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Original Article

Electrometric Study on Nature and Stability of Co^{II}, Ni^{II} and Cu^{II} Complexes with 5-Sulfosalicylic Acid in DMSO-Water Mixtures

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ABSTRACT

Background: The bioavailability of an element and its toxicity based on its chemical species. According to IUPAC the concept of chemical speciation is defined as it is a form of an element according to its oxidation state, isotopic composition, or complex and molecular structure. The speciation studies are profoundly plays a major role in studying the nature of trace elements in a human organism. Speciation of an element has a noticeable impact on bioavailability, distribution and toxicity. These studies have vital role in medical and pharmaceutical sciences. **Materials and Methods:** The present investigation conducted by using pH meter, processing of data done by Gran titration. To obtain best-fit chemical models, a modelling strategy such as SCPHD is used and a computer program MINIQUAD 75 is also employed for the refinement of results. **Results:** In the present investigation we considered the effect of dielectric constants of Dimethyl sulfoxide (DMSO) on stability constants of Co^{II}, Ni^{II} and Cu^{II} with 5-Sulfosalicylic acid (5-SSA) complexes. The formed binary complex species are ML, MLH and ML_2 and obtained skewness values range from -0.15-0.71 for Co^{II}, -0.27-0.32 for Ni^{II} and -0.41-0.32 for Cu^{II} describes the distribution curves are left skewed and right skewed. The peak of the distribution curves shows platykurtic and leptokurtic with regards to the obtained values ranging from 2.89-6.14. **Conclusion:** It is observed that there is a significant influence of co-solvent, Dimethyl Sulfoxide (DMSO)-water mixtures on the stability constants of metal-ligand complexes, also studied how some factors such as changes in concentrations of ligand, acid, base log F and volume of the solution have influence on the protonation constants.

Keywords: Acid-base equilibria, 5-Sulfosalicylic acid, Dimethyl sulfoxide, Binary complexes and Dielectric constant.

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INTRODUCTION

The essential metal ions like Copper, Zinc, Iron, and Manganese in water also become toxic when they have higher concentrations, the non-essential metal ions like Lead, Mercury and Cadmium are very toxic by nature even in lower concentrations. There is a considerable increase in the metal ions in rivers and lakes, which are through anthropogenic inputs in a natural way. The metal ions in the water may be available in the following forms such as free aqua ions, complexes, colloidal phase and etc., these are called species and show various effects. Chemical speciation is an important study by which one can understand the availability of metal ions in organisms and their toxicity. The transportation of metal ions in natural water and in the different compartments of the environment fairly depends on chemical speciation. Chemical speciation will strongly influence some essential properties like toxicity and bioavailability.[1,2] The bioavailability of metal ions varies according to their availability i.e. free state, binding state or complex form with diverse constituents having different concentrations during the biological reactions. The behaviour of metal-ligand complex changes with variations in pH, temperature and ionic strength, complexation of metal ligands is the way to understand the bioavailability of separate metal ions in various biosystems.[3,4] Speciation analysis drives through finding the concentrations of an element about its separate and unique atomic and molecular forms rather than its overall concentration in a single sample; this has gained considerable importance in human biology and toxicology.[5] The speciation of an element extremely affects toxicity and bioavailability.

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Salicylic acid derivative like 5-SSA acid has many applications in drug designing and DMSO is most commonly used in biochemistry. It is a polar solvent, can dissolve many compounds in it, which property makes DMSO to have number of applications in drug designing and synthesis. Cobalt is an essential element; it participates in a biochemical process as a coenzyme. Like Cobalt, Nickel and Copper also have an important role in metabolism, a small change in their concentrations may lead to metabolic disorders. For all the animals, cobalt is an essential element especially in the form of Vitamin B_{12}. Solving of mass-balance equations is generally employed to determine the equilibrium constants of individual reactions and the concentration of species, this is done by using computer programs like HALTAFALL[6] and COMICS.[7] The metal-ligand equilibria in the can also be simulated using other computer programs like ECCLES,[8] MINEQL,[9] SCOGS,[10] SOLMNQ,[11] COMPLOT,[12] SPE,[13] ESTA,[14] GEOCHEM,[15] JESS,[16] visual MINTEQ,[17] CHEAQS[18] and HYSS.[19]As stability constants have wide range of applications in drug synthesis, they act like good tools for chemists and biochemists. The properties of metal-ligand complexes and their reactions in aqueous medium or in biological fluids are dependent on stability constants. The present study aims at understanding the nature of complexes formed, check the adequacy of the best fit model with statistical parameters, the effect of dielectric constant of solvent on the stability constants of the formed complexes. The metal ions Co^{II}, Ni^{II} and Cu^{II} and the ligand 5-SSA and DMSO-water mixtures were taken as model in this investigation.

MATERIALS AND METHODS

Chemicals

The A.R grade5-SSA (TCI, India) substance is used to prepare the ligand solution by dissolving the substance in the required amount of distilled water and few amounts of hydrochloric acid (Qualigens, India) to maintain its strength at 0.05 mol L^{-1}, the purpose of adding hydrochloric acid to increase the solubility of ligand substance. The maintenance of ionic strength in the system is important and is done by adding 2.0 mol L^{-1} of Sodium chloride solution (Qualigens, India). To carry out the reaction in an aqua-organic medium, DMSO (Qualigens, India) is used and it does not require any further purification. The A.R grade substance of Co^{II} chloride (E-Merck, India), Ni^{II} chloride (E-Merck, India) and Cu^{II} chloride (E-Merck, India) used to prepare 0.1 mol L^{-1}concentrated solutions by dissolving in de ionized water and small amount of hydrochloric acid was added to restrain the metal ions from hydrolysis. The metal ion solutions of Co^{II} chloride, Ni^{II} chloride and Cu^{II} chloride were standardized using disodium salt of EDTA (E-Merck, India) solution by using suitable indicators through complex-metric titrations. A stock solution of sodium hydroxide having the strength of 2.0 mol L^{-1} was prepared and standardized with oxalic acid using acid-base titrations. Hydrochloric acid solution standardized using standard sodium hydroxide (Qualigens, India)solution. In order to assess the errors in the concentrations of prepared solutions, a statistical test ANOVA[20,21] is employed and also uses a computer program called COSWT.[22] The concentrations of hydrochloric acid and sodium hydroxide were calculated using Gran titration method.[23,24]

Electrometric Titration Assembly

The data in the present investigation is obtained by using a pH meter (Equiptronics: EQ 614 A), the equipment was calibrated for accurate results using potassium hydrogen phthalate and borax solutions. The glass membrane electrode is allowed to equilibrium in the DMSO-water mixture for 7-10 days to get the best results with steady readings. The equilibration of the electrode has to be continued till calculated pH values and pH meter dial readings were constant, the same procedure was done to equilibrate the electrode in all percentages of DMSO-water mixtures (0.0-60% v/v) before starting the titration in the respective percentage of the aqua-organic medium. The titrations were done in DMSO-water mixtures having various percentages. The correction factor, log F was calculated in each composition of the solution mixture using a computer program SCPHD.[25,26]

Procedure

During the investigation, in the titration the solution mixture is prepared by adding 1 mmol of hydrochloric acid, sodium chloride solution to maintain ionic strength at 0.16 mol dm^{-3}, metal ion solution, ligand solution in 1.0:2.5 to 1.0:5.0 range and the rest is filled with water. The contents of titrant are titrated against standard 0.4 mol dm^{-3} solution. The concentrations of constituents in different percentages of DMSO-water mixtures are given in Table 1.

Modeling Strategy

The chemical speciation of an element is generally studied by using experimental methods; there are some alternative methodologies ways which uses the chemical concepts in a theoretical to find the distribution of chemical species, which uses the calculation of concentrations of species in equilibrium. SCPHD computer program is used to calculate the correction factors, which are very essential obtaining the accurate results. The stability constants of metal-ligand complexes are calculated using the data obtained from pH metric titrations by using a computer program MINIQUAD75.[27,28] The refinement of binary complexes was done by fixing the protonation constant values of 5-Hydroxysalicylic acid and correction factor i.e. log F values.

RESULTS AND DISCUSSION

The different models having different types of species were obtained from the titrimetric data, among them some species were refined well and the others were rejected by the computer program MINIQUAD75. Various combinations of the models with the species were tested at one time. The same refinement process was done with varying concentrations of acid, alkali, ligand, total volume of titrant and log F. The species which are lower than ten percentages were removed from the model. An exhaustive modeling[29] method was employed to check the presence of species, various combinations of species in the models were assumed and evaluated. The computer program CEES was employed to generate various models with different combinations of species.[30]

The models were then subjected to refinement using a computer program MINIQUAD75, it is observed that the best statistical parameters were concerning increase in the percentage of species, which denotes the best-fit model, it confirms the model best fits the obtained experimental data. The best-fit model for the binary complex systems of Co^{II}, Ni^{II} and Cu^{II} with 5-SSA in DMSO-water mixtures of the present study is given in Table 2. The table contains the stability constants of the complex species, standard deviation, pH range, Number of Points (NP), U correction (Ucorr), Chi square (χ^2), skewness, kurtosis and R-factors values of the best fit model. The low standard deviation of stability constants of the complex species evident that they are accuracy and precision, the small values of Ucorr, skewness, kurtosis, standard deviation and R-factor validates the present model.

Residual Analysis

The kurtosis is a measure of tailedness of a distribution and skewness is measure of asymmetry in the data set. If the kurtosis value is three i.e. mesokurtic and skewness is zero, it means the distribution is best or ideal. For the model, if the kurtosis value is more than three it called leptokurtic and if the value is less than three it is platykurtic. The platykurtic values show the distribution curve flat and leptokurtic values gives the distribution curve with a sharp peak. The obtained kurtosis values of the present model are ranging from 2.89 to 6.35 which indicate the distribution is platykurtic as well as leptokurtic for all the metal ions with the ligand in DMSO-water mixtures. The skewness values are ranging from -0.15-0.79 for Co^{II}, -0.27-0.32 for Ni^{II} and -0.41-0.32 for Cu^{II} with 5-SSA predicts that the distribution is left skewed and right skewed. As the data proves the distribution is an ideal distribution least-squares method can be applied for the present system. It is evident that the model is sufficient as the R-factor values are low and the obtained statistical values representing the best fit model of the present system reveal the metal-ligand species in DMSO-water mixtures. The random errors and residuals are tested for ideal distribution, which was understood by the residual

Table 1: Total initial concentrations of ingredients for metal-ligand titrations in DMSO-water mixtures.

Solvent% v/v	Co^{II}		Ni^{II}		Cu^{II}		TL0/ TM0
	TM0	TL0	TM0	TL0	TM0	TL0	
		5-SSA		5-SSA		5-SSA	
		DMSO		DMSO		DMSO	
	0.0984	0.247	0.1004	0.251	0.1005	0.254	2.50
0.0	0.374	0.376	0.375	3.75		0.496	0.498
0.496	5.00		0.0984	0.252	0.1004	0.247	0.1005
0.259	2.50	10.0		0.376		0.373	
0.378	3.75			0.501		0.496	
0.507	5.00		0.0984	0.251	0.1004	0.245	0.1005
0.252	2.50	20.0		0.377		0.368	
0.374	3.75			0.503		0.493	
0.503	5.00		0.0984	0.295	0.1004	0.229	0.1005
0.295	2.50	30.0		0.443		0.343	
0.444	3.75			0.591		0.45	
0.592	5.00		0.0984	0.255	0.1004	0.248	0.1005
0.252	2.50	40.0		0.382		0.372	
0.374	3.75			0.512		0.496	
0.505	5.00		0.0984	0.245	0.1004	0.246	0.1005
0.248	2.50	50.0		0.368		0.368	
0.376	3.75			0.491		0.492	
0.499	5.00		0.0984	0.251	0.1004	0.237	0.1005
0.258	2.50	60.0		0.376		0.357	
0.377	3.75			0.501		0.478	
0.504	5.00						

Table 2: The statistical values of best-fit models of metal ions with the ligand in DMSO-Water mixtures.

% v/v DMSO	log β_{mlh} (SD)			pH-Range	NP	U_{corr}	^{2}	Skewness	Kurtosis	R-factor
	ML	MLH	ML_2							
Co^{II}										
00.0	4.03(90)	13.93(32)	7.52(96)	1.80-9.80	81	53.38	44.24	0.25	4.14	0.03885
10.0	4.11(38)	13.68(36)	7.78(18)	2.8-11.80	17	75.16	39.19	-0.15	3.90	0.0015
20.0	4.27(28)	13.59(72)	7.98(38)	2.11-9.68	73	20.39	11.01	0.24	3.89	0.2871
30.0	4.41(83)	13.84(67)	8.17(39)	2.89-10.10	86	87.18	82.09	0.79	4.12	0.2634
40.0	4.53(84)	13.53(87)	8.26(72)	3.89-10.27	45	84.33	73.23	-0.01	4.29	0.0178
50.0	4.69(72)	13.64(67)	8.39(83)	3.12-10.91	57	49.98	83.32	0.19	3.57	0.0217
60.0	4.81(16)	13.48(98)	8.50(73)	5.75-11.10	73	90.14	36.73	0.48	3.11	0.2189
Ni^{II}										
00.0	4.12(49)	13.57(32)	7.25(94)	1.90-10.10	73	30.36	16.80	0.25	3.86	0.11338
10.0	4.19(12)	13.81(69)	7.38(33)	2.10-10.10	66	72.90	63.78	-0.01	4.56	0.0126
20.0	4.38(26)	13.98(56)	7.72(72)	2.80-10.85	34	73.08	64.36	-0.27	5.13	0.0324
30.0	4.46(17)	13.84(67)	7.91(64)	4.80-10.80	85	28.97	25.72	0.11	6.15	0.0722
40.0	4.61(67)	13.67(79)	8.12(34)	4.70-10.50	74	58.08	53.26	0.03	6.35	0.0214
50.0	4.71(37)	13.74(58)	8.28(84)	4.10-11.10	77	73.47	24.26	0.32	5.48	0.0817
60.0	4.86(16)	13.49(56)	8.41(43)	4.00-11.00	64	63.40	32.89	0.06	3.19	0.0193
Cu^{II}										
00.0	4.74(91)	13.97(30)	7.70(42)	1.80-9.90	58	44.02	27.56	0.23	3.84	0.32120
10.0	4.81(23)	13.85(73)	7.91(37)	2.15-11.00	73	19.11	63.21	0.05	3.14	0.0620
20.0	5.01(63)	13.73(71)	8.14(48)	2.30-10.00	64	38.15	32.12	0.32	4.16	0.0732
30.0	5.27(43)	13.59(82)	8.29(34)	3.10-10.65	73	47.89	63.52	-0.41	2.89	0.0263
40.0	5.41(74)	13.49(63)	8.46(48)	4.00-11.10	89	83.28	32.54	0.07	6.14	0.0236
50.0	5.58(32)	13.69(23)	8.59(74)	4.20-11.00	72	92.21	53.82	0.01	3.21	0.1026
60.0	5.69(64)	13.86(67)	8.78(83)	5.00-11.20	28	73.28	57.09	-0.17	4.77	0.1729

tests such as χ^2, Skewness, Kurtosis and R-factor.[31] The statistical parameters obtained in the study gives the best fit model which represents the metal-ligand species in DMSO-water mixtures.

Effect of Systematic Errors on Best Fit Model

The reliability of the best-fit model was further tested for its accuracy by introducing some negative errors in the important parameters like concentration of acid, base, ligand, the volume of the titrants and correction factor log F. It is observed that changes in the concentration of base, acid affect on stability constants and standard deviation values. In some cases, the species were rejected by changing the base and acid concentration, which confirms the suitability of the experimental conditions under which the data was obtained. The order of parameters which influence more on stability constants by changing their concentrations is log F < volume < ligand < volume < acid < alkali. The effect of errors in the concentrations and their influence on the stability constants of Co^{II} with 5-SSA in 20% v/v DMSO-water mixtures were given in Table 3.

Effect of Solvent

The property dielectric constant is very important in solution chemistry as it one of the most important characteristics of a solvent. The characteristic of a solvent dielectric constant shows high influence stability constants. The ionization of acid changes the dielectric constant there by showing the effect on stability constants; this may be due to electrostatic or non-electrostatic forces which can be understood with Born's classical treatment.[32,33] According to Born's classical treatment stability constants should vary linearly with an increase in the dielectric constants of the solvent. It is observed that there is a linear variation in the stability constants of 5-hydroxysalicylic with dielectric constants (1/D) of the medium, which reveals that the electrostatic forces are dominating over the equilibrium. The plot of log and dielectric constant values (1/D) is represented in the below Figure 1.

Species Distribution

Distribution diagrams are obtained with the computer programs DISPLOT[34] and SCPHD. 5-hydroxysalicylic acid has three

Table 3: Effect of errors in influential parameters on Cu^{II} and 5-SSA complex stability constants in 20% v/v DMSO-water mixture.

Ingredient	% Error	Log β_{mlh}(SD)		
		110	111	120
Acid	0	5.69(64)	13.86(67)	8.78(83)
	-5	5.12(74)	12.89(48)	Rejected
	-2	4.48(48)	Rejected	8.01(58)
	+2	rejected	13.42(34)	8.96(85)
	+5	Rejected	Rejected	8.57(93)
Alkali	-5	Rejected	13.90(37)	Rejected
	-2	4.94(56)	12.37(85)	Rejected
	+2	5.78(38)	Rejected	9.01(73)
	+5	5.82(84)	12.01(19)	8.39(92)
Ligand	-5	5.48(76)	13.65(67)	8.09(47)
	-2	5.18(49)	13.19(83)	8.76(37)
	+2	5.80(57)	13.49(23)	8.69(67)
	+5	5.28(34)	14.00(37)	8.58(47)
Metal	-5	5.01(68)	13.26(45)	7.56(93)
	-2	4.09(83)	13.57(37)	7.68(83)
	+2	4.80(38)	13.07(38)	8.62(37)
	+5	4.57(43)	13.22(23)	8..68(57)
Volume	-5	5.21(81)	13.81(47)	8.37(95)
	-2	5.27(47)	13.93(23)	8.88(78)
	+2	5.73(46)	12.21(34)	8..72(34)
	+5	5.60(46)	12.69(37)	8.34(54)
Log F	-5	5.10(37)	12.99(30)	8.17(49)
	-2	4.98(23)	12.97(11)	8.98(93)
	+2	5.27(27)	13.01(19)	8.43(43)
	+5	4.68(45)	13.56(19)	8.36(73)

dissociable protons from one (–COOH) and two hydroxyl (-OH) groups. One among the three has a high protonation constant and will dissociate at a pH 12.0, this range of pH makes the glass electrode unable to detect the protonation due to its sensitivity. The existence of 5-HSA will be as LH_3at low pH and $LH_2^-$and LH^{2-} in the pH range 1.5-6.5, 1.5–11.5, and5.5-11.5, respectively. In the present study, it is revealed that the binary complexes of metal-ligand existed are in the form of ML, MLH, and ML_2 for Co^{II}, Ni^{II} and Cu^{II}.

The formation of various 5-SSA complex species is shown in the following equilibrium.

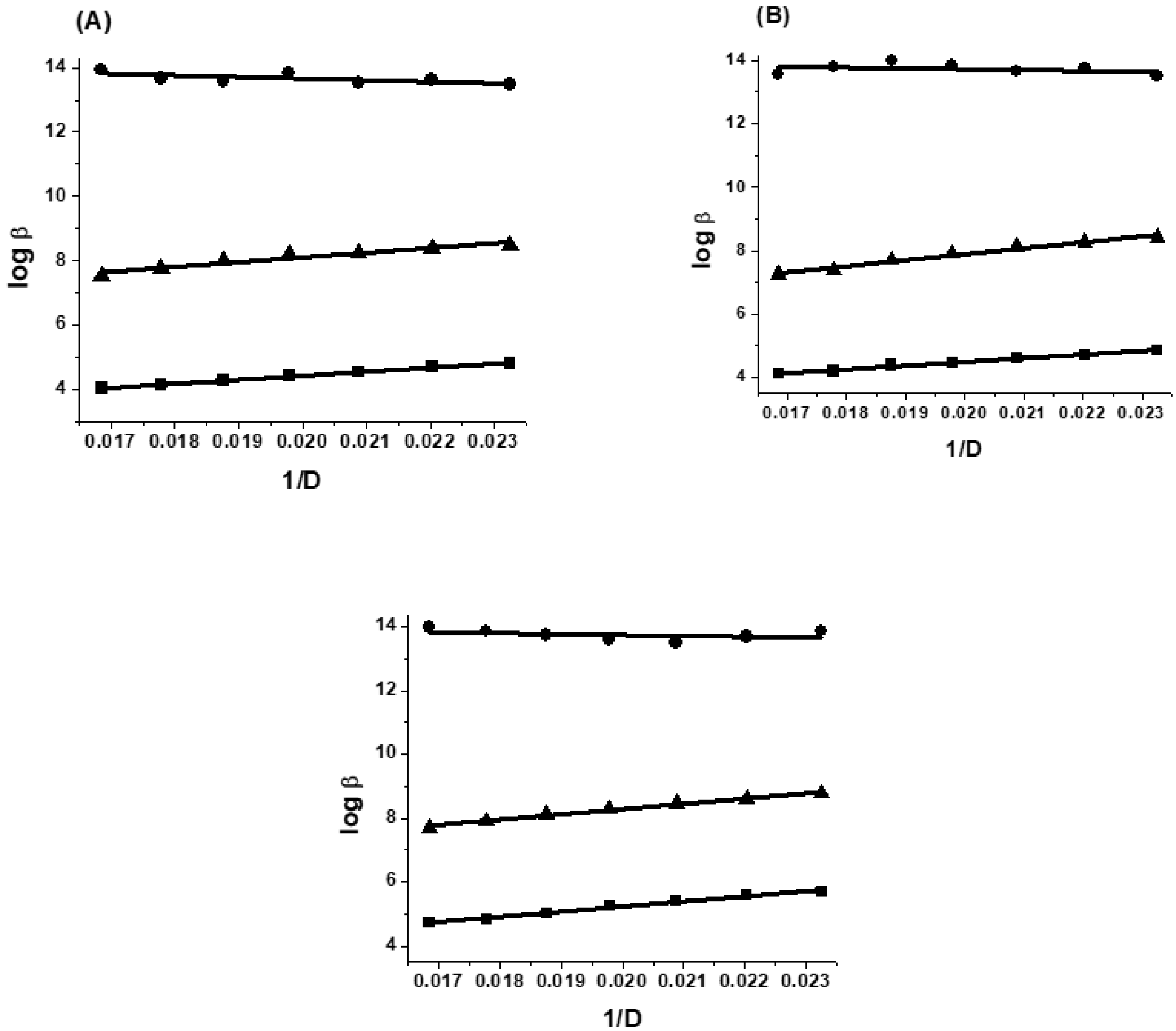

Figure 1: Effect of 1/D of DMSO-water mixtures on stability constant values of metal-5-SSA complexes. (a) Co^{II}; (b) Ni^{II}; (c) Cu^{II}; (■)log β_{ML}; (▲) log β_{MLH}; (●) log β_{ML2}.

M(II) + $3LH_3$	$\rightleftharpoons$	$ML_3H_6^-$+$3H^+$	....…………1
$ML_3H_6^-$	$\rightleftharpoons$	$ML_3H_5^{2-}$+H^+	....…………2
$ML_3H_5^{2-}$	$\rightleftharpoons$	$ML_3H_4^{3-}$+H^+	....…………3
$ML_3H_4^{3-}$	$\rightleftharpoons$	$ML_3H_3^{4-}$+H^+	....…………4
$ML_3H_3^{4-}$	$\rightleftharpoons$	$ML_3H_2^{5-}$+H^+	....…………5
$ML_3H_2^{5-}$	$\rightleftharpoons$	ML_3H^{6-}+H^+	....…………6
ML_3H^{6-}	$\rightleftharpoons$	ML_3^{7-}+H^+	....…………7
M(II) +LH_3	$\rightleftharpoons$	MLH_2^-+H^+	....…………8

MLH_2^-	$\rightleftharpoons$	$MLH^{2-} + H^+$	….…………9
MLH^{2-}	$\rightleftharpoons$	$ML^{3-} + H^+$	….………...10
$M(II) + 2LH_3$	$\rightleftharpoons$	$ML_2H_4^{2-}+2H^+$	….………...11
$ML_2H_4^{2-}$	$\rightleftharpoons$	$ML_2H_3^{3-}+H^+$	….…...……12
$ML_2H_3^{3-}$	$\rightleftharpoons$	$ML_2H_2^{4-}+H^+$	….…...……13
$ML_2H_2^{4-}$	$\rightleftharpoons$	$ML_2H^{5-}+H^+$	….…...……14
ML_2H^{5-}	$\rightleftharpoons$	$ML_2^{6-}+H^+$	….…...……15
$M(II) +2LH_2^-$	$\rightleftharpoons$	$ML_2H_2^{2-}+2H^+$	….………...16
$ML_2H_2^{2-}$	$\rightleftharpoons$	$ML_2H^{3-}+H^+$	….……..….17
ML_2H^{3-}	$\rightleftharpoons$	$ML_2^{4-}+H^+$	….……..….18
$ML_2H_2^{2-}$	$\rightleftharpoons$	$ML_2^{4-}+2H^+$	….……..….19
$M(II) + LH_2^-$	$\rightleftharpoons$	$MLH+H^+$	…..……..…20
MLH	$\rightleftharpoons$	ML^-+H^+	….……..….21
$M(II) +3LH_2^-$	$\rightleftharpoons$	$ML_3H_6^{3-}+3H^+$	….………...22
$ML_3H_6^{3-}$	$\rightleftharpoons$	$ML_3H_5^{4-}+H^+$	….……..….23
$ML_3H_5^{4-}$	$\rightleftharpoons$	$ML_3H_4^{5-}+H^+$	….……..….24
$ML_3H_4^{5-}$	$\rightleftharpoons$	$ML_3H_3^{6-}+H^+$	….……..….25
$ML_3H_3^{6-}$	$\rightleftharpoons$	$ML_3H_2^{7-}+H^+$	….……..….26
$ML_3H_2^{7-}$	$\rightleftharpoons$	$ML_3H^{8-}+H^+$	….……..….27
ML_3H^{8-}	$\rightleftharpoons$	$ML_3^{9-}+H^+$	….……..….28

The species distribution diagrams were shown in Figure 2. The study reveals that the complexes of Co^{II}, Ni^{II} and Cu^{II} are formed in between the pH 1.5-11.8.In the case of Co^{II} and 5-SSA complex, the percentage of MLH speciesare low at pH 1.5 and there is a steady increase of species up pH 9.9 [Equilibrium 20], where the species are 72%, as the pH is increasing the percentage of species decreases slowly up to 11.8 pH. There is a simultaneous formation of ML and ML_2 species, where ML possesses the highest percentage of species i.e. 40% at pH 9.9 [Equilibrium 21] and ML_2 forms highest percentage of species i.e. 79% at 11.8 pH, this is represented in Figure 2(A).

For Ni^{II} and 5-SSA complex, the percentage of MLH species are low at pH 1.4 and there is an increase of species and possess highest percentage i.e. 82% at pH 3.8, There is a simultaneous formation of ML and ML_2 species, where ML possess highest percentage of species i.e. 25% at pH 8.0 and ML_2 forms highest percentage of species i.e. 95% at 11.8 pH, this is represented in Figure 2(B).In the case of Cu^{II} and 5-SSA complex, the percentage of MLH species are low at pH 1.4 and there is an increase of species and possess highest percentage i.e. 58% at pH 3.5, There is a simultaneous formation of ML and ML_2 species, where ML possess highest percentage of species i.e. 62% at pH 9.0 and ML_2 forms highest percentage of species i.e. 95% at 11.3 pH, this is represented in Figure 2(C).

Proposed Structures of Complexes

The proposed structures of metal-ligand complexes are shown in Figure 3.

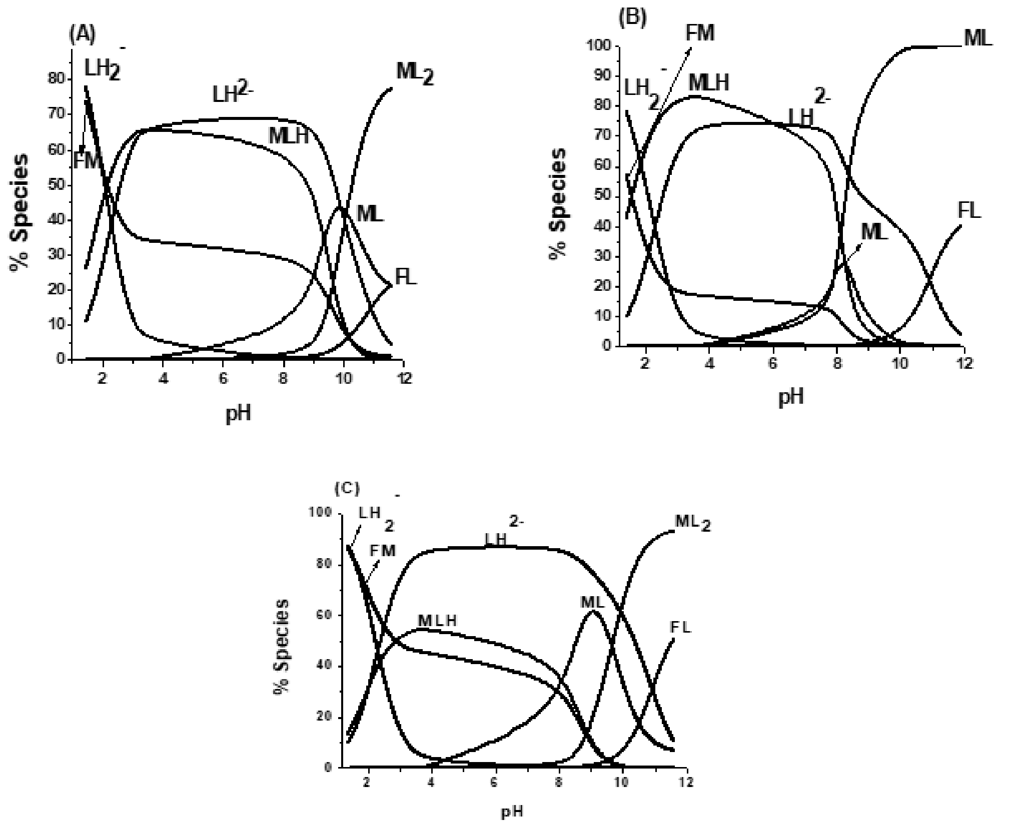

Figure 2: Species Distribution diagrams of metal-ligand complexes in 40% v/v DMSO-water mixture: (a) Co^{II} (b) Ni^{II} and (c) Cu^{II}.

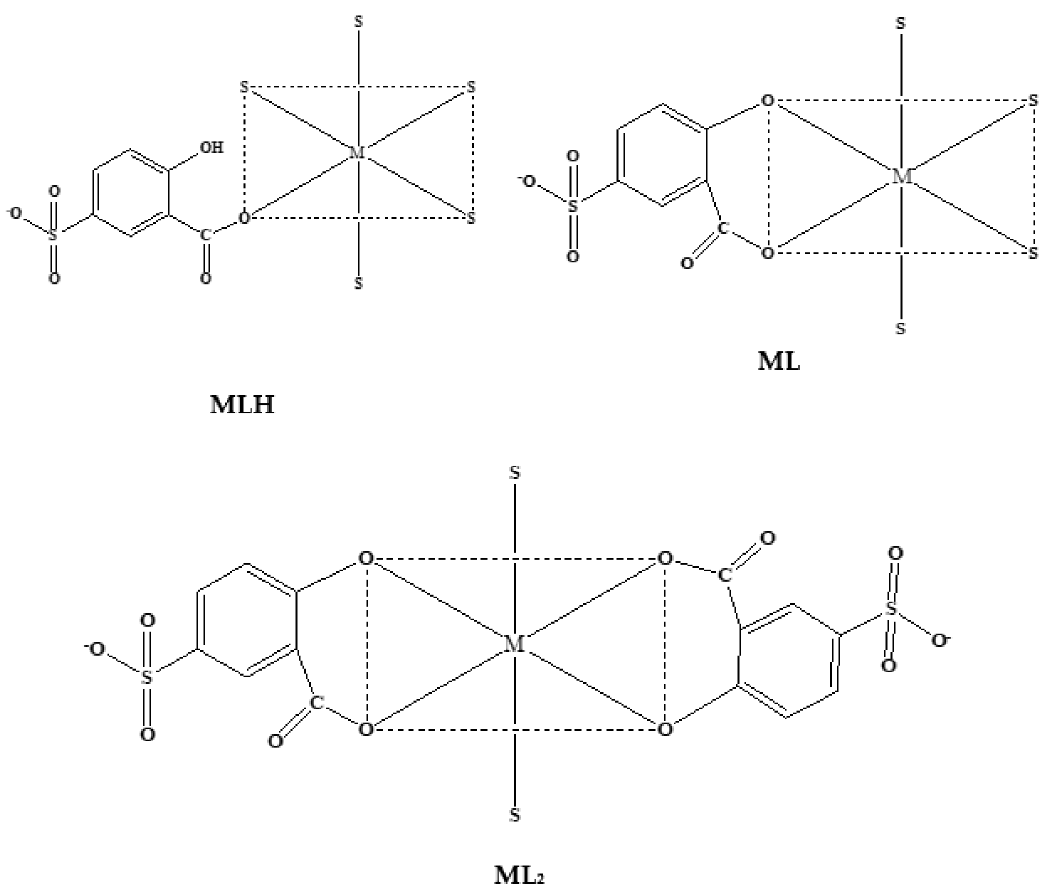

Figure 3: Proposed structures of metal-ligand complexes.

CONCLUSION

The essential metal ions Cot^{II}, Ni^{II} and Cu^{II} forms complexes in the pH range 1.5-11.8 with the ligand 5-SSA and the complexes are represented as ML_2H_2, ML_2H_3 and ML_2H_4 in the pH range 1.6-11.5. A distribution curve shows both the trends platykurtic and leptokurtic pattern, this is by the obtained kurtosis values. Both the left-skewed and right-skewed pattern of distribution curves are observed, this concerns the skewness values. The adequacy and best fit of the model are confirmed with the obtained statistical parameters such as lower standard deviation and R-factor values. The effect of dielectric constants of the medium on the stability constants of metal-ligand complexes shows a linear trend, which indicates the dominance of electrostatic forces. It is found that the stability constants are majorly influenced by a few parameters when some changes are made in their concentrations. The order of effect of influential parameters are as log F < volume of titrants< concentration of metal ion solution < concentration of ligand < concentration of acid < concentration of alkali.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

5-SSA: 5-Sulfosalicylic acid; **MLH:** Metal Ligand Hydrogen; **Co^{II}:** Co^{II} chloride; **Ni^{II}:** Ni^{II} chloride; **Cu^{II}:** Cu^{II} chloride; **EDTA:** Ethylene Diamine Tetra Acetic acid; **HCl:** Hydro Chloric acid; **DMSO:** Dimethyl Sulfoxide.

SUMMARY

Chemical Speciation/Speciation analysis is a vital study to determine the concentrations of an individual metal ion and its molecular forms in human biology and toxicology, as the changes or variations in their concentrations and forms lead to toxicity and biological disorders. In the present study the author has studied the chemical speciation of Co^{II}, Ni^{II} and Cu^{II} with 5-SSA as the above mentioned metal ions plays crucial role in metabolism and changes in their concentrations leads to metabolic disorders. DMSO is selected in these studies to maintain the dielectric properties of the medium at comparable levels to those of the physiological fluids. The present study provides wide knowledge on type of complexes formed, the stability of complexes, and effect of acid, base, and metal and ligand concentrations on stability constants. The pH meter is used for titrations and SCPHD and MINIQUAD 75 software's are used to obtain the statistical data in order to understand the metal-ligand complex behavior. The behavior of the drug with metal ions can be easily understandable with the obtained results. The species refined and their relative concentrations under the present experimental conditions represent the possible forms of metal ions in the biological fluids. Further, computer augmented modeling studies were carried out to arrive at the best fit chemical models and to check their validity.

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