal coordinate analysis. The important infrared absorption bands and spectra of ligand and its metal chelates are shown in Table 1.1.

The spectra of metal chelates (MC) are obtained in the range of  $4000\text{-}400\text{ cm}^{-1}$  using chelates in the form of KBr pellets. The IR spectra indicate the presence of oxine and acyclovir in the ternary chelates. The presence of water molecule in the chelates is indicated by broad band around  $3400\text{ cm}^{-1}$  and some additional bands at  $503\text{ cm}^{-1}$ ,  $517\text{ cm}^{-1}$  and  $910\text{ cm}^{-1}$  assigned to M-OH<sub>2</sub> bands [6]. The oxine molecule shows the following characteristic bands;  $3476\text{-}3080\text{ cm}^{-1}$  (O-H and aromatic C-H stretching),  $1219\text{ cm}^{-1}$  (C-O stretching),  $1582\text{ cm}^{-1}$  and  $1514\text{ cm}^{-1}$  (C=N stretching) [7]. The usual ring skeleton (C-C) and (C-N) bands are observed at  $1600$ ,  $1450$ ,  $1400$  and  $1370\text{ cm}^{-1}$  [8]. The acyclovir molecule shows the following characteristic bands;  $1423$  and  $1501\text{ cm}^{-1}$  (C-O) and (O-H) coupled,  $1695\text{ cm}^{-1}$  (C=O),  $1036\text{ cm}^{-1}$  (C-N) and  $3406\text{-}2916\text{ cm}^{-1}$  (O-H) and (N-H) [9]. In the chelates, the band around  $498\text{ cm}^{-1}$  corresponds to (M-O) suggest that phenolic groups are involved in bond formation with metal ions. In the oxine molecule a band is observed at  $3179\text{-}3050\text{ cm}^{-1}$  due to (O-H) band is absent in chelates due to M-O [10-11]. The (M-N) frequency in the oxine chelate is obtained at higher wave number because of the double bond character of M-N bond due to MN -interaction [12]. Nakamoto [13] has shown that (M-N) frequency undergoes coupling with other stretching bands. The bands around  $788$  and  $643\text{ cm}^{-1}$  may correspond to the coupled M-N vibrations [14]. Schmidt et al. confirmed the original assignments made by Nakamoto [15]. The complex Hg-ACV could be tentatively assigned as a Hg(ACV) polymer based on spectral data which show direct N(7)-Hg interaction, conductometric measurements (no electrolyte) and comparison with other similar structures [Hg (L1) (L2)]  $10\text{H}_2\text{O}$ ].

### Mass Spectra

In the mass spectra of individual ligand and chelates the following observations were made. The mass spectrum of oxine showed  $146\text{ m/z}$  base peak due to oxine + 1. All the three chelates of  $\text{Zn}^{2+}$ ,  $\text{Sr}^{2+}$  and  $\text{Hg}^{2+}$  showed  $178\text{ m/z}$  base peak due to ACV - 1 -  $\text{C}_2\text{H}_5\text{OH}$ . In the mass spectra of  $\text{Zn}^{2+}$  and  $\text{Cd}^{2+}$  chelates, peaks below  $150\text{ m/z}$  were not observable whereas in  $\text{Hg}^{2+}$  chelate the molecular peaks were not observed largely because the molecule proposed seem too huge to be observable in mass spectra. However the  $489\text{ m/z}$  molecular peak of  $\text{Zn}^{2+}$  chelate was observed a very tiny peak along with other.

### Thermal gravimetric Study:

It has been observed that Zn(II) and Cd(II) chelates show loss in weight corresponding to two water molecules in range  $100\text{-}150^\circ\text{C}$  and Hg(II) chelate show loss in weight corresponding to one water molecule in  $100\text{-}150^\circ\text{C}$ . This shows that there is water molecules present in each metal chelate. Decomposition of Zn(II) chelate starts above  $350^\circ\text{C}$ , Cd(II) chelate starts above  $350^\circ\text{C}$ , and Hg(II) chelate starts above  $200^\circ\text{C}$ .

In general, the water of hydration may be considered as either the crystallization water or coordinated water. According to Nikolaev et al. [16] water eliminating below  $150^\circ\text{C}$  can be considered as the water of crystallization and water eliminated above  $150^\circ\text{C}$  may be due to its coordination in the metal.

### Antibacterial Activity

All synthesized chelates were screened for their antimicrobial activity in vitro against both Gram-positive and Gram-negative bacteria. *Staphylococcus Aureus*, *Streptococcus Pyogenes*, *Escherichia coli* and *Pseudomonas aeruginosa* were the microorganism

employed. All the synthesized chelates gave incisive activity against different antimicrobial genus in comparison with the ligand as well as the standard drug which indicates that due to chelation the antimicrobial activity of organic counterpart increases.

In comparison with the standard drug Ampicillin, chelates of  $Cd^{2+}$  and  $Hg^{2+}$  gives enhanced activity against *Escherichia coli*, while the rest of chelates as well as both the ligands did not give even equal activity abutting *Escherichia coli*.

Similarly in comparison with the same standard drug Ampicillin, the chelate of  $Cd^{2+}$  illustrates excellent activity and chelate of  $Hg^{2+}$  illustrate equal activity against *Staphylococcus Aureus*. Moreover oxine also illustrates better activity towards *Staphylococcus Aureus* in comparison with the standard drug Ampicillin.

In this progression, when the synthesized chelates were screened in conjunction with *Pseudomonas aeruginosa*, only the chelate of  $Hg^{2+}$  shows parallel activity as the standard drug while the rest of chelates as well as both the ligands did not give even equal activity against *Pseudomonas aeruginosa*.

Finally when the synthesized chelates were screened in conjunction with *Streptococcus Pyogenes*, not only the chelates but also both the ligands did not give even equal activity abutting *Streptococcus Pyogenes*.

But the study revealed interesting changes in antimicrobial activity on chelation including significant activity by some chelates as they compared with the ligand's activity. The ligand was not sowing even equal activity in comparison with the standard drug, while on chelation it not only gave better activity than the standard drug Ampicillin but also exhibits equal activity as another standard drug such as Chloramphenicol as well as ciprofloxacin (e.g. chelates of  $Cd^{2+}$ ,  $Hg^{2+}$ ... etc).

**Table 1.2** Antibacterial activity table: Minimal inhibition concentration

S.NO	CODE NO.	E.COLI	P.AERUGINOSA	S.AUREUS	S.PYOGENUS
	Compound Molecular Formula	<b>MTCC 443</b>	<b>MTCC 1688</b>	<b>MTCC 96</b>	<b>MTCC 442</b>
1	$C_8 H_{11} N_5 O_3$ ( L1)	250	250	500	500
2	$C_9 H_7 N O$ (L2)	200	500	150	200
3	[Zn (L1) (L2)] $3H_2O$	250	250	500	500
4	[Cd (L1) (L2)] $10H_2O$	50	125	125	250
5	[Hg (L1) (L2)] $10H_2O$ ]	62.5	100	250	250

L1 = Acyclovirand L2 = Oxine

**Table 1.3** Antifungal activity table: Minimal fungicidal concentration

S.NO	CODE NO.	C.ALBICANS	A.NIGER	A.CLAVATUS
	Compound Molecular Formula	<b>MTCC 227</b>	<b>MTCC 282</b>	<b>MTCC 1323</b>
1	$C_8 H_{11} N_5 O_3$ ( L1)	500	1000	1000
2	$C_9 H_7 N O$ (L2)	250	500	500
3	[Zn (L1) (L2)] $3H_2O$	1000	>1000	>1000
4	[Cd (L1) (L2)] $10H_2O$	250	1000	>1000
5	[Hg (L1) (L2)] $10H_2O$ ]	500	>1000	>1000

L1 = Acyclovirand L2 = Oxine

### Antifungal Activity

Three fungii selected viz. *C.albicans*, *A.Niger* and *A.Clavatus*. The synthesized chelates showed antifungal activity against only one organism *C.albicans* compared to the standard drug Nystatin and Greseofulvin. The chelates exerted less activity against *A.Niger* and *A.Clavatus*. The chelates of  $Cd^{2+}$  exhibited better while  $Hg^{2+}$  furnish identical activity than Greseofulvin against *C.albicans*, while ligand oxine showed moderate effect against *C.albicans*. Out of all the chelates, the chelate of  $Cd^{2+}$  exhibited promising antimicrobial activity as a whole.

## 4. CONCLUSION

The confirmation and characterization of the compounds prepared in the present studies are interesting. The formation of metal chelates from various considerations and the structure is tentatively assigned on the basis of above studies. It is suggested that all metal chelates are dimagnetic, four coordinate, two of them crystalline, having ternary; metal: primary ligand: secondary ligand (1:1:1) composition.

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