ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

# A BIOMIMETIC SPECIATION STUDY OF BINARY COMPLEXES OF L-PHENYLALANINE AND MALEIC ACID WITH SOME METAL IONS IN UREA-WATER MIXTURES

**Hadgu Hailekiros Belay**

*Department of Applied Chemistry, Adama Science and Technology University, Adama, Ethiopia*

**Corresponding author: hadgu10@gmail.com*

## ABSTRACT

Speciation of binary complexes of Co(II), Ni(II), and Cu(II) with L-phenylalanine and maleic acid in the presence of Urea water mixtures in the concentration range of 0–50% v/v has been studied potentiometrically at a temperature of 298K and at an ionic strength of 0.16 mol L−1. The selection of best fit chemical models is based on statistical parameters and residual analysis. The species detected were ML, $ML_2$, and $ML_2H_2$ for Co(II), Ni(II), and Cu(II). The appropriateness of the experimental conditions was verified by introducing errors deliberately. The models containing different numbers of species were refined by using the computer program MINIQuAD75. The chemical speciation was explained based on the distribution diagrams drawn using HYSS HYPERQUAD. The trend in variation of stability constants of the complexes with dielectric constant of the medium was attributed for the formation and possible structures of the complex species presented.

**Keywords:** Chemical Speciation, L-Phenylalanine, Maleic Acid, Urea, MINIQuAD75, Hyss Hyperquad.

## 1. INTRODUCTION

In all living systems, the biochemical functions of both essential and toxic metals are mediated through specific chemical species or complexes, and their concentrations are important for the biochemical reactions but not just the total concentration of the metal in the system [1]. For instance, some elements can be highly toxic to various life forms; others are considered essential but can become toxic at higher doses. Many of these effects depend strongly on the particular form in which the element is present in the system [2]. The bioavailability and toxicity of the complexes are critically dependent on their thermodynamic and kinetic stability. Identifying these species (i.e., speciation) and obtaining reasonable estimates of their thermodynamic and kinetic stabilities are the problems that continue to plague environmentalists and toxicologists [3]. Hence, extensive attention has been paid in recent years to the study of the chemical speciation of ligands with metal ions. L-phenylalanine (F) is an essential α-amino acid. It is classified as non-polar because of the hydrophobic nature of the benzyl side chain. It is an electrically neutral amino acid, one of the twenty common amino acids used to biochemically form proteins, coded for by DNA. It is used in the manufacture of food and drink products and sold as a nutritional supplement for its reputed analgesic and antidepressant effects. A non-food source of phenylalanine is the artificial sweetener aspartame. F is the starting compound used in the flavonoid biosynthesis [4].

The genetic disorder phenylketonuria (PKU) is the inability to metabolize phenylalanine. Individuals with this disorder are known as "phenylketonurics" and must regulate their intake of phenylalanine. Phenylalanine uses the same active transport channel as tryptophan to cross the blood–brain barrier and, in large quantities, interferes with the production of serotonin. Individuals who cannot metabolize phenylalanine must monitor their intake of protein to control the buildup of phenylalanine as their bodies convert protein into its component amino acids [5]

Maleic acid (MA) is industrially derived by hydrolysis of maleic anhydride; maleic anhydride is produced by oxidation of benzene or butane. It is an industrial raw material for the production glyoxylic acid by ozonolysis. Maleic acid and fumaric acid do not spontaneously interconvert because rotation around a carbon-carbon double bond is not energetically favorable. However, conversion of the *cis* isomer into the *trans*-isomer is possible by photolysis in the presence of a small amount of bromine [6].

Cobalt is a central component of the vitamin, cobalamin (vitamin $B_{12}$). Cobalt in the form of cyanocobalamin is most efficiently stored in kidneys and liver. Cobalt is essential for the production of red blood cells. It acts as coenzyme in several biochemical processes. Nickel is associated with several enzymes, [7,8] and any variation in its concentration leads to metabolic disorders. Nickel is present in enzymes like urease, present in a wide range of plant species. The signs of nickel deprivation include depressed growth, reproductive performance, and plasma glucose. It also affects distribution and proper functioning of other nutrients including calcium, iron, zinc, and vitamin $B_{12}$. Copper is an essential element for life on earth. The biological functions include electron transfer, dioxygen transportation, oxygenation, oxidation, reduction, and disproportionation [9, 10]. The melanin pigment of the skin is also a copper containing protein.

Urea acts as a denaturant of macromolecules but this action is reversible. The denaturing effect of urea on proteins can occur in two ways; 1) Direct interaction of urea molecules with amide and peptide groups, to destroy intermolecular hydrogen bonds and hydrophobic interaction [11] that are involved in the maintenance of ternary structures, and 2) Urea molecules exert their influence through changes in water structure. [12] The increased solubilities of amino acids [13] and hydrocarbons [14] in presence of urea support the former mechanism. The negative heat capacities of transfer of certain amino acids [15] from water to aqueous urea solution and the increments in the critical micellar concentration [16] of certain surfactants suggest that urea may reduce the co-operative structure of water. So, in the present study, organic solvent Urea is chosen to mimic the permittivity of the biological fluids and L-phenylalanine (F) and maleic acid (MA) are chosen as model compounds to proteins and substrates.

## 2. EXPERIMENTAL, RESULTS & DISCUSSION

### 2.1. Chemicals and Standard Solution

All the chemicals used in this experiment were of analytical reagent grade purity. Triple distilled deionized water was used for the preparation of all the solutions. Solutions of 0.1 mol $L^{-1}$ of Co(II), Ni(II), Cu(II) chlorides (EMerck, India) were prepared maintaining 0.05 mol $L^{-1}$ hydrochloric acid to suppress the hydrolysis of metal salts. A solution (0.05mol $L^{-1}$) of L-phenylalanine and maleic acid (GR grade, E-Merck, Germany) were prepared by maintaining a 0.05mol $L^{-1}$ hydrochloric acid concentration to increase its solubility. Urea (Finar, India) was used as received. Solutions of 0.2 mol $L^{-1}$ hydrochloric acid (GR grade, Merck, India) and 0.4 mol $L^{-1}$sodium hydroxide (E-Merck, India) were prepared. A solution of 2.0 mol $L^{-1}$ sodium chloride (Merck, India) was prepared to maintain the ionic strength in the titrand. All the solutions were standardized by the usual oxalic acid and potassium hydrogen phthalate solutions, while the normality of hydrochloric acid was determined by using the standardized sodium hydroxide and the primary borax solutions [17]. The concentration of the metal ions was determined complex metrically by titrating against a standard solution of EDTA using xylenol orange indicator and hexamethylenetetramine powder as buffer to maintain the pH at 5.0-6.0 [18]. So as to assess the errors that might have crept into the determination of the concentrations, the data were subjected to one-way analysis of variance (ANOVA) by using the computer program, COST [19]. The strengths of alkali and mineral acid were determined using the Gran plot method [20, 21].

### 2.2. Alkalimetric Titrations

The pH measurements of metal-ligand binary systems were carried out in aqueous media containing varying compositions of Urea in the range of 0-50% (v/v) maintaining an ionic strength of 0.16 mol L-1 with sodium chloride at 298K by using a digital pH meter ELICO (Model Li 120, India) type readability of 0.01 (0-14). The electrode of the cell was calibrated with 0.05 mol L-1 potassium hydrogen phthalate solution in the acidic region and with 0.01 mol L-1 borax solution in the alkaline region to measure the response in the pH range 2.0-11.0.The effect of variations in asymmetry potential, liquid junction potential, activity coefficient, sodium ion error and dissolved carbon dioxide on the response of the glass electrode were accounted for in the form of correction factor [22, 23]. Mechanical stirring of the solution was carried out by means of a Teflon stirrer. To verify whether the electrode was equilibrated, a strong acid was titrated with an alkali every day until no appreciable differences were observed between the pH values of two titrations at the corresponding volumes of titrant. A calomel electrode was refilled with Urea-water mixture of the equivalent composition to that of the titrand. Free acid titrations were performed before the metal -ligand titrations to calculate the correction factor. In each of the titrations, the titrand consisted of a mineral acid of approximately 1mmol in a total volume of 50mL.Titrations with different metal-to-ligand ratios

(1:2.5, 1:3.75, and 1:5) were carried out with 0.4 mol $dm^{-3}$ sodium hydroxide.

### 2.3. Modeling Strategy

The computer program SCPHD [24] was used to calculate the correction factor. The binary stability constants were calculated from with the pH-metric titration data using the computer program MINIQuAD75 [25] which exploit the advantage of a constrained least-squares method in the initial refinement and reliable convergence of the Marquardt algorithm. During the refinement of the binary systems, the correction factor and the protonation constants of phenylalanine were fixed.

**Table 1: Parameters of best fit chemical models of M (II)-MA complexes in Urea-water medium**

| % v/v Urea | logβmlh (SD) | | | NP | Ucorr | Skewness | χ2 | R-factor | Kuurtosis | pH-Range |
|---|---|---|---|---|---|---|---|---|---|---|
| | **ML** | **$ML_2$** | **$ML_2H_2$** | | | | | | | |
| **Co(II)** | | | | | | | | | | |
| 0.0 | 4.59(9) | 6.86(2) | 17.74(9) | 68 | 1.00 | 1.09 | 12.57 | 0.0094 | 3.22 | 1.5-8.0 |
| 10.0 | 4.25(3) | 6.07(3) | 17.81(1) | 77 | 1.22 | 0.80 | 12.09 | 0.0003 | 3.55 | 2.2-8.0 |
| 20.0 | 3.41(7) | 6.32(7) | 17.43(0) | 55 | 1.05 | 0.15 | 12.54 | 0.0022 | 3.06 | 2.2-8.0 |
| 30.0 | 3.32(2) | 5.93(0) | 17.02(1) | 99 | 1.00 | 0.30 | 12.70 | 0.0055 | 3.06 | 2.2-8.0 |
| 40.0 | 4.36(1) | 7.12(0) | 18.23(5) | 84 | 1.03 | -0.44 | 12.07 | 0.0121 | 3.33 | 2.0-8.0 |
| 50.0 | 3.15(0) | 6.45(1) | 17.32(2) | 89 | 1.22 | 1.18 | 12.31 | 0.0110 | 4.34 | 2.0-8.0 |
| **Ni(II)** | | | | | | | | | | |
| 0.0 | 5.43(9) | 7.45(1) | 16.35(7) | 76 | 1.09 | 1.50 | 12.26 | 0.0130 | 3.92 | 1.8-6.6 |
| 10.0 | 3.70(3) | 5.60(8) | 17.36(6) | 89 | 1.15 | -0.18 | 12.59 | 0.0084 | 3.38 | 2.1-6.6 |
| 20.0 | 4.36(1) | 7.33(0) | 18.39(0) | 90 | 1.70 | 1.50 | 12.53 | 0.0110 | 3.44 | 2.1-6.5 |
| 30.0 | 4.30(8) | 7.41(0) | 18.31(0) | 56 | 1.70 | -0.11 | 12.97 | 0.0131 | 3.64 | 2.1-6.5 |
| 40.0 | 4.28(9) | 6.90(0) | 18.08(1) | 87 | 1.33 | 1.44 | 12.68 | 0.0204 | 3.26 | 1.9-6.6 |
| 50.0 | 3.44(5) | 6.47(9) | 17.65(8) | 90 | 2.87 | -0.20 | 10.44 | 0.0234 | 2.72 | 1.9-6.6 |
| **Cu(II)** | | | | | | | | | | |
| 0.0 | 4.90(1) | 7.85(5) | 15.83(1) | 77 | 1.50 | 0.04 | 12.84 | 0.0080 | 3.40 | 2.0-5.8 |
| 10.0 | 3.80(2) | 6.20(6) | 16.70(0) | 67 | 1.66 | -0.10 | 12.56 | 0.0040 | 3.31 | 2.0-5.8 |
| 20.0 | 4.76(3) | 7.93(7) | 18.40(3) | 90 | 1.34 | -0.10 | 12.36 | 0.0066 | 2.22 | 2.0-5.7 |
| 30.0 | 3.70(7) | 6.93(2) | 17.30(4) | 80 | 1.22 | 0.60 | 12.69 | 0.0108 | 4.00 | 2.1-5.8 |
| 40.0 | 4.95(1) | 7.89(1) | 18.27(1) | 48 | 1.44 | -0.22 | 12.60 | 0.0200 | 3.30 | 2.1-5.9 |
| 50.0 | 3.33(2) | 7.23(8) | 17.39(8) | 77 | 1.30 | 0.06 | 13.67 | 0.0180 | 3.32 | 2.5-5.8 |

*$U_{corr}$ = U/(NP-m)X10$^8$, where m = number of species; NP=Number of experimental points; SD=Standard deviation.*

A very low standard deviation in log β values indicates the precision of these parameters. The small values of Ucorr (the sum of squares of deviations in concentrations of ingredients at all experimental points) corrected for degrees of freedom indicate that the model can represent the experimental data. Small values of mean, standard deviation, and mean deviation for the systems corroborate that the residuals are around a zero mean with little dispersion. Kurtosis is a measure of the peakedness of the error distribution near a model value. For an ideal normal distribution, kurtosis value should be three (mesokurtic) [26]. If the kurtosis is less than three, the peak of the error distribution curve is flat (platykurtic) and if the kurtosis is greater than three, the distribution shall have sharp peak (leptokurtic). The kurtosis values in the present study indicate that the residuals form leptokurtic as well as platykurtic patterns and very few form mesokurtic patterns. The values of skewness recorded in Tables 1and 2 are between -1.60 and 1.50. These data suggest that the residuals form a part of normal distribution. Hence, least-squares method can be applied to the present data.

The sufficiency of the model is further evident from the low crystallographic R-values. These statistical parameters thus show that the best fit models portray the metal–ligand species in Urea-water media.

**Table 2: Parameters of best fit chemical models of M(II)-F complexes in Urea-water medium**

| % v/v Urea | logβmlh (SD) | | | NP | Ucorr | Skewness | χ2 | R-factor | Kuurtosis | pH-Range |
|---|---|---|---|---|---|---|---|---|---|---|
| | **ML** | **$ML_2$** | **$ML_2H_2$** | | | | | | | |
| **Co(II)** | | | | | | | | | | |
| 0.0 | 5.50(6) | 9.40(9) | 23.82(1) | 77 | 0.70 | 0.18 | 5.01 | 0.0041 | 3.02 | 1.8-8.6 |
| 10.0 | 5.74(7) | 9.60(8) | 24.39(2) | 90 | 0.30 | -0.15 | 5.47 | 0.0100 | 3.12 | 2.5-8.6 |
| 20.0 | 6.63(5) | 10.81(7) | 25.27(2) | 40 | 0.91 | 0.09 | 7.62 | 0.0090 | 3.50 | 2.5-8.6 |
| 30.0 | 6.53(2) | 10.83(6) | 24.83(2) | 55 | 0.45 | 0.75 | 4.68 | 0.0080 | 4.32 | 2.5-8.6 |
| 40.0 | 5.45(0) | 9.34(5) | 24.20(7) | 60 | 0.22 | 0.77 | 5.30 | 0.0076 | 3.01 | 2.5-8.6 |
| 50.0 | 5.80(3) | 9.91(2) | 24.80(6) | 80 | 0.21 | 0.10 | 8.05 | 0.0122 | 3.63 | 2.5-8.6 |
| **Ni(II)** | | | | | | | | | | |
| 0.0 | 8.50(3) | 13.36(1) | 23.50(7) | 77 | 0.71 | 0.70 | 62.28 | 0.0071 | 4.32 | 1.7-8.6 |
| 10.0 | 7.34(1) | 12.18(9) | 25.08(8) | 34 | 0.90 | 0.60 | 31.73 | 0.0072 | 3.43 | 1.7-8.6 |
| 20.0 | 8.75(8) | 13.80(7) | 25.90(1) | 78 | 0.15 | 0.01 | 3.08 | 0.0150 | 2.63 | 2.3-7.5 |
| 30.0 | 7.70(2) | 12.75(5) | 24.90(8) | 67 | 0.93 | 0.10 | 2.87 | 0.0085 | 3.12 | 2.3-7.5 |
| 40.0 | 7.53(9) | 12.30(3) | 24.80(2) | 90 | 0.85 | -0.01 | 4.97 | 0.0030 | 2.62 | 2.3-7.6 |
| 50.0 | 6.40(3) | 10.92(2) | 24.73(4) | 60 | 0.75 | 0.25 | 5.13 | 0.0133 | 3.21 | 2.3-7.6 |
| **Cu(II)** | | | | | | | | | | |
| 0.0 | 9.15(5) | 16.50(8) | 23.63(1) | 50 | 0.60 | 0.17 | 5.85 | 0.0022 | 3.71 | 2.0-8.2 |
| 10.0 | 9.62(5) | 16.51(0) | 24.45(1) | 50 | 0.80 | 0.00 | 11.24 | 0.0054 | 2.83 | 2.0-8.3 |
| 20.0 | 9.85(8) | 18.72(9) | 25.90(0) | 28 | 0.59 | -0.02 | 4.89 | 0.0170 | 3.92 | 2.0-8.3 |
| 30.0 | 8.80(7) | 15.83(6) | 23.83(0) | 67 | 1.61 | 0.35 | 3.33 | 0.0115 | 2.12 | 2.6-8.2 |
| 40.0 | 9.29(6) | 16.35(5) | 24.47(6) | 40 | 0.30 | -1.37 | 8.67 | 0.0056 | 3.01 | 2.3-8.3 |
| 50.0 | 9.70(2) | 17.03(3) | 25.56(5) | 80 | 0.78 | -1.60 | 12.63 | 0.0200 | 3.30 | 1.6-8.3 |

*$U_{corr} = U/(NP-m)X10^8$, where m = number of species; NP=Number of experimental points; SD=Standard deviation.*

**Table 3: Effect of errors in influential parameters on the stability constants of Cu(II)-MA complexes in 0% v/v Urea-water medium.**

| Ingredient | %Error | logβ(SD) | | |
|---|---|---|---|---|
| | | ML | $ML_2$ | $ML_2H_2$ |
| | 0 | 4.59(9) | 6.86(2) | 17.74(9) |
| Alkali | -5 | Rejected | Rejected | Rejected |
| | -2 | Rejected | 5.83(34) | Rejected |
| | +2 | 5.59(55) | Rejected | 18.78(55) |
| | +5 | 7.09(77) | 11.17(45) | Rejected |
| Acid | -5 | Rejected | Rejected | Rejected |
| | -2 | 5.49(33) | 8.82(50) | 18.81(32) |
| | +2 | 5.32(79) | 6.00(34) | 16.19(38) |
| | +5 | Rejected | 5.00(36) | 16.20(44) |
| Ligand | -5 | 4.47(22) | 6.76(34) | 17.84(33) |
| | -2 | 4.93(37) | 6.26(32) | 17.53(22) |
| | +2 | 4..50(47) | 6.67(39) | 17.15(44) |
| | +5 | 4.20(32) | 6.80(40) | 17..87(36) |
| Metal | -5 | 4.63(38) | 7.79(44) | 17.79(27) |
| | -2 | 4.62(39) | 7.82(38) | 17.76(28) |
| | +2 | 4.60(46) | 6.89(33) | 17.71(29) |
| | +5 | 4.69(45) | 6.88(32) | 17.78(30) |

### 2.4. Effect of systematic errors on best fit model

In order to obtain the best chemical model for critical evaluation and application under varied experimental conditions with different accuracies of data acquisition, an investigation was under taken by introducing pessimistic errors in the influential parameters like concentrations of alkali, mineral acid, ligand, and metal (Table 3). The order of the ingredients that influence the magnitudes of stability constants due to incorporation of errors is alkali > acid > ligand > metal. Some species were even rejected when errors are introduced in the concentrations. The rejection of some species and increased standard deviations in the stability constants on introduction of errors confirm the suitability of the experimental conditions (concentrations of ingredients) and choice of the best fit models.

**Table 4: Effect of errors in influential parameters on the stability constants of Cu(II)-F complexes in 10% v/v Urea-water medium**

| Ingredient | %Error | logβ(SD) | | |
|---|---|---|---|---|
| | | ML | $ML_2$ | $ML_2H_2$ |
| | 0 | 9.62(5) | 16.51(0) | 24.45(1) |
| Alkali | -5 | Rejected | Rejected | Rejected |
| | -2 | Rejected | 18.24(24) | 23.58(33) |
| | +2 | 8.73(28) | 17.89(22) | Rejected |
| | +5 | Rejected | 17.76(26) | 23.93(33) |
| Acid | -5 | 10.12(27) | 13.88(27) | 25.20(41) |
| | -2 | 6.85(40) | 15.97(29) | 25.77(27) |
| | +2 | 10.57(30) | 15.23(33) | 25.44(28) |
| | +5 | 10.89(33) | Rejected | Rejected |
| Ligand | -5 | 9.24(43) | 16.26(22) | 24.00(29) |
| | -2 | 9.34(20) | 16.33(19) | 24.13(25) |
| | +2 | 9.51(28) | 15.44(27) | 23.30(24) |
| | +5 | 8.63(28) | 16.53(28) | 24.42(24) |
| Metal | -5 | 9.46(26) | 16.52(28) | 24.45(25) |
| | -2 | 9.44(20) | 16.44(28) | 24.23(35) |
| | +2 | 9.41(20) | 16.33(38) | 24.20(36) |
| | +5 | 9.38(20) | 16.24(38) | 24.18(37) |

### 2.5. Effect of Solvent on Metal-Ligand Equilibria

Co-solvent influences the equilibria in solution due to change in the dielectric constant (D) of the medium that varies the relative contribution of electrostatic and non-electrostatic interactions which in turn vary the magnitude of stability constants [27].

Urea is a dipolar protic solvent. It is a structure former and enhances the water structure in Urea-water mixtures; hence, it removes water from the coordination sphere of metal ions, making them more reactive towards the ligands. As a result, the stability of the complexes is expected to increase. At the same time, it is a coordinating solvent, and it competes with the ligands for coordinating the metals [28]. This decreases the stability of the complexes. Hence, the stability of the complexes is expected to either increase or decrease. The variation of overall stability constants with co-solvent content depends upon electrostatic and non-electrostatic factors.

The co-solvent induced increased basicity of Urea-water mixtures increases the stabilization of protons. The trends of stability constant (log β) values of complexes of F with 1/D of Urea-water mixture are given in Figs 1. The trend is almost linear which indicates that the dielectric constant or long-range interactions are responsible for the stability trend. This linear increase indicates the dominance of the structure-forming nature of Urea over the complexing ability.

### 2.6. Distribution Diagrams

The present investigation reveals the existence of ML, $ML_2$ and $ML_2H_2$ for Co(II), Ni(II) and Cu(II). The $ML_2$ species is the predominant species (Figs.2. & 3.) at higher

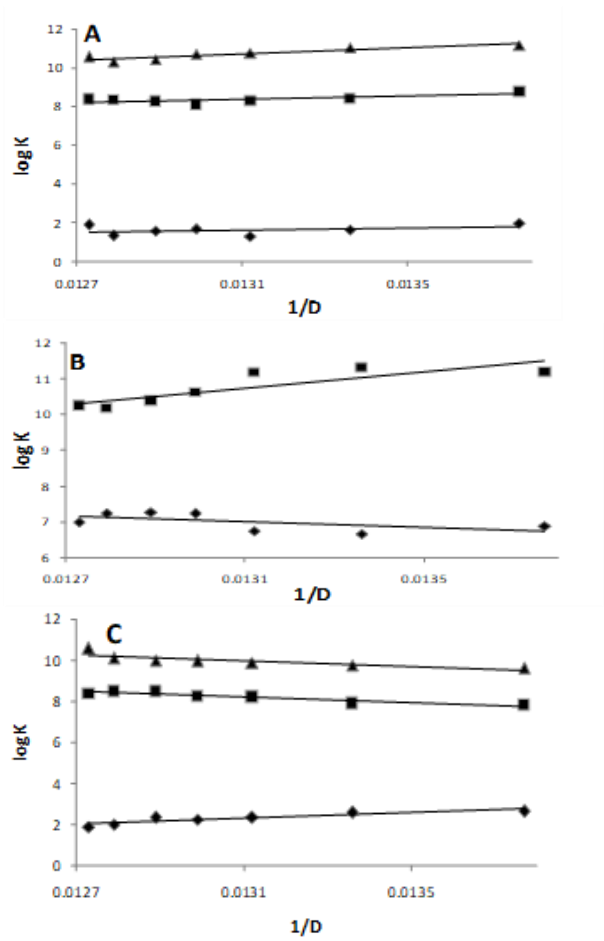



**Fig. 1: Variation of stability constant values of metal-MA complexes species with 1/D of Urea: (A) Co(II); (B) Ni(II); (C) Cu(II)-(♦) log βML; (■) log $\beta ML_2$; (▲) log $\beta ML_2H_2$.**

pH and $ML_2H_2$ is the predominant species at lower pH among all the binary complexes. Low concentration of free metal ion (FM) indicates the strong complexing nature of MA and F.

**The formation of various binary complex species is shown in the following equilibria**

$$M(II) + LH_2 \rightleftharpoons ML + 2H^+ \quad .....(1)$$

$$M(II) + LH \rightleftharpoons ML + H^+ \quad .....(2)$$

$$M(II) + 2LH_2 \rightleftharpoons ML_2H_2 + 2H^+ \quad .....(3)$$

$$ML_2H_2 \rightleftharpoons ML_2 + 2H^+ \quad .....(4)$$

$$ML + LH_2 \rightleftharpoons ML_2 + 2H^+ \quad .....(5)$$

$$ML + LH \rightleftharpoons ML_2 + H^+ \quad .....(6)$$

Equilibria (1), (2) and (3) represent the formation of complexes from metal ion and the ligand. In alkalimetric titrations, protons are removed successively from the complexes by the addition of aliquots of the alkali. Equilibrium (4) represents the successive deprotonation of the complexes with increasing pH of the solution during alkalimetric titrations. Formation of $ML_2$ through the equilibria (4), (5) and (6) is proved by the increase in concentration of $ML_2$ by the decrease in concentration of ML and $ML_2H_2$. Some typical distribution diagrams of M(II)-F and M(II)-MA in Urea-water media are shown in the figs.2 to 7.

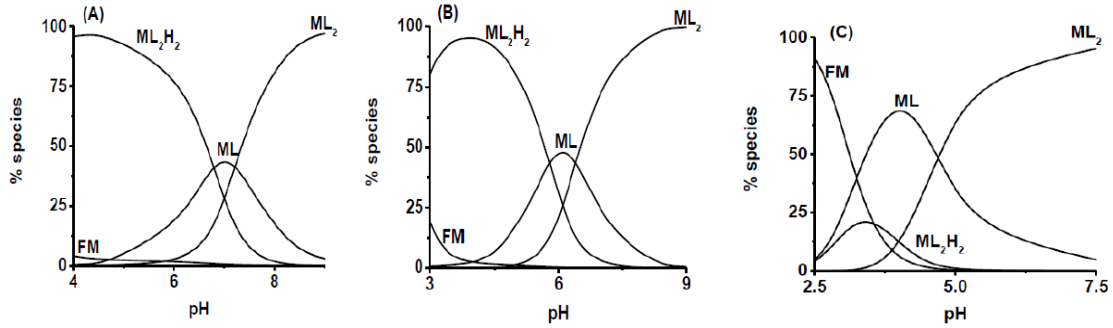



**Fig. 2: Distribution diagrams of F complexes in aqueous medium (A)Co(II)(B) Ni(II) and (C) Cu(II).**

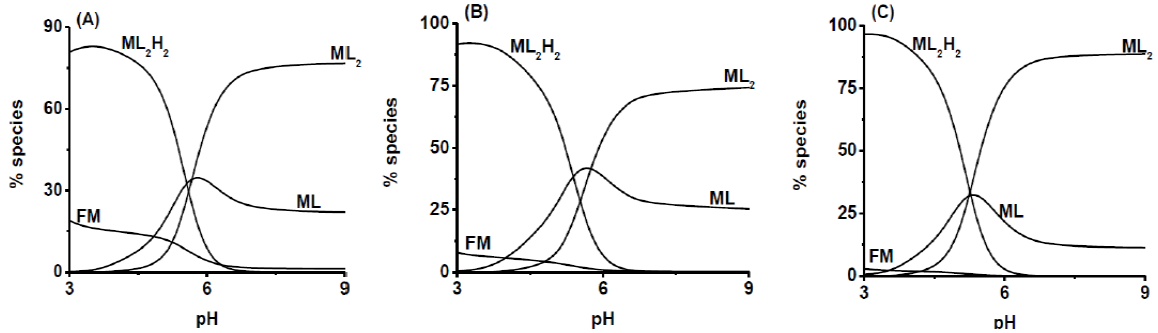



**Fig.3: Distribution diagrams of MA complexes in aqueous medium. (A) Co(II) (B) Ni(II) and (C) Cu(II)).**

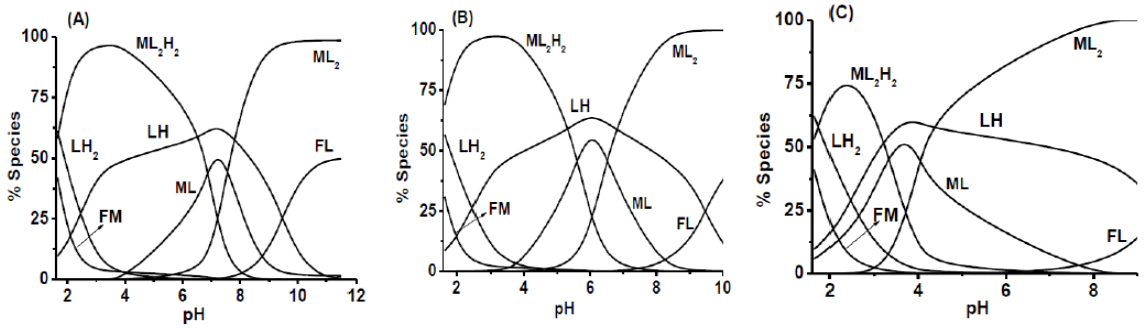



**Fig. 4: Distribution diagrams of F complexes in 10% v/v Urea-water medium (A) Co(II) (B) Ni(II) and (C) Cu(II)**

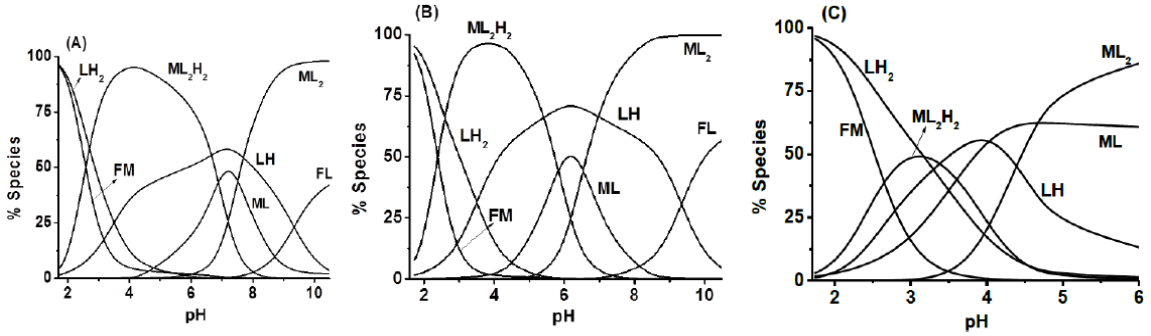



**Fig.5: Distribution diagrams of F complexes in 20% v/v Urea-medium (A) Co(II) (B) Ni(II) and (C) Cu(II)**

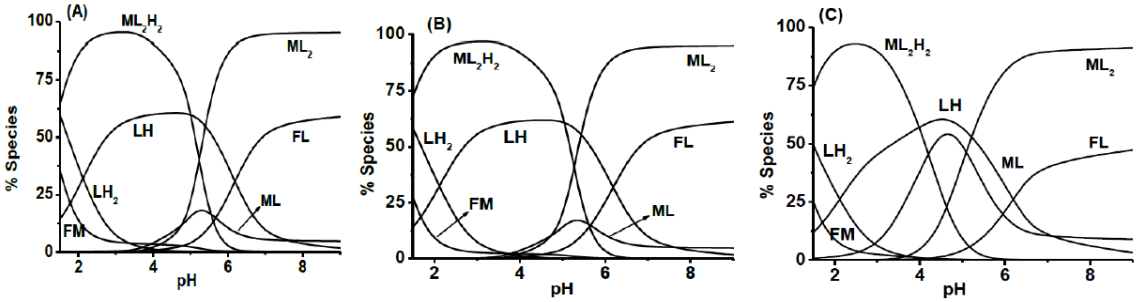



**Fig. 6: Distribution diagrams of binary complexes of MA in 10% Urea-water mixtures (A) Co(II), (B) Ni(II), and (C) Cu(II)**

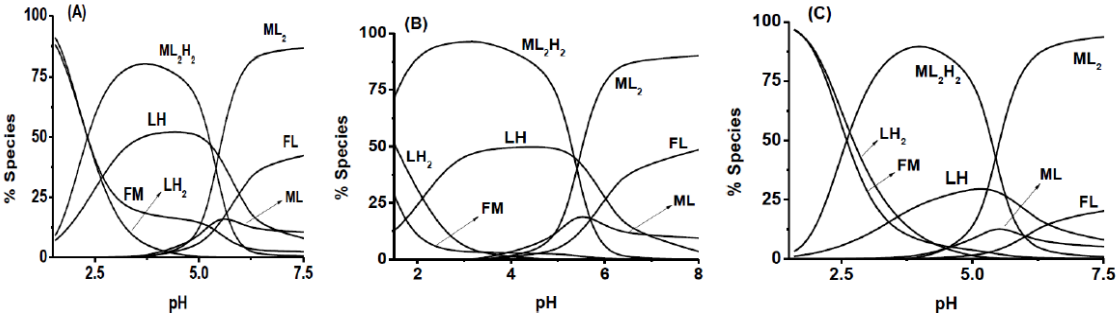
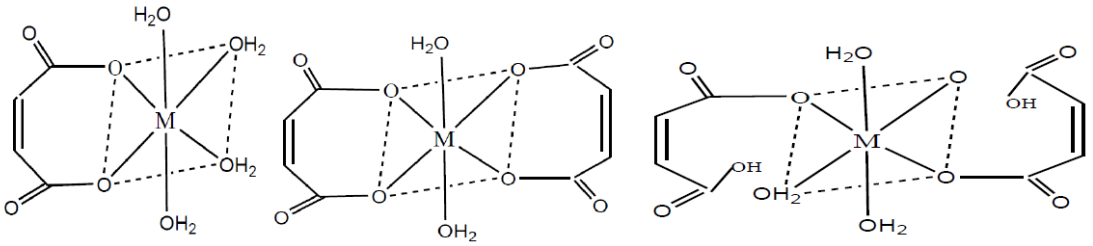



**Fig.7: Distribution diagrams of MA complexes in 20% v/v Urea-water medium. (A) Co(II) (B) Ni(II) and (C) Cu(II).**

### 2.7. Structures of Complexes

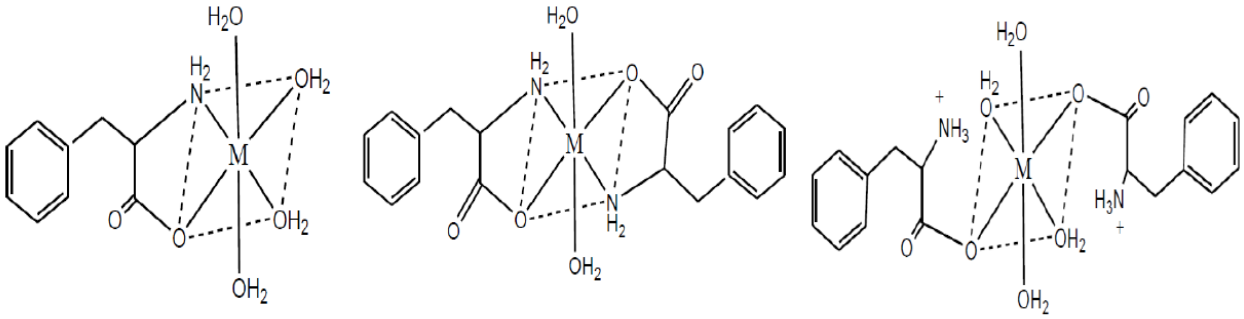
Although it is not possible to elucidate or confirm the structures of complex species potentiometrically, they can be proposed based on the literature reports and chemical knowledge. In aqueous solutions, metal ions are coordinated by six water molecules. Amino acids replace water molecules and form metal-amino acid complexes [29].

Depending upon the nature of the ligands and metal ions and based on the basic chemical knowledge tentative structures of the complexes are proposed as shown in Figs.8 and 9 for F and MA complexes.



ML $ML_2$ $ML_2H_2$

**Fig. 8: Proposed structures of binary complexes of MA with M(II).**



ML $ML_2$ $ML_2H_2$

**Fig. 9: Proposed structures of binary complexes of F with M(II).**

## 3. CONCLUSIONS

The author has investigated the biomimetic chemical speciation of L-phenylalanine (F) and maleic acid (MA) complexes of Co(II), Ni(II) and Cu(II) in Urea-water mixtures. The following conclusions can be drawn based on the biomimetic speciation studies performed on these systems.

1. The binary species detected due to the interaction of F and MA with metals are ML, $ML_2$ and $ML_2H_2$ for Co(II), Ni(II) and Cu(II). These models are validated by statistical treatment of the data.
2. The ingredients that affect the magnitudes of stability constants of metal complexes were found to be alkali >acid > ligand > metal.
3. The stabilities of the complexes followed the Irving-Williams order, i.e., Co(II) < Ni(II) <Cu(II).
4. The study also gave an insight into the metal ion availability/metal ion transport in bio-fluids which may help in assessing the toxicity of these metal ions if found to be in excess. The binary complexes with higher stability were more amenable for "metal transport" because of their extra stability and the binary complexes with less stability constants make the metal ion to be available in physiological systems due to their decreased stability.

## 4. REFERENCES


1. Ramanaiah M, Goutham S. *Journal of Indian Chem. Soc.,* 2014; **91:**351-357.
2. Rama Raju B, Santhee DKV, Padmaja N, Rao GN. *Journal of Chem.,* 2012; **24:**89-96.
3. Andrea MO. "Springer-Verlag," 1984; 359.
4. Nelson Dl, Cox MM. Lehninger, Principles of Biochemistry, 3rd edn., New York: Worth Publishing, 2000.
5. Koley D, bard AJ, *Proc. Nat Acad. Sci.,* 2010; **107(39):**16783-16787.

6. Adams MWW. Biochim. Biophys. Acta, 1990; **1020:**115-145.
7. Cammack R. *Nature*, 1995; 373:556-557.
8. Holm RH, Kennepohl P, Solomon EI. *Chem.Rev*., 1996; **96:**2239-2314.
9. R. Mukherjee. Comprehensive Coordination Chemistry-II: from Biology to Nanotechnology, in amsterdam:*elsevier*, 2003;747.
10. Sengwa RJ, Khatari V, Sankhala S, *Journal of Molecular Liquids*, 2009; **144:**89-96.
11. Nelson DL, Cox MM. Lehninger, principles of biochemistry, 3rd edn., New York: Worth Publishing, 2000.
12. Koley D, Bard AJ. *Acad. Sci.,* 2010; **107**:16783.
13. Gordon JA & Warren JR. *J biol Chem*, 1968; **245:**5663.
14. Hammes GG& Swann JC, *Biochemistry*, 1967; **6:**1591.
15. Wetiaufer DB, Malic SK, Stoller L & Coffin RL. *J Am Chem Soc*, 1964; **86:**508.
16. Kresheck GC & Benjamin L. *J Phys Chem*, 1964; **68:**2476.
17. Jeffery GH, Bassett J, Mendham J, Denney RC. Vogel's Text Book of Quantitative Chemical Analysis., 5th edn., London: Longman, 1991.
18. weltcher FJ, "The Analytical Use of Ethylenediaminetetraacetic Acid," New York, Dvannostrand Company, 1957.
19. Rao RS, Rao GN. Computer Applications In Chemistry, Mumbai, Himalaya Publishing House, 2005.
20. Soldatovic TV, Vasic V, Bugarcic ZD. *Bull. Chem. Soc. Jpn*., 2006; **79(12):**1889-1893.
21. Sigel H, Martin RB, Tribolet R, Haring UK, Balakrishnan RM. *Journal of Eur. Biochem*., 1985; **152:**187-194.
22. Gonzalez G, Rosales D, Ariza JLG, Perez AG, Talanta. 1986; **33:**105-106.
23. Rao GN. "Complex Equilibria Of Some Biologically Important Metal Ions in Aquo-Organic Media [Ph.D. Thesis]," Visakhapatnam, India, Andhra University, 1989.
24. Gans P, Sabatini A, Vacca A. *Inorg. Chim. Acta*., 1976; **18:**237-239.
25. Van Uitert LG, Haas CG. *Journal of Am.Chem.Soc*., 1953; 75: 451-455.
26. Sharman R, Sullivan K, Young RM, Mcgill J. "Depressive Symptoms In Adolescents With L-phenylalanine andtyrosine levels, in gene, 2012; **504:**288-291
27. Naik AB, Narwad M. *Journal of Am. Eurasian. Sci. Res.,* 2008*;* **3:**212.
28. Pedada SR, Bathula SS, Rao SS,.Charla KS, Rao GN. *Bull. Chem. Soc. Ethiop*., 2009; **23:**347.
29. Damaj Z, Naveau A, Dupont L, Henon E, Rogez G, Guillon E. *Inorg. Chem. Commun*, 2009; **12:**17.