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Research Article

Speciation Studies of L-Histidine Complexes of Pb(II), Cd(II), and Hg(II) in DMSO-Water Mixtures

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Equilibrium study on complex formation of L-histidine with Pb(II), Cd(II), and Hg(II) has been investigated pH metrically in DMSO-water mixtures (0–60% v/v) at 303 K and 0.16 mol L^{-1} ionic strength. The predominant species detected for Pb(II) and Cd(II) are ML_2H_4, ML_2H_3, ML_2H_2, ML_2H, and ML_2 and those for Hg(II) are ML_2H_4, ML_2H_3, ML_2, and ML. The appropriateness of experimental conditions is verified by introducing errors intentionally in the concentrations of ingredients. The 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 stability constants of the complexes with dielectric constant of the medium is attributed to the electrostatic and nonelectrostatic forces. The species distribution and the plausible equilibria for the formation of the species are also presented.

1. Introduction

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 aminoacids in biofluids.

Due to its numerous uses and high persistence, lead is a major environmental contaminant [1]. Lead is toxic even at low concentrations for living organisms, who can absorb it in various ways [2]. Lead intake by humans can be due to the consumption of crop plants grown on soils with high plant-available metal concentrations [3]. It can, however, migrate through the soil with dissolved organic matter [4] or mobilized by certain plants [5]. Moreover, carried from the air to the soils as fine particles, lead could be released more easily in soil solution [6].

Cadmium causes iron deficiency by binding to cysteine, glutamate, aspartate, and histidine ligands [7]. Cadmium inhibits enzymes that participate in bilirubine conjunction [8]. It increases urine Ca^{2+} excretion which can cause severe bone pathology [9]. The possible effects of long term low-level exposure to cadmium are of concern because it is readily distributed to tissues of liver and kidney, which are the main target organs in acute and chronic cadmium exposure [10, 11]. Other tissues involved in cadmium toxicity include the testis, heart, bone, eye, and brain [12].

Mercury is one of the most toxic elements and has negative health effects in human populations, highly dependent on fish consumption [13, 14]. Recent research concluded that neither vitamin B12 nor the acetyl-CoA pathways are required for bacterial methylation of mercury [15]. Cysteine enhances Hg methylation by facilitating uptake of Hg^{2+} and promoting enzymatic formation of monomethylmercury [16–18]. Humans are exposed to Hg primarily as monomethylmercury [19], which is the form of Hg that accumulates readily in organisms and biomagnifies in food webs [20].

L-Histidine (His) is one of the strongest metal coordinating ligands among the aminoacids and plays an important role in the binding of metal ions by proteins. Most of the active sites of the biomolecules have histidine as one of the amino acid residues. It has three potential metal-binding sites, namely, carboxylate oxygen ($O_{caboxyl}$), imidazole imidonitrogen (N_{im}) and aminonitrogen (N_{am})

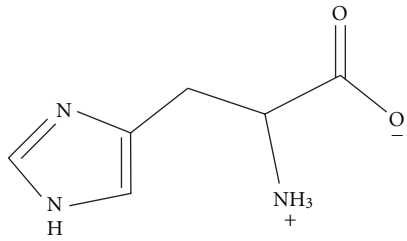

Figure 1: L-Histidine.

[21] (Figure 1). Due to the high reactivity of its imidazole group, histidine residue is often found at the active site of enzymes and involved directly in catalysis [22]. It controls the transmission of metals in biological bases [23] and has been reported to act as a neurotransmitter or neuromodulator in mammalian central nervous system. His is involved in a large number of biochemical processes such as biosynthesis of histamine, secretion of prolactin and antidiuretic hormone, and production of red and white blood cells. It possesses vasodilating and hypotensive actions and may boost the activity of soothing alpha waves in the brain. His is used in the treatment of anemia, allergies, rheumatoid arthritis, and other inflammatory reactions [24–28].

Dimethyl sulfoxide (DMSO) has the largest dielectric constant of the common dipolar aprotic solvents and it has been termed the super solvent. Another important phenomenon about the structure of the DMSO molecule is its trigonal pyramidal geometry. There is a highly directional lone pair of electrons at the apex of the pyramid, which helps in complexation.

His is an important component of active sites of biomolecules and there is a very likely hood for toxic metals to interact with His. Hence the speciation of the title systems has been studied in DMSO-water mixtures. DMSO has been chosen as a medium to decrease the dielectric constant of the medium, since the permittivity of active site cavities is very low [29]. Protonation equilibria of L-His in DMSO-water mixtures have already been studied in this laboratory [30].

2. Experimental

2.1. Materials. L-Histidine.HCl (E-Merck, Germany) solution (0.05 mol L^{-1}) was prepared in triple-distilled deionised water by maintaining 0.05 mol L^{-1} nitric acid concentration to increase the solubility. DMSO (Qualigens, India) was used as received. 2 mol L^{-1} sodium nitrate (Qualigens, India) was prepared to maintain the ionic strength in the titrand. Solutions of Pb(II), Cd(II), and Hg(II) nitrates (0.05 mol L^{-1}) were prepared by dissolving G.R. Grade (E-Merck, Germany) salts in triple-distilled water maintaining 0.05 mol L^{-1} nitric acid to suppress the hydrolysis of metal salts. All the solutions were standardized by standard methods. 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 [31]. The strengths of alkali and mineral acid were determined using the Gran plot method [32, 33].

2.2. Apparatus. The titrimetric data were obtained using ELICO (Model LI-120) pH meter (readability 0.01), which 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 DMSO-water mixture containing the inert electrolyte. All the titrations were carried out in the medium containing varying concentrations of DMSO-water mixtures (0–60% v/v) by maintaining an ionic strength of 0.16 mol L^{-1} with sodium chloride at 303.0 ± 0.1 K. The effect of variation in asymmetry potential, liquid junction potential, activity coefficient, sodium ion error, and dissolved carbon dioxide on the response of glass electrode was accounted for in the form of correction factor [34, 35].

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 DMSO-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 : 3.75 and 1 : 5.0 in the case of Pb(II) and Cd(II) and 1 : 7.5, 1 : 8.5 and 1 : 10.0 in the case of Hg(II)) of metal-to-ligand were carried out with 0.4 mol L^{-1} sodium hydroxide. Other experimental details are given elsewhere [36].

2.4. Modeling Strategy. The computer program SCPHD [37] 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 [38], which exploit 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 histidine 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.

3. Result and Discussion

The results of exhaustive modeling for the Cd(II)-His system in 40% DMSO-water mixture are given in Table 1. The models gave 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 CdL_2H_4, CdL_2H_3, CdL_2H_2, CdL_2H, and CdL_2. This indicates that the final model appropriately fits the experimental data. Such exhaustive modeling was performed for all the systems. The results of the final best-fit models that contain the stoichiometry of the complex species and their overall formation constants along with some of the important statistical parameters are given in Table 2. Very low-standard deviation in overall stability constants (log β) signifies the precision of these constants. The small values of U_{corr} (sum of squares of deviations in concentrations of

Table 1: Exhaustive modeling of Cd(II)-His system in 40% v/v DMSO-water mixture. pH range = 2.0–8.0, $NP = 98$.

Model No.	$\log \beta_{mlh}$ (SD)					$U_{corr} \times 10^8$	Skewness	Kurtosis	χ^2	R-factor
	120	121	122	123	124					
1	12.15 (9)	—	—	—	—	10.927	−1.43	4.96	176.10	0.016
2	—	18.87 (6)	—	—	—	4.649	0.00	6.26	114.71	0.010
3	—	—	25.44 (25)	—	—	34.123	−0.20	12.56	359.17	0.028
4	—	—	—	Rejected	—	—	—	—	—	—
5	—	—	—	—	Rejected	—	—	—	—	—
6	11.27 (12)	18.79 (5)	—	—	—	2.740	−1.32	5.35	100.94	0.008
7	12.11 (7)	—	25.20 (7)	—	—	2.427	−1.36	5.33	100.56	0.007
8	12.15 (9)	—	—	Rejected	—	10.978	−1.43	4.96	176.10	0.016
9	12.15 (9)	—	—	—	Rejected	10.928	−1.43	4.96	176.10	0.016
10	—	18.92 (7)	24.74 (12)	—	—	3.687	0.50	9.42	116.12	0.009
11	—	19.26 (11)	—	30.78 (17)	—	3.448	0.43	8.66	83.63	0.009
12	—	18.87 (6)	—	—	Rejected	4.649	0.00	6.26	114.71	0.010
13	—	—	25.43 (26)	Rejected	—	34.123	−0.20	12.56	359.17	0.028
14	—	—	25.64 (29)	—	35.53 (41)	33.541	−0.20	13.11	412.88	0.028
15	—	—	—	Rejected	Rejected	—	—	—	—	—
16	11.54 (7)	18.75 (4)	24.91 (5)	—	—	1.036	−1.93	6.96	137.95	0.004
17	11.63 (11)	19.17 (8)	—	30.72 (12)	—	1.642	−1.04	4.00	69.05	0.006
18	11.26 (12)	18.88 (5)	—	—	Rejected	2.740	−1.32	5.35	100.94	0.008
19	12.11 (7)	—	25.19 (6)	Rejected	—	2.427	−1.36	5.33	100.56	0.007
20	12.25 (7)	—	25.39 (7)	—	35.34 (11)	1.979	−1.22	6.41	53.76	0.006
21	12.91 (21)	—	—	31.06 (25)	Rejected	8.500	−1.43	5.41	121.02	0.014
22	—	19.16 (12)	24.71 (21)	30.59 (21)	—	3.316	0.55	10.31	151.88	0.008
23	—	19.04 (8)	24.96 (13)	—	35.17 (19)	3.484	0.73	10.39	107.52	0.009
24	—	19.42 (11)	—	31.00 (15)	35.25 (17)	3.168	0.73	9.82	62.68	0.008
25	—	—	25.64 (29)	Rejected	35.53 (40)	33.541	−0.20	13.11	412.88	0.028
26	11.62 (7)	18.89 (6)	24.94 (6)	30.16 (19)	—	0.957	−2.04	7.71	159.99	0.004
27	11.70 (6)	18.87 (4)	25.12 (5)	—	35.20 (8)	0.766	−1.06	5.55	36.56	0.004
28	12.25 (7)	—	25.39 (7)	Rejected	35.34 (11)	1.979	−1.22	6.41	53.76	0.006
29	—	19.32 (11)	24.92 (19)	30.81 (19)	35.28 (16)	2.989	0.93	12.16	126.63	0.008
30	11.80 (11)	19.34 (7)	—	30.96 (10)	35.20 (12)	1.382	−0.50	3.58	26.22	0.005
31	11.78 (6)	19.05 (6)	25.15 (5)	30.45 (13)	35.25 (7)	0.630	−0.75	5.64	56.26	0.003

$U_{corr} = U/(\text{NP} - m)$; m = number of species; NP = number of experimental points; SD = standard deviation.

ingredients at all experimental points) corrected for degrees of freedom, small values of mean, standard deviation, and mean deviation for the systems are validated by the residual analysis [39].

3.1. Residual Analysis. In data analysis with least squares methods, the residuals (the differences between the experimental data and the data simulated based on model parameters) are assumed to follow Gaussian or normal distribution. When the data are fit into the models, the residuals should ideally be equal to zero. If statistical 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, the residuals are tested for normal distribution. Such tests are χ^2, Skewness, Kurtosis, and R-factor. These statistical parameters show that the best-fit models portray the metal-ligand species in DMSO-water mixtures, as discussed below.

In the present study, the χ^2 values are less than the table values, and so the models are accepted. The kurtosis values in this study indicate that the residuals form leptokurtic pattern. The values of skewness recorded in Table 2 are between 0.06 and 1.39 for Pb(II), −0.93 and 2.45 for Cd(II) and −0.78, and 0.19 for Hg(II). These data evince that the residuals form part of a normal distribution. Hence, least square method can be applied to the present data. The sufficiency of the model is further evident from crystallographic R-values. These statistical parameters thus show that the best-fit models portray the metal-ligand species in DMSO media.

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

DMS % v/v	log β_{mlh} (SD) 110	120	121	122	123	124	NP	$U_{corr} \times 10^8$	Skewness	Kurtosis	χ^2	R-factor	pH range
Pb(II)													
0.0	—	9.37 (40)	18.36 (40)	25.07 (41)	31.10 (42)	36.90 (42)	38	0.137	0.67	7.15	32.11	0.002	3.5–9.0
10.0	—	9.65 (29)	19.29 (28)	26.02 (28)	31.78 (30)	37.54 (29)	29	0.385	0.06	2.45	2.66	0.004	3.5–9.0
20.0	—	9.10 (30)	18.59 (30)	25.29 (31)	31.07 (33)	36.67 (35)	19	0.094	0.64	4.22	5.74	0.001	3.7–9.0
30.0	—	9.80 (13)	19.21 (10)	25.65 (12)	30.82 (19)	36.43 (16)	44	0.328	0.59	4.19	10.67	0.004	3.5–9.0
40.0	—	10.81 (34)	19.64 (32)	25.90 (34)	31.35 (39)	36.70 (39)	47	1.323	0.35	3.14	18.38	0.008	3.5–9.0
50.0	—	10.03 (9)	19.29 (8)	25.31 (9)	30.22 (16)	35.46 (15)	45	0.270	1.39	9.68	18.30	0.003	3.5–9.0
60.0	—	9.77 (16)	19.07 (13)	25.02 (17)	29.90 (29)	35.02 (30)	49	0.915	0.86	5.16	9.90	0.006	3.5–9.0
Cd(II)													
0.0	—	10.25 (14)	17.80 (15)	24.35 (16)	30.55 (17)	36.26 (18)	50	0.282	1.85	12.03	59.28	0.003	3.0–8.0
10.0	—	10.63 (26)	18.36 (26)	25.02 (29)	31.19 (29)	36.96 (30)	49	0.522	2.45	13.66	68.13	0.005	3.0–8.0
20.0	—	10.22 (12)	17.63 (12)	23.97 (20)	29.88 (28)	34.95 (69)	37	0.362	1.50	7.91	18.23	0.003	3.0–8.0
30.0	—	11.01 (8)	18.55 (7)	24.90 (10)	30.55 (14)	35.85 (18)	44	0.244	0.77	6.03	13.82	0.003	3.5–8.0
40.0	—	11.78 (6)	19.05 (6)	25.15 (5)	30.45 (13)	35.25 (7)	98	0.630	−0.75	5.64	56.26	0.003	2.0–8.0
50.0	—	12.11 (7)	19.28 (6)	25.22 (6)	30.24 (16)	35.01 (8)	96	0.751	−0.93	6.80	80.00	0.004	2.0–8.0
60.0	—	12.10 (7)	18.91 (6)	24.83 (5)	29.68 (17)	—	22	0.356	1.38	6.32	5.52	0.003	3.5–8.5
Hg(II)													
0.0	10.09 (24)	13.18 (34)	—	—	33.83 (23)	35.21 (87)	90	0.824	−0.78	4.70	47.16	0.004	2.0–8.0
10.0	12.42 (49)	16.78 (85)	—	—	31.60 (65)	—	95	99.96	−0.71	6.23	307.70	.0494	2.0–8.0
20.0	11.57 (33)	14.78 (55)	—	—	32.38 (86)	35.81 (40)	65	4.295	0.19	5.38	107.97	.0103	2.0–9.0
30.0	11.57 (32)	14.59 (35)	—	—	34.56 (29)	37.27 (36)	65	0.533	−0.26	7.16	9.68	0.003	2.0–9.0
40.0	12.31 (20)	16.13 (23)	—	—	34.55 (14)	36.83 (22)	36	0.192	−0.20	4.15	15.70	0.001	2.0–9.0
50.0	12.31 (31)	15.58 (34)	—	—	35.00 (29)	37.36 (36)	106	0.650	−0.55	4.19	20.31	0.003	2.0–9.0
60.0	12.49 (22)	15.55 (28)	—	—	34.87 (19)	37.40 (24)	105	0.668	−0.09	3.40	23.67	0.003	2.0–9.0

Table 3: Effect of errors in influential parameters on Pb(II)-His complex stability constants in 50% v/v DMSO-water mixture.

Ingredient	% Error	$\log \beta_{mlh}$ (SD)				
		120	121	122	123	124
	0	10.03 (9)	19.29 (8)	25.31 (9)	30.22 (16)	35.46 (15)
	−5	14.52 (13)	21.26 (11)	26.28 (17)	31.92 (12)	Rejected
Acid	−2	11.44 (11)	20.00 (9)	25.38 (12)	30.93 (13)	34.98 (34)
	+2	Rejected	18.62 (22)	25.32 (27)	Rejected	35.88 (35)
	+5	Rejected	16.50 (75)	25.12(78)	Rejected	36.29 (86)
	−5	Rejected	15.84 (35)	24.62 (35)	Rejected	35.53 (50)
	−2	Rejected	18.55 (17)	25.25 (21)	Rejected	35.71 (30)
Alkali	+2	11.48 (11)	19.97 (9)	25.37 (12)	30.88 (13)	35.28 (23)
	+5	13.99 (9)	20.67 (8)	25.71 (14)	31.37 (9)	Rejected
	−5	10.00 (17)	19.20 (14)	25.37 (20)	Rejected	35.82 (26)
	−2	10.05 (13)	19.29 (12)	25.36 (13)	30.18 (27)	35.66 (20)
Ligand	+2	10.01 (7)	19.31 (6)	25.28 (7)	30.27 (11)	35.22 (14)
	+5	10.02 (8)	19.36 (6)	25.24 (7)	30.34 (11)	34.73 (26)
	−5	9.94 (12)	19.26 (9)	25.34 (11)	30.32 (18)	35.61 (17)
	−2	9.99 (11)	19.28 (8)	25.32 (10)	30.27 (17)	35.51 (16)
Log F	+2	10.06 (9)	19.31 (7)	25.30 (9)	30.19 (16)	35.39 (15)
	+5	10.12 (8)	19.34 (6)	25.30 (8)	30.15 (15)	35.30 (15)
	−5	10.17 (8)	19.31 (6)	25.22 (8)	30.13 (15)	35.27 (15)
	−2	10.08 (8)	19.30 (7)	25.27 (9)	30.18 (16)	35.38 (15)
Metal	+2	10.06 (8)	19.31 (7)	25.30 (9)	30.19 (16)	35.39 (15)
	+5	10.12 (8)	19.34 (6)	25.30 (8)	30.15 (15)	35.30 (15)
	−5	9.98 (9)	19.24 (8)	25.27 (9)	30.17 (17)	35.40 (16)
	−2	10.01 (9)	19.27 (8)	25.30 (9)	30.21 (16)	35.43 (15)
Volume	+2	10.04 (9)	19.31 (7)	25.33 (9)	30.24 (16)	35.47 (15)
	+5	10.07 (9)	19.34 (7)	25.36 (9)	30.28 (16)	35.50 (15)

3.2. Effect of Systematic Errors on Best Fit Model. 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, log F, and volume (Table 3). The order of the ingredients that influence the magnitudes of stability constants due to incorporation of errors is alkali > acid > metal > ligand > volume > log F. 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.

3.3. Effect of Solvent. The linear variation of stability constants (log β) of his complexes with Pb(II), Cd(II), and Hg(II) with variation of $1/D$ (D is the dielectric constant) of DMSO-water mixtures are given in Figure 2. DMSO is a polar aprotic and coordinating solvent. It is a structure former and it enhances the water structure in DMSO-water mixtures; hence, it removes water from coordination sphere of metal ions, making it 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 the complexes is expected to either increase or decrease. The linear variation indicates that electrostatic forces dominate the equilibrium process under the present experimental conditions.

3.4. Distribution Diagrams. Histidine is a tridentate ligand that has one dissociable (carboxylate group) and two associable (amino, imidazole) protons. The different forms of His are LH_3^{+2} LH_2^{+} LH, and L^{-} in the pH range below 4.0, 2.0–6.0, 6.0–10.0, and above 9.0, respectively. Hence, the plausible binary metal-ligand complexes can be predicted from these data. The present investigation reveals the existence of ML_2H_4, ML_2H_3, ML_2H_2, ML_2H, and ML_2 for Pb(II), and Cd(II). Hg(II) forms ML_2H_4, ML_2H_3, ML_2, and ML species. The formation of various his complex species is shown in the following equilibria.

$$M(II) + 2LH_3^{2+} \rightleftharpoons ML_2H_4^{4+} + 2H^{+}, \quad (1)$$

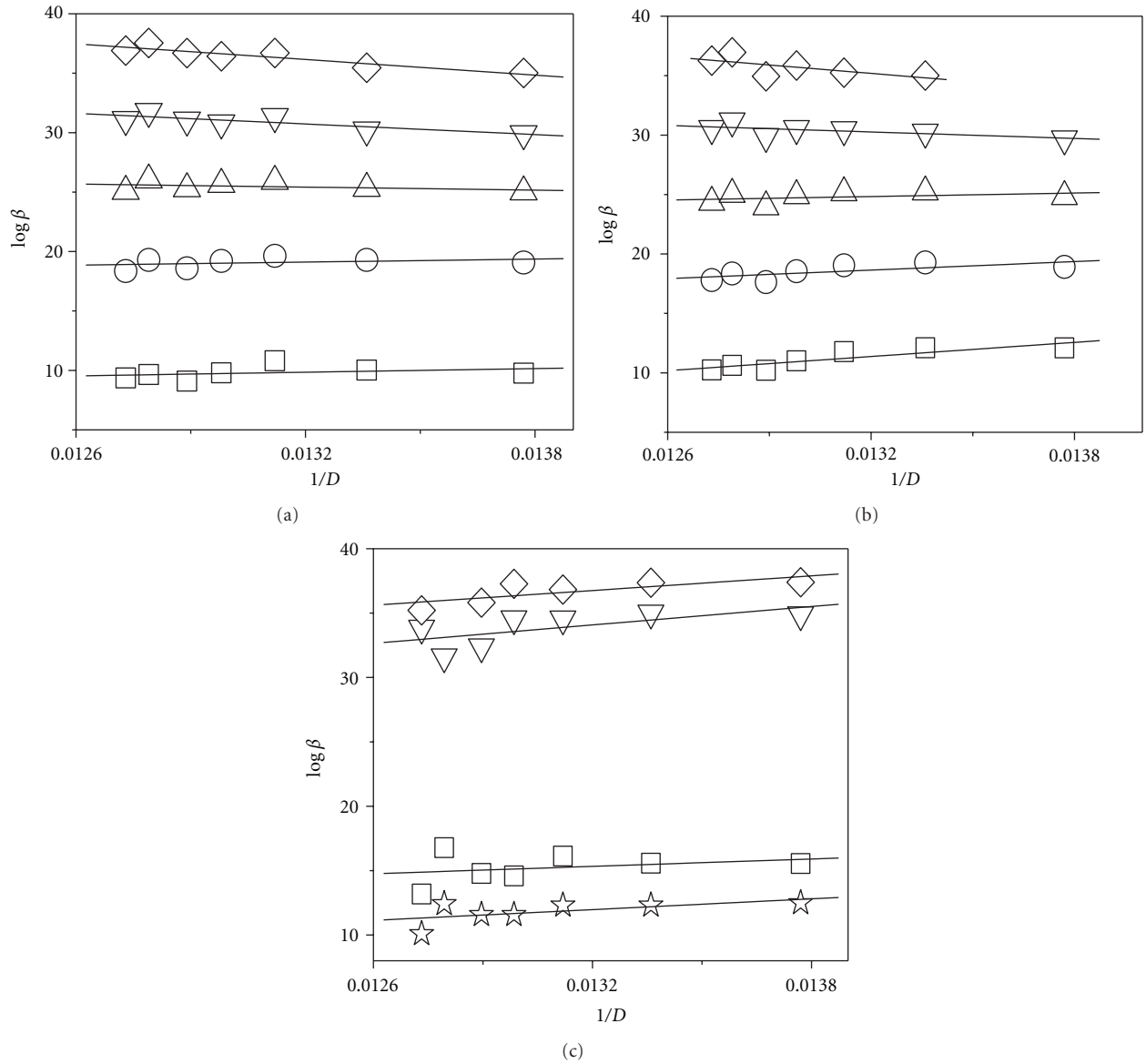

Figure 2: Variation of stability constant values of His complexes with reciprocal of dielectric constant ($1/D$) of DMSO-water mixtures (a) Pb(II); (b) Cd(II); (c) Hg(II); (star) log β_{ML} (square) log β_{ML_2}; (circle) log β_{ML_2H}; (triangle up) log $\beta_{ML_2H_2}$; (triangle down) log $\beta_{ML_2H_3}$; (diamond) log $\beta_{ML_2H_4}$.

$$M(II) + 2LH_3^{2+} \rightleftharpoons ML_2H_3^{3+} + 3H^+, \quad (2)$$

$$ML_2H_4^{4+} \rightleftharpoons ML_2H_3^{3+} + H^+, \quad (3)$$

$$M(II) + 2LH_3^{2+} \rightleftharpoons ML_2H_2^{2+} + H^+, \quad (4)$$

$$M(II) + 2LH_2^{+} \rightleftharpoons ML_2H_2^{2+} + 2H^+, \quad (5)$$

$$ML_2H_4^{4+} \rightleftharpoons ML_2H_2^{2+} + 2H^+, \quad (6)$$

$$ML_2H_3^{3+} \rightleftharpoons ML_2H_2^{2+} + H^+, \quad (7)$$

$$M(II) + 2LH_3^{2+} \rightleftharpoons ML_2H^+ + 5H^+, \quad (8)$$

$$M(II) + 2LH_2^{+} \rightleftharpoons ML_2H^+ + 3H^+, \quad (9)$$

$$ML_2H_4^{4+} \rightleftharpoons ML_2H^+ + 3H^+, \quad (10)$$

$$ML_2H_3^{3+} \rightleftharpoons ML_2H^+ + 2H^+, \quad (11)$$

$$ML_2H_2^{2+} \rightleftharpoons ML_2H^+ + H^+, \quad (12)$$

$$M(II) + LH_3^{2+} \rightleftharpoons ML^+ + 3H^+, \quad (13)$$

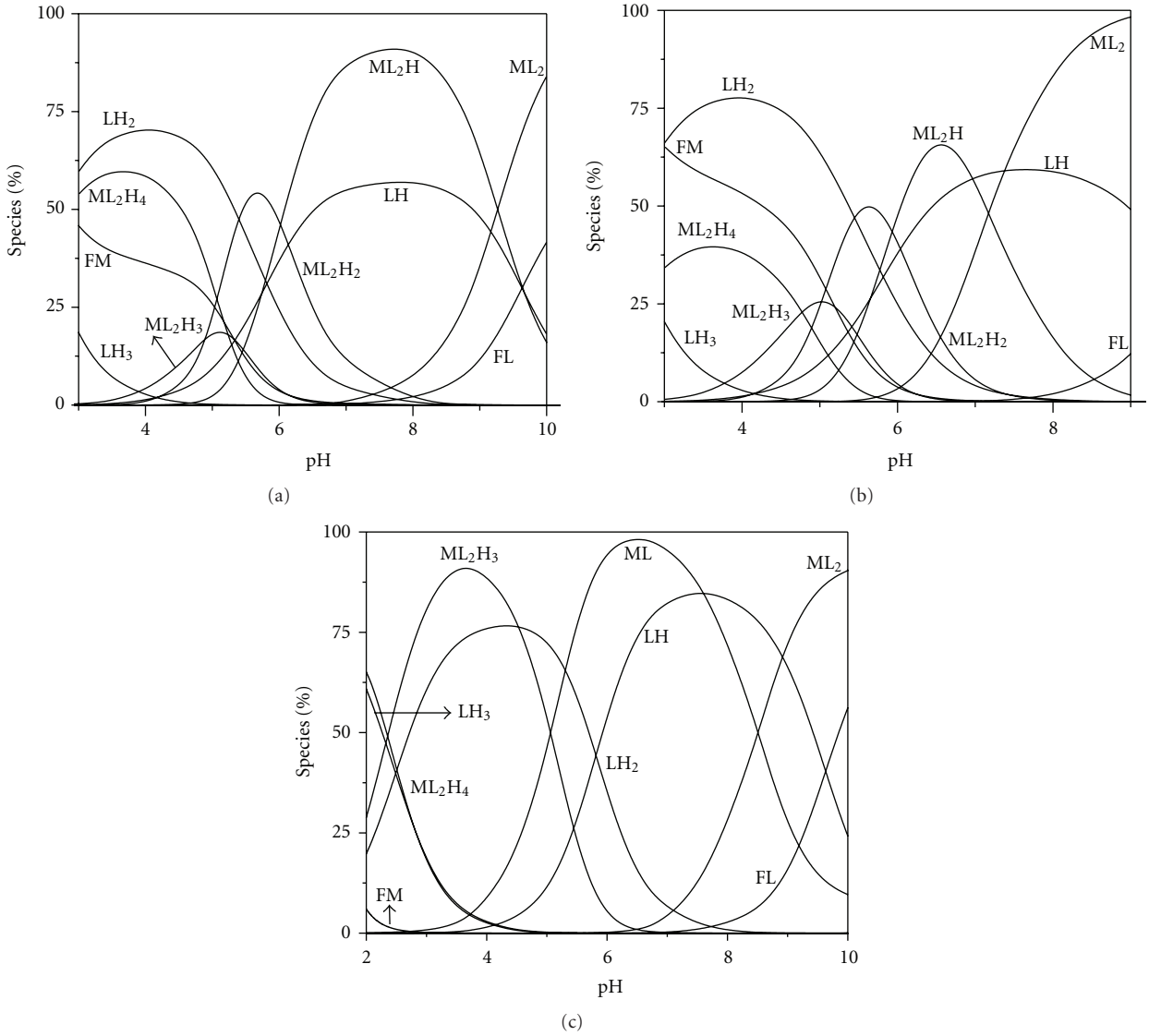

Figure 3: Distribution diagrams of binary complexes of His in 50% v/v DMSO-water mixture: (a) Pb(II), (b) Cd(II) and (c) Hg(II).

$$M(II) + LH_2^{+} \rightleftharpoons ML^{+} + 2H^{+}, \quad (14)$$

$$M(II) + 2LH_2^{+} \rightleftharpoons ML_2 + 4H^{+}, \quad (15)$$

$$M(II) + 2\,LH \rightleftharpoons ML_2 + 2H^{+}, \quad (16)$$

$$ML^{+} + LH \rightleftharpoons ML_2 + H^{+}, \quad (17)$$

$$ML_2H_4^{4+} \rightleftharpoons ML_2 + 4H^{+}, \quad (18)$$

$$ML_2H_3^{3+} \rightleftharpoons ML_2 + 3H^{+}, \quad (19)$$

$$ML_2H_2^{2+} \rightleftharpoons ML_2 + 2H^{+}, \quad (20)$$

$$ML_2H^{+} \rightleftharpoons ML_2 + H^{+}. \quad (21)$$

The species distribution diagrams in DMSO-water mixtures are shown in Figure 3. They indicate that the his complexes of Pb(II), Cd(II), and Hg(II) are formed in the pH range 2.0–9.0. At lower pH, $ML_2H_4^{4+}$ species are formed from free-metal ion that interacts with LH_3^{2+} form of the ligand [Equilibrium (1)]. The species $ML_2H_3^{2+}$ may be formed from M(II) and LH_3^{2+} or by the deprotonation of $ML_2H_4^{4+}$ (Equilibria (2) & (3)). In the same manner, the species ML_2H_2 may be formed either from free-metal ion and LH_3^{+}/LH_2^{+} (Equilibria (4) & (5)) or deprotonation of $ML_2H_4^{4+}$ and $ML_2H_3^{2+}$ (Equilibria (6) & (7)). At lower pH, the interaction of free-metal ion with LH_3^{2+} or LH_2^{+} (Equilibria (4) & (5)) and at higher pH, deprotonation of $ML_2H_4^{4+}$, and $ML_2H_3^{2+}$ (Equilibria (6) & (7)) results in the formation of ML_2H_2 species. Species ML_2H is formed from M(II) and LH_3^{2+} or LH_2^{+} or at lower pH, deprotonation

of $ML_2H_4^{4+}$, $ML_2H_3^{3+}$, and $ML_2H_2^{2+}$ species at higher pH (Equilibria (8)–(12)). The ML_2 species are formed from interaction of free-metal ion, with LH_2^+ or LH (Equilibria 15 & 16) or ML^+ and LH (Equilibrium (17)) or deprotonation of $ML_2H_4^{4+}$, $ML_2H_3^{3+}$, $ML_2H_2^{2+}$, and ML_2H^+ species (Equilibria (18)–(21)). In the case of Hg(II) (Figure 2(c)) the ML species are formed from interaction of free-metal ion and LH_3^{2+} or LH_2^+ (Equilibria (13) & (14)). It is formed at near neutral pH.

4. Conclusions

The following conclusions have been drawn from the modeling studies of the L-Histidine complexes of Pb(II), Cd(II) and Hg(II) in DMSO-water mixture.

(1) L-Histidine forms both protonated and unprotonated complexes under pH range 2.0–9.0. The species detected for the toxic metals Pb(II) and Cd(II) are ML_2H_4, ML_2H_3, ML_2H_2, ML_2H, and ML_2. ML_2H_4, ML_2H_3, ML_2, and ML species are detected the case of Hg(II).

(2) The linear variation of stability constants as a function of $1/D$ of the medium indicates the dominance of electrostatic forces over nonelectrostatic forces. The linear increasing trend with DMSO content supports the dominance of the structure forming nature of DMSO over its complexing ability.

(3) The order of ingredients in influencing the magnitudes of stability constants due to incorporation of errors in their concentrations is alkali > acid > metal > ligand > volume > log F.

(4) Some species are stabilized due to electrostatic interactions and some are destabilized due to the decreased dielectric constant.

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