Available online at www.joac.info

ISSN: 2278-1862

Journal of Applicable Chemistry

2015, 4 (6): 1844-1851

(International Peer Reviewed Journal)

Formation of Binary Complexes of Co (II), Ni (II), and Cu (II) with L-Phenylalanine in TX100 – Water Mixtures

Gowri kumari Vasireddy[1], Nageswara Rao Choppa[2] and Sailaja B.B.V[3]*

*Department of Inorganic & Analytical Chemistry, Andhra University, Visakhapatnam-530 003, **INDIA**

Email: vasireddy.gowri@gmail.com,nageshchoppa@gmail.com,sailajabbv.chem@gmail.com

Accepted on 20th November 2015

ABSTRACT

Chemical speciation of binary complexes of Co (II), Ni (II), and Cu (II) with L-phenylalanine was investigated pH-metrically in TritonX(100) – water mixtures. The stability constants were calculated using the computer program MINIQUAD75. The best-fit chemical models were selected based on statistical parameters and residual analysis. The models for the binary species contained ML, ML_2 and ML_2H_2 for Co(II), Ni(II) and Cu(II) in TritonX(100) – water mixtures. The trend in variation of stability constants with change in the mole fraction of the medium was explained on the basis of electrostatic and non-electrostatic forces. Distribution of species, formation equilibria and effect of influential parameters on the stability constants has been presented. The possible structures of the various species are elucidated on the basis of the analysis of the pH metric data.

Keywords: Chemical Speciation, Binary complexes, L-phenylalanine, MINIQUAD75, TritonX (100), and Stability constants.

INTRODUCTION

A number of studies have been reported on chemical speciation of α-amino acids in different media in recent times [1-4]. The binary complexes of Co (II), Ni (II), and Cu (II) with L-phenylalanine (Phe) are studied in the presence of TritonX (100) – water mixtures to understand the influence of co-solvent on the speciation. In biological fluids, metal ions exist in non-exchangeable form as in metalloproteins or loosely bound to some biological ligands as in metal-activated proteins. The loosely bound metal ions are in equilibrium with similar metal ions present in the bio fluids. These simultaneous equilibria involving a variety of metal ions and ligands are important in biological fluids [5]. Chemical speciation of a molecule is governed by its structure and solvent effects [6, 7]. Phe is an essential α-amino acid. It is classified as nonpolar because of the hydrophobic nature of the benzyl side chain. Phe 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. Phe is the starting compound used in the flavonoid biosynthesis.

Cobalt is essential for the production of the red blood cells and cobalamin acts as the substrate for the final enzymatic reaction that yields the active coenzyme derivatives of cyanocobalamin and aquacobalamin.

Nickel is found in enzymes, such as urease, which is a dinuclear Ni (II) containing metalloenzyme. This enzyme accounts for 6% of the soluble cellular proteins [8-10] and catalyses the hydrolysis of urea to yield ammonia and carbamate. The copper-containing enzymes and proteins constitute an important class of biologically active compounds. The biological functions include electron transfer, dioxygen transport, oxygenation, oxidation, reduction and disproportionation [11, 12].

MATERIALS AND METHODS

Solutions of L-phenylalanine, cobalt (II), nickel(II), and copper(II) chlorides (E. Merck, G. R. Grade) were prepared in triple distilled water. To increase the solubility of ligand, 0.05 mol L^{-1} hydrochloric acid concentrations were maintained in the solution. G. R. sample of poly oxyethylene diisobutyl phenol (Triton X-100 or TX100, $R_8C_6H_4[OCH_2CH_2]_{9.5}OH$) was used as such and the purity was checked by determining critical micelle concentration (CMC) Conductometrically. CMC value of TX100 was 0.54 vol. % at 25^0C. All the solutions were standardized by standard methods. Cobalt, nickel and copper chlorides were standardized using EDTA. To assess the errors that might have crept into the determination of the concentrations, the data were subjected to analysis of variance of one way classification [13]. The strengths of alkali and mineral acid were determined using the Gran plot method [14].

The titrations were carried out in the medium containing varying concentrations (0.5–2.5%v/v) of TX100 in water maintaining an ionic strength of 0.16 mol dm^{-3} with NaCl at 303.0 $\pm$ 0.1 K using an ELICO (Model LI 120, India) pH meter of 0.01 readability (0-14 pH) in conjunction with a glass combination pH electrode was used. The pH meter was calibrated with potassium hydrogen phthalate (0.050 mol L^{-1}) in acidic region and borax (0.010 mol L^{-1}) in basic region. The glass electrode was equilibrated for several days in a well stirred TX100 – water mixture containing inert electrolyte. The effect of variations in asymmetry potential, liquid junction potential, activity coefficient, sodium ion error and dissolved carbon dioxide on the response of glass electrode were accounted for in the form of correction factor [15].

For the determination of stability constants of metal – ligand binary species, initially titrations of strong acid with alkali were carried out at regular intervals to check whether complete equilibration was achieved. Then the calomel electrode was refilled with TX100-water mixture of equivalent composition as that of the titrand. Titrations with different ratios (1:2.5, 1:3.75, 1:5.0) of metal to ligand were carried out with 0.40 mol L^{-1} sodium hydroxide.

Modelling Strategy: The computer program SCPHD [16] was used to calculate the correction factor. The binary stability constants were calculated from the pH metric titration data using the computer program, MINIQUAD75 [17]. During the refinement of binary systems, the correction factor and protonation constants of Phe were fixed. The protonation constants were fixed in the refinement of metal-ligand stability constants in testing various chemical models. The correction factor [18, 19] was used to convert pH meter dial reading into logarithm of reciprocal of hydrogen ion concentration.

RESULTS AND DISCUSSION

The results of the best fit models that contain the type of species and overall formation constants along with some of the important statistical parameters are given in table 1. A very low standard deviation in log β values indicates the precision of these parameters. The small values of U_{corr} (the sum of squares of deviations in concentrations of ingredients at all experimental points corrected for degrees of freedom), indicate that the experimental data can be represented by the model. Small values of mean, standard deviation and mean deviation for the systems corroborate that the residuals are around a zero mean with little dispersion. χ^2 values range between 8.15 and 62.28. For an ideal normal distribution, the values of kurtosis and skewness should be three and zero, respectively. The values of kurtosis and skewness range between 2.38 and 7.34, and -0.35 and 1.08 respectively. The kurtosis values indicate that the residuals form leptokurtic as well as platykurtic patterns [20, 21]. Deviation of the values of kurtosis and skewness form 3 and 0, respectively, shows the tendency of these residuals to concentrate more to the left or right of the mean and broadening of the peak. However, U_{corr} values in all the three mass-balance equations are very low confirming the adequacy of the chemical model to represent the experimental data. These data evince 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-value recorded. These statistical parameters thus show that the best fit models portray the metal-ligand species in TX100 – water mixtures.

Table 1: Parameters of best fit chemical models of M(II) – Phe complexes in TX(100) – water medium

% v/v TX100	**$\log\beta_{mlh}$ (SD)**			**NP**	**U_{corr}**	**Skew-ness**	**χ^2**	**R-Factor**	**Kurt-osis**
	ML	**ML_2**	**ML_2H_2**						
			Co(II) (pH-Range 2.5 – 8.5)						
0.0	5.58(09)	9.41(07)	23.84(03)	66	0.78	0.14	15.01	0.0044	5.08
0.5	6.10(21)	10.62(15)	24.64(06)	119	1.32	0.09	19.40	0.0091	3.84
1.0	6.67(22)	10.94(17)	25.37(05)	67	0.98	0.04	52.89	0.0085	2.63
1.5	5.91(16)	10.13(13)	24.34(09)	49	1.47	0.48	34.93	0.0109	5.00
2.0	6.76(13)	10.93(11)	25.11(06)	70	0.81	0.08	15.75	0.0076	4.35
2.5	7.03(34)	11.48(30)	25.25(26)	45	0.23	0.86	18.66	0.0121	5.44
			Ni(II) (pH-Range 2.3 – 7.5)						
0.0	8.55(10)	13.33(14)	23.50(04)	81	2.70	0.78	62.28	0.0073	7.34
0.5	8.45(24)	13.72(23)	25.71(18)	57	2.91	0.63	23.67	0.0212	4.11
1.0	8.23(25)	13.54(24)	25.66(17)	36	4.19	-0.35	25.63	0.0135	5.39
1.5	7.73(34)	12.83(34)	24.87(18)	36	1.94	0.02	8.15	0.0198	2.24
2.0	8.37(37)	13.35(37)	25.10(21)	64	3.88	-0.01	26.0	0.0198	2.26
2.5	7.46(33)	12.55(34)	24.58(13)	42	3.78	0.16	9.37	0.0197	2.42
			Cu(II) (pH-Range 2.0 – 8.0)						
0.0	9.15(05)	16.51(09)	23.65(07)	70	1.62	0.19	45.85	0.0084	4.71
0.5	10.20(06)	18.06(08)	25.52(03)	76	0.84	0.84	15.09	0.0049	6.66
1.0	10.11(06)	17.90(10)	25.33(07)	51	7.54	1.08	11.86	0.0072	2.91
1.5	8.87(05)	16.18(09)	23.62(08)	50	1.61	0.21	15.33	0.0095	2.47
2.0	8.45(05)	15.66(09)	22.78(13)	50	0.39	-0.00	13.31	0.0097	2.38
2.5	8.64(05)	15.88(09)	23.17(08)	58	38.78	0.15	10.28	0.0089	2.63

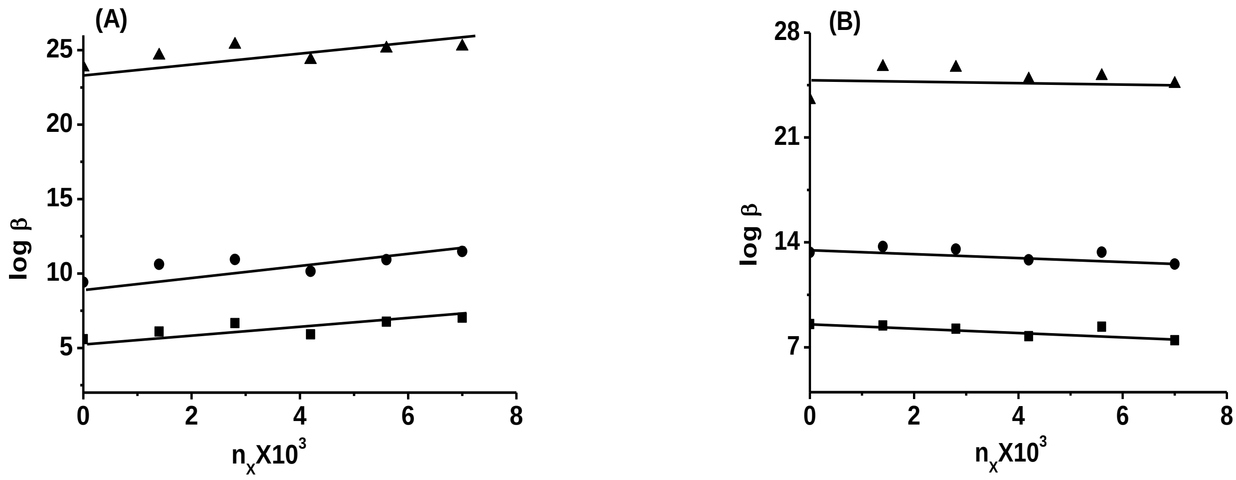
$U_{corr} = U/(NP-m)X10^8$, where m = number of species; NP=Number of experimental points; SD=Standarddeviation

Effect of Systematic Errors on Best Fit Chemical Models: The computer programs refine the stability constants by minimizing the random errors in data. But in the presence of considerable systematic errors, not only the β's are in error, even some species may be rejected. Hence, some representative systems were studied in order to have a cognizance of the effects of errors in concentrations of ingredients on the stability constants of binary metal complexes. These results are given in table 2. The data show that the order of affecting the magnitudes of stability constants is mineral alkali > acid > ligand > metal ion. This type of investigation has significance because the data acquisition was done under varied experimental conditions with different accuracies.

Table 2: Effect of errors in influential parameters on the stability constants of Cu(II)-Phe complexes in 1.5% v/v TX(100) – water medium.

Ingredient	% Error	log β (SD)		
		ML	ML_2	ML_2H_2
	0	8.87(05)	16.18(09)	23.62(08)
Alkali	-5	7.09(31)	Rejected	Rejected
	-2	8.20(36)	15.00(71)	23.21(17)
	+2	9.39(18)	17.19(42)	Rejected
	+5	Rejected	18.16(33)	Rejected
Acid	-5	10.16(82)	18.45(33)	Rejected
	-2	9.52(67)	17.28(28)	23.96(15)
	+2	8.13(16)	14.98(40)	23.00(19)
	+5	7.09(15)	13.21(66)	Rejected
Ligand	-5	8.74(06)	16.09(09)	23.45(09)
	-2	8.82(05)	16.14(09)	23.56(08)
	+2	8.93(05)	16.22(09)	23.68(08)
	+5	9.01(08)	16.29(10)	23.77(08)
Metal	-5	8.93(06)	16.35(10)	23.66(09)
	-2	8.89(06)	16.25(10)	23.64(08)
	+2	8.85(05)	16.12(09)	23.61(08)
	+5	8.82(05)	16.02(09)	23.58(07)

Effect of Surfactant: The variations of stability constants (log β) with mole fraction of different micellar media are shown in figure 1. The stabilities of binary complexes varied almost linearly with the mole fraction of the surfactant. This linear variation, due to the dielectric constant of the medium, decreases with increasing concentration of the surfactant [22, 23]. The non-linear variation depends upon the polarity of the medium, charge on the micellar surface and on the non-electrostatic forces/hydrophobic interactions operating between the complex species and micellar surface. The species should be stabilized in the micellar medium with opposite charges due to electrostatic interactions but these charged species should be destabilized due to the decreased dielectric constant of the medium. This trend reflects in all M(II)-Phe complexes (Figure 1).



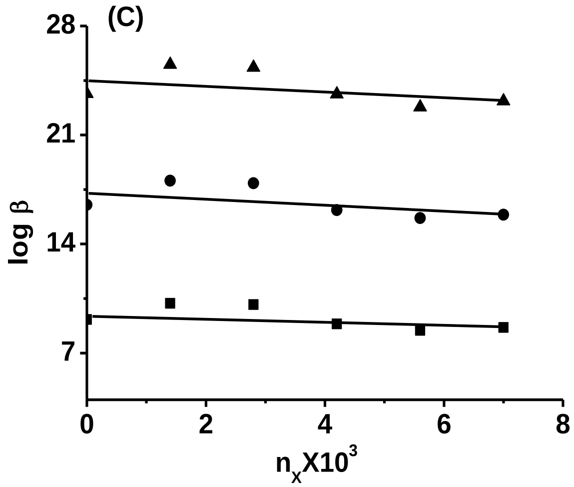


Figure 1 Variation of overall stability constant values of metal – Phe complexes with mole fraction ($n_x \times 10^3$) of TX100 – water mixtures (**A**) Co(II), (**B**) Ni(II), and (**C**) Cu(II); (■)log$\beta_{ML,}$ (●)logβ_{ML2}, (▲)log$\beta_{ML2H2.}$

Distribution Diagrams: Some typical distribution diagrams of M(II)-Phe in TX100 – water medium are shown in the fig. 2. The different forms of Phe are LH_2^+, LH and L^- in the pH-range of 3.0 – 5.0, 3.0 – 10.0 and 8.0 – 10.0 respectively. The plausible binary metal-ligand species in different systems can be predicted from these data. 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 (Fig. 2) at higher 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 Phe. The formation of various binary complex species is shown in the following equilibria. 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. The formation of various binary complex species is shown in the following equilibria.

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

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

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

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

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

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

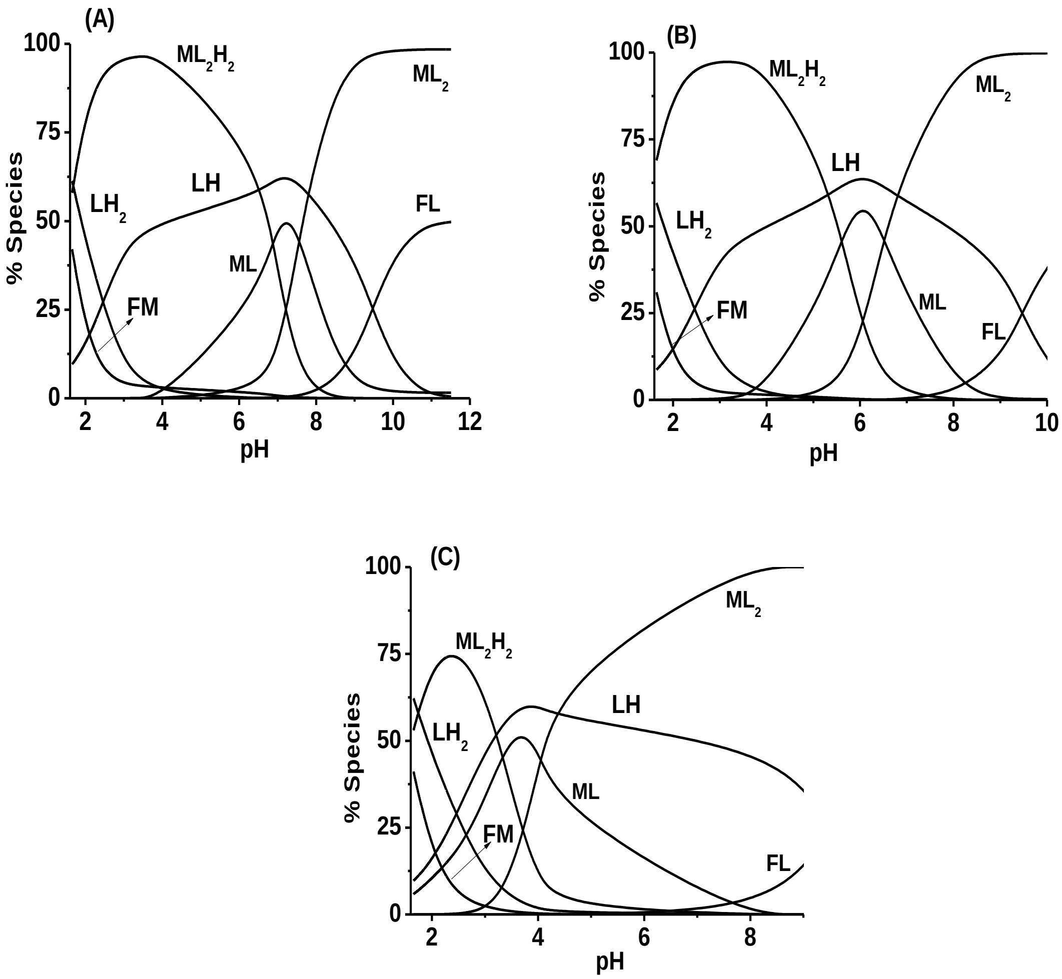


Figure 2: Distribution diagrams of Phe complexes in 1.0 % v/v TX100 – water medium. (A) Co(II) (B) Ni(II) and (C) Cu(II)

APPLICATIONS

The studies carried out on these systems under the present experimental conditions are useful to understand the role played by the active site cavities in biological molecules, the type of complex formed by the metal ion and the bonding behaviour of protein residues with the metal ion. Hence, the speciation studies on the interaction of L-phenylalanine with Co (II), Ni(II) and Cu(II) in varying compositions of TX100 – water mixtures have been carried out.

CONCLUSIONS

1. The predominant species detected were ML_2, ML_2H, and ML_2H_2 for Co(II), Ni(II), and Cu(II). At lower pH, protonated complexes are formed and these are deprotonated as the pH increases.
2. The stabilities of these species in TX100 – water medium do not show a particular trend because of accumulation of metal ion and ligand on the surface of micelles with increased concentration of surfactant and species with lower charge or high hydrophobicity are stabilized in the micellar pseudophase. The present biomimetic studies of metal ion complexes with L-Phenylalanine in TX100 – water mixtures indicate that all the complexes were protonated in acidic pH values.

3. The higher concentration of free metal in low pH values make the metal more bioavailable, more so in the case of toxic metals. At higher pH values, the higher concentrations of complex chemical species indicate that the metals are more amenable for transportation at higher pH values.
4. The order of the compounds influencing the magnitudes of the stability constants due to the incorporation of errors was alkali > acid > ligand > metal.

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AUTHORS' ADDRESSES

1. **Gowri Kumari Vasireddy**
Department of Inorganic & Analytical Chemistry,
Andhra University,Visakhapatnam – 530 003,India.
Email: vasireddy.gowri@gmail.com
Mobile no. 9550787190

2. **Nageswara Rao Choppa**
Department of Inorganic & Analytical Chemistry,
Andhra University, Visakhapatnam – 530 003, India.
Email id: nageshchoppa@gmail.com
Mobile no. 9849942610

3. **Dr. Sailaja B. B. V**
Assistant Professor,
Department of Inorganic & Analytical Chemistry,
Andhra University, Visakhapatnam – 530 003, India.
Email: sailajabbv.chem@gmail.com, Mobile no. 9441328956