



## Synthesis and Biological Studies of Schiff Base Metal(II) Complexes Derived from Isatin

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**Abstract:** Potentially bioactive Schiff base metal complex is a kind of attractive reagents due to specific activities of pharmacology and physiology. Medical inorganic chemistry has exploited metal ions' unique properties to design new drugs. In this study a novel Cu(II), Ni(II), Mn(II) and Co(II) Schiff base complexes have been from p - nitroaniline, isatin and 2, 2' bipyridyl. The elemental analyses of the complexes are confined to the stoichiometry of the type  $L_2L_2M$  [ $M = Cu(II), Ni(II), Mn(II)$  and  $Co(II)$ ], respectively, where L is Schiff base ligand in the ratio of 1:1:1. Structures have been proposed from elemental analyses, IR, UV, <sup>1</sup>H NMR, ESR spectral data and magnetic studies. The measured low molar conductance values in DMF indicate that the complexes are non-electrolytes. The IR data tells us the association of C=N nitrogen atom in co - ordination to the metal ion. The UV spectral studies and magnetic measurements suggested the octahedral geometry around metal ion under investigation. The EPR spectral data shows additional proof for the octahedral geometry. In addition, the antioxidative activity was also determined. The ligand's antioxidative activity and its complexes demonstrate that, compared to the ligand, the complexes exhibit higher scavenging activity. The antibacterial activity of these compounds was studied in vitro by the disc diffusion assay against two Gram-positive bacteria like *Staphylococcus aureus*, *Bacillus subtilis* and two Gram-negative bacteria like *Escherichia coli* and *Klebsilla pneumonia*. The complexes show significant growth inhibitory activity than ligands.

**Keywords:** Isatin, octahedral geometry, DNA Cleavage, schiff base.

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## 1. INTRODUCTION

Schiff base ligands played central role as chelating ligands in the main group and transition metal coordination chemistry<sup>1</sup>. Transition metal complexes of Schiff base ligands find applications as model analogs of certain metal enzymes and catalyst in oxidative addition reactions modifiers for selective electrodes, and different uses in material chemistry. A monometallic core is versatile at the active site of many metalloenzymes and plays an essential role in biological systems by the interplay of a pair of metal ions<sup>2</sup>. In the last decade, many mononuclear Schiff base complexes of different structural types have been synthesized and characterized. These complexes span the gamut in their new applications, donating types, structures and biological activities<sup>3</sup>. Recently, wide varieties of the Cu(II), Ni(II), Mn(II) and Co(II) complexes of Schiff base derivatives, including Schiff base ligands were tested *in vitro* for their antibacterial activities against human pathogenic bacteria (using disc diffusion (DD) method<sup>4</sup>, where the metal complexes have higher antimicrobial activities than the free ligands. Also, a survey highlighting structural properties and biological studies of transition metal complexes derived from Isatin were reported<sup>5</sup>. Having all the above facts in mind, herein we have synthesized and explored the structural determination of isatin based Schiff bases having nitrogen donors, derived from p - nitroaniline, isatin and 2, 2' bipyridyl with Cu(II), Ni(II), Mn(II) and Co(II) metal ions. Their spectral and biological activities are discussed in detail.

## 2. PHYSICAL AND MATERIALS MEASUREMENTS

Diverse agents and chemicals utilized for current analysis were purchased from sources like Loba, Merck and Aldrich chemicals. Metal(II) salts, isatin, p-nitroaniline, and 2, 2' bipyridyl got from Loba chemicals and utilised as same. CH<sub>3</sub>CH<sub>2</sub>OH, Dimethylsulphoxide and Dimethylformamide were taken as solvents, and that are from Aldrich and Merck chemicals. The elemental analyzer herein case for elemental analysis was Carlo Erba Model 1106. Perkin–Elmer FT-IR-8300 spectrophotometer on KBr disks was for recorded IR spectra, range of 4000– 400 wavenumber region. ELICO CM 185 Bridge were measured the molar conductivity values using a freshly prepared DMF solution. Perkin-Elmer Lambda 40 spectrometer using DMF were exactly recorded electronic spectra of complexes at 300 K in the range of 200-800 nm. EPR spectral analysis was recorded on an E-112 ESR spectrometer for powdered samples. BRUKER ADVANCED III 400 MHz spectrophotometer were recorded Proton Nuclear magnetic Resonance spectra in Dimethylsulphoxide - d<sub>6</sub> by Tetramethylsilane here for interior reference. Magnetic moment dimensions run out at room temperature by balance named Gouy. Synthesis of (1-Methyl-4-nitro-benzene(1,2-dihydrogen-indol-3-ylidene-2-imino-)-(4-nitro-phenylene)-amine). (1-Methyl-4-nitro-benzene(1,2-dihydrogen-indol-3-ylidene-2-imino-)-(4-nitro-phenylene)-amine) was derived via adding 4- nitroaniline (2 mmole) in 10 ml of sol. ethanol, Isatin (1 mmole) in CH<sub>3</sub>CH<sub>2</sub>OH sol. (20 ml) and induce heating by refluxation for 2-3 hours as in Fig. 1. The product yellow color precipitate was allowable to cooling process and dried in desiccator using silica gel<sup>6</sup>. Product Yield: 85%. Melting point: 139 ° C. *Analytical calculation For C<sub>20</sub>H<sub>13</sub>N<sub>4</sub>O<sub>4</sub>*: Carbon, 69.30; Hydrogen, 6.11; Nitrogen, 12.92. Found: Carbon, 68.37; Hydrogen, 8.90; Nitrogen, 12.82 %. UV–Visible [λ (nm) (dmf)]: 340 (34, 000)(π→ π\*), 364 (36,400) ( n→ π\*). IR cm<sup>-1</sup> (KBr): ν (C=N)1620.

### 2.1. Synthetic Methodology of Cu(C<sub>30</sub>H<sub>21</sub>N<sub>7</sub>O<sub>4</sub>Cl<sub>2</sub>)

(1-Methyl-4-nitro-benzene (1, 2-dihydrogen-indol-3-ylidene2-imino-)-(4-nitro-phenylene)-amine) (1 mmole) in 20 ml of ethanol, was added with a solution of Cu(II) chloride in 20 ml of ethanol. The solution was refluxed for 3 hrs. The mixture was then reacted with 2, 2' bipyridyl in ethanolic solution for 3-5 hrs on the water bath and then allowed to stand at room temperature for 24 hrs as shown in Figure 2. The resulting darkish green colored precipitate powder was filtered and dried in vacuum<sup>7</sup>. Product Yield: 85%. Melting point:>200 ° C. Elemental analyses, *Analytical calculation For Cu(C<sub>30</sub>H<sub>21</sub>N<sub>7</sub>O<sub>4</sub>Cl<sub>2</sub>)*: Carbon, 56.90 ; Hydrogen,5.54; Nitrogen, 10.52. Found: Carbon, 56.88; Hydrogen, 5.51; Nitrogen, 10.53%. UV–Visible [λ (nm) (dmf)]: 270 (27,000)(π→ π\*), 330 (33,000)( n→ π\*), 345 (34,500) )( L→ M), 510, 609 (51,000) (60,900) (d→d). IR cm<sup>-1</sup> (KBr): ν [C=N :1595, M-N: 468, M-Cl :310].

### 2.2. Synthetic Methodology of Ni(C<sub>30</sub>H<sub>21</sub>N<sub>7</sub>O<sub>4</sub>Cl<sub>2</sub>)

(1-Methyl-4-nitro-benzene (1, 2-dihydrogen-indol-3-ylidene2-imino-)-(4-nitro-phenylene)-amine) (1 mmole) in 20 ml of ethanol, was added with a solution of Ni(II) chloride in 20 ml of ethanol. The solution was refluxed for 3 hrs. The mixture was then reacted with 2, 2' bipyridyl in ethanolic solution for 3-5 hrs on water bath and then allowed to stand at room temperature for 24 hrs as shown in Figure 2. The resulting brownish black coloured precipitate was filtered and dried in vacuum<sup>8</sup>. Product Yield: 85%. Melting point:>200 ° C. Elemental analyses, *Analytical calculation For Ni(C<sub>30</sub>H<sub>21</sub>N<sub>7</sub>O<sub>4</sub>Cl<sub>2</sub>)*: Carbon, 57.69; Hydrogen, 5.60 ; Nitrogen, 10.63. Found: Carbon, 57.65; Hydrogen, 5.58; Nitrogen, 10.63%. UV–Visible [λ (nm) (dmf)]: 285 (28,500)(π→ π\*), 357 (35,700)( n→ π\*), 370 (37,000) )( L→ M), [450(45,000), 582(58,200), 630(63,000)] (d→d). IR wavenumber region (KBr): ν [C=N: 1609, M-N: 454, M-Cl: 317].

### 2.3. Synthetic Methodology of Co(C<sub>30</sub>H<sub>21</sub>N<sub>7</sub>O<sub>4</sub>Cl<sub>2</sub>)

(1-Methyl-4-nitro-benzene (1, 2-dihydrogen-indol-3-ylidene2-imino-)-(4-nitro-phenylene)-amine) (1 mmole) in 20 ml of ethanol, was added with a solution of Co(II) chloride in 20 ml of ethanol. The solution was refluxed for 3 hrs. The mixture was then reacted with 2, 2' bipyridyl in ethanolic solution for 3-5 hrs on the water bath and then allowed to stand at room temperature for 24 hrs as shown in Figure 2. The resulting dark pink colored precipitate powder was filtered and dried in vacuum<sup>9</sup>. Product Yield: 80%. Melting point:>200 ° C. Elemental analyses, *Analytical calculation For Co(C<sub>30</sub>H<sub>21</sub>N<sub>7</sub>O<sub>4</sub>Cl<sub>2</sub>)*: Carbon, 57.68; Hydrogen, 5.61 ; Nitrogen, 10.62. Found: Carbon, 57.64; Hydrogen, 5.57; Nitrogen, 10.63%. UV–Visible [λ (nm),dmf): 285 (28,500)(π→ π\*), 360 (36,7000)( n→ π\*), 370 (37,000) )( L→ M), [470(47,000), 560(56,000), 630(63,000)] (d→d). IR wavenumber region (KBr): ν [C=N:1595, M-N: 468, M-Cl: 310].

### 2.4. Synthetic Methodology of Mn(C<sub>30</sub>H<sub>21</sub>N<sub>7</sub>O<sub>4</sub>Cl<sub>2</sub>)

(1-Methyl-4-nitro-benzene (1, 2-dihydrogen-indol-3-ylidene2-imino-)-(4-nitro-phenylene)-amine) (1 mmole), was added with a solution of Mn(II) chloride in 20 ml of ethanol. The solution was refluxed for 3 hrs. The mixture was then reacted with 2, 2' bipyridyl in ethanolic solution for 3-5 hrs on the water bath and then allowed to stand at room temperature

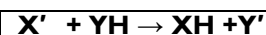
for 24 hrs as shown in Figure 2. The resulting dark brown coloured precipitate powder was filtered and dried in vacuum<sup>10</sup>. Product Yield: 80%. Melting point: >200 ° C. Elemental analyses, *Analytical calculation For*  $Mn(C_{30}H_{21}N_7O_4Cl_2)$ : Carbon, 57.60; Hydrogen, 5.60 ; Nitrogen, 10.71. Found: Carbon, 57.58; Hydrogen, 4.58; Nitrogen, 10.62%. UV-Visible [ $\lambda$  (nm) (dmf)]: 285 (28,500)( $\pi \rightarrow \pi^*$ ), 295 (29,500)( $n \rightarrow \pi^*$ ), 370 (37,000) ( $L \rightarrow M$ ), [525 (52,500), 560(56,000), 695(69,500)] ( $d \rightarrow d$ ). IR wavenumber region (KBr.):  $\nu$  [C=N: 1600, M-N: 444, M-Cl: 312.

## 2.5. Antibacterial Assay

The biological activities of the synthesized Schiff's base and its Cu(II), Ni(II), Mn(II) and Co(II) complexes were screened for their antibacterial properties by the disc agar diffusion method<sup>11</sup> in DMF solvent against *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria) and *Escherichia coli* and *Klebsilla pneumonia* (Gram-negative bacteria). The antibiotic *Streptomycin* was used as a standard reference. The tested compounds were dissolved in DMF to get a concentration of 100  $\mu$ g/mL. The test was performed on medium potato dextrose agar containing an infusion of 200 g potatoes, 6 g dextrose and 15 g agar<sup>12</sup>. Uniform size filter paper discs (three disks per compound) were impregnated by equal volume from the specific concentration of dissolved tested compounds and carefully placed on an incubated agar surface. After incubation for 36 h at 27° C, inhibition of the organism, which was evidenced by clear zone surrounding each disk, was measured and used to calculate the mean of inhibition zones.

## 2.6. Antioxidant Activity

The antioxidant activity assay employed is a technique depending on measuring the consumption of stable free radicals i.e. evaluating the free radical scavenging activity of the investigated component. The methodology assumes that the consumption of the stable free radical ( $X'$ ) will be determined by reactions as follows:



The rate or the extent of the process measured in terms of the decrease in  $X'$  concentration would be related to the ability of the added compounds to trap free radicals. The reduction in color intensity of the free-radical solution due to the scavenging of the free radical by the antioxidant material is measured at a specific wavelength<sup>13</sup>.

## 2.7. DPPH Free Radical Scavenging Activity

The hydrogen atom or electron donation ability of the corresponding compounds was measured from the bleaching of purple colored of the DMF solution of DPPH. This spectrophotometric assay uses the stable radical diphenylpicrylhydrazyl (DPPH) as a reagent<sup>14</sup>. Different concentrations of the chemical compounds were dissolved in DMF to determine IC<sub>50</sub> (concentration makes 50% inhibition of DPPH color). Fifty microliters of various sample concentrations were added to 5 ml of 0.004% DMF solution of DPPH. After 60 min of incubation at dark, the absorbance was read against a blank at 517 nm.

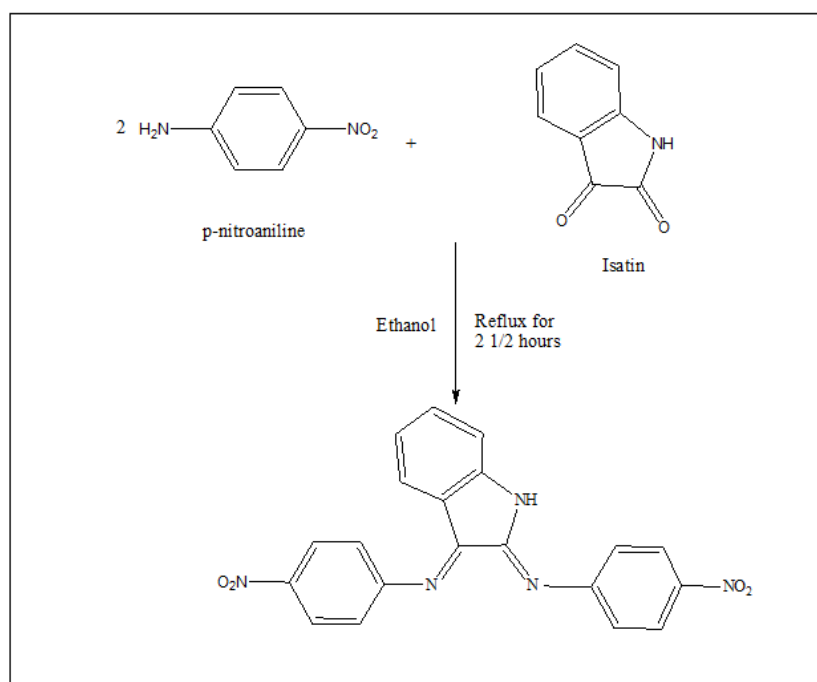
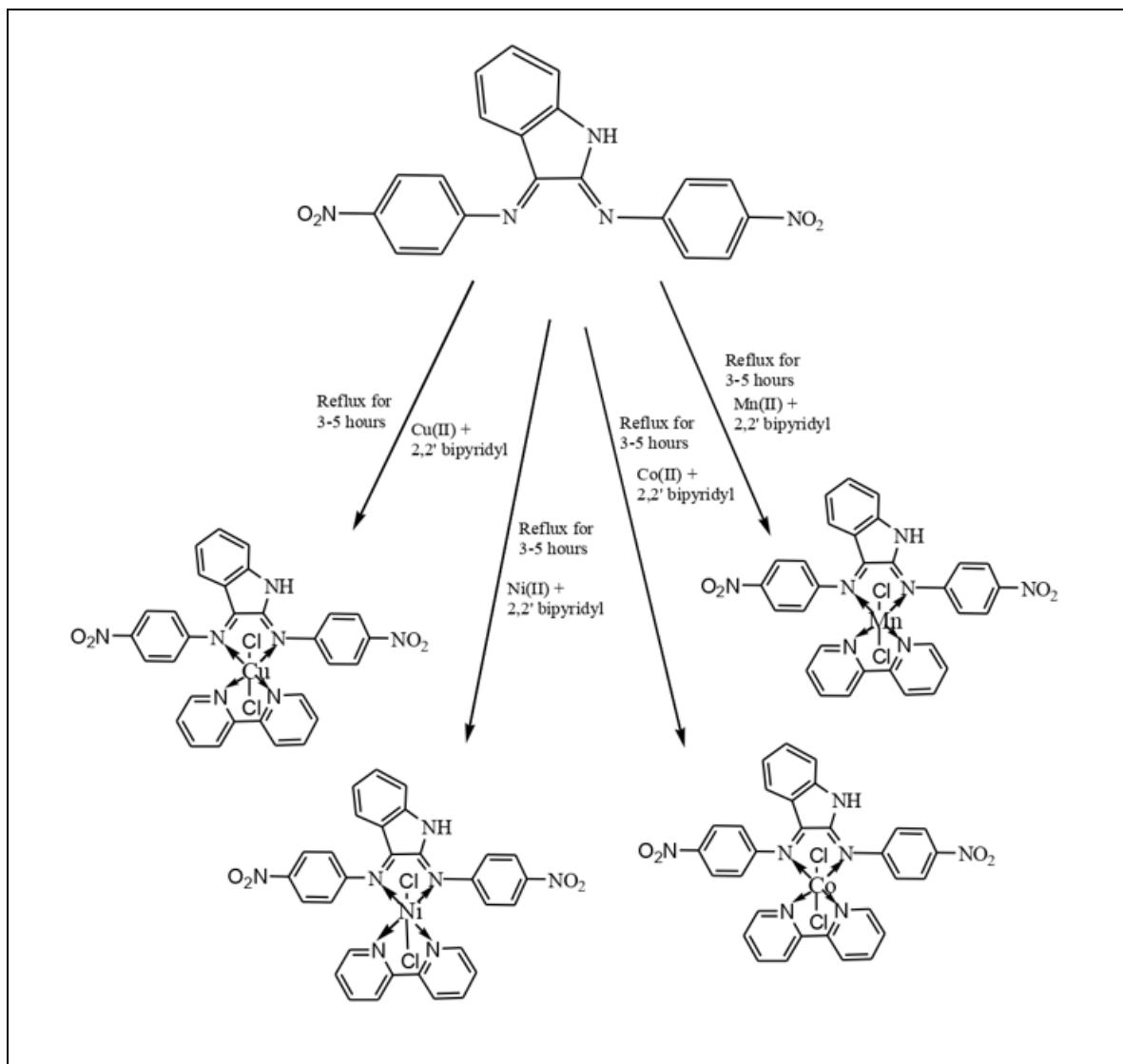


Fig 1: Synthesis of Schiff Base Ligand ( $C_{20}H_{13}N_4O_4$ )



**Fig 2: Synthetic Route of Mononuclear Schiff Base**

## METAL(II) COMPLEXES

### 3. RESULTS AND DISCUSSION

Derived compounds are unsolvable in  $\text{H}_2\text{O}$  along with various organic solvents, which are common. Still, they all are instantly dissolvable in powerful coordinating agents like Dimethylformamide, Acetonitrile as well as Dimethyl Sulphoxide. The physical properties and elemental analysis

data of synthesized compounds listed in Table: I. The derived combinations can be signified as  $\text{ML}_1\text{L}_2$  where: (M= Copper(II), Nickel(II), Cobalt(II), and Manganese(II) and (L = ligand). Lower conductance values of derived complexes in DMF were precised at  $10^{-3}$  Molar concentration, indicates that all reported complexes perform as non-electrolytes<sup>15</sup>.

<b>Table I: Analytical Data of the Schiff Base Ligand and Its Mononuclear Metal Complexes</b>								
Molecular Formula	color	Yield %	Melting Point (°)	% of Nitrogen		% of Metal		Molar conductance $\Lambda_m$ ( $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ )
				Cal	Exp	Cal	Exp	
$\text{C}_{20}\text{H}_{13}\text{N}_4\text{O}_4$	Pale yellow	85	139	12.92	12.82	-	-	-
Cu(II)complex	Dark green	85	>200	10.52	10.53	9.60	9.55	6.7
Ni(II)complex	Dark green	85	>200	10.63	10.63	8.90	8.95	5.8
Co(II)complex	Dark pink	80	>200	10.62	10.63	8.96	8.95	7.9
Mn(II)complex	Dark brown	80	>200	10.71	10.62	8.42	8.45	8.4

\*  $\text{L}_1$ = Ligand I,  $\text{L}_2$ = 2, 2' bipyridyl and X = Chloride ion.

Table I Illustrates the stoichiometry of the complexes as  $\text{ML}_1\text{L}_2$  and Low molar values indicate non electrolytic nature of complexes.

### 3.1. Infrared Spectra

Derived compounds were recorded for IR- spectra to prove the binding form of electron donor atoms with central metal ions. Vibrational frequencies, along with their timid assignments of reported metal(II) complexes, were exactly listed in Table 2. The band is shown at 1620  $\text{cm}^{-1}$  represents

$\nu(\text{C}=\text{N})$  that is shifted near the low region approximately 1595-1609  $\text{cm}^{-1}$  in derived complexes and it clearly tells the confirmation of C=N molecule in the prepared formation of complexes<sup>16</sup>. The formation of non-ligand bands in complexes just about 444-468  $\text{cm}^{-1}$  are due to (Metal-N) bond respectively<sup>17</sup>. The absorption band is at 310-317  $\text{cm}^{-1}$  region that is assigned because of  $\nu$  (Metal-Cl) Vibrations.

Table2: IR Data of the Schiff Base Ligand and Its Mononuclear Metal Complex			
Compounds	(C=N) ( $\text{cm}^{-1}$ )	(M- N) ( $\text{cm}^{-1}$ )	(M- Cl) ( $\text{cm}^{-1}$ )
Ligand	1620	--	--
Co(II)complex	1595	468	310
Mn(II)complex	1600	444	312
Cu(II)complex	1605	460	315
Ni(II)complex	1609	454	317

Table 2 The significant IR absorption bands of the prepared ligand and its complexes are given. In addition, the characteristic absorption bands of the ligand are shifted on complex formation and new characteristic vibrational bands of the complexes appear.

### 3.2. Magnetic Moment and Electronic Spectral

UV spectra of derived ligand in Dimethylformamide exhibits band assigned to  $\pi-\pi^*$  transitions of aromatic ring in ligand and imino group at 340 nm. Another extra band is noted at 364 nm and is dependable for  $n-\pi^*$  transitions<sup>18</sup>. The  $\text{Cu}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  complex gives bands at 505 and 604 nm due to  ${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_{1g}$  and  ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$  transitions. This electronic data shown us octahedral geometry for the reported  $\text{Cu}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  complex. Cu(II) complex have a magnetic moment value at 1.90 B.M. Octahedral geometry for darkish colored derived  $\text{Co}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  complex established by

magnetic moment at 3.60 B.M. And the assignment of the three most intense bands are  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}(\text{F})$ ,  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$ , and  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{P})$  at the range 464, 595 and 625 nm. The Mn(II) complex depicts transition bands by 694, 555 and 522 nm attributed to  ${}^6\text{A}_{1g} \rightarrow {}^4\text{A}_{1g}$ ,  ${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g$ ,  ${}^4\text{A}_{1g}$  and  ${}^6\text{A}_{1g} \rightarrow {}^4\text{A}_{2g}$ , respectively that are depicted to an octahedral geometry about manganese(II) ion. Mn(II) complex shows magnetic moment value at 5.92 B.M<sup>19</sup>. The three bands were shown for  $\text{Ni}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  complex in the range of 446, 578 and 625 nm, responsible to  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ ,  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})$ , and  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$  d-d transitions. Magnetic moment value of  $\text{Ni}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  at 3.12 Bohr magneton.

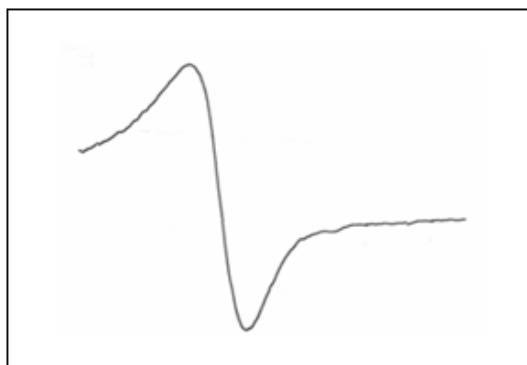
Table 3: UV-V is Absorption Spectral Data of Metal(II) Complexes at 300 K.				
Complex	$\lambda$ max (nm)	Band assignments	Geometry	Magnetic moment (B.M.)
Ni(II)complex	357	INCT	Distorted octahedral	3.14
	370	LMCT		
	450	${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})$ , ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ ${}^3\text{A}_{2g}(\text{F})$		
	582	$\rightarrow {}^3\text{T}_{1g}(\text{P})$		
	630			
Cu(II)complex	345	INCT	Distorted octahedral	1.92
	370	LMCT		
	510	${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_{1g}$ ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$		
	609			
Mn(II)complex	295	INCT	Distorted octahedral	5.90
	370	LMCT		
	525	${}^6\text{A}_{1g} \rightarrow {}^4\text{A}_{1g}$ ,		
	560	${}^6\text{A}_{1g} \rightarrow {}^4\text{A}_{2g}$ ,		
	695	${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g$ , ${}^4\text{A}_{1g}$		
Co(II)complex	360	INCT	Distorted octahedral	3.62
	370	LMCT		
	470	${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$ , ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}(\text{F})$ ${}^4\text{T}_{1g}(\text{F})$		
	560	$\rightarrow {}^4\text{T}_{2g}(\text{P})$		
	630			

Table 3The UV-vis spectra of the ligand and the complexes were recorded in DMF solution in the wavelength range from 200 to 800 nm.

### 3.3. ${}^1\text{H}$ NMR

${}^1\text{H}$  NMR spectral studies of derived ligand ( $\text{C}_{20}\text{H}_{13}\text{N}_4\text{O}_4$ ) indicated signals at 6.40– 7.90 ppm corresponding to aromatic protons at 8.23 ppm which is attributed to azomethine moiety (C=N). These signals afford structural arrangement for the prepared ligand

### 3.4. ESR Studies



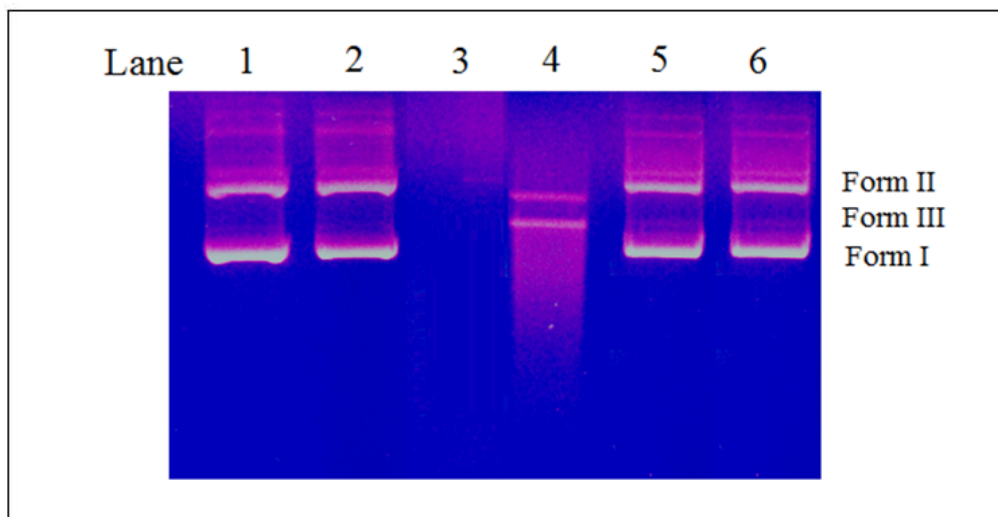
**Fig 3: Epr Spectra of  $\text{Cu}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  Schiff Base Complex**

The Electromagnetic Resonance spectrum of the derived  $\text{Cu}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  compound gives idea of the exact geometry and the nature of ligating sites around the central metal ion <sup>11</sup>. X-band of ESR spectrum for the  $\text{Cu}(\text{C}_{30}\text{H}_{21}\text{N}_7\text{O}_4\text{Cl}_2)$  complex was recorded at a particular frequency range of 9.1 GHz at 77 K, which suggests that this complex has a distorted octahedral geometry.

### 3.5. Gel Electrophoresis Assay

Deoxyribonucleic acid cleavage actions of the prepared complexes been completely monitored by the capability of changing super coiled pUC18 DNA (Form I to Form II to Form III) via suitable gel-electrophoresis method <sup>21</sup>. Figure 4 depicts the exact cleavage pattern. The Deoxyribonucleic acid cleavage competence of derived compounds actually was

binding affinity of complex to Deoxyribonucleic acid molecule. In this case, control did not illustrate noticeable cleavage of DNA (lane 1 & 2). Fig. 4, derived complexes noted to illustrate the nuclease activity in the existence of  $\text{H}_2\text{O}_2$  as (Lanes 3 and 4). There is no cleavage taking place in lanes 5 and 6. According to these results, we infer that complexes  $\text{Cu}(\text{II})$  and  $\text{Ni}(\text{II})$  effectively cleave the DNA and act as a potent nuclease agent. As the compounds were observed to cleave DNA, it can be concluded that the compounds inhibit the growth of the pathogenic organism by cleaving the genome. We have observed a significant effect of conjugation in the sulphur containing Schiff base, reducing the cleavage efficiency. The results are of importance in designing metal-based complexes containing sulfur-containing ligands for pharmacological applications



**Fig 4: Dna cleavage changes in the agarose gel electrophoretic pattern of puc18dna INDUCED BY  $\text{H}_2\text{O}_2$  AND Metal Complexes. Lane 1-Dna Alone; Lane 2- Dna Alone +  $\text{H}_2\text{O}_2$ ; Lane 3-Dna + Cu Complex +  $\text{H}_2\text{O}_2$ ; Lane 4-Dna + Ni Complex+  $\text{H}_2\text{O}_2$ ; Lane5-Dna + Co Complex Lane 6-Dna+ Mn Complex  $\text{H}_2\text{O}_2$ .**

### 3.6. DPPH Radical Studies

The antioxidant activity of the ligand and its complexes have attracted increasing interest and been substantially investigated. DPPH radical scavenging effect is an easy and suitable process that is expansively utilized for assessing the antioxidant capability of derived compounds. Diphenylpicrylhydrazyl radicals are firm but in the existence of prepared compounds competent of contributing H atoms and a radical activity completely damaged ensuing in a

transformation of color from purple to yellow. It is noted that Schiff base, along with its complexes, definitely diminish its attentiveness of Diphenylpicrylhydrazyl radical in the solution and it has been considered a confirmation of their antioxidant capacity <sup>22</sup>. The scavenging activity increases with increasing sample concentration in the range tested. As shown in the Figure, the free ligand L has less scavenging activity than the complexes within the investigated concentration range due to the OH groups which can react with DPPH radical by the typical H-abstraction reaction to form a stable radical As

shown in Figure 5 Cu(II) complex possess more efficient activity in quenching DPPH• radical than the free ligand L consistency with previously reported data for other elements. When the ligand L interacts with the positively charged metal ions, electron density is drawn from the oxygen. This flow of electron density causes the O–H bond to become more polarized; as a result, the H atom have a greater tendency to

ionize than those in the free ligand L not bound to the metal ions in DMF and thus increases the possibility of scavenging ability. Cu(II) complexes displayed the highest scavenging activities than Ni(II), Mn(II) and Co(II) complexes and ligand. Here for comparison, ascorbic acid molecules were used as standard.

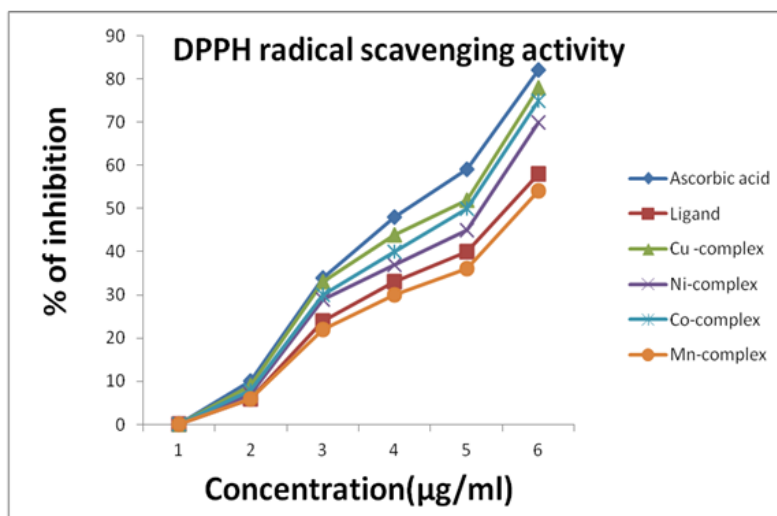


Fig. 5. Dpph Scavenging Activity of  $C_{20}H_{13}N_4O_4$  and its Complexes.

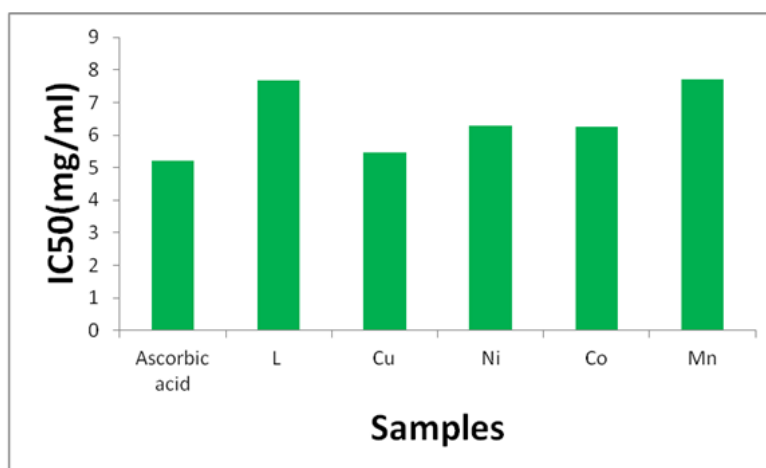


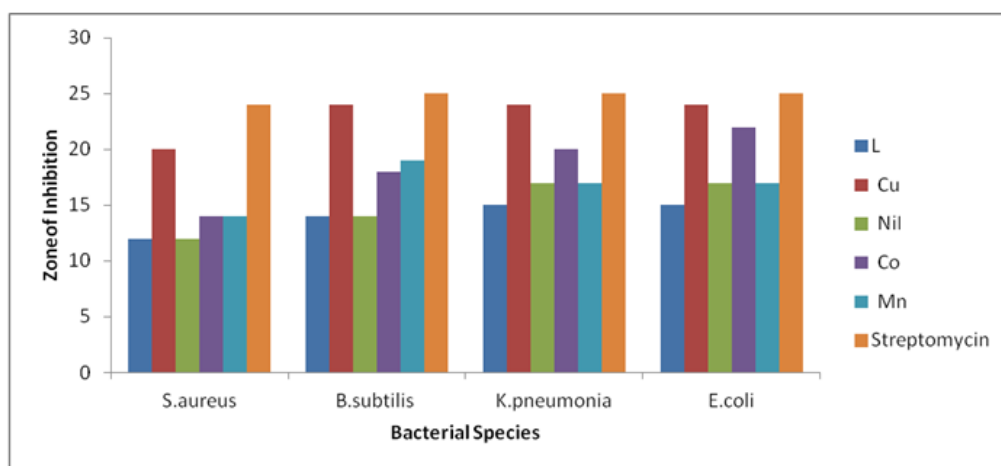
Fig 6: Dpph Radical Scavenging Capacities ( $IC_{50}$ ) of Synthesized Metal Complexes

### 3.7. Antimicrobial Activity

The antimicrobial capacities of all reported samples have been assessed against two pathogenic strains such as *S. aureus*, *B. subtilis* (gram positive) while gram-negative strains are *E. coli* and *K. Pneumonia* species<sup>23</sup>. The disc diffusion technique at a concentration of 50 μg/mL. Streptomycin was taken as the standard drug here. It has been suggested that the ligand with the N donor system might have inhibited enzyme production since enzymes that require free hydroxyl groups for their activity appears to the unique susceptibility to deactivation by the ions of the complexes. The complexes facilitate their diffusion through the lipid layer of spore membranes to the site of action, ultimately killing them by combining with OH groups of certain cell enzymes. The variation in the

effectiveness of different biocidal agents against different organisms depends on the impermeability of the cell. Chelation reduces the polarity of the central metal atom, mainly because of the partial sharing of its positive charge with the ligand. Also, the formation of a hydrogen bond may affect the normal cell process through the azomethine nitrogen atom with the active centers of cell constituents. The chosen compounds used for this investigation are as an example only for this study. Also, the absence of bulkiness observed around the metal ions, which may permit their interaction easily with the cell enzymes, is considered the main cause for the choice. The noted antibacterial studies of reported samples are in figure 7. Also, it was clearly noticed that all complexes showed better inhibition than ligands.





**Fig 7: Antibacterial Activity of Synthesized Compounds Against Four Bacterial Strains**

**Table 4: Antibacterial Activity for Schiff Base Ligands and Its Mononuclear Metal Complexes**

Table 1: Antibacterial Activity for Schiff Base Ligands and Its Mononuclear Nickel Complexes																
Compounds	Zone of inhibition (mm)															
	Gram positive bacteria								Gram negative bacteria							
	Staphylococcus aureus				Bacillus subtilis				Escherichia coli				Klebsiella pneumoniae			
	Concentration (µg/mL)															
	25	50	75	100	25	50	75	100	25	50	75	100	25	50	75	100
Ligand	7	7	8	10	7	7	9	10	6	6	7	9	7	8	8	10
Ni(II)complex	9	8	10	12	9	8	11	12	6	7	7	9	9	8	9	10
Cu(II)complex	10	11	12	14	10	9	12	13	9	9	10	11	10	12	15	17
Mn(II)complex	8	9	9	10	8	9	9	10	7	8	9	9	7	8	9	10
Co(II)complex	10	9	12	13	10	11	12	14	8	9	9	11	9	10	11	12
Streptomycin	16	17	20	22	16	15	17	20	13	13	16	20	13	15	16	18

Table 4 shows the Difference between Anti-bacterial Activities (against different organisms as gram-negative and gram positive using different concentrations.) of the Schiff Base and its Mononuclear Metal Complexes. Standard = Streptomycin Inhibition Zone in mm, Concentration 50 µ g/mL

#### 4. CONCLUSION

This research article explores the synthesis and coordination chemistry of some mono nuclear metal(II) complexes derived from the tetradentate Schiff-base ligand. Based on various physico-chemical and spectral data presented and discussed above, the complexes may tentatively be suggested to have octahedral complexes. The therapeutic promise of the investigated metal (II) complexes was found to exhibit higher antimicrobial activity than the ligand. The interaction of these complexes with pUC18 DNA was investigated by gel electrophoresis and concluded that Ni(II) and Cu(II) complexes cleave DNA in the presence of H<sub>2</sub>O<sub>2</sub>. In contrast, the control DNA and Mn(II) and Co(II) complex are less effective. Moreover, the ligand and its complexes were

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screened for antioxidant activity using DPPH assay. Cu (II) complex shows better antioxidant activity.

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#### 6. AUTHORS CONTRIBUTION STATEMENT

T. Sujeshwari conceptualized and gathered the data with regard to this work. Dr.Akila analyzed these data and necessary inputs were given towards the design of the manuscript. All authors discussed the methodology and results and contributed to the final manuscript.

#### 7. CONFLICT OF INTEREST

Conflict of interest declared none.



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