Influence of propylene glycol on chemical speciation of ternary complexes of bi- and tri-dentate ligands with some essential metal ions

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Abstract : Equilibria of complexation of Co^{II}, Ni^{II} and Cu^{II} ions with L-aspartic acid and ethylenediamine were investigated pH metrically in 0.0–60.0% v/v propylene glycol-water mixtures maintaining an ionic strength of 0.16 mol L^{-1} at 303.0 ± 0.1 K. Stability constants of ternary complexes were calculated and various models were refined with MINIQUAD75. The best fit chemical models were selected based on statistical parameters and residual analysis. The species detected were MLXH, MLX and ML_2X for Co^{II}, Ni^{II} and Cu^{II}. The appropriateness of experimental conditions was verified by introducing errors intentionally in the concentrations of ingredients. The stabilities of the complexes followed the Irving-Williams order, i.e. Co^{II} < Ni^{II} < < Cu^{II}.

Keywords : Chemical speciation, ternary complexes, aspartic acid, ethylenediamine, propylene glycol, MINIQUAD75.

Introduction

Several studies on ternary stability constants of α-amino acids have been reported in different media[1,2]. Metal ions exist in non-exchangeable form, loosely bound to some biological ligands and in equilibrium with a variety of bioligands in different biofluids like blood serum, intestinal fluid, cerebrospinal fluid, gastric juice etc. Thus, simultaneous equilibria involving a variety of metal ions and ligands are possible in bio fluids. Cobalt, nickel and copper have several biological functions[3,4]. Therefore, investigation of ternary complexes containing a metal ion and two different ligands drew the attention of several researchers. Mixed ligand complexes can be considered as models for apoenzyme-metal ion-substrate complexes. In peptides, proteins and amino acids, amide group is one of the important binding sites for the coordination of the metal ions. Acidity and basicity of a molecule is governed by its structure and solvent effects[5]. Propylene glycol (PG) is chosen as a polar organic solvent to mimic the permittivity of the biological fluids. L-Aspartic acid (Asp) and ethylenediamine (en) are chosen as model compounds to proteins and substrates.

Asp, a non-essential amino acid, plays an important role in maintaining the solubility and ionic character of proteins[6]. en is used as an important monodentate, bidentate or a bridging ligand[7]. It is useful in manufacturing accelerator or curing agent in epoxy industry. It is involved in the synthesis of β-enaminoesters[8] and Schiff bases[9]. The protonation constants of ethylenediamine were reported earlier by theoretical calculations[10,11]. Protonation constants[12] and binary stability constants of Asp[13] and en[14] with Co^{II}, Ni^{II} and Cu^{II} in PG-water mixtures were reported earlier. Hence, chemical speciation of their ternary complexes is reported in this communication.

Experimental

Aqueous solutions (0.1 mol L^{-1}) of Co^{II}, Ni^{II} and Cu^{II} chlorides (GR grade, E. Merck, Germany) were prepared by dissolving them in triple distilled water. 0.05 mol L^{-1} aqueous solutions of L-aspartic acid (GR grade, E. Merck, Germany) and ethylenediamine (AR, Qualigen, India) were also prepared. To increase the solubility of the ligands and metal salts, 0.05 mol L^{-1} hydrochloric acid was maintained in the solutions. Propylene glycol (Finar, India) was used as received. The strength of acid in metal ion solutions was determined using the Gran plot method[15,16]. Errors in the concentrations of the ligands, metal ions and alkali were subjected to analysis of vari-

ance (ANOVA)[17].

Titrations were carried out in the medium containing varying concentrations of PG maintaining an ionic strength of 0.16 mol L^{-1} with sodium chloride at 303.0 ± 0.1 K, with ELICO (Model LI-120) pH meter of 0.01 readability in conjunction with a glass and calomel electrode. The pH meter was calibrated with 0.05 mol L^{-1} potassium hydrogen phthalate in acidic region and 0.01 mol L^{-1} borax solution in basic region. The glass electrode was equilibrated in a well stirred PG-water mixtures containing inert electrolyte.

Determination of correction factor :

The effect of variation in asymmetry potential, liquid junction potential, activity coefficient, sodium ion error and/or dissolved carbon dioxide on the response of glass electrode is to be considered for accurate determinations. Correction factor proposed by McBryde[18] and others[19–21] to account for the above parameters was used in the present electrometric titrations. The simulated acid-base titration data (pHC_i) calculated by SCPHD[22] program was used to compute correction factor (log F) for each of the solvent compositions (eq. 1). Thus calculated log F value was used to convert pH meter dial reading (D) into logarithm of reciprocal of hydrogen ion concentration (pHE_i) according using eq. (2).

$$\log F = pHC_i - pHE_i \tag{1}$$
$$pHE_i = D - \log F \tag{2}$$

Each point in the titration data past the equivalence point was corrected for sodium ion error ($\sim$ < 0.05 units) using the data available for aqueous system (Radiometer pH meter operational manual). The values of pOH and subsequently the value of pK_w were calculated from the volume of alkali added.

Titration procedure :

The titrations were carried out in media containing varying amounts (0–60% v/v) of PG maintaining an ionic strength (μ) of 0.16 mol L^{-1} with NaCl at 303.0 K. In these titrations, the titrand consisted of mineral acid and ligand, in the presence and absence of metal ion, in a total volume of 50 mL. Titrations were performed by adding each time 0.1 mL portions of 0.4 mol L^{-1} sodium hydroxide to the titrand. The pH meter reading was recorded only after a constant value was displayed. Typical

duplicate titrations showed that equilibration was fast and titration data did not differ by more than 0.02 units.

Titration of strong acid with alkali was carried out at regular intervals to check whether complete equilibration was achieved. The calomel electrode was refilled with PG-water mixtures of equivalent composition as that of the titrand. In each of the titrations, the titrand consisted of 1 mmol of hydrochloric acid in a total volume of 50 mL. Titrations were carried out in the presence of different relative concentrations of the metal (M) to Asp (L) to en (X) (M : L : X = 1 : 2.5 : 2.5, 1 : 2.5 : 5.0, 1 : 5.0 : 2.5) with 0.4 mol L^{-1} NaOH (Table 1). The best-fit chemical model for each system investigated was arrived at using MINIQUAD75[23], which exploits the advantage of constrained least squares method in the initial refinement and reliable convergence of undammed, unconstrained Marquardt algorithm. The protonation constants and the stability constants of the binary metal complexes of the ligands were fixed in refining ternary complexes.

Table 1. Total initial concentrations of reactants (in mmol) for mixed ligand titrations in PG-water mixture

[NaOH] = 0.4 mol L^{-1}; V_0 = 50 mL; Temperature = 303.0 ± 0.1 K; Mineral acid = 1.0 mmol; Ionic strength = 0.16 mol L^{-1}

PG	TM0			TL0	TX0	TM0 : TL0 : TX0
% v/v	Co^{II}	Ni^{II}	Cu^{II}	Asp	en	
0.0	0.100	0.099	0.102	0.2500	0.2499	1 : 2.5 : 2.5
				0.2500	0.5000	1 : 2.5 : 5.0
				0.4999	0.2499	1 : 5.0 : 2.5
10.0	0.100	0.099	0.102	0.2498	0.2499	1 : 2.5 : 2.5
				0.2498	0.5000	1 : 2.5 : 5.0
				0.4998	0.2499	1 : 5.0 : 2.5
20.0	0.100	0.099	0.102	0.2492	0.2500	1 : 2.5 : 2.5
				0.2492	0.5000	1 : 2.5 : 5.0
				0.5001	0.2500	1 : 5.0 : 2.5
30.0	0.100	0.099	0.102	0.2510	0.2502	1 : 2.5 : 2.5
				0.2510	0.5000	1 : 2.5 : 5.0
				0.4998	0.2502	1 : 5.0 : 2.5
40.0	0.100	0.099	0.102	0.2550	0.2588	1 : 2.5 : 2.5
				0.2550	0.5000	1 : 2.5 : 5.0
				0.4999	0.2515	1 : 5.0 : 2.5
50.0	0.100	0.099	0.102	0.2500	0.2505	1 : 2.5 : 2.5
				0.2500	0.5000	1 : 2.5 : 5.0
				0.5001	0.2505	1 : 5.0 : 2.5
60.0	0.100	0.099	0.102	0.2500	0.2503	1 : 2.5 : 2.5
				0.2500	0.5000	1 : 2.5 : 5.0
				0.5001	0.2503	1 : 5.0 : 2.5

Results and discussion

Modeling strategy :

A preliminary investigation of alkali metric titrations of mixtures containing different mole ratios of Asp and en in the presence of hydrochloric acid and inert electrolyte indicates that no condensed species were formed. The existence of the ternary complexes was determined by performing an exhaustive modeling study and the results of a typical system are given in Table 2. The models were evaluated assuming the simultaneous existence of different combinations of species. Models containing various number and combinations of species were generated using an expert system package CEES and these models were refined using MINIQUAD75. As the number of species increased, the models gave better statistics denoting the best fit. The best fit models were chosen based on the statistical parameters like χ^2, *R*-factor, skewness and kurtosis given in Table 3.

A very low standard deviation (SD) in the overall stability constants (log β) indicates the precision of the parameters. The small values of U_{corr} (sum of squares of deviations in the concentrations of the metal, the ligands and the hydrogen ion at all experimental points corrected for degrees of freedom) indicate that the models 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.

χ^2 *test* :

χ^2 is a special case of gamma distribution whose probability density function is an unsymmetrical function. This distribution measures the probability of residuals forming a part of standard normal distribution[17] with zero mean and unit standard deviation. If the χ^2 calculated is less than the table value, the model is accepted.

Crystallographic R-test :

Hamilton's *R* factor ratio test[24] is applied in complex equilibria to decide whether inclusion of more species in the model is necessary or not. In pH metric method the readability of pH meter is taken as the R_{limit}, which represents the upper boundary of *R* beyond which the model bears no significance. When different values are obtained for models containing different numbers of species, models whose values are greater than *R*-table are rejected. The low crystallographic *R*-values given in Table 3 indicate the sufficiency of the model.

Skewness :

It is a dimensionless quantity indicating the shape of the error distribution profile. A value of zero for skewness indicates that the underlying distribution is symmetrical. If the skewness is greater than zero, 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 skewness is less than zero. For an ideal normal distribution, the value of skewness should be zero. The values of skewness recorded in Table 3 are between –0.46 and 3.46. These data evince 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 modal 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 distribution shall have sharp

Table 2. Exhaustive modeling study performed on Asp-Ni^{II}-en ternary complexes in aqueous medium
pH range = 4.0–10.0, NP = 92; Temperature = 303.0 ± 0.1 K, Ionic strength = 0.16 mol L^{-1}

Model No.	log β (SD)			U_{corr} $\times 10^8$	Skewness	χ^2	Kurtosis	R-Factor
	MLX	ML$_2$X	MLXH					
1.	11.96(12)	–	–	3.84	3.46	0.81	4.82	0.0008
2.	–	22.18(15)	–	3.44	5.32	0.20	10.65	0.0012
3.	–	–	27.58(7)	2.70	4.70	–1.26	76.96	0.0015
4.	12.91(12)	21.30(20)	–	2.04	1.15	–1.06	2.43	0.0109
5.	13.56(8)	–	24.33(6)	1.80	2.46	0.97	4.26	0.0006
6.	–	20.73(16)	22.12(8)	1.69	3.42	1.29	28.91	0.0075
7	15.01(32)	19.87(17)	21.15(10)	0.84	2.97	23.75	7.73	0.0177

Table 3. Best fit chemical models of ternary complexes of Co^{II}, Ni^{II} and Cu^{II} with Asp and en in PG-water mixtures

%v/v PG	log β_{mlxh} (SD)			NP	U_{corr} $\times 10^8$	χ^2	Skewness	Kurtosis	R-factor
	1111	1110	1210						
			Co^{II} (pH = 5.0–10.0)						
0.0	19.33(12)	11.88(8)	15.51(23)	23	0.85	12.35	–0.37	3.65	0.0039
10.0	19.46(12)	12.15(12)	16.16(12)	37	1.52	116.4	2.33	7.97	0.0109
20.0	19.67(22)	12.64(28)	16.7(20)	35	2.68	69.28	3.07	12.75	0.0289
30.0	19.87(12)	12.83(12)	16.86(12)	48	1.90	74.00	3.46	17.27	0.0526
40.0	19.99(12)	12.86(12)	16.93(12)	32	0.16	34.88	1.10	3.71	0.0432
50.0	20.18(12)	13.34(12)	17.10(12)	21	1.14	12.94	2.01	8.80	0.0064
60.0	20.78(12)	13.64(12)	18.37(12)	23	1.52	12.36	1.75	7.55	0.0132
			Ni^{II} (pH = 4.0–10.0)						
0.0	21.15(57)	15.01(32)	19.87(33)	96	7.84	23.75	1.60	7.73	0.0178
10.0	21.95(70)	15.39(49)	19.97(42)	34	9.38	22.09	2.12	8.57	0.0163
20.0	22.28(24)	15.59(22)	20.01(39)	36	6.18	14.55	–0.15	3.01	0.0134
30.0	22.33(25)	15.72(28)	20.24(36)	35	3.14	32.33	2.47	11.20	0.0094
40.0	22.60(18)	16.02(15)	20.40(19)	25	3.28	4.32	–0.22	3.09	0.0093
50.0	22.61(11)	16.33(12)	20.71(15)	26	0.60	23.08	2.79	15.08	0.0041
60.0	23.27(32)	17.11(63)	22.60(54)	27	9.54	12.59	2.61	10.07	0.0178
			Cu^{II} (pH = 2.0–8.0)						
0.0	30.31(24)	25.56(45)	32.65(27)	30	2.66	5.87	–0.19	3.36	0.0096
10.0	30.09(10)	25.61(25)	33.12(22)	37	3.29	4.63	–0.36	3.07	0.0085
20.0	30.83(30)	25.75(35)	33.43(33)	33	2.83	16.11	–0.42	3.38	0.0117
30.0	31.00(42)	26.28(49)	33.58(47)	59	4.58	48.07	–0.38	3.58	0.0199
40.0	31.22(14)	26.49(40)	34.88(23)	36	1.07	32.44	2.01	10.93	0.0083
50.0	31.38(13)	27.66(13)	35.01(13)	37	0.20	17.51	–0.06	4.84	0.0016
60.0	32.24(4)	28.18(8)	35.24(7)	39	0.95	10.15	–0.46	3.09	0.0034

peak (leptokurtic). For an ideal normal distribution, the value of kurtosis should be three. The kurtosis values in the present study indicate that most of the residuals are very nearer to leptokurtic and a few form mesokurtic patterns.

The ternary complex species detected are MLX, ML_2X and $MLXH$ for Co^{II}, Ni^{II} and Cu^{II}. The present values are compared with those reported earlier in ethylene gly-col (EG)-water mixtures (Table 4). The results are similar because both PG and EG are protophilic dipolar protic solvents and act as structure formers.

Solvent effect on stability of ternary complexes :

PG is a protophilic dipolar protic solvent and acts as a structure former. 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 com-

Table 4. Comparison of ternary stability constants reported in literature with the present study. Instrumental method is pH metry.

System	log β_{mlxh}						Ionic strength (M)	Ref.
	1110	1210	1111	1120	1121	1122		
Co^{II}-(L-Asp)-(en)	11.57	14.17	–	14.83	24.29	31.82	0.16	34
Co^{II}-(L-Asp)-(en)	11.88	15.51	19.33	–	–	–	0.16	Present study
Ni^{II}-(L-Asp)-(en)	13.89	16.92	–	18.35	26.62	32.46	0.16	34
Ni^{II}-(L-Asp)-(en)	15.01	19.87	21.15	–	–	–	0.16	Present study
Cu^{II}-(L-Asp)-(en)	17.81	20.98	–	21.97	30.40	37.11	0.16	34
Cu^{II}-(L-Asp)-(en)	25.56	32.65	30.31	–	–	–	0.16	Present study

plexes is expected to increase. At the same time, it is a coordinating solvent and it competes with the ligands for coordinating the metals. This decreases stability of the complexes. Hence, stability of the complexes may increase or decrease. The variation of overall stability constants with co-solvent content depends upon electrostatic and non-electrostatic factors. Born's classical treatment holds good in accounting for the electrostatic contribution to the free energy change[25]. According to this treatment, the energy of electrostatic interaction is related to dielectric constant. Hence, the log β values should vary linearly as a function of reciprocal of the dielectric constant ($1/D$) of the medium. The linear variation observed in the present study (Fig. 1) indicates that electrostatic forces are dominating the equilibrium process under the present experimental conditions. This is due to protophilic dipolar protic and structure forming nature of the solvent. The stabilities of the complexes follow the Irving-Williams order, i.e. $Co^{II} < Ni^{II} << Cu^{II}$.

Effect of systematic errors on stability of ternary complexes :

In order to rely upon the best-fit chemical model for critical evaluation and application under varied experimental conditions with different accuracies of data acquisition, an investigation was undertaken by introducing pessimistic errors in the influential parameters like concentrations of alkali, mineral acid, ligand, metal (Table 5). The order of the ingredients that influence the magnitudes of stability constants due to incorporation of errors is alkali > acid > Asp > en > metal.

The order of concentrations/number of mmols of the ingredients used in the present study is alkali (0.4 M), acid (1.0 mmol), ligand (0.25 mmol) and metal (0.1 mmol). Since the content of alkali is far higher than those of other ingredients, any variation (error) in the concentration of alkali affects the magnitude of the stability constant greatly. The content of acid is the highest next to alkali and hence the above order.

Some species were even rejected when errors were 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.
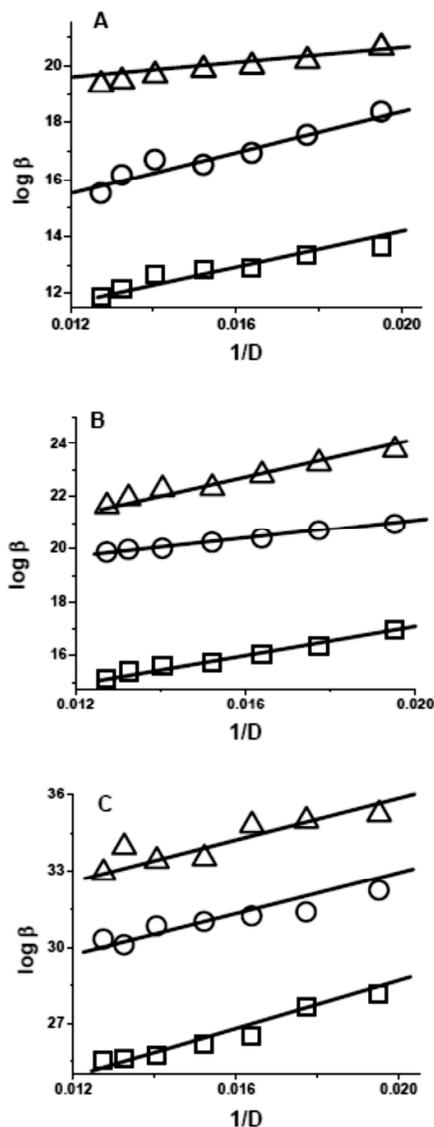

Fig. 1. Variation of stability constants of Asp-metal-en ternary complexes in PG-water mixtures. (A) Co^{II}, (B) Ni^{II} and (C) Cu^{II}; ($\square$) log β_{MLX}, ($\bigcirc$) log β_{ML_2X} and ($\triangle$) log β_{MLXH}.

Stability of ternary complexes :

The change in the stability of the ternary complexes as compared to their binary analogues was quantified[26,27] based on the disproportionation constant (log X) given by eq. (1) which corresponds to the equilibrium ML_2 + $MX_2 \rightleftharpoons 2MLX$. Under the equilibrium conditions one can expect the formation of 50% ternary complexes and 25% each of the binary complexes statistically and the value of log X shall be 0.6. A value greater than this accounts for the extra stability of MLX.

Table 5. Effect of errors in influential parameters on the stability constants of Asp-Co^{II}-en ternary complexes in 50% v/v of PG-water mixture

Ingredient	% Error	log β_{mlxh} (SD)		
		1111	1110	1210
	0	20.18(12)	13.34(12)	17.10(12)
Alkali	–5	Rejected	13.71(29)	Rejected
	–2	16.23(27)	15.70(38)	19.11(48)
	+2	19.92(41)	15.00(35)	Rejected
	+5	Rejected	Rejected	19.15(29)
Acid	–5	19.31(16)	12.82(29)	18.33(29)
	–2	18.90(23)	Rejected	18.96(20)
	+2	Rejected	14.71(35)	14.82(99)
	+5	18.35(43)	Rejected	Rejected
Asp	–5	18.73(35)	14.52(67)	16.30(30)
	–2	18.25(26)	14.17(46)	17.85(27)
	+2	18.20(25)	14.02(42)	16.15(36)
	+5	17.97(28)	13.98(38)	15.83(79)
en	–5	17.56(30)	13.86(17)	17.74(42)
	–2	18.12(26)	13.97(35)	17.23(32)
	+2	18.59(41)	13.98(78)	17.82(43)
	+5	19.98(38)	13.69(58)	17.29(40)
Metal	–5	19.55(30)	14.20(53)	18.99(28)
	–2	19.43(29)	14.04(48)	18.02(31)
	+2	19.27(54)	14.06(57)	18.14(62)
	+5	19.14(24)	14.64(37)	18.59(39)

$$ \text{(1)} $$
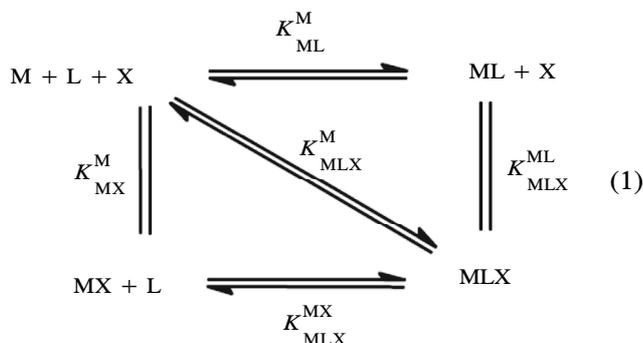
Another approach[28–30] to quantify the extra stability of ternary complexes was based on the difference in stability ($\Delta \log K$) for the reactions ML with X and M (aq) with L and X, where L is the primary ligand (Asp) and X is the secondary ligand (en). It is compared with that calculated purely on statistical grounds as given in eq. (2). The equations for the calculation of $\Delta \log K$ and log X are given in Table 6.

$$ \Delta \log K = \log K^M_{MLX} - \log K^M_{ML} - \log K^M_{MX} \quad \text{(2)} $$

The electrostatic theory of binary complex formation and statistical arguments suggest the availability of additional coordination positions of the hydrated metal ion for the first ligand than for the second. Hence, the usual order of stability $K^M_{ML} > K^M_{ML_2}$ applies. This suggests that $\Delta \log K$ should be negative, although several exceptions have been found[31]. The statistical values of $\Delta \log K$ for triden-

Table 6. log K and log X values of ternary complexes of Co^{II}, Ni^{II} and Asp-Cu^{II}-en in PG-water mixtures

% v/v	$\Delta \log K$		log X	
PG	1110	1210	1110	1111
		Co^{II}		
0.0	–0.47	–5.77	2.48	2.71
10.0	–0.39	–5.75	2.60	3.27
20.0	–0.37	–6.38	2.20	2.73
30.0	–0.29	–5.75	3.05	3.15
40.0	–0.51	–6.67	2.12	3.69
50.0	–0.03	–6.50	2.86	5.05
60.0	–0.19	–6.22	2.69	4.67
		Ni^{II}		
0.0	0.13	–5.19	3.68	4.69
10.0	–0.58	–5.56	3.27	4.40
20.0	–0.33	–5.12	3.78	4.76
30.0	–0.22	–5.49	3.62	5.65
40.0	–0.41	–6.24	3.20	5.69
50.0	–0.34	–6.25	3.62	6.12
60.0	0.51	–6.08	4.87	7.64
		Cu^{II}		
0.0	3.13	–3.24	15.23	15.77
10.0	6.28	–2.49	15.61	15.78
20.0	5.21	–4.93	13.14	–
30.0	4.96	–4.50	14.48	16.14
40.0	5.38	–2.76	15.34	16.46
50.0	6.21	–3.22	17.09	15.51
60.0	7.06	–2.46	18.66	17.55

Equations for the calculation of $\Delta \log K$ and log X

$\Delta \log K_{1110} = \log \beta_{1110} - \log \beta_{1100} - \log \beta_{1010}$

$\Delta \log K_{1210} = \log \beta_{1210} - \log \beta_{1200} - \log \beta_{1020}$

$\Delta \log K_{1111} = \log \beta_{1111} - \log \beta_{1100} - \log \beta_{1010}$

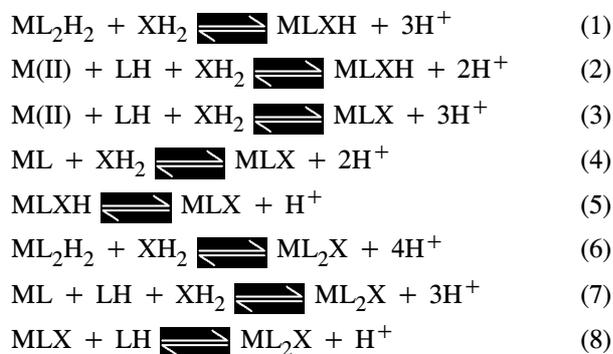$\log X_{1110} = 2 \log \beta_{1110} - \log \beta_{1200} - \log \beta_{1020}$

$\log X_{1210} = 2 \log \beta_{1210} - \log \beta_{1400} - \log \beta_{1020}$

$\log X_{1111} = 2 \log \beta_{1111} - \log \beta_{1202} - \log \beta_{1020}$

tate L and bidentate X are, –6.67 to 7.06 in PG-water mixtures (Table 6). Negative values of $\Delta \log K$ can be understood as the secondary ligand forms a more stable complex with hydrated metal ion than with L. Whenever the experimental values of $\Delta \log K$ exceed the statistical values, it can be inferred that the ternary complex is formed as a result of interaction of ML with X or MX with L. The $\log X$ and $\Delta \log K$ values could not be calculated for some systems due to the absence of relevant binary species. The $\log X$ values range from 2.12 to 18.66, all the values are found to be higher than those expected on statistical bases (0.6). These higher values account for the extra stability of the ternary complexes. The extra stability of ternary complexes makes them more amenable for metal transport. The less stable binary complexes make the metals bioavailable.

Distribution diagrams :

Based on the active forms of the ligands[12] (LH_3^+, LH_2, LH^-, L^{2-} and XH_2^{2+}, XH^+ and X) and the existence of the binary complex species[13,14] (ML, ML_2, ML_2H_2, ML_2H_3 and ML_2H_4 and MX, MX_2 and MX_3), the species are assumed to form through the following equilibria.

$$ML_2H_2 + XH_2 \rightleftharpoons MLXH + 3H^+ \qquad (1)$$

$$M(II) + LH + XH_2 \rightleftharpoons MLXH + 2H^+ \qquad (2)$$

$$M(II) + LH + XH_2 \rightleftharpoons MLX + 3H^+ \qquad (3)$$

$$ML + XH_2 \rightleftharpoons MLX + 2H^+ \qquad (4)$$

$$MLXH \rightleftharpoons MLX + H^+ \qquad (5)$$

$$ML_2H_2 + XH_2 \rightleftharpoons ML_2X + 4H^+ \qquad (6)$$

$$ML + LH + XH_2 \rightleftharpoons ML_2X + 3H^+ \qquad (7)$$

$$MLX + LH \rightleftharpoons ML_2X + H^+ \qquad (8)$$

The distribution of metal ions in various complex species (chemical speciation) with pH is represented as distribution diagrams. Some typical distribution diagrams are given in Fig. 2. The protonated ligands interact with metal ion (Equilibria 2, 3 and 4) to form MLXH and MLX. MLX is also formed by the dissociation of MLXH (Equilibrium 5) which is formed by the interaction of ML_2H_2 with XH_2 (Equilibrium 1). Similarly ML_2X is formed by the interaction of ML_2H_2 with XH_2 (Equilibrium 6), ML and LH with XH_2 (Equilibrium 7) and MLX with LH (Equi-
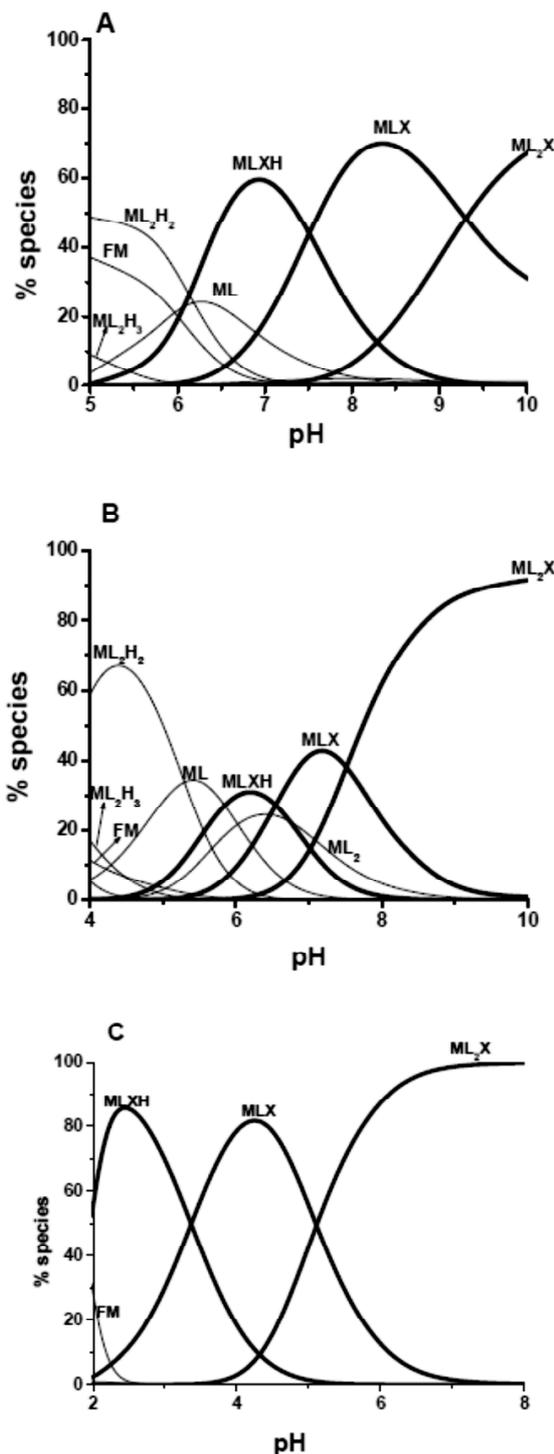

Fig. 2. Species distribution diagrams of ternary complexes of Asp and en in 40% v/v PG-water mixtures. (A) Co[II], (B) Ni[II] and (C) Cu[II]. The amounts of ingredients are M[II] : 1.0 mmol, Asp : 5.0 mmol and en : 2.5 mmol.

librium 8), because the concentrations of both MLX and LH are decreasing with increasing concentration of ML_2X in the pH range 8.0–10.0.

Structures of complexes :

The literature[32,33] suggests that Co^{II}, Ni^{II} and Cu^{II} complexes shall be octahedral. Amino nitrogen can associate with hydrogen ions in physiological pH ranges. Hence, there is often significant competition between hydrogen and metal ion for this donor site. This situation results in the simultaneous existence of a number of equilibria producing an array of protonated complexes, which are detected in the present study. Asp acts as bidentate or tridentate ligand depending on the experimental conditions and en acts as bidentate ligand. Thus based on the above equilibria the speculative structures of the complexes are presented in Fig. 3.
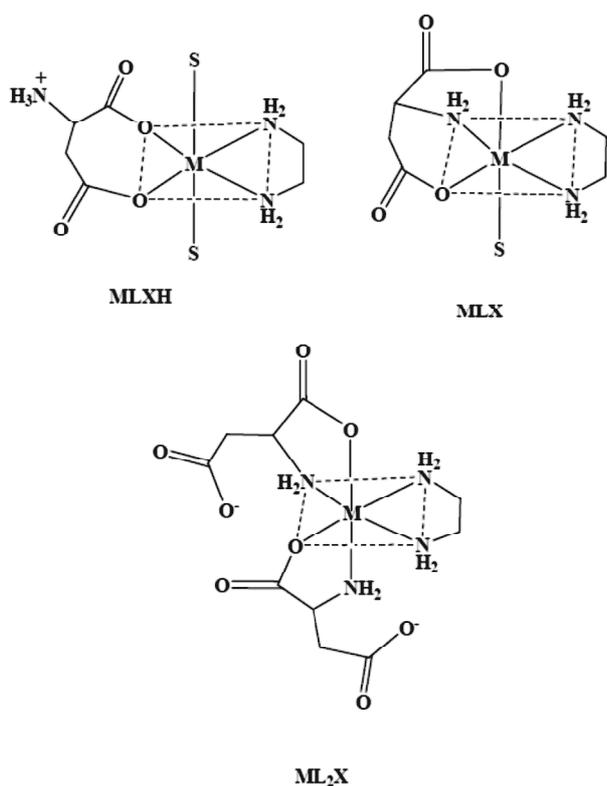

MLXH   **MLX**

ML_2X

Fig. 3. Speculative structures of Asp-M(II)-en complexes, where S is either solvent or water molecule.

Conclusions

The following conclusions have been drawn from the modeling studies of the speciation of ternary complexes of Co^{II}, Ni^{II} and Cu^{II} with Asp and en in PG-water mixtures.

(i) The ternary metal complex species detected are MLX, ML_2X and MLXH for Co^{II}, Ni^{II} and Cu^{II}, where L = Asp and X = en.

(ii) The values of $\Delta \log K$ and $\log X$ indicate that the ternary species have extra stability compared to their binary species.

(iii) The linear increase in the stabilities of ternary complexes with decreasing dielectric constants is due to the dominance of electrostatic forces over non-electrostatic forces.

(iv) The $\Delta \log K$ method is based on statistical grounds and the $\log X$ method takes disproportionation of the binary complexes into consideration. $\Delta \log K$ should be negative if the ternary complex has extra stability. Any value for $\log X$ greater than 0.6 accounts for extra stability.

(v) The order of the ingredients that influence the magnitudes of stability constants due to incorporation of errors is alkali > acid > Asp > en > metal.

(vi) The study also gives an insight into the metal availability/metal transport in biofluids. The ternary complexes are more amenable for "metal transport" because of their extra stability.

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