CHEMICAL SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITY OF P-HYDROXY ACETOPHENONE PRAMIPEXOLE AND ITS Cu(II), Ru(III) COMPLEXES

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ABSTRACT

The present paper deals with the synthesis, characterization and DNA binding studies of metal complexes of new Schiff base derived from Pramipexole (N6-propyl-4,5,6,7-Tetrahydro-,1,3-benzothiazole-2,6-diamine). The bidentate ligand is derived from the inserted condensation of pramipexole with P-hydroxy acetophenone (PHAPP) in a 1:1 molar ratio. Using this bidentate ligand, complexes of Cu(II), Ru(II) with general formula ML2 have been synthesized. The synthesized complexes were characterized by several techniques using Elemental analysis, IR, NMR, UV-Vis Spectrometry, ESR, TG-DTA and Conductometric measurements. The elemental analysis data suggest that stoichiometry to be 1:2 [M:L]. All the complexes are non-electrolytic in nature as suggested by molar conductance measurements. Infrared spectral data indicate the coordination between ligand and central metal ion through deprotonated phenolic oxygen and azomethine nitrogen. In addition, the authors have screened the compounds for biological activity. It was found that the compounds have shown activity against the organisms like Escherichia coli, Klebsiella and Bacillus subtilis.

Keywords: Synthesis, Characterization, Schiff base (PHAPP), Pramipexole, DNA binding, Biological activity.

INTRODUCTION

Coordination complexes are gaining importance in recent years especially in the designing of long acting drugs in metabolism. The metal complexes from bidentate ligands have often been studied recently because of their technical applications1,2 and applications in enhancement of drug action3,4. Transition metals are essential for normal functioning of living organism and are, therefore of great interest as potential drugs5. The coordination chemistry of nitrogen donor ligands is an active area of research. A great deal of attention in this area has been focused on the complexes formed by metals with bidentate ligands using both sulfur and nitrogen6,7. The Schiff bases are an important class of ligands in coordination chemistry. The study of structural and binding features of various Schiff base complexes can play an important role in better understanding of the complex biological process. Schiff bases derived from P-hydroxy Acetophenone are well known for their interesting ligational properties and exclusive applications in different fields8-10. It is well known from the literature that Schiff bases derived from pramipexole have a strong ability to form metal complexes11. The interaction of these donor ligands and metal ions gives complexes of different geometries, and literature survey reveals that these complexes are potentially more biologically active. Thus, in recent years Schiff bases and their metal complexes have attained much attraction because of their extensive biological activities12,13. Keeping the above fact in our mind and in continuation of our earlier work on transition metal complexes with Schiff bases14,15, the ligand PHAPP Schiff base(L) has been synthesized. In the present paper, the synthesis and characterization of the ligand and its complexes with Cu(II), Ru(II) are being reported.

MATERIALS AND METHODS

Instrumentation:
The percentage compositions of the elements (CHNO) for the compounds were determined using an element analyzer CHNO model Fison EA 1108. The Infra red spectra were recorded as potassium bromide (KBr) discs using a JASCO FT/IR-5300. The 1H (400Hz) nuclear magnetic resonance spectra were recorded using the ACF200 Broker Germany Spectrometer. Ultraviolet Spectra were recorded using Perkin-Elmer lab India UV-Vis Spectrometer. The Electron spin resonance spectra were recorded using the JES-FA Series and TG-DTA spectra were recorded using the SPTQ600 PA, Thermo gravimetric analyses of the metal complexes were
carried out by using the Perkin Elmer system in thermal analysis centre Stick Cochin. Melting points were measured on a unimelt capillary melting point apparatus. All materials used in this investigation were purchased from Sigma/Aldrich and AR (Merck). Solvents used were of reagent grade and purified before use by the standard methods.

**Preparation of the ligand and its metal complexes:**

*(Preparation of Pramipexole and P-hydroxy Acetophenone Schiff base (PHAPP))*:

Pramipexole 4.22g (0.02mole) and P-Hydroxy Acetophenone 2.442g (0.02mole) were dissolved in 25ml of methanol were taken in 250ml borosil reflection flask and 1 ml of triethylamine. The mixture was refluxed for 3 hour on water bath and then cooled to room temperature, dark cream colored sharp needles were separated out and washed with methanol and dried in vacuum desiccators over CaCl$_2$ anhydrous.

For the Preparation of Cu(II) and Ru (II) metal chloride salts were used. Dissolve 3.294g(0.01 Mole)of newly synthesized ligand in adequate of methanol. To this solution, aqueous solution of 1.3434 g(0.01Mole) and 1.718g (0.01Mole) metal chlorides, and 1 ml of Sodium acetate. The mixture was refluxed for 6hours in a water bath and then cooled to room temperature, Dark green colored, dark brown colored sharp needles were separated out. The coloured metal complexes were washed with water and then methanol, and were recrystalised from ether and dried in vacuum desiccators over CaCl$_2$ anhydrous. The elemental analysis was carried out for the newly synthesized ligand metal complexes. The prepared metal complexes were in 1:2 ratio. Ligands and metal complexes analytical data was tabulated in Table-1.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Molecular weight</th>
<th>Co lour</th>
<th>Yield</th>
<th>M.P</th>
<th>C % Calculated</th>
<th>Found</th>
<th>H% Calculated</th>
<th>Found</th>
<th>N % Calculated</th>
<th>Found</th>
<th>O% Calculated</th>
<th>Found</th>
<th>M% Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHAPP</td>
<td>329.47</td>
<td>Dark cream</td>
<td>73</td>
<td>185-186</td>
<td>65.65</td>
<td>65.00</td>
<td>6.99</td>
<td>6.45</td>
<td>12.79</td>
<td>12.55</td>
<td>5.079</td>
<td>4.999</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cu(PHAPP)$_2$X$_2$</td>
<td>758.48</td>
<td>Dark green</td>
<td>72</td>
<td>194-196</td>
<td>55.96</td>
<td>55.56</td>
<td>6.59</td>
<td>6.12</td>
<td>11.07</td>
<td>10.75</td>
<td>8.764</td>
<td>8.223</td>
<td>8.37</td>
<td>8.10</td>
</tr>
<tr>
<td>Ru(PHAPP)$_2$X$_2$</td>
<td>796.01</td>
<td>Dark brown</td>
<td>70</td>
<td>202-204</td>
<td>54.22</td>
<td>54.22</td>
<td>6.28</td>
<td>6.12</td>
<td>10.55</td>
<td>10.02</td>
<td>8.342</td>
<td>8.001</td>
<td>12.69</td>
<td>12.40</td>
</tr>
</tbody>
</table>

**RESULTS AND DISCUSSION**

**Infrared spectral analysis:**

Infrared spectra were recorded with a JASCO FT/IR-5300 Spectrometer (4000-400cm$^{-1}$) using KBr pellets. By utilizing this spectroscopy, the presence of important functional groups in the compound can be identified. Table2 through light on the observation made in analyzing IR spectra of ligand and metal complexes. The typical IR spectra are presented in the Fig.1, 2 and 3.

**Interpretation of PHAPP and Cu(II) and Ru(II) complexes:**

The Infrared spectrum of the ligand was compared with the spectra of Cu(II) and Ru(II) complexes. The data was summarized in table along their assignment. The typical IR spectra were shown in Fig.1, 2 and 3. A strong band exhibited at 1670 cm$^{-1}$ in the IR spectrum of the ligand has been assigned to the (C=N) Stretching vibration of the azomethine group. On complexation this band is shifted to 1665 and 1649 cm$^{-1}$ for Cu (II),and Ru(III) complexes respectively . This shift to lower wave numbers supports the participation of the azomethine group of this ligand in binding to the metal ion$^{17}$.This was due to the reduction of electron density on Nitrogen. There by indicating the coordination of the metal in through the nitrogen atoms.

The IR spectra of metal chelates shows the disappearance of the υ(OH)$^{16}$ bond at 3303 cm$^{-1}$. It indicates the proton displacement from the phenolic (OH) group on complexation. Thus bonding of the metal ions to the ligands under investigation takes place through a covalent link with oxygen of the phenolic group.The IR spectra of Cu(II) and Ru(II) metal complexes exhibit a broad band around3309cm$^{-1}$ and 3369cm$^{-1}$ respectively, which can be assigned to υ(OH) of water molecules associated with complex formation. New bands were observed in the complexes, which were not observed in ligand. The bands at 620 cm$^{-1}$ and 680 cm$^{-1}$ were assigned to stretching frequencies of (M-O), the band at 460cm$^{-1}$ and 580cm$^{-1}$ were assigned to the stretching frequencies (M-N) respectively$^{19,21}$. 

Table 1: Analytical data of the ligand and their metal complexes.

\[\text{Table 1: Analytical data of the ligand and their metal complexes.}\]
<table>
<thead>
<tr>
<th>Compound</th>
<th>OH Water</th>
<th>OH Phenolic</th>
<th>C=N</th>
<th>N-H</th>
<th>M-O</th>
<th>M-N</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHAPP</td>
<td>----</td>
<td>3303</td>
<td>1670</td>
<td>3177</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PHAPP-Cu</td>
<td>3309</td>
<td>-</td>
<td>1665</td>
<td>3303</td>
<td>620</td>
<td>460</td>
</tr>
<tr>
<td>PHAPP-Ru</td>
<td>3369</td>
<td>-</td>
<td>1649</td>
<td>3369</td>
<td>680</td>
<td>580</td>
</tr>
</tbody>
</table>

**Table 2: Important IR bands of the Ligand and Their Metal Complexes**

IR Spectra of PHAPP Ligand

IR Spectra of Cu(PHAPP) complex

IR Spectra of Ru(PHAPP) complex
NMR Spectrum of PHAPP Ligand and its Metal complexes:
The $^1\text{H}$ NMR spectra of ligand and metal complexes in DMSO-d$_6$ as solvent were given in fig.4 and 5. The chemical shift values of the ligand and metal complexes were shown in Table 3.

A singlet observed at 2.580 ppm $^{21}$ for $^1\text{H}$ NMR spectrum of the PHAPP ligand is assigned to the methyl protons attached to azomethine (C=N) group. The singlet appeared at 1.8 ppm is attributed to the methylene protons of the cyclohexane ring. Another doublet observed at 6.905-6.927 ppm for $^1\text{H}$ NMR spectrum of the C-H proton of the phenyl ring. A singlet is observed in the region 6.359 due to the aromatic O-H protons of phenolic hydroxyl group. The doublet appeared at 7.909-7.931 ppm due to two C-H proton of the phenyl ring. The another singlet appeared at 7.2 ppm due to N-H proton of ligand.

In the $^1\text{H}$ NMR spectrum of the PHAPP – Cu complex, a signal appeared due to methyl protons attached to azomethine group has been shifted to 2.586 ppm compared to 2.580 ppm in the case of ligand. This downfield shift indicates the deshielding of azomethine proton on coordination through nitrogen atom of azomethine group $^{22}$. The signal observed at 1.719 ppm due to the methylene protons of cyclohexane ring for the (Cu) complex. A signal is appeared due to para at 6.2 ppm due to OH proton on Para position of phenolic group. The multiplet observed in the region 6.6-6.9 ppm due to aromatic two C-H protons of phenyl ring for (Cu) complex may be due to the drifting of ring of electrons towards the metal ion. Another multiplet observed in the region of 7.9-8.2 ppm indicate two C-H protons of phenyl ring. A new signal is observed as a singlet at 4.67 ppm in the case of Cu(II) complex indicating the presence of water molecules coordinated to the metal atom. A signal observed at 7.2 ppm in ligand due to N-H proton is shifted to 7.28 ppm for Cu complex.

In the $^1\text{H}$ NMR spectrum of the PHAPP – Ru complex, a signal appeared due to methyl protons attached to azomethine group has been shifted to 2.6 ppm compared to 2.580 ppm in the case of ligand $^{21}$. This downfield shift indicates the deshielding of azomethine proton on coordination through nitrogen atom of azomethine group. The signal observed at 1.719 ppm due to the methylene protons of cyclohexane ring for the (Ru) complex. A signal is appeared due to para at 6.37 ppm due to OH proton on Para position of phenolic group. The multiplet observed in the region 6.6-6.95 ppm due to aromatic two C-H protons of phenyl ring for (Ru) complex may be due to the drifting of ring of electrons towards the metal ion. Another multiplet observed in the region of 7.93-8.24 ppm indicate two C-H protons of phenyl ring. A new signal is observed as a singlet at 5.01 ppm in the case of Ru(II) complex indicating the presence of water molecules coordinated to the metal atom. A signal observed at 7.2 ppm in ligand due to N-H proton is shifted to 7.28 ppm for Ru complex.

### Conductivity measurements:
The molar conductance values of these complexes d-d transitions were observed in visible region. Magnetic susceptibility measurements of copper (II) and Ruthenium (II) complexes:
The effective magnetic moment values for all the complexes are represented in the Table 6. There are considerable orbital shifts values of the ligand and metal complexes were shown in Table 3. Conductivity measurements:
The molar conductance values of these complexes were determined at 27+20°C using Syntronic 303 direct reading conductivity bridge. A known amount of solid complexes is transferred into 25ml standard flask and dissolved in dimethyl formamide (DMF). The contents are made up to the mark with DMF. The complex solution is transferred into a clean and dry 100ml beaker. The molar conductance of the complexes were less than 20 Ohm cm$^{-2}$ mol$^{-1}$ indicating the Non-electrolytic nature. These values suggest non-electrolytic nature of the present complexes. The molar conductance values of these metal complexes are given in the Table 4.

### Electronic spectra:
In UV-Visible electromagnetic radiation, the transitions are associated with the electronic energy levels of the compound under investigation. The electronic spectra were recorded on a Thermo Spectronic Heylosa spectrophotometer. The transition metal ions occur in a variety of structural environments. Because of this, the electronic structures are extremely varied. The electronic structures have been identified with UV-Visible spectroscopy PHAPP and its metal complexes: The electronic spectral of ligand and its metal complexes were given in the transitions were reported in the Table 5. Ligand shows signal band at 310 nm, assigned to $[\pi-\pi^*]$ transition. In complexes this band was shifted to higher wavelength regions. New bands were observed in the complexes at corresponding to the charge transfer transitions. In high concentration spectra of complexes d-d transitions were observed in visible region.

### Conductance data for Metal-PHAPP Complexes:

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Metal Complex</th>
<th>Molar Conductance (Ohm cm$^{-2}$ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Cu(PHAPP)$_2$</td>
<td>20</td>
</tr>
<tr>
<td>2.</td>
<td>Ru(PHAPP)$_2$</td>
<td>23</td>
</tr>
</tbody>
</table>

### Electronic spectral data

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\lambda_{max}$ of compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHAPP</td>
<td>294</td>
</tr>
<tr>
<td>PHAPP-Cu</td>
<td>316</td>
</tr>
<tr>
<td>PHAPP-Ru</td>
<td>334</td>
</tr>
</tbody>
</table>

### Magnetic susceptibility measurements of copper (II) and Ruthenium (II) complexes:
The effective magnetic moment values for all the complexes are represented in the Table 6. There are considerable orbital shifts values of the ligand and metal complexes were shown in Table 3.

### Table 3: NMR Data of ligands and its metal complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>H$_2$C-C=N</th>
<th>Ar-H</th>
<th>CH$_2$</th>
<th>Ar-OH</th>
<th>N-H</th>
<th>H$_2$O-OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHAPP</td>
<td>2.580</td>
<td>6.905-7.931</td>
<td>1.8</td>
<td>6.359</td>
<td>7.2</td>
<td>4.67</td>
</tr>
<tr>
<td>PHAPP-Cu</td>
<td>2.586</td>
<td>6.6-8.2</td>
<td>1.719</td>
<td>6.2</td>
<td>7.28</td>
<td>5.01</td>
</tr>
<tr>
<td>PHAPP-Ru</td>
<td>2.6</td>
<td>6.6-8.24</td>
<td>1.719</td>
<td>6.37</td>
<td>7.2</td>
<td>5.01</td>
</tr>
</tbody>
</table>
contribution and effective magnetic moments for octahedral complex at room temperature. The magnetic moments of the present \((\text{PHAPP})_2\) Cu complex is 4.72 B.M. and the value is less than the spin only value, it shows reduced Paramagnetism, which suggest the formation of low-spin complex having octahedral geometry. The magnetic moments of the present \((\text{PHAPP})_2\) Ru complex is 1.60 B.M. and this value is less than the spin-only value, showing reduced paramagnetism, which suggest the formation of flow-spin complex having square planar.

Table 6: Magnetic moments of copper and Ruthenium

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Metal Complexes</th>
<th>Effect. In B.M.</th>
<th>Theoretical</th>
<th>Observed</th>
<th>Number of unpaired electron</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>(\text{Cu(\text{PHAPP})}_2)</td>
<td>4.80</td>
<td>4.72</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>(\text{Ru(\text{PHAPP})}_2)</td>
<td>1.79</td>
<td>1.60</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Thermal analysis:
The thermal studies of these complexes are carried out to know the stability of the complexes on thermal decomposition, as well as to know the different final products that are obtained in thermal decomposition having novel catalytic properties.

Study of \(\text{PHAPP and its Cu (II) and Ru (II) metal complexes by TGA-DTA spectra:}\)
Thermo analytical data of metal complexes were given in the Table.8. The representative thermo grams were shown in the fig.8 and 9. The Cu complexes are thermally stable up to 1000°C. The Copper complex of PHAPP shows three main decomposition stages, and the first stage with small endothermic dehydration step in the range of 100°C to 160°C was due to loss of two water molecules coordinated to the metal. The Second step involves two sub steps which involves decomposition of the ligand moiety, Exothermic decomposition of the ligand moiety takes place around 180–200°C, to give the stable intermediate \((\text{PHAPP})_2\) and this was stable up to 440°C, which on further undergoes exothermic decomposition in the region 440-840°C in the third stage forming Copper Oxide (CuO) as final residual product. The Ruthenium complex of PHAPP shows three main decomposition stages, and the first stage with small endothermic dehydration step in the range of 100°C to 110°C was due to loss of two water molecules coordinated to the metal. The Second step involves two sub steps which involves decomposition of the ligand moiety, Exothermic decomposition of the ligand moiety takes place around 310–530°C, to give the stable intermediate \((>\text{C=N})_2\) and this was stable up to 770°C, which on further undergoes exothermic decomposition in the above region of 770°C in the third stage forming Ruthenium Oxide (RuO) as final residual product.

All the experimental mass loss has shown Table.8. At high temperatures, the corresponding metal oxides were formed, as stable products. All the experimental percentage mass loss was compared with the calculated weights. Based on thermal data it was shown that the stability order of the complexes was Cu (II)> Ru (II).

Table 7: Thermal analytical data of the Ligand and their metal complexes

<table>
<thead>
<tr>
<th>Complex (X=\text{H}_2\text{O})</th>
<th>Molecular weight in gms</th>
<th>Weight of the complex taken in mgs</th>
<th>Temperature Range during weight loss in 0°C</th>
<th>% of fraction of weight</th>
<th>Probable assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\text{Cu.L2.X2}])_ (L=\text{C}_1\text{H}_3\text{N}_3\text{SO})</td>
<td>758.48</td>
<td>8.1910</td>
<td>100-160, 180-200, 440-840</td>
<td>3.67, 65.42, 9.85</td>
<td>Loss of 2H2O molecule. Loss of two L molecules. Remaining residue Corresponds to CuO.</td>
</tr>
<tr>
<td>([\text{Ru.L2.X2}])_ (L=\text{C}_1\text{H}_3\text{N}_3\text{SO})</td>
<td>769.01</td>
<td>12.1630</td>
<td>100-110, 310-530, Above 770</td>
<td>5.68, 40.73, 13.91</td>
<td>Loss of 2H2O molecule. Loss of two L molecules. Remaining residue Corresponds to RuO.</td>
</tr>
</tbody>
</table>
DNA Binding studies:
The interactions of all the newly synthesised complexes were monitored by UV–Visible spectral studies. Disodium salt of calf thymus DNA was stored at 5°C. Solution of DNA in the buffer 45 mM NaCl/5 mM Tris HC1 (pH, 7.1) in water gave a ratio 1:9 of UV absorbance at 260 and 280 nm, A260/A280, indicating that the DNA was sufficiently free from protein. The concentration of DNA was measured by using its coefficient at 260 nm (6600 Cm⁻¹) after 1:100 dilutions. Concentrated stock solutions of the complexes were prepared by dissolving in DMSO and diluting suitably with the corresponding buffer to the required concentrations for all the experiments. The absorption spectra of complexes were compared in the absence and presence of CT–DNA. In the presence of increasing amounts of DNA, the spectra of complexes showed a strong decrease (hypochromicity) in intensity with shift in absorption maxima towards higher (red–shift) wavelengths. The binding of intercalative molecules to DNA has been well characterized by large hypochromism and significant red–shift due to strong stacking interaction between the aromatic chromophore of the ligand and DNA base pairs with the extent of hypochromism and red shift commonly consistent with the strength of intercalative interaction. To enable quantitative comparison of the DNA binding affinities the intrinsic binding constants $K_b$ of the complexes for binding with CT DNA were obtained by using the equation.

$$\frac{[DNA]}{(\varepsilon_a - \varepsilon_f)} = \frac{[DNA]}{(\varepsilon_b - \varepsilon_f)} + \frac{1}{K_b (\varepsilon_b - \varepsilon_f)}$$

Where $[DNA]$ is the concentration of DNA in base–pairs, $\varepsilon_a$ is the apparent extinction coefficient obtained by calculating $A_{obs} / [complex]$, $\varepsilon_f$ corresponds to the extinction coefficient of the complex in its free form and $\varepsilon_b$ refers to the extinction coefficient of the complex in the bound form. Each set of data, when fitted to the above equation, gave a straight line with a slope of $1/ (\varepsilon_b - \varepsilon_f)$ and a $y$–intercept of $1/K_b (\varepsilon_b - \varepsilon_f)$ and $K_b$ was determined from the ratio of the slope to intercept. The intrinsic binding constants $K_b$, obtained for the complexes.
Table 8: DNA binding constants of metal complexes

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Complex (X= H$_2$O)</th>
<th>$\lambda_{\text{max}}$ nm</th>
<th>$\Delta\lambda$ nm</th>
<th>H%</th>
<th>$K_b$(M$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Cu (PHAPP)$_2$X$_2$]</td>
<td>304</td>
<td>310</td>
<td>6</td>
<td>6.99</td>
</tr>
<tr>
<td>2</td>
<td>[Ru (PHAPP)$_2$X$_2$]</td>
<td>371</td>
<td>376</td>
<td>5</td>
<td>6.59</td>
</tr>
</tbody>
</table>

Absorption spectra were recorded 240–400 ranges. The ranges were selected where maximum absorption change observed on addition of DNA. Electronic absorption spectral data upon addition of CT–DNA and binding constants were given in Table 10 it was evident that these complexes bind with DNA with high affinities and the estimated binding constants are in the range of $10^5$–$10^6$ M$^{-1}$. This may due to the presence of pi–stacking of the pyridine ring present in the ligand moiety.

![DNA Binding interaction of Cu [PHAPP]](image1)

![DNA Binding interaction of Ru [PHAPP]](image2)

**Biological activity:**
The author in this present investigation attempted to find out antibacterial activity of ligand and their metal complexes against *Escherichia coli, Klebsiella and Bacillus subtilis* choosing serial paper disc method Table 9. The results of the biological activity of the metal complexes indicated the
following facts. A comparative study of the ligand and their complexes indicates that the metal chelates exhibited higher antibacterial activity than that of the free ligand. The increase in the antibacterial activity of metal chelates was found due to the effect of metal ion on the metal chelates which could be explained on the basis of overtones concept and chelation theory. On chelation the polarity of the metal ion reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charges of metal ion with donor groups. It was further noted that the delocalization of electrons to the metal ion through azomethine nitrogen and phenolic – OH group. This has been further confirmed on the basis of physicochemical and spectral studies. Thus, on the basis of above IR and NMR spectral studies the complexes are found to be more.

Table 9: Antibacterial Activity of the Metal complexes Total Area of Zone of clearance in mm

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Compound</th>
<th>Salmonella Typhi</th>
<th>Enterococcus Faecalis</th>
<th>Escherichia coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PHAPP</td>
<td>14</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>CuPHAPP</td>
<td>12</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>Ru(PHAPP)</td>
<td>12</td>
<td>13</td>
<td>13</td>
</tr>
</tbody>
</table>

CONCLUSION

The outcome of the above results confirms the stoichiometry of the complexes to be 1 : 2 [M: L] as indicated by elemental analysis and conductometric measurements. IR spectra suggest that the ligand behaves as bidentate and coordinates to the central metal ion through azomethine nitrogen and phenolic – OH group. This has been further confirmed on the basis of NMR spectral studies. Thus, on the basis of above physicochemical and spectral studies the complexes are found to have higher biological activities as compared to the respective ligand and the parent drug that, somehow, justifies the purpose of the research work. The present work will be further extended to the synthesis of metal complexes using other biologically active metals and evaluation of their biological activities. All the metal complexes carry on charge and are thermally stable. As such no single technique is independent of predicting final structures of the complexes.

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REFERENCES

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