Anionic Surfactant Influence On Binary Complexes Of Ca(II), Mg(II) And Zn(II) Ions With Glycylglycine

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Abstract

A pH metric titration study has been undertaken to determine the anionic surfactant influence on mixed binary systems consisting of calcium (II), magnesium (II) and zinc (II) with glycylglycine (GG) at various concentrations (0.0–2.5% w/v) of the SLS (Sodium Lauryl Sulphate) surfactant solution while maintaining an ionic strength of 0.16 mol L^{-1} (NaCl) at 30 °C. Titrations were performed in the presence of different ratios (M:L = 1:2.50, 1:3.75, and 1:5.00) of metal (M) and glycylglycine (L) using sodium hydroxide. Model systems were developed based on statistical parameters and residual analysis. For Ca(II), Mg(II) and Zn(II), the species detected were ML_2, ML_2H, and ML_2H_2. The electrostatic relationship of the ligands' side chains, charge neutralization, chelate effect and stacking interactions are used to explain the trend in the variation of logarithm of stability constants (log β) values with changing dielectric constant and mole fraction of the surfactant. The variation in species distribution as a function of pH and surfactant composition is also presented and discussed, as are plausible equilibria for the formation of the species and structures of the ternary complexes are also presented and discussed.

Keywords: Binary Complxes, Stability Constants, SLS, Glycylglycine, pH

1. Introduction

Speciation studies of toxic and essential metal ion complexes are useful in order to understand the role played by the active site cavities in biological molecules and the bonding behaviour of their residues with metal ions [Forste, et al., 1983; Meria, E. 1991 and Shehate, et al., 2008]. The possible ligand groups in proteins are the aminoacid side chains, the

terminal amino, carboxyl, hydroxyl and thiol groups and in some cases, the amide group in the peptide backbone. However, the study of metal-protein interactions involves complications due to the complex nature of proteins. An exact model of the metal protein system may be difficult to construct in simple biomolecules like aminoacids and peptides but such models may give a tremendous amount of information about the structure of proteins and function of biomolecules in biological systems. The interaction of metals with amino acids, catechols, carboxylic acids and peptides has been the subject of much interest due to the importance of metals in many biochemical processes such as respiration, metabolism and nerve transmission [Freeman, H.C. 1967; Benzakou, et al., 2004; Rodgersand, et al., 2004 Lippard, et al., 1994]. Investigations of multiple equilibria of dipeptides and their interaction with metal ions at varying ionic strengths and temperatures throw light on the mechanism of enzyme-catalyzed reactions. Chemical speciation of metals is important for an understanding of their distribution, mobility, bioavailability, toxicity and for setting environmental quality standards [Teigen, et al., 1992]. Bioavailability of a particular metal depends on its complex chemical reactions of dissolution, binding and complexation with the constituents of the environmental aquatic media [Di Toro, et al., 2001].

The significance of the present study is to identify the metal complex species formed under the given experimental conditions and to validate the associated models by statistical treatment of the data obtained relating to the binary stability constants of glycylglycine. Surfactant-water mixtures are used in these studies to mimic physiological fluid media. These data are useful in extraction metallurgy, nuclear energy, and medical, environmental, and industrial research [Sachan, S. 2011]. In general, stability constant data are useful in understanding the role and activity of metal complexes in biological systems [Singh P.P., and Kanaujia S. 2013]. The chosen ligands bear immense biological and medicinal importance.

Dipeptides are important bioligands as they have good coordination sites for metal complexation as revealed by chemical literature [Ilavarasi, R. 2014; Dhanalakshmi, B. 2014 and Nair, M.S. 2000]. Study of the chelating ability of glycine peptides and catecholamines, in particular diglycine with some divalent toxic metals were carried out to understand the mode of complexation of these ligands in biological systems which is used for efficacious treatment for patients with metal poisoning [Padmaja, N. 2012].

2. Material and Methods

2.1 Experimental

By dissolving the pure chemical component in distilled water and adding a small amount of 0.05 mol L-1 hydrochloric acid, which boosts glycylglycine's solubility, glycylglycine solution with 0.05 mol L-1 concentration was created. The sodium hydroxide pellets are dissolved in distilled water to create a sodium hydroxide solution with a concentration of 0.4 mol L-1. The titrand solution, which is created with a 2.0 mol L-1 concentration by dissolving the drug in distilled water, uses sodium chloride to maintain ion strength. Metal ion solutions of Ca(II), Mg(II), and Zn(II) chloride were created by dissolving the components in distilled water to a concentration of 0.05 mol L-1. By dissolving in distilled water, hydrochloric acid solution with a concentration of 0.2 mol L-1 is created. SLS is utilized directly from the manufacturer, without being further purified. Glycylglycine is purchased from Qualigens in India, and sodium chloride is purchased from Himedia in India. All solutions are made with triple-distilled water, which is also used to clean glassware equipment. Sodium hydroxide, metal ion solutions, and hydrochloric acid were all standardized using accepted techniques. Any errors in the concentration determination are evaluated using the analysis of variance of one-way classification [Seetharam. P, et al., 2021]. To evaluate the strengths of acids and bases, the widely utilized Gran plot approach is employed [Ramanaiah, et al., 2019 and Gran, G., 1952].

2.2 Procedure

Titration between acid and alkali is the first step in the process of figuring out the stability constants of metal ligand complexes. This will assist determine whether equilibrium has been reached. In order to maintain the electrode in an equilibrium state when using this approach, SLS-water solution must be maintained. For every titration against 0.4 mol L-1 of sodium hydroxide, 1 mmol of mineral acid must be introduced to the titrand using the same method of maintaining the electrode in SLS-water mixtures. By changing the metal-to-ligand ratios (1:2.5, 1:3.75, and 1:5), titrations are performed. The initial concentrations of reactants are given in Table 1. Additional experimental information is provided elsewhere [Gran, G., 1988].

2.3 Modelling strategy

The computer programme MINIQUAD75[Rao, G.N. 1992] was used to generate the best-fit chemical models relating stoichiometric coefficients to the logarithm of stability constants (log β). Some heuristics were followed in refining stability constants andvalidating models [Sailaja B.B.V, et al., 2002 and Rao, R.S. 2005]. The formation constants for acid–base equilibria and those for binary metal complexes of Asp andCit were determined in the refinement of the mixed ligand stability constants using MINIQUAD75.

Table 1: Total initial concentrations of ingredients (in mmol) for metal - ligand titrations in SLS-water mixtures. [NaOH] = 0.4 mol dm^{-3}; V_0 = 50 cm^3; Temperature = 303 K; Mineral acid = 1.0 mmol; μ = 0.16 mol dm^{-3}.

% w/v SLS	Titration curves	TM0			TL0	TL0/TM0
		Ca(II)	Mg(II)	Zn(II)	GG	
0.0	3	0.10031	0.10019	0.10012	0.2488 0.3767 0.4990	2.50 3.75 5.00
0.5	3	0.10031	0.10019	0.10012	0.2497 0.3746 0.4995	2.50 3.75 5.00
1.0	3	0.10031	0.10019	0.10012	0.2497 0.3745 0.4994	2.50 3.75 5.00
1.5	3	0.10031	0.10019	0.10012	0.2490 0.3735 0.4981	2.50 3.75 5.00
2.0	3	0.10031	0.10019	0.10012	0.2492 0.3738 0.4985	2.50 3.75 5.00
2.5	3	0.10031	0.10019	0.10012	0.2494 0.3741 0.4989	2.50 3.75 5.00

3. Results and Discussion

3.1 Complex equilibria

In the presence of a mineral acid and an inert electrolyte, alkali-metric titrations of mixtures containing different mole ratios of glycylglycine revealed that ML_2, ML_2H, and ML_2H_2 species are formed for Ca(II), Mg(II) and Zn(II).The parameters of the best-fit models and statistical parameters are given in Table 2. The very low standard deviationin the log β values reflects the precision of these parameters. This indicates that the generated models appropriately fit theexperimental data. The small values of U_{corr} indicate that the model is consistent with the experimental data[31]. The majority of the systems had kurtosis values around 3, and hence, the residuals form a meso-kurtic pattern.

For some systems, the kurtosis values are greater than 3 (leptokurtic pattern). The values of skewness between –2.15 and 2.41 indicate that the residuals form a part of a normal distribution, and 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-factor values, which indicate the need for the inclusion of additional species in the model. χ2 is a special case of a γ-distribution that measures

the probability of residuals forming a part of standard normal distribution.

Table 2: Parameters of best fit chemical models of M(II) – Glycylglycine complexes in SLS-water medium

% w/v SLS	log β_{mlh} (SD)			pH-Range	NP	U_{corr} $_{\times 10^8}$	χ^2	Skew-ness	Kurt-osis	R-factor
	ML_2	ML_2H	ML_2H_2							
Ca(II)										
0.0	4.80(38)	14.80(22)	22.85(27)	3.0-10.1	28	16.76	0.80	0.16	3.32	0.0280
0.5	5.49(20)	15.29(30)	22.46(37)	3.4-10.8	55	12.08	33.05	2.04	8.86	0.0415
1.0	6.62 27)	16.59(30)	23.33(34)	3.4-10.8	34	13.44	42.16	2.41	11.66	0.0352
1.5	5.98(23)	15.96(26)	24.21(43)	2.2-10.8	22	30.12	15.27	0.11	3.92	0.0383
2.0	6.93(12)	15.75(29)	23.96(20)	2.7-7.5	51	17.86	18.87	-0.08	4.58	0.0217
2.5	7.35(24)	15.76(28)	23.63(20)	2.9-8.2	27	9.23	13.91	0.01	4.22	0.0223
Mg(II)										
0.0	6.97(28)	16.32(25)	23.68(19)	2.2-10.3	73	21.14	56.98	0.14	4.37	0.0343
0.5	7.39(20)	16.16(35)	24.05(44)	2.2-9.1	56	35.88	25.24	0.03	7.26	0.0420
1.0	7.59(34)	16.52(29)	23.36(42)	2.5-10.1	37	29.39	22.69	-2.15	10.07	0.0465
1.5	7.48(33)	16.24(35)	23.62(27)	2.3-9.3	55	39.47	23.75	-0.21	5.84	0.0462
2.0	7.85(15)	15.98(35)	23.55(10)	2.3-7.5	57	10.44	5.61	-0.29	3.49	0.0217
2.5	8.22(28)	15.15(42)	22.73(35)	3.1-10.0	23	14.13	9.72	0.07	4.39	0.0420
Zn(II)										
0.0	7.46(30)	14.76(35)	21.76(40)	2.5-8.1	56	13.94	32.67	0.33	4.55	0.0305
0.5	7.12 (34)	15.35(38)	22.34(31)	2.1-7.5	35	6.40	28.56	0.02	1.84	0.0354
1.0	7.98(16)	16.72(36)	23.98(27)	2.3-7.0	23	3.87	3.93	0.03	3.17	0.0225
1.5	8.73(36)	16.57(30)	23.82(26)	2.4-7.5	32	2.75	15.11	0.18	2.66	0.0314
2.0	8.59(23)	16.51(10)	24.05(10)	2.4-7.5	77	7.94	29.81	-0.17	5.93	0.0160
2.5	8.41(35)	16.89(40)	24.08(36)	2.8 - 7.5	30	11.56	6.18	-0.05	3.64	0.0349

U_{corr} = U/ (NP-m)X10^8, where m = number of species; NP=Number of experimental points; SD=Standard deviatio

3.2 Perturbation in stability constants due to systematic errors

The computer programs refine the stability constants by minimizing the random errors in the data. But in the presence of considerable systematic errors, not only the β's are in errors; even some species may be rejected. MINIQUAD75 has no provision to vary the influential parameters. Hence, some representative systems were studied in order to have a cognizance of the effect of errors in concentrations of ingredients on the stability constants of binary metal complexes. These results are given in Table 3. The data show that the order of affecting the magnitudes of stability constants is alkali > acid > ligand > metal. 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 was done under varied experimental conditions with different accuracies.

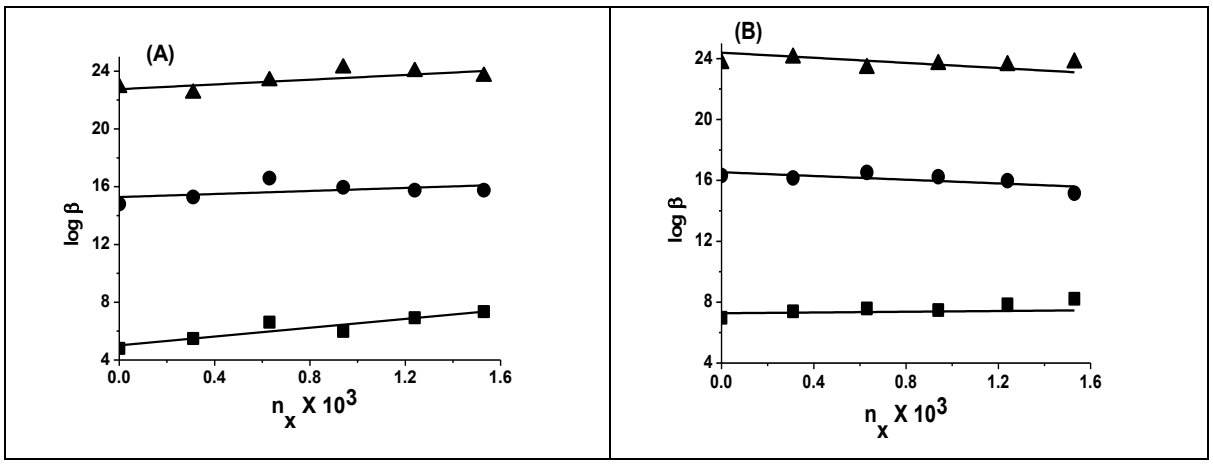
Ingredient	% Error	Log β_{mlh}(SD)		
		120	121	122
Acid	0	8.73(36)	16.57(30)	23.82(26)
	-5	10.78(65)	Rejected	Rejected
	-2	9.55(31)	16.81(37)	23.55(26)
	+2	7.73(34)	15.22(55)	23.70(30)
	+5	Rejected	14.41(60)	22.23(45)
Alkali	-5	Rejected	14.71(64)	23.35(23)
	-2	7.93(24)	14.49 (63)	23.77(22)
	+2	8.28(30)	16.48(37)	23.36(24)
	+5	9.52(49)	17.84(58)	23.89(43)
Ligand	-5	8.72(23)	16.89(33)	23.87(19)
	-2	8.79(25)	16.77(43)	23.98(20)
	+2	8.59(27)	16.56(44)	23.73(22)
	+5	8.68(29)	16.49(45)	23.65(24)
Metal	-5	8.70(28)	16.54(37)	23.74(23)
	-2	8.61(22)	16.51(35)	23.69(27)
	+2	8.69(25)	16.96(32)	23.63(20)
	+5	8.70(24)	16.92(30)	22.79(19)
\				
Volume	-5	8.79(25)	16.52(33)	23.73(20)
	-2	8.72(25)	16.56(33)	23.70(21)
	+2	8.76(26)	16.59(33)	23.66(21)
	+5	8.78(26)	16.62(33)	23.69(21)

Log F	-5	8.55(26)	15.98(33)	23.72(22)
	-2	8.55(26)	15.98(33)	23.72(22)
	+2	8.54(26)	15.98(33)	23.86(22)
	+5	8.54(26)	15.98(33)	23.76(22)

Table 3: Effect of errors in influential parameters on the stability constants of Zn(II)-Glycylglycine complexes in 1.5% W/v SLS – water medium.

3.3 Effect of micelles on stability of complexes

The variations of stability constants (log β) with mole fraction of different micellar media are shown in Figure 1. The stability of a complex depends on the charge of the Stern layer [Bunton, et al., 1972;]. The stabilities of binary Ca(II), Mg(II) and Zn(II) complexes varied linearly with mole fraction due to the polarity of the medium, charge on the micellar surface and due to the non-electrostatic forces/hydrophobic interactions operating between the complex species and micellar surface. The species should be stabilized in the micellar medium with opposite charges due to electrostatic interactions but these charged species should be destabilized due to the decreased dielectric constant of the medium. The deviation from linearity may be due to some contributions from non-electrostatic forces [Feakins, et al., 1983].



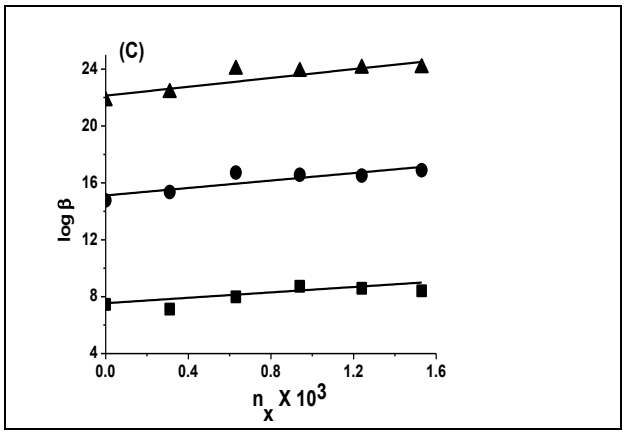


Figure 1: Variation of stability constants of GG complexes of (A) Ca(II), (B) Mg(II) and (C) Zn(II);(■)logβ_{ML_2}; (●)logβ_{ML_2H};(▲)log$\beta_{ML_2H_2}$ with mole fraction of SLS-water mixtures.

3.4 Distribution Diagrams

Glycylglycine has one associable (amino) and one dissociable (carboxylate) proton. LH^{2+}, LH+, and L-, which have pH ranges of 1.8 to 3.0, 3.0 to 10.0, and 8.0 to 10.0, respectively [Seetharam. P, et al., 2016 and Seetharam. P, et al., 2020], are the three distinct forms of glycylglycine. These data allow for a prediction of the likely binary metal-ligand species in various systems, which MINIQUAD75 then confirms.

The current analysis shows that Ca(II), Mg(II), and Zn(II) all have ML_2H_2, ML_2H, and ML_2.The fact that Ca(II), Mg(II), and Zn(II) may produce ML_2H_2 suggests that the side chain amino group is still protonated in their presence. Among all the binary complexes, the ML_2 species predominates at higher pH levels while ML_2H_2 predominates at lower pH levels. The strong complexing character of glycylglycine is indicated by the low concentration of free metal ions (FM). The following equilibria demonstrate how distinct binary complex species develop. Figure 2 shows some typical distribution diagrams for SLS-water media. When observed in Equilibrium (4), ML_2H_2 is produced when the concentration of the free metal ion and LH^{2+} decreases. Equilibria (7) and (8) are suggested for the creation of ML_2H, however ML_2H is more likely to occur in equilibria (8) than in equilibria (7) since it does so with a decreasing concentration of MLH. Equilibria (9) and (10) both describe possible pathways for the formation of ML_2H, but (10) is more appropriate because, during this process, the concentration of ML decreases and the percentage of ML_2 increases as the concentration of ML and ML_2H are decrease at the same pH range. The following equilibria illustrate how different glycylglycine complex species form:

$$M(II) + LH_2^{+} \rightleftharpoons MLH^{2+} + H^{+} \quad (1)$$

$$MLH^{2+} \rightleftharpoons ML^{+} + H^{+} \quad (2)$$

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

$$M(II) + 2LH_2^{+} \rightleftharpoons ML_2H_2^{2+} + 2H^{+} \quad (4)$$

$$MLH^{2+} + LH_2^{+} \rightleftharpoons ML_2H_2^{2+} + H^{+} \quad (5)$$

$$ML_2H_2^{2+} \rightleftharpoons ML_2H^{+} + H^{+} \quad (6)$$

$$M(II) + 2LH_2^{+} \rightleftharpoons ML_2H^{+} + 3H^{+} \quad (7)$$

$$MLH^{2+} + LH \rightleftharpoons ML_2H^+ + H^+ \quad (8)$$

$$ML^+ + LH_2^+ \rightleftharpoons ML_2H^+ + H^+ \quad (9)$$

$$ML_2H^+ \rightleftharpoons ML_2 + H^+ \quad (10)$$

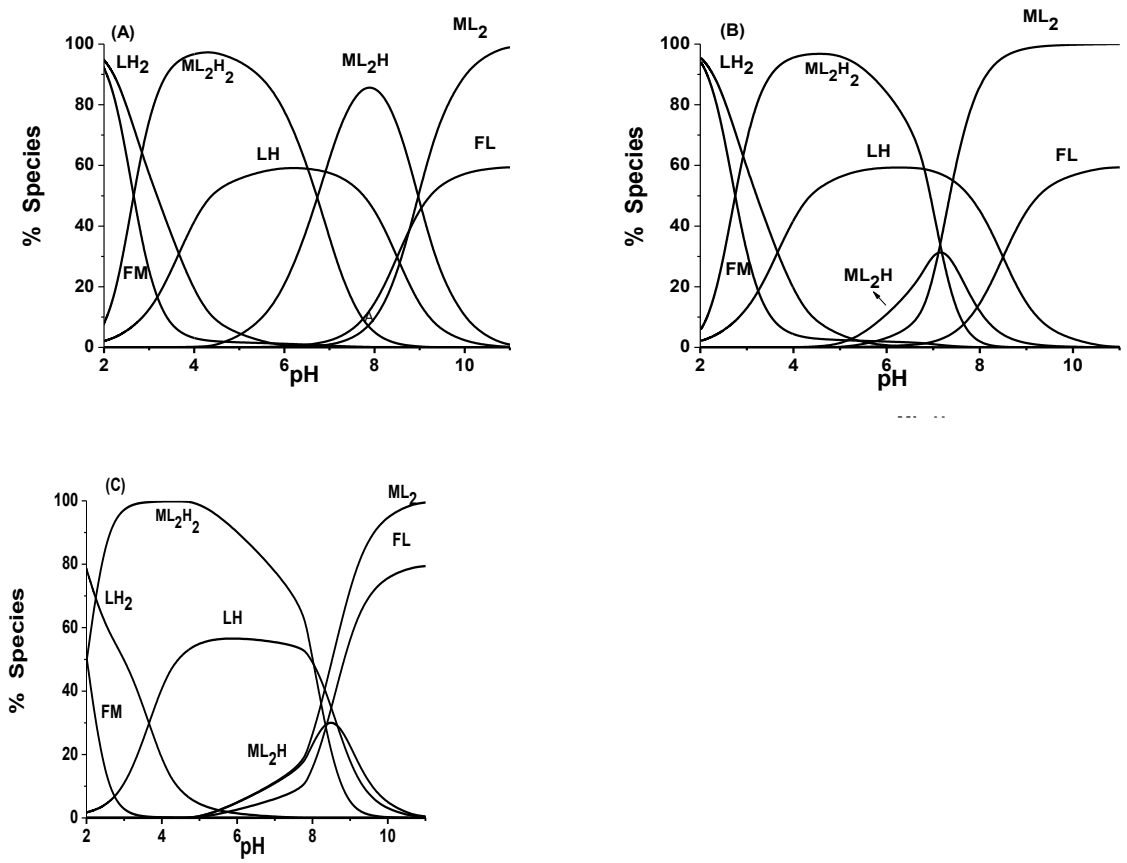


Figure 2: Distribution diagrams of GG complexes in 1.0 % w/v SLS-water medium. (A) Ca(II) (B) Mg(II) and (C) Zn(II)

3.5 Structures of Complexes

Octahedral structures are proposed to the complexes of Ca(II), Mg(II) and Zn(II). Amine nitrogen atoms can associate with hydrogen ions in the lower pH ranges. Hence, there is often significant competition between hydrogen and metal ion for this second donor site. This situation results in the simultaneous existence of equilibria producing protonated and un protonated complexes. The possible structures for the species of M(II)-GG complexes are given in Figure 3.

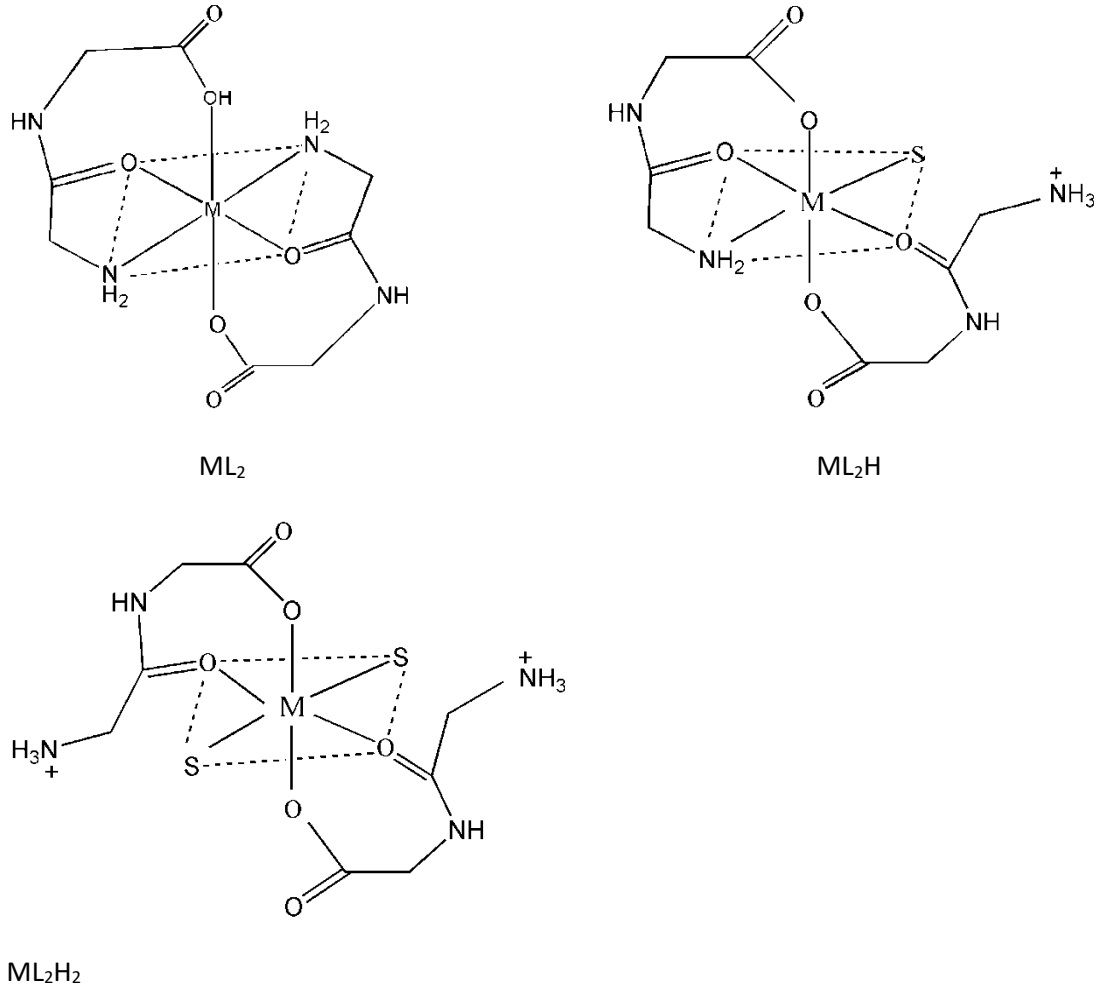


Figure 3: GG-M(II) metal ligand complexes, S is solvent or water

4. CONCLUSION

In the pH range 2.0-10.0, glycylglycine forms complexes with metal ions of calcium, magnesium and zinc, which divalent. The metal ligand complexes formed in the present study are ML_2, ML_2H, and ML_2H_2. It is observed that there is a measurable change in the stability constants of the metal complexes with respective to SLS composition, it describes the predominant role of electrostatic forces. As the concentration of SLS is increasing, the $\log_{mlh}$ values of Ca(II), Mg(II) and Zn(II) complexes were increased. Stabilization and destabilization of species are caused by electrostatic interactions and a decreasing dielectric constant. The stability of reactant modified complexes is in the order alkali component > acid component > ligand component > metal component > total volume component > log F component. This study contributes to our understanding of the interactions between metals and ligands in aqueous-surfactant combinations and has the potential to be extremely instructive for future research on medicinal applications.

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