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Research Article

EVALUATION AND BIOLOGICAL ROLE OF SCHIFF BASE METAL COMPLEXES

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ABSTRACT

The versatile nature of the lanthanide Schiff base complexes, make them an important candidate in catalysis of numerous organic transformations like oxidation of amines to their corresponding oxygen containing derivatives. 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 antifungal, antibacterial, 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 Schiff base ligand was synthesized by aldehyde with Aromatic Amine to form Schiff base ligand. It is mixed with 1st Row transition metal ions to form metal complexes. Complexes are characterized by Elemental analysis, UV- spectroscopy, Infrared spectroscopy and NMR. Elemental analysis of the metal complexes suggested that the stoichiometry ratio is 1:2 (metal-ligand). The UV-spectrum gives clear idea about the metal complexes. The Schiff base complexes have been screened for their invitro antibacterial activity against three bacteria via; (*Staphylococcus sp, Pseudomonas sp, Bacillus sp.*) and also studied antifungal activities (*Aspergillus sp* and *Aspergillus sp*). Similarly, anti-oxidant studiesof metal complexes were also performed.

Keywords: Schiff base, Natural metal complexes, Spectral characterization, Biological activities, Antioxidant.

1. INTRODUCTION

Schiff bases have been playing an important part in the development of Co-ordination chemistry. Schiff base metal complexes have been studied extensively because of their attractive chemical and physical properties and their wide range of applications in numerous scientific areas. They play an important role in both synthetic and structural research, because of their preparative accessibility and structural diversity [1].

Schiff base compounds as ligands have gained importance because of the physiological and pharmacological activities associated with them. They constitute an interesting class of chelating agents capable of coordination with metal ions given complex which serve as models for biological system [2]. Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Hugo Schiff in 1864. The common structural feature of these compounds is the azomethine group with a general formula $RN=CH-R^1$, where R and R^1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines [3].

Metal complexes containing Schiff- base ligands also have shown attractive properties, such as antibacterial behavior exhibit interesting magnetic properties and catalytic oxidation [4]. During the recent years there have been intense investigations of different classes of indole derivative compounds. Many of these possess interesting biological properties such as antimicrobial and analgesic activities. The important criteria for the development of metallo drugs as chemotherapeutic agents are the ability of the metallo drug to bring about DNA cleavage. A large number of transition metal complexes because of their redox properties, have been found to promote DNA cleavage [5]. Schiff bases are known to be medicinally important and are used to design medicinal compounds [6]. The bio medicinal properties of free organic molecule upon chelation with suitable metal ion led to the implementation of metal complexes for several biomedical applications as therapeutically active possessing analgesic [7], antipyretic [8], anti-inflammatory [9], cytotoxic [10], antiviral [11], anti-tumorous [12] and anti-tubercular activity [13] etc. Besides their applications as Anti oxidant can be defined as substances whose presence in relatively low concentrations significantly inhibits the rate of oxidation. These are the substances that may protect cells from the damage caused by unstable molecules known as free radicals. Scientific research now confirms that free radicals play a major role in the development of cancer, heart disease, aging, cataracts and impairment of the immune system [14]. In our current research work studied about important biological role of natural schiff base metal complexes and to study the biological activity of the compounds prepared and to attempt to elucidate their structure-activity relationships.

2. MATERIAL AND METHODS

All the chemicals and solvents used were of AR grade. All the reagents used for the preparation of the ligand and metal complexes were obtained from Sigma Aldrich.

2.1. Synthesis of 2,6-diamino pyridine-2-furaldi-mine

A Solution of 2-Furaldehyde was added to 2,6-diamino pyridine in 20 ml alcohol and 2 drops of dil. Acetic acid were added. The mixture was refluxed for about 6 hours. 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 to obtain pure ligand.

2.2. Synthesis of Metal Complexes

To an ethanolic solution of the Schiff base, Ligand and the solution of metal (Copper acetate (II), Nickel Sulphate (II), Vanadium (II) 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.

2.3. Spectral characterization of schiff base metal complexes

2.3.1. UV-Visible Spectral Analysis

The UV visible electronic spectra (200-800nm) were recorded by UV-Vis-1800 series (Shimadzu) double beam spectrophotometer using DMSO solvent. The electronic spectral measurements were used for assigning the stereo chemistry of metal ions in the complexes based on the positions and number of d-d transition peaks. It is very useful to measure the number of conjugated double bonds and also aromatic conjugation within the various molecules. The electronic absorption spectra of the Schiff base and its metal complexes were recorded at room temperature.

2.3.2. FT-IR spectra analysis of metal complex

FT-IR spectra were recorded using KBr pellets in Schimadzu FT-IR 8201 spectrometer (4000-400cm^{-1}).

2.3.3. Fluorescent studies

Fluorescent transition metal centers are particularly attractive moieties because they often possess distinctive electrochemical or photo physical properties thus enhancing the functionality of the binding agent. The fluorescence characteristics of metal complexes were studied at room temperature in solid state.

2.3.4. NMR spectra analysis of schiff base complex

Proton magnetic resonance spectral measurements were made on a Brucker 300 MHz (or) Perkin-Elmer R32, 90 MHz (or) Joel, GSX 400, 400 MHz spectrometer in deuterated organic solvent DMSO with tetramethylsilane (TMS) as the internal standard. Frequencies were measured by the side band technique and area was determined planimetrically.

2.4. Biological properties of schiff base complexes

2.4.1. Antibacterial activity

Antibacterial activity of the extract of compounds was determined using well diffusion method [22]. It was performed by sterilizing Muller Hinton agar media. After solidification, wells were cut on the Muller Hinton agar using cork borer. The test bacterial pathogens were swabbed onto the surface of Muller Hinton agar plates. Wells were impregnated with 25μl of the test samples. The plates were incubated for 30 min to allow the extract to diffuse into the medium. The plates were incubated at 30°C for 24 hrs, and then the diameters of the zone of inhibition were measured in millimeters. Each antibacterial assay was performed in triplicate and mean values were reported.

2.4.2. Antifungal activity

Antifungal activity of the extract of compounds was determined using well diffusion method. It was performed by sterilizing Mueller Hinton agar media. After solidification, wells were cut on the Mueller Hinton agar using cork borer. The test fungal pathogens were swabbed onto the surface of Mueller Hinton agar plates. Wells were impregnated with 25 μl of the test samples. The plates were incubated for 30 min to allow the extract to diffuse into the medium. The plates were incubated at 30°C for 24 hrs, and then the diameters of the zone of inhibition were measured in millimeters. Each antifungal assay was performed in triplicate and mean values were reported.

2.5. Antioxidant activities of schiff base complexes

Anti Oxidant investigations are usually regarded as the potential method to cure various life-style related diseases [15]. Antioxidant activity of the ligand and its transition metal complexes was studied by comparing their scavenging effects on superoxide anion and hydroxyl radical. The inhibitory effects of the tested compounds on $O_2^{\cdot(-)}$ and HO. are concentration related and the suppression ratio increases with the increasing sample concentration in the range of the tested concentrations. The antioxidant activity of the compounds is expressed as 50% inhibitory concentration (IC_{50} in μM). Inhibitor was dissolved in buffer to make various concentrations. Buffer was ethanol (or) DMSO (depending on solubility). The different concentration of standard was centrifuged at 3000 rpm using a centrifuge machine for 10 minutes and supernatant was collected. DPPH was dissolved in buffer to make 300 micro molar concentrations. The supernatant of the extract was added to DMSO solution of DPPH in a test tube, shaken at 37°C for 30minutes. The absorbance of the residual DPPH solution was determined at 517 nm in a UV-Visible Spectrophotometer. The experiment was performed in triplicate. Vitamin C (Ascorbic acid) was used as positive control. The percentage of inhibition (I) was calculated in following formula,

$$I\,(\%) = \{(A_0 - A_1)/A\} \times 100$$

Where, A_0 is the absorbance of the control, A_1 is the absorbance of the standard, respectively.

A percent inhibition versus concentration curve was plotted and the concentration of sample required for 50% inhibition was determined and expressed as IC_{50} value. The lower the IC_{50} value indicates high antioxidant capacity.

3. RESULT AND DISCUSSION

The metal complexes are insoluble in water and soluble in DMSO, DMF, $CHCl_3$ and acetone, slightly soluble in methanol and ethanol. The physical properties of the ligand and complexes are presented in Table-1.

Table 1: Elemental analysis of ligand and complexes

Compounds	Physical appearance	Melting point (°C)	Elemental (%) Calc. (found)					m/z
			C	H	N	O	M (metal)	
Ligand (L)	Black	300	61.16	4.87	22.43	8.56	-	187.09
			(63.12)	(4.80)	(22.44)	(8.51)		
Cu - L	Green	320	52.06	4.02	18.65	7.15	14.13	449.05
			(53.05)	(4.03)	(5.43)	(7.17)	(14.15)	
V - L	Yellow	310	55.28	4.61	17.72	13.55	10.73	473.18
			(55.25)	(4.62)	(17.71)	(13.57)	(10.71)	
Ni - L	Red	300	53.42	4.64	17.76	13.58	10.78	473.15
			(53.40)	(4.65)	(17.73)	(13.54)	(10.75)	
Ru - L	Brown	305	53.38	4.62	16.26	6.19	19.53	518.14
			(53.40)	(4.66)	(16.29)	(6.14)	(19.58)	

3.1. Elemental analysis of schiff base 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 [16].

3.2. Spectral characterization of schiff base complexes

3.2.1. UV-Visible spectra analysis of schiff base complexes

The electronic absorption spectra are often very helpful in the evaluation of results furnished by other methods of structural investigation. The electronic spectral measurements were used for assigning the stereo chemistry of metal ions in the complexes based on the positions and number of d-d transition peaks. The electronic absorption spectra of the Schiff base and its metal complexes were recorded at room temperature. Simultaneously, the Schiff base ligand shows two type of transition $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ respectively these transition were existed also in the spectra of the complexes, but they shifted to lower intensity, confirming the co –ordination of the ligand to the metal ion. These spectra the weak band should be at 400-

500nm are due to intra ligand charge transfer bands in the complexes which is absence in the ligand. The lower wave lengths for the Schiff bases have a range between 215nm to 230nm.The UV data's are shown in fig.1.

Hence in the UV-visible spectrum of Nickel complex in DMSO shows a broad band at 275.50nm (36291.64cm^{-1}) and 211.50nm (47281.32cm^{-1}) which can be assigned to$^2B_{1g}\rightarrow{}^2B_{2g}$ and$^2B_{1g}\rightarrow{}^2A_{1g.}$ The expected structure is Octahedral for Nickel complex. The UV-visible spectrum of Vanadium complex in DMSO shows a broad band at 599.50nm (16680.57cm^{-1}) and 275.50nm (36297.64cm^{-1}) which can be assigned to ligand to metal (LMCT). The expected structure has isoctahedral geometry [17].

3.2.2. *FT-IR spectra analysis of schiff base complex (L3)*

The FT-IR spectrum of ligand confirms the formation of Imine bond (-C=N-H) and the absence of carbonyl bond (C=O). Actual band at 1643-1530cm^{-1} is assigned to stretching vibration of the imine group at (-C=N-H). The Schiff base showed the absence of bands at 1735 cm^{-1} and 3420cm^{-1} due to carbonyl (C=O) and NH_2 Stretching vibration. A strong new band was observed at 1606.7 cm^{-1} assigned to the azomethine (HC=N) linkage. It is suggested that amine and aldehyde moieties of the starting reagents are absent and have been converted into the azomethine moiety [18]. The comparison of the IR spectra of the Schiff base and their metal chelates indicated that the functional group present in the metal complexes. Schiff base were principally coordinated to the metal atom in three ways, representing thus ligand acting in a bidentate manner and the intermolecular H bonded OH group was around at 3446cm. Ligand (L) was found to be 1666.50 cm^{-1}. In all the complexes the co-ordination of the azomethine nitrogen to the metal centers. The IR data were noted in fig.2.

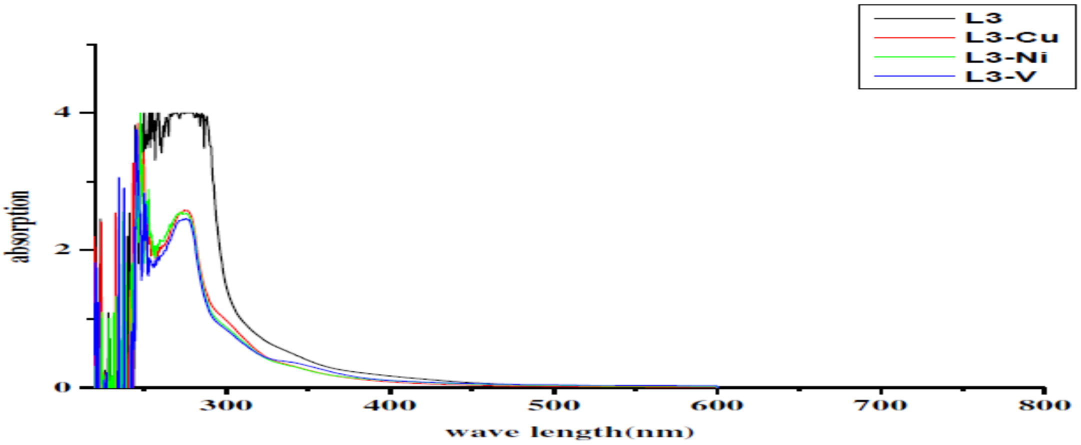

Fig. 1: UV spectra for ligand and its metal complexes (L3)

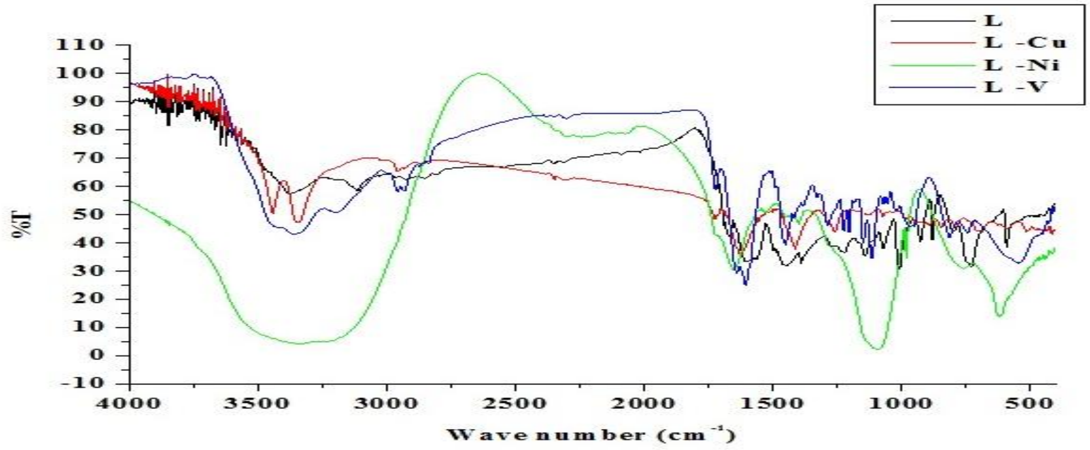

Fig. 2: FT-IR spectra for ligand and its metal complexes

3.3. Fluorescent studies for ligand and its metal complexes

The fluorescent studies Schiff base metal complexes of the ligand and its studies. The emission spectrum of the free ligand revealed the broad fluorescent band centered at 410nm attributed to responsible peaks. The results were recorded in fig.3. The Cu, Ni and V complexes exhibit the characteristic emission spectral of these groups. These complexes indicates that the Schiff base ligand was a highly effective it can be used to absorb and transfer energy to the Ligand complexes. The above complexes, were analyzed the emission spectrum shows three luminescence bands at 220 to 470nm which was corresponding to the respective emission of the transitions respectively. The Schiff base complexes of ligand, the emission of ions groups can be mainly recorded in the process depends upon the excitation of the Schiff base moiety, since the large molar absorption similar with the several orders as compared with these complexes [19].

3.4. NMR spectral analysis of schiff base complexes

NMR signal is usually plotted with magnetic field strength increasing to the right [20, 21]. Thus the signal for TMS appears at the extreme right of spectrum with δ=0ppm. Greater the deshielding of protons, larger will be the value of δ7.34ppm. In L$_3$ NH$_2$ proton for the bidentate ligand appear at 7.74ppm and methoxy group at 3.83ppm and aromatic proton is multiplet in the range 6.22-8.21ppm.In L$_3$ NH$_2$ proton for the bidentate ligand appears at 4.0ppm and aromatic proton appears at 6.6-7.4ppm and five membered ring appear at 6.3-7.4ppm. The results were noted in Fig.4 5.

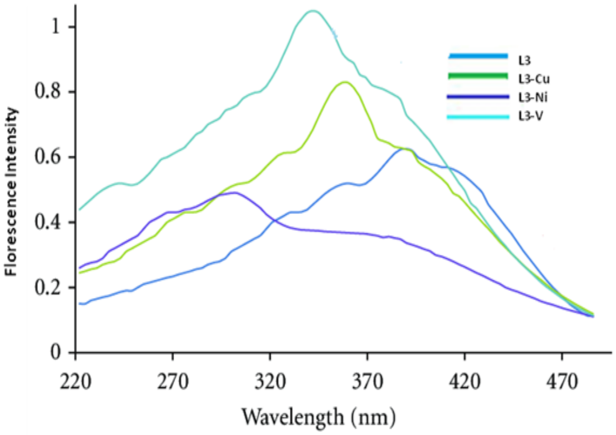

Fig. 3: Fluorescent spectra of ligand (L3) and metal complexes

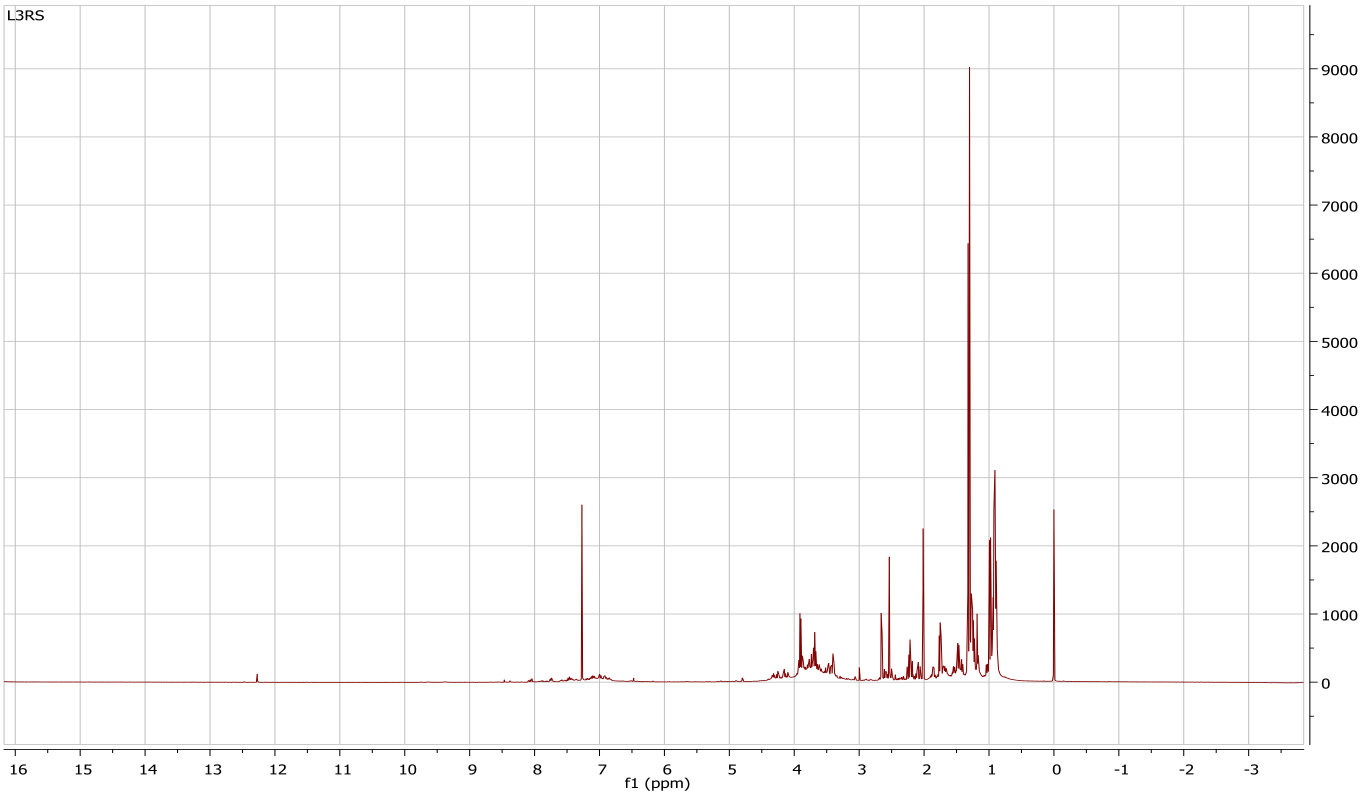

Fig. 4: ^{1}H-NMR spectrum for (L3) 2,6 diamino pyridine-2-furaldimine

3.5. Biological Screening

3.5.1. Antibacterial activity

The antimicrobial studies of Schiff base ligand complex were performed. From the results it is inferred that metal complexes were more active than their ligands. The Copper (II) Schiff base complex show higher efficiency when compared with the standard. This would suggest that the chelation could facilitate the ability of a complex to cross a cell membrane [22] and can be explained by Tweedy's chelation theory [23]. The results were noted in fig.6.

3.5.2. Antifungal activity

From the results, it is inferred that metal complexes were more active than their ligands. The Nickel Schiff base complex show superior efficiency against *Aspergillus sp* and *Aspergillus sp* fungi [24]. The results were recorded in fig.7.

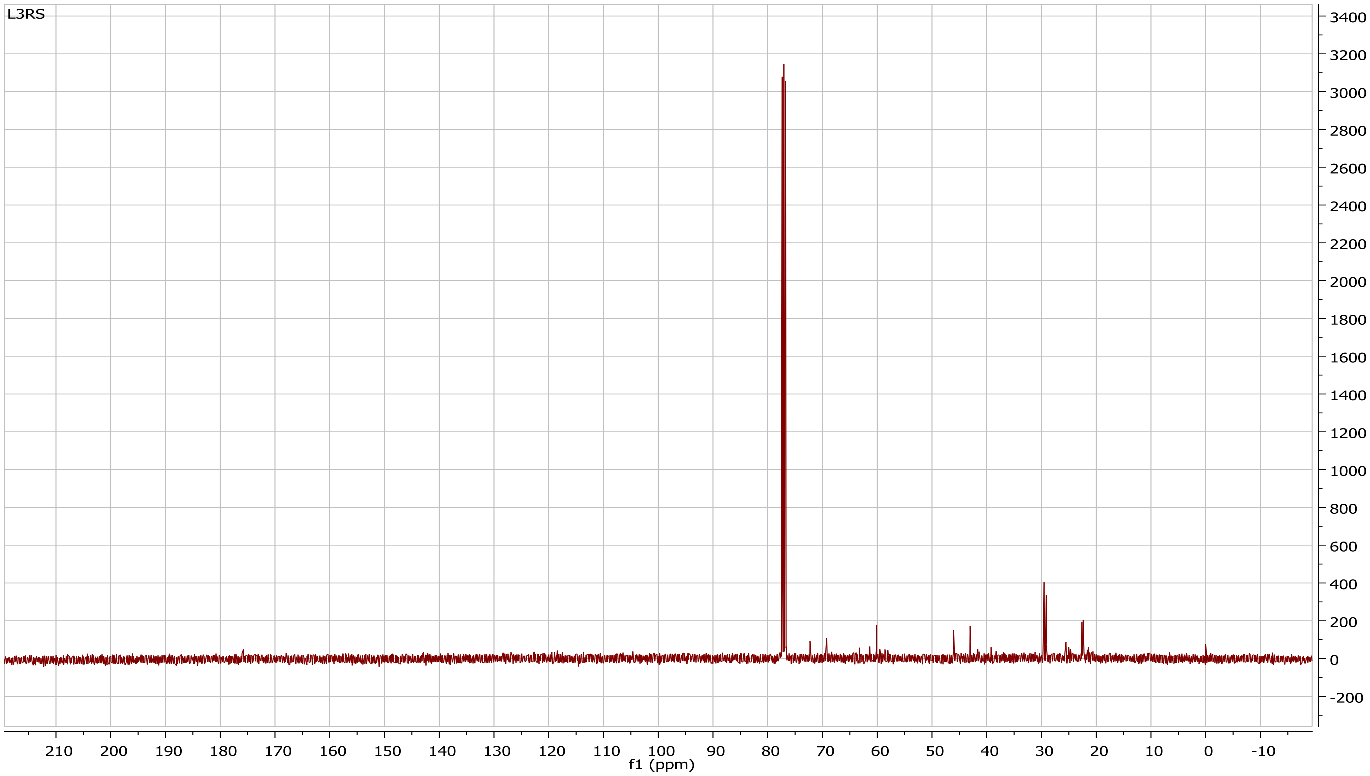

Fig. 5: C^{13}-NMR spectrum for (L3) 2,6 diamino pyridine-2-furaldimine

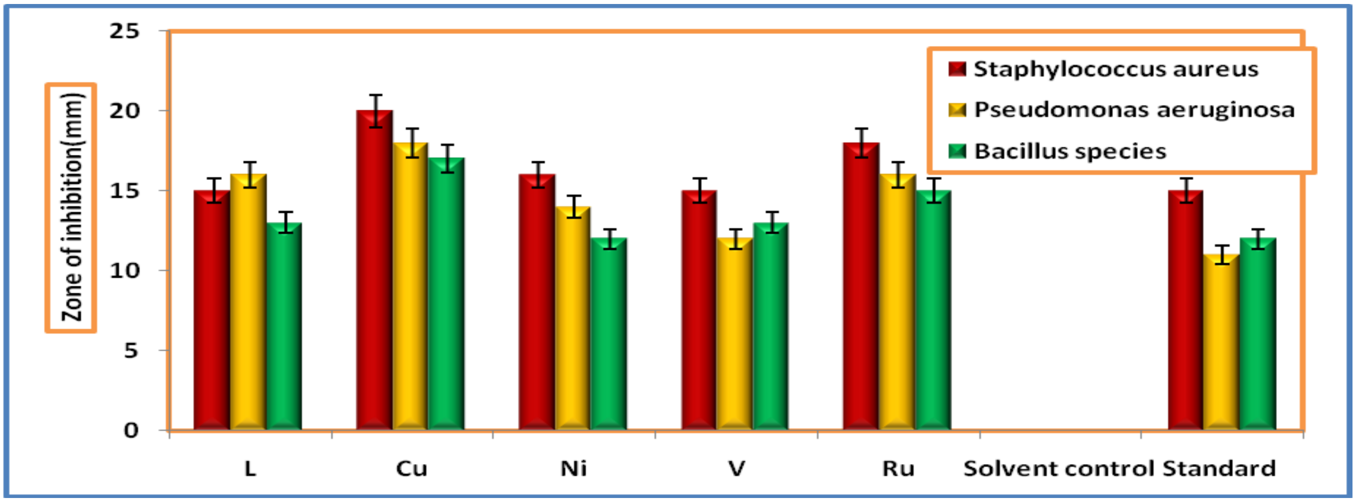

Fig. 6: Antibacterial activity of the ligand (L3) and its complexes

3.6. Antioxidant activity of the ligand complexes

3.6.1. DPPH radical scavenging activity assay

Antioxidants react with DPPH, a stable free radical that is thus reduced, and as a result the absorbance decreases due to the formation of the DPPH-H from the DPPH radical [25].The degree of discoloration indicates the scavenging potential of the antioxidant compounds or samples in terms of hydrogen donating ability [26]. It was observed that metal (II) complexes had higher activity than that of the free Schiff base. At the lowest concentration (100µg/mL) the antioxidant activity of the free ligand was found to be 24.20% but, upon complexation, it increased significantly within the range 29.80%-45.01%. The results were depicted in fig.8.

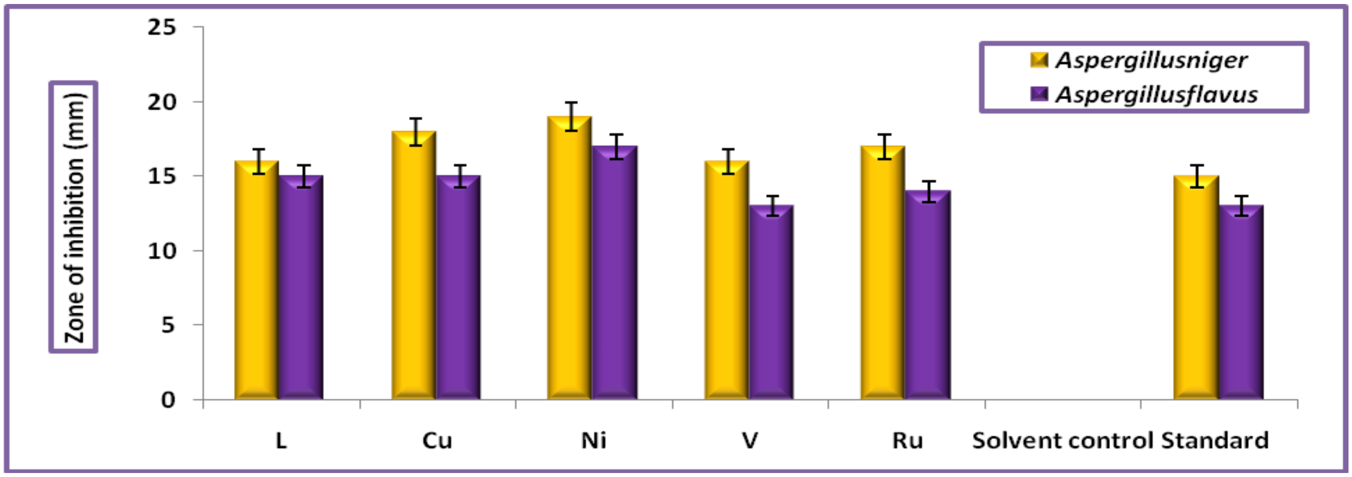

Fig. 7: Antifungal activity of the ligand and its complexes

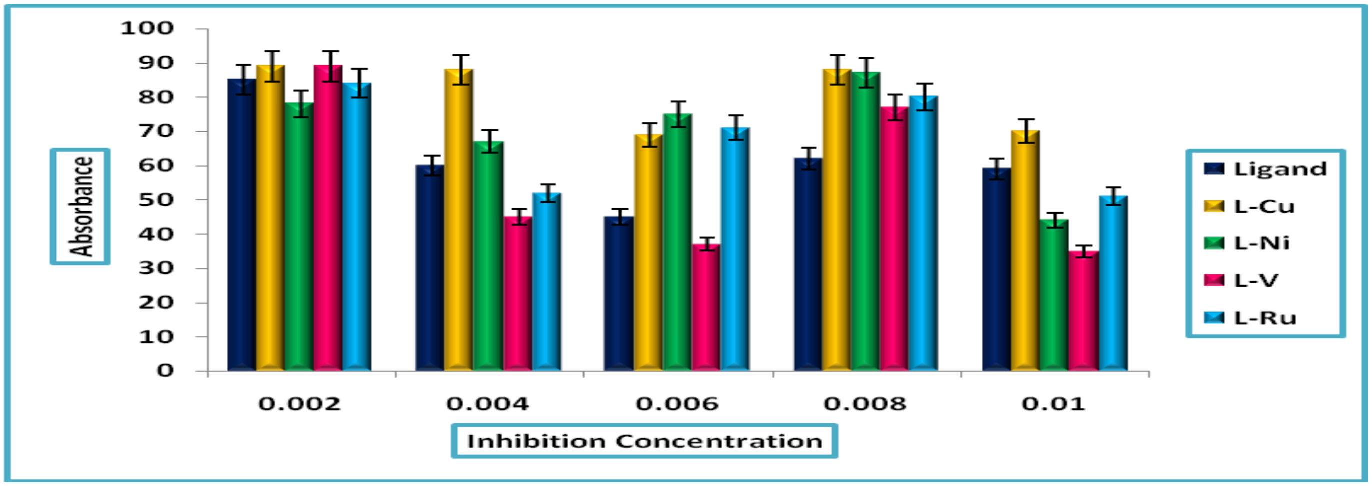

Fig. 8: Anti-oxidant activity for ligand and its metal complexes

4. CONCLUSION

In the current research work, the Schiff base ligand derived from 2, 6-diamino pyridine with furaldehyde and its Copper (II), Nickel(II), and Vanadium(V) complexes have been synthesized. The ligand structure is confirmed by ^{1}H-NMR spectrum. The ligand and its complexes have been characterized by UV, FT-IR spectral techniques. Based on the spectral data, the geometry of complexes can be predicted. Ni and V complexes are Octahedral and Cu complex has tetrahedral geometry. Anti-oxidant studies with different concentration of ligand and its metal complexes were also be studied. The Scavenging activities at lower concentration will be greater. Copper(II) complex is having higher activity than other complexes. The Anti-microbial activities have also been studied. Copper complex has higher anti-bacterial activity and Nickel complex has higher Anti -fungal activity than the ligand. The complexes have highest anti-oxidant activity than the free ligand.

Conflict of interest

None declared

5. REFERENCES

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