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Synthesis, Characterization and Antimicrobial Activity of Manganese (Ii), Iron (Ii) and Cadmium (Ii) Complexes Containing Oxine and L- Valine

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Abstract

The mixed ligand complexes of Manganese (II), Iron (II) and Cadmium (II) complexes with oxine and L- valine were synthesized. The complexes were characterized by melting point, solubility, molar conductance, UV spectra, IR spectra, XRD and TGA- DTA studies, antimicrobial and antifungal activities. The lower conductivity values indicated the non- electrolytic nature of the compounds. The complexes are found to be semi-crystaline from XRD data. The thermogram of the complexes shows that they are thermally quite stable. The [M(ox)(val)] complexes exhibit good activity against the bacterial strains Escherichia coli, Bacillus species and Pseudomonas aeruginosa and fungal strains such as Aspergillus niger and Candida albicans compared with the standard. The increase in antimicrobial activity is due to metal chelation. The cadmium complex is found to be more active compared to other metal complexes.

Key words: Transition metal complexes, oxine complexes, Valine, Antimicrobial activity. Antifungal activity, Antilarvicidal activity, Thermal studies.

Keywords

Nanomedicines · Pharmacokinetics · Delivery · Guidelines

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INTRODUCTION

The transition elements are those elements having a partially filled d or f sub-shell in any common oxidation state. Transition metal complexes are important in catalysis, synthesis, photochemistry and biological systems. Comprehensive research has been carried out for the study of mixed ligand complexes and their importance in various biological processes. [1-2] It has been found that many ternary complexes of some metals are significant for activation of enzymes and they are used for storage as well as for transport of active materials. [3] The correlation between the stability of the metal-ligand complexes with their antimicrobial activity has been studied.

Oxine (8-hydroxyquinoline) is an important organic ligand which are widely studied and used in the field of synthesis of organic compounds and metal ion complex. Oxine is a derivative of the heterocyclic quinoline by placement of an –OH group on carbon number 8. [4] Oxine is a monoprotic bidentate chelating agent. In neutral solution, the hydroxyl is in the protonated form (pKa=9.89) and the nitrogen is not

protonated (pKa=5.13). [5] However, an excited-state zwitterionic isomer exists in which H+ is transferred from the oxygen (giving an oxygen anion) to the nitrogen giving a protonated nitrogen cation. [6] Earlier work reported that some drugs showed increased activity, when administered as metal chelates rather than as organic compounds. [7]

A broad spectrum of biological activity is reported to be associated with a large number of heterocyclic compounds. If hydroxyl group is blocked so that the compound is unable to chelate, the antimicrobial activity is destroyed. [8] Oxine with cu (II), Zn (II) and Cd (II) complexes give little information about their thermal stability by using thermogravimetric analysis. As out of seven possible hydroxyquinoles, 8-hydroxyquinoline forms chelate with metal ions found to have antimicrobial activity.

A survey of the literature reveals that the ternary complexes of Zn (II) and Cd (II) with 8-hydroxyquinoline as primary ligand and glycine, L-lysine and L- alanine as secondary ligand have been studied, the synthesized complexes have shown antimicrobial activity against some strains of bacteria. [9] The chelating ability of amino acids has been used in fertilizers for agriculture to facilitate the delivery of minerals to plants in order to correct mineral deficiencies, such as iron chlorosis. These fertilizers are also used to prevent deficiencies from occurring and improving the overall health of the plants. The remaining production of amino acids is used in the synthesis of drugs and cosmetics.

Valine is an essential amino acid, hence must be ingested through foods or supplements. Out of both configurations, L-Valine mainly involves in biochemical processes and is actively taken by muscles. L- Valine also regulates the immune system and essential for muscle tissue repair and muscle metabolism as well as increases exercise endurance. L- Valine required for the proper performance of the nervous system and prevents the nervous and digestive disorders. Mixed ligand complexes plays an important role in numerous chemical and biological systems like water softening, ion exchange resin, electroplating, dying, antioxidant, photosynthesis in plants, removal of undesirable and harmful metal from living organisms. Many of these metal complexes are shown good biological activity against pathogenic microorganism. [10]

The ternary complexes play a decisive role in the activation of enzymes and also in the storage and transport of active substances. The ternary transition metal complexes have shown catalytic activity and have also shown biological activity. Ternary complexes containing an amino acid as a secondary ligand are of significant as they are potential models for enzyme metal ion substrate complexes. [11]

The mixed-ligand complexes containing Mn (II), Co(II), Ni(II), Cu(II) and Cd(II) , amino acid (L-Valine) and saccharin is synthesized. They suggested that the ligands L-Valine and Saccharin coordinate with M(II) forming octahedral geometry. The antibacterial activity of mixed ligand complexes against E.coli, Salmonella typhi, Pseudomonas aeruginosa, Staphylococcus were carried out and its zone of inhibition is measured. It is shown that the antibacterial activity significantly increased on coordination. It has been suggested that the ligands with nitrogen and oxygen donar systems inhibit enzyme activity. Hence metal chelates can be employed as antibacterial agent.The present paper deals with the synthesis , spectral and thermal studies of transition metal complexes with oxine as aprimary ligand and L-valine as a secondary ligand. These metal complexes have shown good antimicrobial activity and antilarvicidal activity. [12]

MATERIALS AND METHODS

Reagents and solvents: All the chemicals ($MnSO_4$, $FeSO_4$ & $CdCl_2$) and reagents used for the preparation of complexes were commercial products (Sisco Research Laboratories Pvt Ltd and Nice Chemicals Pvt Ltd) and used without further purification. DMF and DMSO were purchased from Nice Chemicals Pvt Ltd.

Melting points of the synthesized compounds were measured using a melting point apparatus obtained from Guna Enterprises, Chennai.

The molar conductivities were measured with the conductivity meter of model DCM 900 using the freshly prepared solution of the complexes (10^{-3} M) in DMSO.

The ultraviolet visible spectra of the compounds were recorded on a SYSTRONICS 2201 spectrometer using DMSO as solvent in the wavelength range of 800 - 200 nm.

The IR spectra of the synthesized compounds were recorded using SHIMADZU spectrophotometer in 4000 – 400 cm^{-1} range, using KBr pellet.

The X – ray diffraction patterns of the samples were tested by an X – ray scattering SHIMADUZ XD – DI

diffractometer using in filter Cu Kα radiation source (LAMDA = 0.154 nm), set a scan rate = 10 / min, using a voltage of 40 Kv and a current of 30 Ma.

The complexes were tested in a SDT Q600 V8.0 build 95 instrument at IIT, Madras. The temperature range was varied from room temperature to 800 °C with heating rate of 20 °C/min in oxygen atmosphere.

The effect of various metal complexes on the several bacterial strains and fungal strains were assayed by Agar well diffusion method.

The larvicidal activity of metal complexes have been studied. The egg and egg rafts of culex quinquefasciatus were procured from Zonal entomological unit, Velapadi, Vellore, Tamil Nadu.

Preparation of metal complexes

Complexes of the type [M(oxine)(valine)]

2.9 g of oxine was dissolved in 10 ml ethanol and 20 ml of 2 M NaOH. The mixture was added to an aqueous solution of metal salt ($MnSO_4$, $FeSO_4$ & $CdCl_2$) in 250ml beaker and stirred well for half an hour using magnetic stirrer. 2.34 g of L- valine was dissolved in 20 ml of 2 M NaOH and 5 ml of DMF. This solution was added slowly and heated in a boiling water bath for half an hour. The precipitate formed was filtered using Whatmann no.1 filter paper, washed with water, washed with ether and then dried.

Results and discussion

The metal complexes obtained were solid and coloured. They were insoluble in water and soluble in solvents like dimethyl sulphoxide and dimethyl formamide.

Table 1: Analytical data of synthesized transition metal complexes

Properties	[Mn(ox)(val)]	[Fe(ox)(val)]	[Cd(ox)(val)]
Molecular Formula	$MnC_{14}H_{16}O_3N_2$	$FeC_{14}H_{16}O_3N_2$	$CdC_{14}H_{16}O_3N_2$
Molecular weight	316.44	317.35	373.92
Colour	Green	Dark black	Fluorescent green
Melting point ℃	> 360	> 350	> 350
Molar Conductance ohm^{-1} cm^{-2} mol^{-1}	0.023	0.025	0.020

The lower molar conductivity values showed the non-electrolytic nature of the complexes.[13]

1. UV Spectra

The spectrum of free ligand valine display absorption bands at 257 nm and an intense peak at 322 nm which are attributed to $\pi \rightarrow \pi*$ and $n \rightarrow \pi*$ transitions respectively. Similarly, the spectrum of free ligand oxine display absorption bands at 257 nm and 317 nm which are assigned to $\pi \rightarrow \pi*$ and $n \rightarrow \pi*$ transitions respectively.

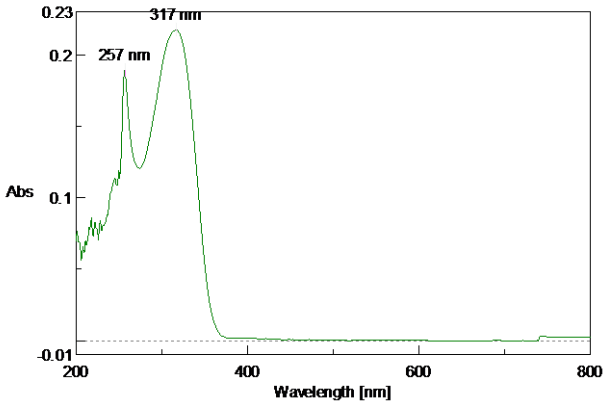


Fig.1: UV - Visible Spectra of Oxine

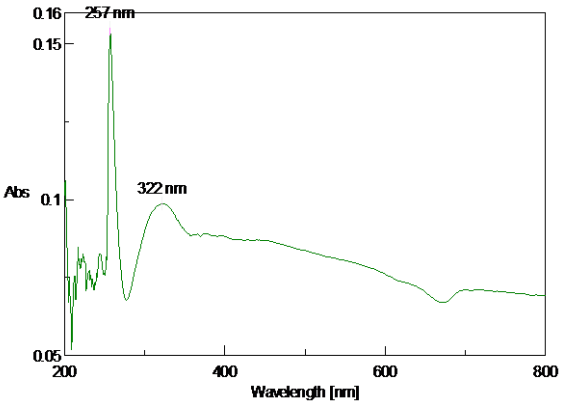


Fig.2: UV - Visible Spectra of Valine

The electronic spectrum of [Mn(ox)(val)] complex exhibit three bands in the region 260nm, 333 nm and 394 nm which are assigned to the $\pi \rightarrow \pi*$, $n \rightarrow \pi*$ and charge transfer from ligand to metal respectively which indicates the presence of tetrahedral symmetry.[14] The electronic spectrum of [Fe(ox)(val)] complex exhibits an intense band in the region 259 nm which is assigned to $\pi \rightarrow \pi*$ transition and also this complex exhibits three d-d transition bands centered at 374 nm, 462 nm and 583 nm indicating tetrahedral geometry.

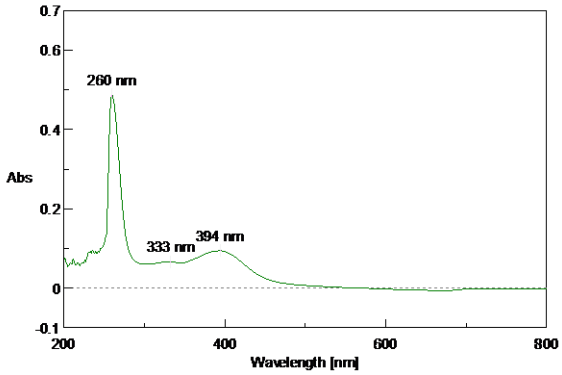


Fig. 3: UV - Visible Spectra of [Mn(ox)(val)]

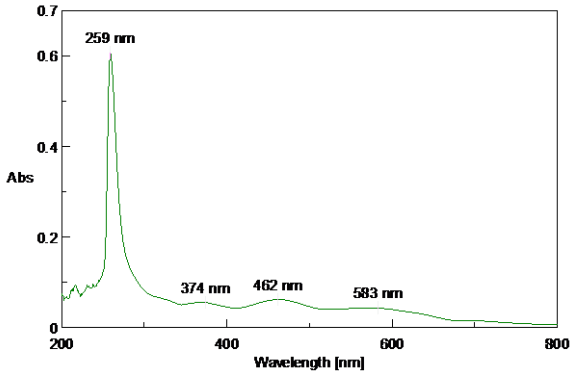


Fig. 4: UV - Visible Spectra of [Fe(ox)(val)

The electronic spectrum of [Cd(ox)(val)] complex exhibit three bands in the region 265 nm, 341 nm and 397 nm which are assigned to the $\pi \rightarrow \pi*, n \rightarrow \pi*$ and charge transfer from ligand to metal respectively which indicates the presence of tetrahedral symmetry. Here cadmium (II) complex is diamagnetic in nature and its electronic spectra do not furnish any characteristic d-d transitions except charge transfer (LMCT) bands as expected for d^{10} systems.

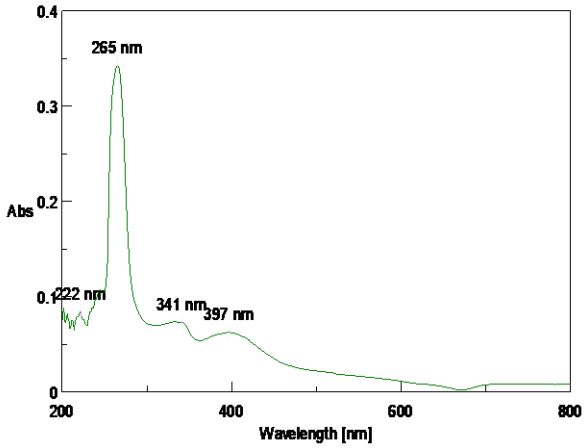
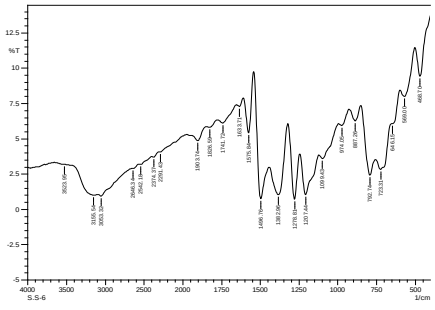


Fig. 5: UV - Visible Spectra of [Cd(ox)(val)]

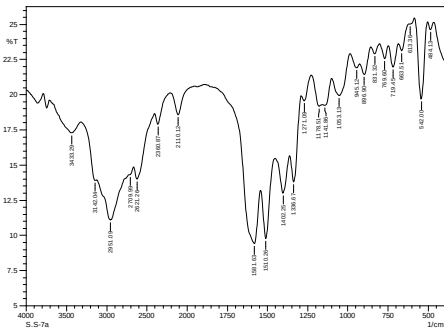
2. Infrared spectra

The IR spectra provide valuable information regarding the nature of the functional groups attached to the metal ion. The transition metal complexes show characterised functional bands such as N - H, C - O, C - N, COO^-, M - O and M - N bands. Formation of metal-nitrogen and metal-oxygen bonds were further confirmed by the presence of the stretching vibration of υ(M-N) and υ(M-O) around (401-578) cm^{-1} and (648-486) cm^{-1} respectively.



Wavenumber (cm^{-1})

Fig.6: IR Spectrum of oxine



Wavenumber (cm^{-1})

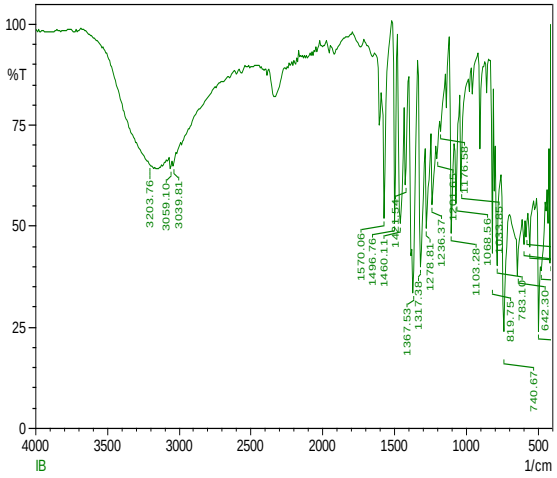
Fig. 7: IR spectrum of L-Valine

The N - H asymmetric and N - H symmetric vibrations observed at 3142.04 cm^{-1} in the free amino acid are shifted to higher wave number 3203.76 cm^{-1}, in the spectra of the complexes suggesting the coordination of amino group through nitrogen with the metal ion. [15]

The $\nu(COO)_{asym}$ band of the free amino acids observed at 1581.63 cm^{-1} is shifted to lower wave number 1570.06 cm^{-1} and the $\nu(COO)_{sym}$ band observed at 1402.25 cm^{-1} in the spectra of free amino acids is found to be shifted to lower wave number 1367.53 cm^{-1} indicating the coordination of the carboxylic acid groups via oxygen with the metal ion.[16]

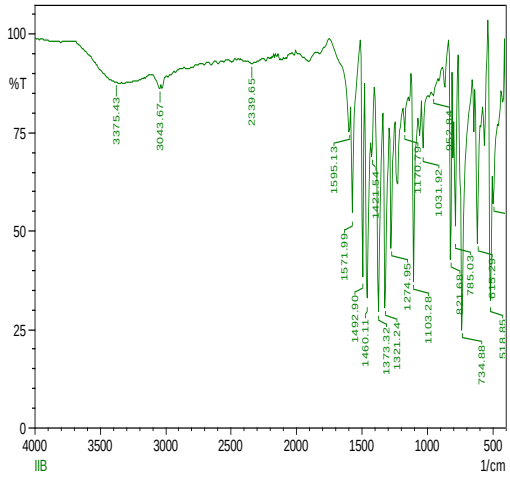
The ν (C = N) band observed at 1575.84 cm^{-1} in the spectrum of free oxine ligand is found to be shifted to lower wave number in the range of 1496.76 cm^{-1} in the spectra of the complexes suggesting the coordination through tertiary N - donor of oxine.

A new band at 497.63 cm^{-1} due to ν(M - N) is further confirmed the coordination of metal to nitrogen and band at 642.30 cm^{-1} due to ν (M - O) and also 563.21 cm^{-1} due to ν(M - O - C) in IR spectrum of [Mn(ox)(val)].



Wave number (cm^{-1})

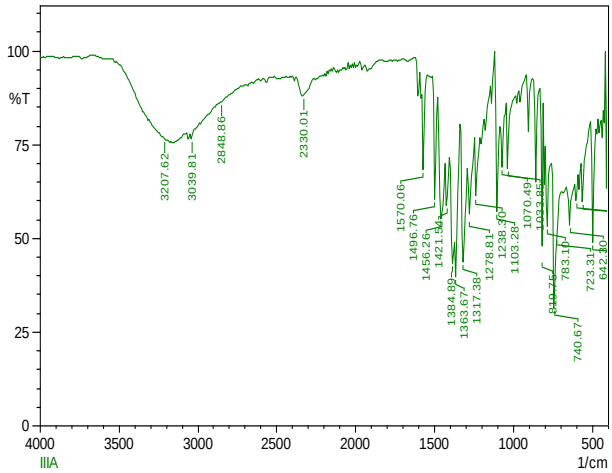
Fig 8:IR Spectra of [Mn(ox)(val)]



Wave number (cm^{-1})

Fig 9: IR Spectra of [Fe(ox)(val)]

Similarly, a new band at 497.63 cm^{-1} due to ν(M - N) is further confirmed the coordination of metal to nitrogen and band at 615.29 cm^{-1} due to ν (M - O) and 518.85 cm^{-1} due to ν(M - O - C) in IR spectrum of [Fe(ox)(val)]. A new band at 525.15 cm^{-1} due to ν(M - N) is further confirmed the coordination of metal to nitrogen and band at 642.30 cm^{-1} due to ν (M - O) and also 580 cm^{-1} due to ν(M - O - C) in IR spectrum of [Cd(ox)(val)].



Wave number (cm^{-1})

Fig10:IR Spectra of [Cd (ox)(val)]

3. X-Ray Diffraction Analysis

XRD analysis is used to determine the percentage of crystallinity present in the material. The crystal size has been calculated using Debye-Scherrer's equation [17] which was shown in the table.

Table 2: X-Ray Diffraction of [M(ox)(val)]

Complexes	FWHM (deg)	θ (deg)	Crystal size (nm)
[Mn(ox)(val)]	46.67	8.5	0.0300
[Fe(ox)(val)]	40.442	12.25	0.0351
[Cd(ox)(val)]	48.52	15	0.0295

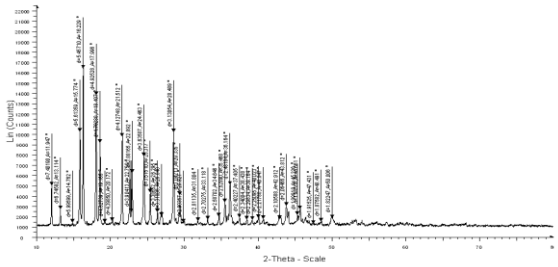


Fig.11: X-Ray Diffraction of [Fe(ox)(val)]

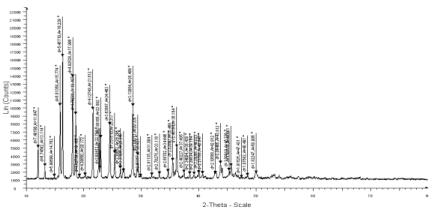


Fig.12: X-Ray Diffraction of [Cd(ox)(val)]

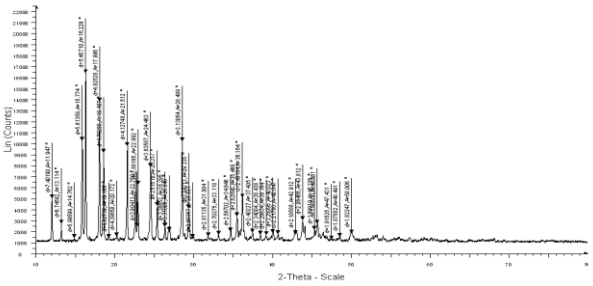


Fig.13: X-Ray Diffraction of [Mn(ox)(val)]

4. Thermal Data

The thermograms of the complexes have shown that they are thermally quite stable to varying degree. The complexes show gradual loss in weight due to decomposition by fragmentation with increasing temperature. The complex [Mn(ox)(val)] is found to be observed that there are two exothermic peaks, one at 120°C and 340°C. The peak at 340°C is the prominent one. The exothermic peaks are due to oxidative degradation.[18]

The complex [Fe(ox)(val)] shows that there is one prominent exothermic peak at 345 °C, the exothermic peaks are due to oxidative degradations. The complex [Cd(ox)(val)] that there are two exothermic peaks, one at 120 °C and another at 420 °C. The peak at 420 °C is the prominent one and the exothermic peaks are due to oxidative degradation.

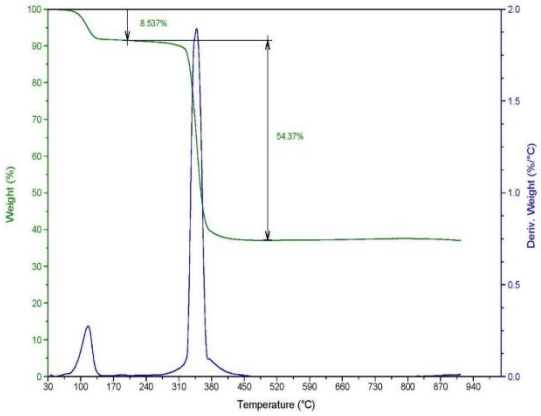


Fig. 14: Thermal data of [Mn(ox)(val)]

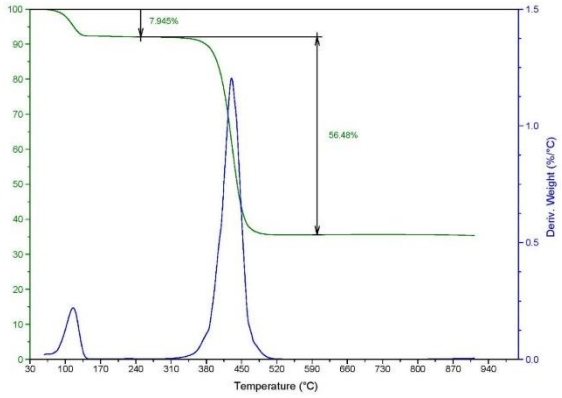


Fig. 15: Thermal data of [Cd(ox)(val)]

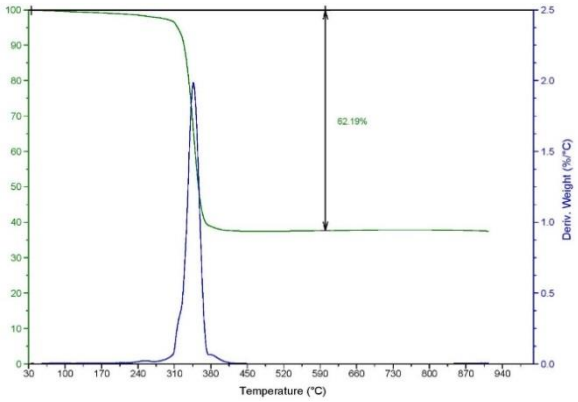


Fig. 16: Thermal data of [Fe(ox)(val)]

5. ANTIMICROBIAL ACTIVITY

Antimicrobial studies of the transition metal complexes were tested against bacteria such as *Escherichia coli, Bacillus species and Pseudomonas aeruginosa* and fungi such as *Aspergillus niger and canida albicans* using well diffusion method.

Antibacterial activity of Metal Complexes

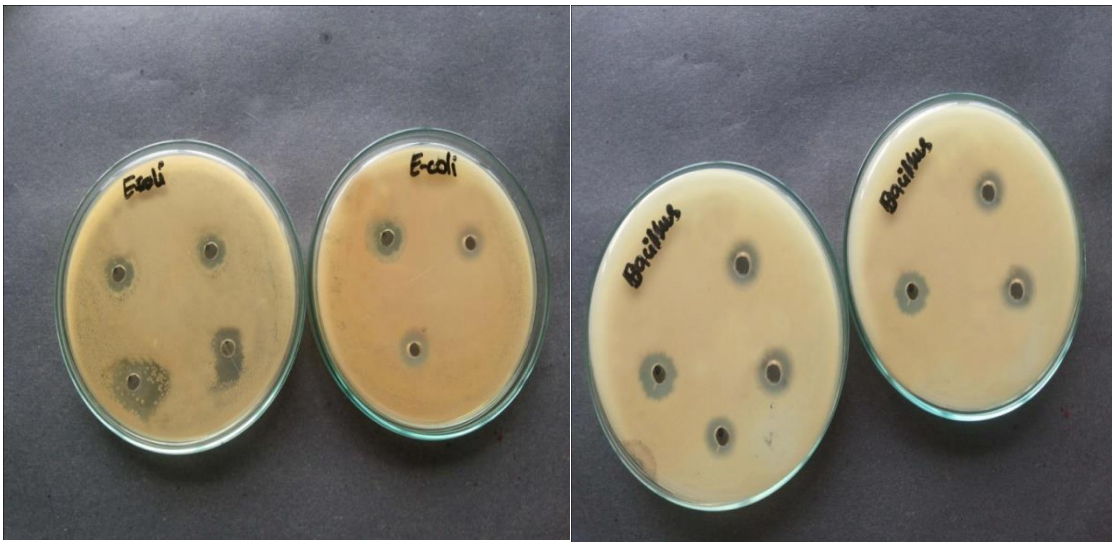
The antibacterial activities of the complexes were studied using Agar well diffusion method. The bacterial species used in the screening were Bacillus species (gram positive) and E.coli (gram negative).

The zone of inhibition values of the synthesised compounds and ligands against the growth of selected bacteria are given below. The results of antimicrobial activity indicated that most of the test compounds exhibited very good antibacterial and antifungal activity.[4]

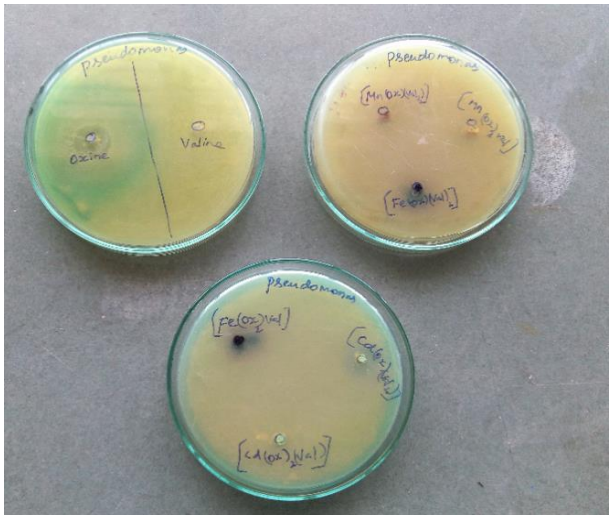
Table 3: Antibacterial Activity Data of Ligands and [M(ox)(val)] Complexes

Compounds	Zone of inhibition (mm)			
	E - Coli	***Bacillus***	***Pseudomonas aeruginosa***	***Ampicillin (Standard)***
Oxine	19	17	15	16
L - Valine	12	12	9	16
[Mn(ox)(val)]	14	11	10	16
[Fe(ox)(val)]	15	13	12	16
[Cd(ox)(val)]	17	15	13	16

Images of Antibacterial Activity of [Mn(ox)(val)], [Fe(ox)(val)] and [Cd(ox)(val)].



Echerichia coli ***Bacillus species***



Pseudomonas aeruginosa

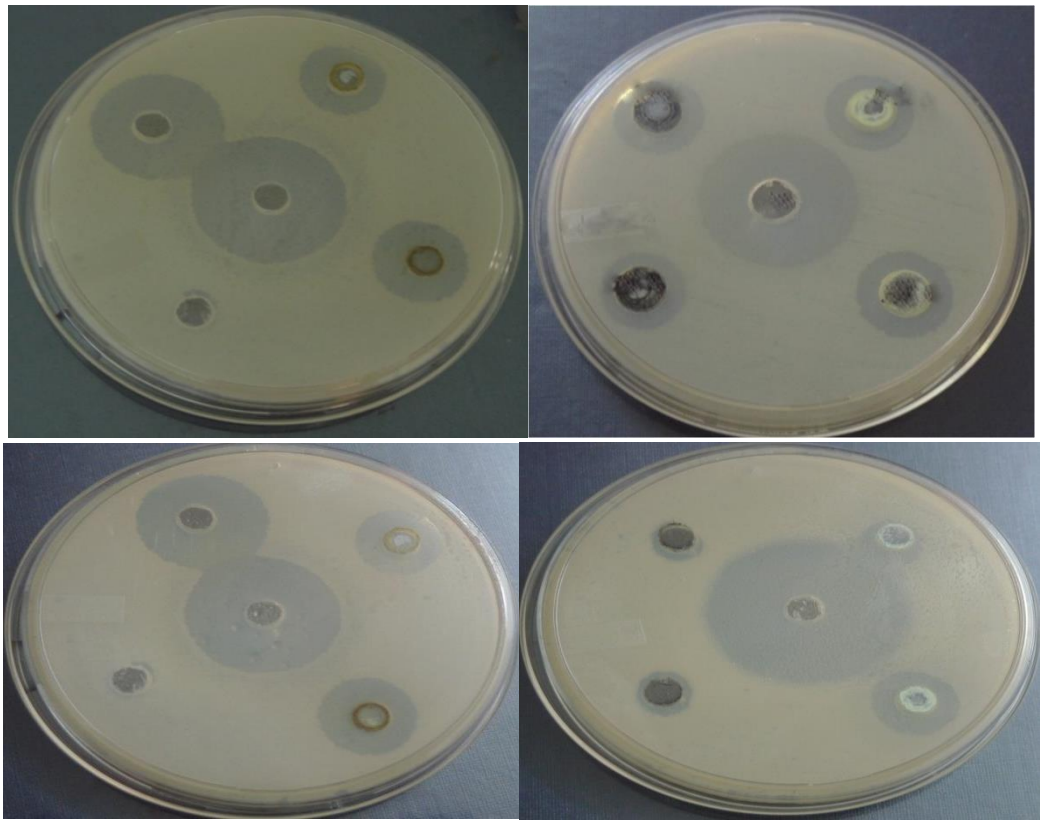
6.Antifungal activity of metal complexes

The Antifungal activity of standard fungicide (*Ciprofloxacin)* and complexes were tested for their effects on the growth of microbial cultures and studied for their interaction with *Aspergillus niger* and *Canida albicans*. The zone of inhibition measured for standard, ligands and complexes have been listed below.

Table 4: Antifungal activity data of Ligands and [M(ox)(val)] Complexes.

Compounds	Zone of inhibition (mm)		
	Aspergillus niger	***Candida albicans***	**Ciprofloxacin**
Oxine	24	25	35
L - Valine	2	2	35
[Mn(ox)(val)]	17	16	35
[Fe(ox)(val)]	10	15	35
[Cd(ox)(val)]	15	16	35

Images of Antifungal Activity of [Mn(ox)(val)], [Fe(ox)(val)] and [Cd(ox)(val)].



Aspergillus niger ***Candida albicans***

7.Antilarvicidal Activity

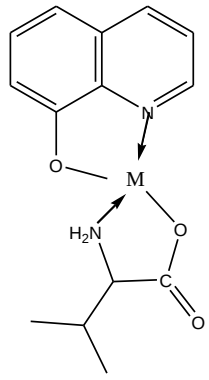
The larvicidal activity of the synthesised metal complexes was performed against *Culex quinquefasciatus* and the values were noted. All the synthesized complexes showed moderate to stronger toxic effect against *Culex quinquefasciatus.* The mortality values of the complexes are listed.

Table 5: Larvicidal Activity of [M(ox)(val)] Complexes

Compounds	Concentration/ Mortality			
	4mg/200 ml	2mg/200 ml	1mg/200 ml	0.5mg/200 ml
[Mn(ox)(val)]	18	14	13	9
[Fe(ox)(val)]	16	14	11	8
[Cd(ox)(val)]	19	14	13	9

The results are corroborated with the findings of other researchers.

The proposed structure of the complexes is given below



Where M = Mn^{2+}, Fe^{2+} and Cd^{2+}.

Conclusion

The complexes of Mn (II), Fe(II) and Cd(II) were synthesized using mixed ligands oxine and L-valine. The complexes were coloured and they are insoluble in water and soluble in DMF & DMSO. The Complexes were characterized by melting point, solubility, molar conductance, UV spectra, IR spectra, XRD and TGA-DTA techniques.

The lower conductivity values indicated the non-electrolytic nature of the complexes. The melting points of metal chelates are higher which suggests

their thermal stability. The thermal properties for [M(ox)(val)] complexes have been investigated. All the stages of decomposition follow one after the other without any stable compound in between. The thermal degradation steps were identified and are mainly due to the direct decomposition of oxine and L- valine from metal complex leaving the corresponding metal oxide. The exothermic peaks are due to oxidative degradation of the complexes and endothermic peaks are due to thermal decomposition of the complexes.

The [M(ox)(val)] complexes exhibit good activity against bacterial strains Escherichia coli, Bacillus species and Pseudomonas aeruginosa and the fungal strains such as Aspergillus niger and Candida albicans compared with the standard drugs. The increase in antimicrobial activity may be due to metal chelation. [Cd(ox)(val)] complex is more effective when compared to other complexes. Similarly, antilarvicidal activity is more effective in Cd(ox)(val)] complex.

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