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Effect of Cationic Micelles on Chemical Speciation of Binary Metal-Ligand Complexes of Co(II), Ni(II) and Cu(II) Metal ions with an essential Amino acid L-Methionine

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Abstract

Chemical speciation of binary complexes of L-Methionine with transition trace metal ions was studied potentiometrically. The study was conducted by varying concentrations (0.0-2.5% w/v) of CTAB, water mixture and at an ionic strength of 0.16 mol dm^{-3} using NaNO$_3$ as an electrolyte at 303.0 ± 0.1 K. The stability constants of various binary species were established by modelling studies using the computer program MINIQUAD75. Alkalimetric titrations were carried out in presence of relative concentrations of metal(M) to L-Methionine(L) (M:L=1:2.5, 1:3.5, 1:5) with sodium hydroxide as titrant.

The shift in the variation of stability constants with change in mole fraction of the surfactant (cationic micellar) media is described on the basis of two opposite forces namely electrostatic and non-electrostatic. Distribution of species in relation to pH at various compositions of micellar medium and plausible structures was presented.

Keywords: Chemical Speciation, binary complexes, CTAB, MINIQUAD75 and L-Methionine.

Introduction

Chemical speciation of elements is a key topic for systems like natural waters and biofluids, which is much essential for discussing constituent's chemical behaviour in these systems. This clearly understands the chemical form of a metal or metalloid that describes the reactivity, life time and fate in the environment. Speciation analysis is also significant from a chemical and toxicological point of view because it gives necessary information about geochemical behaviour of chemical species as well as the biological availability and toxicity of elements. The knowledge of speciation is critical to understand i) transport ii) accumulation iii) bioavailability and iv) toxicity of elements within and between the environmental compartments of air, soil, water, sediments and biota [2, 19, 12].

Since last three decades, a growing interest is developing on chemical speciation of metal complexes from researchers due to wide applications in various fields (medicinal, industrial, analytical and environmental chemistry) in addition to pharmacokinetics and pharmacodynamics in biological systems, where the former one is the study of a) absorption b) distribution c) metabolism and d) excretion of drugs in living bodies and later theory explains how the body reacts to drugs.[1,3,36] The present study investigates the binding affinity of essential ligand L-Methionine with '3d' transition trace metal ions such as Co(II), Ni(II) and Cu(II) in cationic micellar medium. Stability of metal complexes can be determined by different authors using various techniques like Potentiometry, Spectrophotometry and Paper Ionophoretic Technique, but results obtained from potentiometric method provide universally allowed values of stability constants[39].

A lot of data is available on stability constants in literature[7] but we still need some more data at different experimental conditions because the formed coordination compounds were treated as models in synthesizing novel complexes for therapeutic use.

L- Methionine (L-Met) plays critical role of cell metabolism and in proteins. It is the only amino acid which starts the process of making new proteins inside the cell. Because of its high hydrophobicity, most of the methionine residues in globular proteins are found in the hydrophobic core; in membrane-spanning protein domains, methionine is often found to interact with the lipid bilayer [7]. The exposed methionine residues are oxidized to methionine sulphoxide residues, which acted as endogenous antioxidants in proteins[22].

The catalytic activity of the enzyme methionine sulphoxide reductase reduces methionine residues to methionine. Thus, an oxidation-reduction cycle occurs. The impaired activity of methionine sulfoxide reductase and the subsequent accumulation of methionine sulfoxide residues are associated with age-related diseases, neuro degeneration and shorter life span[25]. The role of '3d' transition trace metals in biological systems is well recognized[37]. Trace metal ions like Co(II), Ni(II) and Cu(II) are essential and any variation in their homeostasis leads to metabolic disorders.[11,41]

Most of the speciation studies are performed in aqueous media under conditions comparable to those existing in physiological systems. These are taken as models for the systems existing in biofluids and natural waters. But biosystems are associated with low dielectric media of different magnitude and metabolic reactions are carried out under strictly compartmentalized conditions. The selected medium, cetyltrimethyl ammonium bromide(CTAB), a cationic surfactant, forms micelles in aqueous solution, when concentration is more than its CMC (critical micelle concentration) value in which micellisation leads to compartmentalization[4].

Generally, CTAB tends to denature proteins and profoundly influences the bulk properties of physiological systems and is also used for isolating DNA from plant tissues. It can solubilize, concentrate and compartmentalize ions and molecules.[14,18]

Hence, the chemical speciation of the entitled system has been carried out to examine the species distribution and the effect of cationic micelles on binary complexes of trace metal ions with selective bio-ligand.

Material and Methods

Solution of 0.05 mol dm^{-3}, L-Methionine (Merck, India) was prepared in triple-distilled deionized water by maintaining nitric acid (0.05 mol dm^{-3}) to increase the solubility. CTAB (Merck, India) was used as received. 2.0 mol dm^{-3} of sodium nitrate was prepared to maintain the ionic strength in the titrand, 0.4 mol dm^{-3} of sodium hydroxide and 0.2 mol dm^{-3} of nitric acid were prepared. Nitrates of Co(II), Ni(II) and Cu(II) solutions were prepared by dissolving AR Grade salts in triple distilled water by maintaining 0.05 mol dm^{-3} mineral acid(HNO_3) to suppress the hydrolysis of metal salts. All the solutions were standardized by standard methods[42]. To assess the errors in the concentration, the data was treated with analysis of variance of one way classification (ANOVA). The strengths of alkali and mineral acid was determined using the gran plot method.[16,17,34]

Instrumentation: An Elico (Model L1-120) digital pH meter of readability 0.01 was used for the titrimetric data which is calibrated with Potassium hydrogen phthalate (0.05 mol dm^{-3}) in acidic region and borax (0.01 mol dm^{-3}) in basic region. The glass electrode was equilibrated in a well stirred CTAB-water mixture containing 2.0 mol dm^{-3} of sodium nitrate and acts as an inert electrolyte. All the titrations were performed in aqua surfactant media of concentration ranges from 0.0 to 2.5% (w/v) at 303.0 ± 0.1 K and constant ionic strength of 0.16 mol dm^{-3}. During the experiment, the change in asymmetric potential, liquid junction potential, activity coefficient, sodium ion error and dissolved carbon dioxide were accounted on the glass electrode in the form of a correction factor[30].

Analytical Procedures: In order to determine the stability constants of the 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 equilibrated in CTAB-water mixture containing inert electrolyte for several days to attain the composition of the titrand. Titrations with different metal to ligand ratios (1:2.5, 1:3.5 and 1:5.0) were carried out with 0.4 mol dm^{-3} of sodium hydroxide. Other experimental details are given elsewhere [27].

Results and Discussion

Modelling Strategy: The computer program SCPHD [33] was used to calculate the correction factor. The stability constants of the binary species were calculated from the computer program MINIQUAD75[15] using the potentiometric titration data, which exploit the advantage of a constrained least- squares method in the initial refinement and reliable convergence of Marquardt algorithm. The correction factor and protonation constants of L-Methionine were fixed throughout the refinement.[20,32] The initial concentrations of metal to ligand ratios were listed in table 1.

Alkalimetric titrations curves in CTAB-water mixture of L-met are active in the pH range of 2.0-10.5. Based on the active form of the ligand in this pH range, models containing various compositions of the complex species were fed to MINIQUAD75 along with titration data. The results of the best fit models that contain stoichiometry of the complex species and their overall formation constants (log β) along with some of the important stastical parameters are given in table 2.

A very low value of standard deviation of log β's (formation constants) signifies the precision of these constants. The small values of Ucorr (sum of squares of deviations in concentration of ligand and hydrogen ion at all experimental points) corrected for degrees of freedom, small values of mean, standard deviation and mean deviation for systems are validated by the residual analysis.

Residual analysis of the data analyzed by least squares methods, the residuals (the difference between the experimental data and the data simulated based on model parameters) are assumed to follow Gaussian or normal distribution[29]. When the data fit into the models, the residuals should ideally be equal to zero. If stastical measures of the residuals and the errors assumed in the models are not significantly different from each other, the model is said to be adequate. Further, a model is considered adequate only if the residuals do not show any trend.

Respecting the hypothesis that the errors are random following normal distribution in the least squares analysis, the residuals are tested for normal distribution. Such tests are skewness, kurtosis, χ^2 and R-factor. These stastical parameters show that the best fit models portray the binary complexes of L-Met with Co(II), Ni(II) and Cu(II) metal ions in CTAB- water mixtures.

χ^2 test(chi square): χ2, a special case of gamma distribution, is a probability density function, which is a function of symmetry.

Table 1
Total concentrations of reactants (in mmol) for metal-ligand titrations in CTAB, Water mixtures.

% w/v CTAB	TM0			TL0	TM0:TL0
	Co(II)	Co(II)	Ni(II)	Met	
0.0	0.0999	0.0997	0.1001	0.2505	1.0:2.5
				0.3506	1.0:3.5
				0.5009	1.0:5.0
0.5	0.0998	0.0997	0.0999	0.2508	1.0:2.5
				0.3512	1.0:3.5
				0.5015	1.0:5.0
1.0	0.1001	0.0997	0.0998	0.2503	1.0:2.5
				0.3504	1.0:3.5
				0.5005	1.0:5.0
1.5	0.0999	0.1002	0.0996	0.2500	1.0:2.5
				0.3500	1.0:3.5
				0.5000	1.0:5.0
2.0	0.0998	0.0999	0.0997	0.2498	1.0:2.5
				0.3497	1.0:3.5
				0.4995	1.0:5.0
2.5	0.0998	0.0998	0.1001	0.2498	1.0:2.5
				0.3497	1.0:3.5
				0.4995	1.0:5.0

This distribution measures the probability of residuals forming a part of standard normal distribution with zero mean and unit standard deviation. If the χ^2 calculated is less than the table 2 value, the model is accepted.

Crystallographic R-Test: Hamilton's R- factor ratio test is applied in complex equlibria to decide whether involvement of more species in the model is necessary or not. The readability of pH meter in pH metric method and the value of R represent the upper boundary limit of the model value beyond which the model has no significance. The simulated models obtained from the refinement whose values are greater than R-table, are rejected. The low crystallographic R-values given in table indicate the sufficiency of the model.

Skewness: Skewness describes the shape of the error distribution, which is a dimensionless quantity. A value of zero for skewness indicates that the underlying distribution is symmetrical. The negative value of skewness signifies the peak of the error distribution curve is to the left of the mean and the peak is to the right of the mean if the skewness values are positive [31]. The values of skewness recorded in the table are in between -0.61 to 0.18 for Cobalt(II), -0.51 to 0.68 for Nickel(II) and -0.32 to 0.12 for Copper(II). This data suggested that the residuals form a part of normal distribution, hence least-squares method can be applied to the present data.

Kurtosis: It 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). If the calculated kurtosis is less than three, the peak of the error distribution curve is flat(platykurtic) and if the kurtosis is greater than three, the error distribution is a sharp peak(leptokurtic)[5]. The kurtosis values in the present study indicate that most of the systems follow leptokurtic pattern, some of the copper systems follow platykurtic pattern.

Effect of Systematic errors on Best fit models: In order to get best fit models for critical assessment and application with various experimental conditions with different accuracies of data obtainment, a study made knowingly enters the pessimistic errors in the concentrations of alkali, mineral acid, ligand, metal and correction factor. Obtained results were shown in table 3.

From table 3, it is observed that the magnitudes of stability constants influenced by concentration of alkali, acid and ligand were more compared to concentration of metal, volume and correction factor (log F).

The rejection of some species and increased standard deviations in the overall formation constants on introduction of errors in concentration confirm the suitability of the experimental conditions and choice of the best fit models.

Effect of the Medium: Variations in magnitude of formation constants for the complex species formed due to the interaction between metal ions and L-Met with mole fraction of the surfactants are shown in figure 1, which indicate that the stabilities of the metal complexes were increasing linearly with mole fraction of the CTAB medium.

The increase in stability of the complexes with increased surfactant concentration may be due to the increased micelles size and decreased dielectric constant of the medium.

Table 2
Parameters of best fit chemical models of M(II)-Met complexes in CTAB, Water mixtures; Temperature=303 K, Ionic strength=0.16 mol dm^{-3}.

% w/v CTAB	log β_{mlx} (SD)			pH range	NP	Ucorr	Skewness	Kurtosis	$\chi2$	R-factor
	MLH	ML	ML_2							
Co(II)										
0.0	10.53(13)	3.28(20)	5.65(37)	1.69-8.7	86	7.92	-0.27	3.78	53.01	0.0220
0.5	11.33(13)	3.94(14)	6.69(19)	2.16-8.4	79	2.21	0.02	5.87	10.31	0.0177
1.0	11.78(18)	4.14(16)	7.17(23)	2.18-9.5	99	1.75	0.18	5.87	92.36	0.0153
1.5	12.63(21)	4.59(24)	6.92(29)	2.00-9.5	104	5.68	0.02	5.79	94.87	0.0078
2.0	12.79(11)	4.78(14)	7.54(27)	2.02-8.8	92	3.42	0.17	7.89	41.45	0.0107
2.5	13.20(18)	4.76(22)	8.39(22)	2.08-9.2	122	1.06	-0.61	5.06	56.78	0.0171
Ni(II)										
0.0	11.56(06)	5.59(08)	8.98(12)	1.69-8.7	126	0.98	0.09	5.56	64.50	0.0097
0.5	11.83(15)	5.62(05)	9.24(11)	2.16-8.5	86	2.81	0.20	7.73	84.70	0.0087
1.0	12.06(18)	5.76(27)	9.03(37)	2.18-8.5	92	2.59	0.05	5.1	64.58	0.0113
1.5	12.18(11)	5.78(14)	9.51(21)	2.00-9.5	110	3.31	0.18	4.89	43.09	0.0123
2.0	11.87(12)	5.83(14)	9.64(12)	2.02-8.5	106	3.36	0.68	32.9	81.27	0.0096
2.5	13.03(20)	6.08(32)	9.65(39)	2.08-8.5	114	1.54	-0.51	4.49	47.24	0.0233
Cu(II)										
0	11.18(08)	7.19(13)	13.56(12)	1.63-5.2	134	2.56	-0.19	3.38	26.7	0.0154
0.5	11.32(10)	7.51(08)	14.12(10)	2.16-4.7	27	3.78	0.12	5.13	56.58	0.0076
1.0	12.29(11)	8.56(09)	13.85(44)	2.28-5.8	81	1.85	-0.19	3.68	8.69	0.0058
1.5	13.01(14)	8.72(20)	15.30(16)	1.64-4.7	86	0.77	-0.03	2.68	5.88	0.0072
2.0	12.54(04)	9.18(05)	15.94(14)	1.64-4.8	81	5.91	-0.23	2.57	3.55	0.0085
2.5	12.89(23)	10.06(10)	17.22(15)	1.64-5.0	86	14.3	-0.32	3.22	27.52	0.0135

U_{corr} = U/ (NP-m).10^8; NP = Number of points; m = number of formation constants; SD = Standard deviation

The dielectric constant of the medium has a direct influence on the protonation-deprotonation equilibria[9,10]. The variation in log K^M or change in free energy (ΔG^1) with surfactant content can be written as the sum of the changes in ΔG^1 due to electrostatic and non-electrostatic factors.

$$\Delta G^1 = RT (\ln K^M - \ln K^W) = \Delta G_{el} + \Delta G_{nel} \quad (1)$$

According to Born's classical treatment[6], the electrostatic factors contribute to the free energy change. According to this treatment, the energy of the electrostatic interactions is related to the dielectric constant(Ds) of the medium given by

$$\Delta Gel = {}^{re2}/_{Z} * {}^{1}/_{Ds} * {}^{1}/_{r} \quad (2)$$

From equations (1) and (2), the logarithm of stability constants should vary linearly as a function of reciprocal of dielectric constant of the medium. The Stern layer[8] of the cationic micelles(CTAB) has positively charged head groups and corresponding anions are presented in Gouy-Chapmann double layer.

Hence, the formed positively charged complex species should be stabilized on the surface of the micelles. The species should be stabilized in the micellar medium with opposite charges in CTAB due to electrostatic interactions[28].

Distribution Diagrams: L-Met, a bidentate ligand has two protonation constants. It exists as LH_2^+, LH and L^- in the pH region 1.7-6.0, 1.8-10.5 and 4.0-10.5 respectively. The chemical species identified in the present study were MLH, ML and ML_2 for the three systems Co(II), Ni(II) and Cu(II). The above species existed in the pH range 1.69-9.5 for Co(II) and Ni(II) and for Cu(II) in the pH range 1.63-5.8. The distribution diagrams were drawn using the formation constants of the best fit models as shown in figure 2.

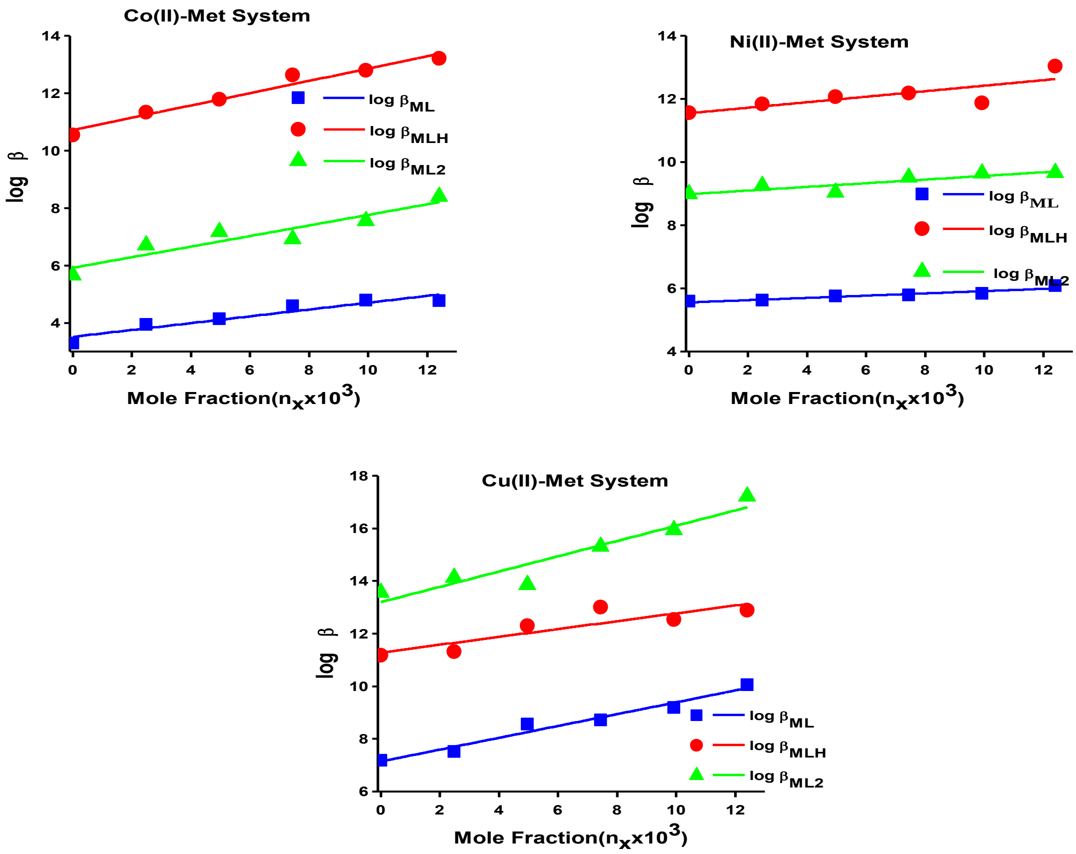

Figure 1: Variation in overall stability constant values of Metal-Met complexes with mole fraction (n_x x 10^3) of CTAB-water mixtures

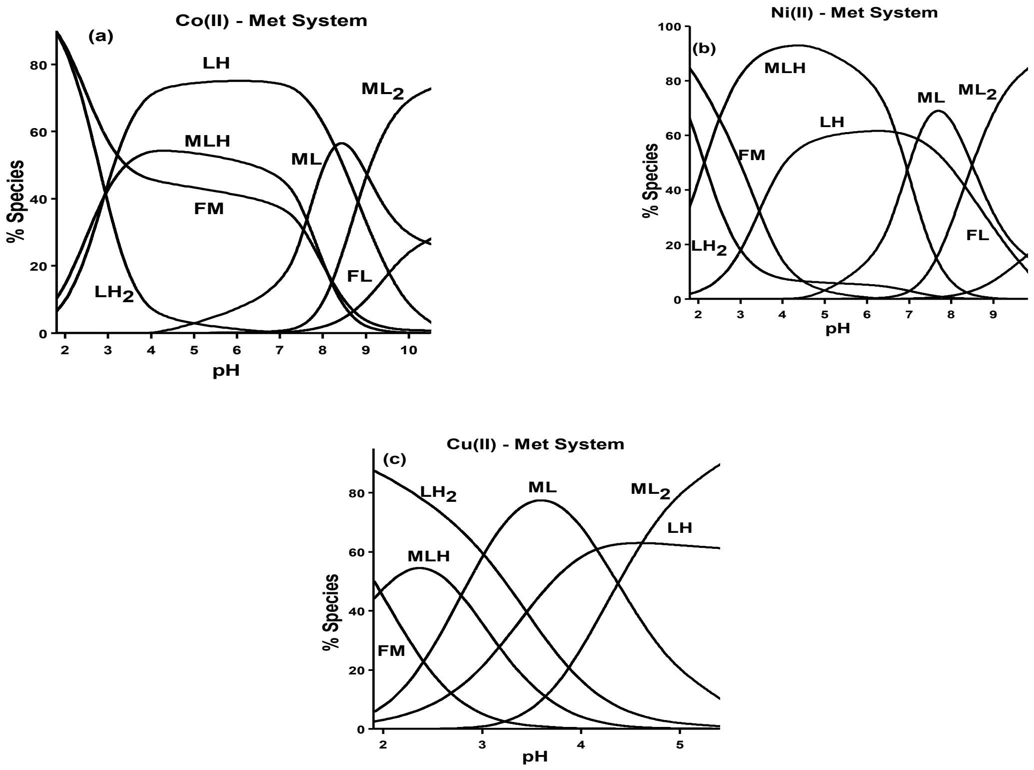

Figure 2: Distribution diagrams of binary complexes (a) 1.0 % (b) 1.5 % and (c) 2.5 % w/v in CTAB-Water medium

Table 3
Effect of errors in influential parameters on Ni(II)-Met complexes stability constants in 0.5% w/v of CTAB-water mixtures.

Ingredient	% of error	log β_{mlh}(SD)		
		MLH	ML	ML_2
	0	11.83(15)	5.62(05)	9.24(11)
Alkali	-5	10.31(10)	4.40(21)	6.42(36)
	-2	11.45(18)	5.18(16)	8.18(28)
	+2	12.21(16)	6.06(16)	10.30(18)
	+5	13.59(55)	7.55(54)	12.33(54)
Acid	-5	10.40(12)	4.56(25)	6.80(36)
	-2	11.49(23)	5.32(24)	9.47(23)
	+2	11.24(21)	5.08(15)	8.19(27)
	+5	Rejected	4.41(18)	8.94(21)
Ligand(L)	-5	11.49(15)	5.41(13)	6.86(53)
	-2	11.70(14)	5.54(14)	9.11(19)
	+2	11.96(16)	5.73(16)	9.19(20)
	+5	12.17(20)	5.90(20)	9.33(22)
Metal	-5	11.88(16)	5.65(17)	9.46(21)
	-2	11.85(15)	5.64(15)	9..38(21)
	+2	11.85(15)	5.63(15)	9.23(21)
	+5	11.89(15)	5.67(15)	9.14(21)
log F	-5	11.53(14)	5.40(13)	9.03(20)
	-2	11.67(15)	5.51(14)	9.12(20)
	2	11.95(16)	5.73(16)	9.37(21)
	5	12.11(19)	5.87(19)	9.53(24)
volume	-5	11.78(15)	5.59(15)	9.23(21)
	-2	11.81(15)	5.61(15)	9.24(21)
	+2	11.85(15)	5.64(15)	9.26(21)
	+5	11.87(15)	5.66(15)	9.28(21)

The pattern of species distribution with pH shows that the concentration of species was affected by Surfactant-Water mixtures. The formation of binary species based on the above observations is represented by the given equilibria.

$$M(II) + LH_2^+ \rightleftharpoons MLH^{2+} + H^+ \qquad (1)$$
$$MLH^{2+} \rightleftharpoons ML^+ + H^+ \qquad (2)$$
$$M(II) + LH_2^+ \rightleftharpoons ML^+ + 2H^+ \qquad (3)$$
$$M(II) + 2LH_2^+ \rightleftharpoons ML_2H_2^{2+} + 2H^+ \qquad (4)$$
$$ML_2H_2^{2+} \rightleftharpoons ML_2 + 2H^+ \qquad (5)$$
$$M(II) + 3LH_2^+ \rightleftharpoons ML_3H_3^{2+} + 3H^+ \qquad (6)$$
$$M(II) + 2LH_2^+ \rightleftharpoons ML_2H^+ + 3H^+ \qquad (7)$$
$$M(II) + 2LH_2^+ \rightleftharpoons ML_2 + 4H^+ \qquad (8)$$
$$M(II) + 3LH_2^+ \rightleftharpoons ML_3H_2^+ + 4H^+ \qquad (9)$$
$$M(II) + 3LH_2^+ \rightleftharpoons ML_3H + 5H^+ \qquad (10)$$
$$M(II) + 3LH_2^+ \rightleftharpoons ML_3^- + 6H^+ \qquad (11)$$

The cationic micelles(CTAB) have positive surface charge which can easily form complexes with negatively charged species. Hence, the stabilities of the complexes are increasing linearly with mole fraction of CTAB. At low pH level, MLH is the dominative species and at high pH level ML and ML_2 are dominative, besides ML is the predominant existed species for Co(II) and Ni(II) systems at physiological pH range.

Proposed Structures for Binary Complexes: The proposed structures for Co(II) and Ni(II) complexes were found to be in octahedral geometry in literature by various authors. But apart from these complexes, Cu(II) complexes have been suggested geometry of square planar or distorted octahedral. This distortion was caused by the effect of Jahn-Teller distortion[35,40]. Besides, nitrogen donor sites of amino acids have greater tendency towards electron pair acceptors in pH of the physiological region. Hence, metal ions and protons become the contestants in binding the ligand sites, hence forming protonated and deprotonated species existed in the solution equlibria of the metal-methionine complexes.

Met is a bidentate chelate ligand containing carboxylate (-COO^-) and amino (-NH_2) groups binded the metal ions via the donor atoms of ‘O’ and ‘N’ forming a stable five membered chelate rings.[13,21,23,24,26,38] At lower pH, the protonated species(MLH) are formed by the donation of electron pair from oxygen atom of the carboxylate group leaving the lone pair electrons in amino group donated to the proton.

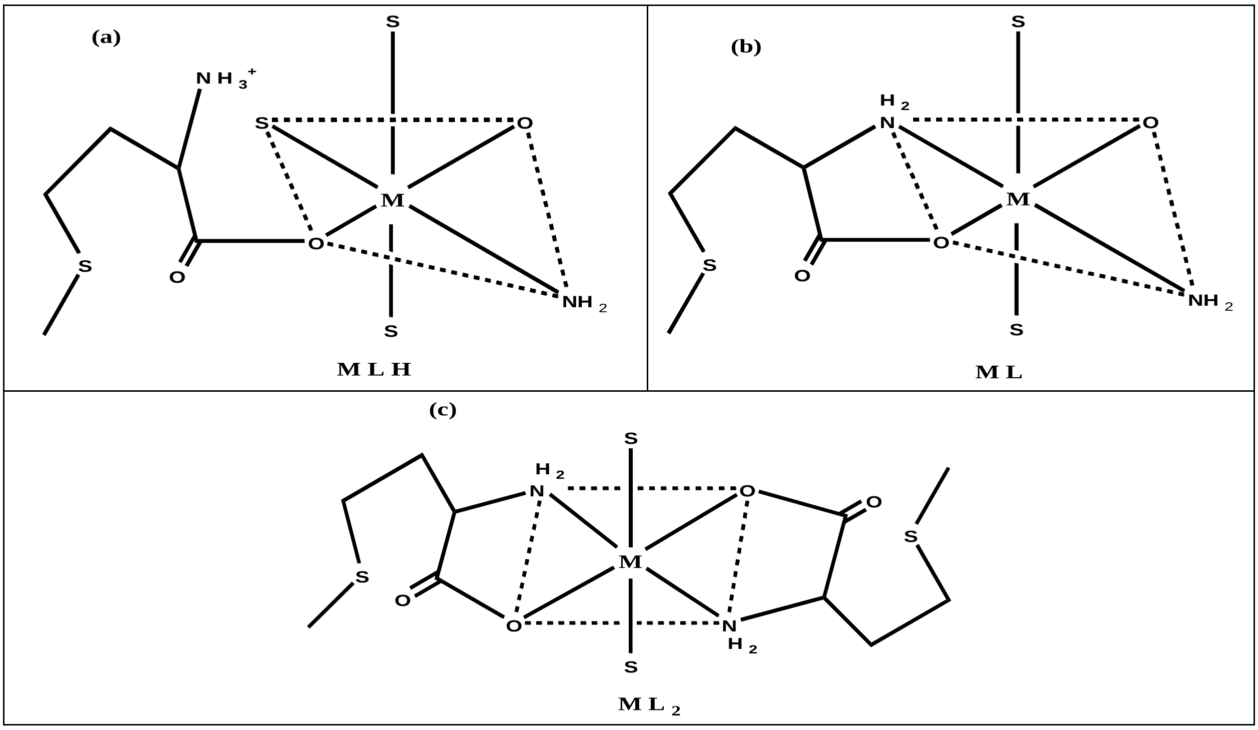

Figure 3: Proposed structures for binary complexes (S is either solvent or water molecules)

At high pH level, the two active sites contain donor atoms ‘N and O’ of Met bonded with metal ions forming deprotonated species (ML and ML_2). In addition to this theoretical evidence from valence shall electron pair repulsion theory, it is suggested that binary complexes of metal (Co(II), Ni(II) and Cu(II))-Methionine systems must be octahedral in shape and the proposed structures are presented in figure 3.

Conclusion

The following conclusions have been inferred from the modeling studies.

1. The bio mimic studies of the metal ion complexes with L-Met indicate that all the complexes are protonated in the pH range 1.8-10.5.
2. The binary species detected are MLH, ML and ML_2 for Co(II), Ni(II) and Cu(II) metal ions when interacted with L-Met in cationic micellar medium of CTAB. Only these species are refined due to the restricted pH ranges and the possible active forms of ligands like LH_2^+ and LH for Met.
3. The order of stability of these complexes was formed to be Co(II) < Ni(II) << Cu(II).
4. The linear increase in stabilities of binary complexes with decreasing dielectric constant due to the dominance of electrostatic forces and some nonlinearity is due to dominance of non-electrostatic forces.
5. The effect of systematic errors in influential parameters shows that the errors in the concentration of alkali and mineral acid will affect the formation constants more than that of the ligand.

The study also gives an insight into the metal availability / metal transport in bio fluids.

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