Spectroscopic Studies of Cu2+ and Zn2+ Binding to Prodigiosin Analogs

Karen Chichetu  
*Portland State University*

Papireddy Kancharla  
*Portland State University*

Shilah Bonnett  
*Portland State University*

Kevin Reynolds  
*Portland State University*

Follow this and additional works at: [https://pdxscholar.library.pdx.edu/studentsymposium](https://pdxscholar.library.pdx.edu/studentsymposium)

Part of the Molecular Biology Commons

Let us know how access to this document benefits you.

Chichetu, Karen; Kancharla, Papireddy; Bonnett, Shilah; and Reynolds, Kevin, "Spectroscopic Studies of Cu2+ and Zn2+ Binding to Prodigiosin Analogs" (2013). Student Research Symposium. 9.  
[https://pdxscholar.library.pdx.edu/studentsymposium/2013/Poster/9](https://pdxscholar.library.pdx.edu/studentsymposium/2013/Poster/9)

This Poster is brought to you for free and open access. It has been accepted for inclusion in Student Research Symposium by an authorized administrator of PDXScholar. Please contact us if we can make this document more accessible: pdxscholar@pdx.edu.
Spectroscopic Studies of Cu$^{2+}$ and Zn$^{2+}$ Binding to Prodigiosin Analogs and Tambjamins

Karen Chichetu, Papireddy Kancharla, Shilah Bonnet and Kevin Reynolds
Department of Chemistry, Portland State University, Portland, Oregon, 97201

Background

Prodigiosins (prodiginines) are a family of secondary metabolites that were first isolated from the bacterium Serratia marcescens. These natural compounds are red pigmented and characterized by a tri-pyrrole skeleton with a C-4 methoxy group (Figure 1). They have been reported to have good biological properties that include antitumor, antimalarial, antimicrobial and immunosuppressive activities. In continuation of our drug discovery program on efficient antimalarial agent, we have synthesized a library of novel analogs of the natural prodigiosins and tambjamins (Figure 2). Most of these analogs exhibited enhanced antimalarial activity against chloroquine-sensitive (CQ) D6 and chloroquine-resistant (CQR) Dd2 and 7G8 strains of P. falciparum and improved toxicological profiles in human liver hepatocellular carcinoma cell line (HepG2). In this work, we studied the interaction between prodigiones and Cu$^{2+}$ and Zn$^{2+}$ using UV and Mass Spectroscopy techniques. Early results show that our prodigiosin analogs have good metal binding properties with dissociation constants (Kd) in the micromolar range. Understanding metal binding activities of prodigiones can be key in understanding their pharmacological action. With some drug-metal complexes already in use for the management of conditions such as cancer, diabetes, ulcers and rheumatoid arthritis there is increased interest in this area.

UV Binding Studies

**Cu$^{2+}$ Titration**

![Figure 3. UV-Vis titration of 1 (10 µM) with Cu(DC1)2 added in 0.1 equiv at 25 °C. The UV-Vis titration studies confirmed the binding of Cu$^{2+}$ to 1 to form 1-Cu complex as indicated by loss of absorbance of 1 at 467 nm and gain of absorbance at 500 and 600 nm.](image)

**Zn$^{2+}$ Titration**

![Figure 4. UV-Vis titration of 1 (10 µM) with ZnCl2 added in 0.1 equiv at 25 °C. The UV-Vis titration studies confirmed the binding of Zn$^{2+}$ to 1 to form 1-Zn complex as indicated by loss of absorbance of 1 at 467 nm and gain of absorbance at 505 and 527 nm.](image)

**Table 1.** Experimental Kd values for metal ion binding to synthetic prodigiones and tambjamins. Data shown is mean ± s.d. dev.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cu$^{2+}$ Kd, µM</th>
<th>Zn$^{2+}$ Kd, µM</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPR-E3</td>
<td>14.84 ± 2.1</td>
<td>10.85 ± 6.1</td>
</tr>
<tr>
<td>KPR-99</td>
<td>4.25 ± 1.2</td>
<td>1.85 ± 0.7</td>
</tr>
<tr>
<td>KPR-276</td>
<td>13.27 ± 2.2</td>
<td>No binding</td>
</tr>
<tr>
<td>KPR-421</td>
<td>7.36 ± 0.9</td>
<td>No binding</td>
</tr>
<tr>
<td>KPR-528</td>
<td>6.46 ± 0.01</td>
<td>No binding</td>
</tr>
<tr>
<td>KPR-655</td>
<td>19.14 ± 4.9</td>
<td>No binding</td>
</tr>
</tbody>
</table>

**Mass Spec. analysis of undecylprodiginine(2)-Cu complex**

![Figure 5. (A) ES$^+$ of undecylprodiginine, and (B) undecylprodiginine-Cu complex](image)

Discussion

- UV titration of prodigiosin with Cu and Zn confirm previous work by Park et al., 2003 in which prodigiosin was shown to form complexes with the two metal ions.
- Prodigiosin analogs are more selective towards Cu$^{2+}$ than Zn$^{2+}$.
- The differences in selectivity for metal binding could be a result of selection by preferential binding geometry of the 2 metal ions.
- Cu$^{2+}$ binds to most ligands more strongly than Zn$^{2+}$ and it has a preference for tetragonal geometry which arises from the Jahn-Teller effect, a result of its d$^{10}$ configuration. Zn$^{2+}$ has d$^{10}$ configuration and a preference for tetrahedral geometry.
- MS analysis of the 2-Cu complex suggests formation of a mixture of different Cu complexes.
- More work needs to be done with the synthetic prodigiones and tambjamins to determine the nature of the complexes they form with Cu$^{2+}$ and Zn$^{2+}$ and the geometry of the metals in these complexes in order to fully understand their selectivity.

Acknowledgements

This work was supported by a grant from the National Institutes of Health (Grant GM077147).

References

