Chemistry and Materials Research
ISSN 2224- 3224 (Print) ISSN 2225- 0956 (Online)
Vol.7 No.5, 2015

Chemical Speciation Study of Ternary Complexes of Cu (II) with Succinic Acid Dihydrazide and Some Amino Acids in Aqueous Solution

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Abstract
Solution equilibrium studies on the systems of Cu (II) with succinic acid dihydrazide (SADH) as a primary ligand (L) and selected amino acids (X) as secondary ligand were investigated with a potentiometric titration technique. The formation constants of the complexes were determined at 30 ± 1°C and ionic strength 0.1 mol dm $^{-3}$ NaCl. The formation constants determined, suggests the formation of mixed ligand complexes. The relative stabilities of the ternary complexes are compared with those of the corresponding binary complexes in terms of ΔlogK values. The stability constants were calculated by using MINIQUAD 75 computer program, and species distribution diagrams were produced using the HYSS computer program. Selection of the best fit chemical models was based on statistical parameters. Distribution diagram and plausible equilibria for the formation of the complex species are presented.
Keywords: stability constant, ternary complex, best fit model, Δlog K

1. INTRODUCTION

The study of mixed ligand complexes has received a considerable attention due to their ability as metal systems for metal–protein complexes such as metallo-enzymes. Metal ions are known to support most of the physiological activities regarding nucleic acid interactions through the formation of ternary (mixed-ligand) complexes.[1-5]Copper is important in a large number of different biological processes. Copper enzymes distributed within the body function, as oxygen and electron transport[6], catalysis in redox reaction[7], protection of cell against damaging oxygen radicals[8] (superoxide dismutase [9,10]) etc.

Dihydrazides and their derivatives are found to act as ditopic ligands that can accommodate two metal ions in different coordination pockets of the same ligand to form bimetallic complexes. The presence of two coordinating sites separated by a flexible bridging part of the ligand may lead to supramolecular structure such as double helices. The selectivity and specificity achieved by nature in biological systems is certainly due to the formation of such complexes. Hydrazides display antimicrobial, antifungal, antibacterial and anti-tubercular properties[11-14], based on their tendency to form metal chelates with transition metal ions.

The study focused on the interaction of copper with the dihydrazide of succinic and typical biomolecules-amino acids help to understand the way enzymes function and give insight into the molecular mechanism of actions of metal ion complexes of SADH and its derivatives as drugs. Furthermore, the information that we get through investigation of the structure of model ternary complexes helps to understand how biological systems achieve their specificity and stability. A survey of the literature reveals that works reported on the ternary complexes of Cu (II) with succinic acid dihydrazide and amino acid containing different functional groups was scanty. Therefore, we developed an interest to conduct investigations of binary and ternary complexes of copper (II) with the ligand succinic acid dihydrazide (SADH) as primary ligand and amino acids-histidine and alanine as secondary ligands. The objective of this work is to determine the formation constant values of the different binary and ternary complexes that are liable to form in such systems.

2. EXPERIMENTAL

2.1 Material and Solution

Succinic acid dihydrazide SADH (Fluka) was recrystallized twice from the water, dried at 100^0 C and a~0. 05 mole dm^{-3} solutions were prepared in 0.1 mol dm $^{-3}$ HCl freshly just before the titrations in aqueous. Cu (II) metal ion (Merck) was used in the form of chloride without further purification and its solution was prepared in doubly distilled water, slightly acidified to repress metal ion hydrolysis[15]. It was titrated for its metal content using complexometric[16, 17] titration. The acid content of the metal solution was determined by titration with 0.1 mol.dm^{-3} NaOH solution after liberation of the H^+ ions by cation exchange[18]. Histidine and L-alanine (Merck, proanalysi) were recrystallized from 1:1 ethanol-water mixtures and dried in vacuum. A~ 0.1 mole.dm^{-3} solutions of the ligands were prepared for use in pH-metric titrations. A ~0.2 mol.dm^{-3} solution of sodium hydroxide (E.Merck proanalysi) was prepared in double distilled/ deionized water and was standardized against

potassium hydrogen phthalate (Merck). It was then preserved under nitrogen atmosphere and regularly Gran-titrated to check the absence of carbonates[19, 20]. Solution of ~0.2 mol-dm^{-3} hydrochloric acid, prepared by successive dilutions (E. Merck proanalysi) was standardized against sodium hydroxide solution. All potentiometric titrations were carried out in aqueous medium at an ionic strength of 0.1 mol.dm^{-3} using NaCl (B.D.H. AnalaR) as the background electrolyte.

2.2 pH-potentiometric Measurements

2.2.1 Apparatus

The pH-metric titrations were carried out with a Control Dynamics pH meter model APX 175 E/C in conjunction with a 0-14 pH range combined glass and calomel electrode. The electrode system was standardized in terms of hydrogen ion concentration in aqueous solution. The correction factor to convert the pH meter dial reading into logarithm of reciprocal of hydrogen ion concentration was calculated before each set of experimental titrations by performing an acid base titration at the chosen ionic strength and analyzing the data by Gran method[19, 20] and ACBA[21] computer program.

A tip less double walled Pyrex glass vessel of 100 ml capacity fitted with a Perspex lid, through which the glass calomel electrode, gas inlet and out let tubes and burette tip were admitted, was used for carrying out the potentiometric titrations. The temperature of the solution was maintained by passing thermostatted water through the annular space between the walls of the titration cell. The experimental solution was earthed by means of a platinum wire sealed in a glass tube. In order to prevent the introduction of an earth loop, the pH meter, thermostat and magnetic stirrer were earthed to the same terminal. Purified nitrogen gas was passed through the experimental solution both before and during titration to expel carbon dioxide.

2.2.2 Titration Procedure

Calvin-Wilson titration technique as used by Rossotti[22, 23] was employed for the study of protonation, binary and ternary complex equilibria of the ligands. Requisite volume of hydrochloric acid (to give an overall concentration of 2.0×10^{-2} mole.dm^{-3}), sodium chloride (ionic strength was maintained at 0.1 mole.dm^{-3}), primary ligand (SADH), and secondary ligands (amino acids) solution, in the presence and absence of metal ion in a total volume of 50.0 cm^3 was titrated with ~0.2 mole.dm^{-3} sodium hydroxide at 30.0 ± 0.1°C. The protonation and binary system of the dihydrazide and amino acids was determined under the same experimental conditions for ternary. The concentration of the ligands was 0.004 to 0.015 mol.dm^{-3} in different experiments. Titrations were carried out at 1:1:1, 1:1:2, 2:1:1 and 2:1:2 M: L: X (M= Cu (II) metal ion, L= succinic acid dihydrazide and X= amino acid) ratios of initial concentrations of metal to primary and secondary ligands. After addition of each aliquot (0.1 ml) of sodium hydroxide, the pH-meter dial reading was recorded at regular intervals of time until two successive readings do not differ in more than 0.01 pH units. The titrations were carried out up to a pH of ~12.0. In some of the titrations, the upper pH limit of rejecting data was determined by the appearance of opalescence leading to precipitation indicated by a downward drift of the pH meter dial readings.

2.2.3 Data Analysis

For a system containing one metal ion and one primary and one secondary ligands forming N complexes, the formation of a complex can be represented as,

$$mM+lL+xX+hH \Leftrightarrow MmL_lX_xH_h$$

and the overall stability constant is given by,

$$\beta = [MmL_lX_xH_h]/[M]^m.[L]^l.[X]^x.[H]^h$$

Where, [M], [L], [X] and [H] are the free concentrations of metal, primary ligand, secondary ligand and hydrogen ion respectively at any experimental point. Different species in solution possess different values of stoichiometric coefficients *m, l, x* and *h*. The potentiometric titration data obtained in the present investigation was subjected to analysis by Miniquad-75 program[24]. The stoichiometry and stability constants of the species formed in solution were determined by examining various chemically possible composition models for the systems studied. The best-fit models were selected on the basis of U (sum of the squares of residuals in mass balance equations), standard deviations in formation constants and other statistics like χ^2 test which tests the distribution of errors against a normal one. Species distribution diagrams for all the systems under study were generated using HYSS[25]program. The data from different experiments with different metal to ligand ratios were refined separately using Miniquad-75 program, to yield species relevant to that particular composition. This method has been found to be superior[26]compared to the analysis of the entire data from all the titrations at a time, as the main part of the error in the stability constants derives from the variability from one titration to another. Therefore, the authors processed the data from the different compositions separately using Miniquad-75 program.

3. RESULTS AND DISCUSSION

3.1 protonation and binary metal ligand equilibria of the ligands

To understand the various interactions that exist in a solution containing a metal ion and several ligands,

knowledge on the distribution of various protonated and binary species of the ligands is an essential prerequisite. Therefore, as a prelude to the determination of formation constants of mixed -ligand complexes, the protonation equilibria and metal-ligand systems of succinic acid dihydrazide (SADH), α-alanine and L-histidine under the present experimental conditions has been studied. The results of analysis are presented in Table 1.

Table 1 Formation constants (**Log β_{mlh}**)[a] of proton ligand and binary Cu (II) complexes with SADH, L-histidine and alanine in aqueous solution, ionic strength, I = 0.1 mol dm^{-3} (NaCl) at 30 ± 1°C.

System	m	l	h^a	$log\beta_{mlh}{}^b$	S^c
SADH	0	1	1	03.59(1)	1.527 X 10^{-8}
	0	1	2	06.16 (1)	
	0	1	-1	-11.89 (2)	
	1	1	1	08.22 (8)	4.288X 10^{-8}
	1	1	0	05.72 (6)	
	1	1	-1	-5.35 (9)	
	1	2	2	16.66 (8)	8.190X 10^{-8}
	1	2	1	14.06 (5)	
	2	1	0	08.06(0)	2.195 X 10^{-8}
	2	1	-2	-1.61(5)	
Histidine	0	1	1	08.97	4.000 X 10^{-8}
	0	1	2	15.03	
	0	1	3	16.76	
	1	1	1	13.70(4)	9.721X 10^{-8}
	1	1	0	09.98 (2)	
	1	2	2	28.44(2)	1.337 X 10^{-9}
	1	2	1	24.03(2)	
	1	2	0	18.14(2)	
Alanine	0	1	1	09.65	1.272 X 10^{-8}
	0	1	2	11.98	
	1	1	1	12.04 (2)	4.856X 10^{-8}
	1	1	0	08.48 (2)	
	1	2	2	24.55 (4)	8.456X 10^{-8}
	1	2	1	20.88 (7)	
	1	2	0	16.05 (10)	

[a] m, l and h are the stoichiometric coefficient corresponding to Cu(II), SADH or amino acids and H^+, respectively.
[b] Standard deviations are given in parentheses in least significant figures.
[c] Sum of square of residuals.

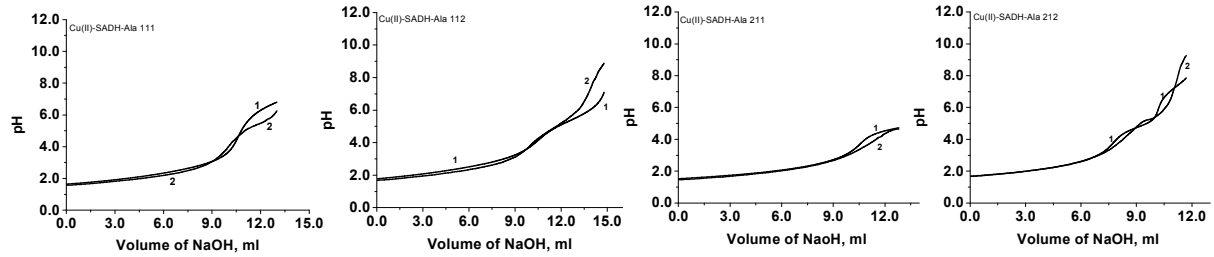
The best-fit model of the SADH contains three protonation constants β_{011}, β_{012} and β_{01-1} corresponding to the protonation (LH^+, LH_2^{2+} and LH_{-1}) at the two terminal NH_2 groups and one of the enolic form. In high alkaline conditions hydrazides are known to lose a proton[27] from the enolic form as a result LH_{-1} is formed. Although SADH contains two such groups, the formation of LH_{-2} species was not observed as its equilibrium may lie well above the pH range of study. However, in the presence of a metal ion the ligand may also lose the second enolic proton forming both deprotonated $M_m L_l H_{-1}$ and $M_m L_l H_{-2}$, type of species.[28]

The best-fit models for Cu (II) ion- SADH systems (Table 1) indicate the formation of ML, MLH, ML_2H, ML_2H_2, MLH_{-1}, M_2L, and M_2LH_{-2} species. The species M_2L, and M_2LH_{-2} contain two metal ions bonded to different hydrazide groups of the same molecule. In the case of α-alanine the species MXH and MX_2H_2 contain the neutral, mono-dentate zwitter ion form of the ligand bonding through the carboxyl oxygen, whereas in the species MX and MX_2 the bidentate form of the ligand is involved in bonding. In the case of L-histidine for the species MXH, it is bonded to the metal through α-amino or imidazole and carboxyl oxygen acting as a bidentate ligand and this has been supported by different structural studies.[29-35] In the species MX_2H_2, histidine acts as a monodentate while the imidazole group is deprotonated and non-bonding, while for the species MX and MX_2 the tridentate form of the ligand is participating in which it binds through imidazole, carboxyl and amino groups. The step wise protonation constant value of MX_2 ($\Delta\log\beta$= Log β_{121}- Log β_{120}=5.89) for the formation of MX_2H is close to the protonation constant of imidazole (i.e., 6.06). This indicates that the imidazole-N is either not participating in coordination or weakly interacting with Cu^{2+} which is already bound to carboxylate group.

3.2 Metal-ligand stability constants of the ternary complexes

The formation constants of simple mono-nuclear complexes like ML, MX, ML_2, MX_2 etc., of Cu (II) -ligands were determined by analysising the data obtained for mixed-ligand equilibria with the help of classical procedures[19]. Simulated titration curves were then generated using computer program SOPHD[36] developed in our laboratory to see whether these species satisfy the experimental data. The simulated titration curves thus obtained were plotted along with the experimental ones and the curves for Cu (II) -SADH- Amino acid system for all the compositions are shown in Fig.1. The wide difference between the simulated and experimental curves reveals the presence of other mixed major species in addition to simple mono-nuclear complexes.

Different chemical models containing chemically plausible species depending on the nature of the ligands, metal and the pH region of difference in the curves were tested for ternary system using Miniquad-75 program. The required initial estimates of the formation constants were calculated basing on the formation constants of simple complexes and protonation/ deprotonation constants of the ligand.



(a)

(b)

Figure 1. Simulated and experimental titration curves for (a) Cu(II)-SADH-Ala and (b) Cu(II)-SADH-His systems for 1:1:1, 1:1:2, 2:1:1 and 2:1:2 compositions. (1.Simulated titration curve 2. Experimental titration curve)

Table 2 Formation constants (**Log β_{mlxh}**)[a] of ternary complexes of Cu (II) 1:1:1, 1:1:2, 2:1:1and 2:1:2 ratio with SADH and amino acids- L-histidine and alanine in aqueous solution, ionic strength, I = 0.1 mol dm^{-3} (NaCl) at 30 ± 1°C.

System	Concentration ratio M:L:X:H				$log\beta_{mlh}$[b]	S^c	$\Delta logK$
	m	l	x	h^a			
Histidine	1	1	1	3	26.13 (9)	2.588X10^{-8}	-
	1	1	1	2	23.82 (7)		1.90
	1	1	1	1	19.81 (8)		0.39
	1	1	1	0	15.56 (7)		-0.14
	1	1	1	-1	08.09(12)		
	1	1	2	5	42.52 (8)	3.411X10^{-9}	-
	1	1	2	4	40.35 (6)		-
	1	1	2	3	36.52 (7)		-0.14
	1	1	2	2	32.79 (6)		-1.37
	1	1	2	1	27.37 (6)		-2.37
	1	1	2	0	21.09(6)		-2.77
	2	1	1	2	27.61 (8)	3.730X10^{-8}	-
	2	1	1	1	24.29 (8)		2.53
	2	1	1	0	20.41 (9)		2.37
	2	1	1	-1	15.09 (10)		-
	2	1	2	4	44.50 (3)	6.018X10^{-9}	-
	2	1	2	2	37.64 (4)		1.14
	2	1	2	1	33.63 (3)		1.55
	2	1	2	0	29.00 (4)		2.80
Alanine	1	1	1	2	21.94 (4)	7.568X10^{-9}	1.68
	1	1	1	1	19.26 (3)		1.50
	1	1	1	0	14.28 (4)		0.08
	1	1	1	-1	07.53 (3)		-
	1	1	2	3	31.84 (2)	6.256X 10^{-8}	-0.93
	1	1	2	2	29.08 (1)		-1.19
	1	1	2	1	24.30 (3)		-2.30
	1	1	2	0	17.60 (4)		-4.17
	2	1	1	1	19.18 (1)	5.219X10^{-8}	-0.17
	2	1	1	0	14.92 (2)		-0.91
	2	1	1	-1	09.39 (6)		-
	2	1	2	2	31.82 (4)	9.786X10^{-8}	-0.79
	2	1	2	1	27.76 (7)		-1.18
	2	1	2	0	22.67 (7)		-1.44
	2	1	2	-1	16.89 (8)		-

[a] m, l, x and h are the stoichiometric coefficient corresponding to Cu(II), SADH, amino acids and H^+, respectively.
[b] Standard deviations are given in parentheses in least significant figures.
[c] Sum of square of residuals.

The titration data of the ternary complexes with SADH and amino acids for different ratio fit satisfactorily with formation of different species and the best-fit models obtained for all the compositions are shown in Table 2. For 1:1:1 and 1:1:2 compositions the species converged include protonated MLXH, $MLXH_2$, $MLXH_3$, MLX_2H, MLX_2H_2, MLX_2H_3, MLX_2H_4, MLX_2H_5 and deprotonated $MLXH_{-1}$, in addition to simple MLX and MLX_2 type of complexes. In the case of 2:1:1 and 2:1:2 compositions, formation of homo-binuclear ternary species M_2LX, M_2LXH, M_2LXH_2, M_2LXH_{-1}, M_2LX_2, M_2LX_2H, $M_2LX_2H_2$, $M_2LX_2H_4$, and $M_2LX_2H_{-1}$ were observed. Charges on the species are omitted for brevity.

In both the systems [Cu (II)-SADH-alanine and Cu (II)-SADH-Histidine] for 1:1:1 and 1:1:2 compositions in protonated species most probably, one of the hydrazide groups of SADH (L) is involved in bonding as a bidentate[37, 38] bonding through carbonyl oxygen and terminal nitrogen while the other hydrazide group remains protonated at the terminal nitrogen. With increase in pH, the protonated species lose proton on the non-bonding side of SADH and forms the unprotonated MLX and MLX_2 species and the deprotonated $MLXH_{-1}$. In the unprotonated species MLX_2 and MLX, and protonated MLXH, SADH participates in its neutral form. In the case of 2:1:1 and 2:1:2 metal to ligand concentration ratios, all the Cu (II) -SADH species exhibit the

formation of homo binuclear complexes, in which SADH acts as a ditopic ligand and is attached to two metal ions (Fig. 4) either in neutral or deprotonated enolic form.

In the protonated ternary species $MLXH_2$, MLX_2H_3, M_2LXH and $M_2LX_2H_2$ of Cu (II)-SADH-alanine system, α-alanine is involved in its mono-dentate zwitter ion bonding through the carboxylate group as seen from the stepwise deprotonation constants that is included in Table 2. For the species MLXH, MLX, $MLXH_{-1}$, MLX_2H, MLX_2, M_2LX, M_2LXH_{-1}, M_2LX_2 and $M_2LX_2H_{-1}$ alanine acts as a bidentate ligand, while for the protonated species MLX_2H_2 and M_2LX_2H it binds in mixed form, i.e., one of the molecule acts as mono dentate and the other as bidentate as indicated in Fig. 5.

This can be ascertained from the step-wise deprotonation constants given in **Table 3**. The values clearly indicates that the step-wise formation constants, for the formation of MLX_2H_2 from MLX_2H and for the formation of MLX_2H from MLX_2 are 4.78 and 6.70 indicating the release of α-ammonium proton of alanine on complexation, while the step-wise dissociation constant of MLX_2H_3 to form MLX_2H_2 is 2.82 (Table 3) which is less than or equal to the protonation constant (3.60) of SADH (L). This clearly shows that one proton in MLX_2H_3 type of species is attached to dihydrazide [M. (LH). $(XH)_2$]. In the case of 2:1:1 ratio alanine is bonded to one of the metal ions as a monodentate (in M_2LXH) bonding through carboxylate oxygen and as a bidentate in M_2LX type of species bonding through both carboxylate oxygen and α-amino nitrogen. The step-wise formation constants for the protonation of M_2LX to form M_2LXH is 4.26. This clearly shows that the deprotonation is of the α-ammonium group on complexation to the metal ion. The formation of a M_2LXH_{-1} type of species may be due to the deprotonation of enolic forms of the two hydrazide groups or hydroxylation.
For 2:1:2 concentration composition, in the symmetric $M_2LX_2H_2$ type of species, succinic acid dihydrazide binds to metal ions on either side as a bis bidentate bonding through carboxyl and terminal amino groups. Two molecules of α-alanine (XH) also participate in complexation as monodentates bonding through carboxylate groups. The α-amino groups of alanine are protonated and non-binding. With the increase in pH this species deprotonates to M_2LX_2H and M_2LX_2 on complexation through amino groups.

Table 3 Step-wise protonation constants of MLX_2H_3 type of species of Metal ion-SADH-alanine systems

Metal ion	**$\log \beta_{1123} - \log \beta_{1122}$**	**$\log \beta_{1122} - \log \beta_{1121}$**	**$\log \beta_{1121} - \log \beta_{1120}$**
Cu^{2+}	2.82	4.78	6.70

L-histidine is potentially a tridentate ligand and bonds to metals in different forms- histamine like, glycine like and imidazole propionic acid-like[39-46]. With this premise in Cu (II)-SADH-histidine system, in the species MLXH, MLX, MLX_2H, MLX_2, M_2LX, M_2LX_2H and M_2LX_2

M_2LXH_{-1} and MLX_2H_2 histidine coordinates as mixed tri and bidentate form in which one molecule acts as tridentate and the other as bidentate and involved in bonding probably through all its binding centers- imidazole, carboxylate and amino groups[47]. In the species $MLXH_2$, $M_2LX_2H_2$ and M_2LXH, histidine coordinates as a bidentate ligand may be through the amine nitrogen and carboxylate oxygen groups and the side chain remain protonated. In the case of species MLX_2H_5, $M_2LX_2H_4$ and M_2LXH_2 histidine acts as a mono dentate ligand and binds through the carboxylate oxygen. In the species MLX_2H_4 mixed mono and bidentate form of histidine is participating in the bonding. This can be ascertained from the step-wise deprotonation constants given in Table 4.

The species distribution diagram of complex species existing in the solution as a function of pH was obtained by means of the HySS computer program. In the case of Cu (II)-SADH-alanine system the species distribution diagram for all compositions is shown in Fig. 2. The formation of protonated complexes starts at very low pH and are prevailing below pH 3.5, except in 1:1:2 compositions, the species MLX_2H reaches maximum concentration (78.42%) at pH 5.75. On increase in pH the concentration of the species MLXH, MLX_2H_2, MLX_2H_3, M_2LXH, $M_2LX_2H_2$and M_2LX_2H increase and become dominant below pH 4 reaching maximum content relative to metal of 77.7%, 74.21%, 54.42%, 71.84%, 83.16% and 58.42% at pH 3.8, 3.8, 2.2, 3.2, 2.8 and 4.5 respectively. On further increase of pH the protonated species consumed and changed to the simple ternary complexes MLX, M_2LX, MLX_2 and M_2LX_2 which has already started to appear at low pH and attains maximum concentration of 80.72%, 62.89%, 99.7% and 50.79% at pH 5.9,4.9,9.2, and 5.5 respectively. Beyond this point the deprotonated complexes M_2LXH_{-2}, $M_2LX_2H_{-2}$ and $M_2LX_2H_{-1}$ are prevalent in the system.

Table 4 Step-wise deprotonation constants of $MLXH_3$ type of species of Metal ion-SADH-histidine systems

Metal ion	**(a)**	**(b)**	**(c)** $\log K^{1111}_{1110} = \log\beta_{1111} - \log\beta_{1110}$
Cu^{2+}	2.31	4.04	4.25

The concentration distribution curves for the Cu (II) -SADH-Histidine system at 1:1:1, 1:1:2, 2:1:1 and 2:1:2 molar ratios are presented in Fig. 6. For all the ratios the protonated species exists in acid solution and complex formation starts around pH ~ 1.8 except for the species MLX_2H which is formed in neutral region and reaches concentration maxima (~71.58%) around pH 6.0.

For homo-binuclear complexes M (II) -SADH-histidine system the protonated as well as the unprotonated complexes occur below pH 4.6 which is relatively acidic. With an increase in pH, the percentage of $M_2LX_2H_4$ increases sharply and attains its maximum around pH 2.5 (91.32%) and drops suddenly a narrow pH range. A further increase in pH is accompanied by a decrease in $M_2LX_2H_4$ complex concentration and an increase of $M_2LX_2H_2$ (52.11% at pH 3.7) complex concentration. The SADH unprotonated ternary complex, M_2LX_2, appears as the major Cu (II) containing species at pH > 4 and reaches maximum at about pH 7.1 (99.5%). This investigation evinces that in the physiological pH region the unprotonated form of the mixtures is the predominant species.

The relative stability of ternary complexes compared to that of the corresponding binary systems, can be quantitatively expressed in different ways. Among the most suitable comparison is in terms of $\Delta\log K$.[48, 49] *ΔlogK*, represents the difference between the stability of the ternary and the two correspondent binary complexes; it shows the tendency of the formation of ternary species.

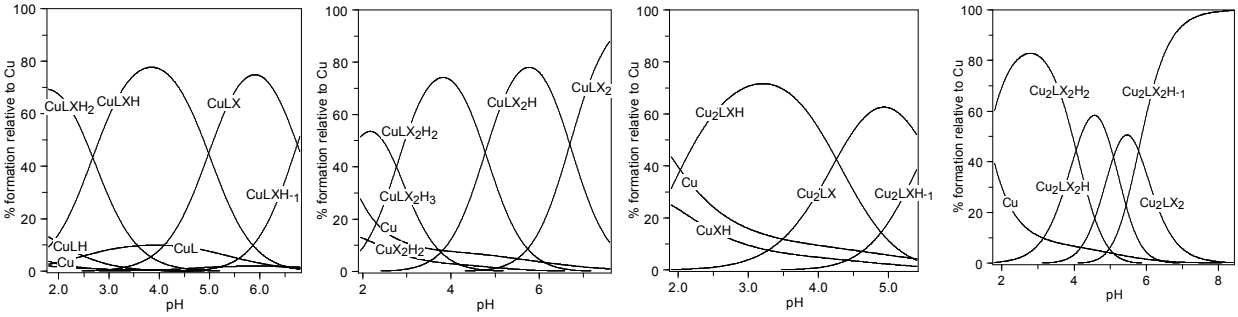


Figure 2. Distribution diagrams of Cu(II):SADH: Alanine 1:1:1, 1:1:2, 2:1:1 and 2:1:2, system in aqueous medium at 30 ± 1°C and ionic strength, I = 0.1 mol dm^{-3} (NaCl) as a function of pH (L=SADH and X= alanine).

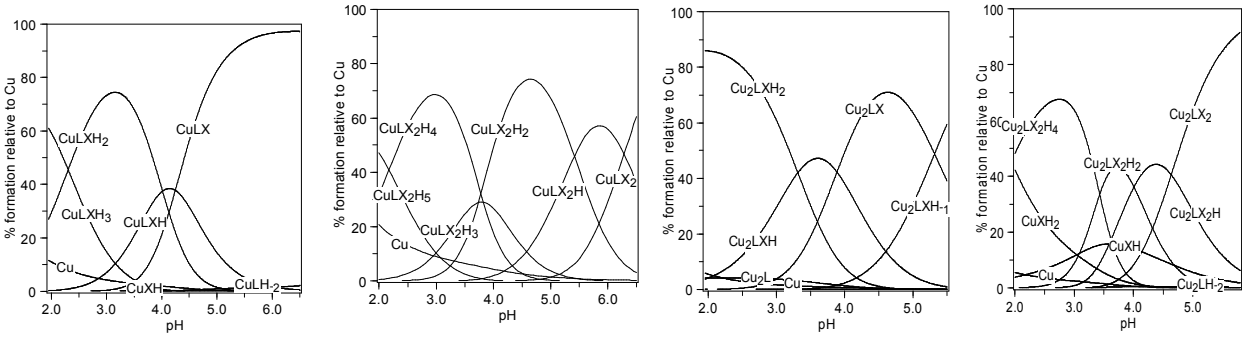


Figure 3. Distribution diagrams of Cu(II):SADH: histidine system 1:1:1, 1:1:2, 2:1:1 and 2:1:2, in aqueous medium at 30 ± 1°C and ionic strength, I = 0.1 mol dm^{-3} (NaCl) as a function of pH (L=SADH and X= histdine). Considering the formation of the ternary system in stepwise mechanism, the *ΔlogK* procedure is derived as:

$$M + X \rightleftharpoons MX \qquad K^{M}_{MX} = \frac{[MX]}{[M][X]} \qquad \text{……..} \text{…….(6)}$$

$$ML + X \rightleftharpoons MLX \qquad K^{ML}_{MLX} = \frac{[MLX]}{ML[X]} \qquad \text{……(7)}$$

$$\Delta logK = K_{MLX}^{ML} - K_{MX}^{M} \quad \text{.....(8)}$$
$$= K_{MLX}^{MX} - K_{ML}^{M} \quad \text{.....(9)}$$

or

$$\Delta logK = log\beta_{MLX} - (log\beta_{ML} - log\beta_{MX}) \quad \text{.....(10)}$$

or generalizing for any mixed-ligand complex $ML_lX_xH_h$

$$\Delta logK = log\beta_{ML_lX_X} - \left(log\beta_{ML_l} + log\beta_{MX_x}\right) \quad \text{.....(11)}$$

According to Sigel, when Δlog*K* values are positive the ternary complexes are more stable than the corresponding binary complexes, while if the values for Δlog*K* are negative, the reverse is true. However, the negative values of Δlog*K* do not preclude the formation of ternary complexes in solution.

The values of Δlog*K* were calculated and are included in Table 2. For the Cu (II) -SADH-histidine 1:1:1 ratio system, the value of ΔlogK is negative for simple complex (MLX) and positive for the protonated (MLXH and $MLXH_2$) complexes. For 1:1:2 ratio system Δlog*K* is negative for all the species of the system invariably. In the case of homo-binuclear complexes (2:1:1 and 2:1:2 ratio) for all complexes the values are exclusively positive. This indicates that in the case of 1:1:1 and 1:1:2 systems, more coordination positions are available in histidine than SADH and Cu (II) forms more stable complexes with L-histidine than SADH ligand and binary complexes are more stable than the ternary complexes. Thus, the secondary ligand histidine is expected to bind the Cu (II) -SADH complex with a smaller formation constant than that with the aquated metal ion. The negative value or low stability of the ternary complex compared to binary may also show either higher stability of the binary complexes and/or reduced number of coordination sites in the primary ligand or it may indicate that no interaction occurs between the ligands in the ternary complexes. However, this deed does not mean that the complex is not formed in the system. Because, other contributing factors, electronic[50,51] and structural factors such as steric hindrance [52-55], difference in bond type, and geometrical structure are also expected to operate in the system and have an effect on negative Δlog*K* values observed. In the case of the binuclear (2:1:1 and 2:1:2) Cu (II) -SADH-Histidine systems the observed result reveals that Cu (II) forms more stable ternary complexes compared to the binary complexes. As it can be inferred from the values, the formation of mixed – ligand complex is favored as a result of interaction of ML with X or MX with L.

For the Cu (II)-SADH-alanine system, Δlog*K* is exclusively negative for all the complexes of 1:1:2, 2:1:1 and 2:1:2 ratio systems, while for 1:1:1 ratio system it is invariably positive for all the species. This result reveals that the ternary complexes are relatively less stable than the corresponding binary complexes for most of alanine system. This indicates that histidine prefer to form the ternary complexes of the type M_2LXH and M_2LX_2H rather than the binary complexes MX or ML; while alanine more preferably forms the binary complexes under this study.

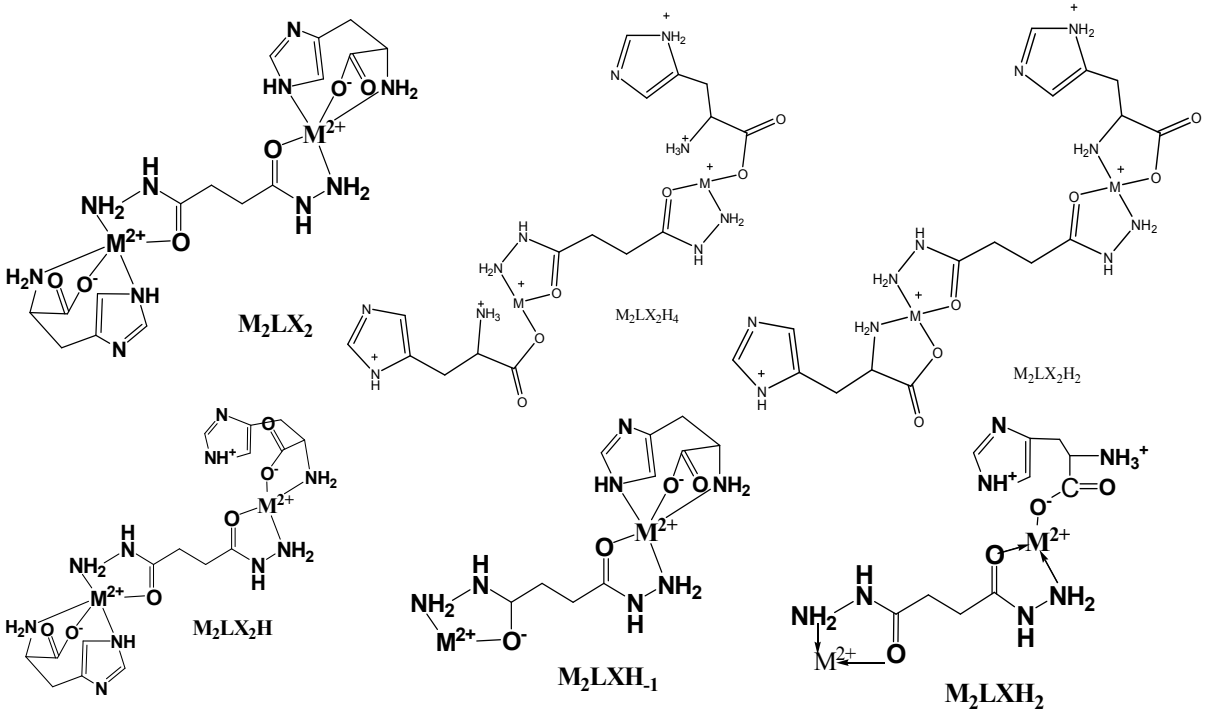


Figure 4: Proposed structures for homo-binuclear species of Cu (II)-SADH-Histidine system

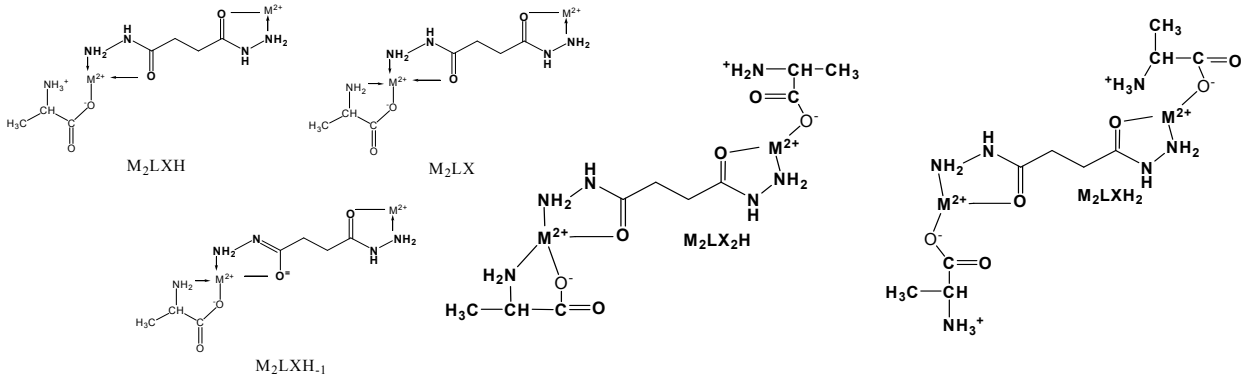


Figure 5: Proposed structures for homo-binuclear species of Cu (II)-SADH-Alanine system.

Conclusion

Examination of complex formation equilibria revealed that Cu (II) metal ion form complexes with succinic acid dihydrazide and amino acids histidine and alanine. The mixed complexes are formed in a stepwise mechanism. The relative stabilities of the ternary complexes are compared with those of the corresponding binary complexes using the $\Delta \log K$ procedure and it was observed that in homo-binuclear bonding, SADH forms more stable ternary complexes compared to binary in the case of histidine than alanine. This is may be attributed to the side chain imidazole which has a structure stabilizing tendency due to its electron donating ability. Finally, the stability constants of complexes in solution have been calculated and distribution of species for all complexes was also evaluated.

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