Chemical Distribution, Stability and Structures of Ternary Metal Chelates in Ethylene glycol-Water Media Involving Mercaptosuccinic acid and Some Non-Essential Amino acids

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ABSTRACT

There has been focus upon the study of stability constants of amino acids with metal ions since they processes antibacterial activities. The stability constants of ternary complexes were determined by pH metric analysis in aqueous solution at 25.0°C between ligands (Mercaprosuccinicacid (MSA), Glycine (GLY), L-Aspartic acid (ASP) and L-Asparagine (ASN)) and some transition metal ions(Co(II), Ni(II), Cu(II) and Zn(II)) in varying Ethylene glycol-water media. The “MINIQUAD75” software tool analysed the potentiometric data to create a complexation model for each system. Based on the calculated equilibrium and stability constants, the most likely binding mechanism for each ternary species was discussed. Their relative stabilities and plausible structures were also proposed.

Keywords: Glycine, L-Aspartic acid, BestFit, MINIQUAD75, Chemical speciation.

INTRODUCTION

In recent years, attention has been focused on transition metals amino acid complexes because they are effective antibacterial agents against \textit{Staphylococcus aureus} and \textit{Escherichia coli} and can be utilised to produce food for humans and animals\textsuperscript{1}. Many attempts have been made to evaluate different factors affecting the stability of the metal chelates along with their stability constants\textsuperscript{2,3}. There are 20 different amino acids that make up proteins out of which 9 are essential and 11 are non-essential amino acids\textsuperscript{4}. Through their amine and carboxylate groups, amino acids combine with different metal ions to form stable five-membered chelates\textsuperscript{5-7}.

Glycine (Gly) is an important building block for all proteins in the body (Fig. 1(b)). It helps the body absorb calcium, build muscle protein, regulates protein turnover, heal after surgery or an injury, and make hormones, enzymes, and antibodies\textsuperscript{8}. L-Aspartic acid (Asp) is an amino acid that is found in large amounts in plant proteins but is not essential to life (Fig. 1(c)). It is an important part of keeping
proteins soluble and ionic. Asp is often used to treat chronic fatigue because it is a key part of how cells make energy. One of the 20 most common natural amino acids is L-Asparagine (Asn). Its side-chain group is carboxamide (Fig. 1(d)). It plays a role in how the brain and nervous system work. It is needed by the nervous system to keep things in balance, and the liver needs it to change amino acids from one form to another. Mercaptosuccinic acid (MSA) is a potentially important tridentate ligand that can form strong complexes with many metal ions and has chemotherapeutic uses in a variety of solvents. Metals like cobalt, nickel, copper, and zinc are important for living things.

**EXPERIMENTAL**

**MATERIALS AND METHODS**

Standardized sodium hydroxide was used to test acid solutions. Merck p.a. reagent sodium chloride was used as a background electrolyte. By adding NaCl as a supporting electrolyte, the amount of ions in each solution was changed to 0.16 M. Himedia India was used to buy MSA, Glycine, L-Aspartic acid, and L-Asparagine. Using standard HCl, the Gran method was used to check the solutions’ purity and figure out their exact concentrations. The metal(II) stock solutions were standardised by titrating them with EDTA and a suitable indicator.

Measurements

The ternary stability constants of MSA as primary ligand, glycine, L-aspartic acid and L-asparagine as secondary ligands were determined using pH titration with following composition.

\[ \text{a — HCl} + \text{MSA} + \text{glycine} + \text{metal(II)}; \]
\[ \text{b — HCl} + \text{MSA} + \text{L-aspartic acid} + \text{metal(II)}; \]
\[ \text{c — HCl} + \text{MSA} + \text{L-asparagine} + \text{metal(II)}. \]

Metal(II) = Co(II) or Ni(II) or Cu(II) or Zn(II).

**Approach**

pH metric titrations were conducted in 0-60%v/v EG-Water media by using an auto-titrator Metrohm 877 titrino plus Switzerland in conjunction with pH sensitive electrode under the temperature of 298 K as described elsewhere. The electrode was standardized with standard buffer solutions.

**Metal-Ligand Ternary Systems**

MINIQUAD75 computer programme was used to calculate stability constants. A set of typical species formed for the different 1:1:1 M(II): MSA: GLY, M(II): MSA: ASP and M(II): MSA: ASN systems is shown in Fig. 2.

**RESULTS AND DISCUSSION**

**Modelling of chemical species**

The metal-ligand stability constants of ternary complexes were evaluated assuming that the
formation of polynuclear complexes and hydrolyzed products were not formed. In this ternary (M-L-X) complexes it is observed that the metal forms the complex first with the primary ligand (L) at lower pH and then metal-primary ligand (M-L) curves comes in to contact with the secondary ligand (X) to form the mixed ligand complex at higher pH. Secondary ligand does not come into contact with metal ions at lower pH. In other words mixed ligand complex formation takes place when M-L complex formation is complete. The best fit models for ternary complexes with MSA and chosen amino acids (GLY, ASP & ASN) have been given in Tables 1-3. Species like MLX, MLX2 and MLXH were detected for M(II)-MSA-X (X=GLY or ASN or ASP). Overall stability constants (log β) with minimal standard deviation (SD) in specifies the exactness of these constraints.

Species Distribution Plots
The weak binary metal complexes render the essential metals accessible, while the stable ternary complexes transport metal ions in biological systems. The plausible forms and their distribution of protonated un-protonated complexes observed in 20% v/v EG–water mixtures that suit best for ternary complex hypothesis and their respective relative distribution plots of several species was plotted using computer program ORIGIN 8.5 and shown in Fig. 3. The present study found MLX, MLX2 species for M(II)-MSA-Glycine and M(II)-MSA-L-Asparagine and MLX, MLXH species for M(II)-MSA-L-Aspartic acid in the pH range 3.0-9.5. At lower pH concentration of MLX species is high (Equilibria 1, 2, 3, 6, 7 and 8). As the concentration of MLX decreases with increasing pH the concentration of MLX2 (Equilibria 4, 5 and 9) increases gradually for M(II)-MSA-Glycine and and M(II)-MSA-L-Asparagine. As in the case of M(II)-MSA-L-Aspartic acid the pH increases the concentration of MLX decreased (Equilibria 1-3 and 6-8) and the concentration of MLXH are increased (Equilibria 10-12).

Table 1: Best fit model of M(II)-MSA- Glycine ternary complexes in 0-60% v/v EG-water mixtures

| %V/V | MLX  | log βMLX(SD) | MLXH | log βMLXH(SD) | MLX  | log βMLX(SD) | MLXH | log βMLXH(SD) |
|------|------|--------------|------|---------------|------|--------------|------|---------------|
| 0.0  | 11.74(11) | 20.17(14) | 13.02(08) | 23.98(09) | 11.97(09) | 20.57(22) | 13.25(18) | 23.40(17) |
| 10   | 12.11(13) | 20.98(15) | 13.49(13) | 24.83(15) | 12.46(22) | 21.40(11) | 13.74(10) | 25.27(11) |
| 20   | 12.71(18) | 20.83(18) | 13.98(11) | 25.71(14) | 12.96(14) | 22.77(21) | 14.23(23) | 26.17(18) |
| 30   | 13.22(09) | 22.77(09) | 14.49(21) | 26.63(20) | 13.22(09) | 22.77(09) | 14.49(21) | 26.63(20) |

Table 2: Best fit model of M(II)-MSA- L-aspartic acid ternary complexes in 0-60% v/v EG-water mixtures

| %V/V | MLX  | log βMLXH(SD) | MLXH | log βMLXH(SD) | MLX  | log βMLXH(SD) | MLXH | log βMLXH(SD) |
|------|------|--------------|------|---------------|------|--------------|------|---------------|
| 0.0  | 12.45(15) | 15.09(14) | 14.56(17) | 16.66(11) | 12.67(21) | 15.51(21) | 14.77(20) | 17.17(21) |
| 10   | 12.90(11) | 15.13(15) | 14.98(11) | 17.68(24) | 12.90(11) | 15.13(15) | 14.98(11) | 17.68(24) |
| 20   | 13.18(18) | 16.36(10) | 15.19(14) | 18.21(09) | 13.18(18) | 16.36(10) | 15.19(14) | 18.21(09) |
| 30   | 13.37(09) | 16.80(18) | 15.41(08) | 18.74(15) | 13.37(09) | 16.80(18) | 15.41(08) | 18.74(15) |
| 40   | 13.61(24) | 16.24(26) | 15.63(16) | 19.29(12) | 13.61(24) | 16.24(26) | 15.63(16) | 19.29(12) |
| 50   | 13.88(18) | 16.70(09) | 15.85(11) | 19.85(14) | 13.88(18) | 16.70(09) | 15.85(11) | 19.85(14) |
| 60   | 18.34(07) | 22.21(17) | 11.43(09) | 14.84(11) | 18.34(07) | 22.21(17) | 11.43(09) | 14.84(11) |
Table 3: Best fit model of M(II)-MSA- L-asparagine ternary complexes in 0-60% v/v EG-water mixtures

| %V/V | MLX | MLX2 | MLX | MLX2 |
|------|-----|------|-----|------|
|      | Co(II) pH Range: 2.5-9.5 | Ni(II) pH Range: 2.5-9.5 |
| 0.0  | 11.06(14) | 20.25(10) | 12.87(21) | 23.61(11) |
| 10   | 11.21(18) | 20.53(14) | 13.08(19) | 23.89(18) |
| 20   | 11.37(08) | 20.82(19) | 13.29(08) | 24.18(06) |
| 30   | 11.53(21) | 21.11(21) | 13.50(11) | 24.47(24) |
| 40   | 11.69(14) | 21.41(09) | 13.72(17) | 24.76(19) |
| 50   | 11.86(16) | 21.71(21) | 13.94(23) | 25.06(22) |
| 60   | 12.02(10) | 22.01(15) | 14.16(10) | 25.36(15) |

Fig. 2. The plausible forms of equilibria and their distribution of protonated and un-protonated complexes observed in the present study

Fig. 3. Species distribution plots of [A]: Co(II)–MSA–GLY; [B]: Ni(II)–MSA–ASP; [C]: Cu(II)–MSA–ASN in 20% v/v EG–water media

Inter Comparison of Stability Constants

By looking at Tables 1-3, we can see that due to the smaller size of Cu(II) makes its stability
constants higher than those of other studied metal complexes and shown in Fig. 4. This behaviour is in line with the Irving–Williams order.\(^{21}\)

nature of EG, eliminates water from the metal ions coordination sphere and creating them highly reactive to ligands resulting the complexes more stable. Thus, log β values should be directly related to the reciprocal of the medium’s dielectric constant (1/D), as shown in present study Fig. 5.

**Role of dielectric constant**

Being a protophilic and structural forming
Proposed structure

Depending upon the nature of the ligands and the metal ions and based on the basic chemical knowledge the structures of the ternary complexes are proposed and sketched using Chem Draw 18.1 computer program as shown in Fig. 6. MSA form strong bidentate complexes with transition metals. MSA at higher pH favors the (O, S) coordination and at physiological pH amino acids bound only through the amino acid side chain\textsuperscript{22-28}.

CONCLUSION

In this study, the results of a pH-metric study of ternary systems of MSA and three non-essential amino acids (Glycine, L-Aspartic acid, and Asparagine) with transition metal ions were used to figure out the constants. It was clear that MSA could form stable ternary complexes with studied metal ions, with glycine, L-aspartic acid, and L-asparagine as the secondary ligands. Due to the effect of the N- and O- donors, the formation of mixed-ligand complexes probability is more than binary.

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