

# Biological accomplishments of Transition metal complexes incorporating novel Schiff base ligand 2-(1-(3-aminopropylimino) ethyl) phenol).

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## Abstract:

Schiff bases and their complexes are versatile compounds synthesized from the condensation of an amino compound with carbonyl compounds and widely used for industrial purposes and also exhibit a broad range of biological activities including anti-fungal, anti-bacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties. Development of a new chemotherapeutic Schiff bases and their metal complexes is now attracting the attention of medicinal chemists.

A novel schiffbase ligand is synthesized by Ketone with Aromatic Amine to form Schiffbase ligand (L). It is mixed with 1<sup>st</sup>Row transition metal ions to form metal complexes. Complexes are characterized by Elemental analysis, UV-Visible spectroscopy, FTIR spectroscopy and H<sup>1</sup> NMR, C<sup>13</sup> NMR spectroscopy. Elemental analysis of the metal complexes was suggested that the stoichiometry ratio is 1:2 (metal-ligand). The UV-Visible spectrum gives clear idea about the metal complexes. Fluorescent studies of ligand and complexes also performed. The Schiff base complexes have been screened for their invitro antibacterial activity against three bacteria via; (Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus sp.) also studied antifungal activities (Aspergillus Niger and Aspergillus flavus). Anti-oxidant properties of metal complexes also have been studied.

## Keywords:

Schiff base, Transition metal complexes, spectroscopy, Fluorescent analysis, Biological activity, Anti-oxidant study.

## 1. INTRODUCTION

Schiff bases are an important class of ligands in co-ordination chemistry and have studied extensively as they are selective and sensitive toward various metal ions. Metal complexes of Schiff bases have found diverse applications in addition to interesting structural chemistry. Schiff bases easily form stable complexes with most transition metal ions. Schiff bases have played a special role as chelating ligands in main group and transition metal coordination chemistry because of their stability under a variety of redox conditions and because imine ligands are borderline Lewis bases. The important physical and biological properties of the Schiff bases are directly related to intermolecular hydrogen bonding and proton transfer equilibria. Co-ordination complexes play a major role in important biological activities. Transition metals are involved in many biological processes which are essential to life process. Transition metal complexes have attracted curiosity due to DNA binding and cleavage properties under physiological conditions. Applications of metal complexes as chemical nucleases are the focus of current research. It has been demonstrated that Inorganic complexes as chemical nucleases are the

focus of current research. It has been demonstrated that inorganic complexes can be used in foot printing studies as sequence specific DNA binding agents, as diagnostic agents in medicinal applications and for genomic research [1].

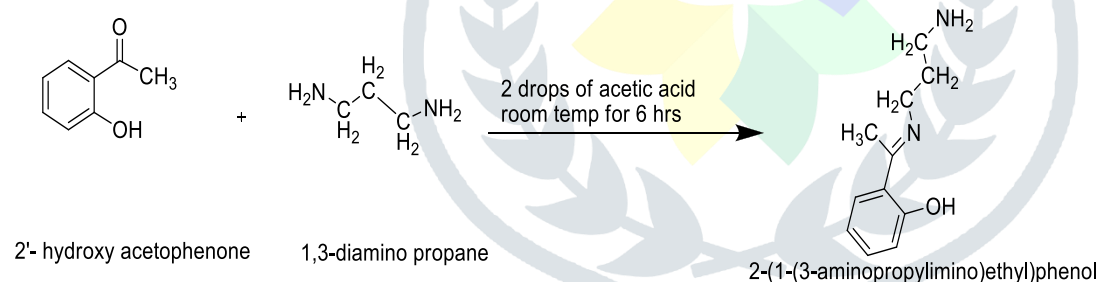
Schiff bases have a large number of synthetic uses in organic chemistry. Acylation of Schiff bases by acid anhydrides, acid chlorides and acyl cyanides is initiated by attack at the nitrogen atom and leads to net addition of the acylation agent to the carbon-nitrogen double bond. Reactions of this type have been put to good use in natural product synthesis. Schiff bases appear to be an important intermediate in a number of enzymatic reactions involving interaction of an enzyme with an amino or a carbonyl group of the substrate.

## 1.1. EXPERIMENTAL WORK

### 1.1.1 SYNTHESIS OF LIGAND (L)

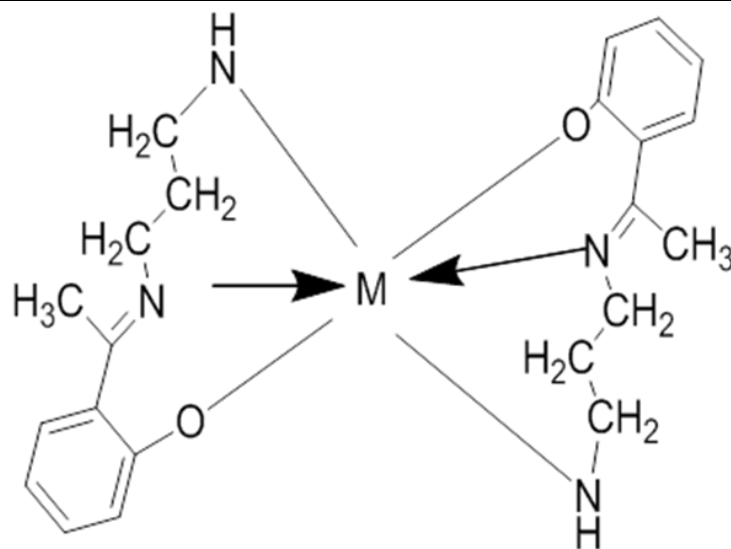
A Solution of 2'-Hydroxy acetophenone and 1, 3- diamino propane in 20 ml alcohol and drops of dilute acetic acid was added. The mixture was refluxed for about 6 hrs. The mixture was cooled in ice. The resulting precipitate was then filtered, washed with ethanol and dried. The product was re-crystallized from hot ethanol gave ligand (L).

#### SCHEME: 1 SYNTHESIS OF LIGAND (L)



### 1.1.2. SYNTHESIS OF METAL COMPLEXES

To an ethanolic solution of the Schiff base Ligand and the solution of metal (Copper, Vanadium, Manganese and Ruthenium) was added in a molar ratio (1:2). The mixture was refluxed for about 2 hours. The mixture was cooled in ice. The resulting precipitate was collected by filtration, washed with ethanol and dried. Crystallization from aqueous ethanol gave pure crystals of metal complexes.



Where M= Cu(II), Mn(II), V(V) and Ru(III)

FIG: 1.1 STRUCTURE OF METAL COMPLEXES (L<sub>4</sub>)

## 1.2 RESULT AND DISCUSSION

### 1.2.1 ELEMENTAL ANALYSIS OF LIGAND (L) WITH METAL COMPLEXES

The micro-elemental analysis for C, H, N and S as well as the molecular weight of the complexes obtained were in agreement with the predicted formula for complexes. Table: 7.1. Shows the list of the elemental analysis of the Schiff base ligand (L<sub>4</sub>) and synthesized Schiff base complexes which are in good agreement with the calculated values.

TABLE: 1.1. ELEMENTAL ANALYSIS OF SCHIFF BASE METAL COMPLEXES

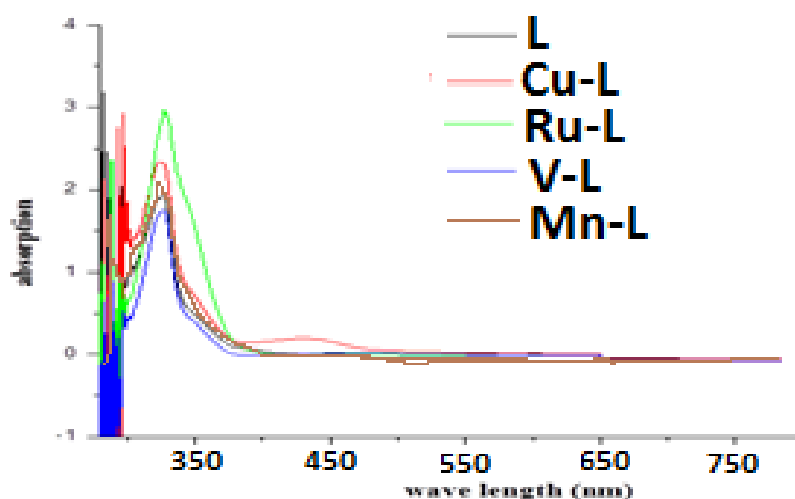
Compounds	Physical appearance	Melting point (°C)	Elemental (%) Calc (found)					m/z
			C	H	N	O	M (metal)	
Ligand (L)	Red	135	68.72	8.39	14.57	8.32	–	192.13
			(68.74)	(8.41)	(14.55)	(8.34)		
Cu- L	Black	158	61.94	8.00	11.11	6.35	12.60	503.24
			(61.92)	(7.97)	(11.09)	(6.32)	(12.57)	
Mn- L	Pale brown	163	65.43	8.45	11.74	6.70	7.67	715.41
			(65.40)	(8.46)	(11.73)	(6.72)	(7.69)	

<b>V- L</b>	Pale yellow	96	63.53	8.20	11.40	6.51	10.36	491.26
			(63.51)	(8.22)	(11.38)	(6.53)	(10.38)	
<b>Ru- L</b>	Brown	132	57.65	7.44	10.34	5.91	18.66	542.22
			(57.67)	(7.48)	(10.37)	(5.93)	(18.69)	

### 1.2.2 UV-VISIBLE SPECTRAL ANALYSIS

The UV-visible absorption spectra of the Schiff base ligand (L) and its complexes, the results were recorded and study was carried out at room temperature. The values of the absorption wavelength and its band assignments of the comparative spectrum were shown in Fig: 1.2. The absorption of the ligand (L) was characterized by main absorption bands at 222 nm, 345 nm. The band appearing at 222 nm was attributed to  $\pi \rightarrow \pi^*$  transition [2,3]. The bands appearing at 345 nm was attributed to  $n \rightarrow \pi^*$  transition [4,5].

The UV-Visible absorption spectra of all the schiff base complexes show similarities, which indicates coincides with their structures and generally shown the characteristic bands of the free ligands with some changes both in frequencies and intensities. Upon complexation, the absorption bands of the complexes are slightly shifted to shorter wavelength (Blue shift) compared to those of the free ligand. In Cu(II)Complex the  $\pi \rightarrow \pi^*$  transition occur at 230 nm and in Ru(III) complex the  $n \rightarrow \pi^*$  transition is at 376 nm. These modifications of the shifts and intensity of the absorption bands indicates the coordination of the ligand to the metal ion. From the data the structure of the complexes is concluded as octahedral. The data given by Table 1.2 and Fig: 1.2



**FIG: 1.2. UV-VISIBLE SPECTRAL ANALYSIS OF LIGAND (L) AND COMPLEXES**

TABLE: 1.2. UV-VISIBLE SPECTRA FOR LIGAND AND ITS METAL COMPLEXES

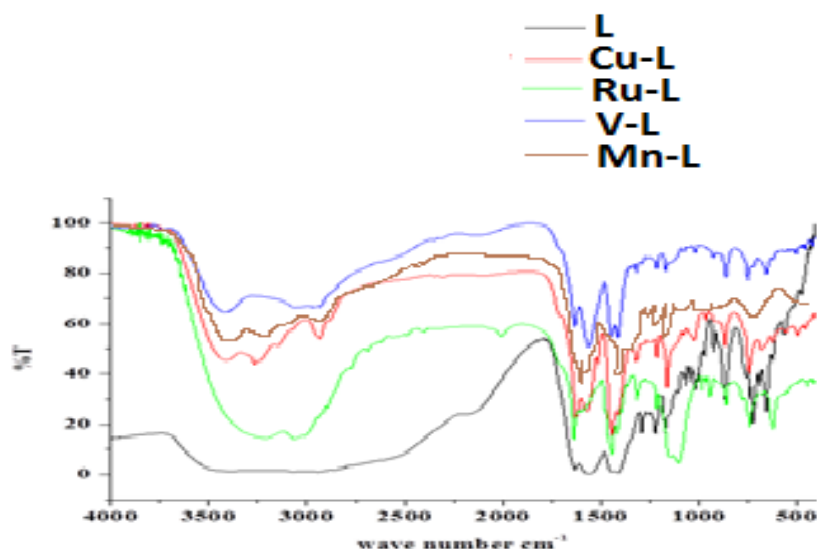
Compounds	Frequency		$\epsilon_{\max}$	Transition	Geometry	BM
	nm	cm <sup>-1</sup>				
Ligand (L)	345	28985.50	-	n $\rightarrow$ $\pi^*$	-	-
	222	45045.04		$\pi\rightarrow\pi^*$		
Cu(II)- complex	380	26315.78	10	$^2E_g\rightarrow^2T_{2g}$	Octahedral	2.02
	230	43478.26	102	$\pi\rightarrow\pi^*$		
Mn(II)- complex	382	26178.01	102	$^2E_g\rightarrow^2T_{2g}$	Octahedral	3.6
V(V)- complex	352	28409.09			Octahedral	-
	340	29411.76	103-4	LMCT		
Ru(III)- complex	376	26595.74	102	n $\rightarrow$ $\pi^*$	Octahedral	2.02
	381	26246.71	102	$^3A_{2g}(F)\rightarrow^3T_{2g}(F)$	Octahedral	2.97

### 1.2.3 FT-IR SPECTRAL ANALYSIS OF LIGAND (L) AND ITS COMPLEXES

The broad band at 1695 cm<sup>-1</sup> for the azomethine group of free ligand was shifted to lower frequency of 1607 cm<sup>-1</sup> in the Cu(II) mixed ligand complex indicating the coordination of the azomethine nitrogen atom to Cu(II). The band at 1663 cm<sup>-1</sup> in the Ru(III) mixed ligand complex corresponds to ketamine. Similarly there is a band at 1669 cm<sup>-1</sup> and 1566 cm<sup>-1</sup> for HC=N stretching of Mn(II) and V(V) complexes respectively. The band at 1721 cm<sup>-1</sup> for the carbonyl group of free ligand was shifted to lower frequency of 1708 cm<sup>-1</sup> in the mixed ligand complex indicating the coordination of the carbonyl oxygen with the metal ion. Similar lower frequency bands appear in other complexes also [6,7].

The band at frequency 3337 cm<sup>-1</sup> is due to the linkage between N and H atoms. The spectrum of the complex shows new bands at 559 cm<sup>-1</sup> and 449 cm<sup>-1</sup> due to the formation of M-O and M-N bonds respectively [8]. Similar bands appear in other complexes also.

The remaining peaks were disappearance of aromatic hydroxyl group after complexation denotes the coordination with -OH with the central metal ion [9]. The data's were noted in the Fig: 1.3. and Table 1.3



**FIG: 1.3. FT-IR SPECTRA FOR LIGAND AND ITS METAL COMPLEXES**

**TABLE: 1.3. FT-IR SPECTRA FOR LIGAND AND ITS METAL COMPLEXES**

Compound	$\nu_{\text{HC=N}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{C=O}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{M-O}}$ ( $\text{cm}^{-1}$ )	$\nu_{\text{M-N}}$ ( $\text{cm}^{-1}$ )
Ligand(L)	1695	1721	-----	-----
Cu-L	1607	1708	559	449
Mn-L	1669	1710	550	464
Ru-L	1663	1715	542	471
V-L	1566	1719	525	452

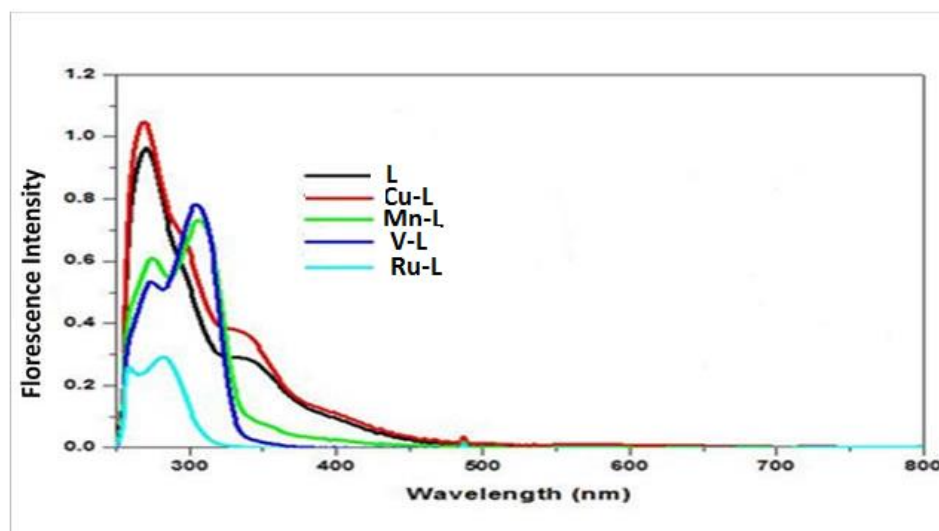
#### 1.2.4 FLUORESCENCE STUDIES FOR SCHIFF BASE COMPLEXES

The rare earth elements still have a unique and important impact on our lives. The unfilled 4f electronic structure of the rare earth elements makes them have special properties in luminescence, magnetism and electronics, which could be used to develop many new materials for various applications such as phosphors, magnetic materials, hydrogen storage materials and catalysts.

The emission spectra of the Schiff base ligand and its complexes are shown in Fig: 1.4. It shows that the free ligand (L) exhibits broad fluorescence band around 270 nm [10, 11]. The emission spectrum of Cu (II) displays luminescence band corresponding to the transition at 260 nm. [12]. For Mn (II) complex, the emission spectrum excited at 270 nm & 300 nm and shows luminescence bands.

For vanadium complex, the emission spectrum excited at 268nm & 300nm shows luminescence bands. These results were indicated that the ligand (L) which were high activity than the Schiff base complex it

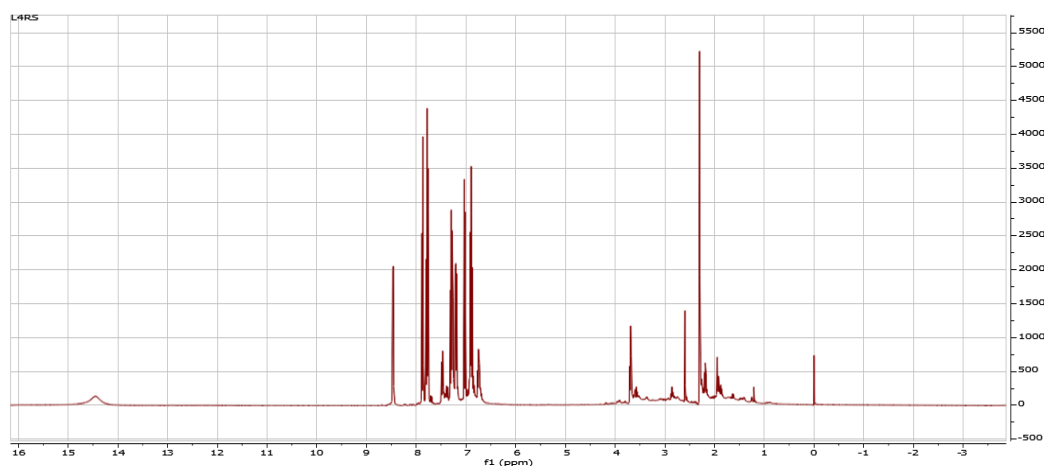
can be used to absorb and transfer energy to the complexes. The Ru (III) complexes, shows a broad emission band around 252nm & 280 nm, which was assigned to transition. The fluorescence intensity of this complex was less while compared with other complexes, these complex may be attributed to the complexation coincides with ligands evident from lesser binding constant values.



**FIG: 1.4. FLUORESCENCE STUDIES OF EMISSION SPECTRA FOR LIGAND AND COMPLEXES**

### 1.2.5 $^1\text{H}$ AND $^{13}\text{C}$ -NMR SPECTRAL ANALYSIS OF SCHIFF BASE LIGAND

The  $^1\text{H}$  and  $^{13}\text{C}$ -NMR Spectra of Schiff base ligand (L) the results were noted in Fig: 1.5. shows signal of triplets at 2.4 ppm and doublet at 4.15 were due to  $\alpha$ , methine and methylene hydrogen atom respectively [13, 14]. The broad singlet at 6.9–8.5 ppm and is due to the aromatic protons. The strong singlet at 8.91 ppm was assigned for the azomethine proton [15]. The same basis  $^{13}\text{C}$ -NMR spectra revealed the 10 ppm to 170 ppm highest ranges in the 140 ppm to 160 ppm respectively. These results was similar with the above mentioned IR data have revealed. The data are in Fig: 1.5&1.6 and Table 1.4.



**FIG: 1.5.  $^1\text{H}$ -NMR SPECTRUM OF LIGAND**



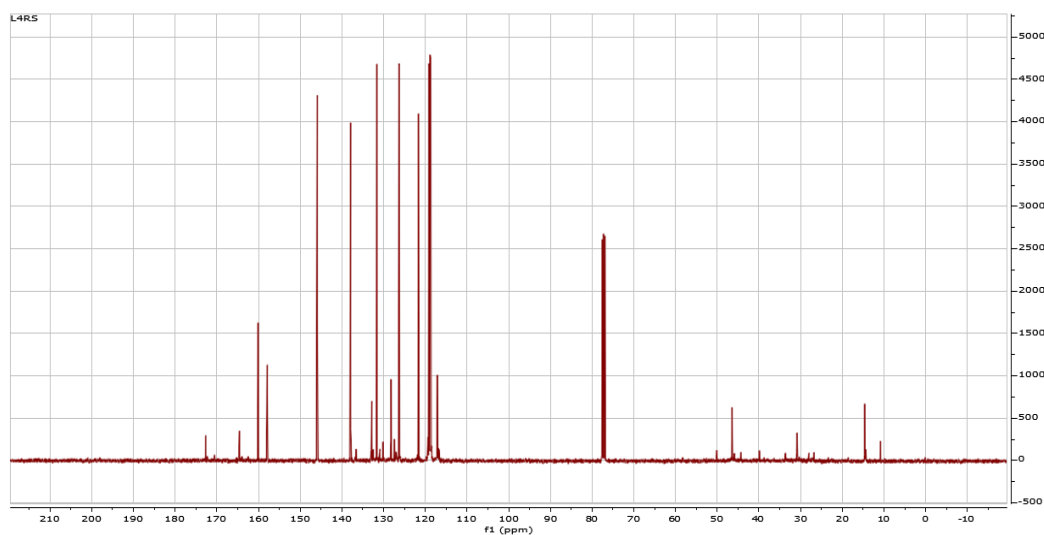


FIG: 1.6.  $^{13}\text{C}$ -NMR SPECTRUM OF LIGAND

TABLE: 1.4.  $^1\text{H}$ -NMR SPECTRUM OF LIGAND

Compound	Signals ( $\delta$ , ppm)	Assignment
(L)	6.9 – 8.5	Aromatic protons
	8.91	-HC=N- Protons
	6.02	-NH <sub>2</sub> Protons
	2.4	=C-CH <sub>3</sub> protons

### 1.2.6 ANTI-BACTERIAL ACTIVITY FOR SCHIFF-BASE LIGAND (L) AND ITS COMPLEXES

The Schiff-base ligand (L) and its complexes evaluated for anti-microbial activity against *Bacillus sp*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* and the percentage of inhibition details were depicted in Table: 1.5. and Fig: 1.7(a) and 1.7(b). The Schiff base ligand (L) was biologically active. However, its Ligand (L) complexes showed remarkable anti-bacterial activity as a result of chelation of metal with ligand synergistically increasing its effect [16]. From the results obtained, the anti-bacterial activity of copper complex is found to be higher than that of a free Schiff base ligand, against the same microorganism under identical experimental conditions. The results were coincides with the previous report. [17].

Fig:1.7(a) Anti-microbial activity for Ligand (L) and Cu(II), Mn(II), V(V) and Ru(III) complexes against bacterial pathogens



a) *Bacillus* species(b) *Staphylococcus aureus*(c) *Pseudomonas aeruginosa*

Where 1,2,3,4 = Cu(II), Mn(II), V(V) and Ru(III) complexes

TABLE: 1.5. ANTI-BACTERIAL ACTIVITY OF THE LIGAND AND ITS COMPLEXES

Test Organisms	Compounds L	Zone of inhibition (in diameter)					Solvent Control	Standard Streptomycin
		Cu-L	Mn-L	V-L	Ru-L			
<i>Staphylococcus aureus</i>	17	19	18	17	14	NZ	18	
<i>Pseudomonas aeruginosa</i>	15	13	11	15	18	NZ	15	
<i>Bacillus species</i>	17	13	14	16	19	NZ	17	

Solvent used: DMSO (Dimethyl Sulphoxide)

Standard used: Streptomycin

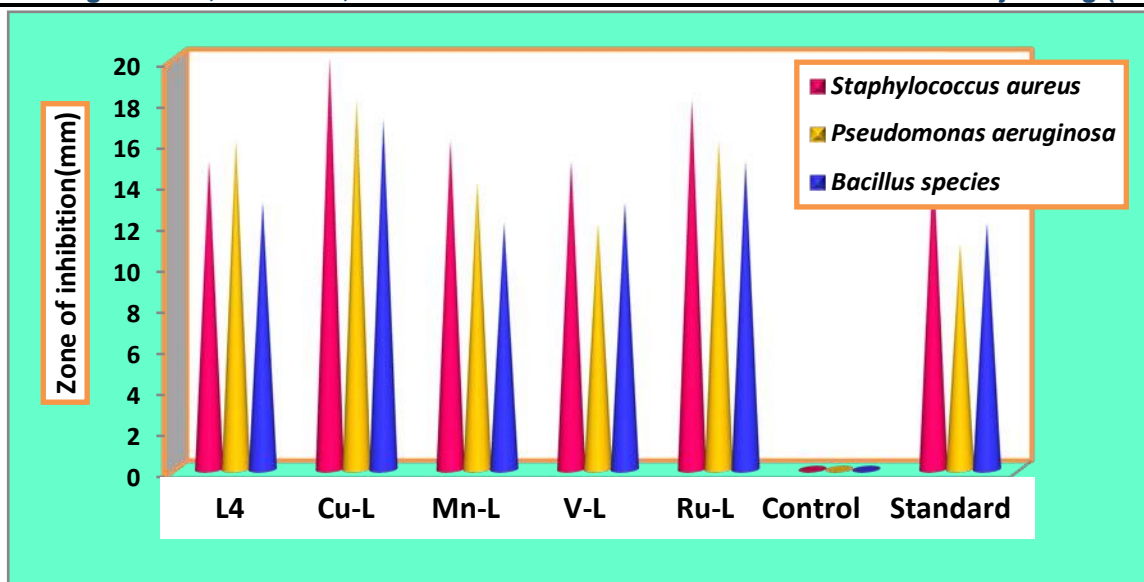


FIG: 1.7(b) ANTI-BACTERIAL ACTIVITY OF THE LIGAND AND COMPLEXES

### 1.2.7 ANTI-FUNGAL ACTIVITY FOR SCHIFF BASE LIGAND AND COMPLEXES

The anti-fungal activity of the Schiff-base ligand (L) and its complexes against *Aspergillus niger* and *Aspergillus flavus* percentage of zone of inhibition were studied. The results were noted in Table: 1.6

The comparative anti-fungal activities have been depicted in Fig: 1.8(a) & 1.8(b). The Schiff base ligand (L) and all the complexes show high anti-fungal activity against the fungal pathogens. However the complexes revealed remarkable anti-fungal activity than the Schiff base ligand. The findings were similar with this earlier report [18].

It was observed that the anti-fungal activity of few complexes were very near to the standard anti-fungal agent. Compared with all other complexes, Mn(II) complex exhibited highest activity against the species *Aspergillus niger* and Simultaneously, *Aspergillus flavus* exhibited all the complex has higher activity among complexes.

Beyond, which was evident from the results showed that the activities were significantly increased on coordination. The efficient activity which has been suggested that the Schiff base with nitrogen and oxygen donor systems inhibit enzyme activity, since the enzymes which require these groups of their activity appear to be especially more susceptible to deactivation by metal ions on coordination [19,20].

TABLE.1.6. ANTI-FUNGAL ACTIVITY OF THE LIGAND (L) AND ITS COMPLEXES

Test Organisms	Compounds	Zone of inhibition (in diameter)					
	L	Cu	Mn	V	Ru	Solvent control	Standard Amk. 30µg
<i>Aspergillus niger</i>	13	15	17	13	12	NZ	19
<i>Aspergillus Flavus</i>	17	14	19	11	15	NZ	17

Solvent used: DMSO (Dimethyl Sulphoxide) Standard used: Amk. 30µg

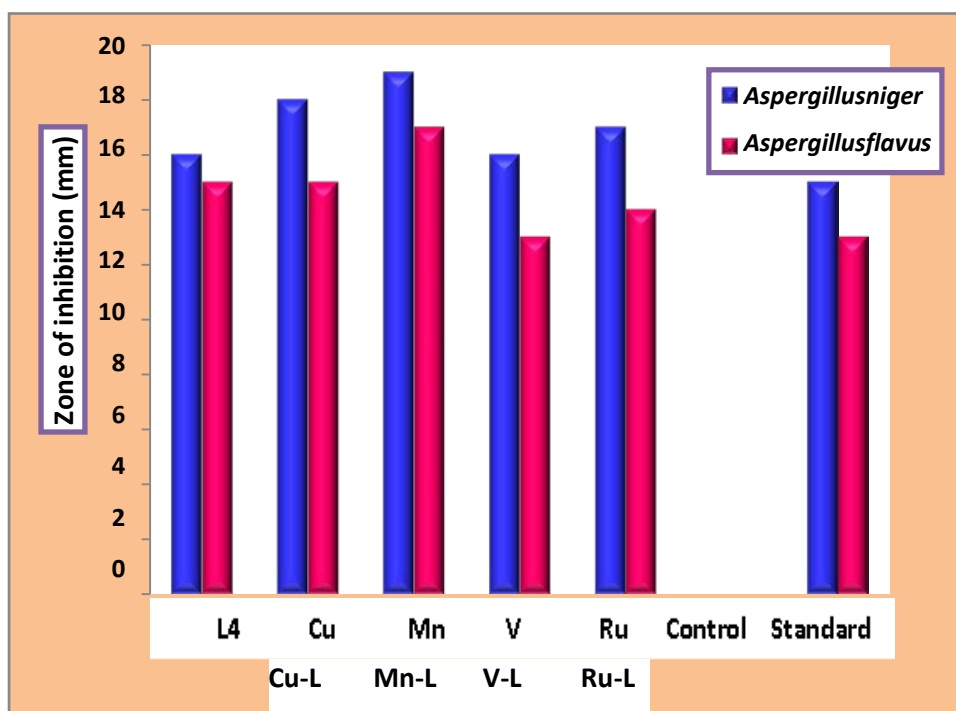


FIG: 1.8(a) ANTI-FUNGAL ACTIVITY OF THE LIGAND AND ITS COMPLEXES

Fig: 1.8(b). Plates: 1,2: Anti-fungal activity of the Ligand and Cu, Mn,V and Ru Complexes treated against *Aspergillus flavus* and *Aspergillus niger*

*Aspergillus flavus*

*Aspergillus niger*



(1)

(2)

(3)

Where plate:1

1=Cu(II) complex, 2=V(V) complex  
3=Mn(II) complex, 4=Ru(III) complex

Where plate:3

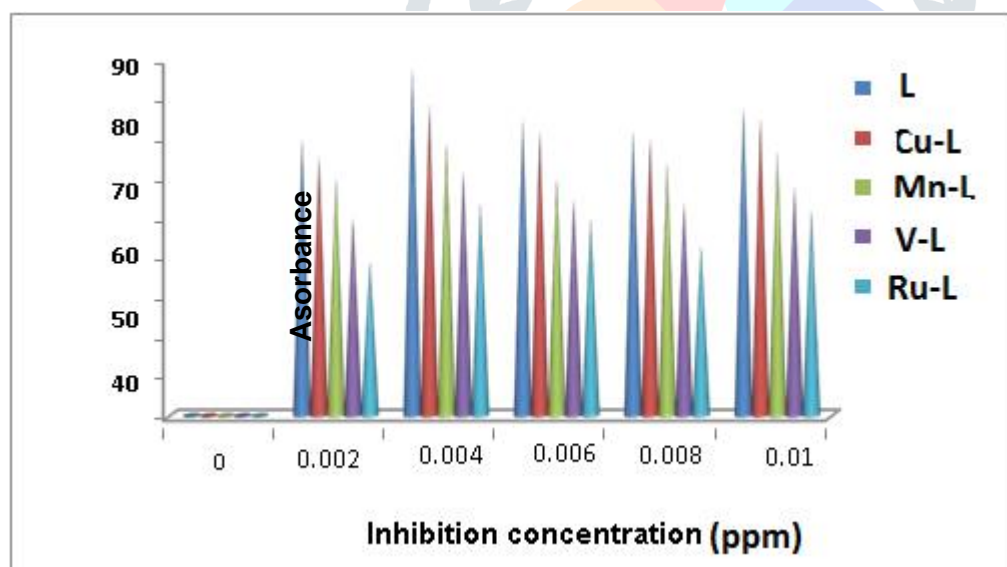
1=Cu(II) complex, 2= Ru(III) complex  
3=V(V) complex, 4= Mn(II) complex

### 1.2.8 ANTI-OXIDANT STUDY OF METAL COMPLEXES

The anti-oxidant properties were studied. The results were depicted in Table:1.7 and Fig.1.9. From the results it was observed that complexes had higher activity than that of the free Schiff base ligand. At the lowest concentration (100 µg/ml) the anti-oxidant activity of the free ligand was found to be low but, upon complexation, it increased significantly.

**TABLE: 1.7. ANTI-OXIDANT PROPERTY OF COMPLEXES**

S. No	Complex	Concentration (µg/mL)				
		0.002	0.004	0.006	0.008	0.010
1.	Ligand	0.070	0.066	0.060	0.050	0.039
2.	Cu	0.088	0.079	0.069	0.062	0.054
3.	Mn	0.075	0.072	0.060	0.055	0.050
4.	V	0.072	0.070	0.064	0.054	0.043
5.	Ru	0.078	0.075	0.067	0.058	0.052



**FIG: 1.9. ANTI-OXIDANT PROPERTY OF COMPLEXES**

The synthesized ligand (L) and metal complexes revealed that all the compounds exhibit a high to moderate activity. The metal complexes denoted more radical scavenging activity than that of the ligand. Cu (II) complex exhibited highly effective anti-oxidant activity than other complexes.

### 1.3 SUMMARY AND CONCLUSION

The spectral studies of Schiff base ligand (L) and their complexes were studied and elucidate the structures. The fluorescence results noted for the ligand and Cu(II), Mn(II), V(V) and Ru (III) Schiff base

complexes, which indicates that the ligand (L) which was a good absorbance and transfer energy to all the complexes. The  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR studies of the complexes were performed. The anti-bacterial, anti-fungal and anti-oxidant activity results were shown that most of the synthesized complexes possess a good anti-microbial activity against the pathogens tested. Manganese complex has high anti-fungal and copper complex has anti-bacterial activity than the corresponding free Schiff base ligand. Cu (II) complex exhibited highly effective anti-oxidant activity than other complexes.

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