Cobalt(II) complexes with 1,10-phenanthroline alone and mixed with cytoside: Synthesis and antibacterial activities

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ABSTRACT

Cobalt can bind to a range of biomolecules forming complexes that are suitable for use in various biological applications. Different ligands could be used to tune the properties of cobalt compounds whose ligand exchange rates become close to those of cellular processes. In this study, two complexes were synthesized from 1,10-phenanthroline alone as [Co(phen)(H2O)2]Cl2 and from both 1,10-phenanthroline and cytoside as [Co(phen)2(Cyt)H2O]Cl. The synthesis was checked using halide test, conductance measurement as well as spectroscopic (AAS, FTIR, Uv-vis) analysis. In vitro antibacterial activities of the two metal complexes were tested against Staphylococcus aureus, methicillin resistant staphylococcus aureus (MRSA), Streptococcus pneumoniae, Escherichia coli, Klebsiella pneumoniae and Shigella boydii. These complexes showed better activities than the commercially available control drugs (chloramphenicol and ciprofloxacin) against certain strains of bacteria. Better inhibition zones were exhibited by [Co(phen)2(Cyt)(H2O)]Cl on MRSA (4.8%) and E. coli (21.4%) than chloramphenicol. Likewise, 11.9% and 22.8% more zones of inhibition than ciprofloxacin were shown against MRSA and E. coli, respectively. On the other hand, [Co(Phen)(H2O)2]Cl showed 5.3% and 3.0% more zones of inhibition against S. aurous and S. boydii, respectively, better than ciprofloxacin.

Keywords/phrases: Mixed ligand complex, 1,10-phenanthroline, Cytosine, Cytoside, Antimicrobial activity

INTRODUCTION

The rapid increase in the number of multidrug-resistant bacteria is becoming a global concern making the discovery of novel active compounds a matter of urgency (Henderson 2006). Originating many of the crude drugs used for medicinal preparations from wild growing plants and animals is threatening the ecology of the globe (Cordell, 2011). Transition metal complexes have several features that are made use of in many areas of modern medicine (Orvig and Abrams 1999). For instance, pharmaceutical industries have considered them as alternatives to conventional drugs which originate from wild sources. This is because the properties of the transition metals can be tuned by coordinating with different ligands (Wilkins, 1974; Lawrence, 2010; Sears et al., 2010). These include stabilization of different oxidation states and modulation of the solvophilicity, electrophilic and nucleophilic properties of the metal ion (Tolman, 1977; Boyer

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et al., 2010; Goo et al., 2015). In coordination, it is not only the properties of metal ions that are modified but also are the properties of the ligands themselves (Atakilt Abebe and Tizazu Hailemariam, 2016). The pharmacological activities and their crucial role in DNA/RNA base pairing through several hydrogen-bonding patterns of free oxypyrimidines such as cytosine can significantly change after complex formation (Patel et al., 2012; Mohapatra and Verma, 2013). The medicinal activities (Mesmaeker et al., 1996; Turel 2002; Leung et al., 2015) of transition metal complexes occur due to their penetration into the lipid membrane which enables them to disrupt the normal activities of the bacteria (Lakshmi et al., 2009) and their potential to bind DNA via a multitude of interactions and to cleave the duplex by virtue of their intrinsic chemical, electrochemical and photochemical activities (Singh et al., 1983; Barton et al., 1986; Barton, 1990; Long and Barton, 1990; Turro et al., 1991; Murphy and Barton, 1992; Sigel and Sigel, 1996; Arounagueri and Maiya, 1999). Prominent among the various metal complexes employed so far are those complexes which incorporate 1,10-phenanthroline (phen) as a ligand (Atakilt Abebe et al., 2017; Turel et al., 2015). One advantage in the use of these metallo-intercalators for such studies is that the ligands or the metal ion in them can be varied in an easily controlled manner to facilitate individual applications (Richards and Rodger, 2007; Terron et al., 2007). In this regard, numerous investigations on the properties and applications of cobalt complexes were made (Kong and Xie, 2000; Boerner and Zaleski, 2005; Jiao et al., 2005; Zeglis et al., 2007; Keene et al., 2009). Nevertheless, there is no report on the chemistry of Co(II) complex containing 1,10-phenanthroline alone as $[\text{Co}(\text{phen})_2(H_2O)_2]\text{Cl}_2$ and/or mixed with cytoside as $[\text{Co}(\text{phen})_2(\text{Cyt})(H_2O)]\text{Cl}$ (Hiort et al., 1993; Dow et al., 1996; Cheng et al., 1999; Guest et al., 2004; Chen et al., 2010; Zhang et al., 2010).

The conveniently placed nitrogen atom along with its rigid planar structure, hydrophobic, electron-poor heteroaromatic and π-acidic properties cooperatively make 1,10-phenanthroline a classic chelating bidentate ligand. These properties enable it to have stacking interaction ability with DNA base pairs (Pyle et al., 1989; Schaeffer et al., 1996; Coury et al., 1997; Lincoln and Norden, 1998).

Cytosine is a chemically inert oxypyrimidine heteroaromatic molecule. Its inertness is changed by complex formation. Its activity is favored in its cytoside (Cyt) form which is derived by deprotonation of cytosine. It plays a crucial role in DNA/RNA base pairing through several hydrogen-bonding patterns (Portalone, 2011; Verma et al., 2012). The ring nitrogen with the acidic hydrogen is the binding site.

The purpose of this study is to examine the effects of 1,10-phenanthroline alone and mixed with cytoside on the biological activity of Co(II). The complex would orchestrate the inherent properties of its components. This includes the binding ability of cobalt with a range of biomolecules, the unique stacking interaction ability of 1,10-phenanthroline on cell genetic material, the interaction of cytoside through hydrogen bonding with guanine residue of the genetic material. The latter phenomena ultimately results strong antimicrobial activity of the complexes.
EXPERIMENTAL

Chemicals

All chemicals used in this work are: 1,10-Phenanthroline monohydrate (BDH chemical Ltd., Poole, England), cytosine (ACROS), Mueller-Hinton agar powder (Oxoid, England), KBr, CoCl2.6H2O, NaCl, AgNO3, NaOH, concentrated H2SO4, concentrated HNO3 (69-27%), and BaCl2.2H2O (all Blulux Laboratories Ltd., India).

Instruments and methods

The electronic conductance were measured using 10^{-3} M solution of each complex in deionized water with JENWAY 4200 conductivity meter at room temperature. The electronic spectra were recorded in the 200-800 nm region on Sanyo SP65 UV/VIS spectrophotometer. IR spectra were recorded using KBr discs in the 4000-400 cm^{-1} region on AVATAR 330 FT-IR Thermo Nicolet spectrophotometer. Cobalt content was determined by Analytik Jena nov AA300 model atomic absorption spectrophotometer digesting 5.75 mg of each complex in concentrated nitric acid and diluting using distilled water. Melting points were determined using STONE, STAFFORDSHIRE, ST15 OSA, UK digital melting point apparatus. Chloride ions were determined thermogravimetrically using the AgCl precipitate obtained from the mixture of 10 mL solution of 8 mg of each complex in distilled water with excess AgNO3 solution. The different bacterial isolates were collected from the University of Gondar, College of Medicine and Health Sciences Hospital. The antibacterial activities were tested at Microbiology Laboratory of Biology Department, Bahir Dar University.

Synthesis

Synthesis of [Co(phen)2(H2O)2]Cl2

A methanolic solution of 1,10-phenanthroline monohydrate (0.80 g, 4.0 mmol) was added from a dropping funel to a methanolic solution of CoCl2 .6H2O (0.461 g, 2.0 mmol) while stirring magnetically in an ice bath for about three hours. The stirring continued for additional three hours after the final drop of the solution containing the ligand when the thin layer chromatography (TLC) follow up indicated the completion of the reaction. A pinkish homogeneous solution was obtained. The solvent was removed in vacuum. Brown powder was collected and washed three times with acetone to remove any unreacted 1,10-phenanthroline (Atakilt Abebe and Tizazu Hailemariam, 2016).

Synthesis of [Co(Phen)2(Cyt)(H2O)]Cl

An aqueous solution of sodium cytoside obtained from a reaction between cytosine (0.126 gm, 1.0 mmol) and sodium hydroxide (0.046 gm, 1.0 mmol) was added from a dropping funnel to an aqueous solution of [Co(Phen)2(H2O)2]Cl2 (0.724 gm, 1 mmol) while stirring at room temperature. The mixture was allowed to stir for three hours when the TLC follow up indicated the completion of the reaction. The resulting reaction product mixture was mixed with 50 ml dichloromethane and stirred for 15 minutes and allowed to stand overnight. The organic (dichloromethane) phase in which the intended complex product is soluble was separated using separatory funnel. The dichloromethane was removed using rotary evaporator and a dark brown powder was collected (Atakilt Abebe and Tizazu Hailemariam, 2016). The product was re-crystallized from methanol. The synthetic strategy is indicated in Scheme 1.
Antimicrobial activity testing

The *in vitro* antibacterial activity of the salt, ligands and complexes were tested against three Gram-positive bacteria: *Staphylococcus aureus*, Methicillin resistant *Staphylococcus aureus* (MRSA), *Streptococcus pneumoniae* and three strains of Gram-negative bacteria: *Escherichia coli*, *Klebsiella pneumonia* and *Shigella boydii* by the cork borer method using nutrient agar as medium (Das *et al*., 2010). Ciprofloxacin (3μg) and chloramphenicol (30μg) were used as standard drugs.

A stock solution (10⁻² mol L⁻¹) of [Co(phen)₂(Cyt) (H₂O)]Cl in water was prepared and serially diluted in order to find the minimum inhibitory
concentration (MIC) value (Neube et al., 2008). Test extract loaded discs inoculated with microorganisms were incubated at 37 °C for 24 h. During the incubation period, the test solution diffused and the growth of the inoculated microorganisms was affected.

RESULTS AND DISCUSSION

The appearance, melting point, elemental estimation, yield and molar conductivity data of the complex are shown in Table 1.

Electronic spectra

The electronic spectra of the ligands and complexes are displayed in Table 2 and Figure 1. The coordination of the ligands to the metal ion is evident from the change in the transition absorptions. The complexes exhibited simple characteristic d–d transitions. The difference in the band position for d-d transition absorption of CoCl$_2$.6H$_2$O and the complexes may be explained by assuming different electronic environment around the metal ion following the coordination. The maximum absorption wave length of the complexes shows significant difference from that of CoCl$_2$.6H$_2$O and shifts to lower frequencies indicating different splitting pattern of the d-orbitals (Table 2).

Table 1: Physical and analytical data of the complexes

<table>
<thead>
<tr>
<th>Complex (color)</th>
<th>Melting point/°C</th>
<th>Yield, (%)</th>
<th>Elemental estimation</th>
<th>Λ$_M$ (S cm$^2$ mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Co(phen)$_2$(H$_2$O)$_2$]Cl$_2$ (Yellow)</td>
<td>325-327</td>
<td>73.5</td>
<td>11.21 (10.98) 13.49(13.25)</td>
<td>138.46</td>
</tr>
<tr>
<td>[Co(phen)$_2$(Cyt)(H$_2$O)]Cl (Dark brown)</td>
<td>177-179</td>
<td>75.37</td>
<td>10.13(9.95) 6.09(5.92)</td>
<td>83.23</td>
</tr>
</tbody>
</table>

Molar conductance of the metal complexes

The conductance measurements recorded for 10$^{-3}$ M solutions of the metal complexes in water are indicated in Table 1. [Co(phen)$_2$(H$_2$O)$_2$]Cl$_2$ and [Co(phen)$_2$(Cyt)(H$_2$O)]Cl are 1: 2 and 1:1 type electrolytes, respectively (Bard et al. 1980), which supports the chloride estimation experiment result. The decreased conductivity of [Co(phen)$_2$(Cyt)(H$_2$O)]Cl compared with [Co(phen)$_2$(H$_2$O)$_2$]Cl$_2$ absorptions. The complexes exhibited simple characteristic d–d transitions. The difference in the band position for d-d transition absorption of CoCl$_2$.6H$_2$O and the complexes may be explained by assuming different electronic environment around the metal ion following the coordination. The maximum absorption wave length of the complexes shows significant difference from that of CoCl$_2$.6H$_2$O and shifts to lower frequencies indicating different splitting pattern of the d-orbitals (Table 2).
As 1,10-phenanthroline is a very strong field chelating ligand, it forms shorter and stronger bonds than the weak field H₂O. This results in splitting patterns of the energy states \( ^4T_{2g} \) and \( ^4T_{1g}(F) \), which equate with a \( t_{2g}^5e_g^2 \) configuration (Housecroft and Sharpe, 2005; Missler and Tarr, 2004). The splitting of \( ^4T_{2g} \) (\( t_{2g}^5e_g^2 \) to \( t_{2g}^5 \) and \( e_g^2 \)) is significant in \([\text{Co(Phen)}_2(H_2O)_2]\)Cl₂, consequently, the energy gap of \( ^4T_{2g} \) (\( e_g \)) orbital from \( ^4T_{1g}(F) \) is minimized and the absorption wave length increases. Similarly, when the water molecule is replaced by a stronger field cytoside to form [Co(Phen)]₂(Cyt)(H₂O)]Cl, the energy gap between \( t_{2g}^5 \) and \( e_g^2 \) of \( (^4T_{2g}) \) increases while the gap between \( ^4T_{1g}(F) \) and \( ^4T_{2g} \) states decreases such that a lower energy is absorbed for the transition. Distorted octahedral geometry is proposed to the complex. Table 2 gives a summary of the electronic transitions of the ligands, the salt and the synthesized complexes.
IR Spectrum of the Ligands and Co(II) Complexes

The IR spectra of the complexes demonstrate that all the ligands are coordinated to the metal (Figure 2). The bands at 1506 cm\(^{-1}\) (s), 1585 cm\(^{-1}\) characteristic for νC=C and 1418 cm\(^{-1}\) (s) characteristic for νC=N stretching in the free 1,10-phenanthroline monohydrate appear shifted to 1525 cm\(^{-1}\) (w), 1644(w) and 1384 cm\(^{-1}\) (s), respectively, in [Co(Phen)\(_2\)(H\(_2\)O)\(_2\)]Cl. They also appeared at 1522 cm\(^{-1}\) (w), 1628 cm\(^{-1}\) (w), respectively, in [Co(Phen)\(_2\)(Cyt)(H\(_2\)O)]Cl. Similarly, the coordination of cytoside to the metal ion is evident from the appearance of strong sharp peaks at 1684 cm\(^{-1}\) characteristic for νC=O. The shift in the characteristic νC=O of free cytosine from 1669 cm\(^{-1}\) to 1684 cm\(^{-1}\) indicates the increase in the C=O bond multiplicity. Furthermore, 3465 cm\(^{-1}\) and 3352 cm\(^{-1}\) regions were assignable, respectively, to the asymmetric and symmetric stretching of terminal NH\(_2\) of cytoside mixed with ν\(_{OH}\) of the coordinated water (Verma et al., 2012) (Figure 2). Because the two phenanthroline molecules already occupied the four coordination sites in a square planar geometry, cytoside is acting as a monodentate ligand coordinated to Co(II) via deprotonated ring nitrogen. The justification for this is that metal ions with oxidation state +2 at the right of Mn in the 3d series of the periodic table are classified as acids with intermediate hardness. These ions prefer to bind to bases with similar hardness. The latter include \(sp^3\) hybridized N containing molecules (Huheey et al., 1993). The side primary amine nitrogen cannot be used for binding. This is due to the fact that the electron pairs that could be used for coordinate covalent bonding are engaged in the resonance of the ring system. Moreover, the cytoside carbonyl oxygen is \(sp^2\) hybridized hard base that does not form a stable bond with Co(II).

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Absorption bands/nm</th>
<th>Transitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoCl(_2).6H(_2)O</td>
<td>301</td>
<td>LMCT</td>
</tr>
<tr>
<td></td>
<td>472</td>
<td>(4^T_{lg} \rightarrow 4^A_{lg})</td>
</tr>
<tr>
<td></td>
<td>491</td>
<td>(4^T_{lg} \rightarrow 4^T_{2g})</td>
</tr>
<tr>
<td>[Co(Phen)(_2)(H(_2)O)(_2)]Cl</td>
<td>362</td>
<td>n →(\pi^*(C=N))</td>
</tr>
<tr>
<td></td>
<td>643</td>
<td>(4^T_{lg}(F) \rightarrow 4^T_{lg}(P))</td>
</tr>
<tr>
<td></td>
<td>662</td>
<td>(4^T_{lg} \rightarrow 4^A_{2g})</td>
</tr>
<tr>
<td></td>
<td>709</td>
<td>(4^T_{lg} \rightarrow 4^T_{2g})</td>
</tr>
<tr>
<td>[Co(Phen)(_2)(Cyt)H(_2)O)]Cl</td>
<td>412</td>
<td>n →(\pi^*(C=O))</td>
</tr>
<tr>
<td></td>
<td>647</td>
<td>(4^T_{lg}(F) \rightarrow 4^T_{lg}(P))</td>
</tr>
<tr>
<td></td>
<td>665</td>
<td>(4^T_{lg} \rightarrow 4^A_{2g})</td>
</tr>
<tr>
<td></td>
<td>715</td>
<td>(4^T_{lg} \rightarrow 4^T_{2g})</td>
</tr>
</tbody>
</table>

Table 2: The maximum absorption wave length and the corresponding transitions of the salt and complexes
Antimicrobial activities of the salt, ligands and complexes

The biological activity investigations result shows that the complexes demonstrated biological activities against all the tested strains (Figure 3, Table 4). The observed increase in antibacterial activity can be explained on the basis of Overtone’s concept (Dharmaraj et al., 2001) and Tweedy’s chelation theory (Tweed, 1964). The lipid membrane that surrounds the cell favors the passage of only lipid soluble materials due to which lipophilicity is an important factor which controls the antimicrobial activity. On coordination, the polarity of the metal ion will be reduced to a greater extent.
due to the overlap of the ligand orbitals and partial sharing of the positive charge of the metal ion with the donor groups. Further, it increases the delocalization of π-electrons over the whole chelate ring and hence enhances the liposolubility of the complexes. This increased liposolubility enhances the penetration of the complexes into the lipid membrane and interferes with the normal activities of the bacteria (Lakshmi et al., 2009).

![Gram-positive bacterial species](image1)

![Gram-nogative bacterial species](image2)

**Table 4: Antibacterial activity of CoCl₂.6H₂O, ligands, metal complexes and reference antibiotic**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>S. aureus (µg)</th>
<th>MRSA (µg)</th>
<th>S. pneumoniae (µg)</th>
<th>E. coli (µg)</th>
<th>K. pneumoniae (µg)</th>
<th>S. boydii (µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Co(Phen)₂(Cyt)(H₂O)]Cl</td>
<td>25.3 ± 1.15</td>
<td>28.3 ± 0.57</td>
<td>28.0 ± 1.00</td>
<td>32.3 ± 0.57</td>
<td>28.0 ± 1.00</td>
<td>23.3 ± 0.57</td>
</tr>
<tr>
<td>[Co(Phen)₂(H₂O)₂]Cl₂</td>
<td>23.3 ± 0.57</td>
<td>23.3 ± 1.52</td>
<td>25.6 ± 1.15</td>
<td>26.3 ± 1.52</td>
<td>26.3 ± 0.57</td>
<td>24.0 ± 1.00</td>
</tr>
<tr>
<td>CoCl₂.6H₂O</td>
<td>23.0 ± 1.00</td>
<td>21.3 ± 0.57</td>
<td>22.6 ± 1.50</td>
<td>20.3 ± 1.52</td>
<td>22.6 ± 1.15</td>
<td>21.3 ± 1</td>
</tr>
<tr>
<td>Cytosine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1,10-Phenanthroline</td>
<td>40.0 ± 1.00</td>
<td>34.6 ± 1.15</td>
<td>36.3 ± 0.57</td>
<td>34.0 ± 1.00</td>
<td>39.0 ± 1.00</td>
<td>21.3 ± 1.00</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>26.0 ± 1.00</td>
<td>25.3 ± 1.15</td>
<td>24.3 ± 0.15</td>
<td>26.3 ± 1.50</td>
<td>30.6 ± 0.57</td>
<td>23.3 ± 1.00</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>28.6 ± 0.57</td>
<td>27.0 ± 1.00</td>
<td>28.3 ± 0.57</td>
<td>26.6 ± 1.50</td>
<td>33.6 ± 0.57</td>
<td>26.3 ± 0.57</td>
</tr>
<tr>
<td>Methanol</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Distilled water</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

IZ= inhibition zone. SD= Standard deviation,
The result showed that around 200 μL/mL of \([\text{Co(Phen)}_2(\text{Cyt})(\text{H}_2\text{O})]\text{Cl}\) is sufficient to inhibit *S. pneumoniae* and *K. pneumoniae* and *E. coli* need around 300 μL/mL. *S. aureus* and *S. boydii* require minimum of 400 μL/mL.

**Table 5: MIC Assay of [Co(Phen)\(_2\)(Cyt)(H\(_2\)O)]Cl against tested bacterial pathogens**

<table>
<thead>
<tr>
<th>Bacterial strains</th>
<th>Observation of growth for each concentrations/ μL/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 200 300 400 600 800 1000</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>+    +    +    -    -    -    -</td>
</tr>
<tr>
<td>MRSA</td>
<td>+    +    -    -    -    -    -</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>+    -    -    -    -    -    -</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>+    +    -    -    -    -    -</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>+    -    -    -    -    -    -</td>
</tr>
<tr>
<td><em>S. boydii</em></td>
<td>+    +    +    -    -    -    -</td>
</tr>
</tbody>
</table>

Note: + = Growth of bacteria, - = No growth of bacteria.

Figure 4: Comparative antibacterial activity of metal salt, ligands, complexes and reference antibiotic.

Salt= CoCl\(_2\)6H\(_2\)O, Cyt=Cytosine, Phen=1,10-Phenanthroline, C1= [Co(Phen)\(_2\)(H\(_2\)O)\(_2\)]Cl\(_2\), C2= [Co(Phen)\(_2\)(Cyt)(H\(_2\)O)]Cl, RA1= Ciprofloxacin, RA2= Chloramphenicol

The result showed that around 200 μL/mL of [Co(Phen)\(_2\)(Cyt)(H\(_2\)O)]Cl is sufficient to inhibit *S. pneumoniae* and *K. pneumoniae*

MRSA and *E. coli* need around 300 μL/mL. *S. aureus* and *S. boydii* require minimum of 400 μL/mL.
**Determination of the Minimum Inhibitory Concentrations (MIC) of \([\text{Co(Phen)}_2(\text{Cyt})(\text{H}_2\text{O})]\text{Cl}\)**

MIC is the lowest concentration that completely inhibited the growth of microorganisms for 24 hours. The percent activity indexes of the complexes about the reference antibiotics were investigated, and they demonstrated significant comparative activity (Table 6). \([\text{Co(Phen)}_2(\text{Cyt})(\text{H}_2\text{O})]\text{Cl}\) demonstrated better activities than ciprofloxacin against MRSA, *S. pneumoniae*, and *E. coli* and equivalent activity against *S. boydii*. (Table 6). Similarly, it showed better activities than ciprofloxacin against MRSA and *E. coli* (Table 6). On the other hand, \([\text{Co(Phen)}_2(\text{H}_2\text{O})_2]\text{Cl}_2\) showed better activities than chloramphenicol against *S. pneumoniae* and *S. boydii* and equivalent activity against *E. coli*.

Table 6: The % Activity Index data of the complexes against the tested bacteria compared to ciprofloxacin and chloramphenicol

<table>
<thead>
<tr>
<th>Compound</th>
<th><em>S. aureus</em></th>
<th>MRSA</th>
<th><em>S. pneumoniae</em></th>
<th><em>E. coli</em></th>
<th><em>K. pneumoniae</em></th>
<th><em>S. boydii</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cip</td>
<td>Chlo</td>
<td>Cip</td>
<td>Chlo</td>
<td>Cip</td>
<td>Chlo</td>
</tr>
<tr>
<td>([\text{Co(Phen)}_2(\text{H}_2\text{O})_2]\text{Cl}_2)</td>
<td>-10.38</td>
<td>-18.53</td>
<td>-7.91</td>
<td>-13.70</td>
<td>5.35</td>
<td>-9.54</td>
</tr>
<tr>
<td>([\text{Co(Phen)}_2(\text{Cyt})(\text{H}_2\text{O})]\text{Cl})</td>
<td>-2.70</td>
<td>-11.54</td>
<td>11.86</td>
<td>4.81</td>
<td>15.23</td>
<td>-1.06</td>
</tr>
</tbody>
</table>

MRSA = Methicillin resistant *S. aureus*, Cip = ciprofloxacin, Chlo = chloramphenicol

**CONCLUSION**

The synthesis brought about Co(II) and the ligands in a rigid configuration. This resulted in convenient electronic environment by the delocalization of π-electrons over the whole cationic unit. The latter phenomena reduced the polarity of the complexes which increased the liposolubility. Consequently, the penetration of the complexes into the cell wall and lipid membrane is enhanced which inhibits the growth of the tested gram-positive and gram-negative bacteria. The latter phenomenon demonstrates the wide-range activities of the complexes.

**ACKNOWLEDGEMENTS**

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