ABSTRACT

Tyrosine is indirectly involved in nerve transduction in CNS (Central Nervous System) and behaves as a good chelating agent for many metal ions, because of its structure. This prompted us to carry investigations of several mixed ligand complexes forming equilibria involving tyrosine as one of the ligand with nutrient and toxic metal ions. Present piece of work describes investigation of ternary systems of Tyrosine with alanine, phenylalanine, Glycine, valine, leucine and cadmium at 35±1°C at three different ionic strengths in aqueous medium. The values of proton dissociation constants of ligands and formation constants of complexes were calculated by algebraic method of Chaberek and Martell as modified by Dey et al. pH-metric data was subjected to SCOGS computer program. Thermodynamic formation constants were obtained by extrapolating the values to zero ionic strength in log β vs. √μ curve. Finally, all the systems are explained on the basis of speciation of species in entire pH range of the experiment.

Key words: Mixed Ligand Complexes, Ternary systems, Thermodynamic formation constant.

INTRODUCTION

Tyrosine (Tyr) is enzymatically produced from L-phenylalanine. It plays a key role in signal transduction[1]. Physiologically, tyrosine is involved in synthesis of (3,4-dihydroxyphenyl)alanine (DOPA) which is precursor to neurotransmitters[2]. All the other selected ligands are also structurally and biologically related to each other and physiologically active.

In the series of various studies[3-5] investigations were carried out for several metal ions, such as Ni(II), Co(II), Cd(II) and organometallic compounds etc[6-12]. Present paper describes the results of studies on Cd(II)-Tyr-Ala/Gly/Val/Lue/Phe biligand systems at 35±1°C at μ =0.05M,0.10M and 0.15M(NaNO₃) in aqueous medium in equimolar conditions (Where, Tyr = Tyrosine, Ala = Alanine, Gly = Glycine, Val = Valine, Lue = Leucine and Phe = Phenylalanine).
These studies are helpful in understanding interference of cadmium in Central Nervous System (CNS) and therapeutic approach to cadmium toxicity.

MATERIALS AND METHODS

All the reagents used were of highest purity Merck products. Solutions were prepared in CO$_2$ free doubly distilled water (pH 6.8). Proton-ligand, monoligand, and biligandequilibria were investigated by pH-metric method using an Elico digital pH-meter model LI-127 with ATC probe and combined electrode type (CL-51B- Glass Body; range 0-14 pH unit; 0-100°C Automatic/Manual) with accuracy ±0.01. Titration mixtures were prepared as described elsewhere at 35±1°C and µ = 0.05M, 0.10M and 0.15M (NaNO$_3$) in aqueous medium and titrated against 0.1M NaOH:

Titration curves obtained by plotting pH against ‘α’ (where, ‘α’ is the moles of alkali added per mole of metal/ligand). Representative curves are shown in fig. 1.

RESULTS AND DISCUSSION

The qualitative analysis of proton-ligand, metal-monomoligand and metal-biligandequilibria were done by examination of titration curves (Fig. 1). This examination reveals that Cd(II) ion coordinates simultaneously with both the ligands tyrosine and ligand ‘B’ forming MAH, MA, MB type monoligand and MABH and MAB type biligand complexes (where, Ligand ‘A’ = Tyrosine and Ligand ‘B’ = Alanine/Glycine /Valine /Leucine /Phenylalanine). The proton dissociation constants of ligands and formation constants of monoligand and biligand complexes were determined by using algebraic method of Chaberek& Martell[13,14] as modified by Dey et. Al[15]. These values were refined by SCOGS (Stability Constants of Generalized Species) computer program[16-18]. Log β values were plotted against √µ and extrapolated to zero ionic strength in order to obtain thermodynamic formation constants.

The order of formation constants was found to be as follows:
Cd(II)-Tyr-Ala>Cd(II)-Tyr-Gly>Cd(II)-Tyr-Val >Cd(II)-Tyr-Leu>Cd(II)-Tyr-Phe

Higher value of alanine complexes is due to +I effect of – CH$_3$ group. Further, the stability of valine and leucine complexes is justified on the basis of vibrational effects and starichindrence of side groups.

Speciation curves for these systems (Fig. 2.1 and 2.2) show that the concentrations of Cd(II)AH and Cd(II)B increase in solution up to pH ≈ 7.5. Simultaneously, Cd(II)ABH is also come in existence and its percentage concentration increases up to pH ≈8.0. Nonprotonated ternary complex Cd(II)AB start forming near pH 7.5 and its concentration increases appreciably above pH 8.0. Pattern of curves indicate that Cd(II)AB is formed by all the monoligand and monoprotonatedbiligand species (Scheme 1), which is also supported by an inflection at ‘α’ ≈ 3.0 (pH ≈ 9.8) in biligand titration curve. Formation of Cd(II)A is found to be negligible.

Scheme 1 Complexation Equilibria for Cd(II)-Tyr-Ala/Gly/Val/Leu/Phe (1:1:1)Systems
Percentage concentration of nonprotonated Cd(II)AB complex is found to be low in case of Cd(II)-Tyr-Phe system as compared to Cd(II)-Ligand A-Ligand B systems. This is attributed to the repulsion between bulky side groups of two ligands in the former system as well as hydrophobic nature of phenyl ring of phenylalanine, whose free ligand concentration increases at higher pH.

All the selected ligands are physiologically active and selected conditions are also biomimimetic. Hence present work is helpful in understanding physiological and medicinal chemistry of cadmium.

Table 1 Thermodynamic Formation Constants of Proton-Ligand and Monoligand(1:1) Complexes of Cadmium and Dissociation Constant of Protonated Complex at 35±1°C

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Tyr</th>
<th>Ala</th>
<th>Gly</th>
<th>Val</th>
<th>Leu</th>
<th>Phe</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \log \beta_{HA} )</td>
<td>10.15</td>
<td>9.93</td>
<td>9.65</td>
<td>9.52</td>
<td>9.26</td>
<td>9.10</td>
</tr>
<tr>
<td>( \log \beta_{H2A} )</td>
<td>19.12</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>( \log \beta_{MAH} )</td>
<td>14.55</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>( \log \beta_{MA} )</td>
<td>5.02</td>
<td>4.88</td>
<td>4.71</td>
<td>4.46</td>
<td>4.35</td>
<td>4.18</td>
</tr>
<tr>
<td>( \log \beta_{MAH} )</td>
<td>4.37</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>( \text{pK}_{\text{MAH}} ) &amp; 9.5 &amp; - &amp; - &amp; - &amp; - &amp; -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All, Gly, Val, Leu, Phe become ligand ‘B’ in biligand systems

\( \text{pK}_{\text{MAH}} = \text{Dissociation Constant of Protonated Complex} \)

Table 2 Thermodynamic Formation Constants for Cd(II)-Tyr-Ligand ‘B’ (1:1:1) Biligand Systems at 35±1°C

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ala</th>
<th>Gly</th>
<th>Val</th>
<th>Leu</th>
<th>Phe</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \log \beta_{MAH} )</td>
<td>19.44</td>
<td>19.18</td>
<td>18.73</td>
<td>18.54</td>
<td>18.11</td>
</tr>
<tr>
<td>( \log \beta_{MA} )</td>
<td>10.92</td>
<td>10.66</td>
<td>10.23</td>
<td>10.11</td>
<td>9.65</td>
</tr>
<tr>
<td>( \log K_{MAH} )</td>
<td>9.29</td>
<td>9.03</td>
<td>8.58</td>
<td>8.39</td>
<td>7.96</td>
</tr>
<tr>
<td>( \log K_{MA} )</td>
<td>4.89</td>
<td>4.63</td>
<td>4.18</td>
<td>3.99</td>
<td>3.56</td>
</tr>
<tr>
<td>( \log K_{MAH} )</td>
<td>4.41</td>
<td>4.32</td>
<td>4.12</td>
<td>4.04</td>
<td>3.78</td>
</tr>
<tr>
<td>( \log K_{MA} )</td>
<td>5.58</td>
<td>5.34</td>
<td>4.93</td>
<td>4.79</td>
<td>4.33</td>
</tr>
<tr>
<td>( \log K_{MAH} )</td>
<td>6.02</td>
<td>5.95</td>
<td>5.79</td>
<td>5.76</td>
<td>5.47</td>
</tr>
<tr>
<td>( \text{pK}_{\text{MAH}} ) &amp; 8.54 &amp; 8.52 &amp; 8.48 &amp; 8.43 &amp; 8.46</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( \text{pK}_{\text{MAH}} = \text{Dissociation Constant of Protonated Complex} \)
Fig 1. Representative pH vs. ‘a’ Curves
Curve 1 represents Ligand ‘A’ (Tyr) Titration Curve
Curve 2 represents Ligand ‘B’ (Ala/Gly/Val/Lue/Phe) Titration Curve
Curve 3 represents Metal-Ligand ‘A’ (1:1) Titration Curve
Curve 4 represents Metal-Ligand ‘B’ (1:1) Titration Curve
Curve 5 represents Mixed-Ligand (1:1:1) Titration Curve
Curve ‘T’ represents Theoretical Composite Curve

Representative speciation curve for Cd(II)-Tyr-Ala/Gly/Val/Lue/Phe (1:1:1) Systems

Fig. 2.1     Fig. 2.2
Where, Curve 1: [M]; 2: [MB]; 3: [MAH]; 4: [MA]; 5: [MABH]; 6: [MAB]
REFERENCES


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