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Chemical speciation studies of binary complexes of malonic acid with some essential biologically important metal ions in 1, 2-propanediol-water mixtures

Belete Yilma Hirpaye[1] Mekonen Tirfu Zekarias[2] and Gollapalli Nageswara Rao[3]*

Department of Inorganic & Analytical Chemistry, School of Chemistry, Andhra University, Visakhapatnam, India

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ABSTRACT

Chemical speciation of Co(II), Ni(II), Cu(II) and Zn(II) complexes of malonic acid in 0.0-60.0% v/v 1, 2-propanediol-water mixtures maintaining an ionic strength of 0.16 M at 303±0.1 K has been studied pH metrically. The predominant complexes formed are ML, ML_2, ML_2H and ML_2H_2 for Co(II) and Cu(II) and ML_2, ML_2H and ML_2H_2 for Ni(II) and Zn(II). Models containing different numbers of species were refined by using the computer program MINIQUAD75. Selection of the best-fit chemical models was 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. Distributions of species, formation equilibria and effect of influential parameters on the stability constants have been presented. Possible structures of the various species present in solution are also indicated on the basis of the analysis of the pH metric data.

Keywords: Binary species, Stability constant, Chemical speciation, Malonic acid, 1, 2-Propanediol.

INTRODUCTION

Malonic acid (MA) has received considerable attention following reports that it can be metabolized to acetyl coenzymeA (AcCoA) and that it is involved in fatty acid synthesis, aromatic synthesis, and mevalonate synthesis [1, 2]. It is important intermediates in synthesis of vitamins B_1 and B_6, barbiturates, non-steroidal anti-inflammatory agents, other numerous pharmaceuticals, agrochemicals, flavors and fragrance compounds [3]. Malonate is an inhibitor of cellular respiration; it binds to the active site of the succinate dehydrogenase in the citric acid cycle but does not react, thereby competing with succinate. For the oxidative phosphorylation reaction, malonate is an inhibitor for complex II, which again contains succinate dehydrogenase [4, 5].

Living organisms store and transport some important essential metal ions both to provide appropriate concentrations of them for use in metalloproteins or cofactors and to protect themselves against the toxic effects of metal excesses; metalloproteins and metal cofactors are found in plants, animals and microorganisms. The normal concentration range for each metal ion in biological systems is narrow, with both deficiencies and excesses causing pathological changes [6-8]. Hence, chemical speciation study of essential metal ions complexes is important for an understanding of their distribution, mobility, bioavailability, toxicity and for setting environmental quality standards [9, 10].

Cobalt is essential for the production of red blood cell. It acts as coenzyme in several biochemical processes. It speeds up ATP turnover. It present as corrin coenzyme in glutamate mutase, dialdehydrase and arginase and in non corrin form in dipeptidase [11]. Nickel is associated with several enzymes [12-14] and any variation in its concentration leads to metabolic disorders [15]. Copper is largely rejected from cells but outside the cell, it is essential for the metabolism of many hormones and connective tissue. The biological functions include electron transfer, dioxygen transport, oxygenation, oxidation, reduction and disproportionation [16-19]. Zinc is the second most abundant essential trace metal after iron and it plays vital roles in biological systems [20-23].

Mixed solvents have been employed in different fields including pharmaceutical and analytical sciences. So far no systematic report has appeared on studies speciation of MA with essential elements in PG-water mixtures of various concentrations. Hence, stability constants and chemical speciation studies of MA with some essential metals like Co, Ni, Cu and Zn in PG-water mixtures are reported in this paper.

EXPERIMENTAL SECTION

Chemicals

1, 2-Propanediol (propylene glycol, PG), obtained from Merck, India, was used as received. A solution 0.05 mol dm^{-3} of malonic acid (Himedia, India) was prepared in triple distilled water. 0.1 mol dm^{-3} aqueous solutions of Co(II), Ni(II), Cu(II) and Zn(II) chlorides(Merck, India) were prepared. To increase the solubility of Malonic acid and to suppress the hydrolysis of metal salts, hydrochloric acid concentration was maintained at 0.05 mol dm^{-3}. Metal ion solutions were estimated using the conventional standard method [24]. Carbonate free sodium hydroxide solution was prepared and standardized by oxalic acid and potassium hydrogen phthalate. Hydrochloric acid solution was prepared and used after standardization using borax. To assess the errors that might have entered into the determinations of the concentrations, the data were subjected to analysis of variance of one way classification (ANOVA) [25]. The strength of the alkali and mineral acid were determined using the Gran plot method [26].

Apparatus

The titrimetric data were obtained with a calibrated Elico (Model L1-120) pH meter (readability 0.01), which can monitor changes in the H^+ concentration. The pH meter was calibrated with a 0.05 mol dm^{-3} potassium hydrogen phthalate solution in the acidic region and a 0.01 mol dm^{-3} borax solution in the basic region. The glass electrode was equilibrated in a well-stirred PG-water mixture containing an inert electrolyte. The effects of variations in the asymmetry potential, liquid junction potential, activity coefficient, sodium ion error and dissolved carbon dioxide on the response of the glass electrode were accounted for in the form of correction factors (log F) [27, 28].

Procedure

The titrations were performed at 303±0.1 K in media containing 0.0-60.0 % v/v PG, whereby the ionic strength was maintained constant at 0.16 mol dm^{-3} with sodium chloride and a total volume was kept constant 50ml. The electrode was kept, usually for 2-3 days, in the required solvent system for equilibration. To verify whether the electrode was equilibrated, a strong acid was titrated with an alkali every day until no appreciable differences were observed between the pH values of two titrations at the corresponding volumes of titrant. Under the above conditions, the electrode was assumed to be equilibrated. A calomel electrode was refilled with PG-water mixture of the equivalent composition to that of the titrand. Free acid titrations were performed before the metal–ligand titrations to calculate the correction factor. In each of the titrations, the titrand consisted of a mineral acid of approximately 1 mmol in a total volume of 50 cm^3. Titrations with different ratios (1:2.5, 1:3.75 and 1:5.0) of metal–ligand were performed with 0.4 mol dm^{-3} sodium hydroxide. Other experimental details are given elsewhere [29]. During the titrations a stream of nitrogen was bubbled through for both stirring and for maintaining an inert atmosphere.

Modeling strategy

The approximate complex stability constants of metal–MA complexes were calculated with the computer program SCPHD [30]. The best fit chemical model for each investigated system was arrived at using MINIQUAD75 [31].

RESULTS AND DISCUSSION

The results of the best fit models that contain the type of species and overall formation constants along with some of the important statistical parameters are given in Tables 1. A very low standard deviation in the log β values indicates the precision of these parameters. The small values of U_{corr} (sum of the squares of the deviations in the concentrations of ligand and hydrogen ions at all experimental points corrected for degrees of freedom) indicate that the experimental data can be represented by the model. Small values of the mean, standard deviation and mean deviation for the systems corroborate that the residuals are around a zero mean with little dispersion. For an ideal normal distribution, the values of the kurtosis and skewness should be three and zero, respectively. The kurtosis values in the present study indicate that the residuals form a leptokurtic pattern and a few form a platykurtic pattern. The values of the skewness given in the Tables are between -1.34 and 0.97. These data evince that the residuals form a 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 recorded. Thus, these statistical parameters show that the best fit models portray the metal–ligand species in PG-water mixtures.

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 concentrations of alkali, mineral acid, ligand, metal and volume (Table 2). The order of the compounds that influence the magnitudes of the stability constants due to incorporation of errors is alkali > acid > ligand > metal > volume. The increased standard deviation in stability constants and even rejection of some species on the introduction of errors confirms the correctness of the proposed models. This type of investigation is significant as the data acquisition were done under varied experimental conditions with different accuracies.

Table 1: Parameters of the best fit chemical models of Co(II), Cu(II), Ni(II) and Zn(II) MA complexes in PG-water mixtures.

Temperature 303±0.1 K, ionic strength 0.16 mol dm^{-3}

% v/v PG	log β_{mlh} (SD)				NP	U_{Corr}	χ^2	Skewness	Kurtosis	R-Factor	pH-Range
	ML	ML_2	ML_2H	ML_2H_2							
Co(II)											
0.00	2.59(58)	4.97(52)	10.17(69)	14.71(22)	53	3.392	31.54	-0.51	4.02	0.0156	2.50-6.50
10.00	2.13(88)	5.49(11)	10.65(17)	13.90(65)	51	0.547	22.63	-1.00	6.27	0.0064	2.60-6.40
20.00	3.08(38)	5.55(32)	10.66(68)	14.58(60)	39	2.210	8.47	0.53	3.31	0.0143	3.00-6.20
30.00	3.18(19)	6.15(7)	11.29(18)	15.49(11)	36	0.288	14.96	0.36	4.65	0.0050	3.00-6.20
40.00	3.37(58)	6.42(19)	11.78(47)	16.33(15)	45	2.837	12.02	-0.14	2.59	0.0150	2.90-6.60
50.00	2.99(80)	6.22(18)	11.77(51)	16.90(11)	55	2.453	28.31	-0.55	3.61	0.0113	2.40-6.20
60.00	3.56(17)	6.37(10)	12.12(30)	17.22(6)	33	3.903	20.03	0.00	5.39	0.0051	3.10-6.10
Cu(II)											
0.00	5.33(77)	8.85(11)	12.71(11)	15.98(8)	77	1.680	13.05	-0.39	3.99	0.0088	2.10-6.20
10.00	5.52(13)	9.16(7)	12.97(47)	16.34(12)	40	0.597	13.07	0.09	4.98	0.0068	2.20-6.30
20.00	5.81(9)	9.60(8)	13.84(16)	16.55(22)	46	0.237	4.14	0.88	3.19	0.0045	2.60-6.80
30.00	6.07(21)	9.99(10)	14.19(29)	17.73(8)	79	2.182	9.51	-0.73	6.99	0.0098	2.00-6.20
40.00	5.91(14)	9.54(10)	13.81(42)	16.86(42)	51	1.671	29.33	-0.02	1.91	0.0105	2.50-6.10
50.00	6.09(5)	9.30(4)	13.78(37)	17.62(8)	56	0.217	14.00	-0.30	5.58	0.0034	2.40-6.10
60.00	5.74(29)	10.32(5)	15.54(6)	18.72(6)	55	0.470	12.50	-0.11	3.12	0.0049	2.40-6.10
Ni(II)											
0.00	---	5.90(11)	10.91(16)	15.01(17)	77	6.200	19.70	-0.26	3.21	0.0171	2.10-6.20
10.00	---	6.13(7)	11.27(9)	14.96(22)	41	1.256	16.64	-1.03	5.18	0.0093	2.20-6.30
20.00	---	6.14(11)	11.59(13)	15.99(9)	63	5.000	19.13	-0.85	4.83	0.0165	2.20-6.00
30.00	---	5.94(7)	11.46(9)	15.25(24)	60	2.034	37.78	-1.34	6.69	0.0105	2.30-6.10
40.00	---	6.78(6)	12.25(6)	16.26(9)	70	1.376	14.00	-0.71	3.99	0.0080	2.20-6.20
50.00	---	6.31(12)	12.05(18)	16.95(15)	61	4.780	26.70	-0.74	4.30	0.0146	2.20-6.00
60.00	---	6.10(8)	12.31(9)	16.49(35)	72	1.814	54.22	0.97	3.95	0.0082	2.10-6.20
Zn(II)											
0.00	---	5.52(16)	10.89(21)	15.70(16)	53	7.902	37.58	-0.27	3.92	0.0235	2.40-6.40
10.00	---	6.14(9)	11.21(15)	15.56(12)	45	2.158	24.11	-1.00	4.38	0.0116	2.10-6.30
20.00	---	6.18(15)	11.58(19)	16.21(13)	62	10.32	18.04	-0.40	3.52	0.0241	2.20-6.00
30.00	---	6.13(10)	11.63(13)	16.24(11)	54	4.077	9.85	-0.77	4.55	0.0162	2.40-6.50
40.00	---	6.10(7)	11.70(8)	15.97(13)	66	1.562	29.72	-0.30	3.03	0.0085	2.20-6.10
50.00	---	6.25(14)	11.97(22)	17.26(15)	58	7.357	24.80	-0.97	4.62	0.0198	2.30-6.40
60.00	---	7.15(12)	12.95(17)	18.29(9)	57	5.036	32.27	-1.25	7.54	0.0159	2.30-6.30

$U_{corr} = U/(NP-m) \times 10^8$; NP = number of points; m = number of protonation constants; SD = standard deviation

Table 2: Effect of errors in influential parameters on Cu(II)-MA complex stability constants in 30% v/v PG-water mixture.

Ingredient	% Error	log β_{mlh} (SD)			
		ML	ML_2	ML_2H	ML_2H_2
	0	6.07(21)	9.99(10)	14.19(29)	17.73(8)
Acid	-5	7.85(56)	13.15(57)	15.54(**)	18.71(**)
	-2	6.80(22)	11.38(14)	14.65(65)	18.10(23)
	+2	5.52(21)	8.35(16)	13.16(70)	17.25(7)
	+5	3.75(9)	Rejected	12.35(10)	16.40(5)
Alkali	-5	Rejected	Rejected	11.77(11)	16.37(7)
	-2	5.37(29)	7.74(37)	13.25(57)	17.34(7)
	+2	6.77(26)	11.53(16)	14.36(**)	17.99(29)
	+5	7.43(62)	13.19(35)	14.10(98)	18.75(57)
Ligand	-5	6.20(30)	10.75(13)	14.33(46)	17.84(14)
	-2	6.13(24)	10.31(11)	14.26(34)	17.77(10)
	+2	5.99(24)	9.63(11)	14.13(30)	17.71(9)
	+5	5.84(30)	8.99(14)	14.03(32)	17.68(9)
Metal	-5	6.18(24)	10.27(11)	14.30(32)	17.80(10)
	-2	6.11(23)	10.10(10)	14.24(31)	17.80(9)
	+2	6.03(22)	9.88(10)	14.15(31)	17.71(9)
	+5	5.47(14)	8.00(21)	12.75(**)	17.32(6)
Volume	-5	5.98(21)	9.89(10)	14.10(28)	17.62(8)
	-2	6.03(22)	9.95(10)	14.16(30)	17.69(9)
	+2	6.11(23)	10.03(11)	14.23(32)	17.78(9)
	+5	6.17(24)	10.10(11)	14.29(34)	17.86(10)

*** Indicates high standard deviation*

Effect of solvent

The dielectric constant is one of the characteristics of solvents. The metal-ligand stability constants are strongly affected by the dielectric constant of the medium because of the fact that at least one of the constituents is charged and other is either changed or has a dipole. Variations in the relative strengths of acids and bases with changing solvents should be a function of the charge, the radius of the ion and the dielectric constants of the medium [32].The dielectric constants of PG at different percentages (0.0-60.0% v/v) of water were taken from literature [33]. PG is an amphiprotic and coordinating solvent. It is a structure former and hence it enhances the structure of water in PG-water mixtures. It also removes water from coordination sphere of metal ions, making them more reactive towards ligands. As a result, the stability of the complexes is expected to increase with increasing concentration of PG. On the other hand, PG is a coordinating solvent and competes with ligands for coordination with the metals.This decreases the stability of the complexes. Hence, variation in the stability of complex with solvent is a result of both the opposing behaviors.

The variation of the values of the overall stability constant or change in free energy with content of co-solvent depends upon two factors, *viz*. electrostatic and non-electrostatic. The Born classical treatment accounts well for the electrostatic contribution to the free energy change [34, 35]. According to this treatment, the energy of electrostatic interaction is related to the dielectric constant. Hence, the log β values should vary linearly with the reciprocal of the dielectric constant of the medium. The plots given in Figure 1 show that the values of log β increase linearly with decreasing value of the dielectric constant. This trend indicates the dominance of the structure forming nature of PG over its complexing ability.

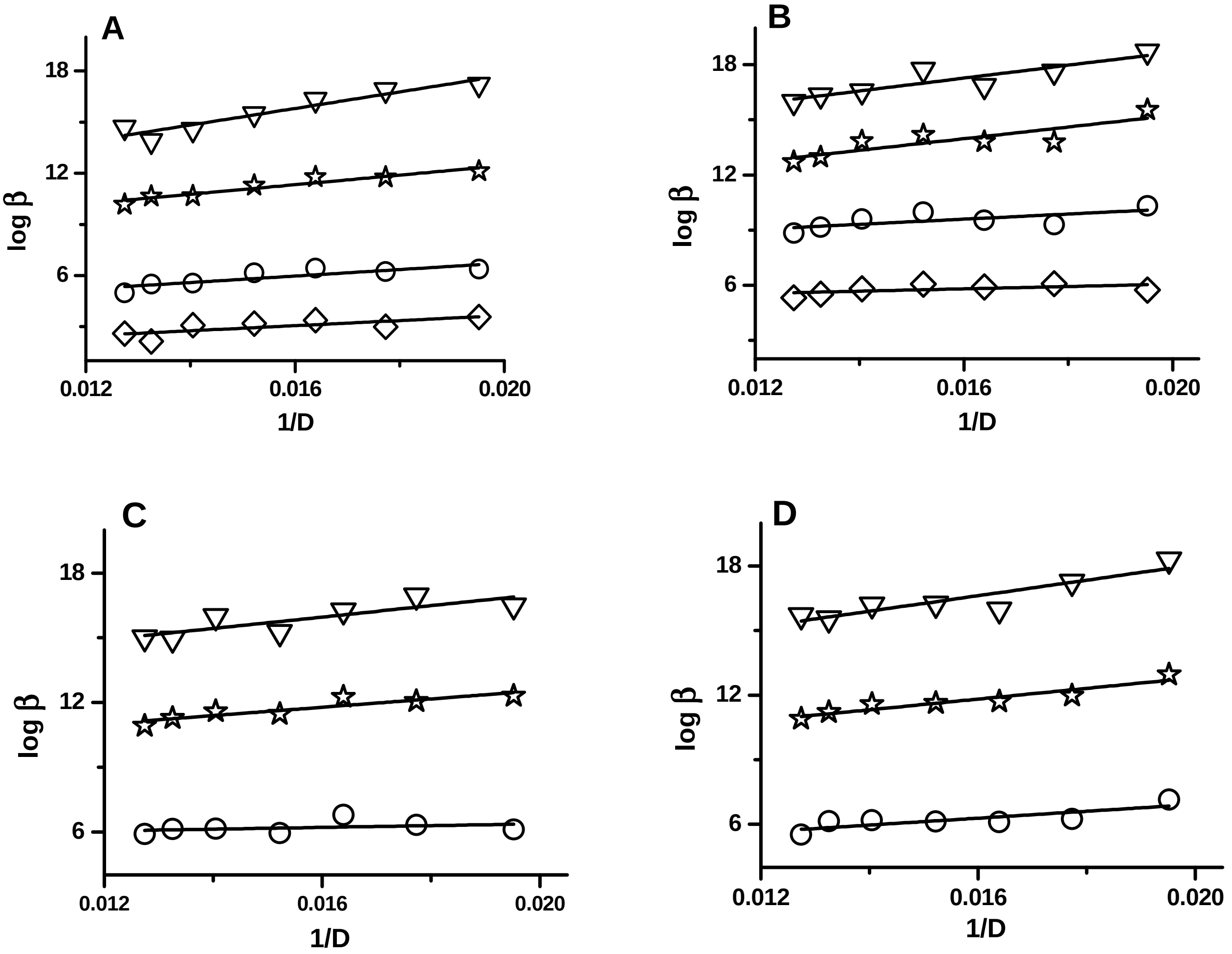

Figure 1: Variation of stability constants of metal-MA complexes with reciprocal of dielectric constant (1/D) in PG-water mixtures. (A) Co(II); (B) Cu(II); (C) Ni(II) and (D) Zn(II); (▽) log β_{ML2H2}, (☆) log β_{ML2H},(○) log β_{ML2}, (◇) log β_{ML}

The cation stabilizing nature of co-solvents, specific solvent-water interactions, charge dispersion and specific interactions of the co-solvent with the solute (indicated by the changes in the solubility of different species in aqua–organic mixtures) account for the small deviation from a linear relationship. Since the complex formation can be viewed as the competition between pure and solvated forms of the ligand and metal ion, solute-solvent interactions, relative thermodynamic stabilities, kinetic labilities play an important role [36, 37].

Distribution diagrams

MA has two dissociable carboxyl protons. The different forms of MA that exist in the pH regions 1.7– 3.5, 1.7-6.0 and 4.0–7.0.0 are LH_2, LH^- and L^{2-}, respectively. Hence, the probable species existing in different systems can be predicted from these data. The present investigation reveals the existence of ML, ML_2, ML_2H and ML_2H_2 for Co(II) and Cu(II) and ML_2, ML_2H and ML_2H_2 for Ni(II) and Zn(II).

Typical species distribution diagrams of various systems are shown in figure 2 which indicate the formation of MA complexes of Co(II), Cu(II), Ni(II) and Zn(II) in the pH ranges 2.4-6.50, 2.1-6.8, 2.1-6.3 and 2.1-6.50, respectively. ML_2H, ML_2H_2 and ML_2 are formed simultaneously and their percentage increase in the same order with increase in pH. From the distribution diagram the percentage of ML for Co(II) and Cu(II) are greater at higher solvent concentration. Except Zn(II) the percentage of ML_2H_2 is very low in all composition of solvent.

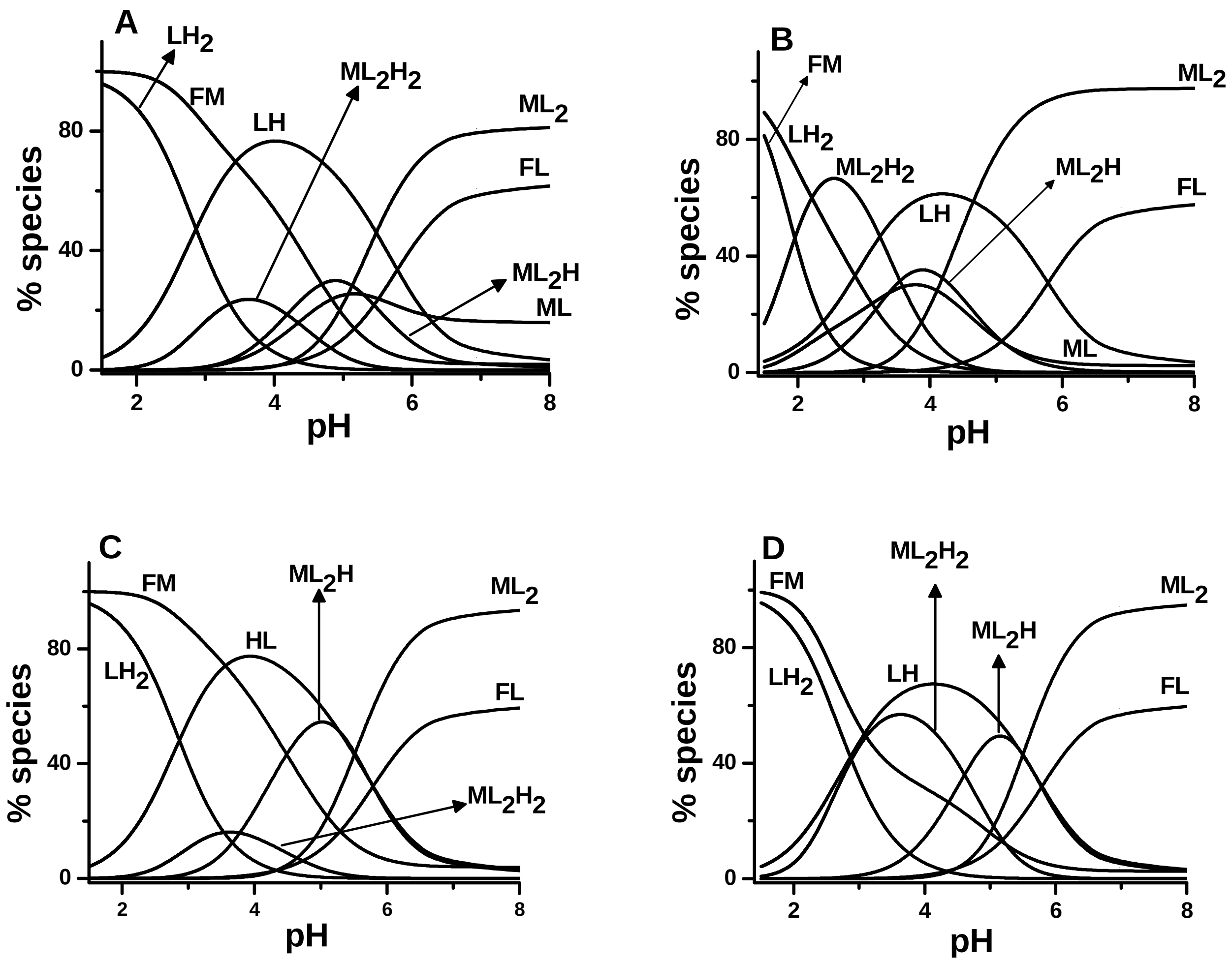

Figure 2: Distribution diagram of MA-metal complexes in 30% PG-water mixtures. (A) Co(II), (B) Cu(II) (C) Ni(II), and (D) Zn(II)

The equilibria for the formation of various binary complexes can be represented as;

$$\mathrm{M(II)} + 2\mathrm{LH_2} \rightleftharpoons \mathrm{ML_2H_2} + 2\mathrm{H^+} \qquad \text{————} \qquad (1)$$

$$\mathrm{M(II)} + 2\mathrm{HL} \rightleftharpoons \mathrm{ML_2H} + \mathrm{H^+} \qquad \text{————} \qquad (2)$$

$$\mathrm{ML_2H_2} \rightleftharpoons \mathrm{ML_2H} + \mathrm{H^+} \qquad \text{————} \qquad (3)$$

$$\mathrm{M(II)} + \mathrm{LH_2} \rightleftharpoons \mathrm{ML} + 2\mathrm{H^+} \qquad \text{————} \qquad (4)$$

$$\mathrm{M(II)} + \mathrm{LH} \rightleftharpoons \mathrm{ML} + \mathrm{H^+} \qquad \text{————} \qquad (5)$$

$$\mathrm{M(II)} + 2\mathrm{LH_2} \rightleftharpoons \mathrm{ML_2} + 4\mathrm{H^+} \qquad \text{————} \qquad (6)$$

$$\mathrm{ML_2H_2} \rightleftharpoons \mathrm{ML_2} + 2\mathrm{H^+} \qquad \text{————} \qquad (7)$$

$$\mathrm{ML_2H} \rightleftharpoons \mathrm{ML_2} + \mathrm{H^+} \qquad \text{————} \qquad (8)$$

$$\mathrm{M(II)} + 2\mathrm{LH} \rightleftharpoons \mathrm{ML_2} + 2\mathrm{H^+} \qquad \text{————} \qquad (9)$$

At low pH, ML_2H_2 species is formed from free metal ions interact with LH_2 form of the ligand (equilibrium 1). The interaction of free metal ions with LH at lower pH (equilibrium 2) and deprotonation of ML_2H_2 at higher pH (equilibrium 3) result the formation of ML_2H species. Higher concentration of ML_2H than that of ML_2H_2 signifies the ML_2H is formed from equilibria of 2 and 3. The ML_2 species is formed from interaction of free metal ion with LH_2 and LH (equilibria 6 and 7) or deprotonation of ML_2H_2 and ML_2H (equilibria 8 and 9). In the case of Co(II) and Cu(II) (Figure 2A and 2B) the ML species may be formed from the interaction of free metal ion with LH_2 or LH (equilibria 5 and 6).

The distribution of the species over the entire pH range is useful to understand the pH where a particular species is likely to form. By using these data, the bioavailability of a metal can be predicted. For instance, in Figure 2 the concentration of free metal ion (FM) is very high in acidic pH values. Hence, in these pH ranges the metals are more bioavailable than in higher pH ranges. Hence, the concentrations of the complex chemical species have more significance than the total concentrations for the bioavailability and toxicity of essential metals in soils and water.

Structures of Complexes

MA acts as a bidentate ligand from two strong oxygen of carboxylic acid that can form complexes with metal ions. Generally, from table 1 the final model containing ML, ML_2, ML_2H and ML_2H_2 appropriately fits the experimental data. Octahedral structures (Figure 3) are proposed to the complexes of all the metal ions. The VSEPR theory suggests that (Cu(II), Ni(II), Cu(II) and Zn(II) complexes shall be octahedral because there are six outer electron pairs.

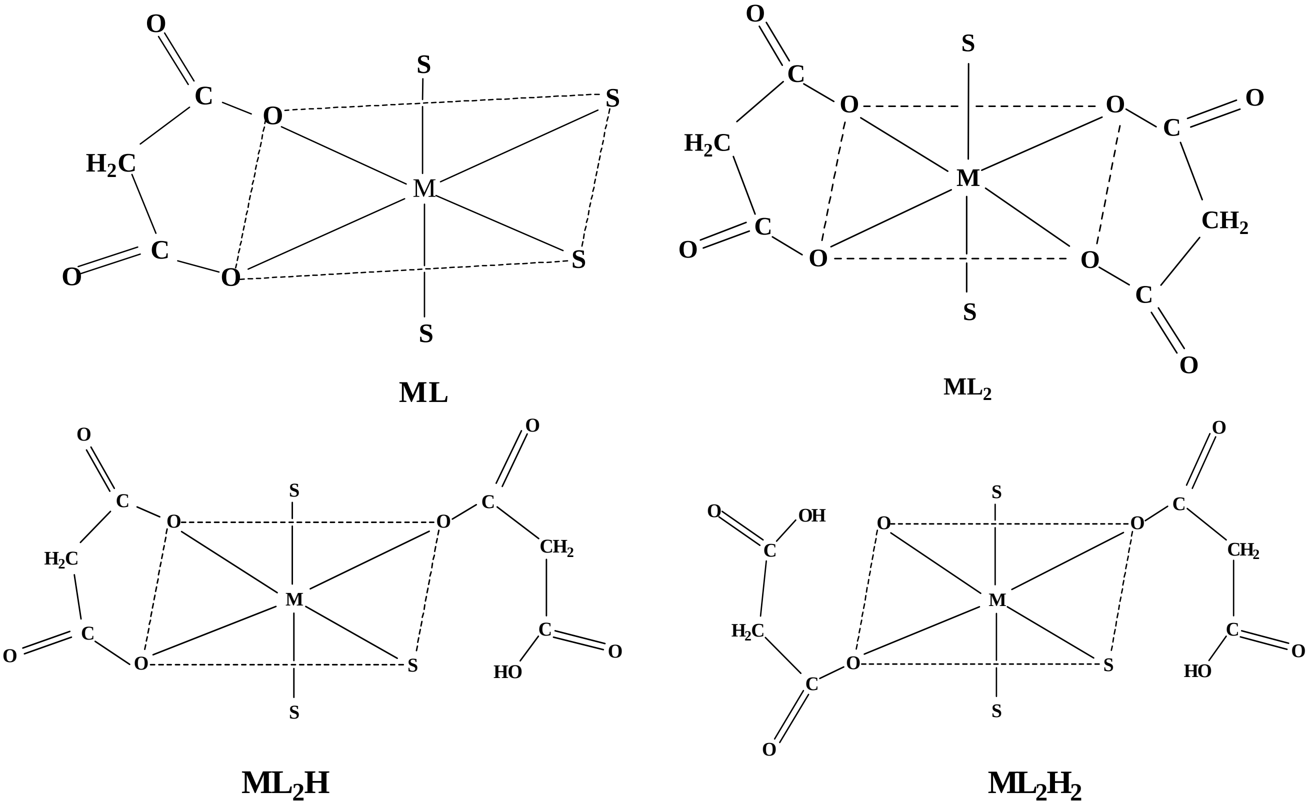

Figure 3: Structure of MA complexes of Co(II), Cu(II), Ni(II) and Zn(II). S is either solvent or water molecule

CONCLUSION

In the present work, pH-metric study was performed to determine stability constants and to asses binary species for MA with essential metal ions in 0.0-60.0% PG-water mixtures in pH range of 2.0-7.0. The following conclusion have been drawn: (1) The binary species formed due to the interaction of MA with metals are ML_2H_2, ML_2H, ML_2 and ML for Co(II) and Cu(II) and ML_2H_2, ML_2H, ML_2. For Ni(II) and Zn(II). These models are validated by statistical treatment of data. (2) The linear variation of stability constants as a function of 1/D of the medium indicates the dominance of electrostastic forces over non-electrostatic forces and the dominance of structure forming nature of the co-solvents over its coordinating power. (3) The order of ingredients influencing the magnitudes of stability constants due to incorporation of errors in their concentrations is alkali > acid > ligand > metal > volume.

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