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Chemical Speciation of Binary Complexes of Pb(Ii), Cd(Ii) and Hg(Ii) with L-Methionine in Propylene Glycol -Water Mixture

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Abstract

Chemical speciation of Pb (II), Cd (II) and Hg (II) complexes of L-methionine in 0.0-60.0 % v/v propylene glycol-water mixtures has been studied pH metrically maintaining an ionic strength of 0.16 M at 303 K. The active forms of ligand are LH_3^+, LH_2 and LH. The predominant species detected are MLH, ML and ML_2. Models containing different numbers of species were refined by using the computer program MINIQUAD75. The best-fit chemical models were arrived at based on statistical parameters. The trend in variation of complex stability constants with change in the dielectric constant of the medium is explained on the basis of electrostatic and non-electrostatic forces.

Keywords: Complex equilibria; Chemical speciation, L-Methionine; Propyleneglycol; Metals.

Introducton

The speciation study of toxic metal ion complexes is useful to understand the role played by the active site cavities in biological molecules and the bonding behavior of protein residues with the metal ion. The species refined and their relative concentrations under the experimental conditions represent the possible forms of amino acids in biofluid. Lead affects every organ of the body, especially the bones and teeth, the kidneys, the nervous, cardiovascular, immune and reproductive systems[1]. Lead and other heavy metals create reactive radicals which damage cell structures including DNA and membranes.[2-4] Lead interferes with the normal metabolism of calcium, DNA transcription, enzymes that help in the synthesis of vitamin D and enzymes that maintain the integrity of the cell membrane. Lead may also be harmful to the developing immune system, causing production of excessive inflammatory proteins.

Cadmium enters the environment through volcanic activity and forest fires.[5] Cadmium affects different kinds of organisms, ranging from microbes to humans. Human exposure to cadmium mainly occurs through cigarette smoking, but exposure can also occur through contaminated food, water or air.[6] Cadmium is a known carcinogen to mammals.[7] Cadmium accumulates in plants, where it is detoxified by binding to phytochelatins[8-10], a family of thiol-rich peptides. Mercury affects the immune system, alters genetics and enzyme systems, and damages the nervous systems, and the senses of touch, taste and vision.[11,12]

Hence, the speciation of Pb(II),Cd and Hg(II) complexes with a sulphur-containing amino acid L-methionine (Met) has been studied. Met is chiefly available in cheese, eggs, fish, meat and poultry. The protonation constants of Met in PG-water mixtures were reported earlier.[13]

EXPERIMENTAL

2.1 Materials

1, 2-Propanediol or propylene glycol (PG) (Merck, Mumbai) was used as received. Aqueous solutions of L-methionine and sodium nitrate (E-Merck, Germany) were prepared. Solutions of Pb(II), Cd(II), Hg(II) nitrates were prepared. To increase the solubility of Met and to suppress the hydrolysis of the metal salts, mineral acid concentration in the above solutions was maintained at 0.05 M. 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 (ANOVA). The strength of alkali was determined using the Gran plot method.[14,15]

2.2 Apparatus

The alkali metric data were obtained with a ELICO (Model L1-120) pH meter (readability 0.01), which was calibrated with 0.05 M potassium hydrogen phthalate in acidic region and 0.01 M borax solution in basic region. The glass electrode was equilibrated in a well-stirred PG-water mixture containing inert electrolyte. All the titrations were carried out in the medium containing varying concentrations of PG (0-60.0 % v/v) maintaining an ionic strength of 0.16 M with sodium nitrate at 303.0 ± 0.1 K. 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[16].

2.3 Procedure

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 PG-water mixture of equivalent composition as that of titrand. In each of the titrations, the titrand consisted of approximately 1 mmol mineral acid in a total volume of 50 mL. Titrations with different ratios (1:2.5, 1:3.5, 1:5) of metal-to-ligand were carried out with 0.4 M sodium hydroxide. Other experimental details are given elsewhere[17].

2.4 Modeling Strategy

The computer program SCPHD[18] was used to calculate the correction factor. By using the pH metric titration data, the binary stability constants were calculated with the computer program MINIQUAD75[19], which exploits the advantage of the constrained least-squares method in the initial refinement and reliable convergence of Marquardt algorithm. During the refinement of binary systems, the correction factor and the protonation constants of methionine[13] were fixed. The variation of stability constants with the dielectric constant of the medium was analyzed on electrostatic grounds on the basis of solute-solute and solute-solvent interactions.

Results and Discussion

Alkali metric titration curves in PG-water mixtures revealed that the acido-basic equilibria of L-methionine were active in the pH range 2.0-9.0. Based on the active forms of the ligands in this pH range, models containing various numbers and combinations of complex species were fed to MINIQUAD75 along with the alkali metric titration data. Exhaustive modeling was performed for a typical system (Table 1).

Table 1: Exhaustive modeling of Cd(II)-methionine complexes in 30% v/v PG-water mixture. pH range = 2.0-9.0; Number of points = 71.

v/v % PG	log β_{mlh} (SD) 110	111	120	NP	U_{corr}	Ske-wness	Kur-tosis	χ^2
1	4.29(22)	---	---	29.57	-0.54	3.5	43.71	0.0360
2	---	7.31(32)	---	23.38	-1.18	4.87	66.10	0.0314
3	---	---	12.24(42)	90.70	0.80	7.22	147	0.0622
4	---	8.76(30)	12.67(29)	12.69	-0.12	4.27	18.04	0.0206
5	5.71(43)	---	12.71(40)	16.05	0.65	3.98	28.40	0.0262
6	3.69(39)	7.28(22)	---	23.38	-1.24	4.91	58.88	0.0317
7	4.92(6)	8.36(9)	12.42(4)	4.40	0.04	4.51	20.28	0.0020

$U_{corr} = U/(NP-m) \times 10^8$, where, m = number of species; NP = number of experimental points.

The models indicated better statistics as the number of species was increased, confirming better fit. There was no further improvement in the fit on inclusion of some more species in the model containing CdLH, CdL and CdL_2. This indicates that the final model appropriately fits the experimental data. Such exhaustive modeling was performed for all the systems. The best-fit model was selected using the statistical parameters[20] of the least squares residuals. The final models along with the statistical parameters are given in Table 2. The results of the best-fit models contain the type of species and overall formation constants. A very low standard deviation in log β values indicates the precision of these parameters. The small values of U_{corr} (sum of squares of deviations in the 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 zero mean with little dispersion.

Table 2: Best fit chemical models of Pb(II), Cd(II) and Hg(II) complexes with Methionine in PG-water mixtures.

v/v% PG	log β_{mlh} (SD)			NP	U_{corr}	Skewness	Kurtosis	χ^2	R-Factor
	110	111	120						
Pb(II) (pH range:1.9-7.0)									
0.0	8.51(7)	12.21(16)	13.60(4)	78	5.6	-0.35	2.51	18.58	0.0134
10.0	8.54(5)	11.41(4)	13.71(6)	82	1.3	-1.07	4.45	32.83	0.0098
20.0	9.00(5)	11.50(6)	13.80(8)	77	3.75	-0.37	4.08	28.01	0.0108
30.0	9.02(6)	11.61(6)	13.90(10)	83	4.21	-0.53	6.93	42.80	0.0121
40.0	9.04(5)	11.66(12)	13.95(8)	83	4.23	-1.14	7.93	44.80	0.0109
50.0	9.23(6)	11.70(9)	13.98(8)	82	1.23	0.82	4.36	8.23	0.0209
60.0	9.05(13)	12.06(32)	13.71(12)	82	4.21	0.00	2.21	57.48	0.0145
Cd(II) (pH range:2.0-9.0)									
0.0	3.34(10)	7.50(6)	11.14(8)	81	1.96	0.38	4.33	56.95	0.0085
10.0	4.39(18)	7.94(12)	11.21(14)	77	4.06	0.22	4.32	67.23	0.0140
20.0	4.56(18)	7.97(22)	12.43(21)	79	1.42	0.24	5.76	62.67	0.0228
30.0	4.92(6)	8.36(9)	12.42(4)	71	4.40	0.04	4.51	20.28	0.0020
40.0	5.14(20)	9.04(13)	12.48(19)	76	6.70	0.37	4.46	34.07	0.0161
50.0	5.75(30)	9.28(22)	12.99(41)	79	1.77	0.44	4.45	37.79	0.0164
60.0	5.76(20)	9.42(28)	13.08(14)	80	5.61	0.04	4.00	25.14	0.0145
Hg(II) (pH range:1.8-8.0)									
0.0	9.00(8)	12.56(11)	14.00(6)	86	1.96	0.85	3.91	34.39	0.0153
10.0	9.25(6)	12.26(10)	14.56(8)	92	2.79	0.56	3.51	8.58	0.0092
20.0	9.30(4)	12.31(11)	14.60(6)	102	2.41	0.37	3.71	61.54	0.0242
30.0	9.47(14)	12.69(15)	14.70(31)	98	8.19	0.15	3.48	12.07	0.0139
40.0	9.51(12)	12.72(14)	15.14(30)	84	7.80	0.14	3.44	39.98	0.0126
50.0	9.71(10)	12.80(9)	15.20(8)	88	1.21	0.69	3.49	12.17	0.0190
60.0	10.09(6)	12.81(9)	15.35(6)	84	2.21	0.45	4.33	11.68	0.0081

$U_{corr} = U/(NP-m) \times 10^8$, where, m = number of species; NP = number of experimental points.

For an ideal normal distribution, the values of kurtosis and skewness should be three and zero, respectively. Kurtosis is a measure of the peakedness of the error distribution near a modal value. For an ideal normal distribution kurtosis 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 peak (leptokurtic). The kurtosis values in the present study indicate that the residuals form leptokurtic as well as platykurtic patterns and very few are nearer to mesokurtic patterns. The values of skewness recorded in the table are between -1.14 and 0.85. These data evince that the residuals form part of a normal distribution. Hence, the least-squares method can be applied to the present data. The sufficiency of the model is further evident from the low crystallographic R-value. These statistical parameters thus show that the best-fit models portray the metal-ligand species in PG-water mixture.

Effect of Systematic Errors on Best-Fit Model

In order to rely upon the best chemical model for critical evaluation and application under varied experimental conditions with different accuracies of data acquisition, an investigation was made by introducing pessimistic errors in the influential parameters[21] like concentrations of alkali, mineral acid, ligand and metal (Table 2). The order of the ingredients that influence the magnitudes of stability constants due to incorporation of errors was alkali > acid > ligand > metal. Some species were even rejected when errors were introduced in the concentrations. This study confirms the appropriateness of the chosen best-fit models and indicates the relative sensitivities of model parameters.

Table 2: Effect of errors in influential parameters on stability constants of Cd(II) complexes with methionine in 30%v/v PG-water mixture.

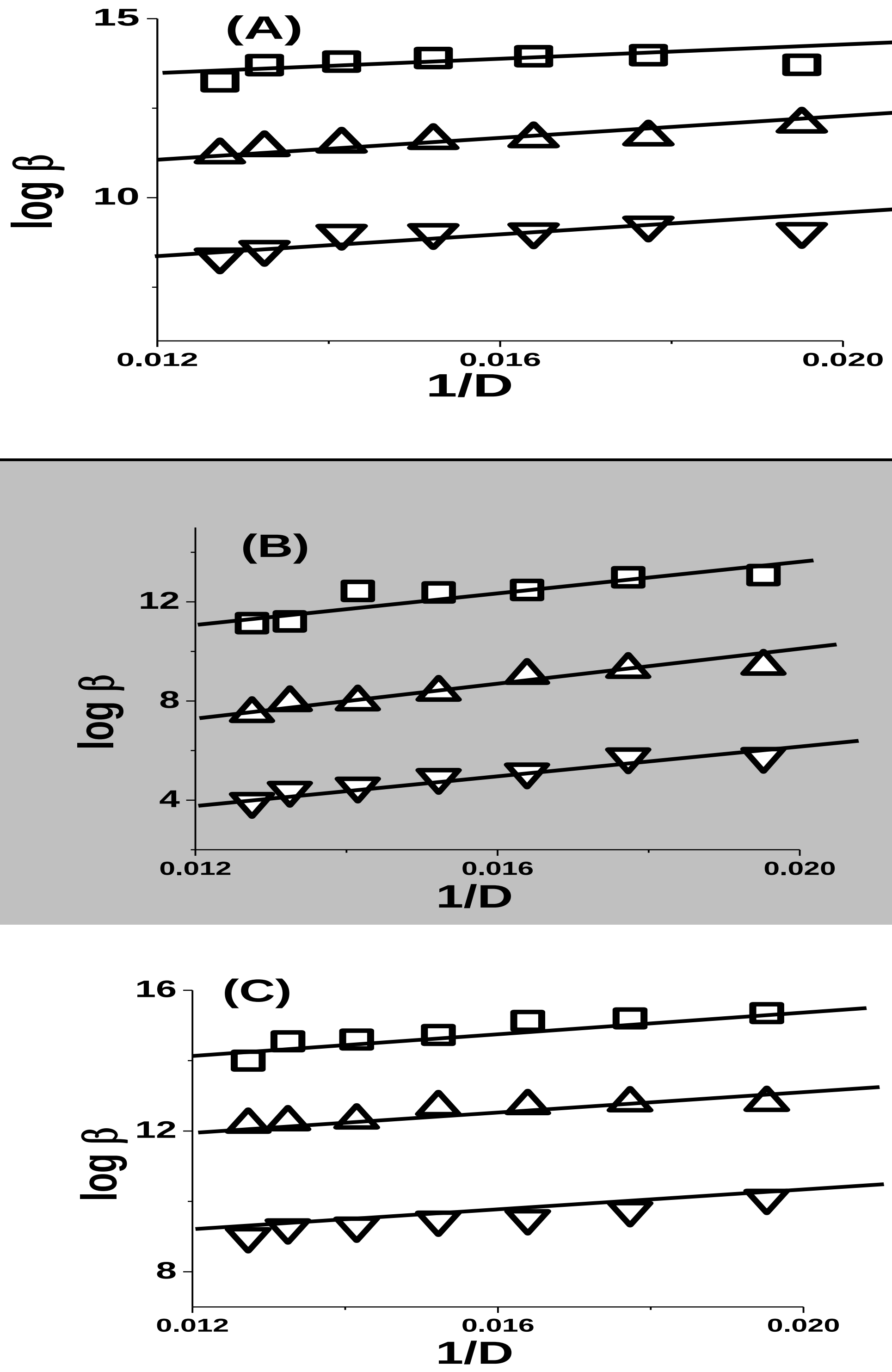
Ingredient	% Error	log β (SD)		
		110	111	120
	0	4.91(8)	8.36(9)	12.42(4)
Alkali	-5	2.84(28)	Rejected	Rejected
	-2	3.42(26)	6.33(21)	Rejected
	+2	4.81(24)	8.66(18)	11.97(14)
	+5	6.42(92)	10.86(88)	13.21(86)
Acid	-5	Rejected	Rejected	Rejected
	-2	5.12(23)	8.86(24)	12.29(16)
	+2	3.40(28)	6.45(22)	Rejected
	+5	2.88(55)	5.12(41)	Rejected
Ligand	-5	3.71(27)	7.31(19)	10.37(72)
	-2	3.94(23)	7.39(35)	11.08(22)
	+2	4.20(22)	7.51(52)	11.50(15)
	+5	4.40(22)	7.61(45)	11.74(15)
Metal	-5	4.05(26)	7.55(25)	11.30(18)
	-2	4.04(23)	7.48(26)	11.28(18)
	+2	4.04(22)	7.39(31)	11.25(18)
	+5	4.03(21)	7.32(33)	11.23(18)

Effect of Solvent

PG is an amphiprotic and coordinating solvent. It is a structure former and it enhances the water structure in PG-water mixtures; hence, it removes water from 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 competes with the ligands for coordinating the metals. This decreases the stability of the complexes. Hence, the stability of complex is expected to either increase or decrease.

The variation of overall stability constant values or change in free energy with co-solvent content depends upon two factors, viz., electrostatic and non-electrostatic. Born's classical treatment[22] accounts for the electrostatic contribution to the free energy change. 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 of the medium[21], which is observed in the present study (Figure 1). The linear variation indicates that electrostatic forces dominate the equilibrium process under the present experimental conditions.

Figure 1: Variation of stability constant values of metal-methionine complexes with reciprocal of dielectric constants (1/D) in PG-water mixtures at 303 K, ionic strength = 0.16 M. (A) Pb(II), (B) Cd(II) and (C) Hg(II); (▽) log 110, (Δ) log 111, (□)log120.

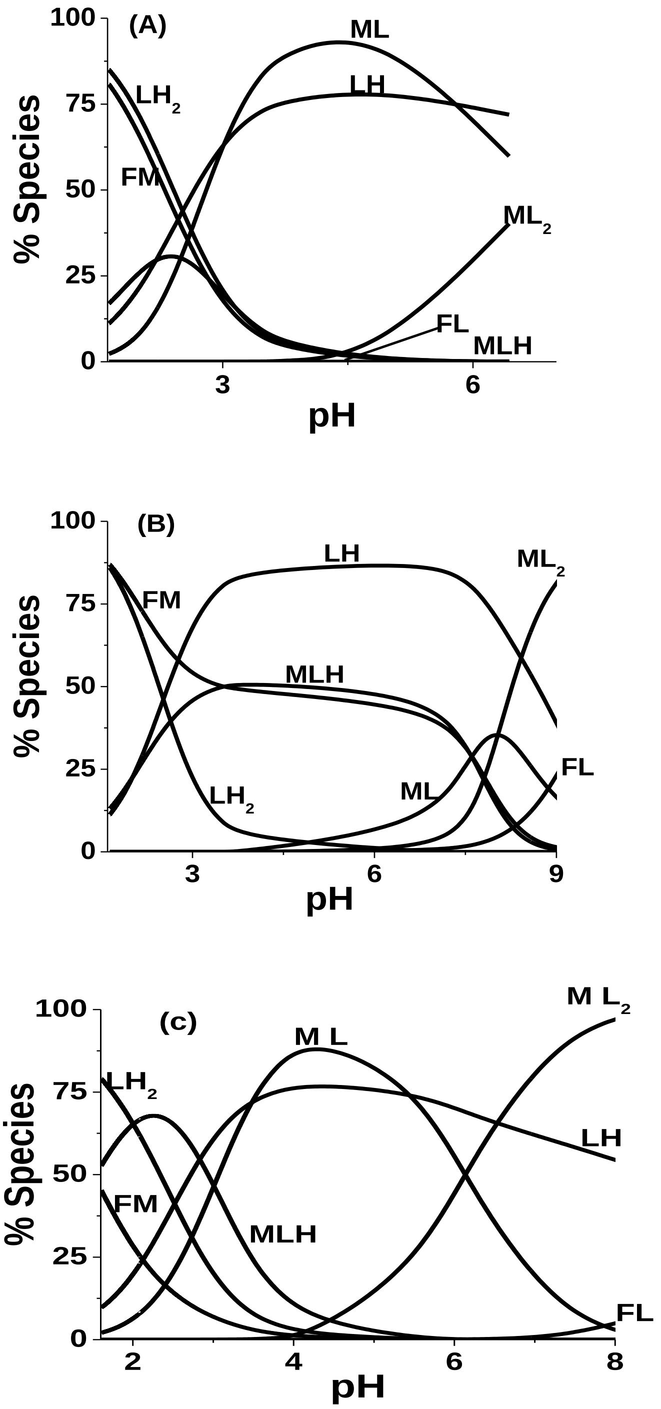


The linear increase indicates the dominance of the structure forming nature of PG over its complexing ability. The cation stabilizing nature of co-solvents. specific solvent-water interactions, change dispersion and specific interactions of co-solvents with solute (indicated by the changes in the solubility of different species in the aqua-organic mixtures) account for little deviation from the linear relationship.

Distribution Diagrams

Met has one dissociable carboxyl proton and an amino group that can associate with a proton. The different forms of Met are LH_2^+, LH and L^- in the pH-regions 2.0-4.0, 4.0-10.0 and 9.0-12.0, respectively. Hence, the plausible species in different systems can be predicted from these data. The species refined and determined are MLH, ML and ML_2 for Pb(II), Cd(II) and Hg(II).

Figure 2: Distribution diagrams of methionine complexes in 20% v/v PG-water mixture at 303 K, ionic strength = 0.16 M. (A) Pb(II) = 0.0999 mmol, (B) Cd(II) = 0.1057 mmol and (C) Hg(II) = 0.0516 mmol. The number of mmols of Met is 0.50.



The species distribution diagrams of various systems are shown in Figure 2. The formation of various binary complex species is shown in the following equilibria.

(a) $M(II) + LH_2 \rightleftharpoons MLH + H^+$

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

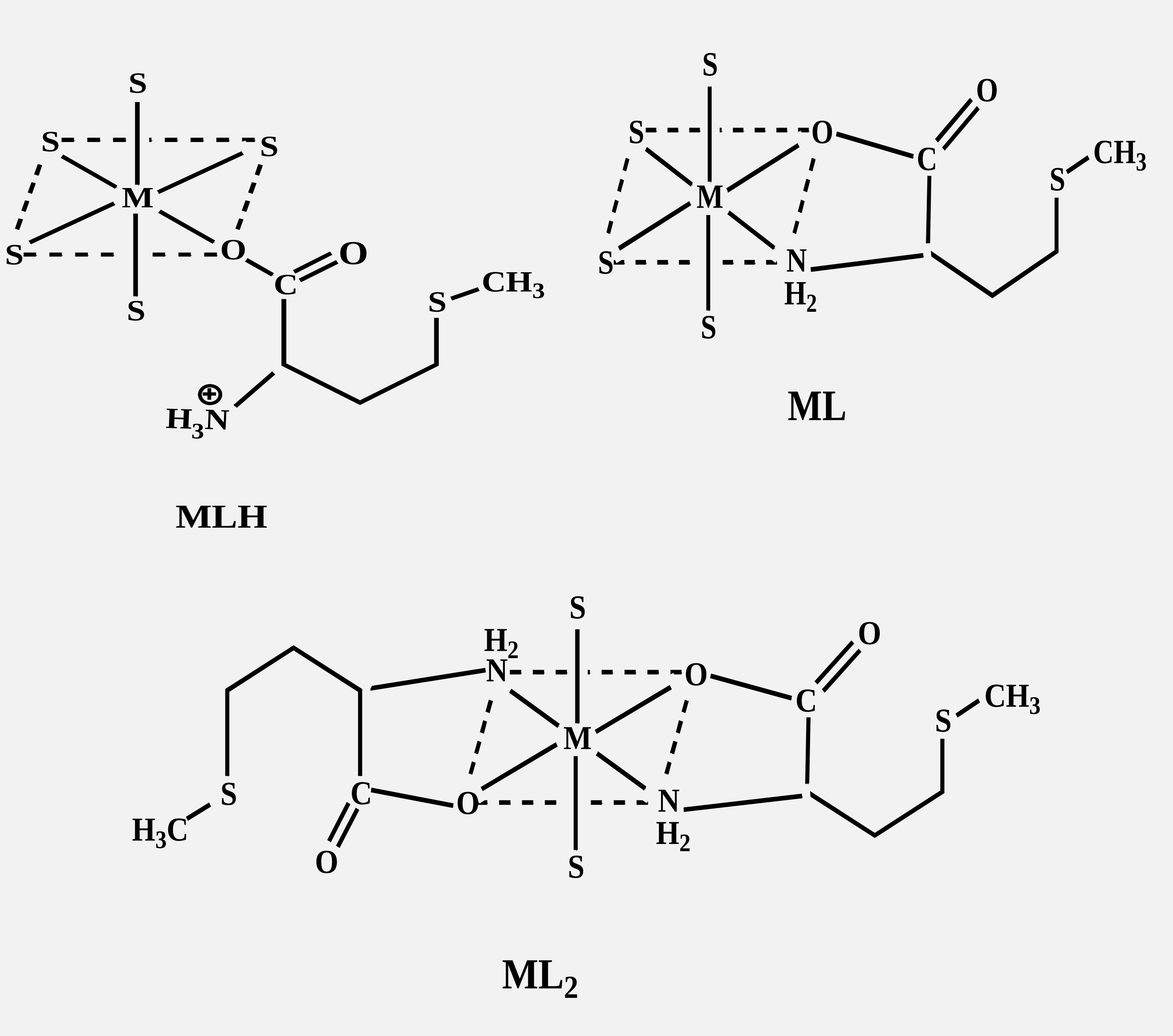
(c) $MLH \rightleftharpoons ML + H^+$

(d) $M(II) + 2LH_2 \rightleftharpoons ML_2 + 4H^+$

(e) $M(II) + 2LH \rightleftharpoons ML_2 + 2H^+$

Equilibrium (a) is proposed for MLH species. Equilibria (b) and (c) are proposed for the formation of ML species. The (b) appears to be more appropriate between them because ML is formed with decreasing concentration of MLH. Equilibria (d) and (e) are possible for ML_2 species, and (d) appears to be more appropriate because the concentration of LH_2 is decreasing with increasing concentration of ML_2. Depending on the coordinating atoms in the ligand and the nature of the metal ions, structures of the complexes are proposed for the species detected as shown in Figure 3.

Figure 3: Structures of binary complexes of Pd(II), Cd (II) and Hg (II) with Met.



MLH

ML

ML_2

Conclusions

1. The species formed due to the interaction of L-methionine with Pb(II), Cd(II) and Hg(II) metals are MLH, ML and ML_2.
2. The linear variation of stability constants with dielectric constants of the medium indicates the dominance of electrostatic forces over non-electrostatic forces. A linear increasing trend with PG content supports the predominance of the structure forming nature of PG over its complexing ability.
3. The order of the ingredients in influencing the magnitudes of stability constants due to incorporation of errors is alkali > acid > ligand > metal.

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