ABSTRACT

The present work describes the complex formation of the Cd (II) with amino acids (L-glutamine, L-asparagine, L-valine, L-leucine, α-alanine and glycine) as primary ligands and vitamin-B7 (β-biotin) as secondary ligand by polarographic technique. The Cd (II) formed 1: 1, 1: 2 and 1: 2: 1 complexes at pH = 7.30 ± 0.01, μ = 1.0 M KNO₃. The Cd (II) showed the two electrons reversible reduction wave with diffusion controlled nature. The trend of the stability constants of the complexes with respect to primary ligand was L-glutamine < L-asparagine < L-valine < L-leucine < α-alanine < L-glycine. The thermodynamic parameters like enthalpy, free energy, and entropy change is also determined. The results showed that the complexes were lesser stable at high temperature and formed with the evolution of heat.

Keywords: [Cd-L-amino - acids-vitamin-B₇] complexes, Cd complexes.

INTRODUCTION

The metal such as Cd ((II) are required for biological processes such as oxygen transport, electron transfer, and catalysis and also necessary to maintain body function to optimize growth, reproductive performance, and immune response. The minerals mis-regulation leads to many serious diseases such as oxidative stress diabetes, amyotrophic lateral sclerosis, cancer, inflammatory, neurodegenerative, and potential to various toxic effects etc. Weak interactions involving functional groups of coordinated amino acids in metal complexes may mimic the modes and effects of the interactions in metalloproteins. Complexes of amino acids and vitamins with metal ions have great importance because of their physiological and pharmacological activities. Some of the research work reported antitumor activities. Biotin is a co-factor and coenzyme involved in vital biological process such as fatty acid synthesis, gluconeogenesis, amino acids metabolism, and carbon dioxide fixation reaction. Therefore the combination of the amino acids and vitamin-B7 with Cd (II) are used to reduce excess metal accumulation and toxicity.

Amino acid side chain groups are involved in various biological functions such as the molecular recognition and catalytic activity of the enzyme active center and formation of an environment with the metal ions used to in medicinal fields. Weak interactions involving functional groups of coordinated amino acids in metal complexes may mimic the modes and effects of the interactions in metalloproteins. Complexes of amino acids and vitamins with metal ions have great importance because of their physiological and pharmacological activities. Some of the research work reported antitumor activities. Biotin is a co-factor and coenzyme involved in vital biological process such as fatty acid synthesis, gluconeogenesis, amino acids metabolism, and carbon dioxide fixation reaction. Therefore the combination of the amino acids and vitamin-B7 with Cd (II) are used to reduce excess metal accumulation and toxicity. The coordination chemistry of the Cd (II) metal ion has shown too significant for the organisms. The minerals mis-regulation leads to many serious diseases such as oxidative stress diabetes, amyotrophic lateral sclerosis, cancer, inflammatory, neurodegenerative, and potential to various toxic effects etc. Weak interactions involving functional groups of coordinated amino acids in metal complexes may mimic the modes and effects of the interactions in metalloproteins. Complexes of amino acids and vitamins with metal ions have great importance because of their physiological and pharmacological activities. Some of the research work reported antitumor activities. Biotin is a co-factor and coenzyme involved in vital biological process such as fatty acid synthesis, gluconeogenesis, amino acids metabolism, and carbon dioxide fixation reaction. Therefore the combination of the amino acids and vitamin-B7 with Cd (II) are used to reduce excess metal accumulation and toxicity.

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MATERIAL AND METHODS

Reagents

All chemicals were of reagent grade and used without further purification and their solutions were prepared in double distilled water. The concentrations of Cd (II), L-amino acids and vitamin-B7 (biotin) were taken in the ratio of 1: 40: 40 and the pH of the analyte were fixed at 7.30 ± 0.01 which were adjusted with the required amount of HCl or sodium hydroxide as needed. The pH of the analyte was stabilized by the addition of potassium dihydrogen phosphate buffer.

Instruments

The polarograms were obtained on a manual polarograph using polyflex galvanometer (PL-50). The polarographic cell was of Laitinen and Lingane type in which capillary of 5.0 cm in length with 0.04 mm in diameter was used. The value of m¹/₂ was 2.40 mg²-s¹/₂ at 60.02 cm. The pH of the analyte was measured using digital pH Meter Model (III-101 E).

Polarographic procedure

In complex formation of [Cd - L-amino acidate - vitamin-B7] system, the concentrations of primary ligands i.e. L-amino acids varied from 0.5 mM to 30.0 mM at 0.025 M and 0.050 M (fixed) concentration of secondary ligand (vitamin-B7). The concentrations Cd (II), KNO₃ and gelatin (as suppressor) in the analyte were 0.50 mM, 1.0 M and 0.001 % respectively. The E₁/₂ showed more negative with the addition of secondary ligand (vitamin-B7) to binary complexes of the [Cd - L-amino acids] system that showed ternary complex formation of 1: 1, 1: 1: 2 and 1: 2: 1 complexes. Cd (II) showed the well-defined two electron reversible reduction wave with half-wave potential -0.586 V vs. S. C. E. at pH = 7.30 ± 0.01 and μ = 1.0 M KNO₃ at 25°C and 35°C.

RESULTS AND DISCUSSION

The values of stability constant were given in Table 1 and the polarographic characteristics and data plots of Fij [X, Y] against [X][Where Fij is a Schaar and McMaster function to evaluate the stability constant [ij, X = glycine, Y = vitamin-B7 and i and j are their stoichiometric numbers respectively] for [Cd -glycinate - vitamin-B7] system were given in Table 2 and Figure 1 respectively, to determine the values of function F₁₁, F₂₁, F₁₂ and F₃₀. The comparisons of the stability of binary and ternary complexes by the values of log K were given by the following equation:

**log K = log β̃₁ + 1/2 log β̃₂ + log β̃₃**

The calculated values are as follows 0.463, 0.447, 0.436, 0.620, 0.606 and -0.277 respectively for [Cd -glycinate - vitamin-B7], [Cd - α-alaninate - vitamin-B7], [Cd - L-leucinate - vitamin-B7], [Cd - L-valinate - vitamin-B7], [Cd - L-asparaginate – vitamin-B7] and [Cd - L-glutaminate - vitamin-B7] systems respectively. The positive values of logKm confirmed that the ternary complexes are more stable than their corresponding binary complexes and the negative values showed that the binary complexes are more stable than the corresponding ternary complexes.

The trend of stability constant of the complexes followed as L-glutamine < L-asparagine < L-valine < L-leucine < α-alanine < L-glycine. The increase of stability constant of Cd complexes with amino acids can be explained on the basis of side chain. The amino acids act as bidentate ligands which bond through COOH and amino groups to Cd (II) metal and form five member chelate ring system. The β-biotin coordinates through the oxygen and nitrogen atoms of ureidyl group with Cd (II) metal ion. But in case of the L-valine and L-leucine the order of the stability is reversed due to higher basicity of L-leucine than L-valine.

It is cleared from the values of stability constants that the complexation of the amino acids and vitamin with the Cd (II) complexes are used to in metal toxicity and in oxidative stress.

**Thermodynamics parameters**

The thermodynamic stability of complexes is also ascertained. The values of thermodynamic parameters such as enthalpy change (ΔH), free energy change (ΔG), and entropy change (ΔS) of complexes were given in Table 3.
which showed that these complexes were lesser stable at higher temperatures\(^{28}\). The values of \(\Delta H\) of complexes showed that there is greater interaction between metal and ligands. As the composition of complex changes, the value of enthalpy varied. The values of \(E_{1/2}\) of complexes with increase of concentration also supported this (Fig. 2, Table 2). The negative values of enthalpy confirmed that the complexes are formed with the evolution of heat. The negative values of \(\Delta H\) indicated that the complexes were formed with the evolution of heat. The thermodynamic parameters of complexes were calculated by the following equations\(^{29}\):

\[
\Delta H = 2.303 \frac{RT_2}{T_2 - T_1} (\log \beta_2 - \log \beta_1) / T_2 - T_1 \tag{i}
\]

\[
\Delta G = -2.303 RT \log \beta \tag{ii}
\]

\[
\Delta G = \Delta H - T\Delta S \tag{iii}
\]

| Table 1. Stability constant of [Cd -L-amino acidate - vitamin-B\(_7\)] system. |
|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Primary ligands  | \(\log \beta_{01}\) | \(\log \beta_{02}\) | \(\log \beta_{03}\) | \(\log \beta_{10}\) | \(\log \beta_{11}\) | \(\log \beta_{12}\) | \(\log \beta_{20}\) |
| L-glycine        | -                | -                | -                | 4.30             | 7.60             | 9.64             | 4.71             |
| a-alanine        | -                | -                | -                | 4.23             | 7.46             | 9.43             | 4.60             |
| L-leucine        | -                | -                | -                | 4.17             | 7.35             | 9.34             | 4.53             |
| L-valine         | -                | -                | -                | 4.11             | 7.21             | 9.16             | 4.45             |
| L-asparagine     | -                | -                | -                | 4.07             | 7.18             | 9.10             | 4.32             |
| L-glutamine      | -                | -                | -                | 4.00             | 7.04             | 8.91             | -                |
| vitamin-B\(_7\)  | 2.01             | 2.86             | -                | -                | -                | -                | -                |

| Fig. 1: Plots of \(F_{ij}[X, Y]\) vs. \([X]\) for [Cd -L-amino acids - vitamin-B\(_7\)] system. |

| Table 2. Polarographic characteristics and \(F_{ij}[X, Y]\) values for the [Cd - glycinate - vitamin-B\(_7\)] system Cd (II) = 0.5mM, \(\mu = 1.0M\) KNO\(_3\), pH = 7.30± 0.01, Temp. = 25ºC. |
|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| \([gly]\) \times 10^3 M | \(E_{1/2}'-V\) vs. SCE | \(\log I_{a}/I_{c}\) | \(F_{as}[X,Y]\) \times 10^6 | \(F_{as}[X,Y]\) \times 10^6 | \(F_{as}[X,Y]\) \times 10^6 | \(E_{1/2}'-V\) vs. SCE | \(\log I_{a}/I_{c}\) | \(F_{as}[X,Y]\) \times 10^6 | \(F_{as}[X,Y]\) \times 10^6 | \(F_{as}[X,Y]\) \times 10^6 |
| 0.00             | 0.586            | -                | 4.011            | 83.73            | 174.07           | 43.65            | -                | 7.93              | 272.52           | 308.33           |
| 0.50             | 0.648            | 0.0073           | 131.81           | 255.59           | 176.25           | 43.65            | 0.061            | 0.0073            | 358.07           | 700.29           |
| 1.00             | 0.660            | 0.0073           | 266.18           | 262.17           | 178.44           | 43.66            | 0.067            | 0.0147            | 593.14           | 585.22           |
| 2.00             | 0.673            | 0.0147           | 902.68           | 449.33           | 182.8            | 43.65            | 0.682            | 0.0222            | 1821.21          | 906.64           |
| 3.00             | 0.682            | 0.0222           | 1943.74          | 645.24           | 187.67           | 43.66            | 0.691            | 0.0222            | 3718.34          | 1236.8           |
| 4.00             | 0.689            | 0.0299           | 3430.55          | 849.89           | 191.54           | 43.67            | 0.697            | 0.0299            | 6310.65          | 1575.68          |
| 5.00             | 0.695            | 0.0378           | 5120.18          | 1063.23          | 195.9            | 43.66            | 0.703            | 0.0378            | 9624.53          | 1923.32          |
| 6.00             | 0.699            | 0.0457           | 7716.21          | 1285.36          | 200.27           | 43.67            | 0.707            | 0.0457            | 13685.77         | 2279.64          |
| 8.00             | 0.707            | 0.0457           | 14047.83         | 1755.48          | 208.97           | 43.66            | 0.714            | 0.0457            | 24156.59         | 3018.58          |
| 10.00            | 0.713            | 0.0539           | 22611.35         | 2260.73          | 217.7            | 43.66            | 0.719            | 0.0539            | 37931.13         | 3792.32          |
| 20.00            | 0.733            | 0.0621           | 106214.69        | 5310.53          | 261.34           | 43.65            | 0.738            | 0.0621            | 163841.66        | 81916.87         |
| 30.00            | 0.745            | 0.0621           | 277034.03        | 9324.33          | 305.02           | 43.65            | 0.750            | 0.0621            | 403535.53        | 13450.92         |

\(\log A = 0.60, \log B = 4.92, \log C = 8.24, \log D = 9.64\)

\(\log A = 0.89, \log B = 5.43, \log C = 8.49, \log D = 9.64\)
Fig. 2: Current – Voltage curves for [Cd – L-amino acids – β-biotin] system, [β-biotin] = 0.025M (fixed).
Table3. Thermodynamic Parameters of [Cd -L-amino acids - vitamin- B<sub>j</sub>] ternary system Cd (II) = 0.5mM, μ = 1.0M KNO<sub>3</sub>, pH = 7.30± 0.01, Temp. = 25ºC/35ºC.

<table>
<thead>
<tr>
<th>System</th>
<th>Stability Constant</th>
<th>-ΔH</th>
<th>-ΔG</th>
<th>-ΔS</th>
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<tr>
<td></td>
<td>log β&lt;sub&gt;11&lt;/sub&gt;</td>
<td>log β&lt;sub&gt;12&lt;/sub&gt;</td>
<td>log β&lt;sub&gt;13&lt;/sub&gt;</td>
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<td></td>
<td>25ºC/35ºC</td>
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<td>25ºC/35ºC</td>
<td>(35ºC-25ºC)</td>
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<td></td>
<td>4.10</td>
<td>7.32</td>
<td>9.09</td>
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<td>7.11</td>
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CONCLUSION

The paper suggested that L-amino acids coordinate bidentate towards the metal ion and to form a planar five membered chelate ring and bonded through the amino nitrogen and COOH with the Cd (II) ion. The stability constant may be used to reduce metal toxicity, oxidative stress and nephrotoxicity. The thermodynamics parameters showed that the complexes were lesser stable at high temperature and formed with the evolution of heat.

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