STUDY OF BINARY AND TERNARY COMPLEXES OF MERCAPTO SuccINIC ACID AND L-ORNITHINE WITH ESSENTIAL METAL IONS IN ETHYLENE GLYCOL-WATER MEDIA

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ABSTRACT
During this study, the stability constants of the metals with mercaptosuccinic acid (MSA) and L-ornithine (L-Orn), as well as their ternary system have been studied in 0-60% ethylene glycol (EG)-water medium using the Metrohm 877 titrino plus auto-titrator between a pH ranges 0-14 at a temperature of 298 K. The modified Calvin-Wilson titration method was used to figure out the relative compositions of chemical species that were formed with metal ions and ligands. The MINIQUAD75 computer program was used to figure out the stability constants of the complexes. Some statistics have been discussed about the formed binary metal complexes and their ternary system, as well. The structures were proposed based on the observations.

Keywords: Ethylene glycol, Calvin-Wilson, Ternary Complexes.

INTRODUCTION
“In reaction with ligands, a metal ion can form a range of species dependent on the metal ion and other circumstances”.¹,² Speciation investigations can indicate species formation nature and degree with change in pH.³,⁴ Recent work has focused on aqueous and aqueous-organic binary and ternary complexes of important biological ligands. In aqueous-organic solvents, compounds evolve in new ways. Mercaprosuccinic acid (MSA) and L-Ornithine (L-Orn) are potentially important tridentate ligands that can form strong complexes with numerous metal ions with chemotherapeutic applications in a range of solvents.⁵-⁸ Despite extensive literature research⁹-¹² in this sector, nothing is known about MSA and L-Orn stability constants in ethylene glycol(EG)-water media. In the current study, the stability constants of binary complexes along with their ternary complexes of selected divalent metal ions with MSA and L-Orn have been reported in an aqueous-EG medium. This study gives insight into information about the formation of several species as a role of pH.

EXPERIMENTAL
0.05mol L⁻¹ MSA (Himedia, India) and L-Orn (Himedia, India) solutions were prepared with hydrochloric acid to improve the solubility. Ethylene Glycol (Merck, India) was used as received. All metal ion solutions were prepared using G.R. Grade chloride salts and an acidic strength of 0.05 mol L⁻¹ was maintained using HCl to inhibit metal salt hydrolysis. Standard approaches were used for the preparation and standardization of all solutions and data were subjected to ANOVA¹³ to identify any errors by the Gran plot approach.¹⁴,¹⁵
RESULTS AND DISCUSSION

Binary Metal-Ligand Complexes

Chemical species formed by metal-ligand interactions were measured using a modified\textsuperscript{17} Calvin-Wilson titration approach. On the electrode response, a correction factor was determined using SCPHD.\textsuperscript{18} MINIQUAD 75 computer programme\textsuperscript{19,20} was used to refine stability constants.

Modeling of Chemical Species

Tables 1 and 2 show the results of the models that suit best the M(II)-MSA and M(II)-L-Orn binary systems, respectively. The possible forms and their distribution of protonated and un-protonated complexes observed that suit best for the metal-ligand hypothesis has been shown in Fig.-1. The $\chi^2$, skewness, kurtosis, and crystallographic R-factors were used to assess the rationality and adequacy of the chemical models that reflect the metal-ligand system.

### Table 1: Best Fit Models for M(II)-MSA Binary Complexes in Solvent-Water Mixtures

| % V/V | Log $\beta_{MLXH}$ (SD) | NP | $U_{corr}$ x10$^{-8}$ | Skewness | Kurtosis | $\chi^2$ | R-Factor |
|-------|-------------------------|----|------------------------|----------|----------|---------|----------|
| ML    | MLH                    | ML2       | ML2H                  |          |          |         |          |
| 0.0   | 6.51(14)               | 10.71(19) | 11.71(11)             | 15.16(28)| 139      | 4.4     | 1.23     | 14.64    | 26.1     | 0.028    |
| 20    | 7.32(16)               | 11.59(16) | 12.84(22)             | 16.13(23)| 123      | 1.23    | -1.49    | 11.27    | 11.93    | 0.014    |
| 40    | 8.32(18)               | 12.17(14) | 13.85(16)             | 17.04(05)| 109      | 4.5     | -1.72    | 11.05    | 23.89    | 0.031    |
| 60    | 9.16(18)               | 13.05(21) | 14.34(22)             | 17.93(06)| 114      | 4.52    | 1.31     | 8.34     | 11.97    | 0.012    |

### Table 2: Best Fit Models for M(II)-L-Orn Binary Complexes in Solvent-Water Mixtures

| % V/V | Log $\beta_{MLXH}$ (SD) | NP | $U_{corr}$ x10$^{-8}$ | Skewness | Kurtosis | $\chi^2$ | R-Factor |
|-------|-------------------------|----|------------------------|----------|----------|---------|----------|
| ML    | MLH                    | ML2       | ML2H                  |          |          |         |          |
| 0.0   | 7.23(21)               | 11.23(19) | 13.41(11)             | 16.27(14)| 121      | 3.91    | 1.05     | 8.23     | 31.14    | 0.018    |
| 20    | 8.13(23)               | 12.14(19) | 14.13(31)             | 17.38(21)| 128      | 6.18    | 0.85     | 10.22    | 23.46    | 0.036    |
| 40    | 9.05(15)               | 12.98(27) | 15.02(15)             | 18.31(14)| 108      | 5.66    | 2.28     | 16.52    | 19.25    | 0.022    |
| 60    | 10.14(17)              | 15.52(22) | 15.92(24)             | 19.31(13)| 129      | 3.64    | 0.68     | 14.70    | 41.54    | 0.032    |

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Selected metal ions interacted with the ligand to produce stable M(II)-L binary complex species. The plausible species with varying pH and their relative distribution have been depicted and plotted using ORIGIN 8.5 as shown in Fig.-2a. The present study found ML, MLH, ML$_2$, and ML$_2$H$_2$ species for M(II) - MSA systems, as well as ML, MLH, ML$_2$, and ML$_2$H species for M(II)-Orn.

Inter Comparison of Stabilities of M(II)-L Binary Complexes

The gradual decrease in the free metal (FM) distribution curve compared with the free ligand (FL) signifies the development of binary complexes. Copper(II) has the maximum stability among all M(II)-L binary complexes with MSA and L-Ornithine (Fig.-2b). This is consistent with the “Irving–Williams stabilities order”.*,21

Role of Dielectric Constant

The present investigation indicated that the stability constants increased linearly with increasing solvent composition. Because the solvent has a lower dielectric constant than water, the metal-ligand complexes are more stable as illustrated in Fig.-2c.

Species Distribution Plots

Selected metal ions interacted with the ligand to produce stable M(II)-L binary complex species. The plausible species with varying pH and their relative distribution have been depicted and plotted using ORIGIN 8.5 as shown in Fig.-2a. The present study found ML, MLH, ML$_2$, and ML$_2$H$_2$ species for M(II) - MSA systems, as well as ML, MLH, ML$_2$, and ML$_2$H species for M(II)-Orn.

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plausible structures of observed complexes of M(II)-L (L=MSA or L-Orn) generated from electrical repulsions and Jahn-Teller distortion effect is shown in Fig.-3a and 3b respectively.
Ternary Complexes of MSA and L-Orn Modelling of Chemical Species

The best fit model for ternary complexes with MSA and L-Orn has been chosen by considering all statistical parameters given in Table-3. MLX, MLX₂, and ML₂X species were detected. Overall stability constants (log \( \beta \)) with minimal standard deviation (SD) in specifies the exactness of these constraints.

Table-3: Best Fit Model of M(II)-MSA-L-Orn Ternary Complexes in 0-60% v/v EG-Water Mixtures

| % V/V | \( \log \beta_{MLX} \) (SD) | \( \log \beta_{MLX_2} \) | \( \log \beta_{ML_2X} \) | NP | \( U_{corr} \times 10^{-8} \) | Skewness | Kurtosis | \( \chi^2 \) | R-Factor |
|-------|--------------------------|--------------------------|--------------------------|-----|--------------------------|--------|--------|--------|--------|
|       | MLX                      | MLX₂                     | ML₂X                     |     |                           |        |        |        |        |
| 0.0   | 10.61(12)                | 18.13(29)                | 20.61(07)                | 111 | 1.21                     | 1.61   | 3.72   | 12.61  | 0.020  |
| 20    | 11.81(11)                | 19.88(23)                | 22.28(25)                | 168 | 7.19                     | 0.85   | 1.17   | 37.12  | 0.017  |
| 40    | 12.92(18)                | 20.80(21)                | 22.82(08)                | 148 | 1.14                     | -1.24  | 6.84   | 38.27  | 0.018  |
| 60    | 13.69(09)                | 22.91(08)                | 23.86(17)                | 149 | 2.94                     | -1.14  | 7.21   | 69.89  | 0.011  |

|       | MLX                      | MLX₂                     | ML₂X                     |     |                           |        |        |        |        |
| 0.0   | 11.34(19)                | 20.15(09)                | 22.64(28)                | 131 | 3.91                     | -1.49  | 4.22   | 29.38  | 0.024  |
| 20    | 13.02(14)                | 21.09(14)                | 23.89(24)                | 147 | 2.50                     | 2.07   | 1.93   | 53.16  | 0.016  |
| 40    | 14.12(25)                | 22.59(19)                | 24.22(21)                | 128 | 1.84                     | 0.69   | 3.01   | 39.25  | 0.015  |
| 60    | 15.64(14)                | 23.44(25)                | 25.64(21)                | 161 | 2.08                     | 1.19   | 5.27   | 36.58  | 0.019  |

|       | MLX                      | MLX₂                     | ML₂X                     |     |                           |        |        |        |        |
| 0.0   | 15.75(25)                | 28.23(21)                | 30.97(14)                | 108 | 2.81                     | 1.02   | 3.80   | 29.56  | 0.032  |
| 20    | 16.38(09)                | 30.22(09)                | 31.39(11)                | 153 | 1.56                     | -0.63  | 2.68   | 10.41  | 0.011  |
| 40    | 18.32(26)                | 31.14(28)                | 32.19(16)                | 171 | 2.96                     | 2.08   | 3.29   | 66.14  | 0.015  |
| 60    | 18.45(24)                | 31.84(21)                | 33.11(14)                | 125 | 2.44                     | -0.75  | 7.92   | 49.16  | 0.025  |

|       | MLX                      | MLX₂                     | ML₂X                     |     |                           |        |        |        |        |
| 0.0   | 10.23(12)                | 17.11(11)                | 18.61(21)                | 112 | 1.91                     | 1.08   | 3.01   | 21.65  | 0.021  |
| 20    | 11.01(20)                | 17.69(09)                | 19.53(18)                | 133 | 11.09                    | 1.03   | 3.22   | 11.62  | 0.03   |
| 40    | 11.92(17)                | 18.80(11)                | 20.14(13)                | 129 | 5.31                     | -1.63  | 4.41   | 32.53  | 0.011  |
| 60    | 12.29(19)                | 19.91(18)                | 21.01(26)                | 136 | 5.18                     | 0.09   | 1.63   | 29.56  | 0.023  |

Species Distribution Plots

Fig.-4 depicts the plausible forms and their distribution of protonated and un-protonated complexes observed that suit best the ternary complex hypothesis. The present study found MLX, ML₂X, and MLX₂ species in the pH range 3.0-9.5 for M(II)-MSA-L-Orn ternary complexes. The relative distribution plots of several species were plotted shown in Fig.-5a.

\[
\begin{align*}
\text{MLH} + \text{XH}_3 & \quad \text{MLX} + \text{4H}^+ \\
\text{M(II)} + 2\text{LH} + \text{XH}_3 & \quad \text{MLX}_2 + \text{6H}^+ \\
\text{MLH} + 2\text{XH}_3 & \quad \text{MLX}_2 + 7\text{H}^+ \\
\text{MXH} + \text{LH} + \text{XH}_3 & \quad \text{MLX}_2 + 7\text{H}^+ \\
\text{MLXH} & \quad \text{MLX}_2 + \text{H}^+ 
\end{align*}
\]

Fig.-4: Possible Binary Complex Formation Equilibria for M(II) – L Binary Complexes

Inter Comparison of Stability Constants

As illustrated in Fig.-5b, the lower size of Cu(II) causes the stability constants to be higher than those of Co(II), Ni(II), and Zn(II) ternary complexes.

Role of Dielectric Constant

Being a protophilic and structural forming nature of EG, eliminates water from the metal ions coordination sphere and creates them highly reactive to ligands resulting in the complexes being more stable. Thus, log values should be directly related to the reciprocal of the medium's dielectric constant (1/D), as shown in the present study (Fig.-5c).
Proposed Structure
The structures of the ternary complexes are hypothesized and sketched using Chem Draw 18.1 as shown in Fig.-6.
CONCLUSION

According to the current biomimetic research ML, MLH, MLH$_2$, and ML$_2$H$_2$ were identified. Statistical data validated the species detected. Protonated species changes to un-protonated species when the pH of the titration mixture increased. MLH and ML$_2$H are protonated at low pH while ML is non-protonated. Statistical data validated the species detected. Among all the M(II)- binary complexes with MSA as well as L-Ornithine, copper exhibits the highest stability and adheres to the Irving–Williams order of stabilities. Ternary complex species MLX, MLX$_2$ and ML$_2$X were found (L = MSA, X = L-Orn). The linear increase in ternary complex stabilities with the percentage of solvent is due to electrostatic forces. The study also examines metal obtainability/transportation in biofluids and metal toxicity. Because Cu(II) is smaller than other studied metal ions, its stability constants are larger.

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