A CATIONIC SURFACTANT, TBAB INFLUENCE ON CHEMICAL SPECIATION OF COPPER(II) AND ZINC(II) TERNARY COMPLEXES WITH BIOLOGICALLY IMPORTANT LIGANDS L-GLUTAMINE AND SUCCINIC ACID

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Abstract

Tetrabutylammonium bromide(TBAB), a cationic surfactant influence on chemical speciation of Copper(II) and Zinc(II) ternary complexes with L-glutamine(Gln) and Succinic acid(Suc) have been studied with a Control Dynamics-APX 175E/C pH-meter at an ionic strength of 0.16 mol dm^{-3} and temperature 303 K in varying concentrations (0.0-3.0%, w/v). Various models for the species of these biologically important ligands are refined by using the computer programs SCPHD and MINIQUAD75. The active forms of both copper(II) and zinc(II) are MLX, MLX_2 and MLXH. The trend in the formation constants and TBAB influence are explained on the basis of electrostatic and non-electrostatic forces. The species distribution with pH at different solvent composition, formation equilibria and plausible structures for the formed specie are also presented in the present study.

Keywords: complex equilibria, speciation, L-glutamine, succinic acid, copper(II), zinc(II), TBAB, MINIQUAD 75

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Introduction

Metalloenzymes are catalyses most of the metabolic reactions, activities of these enzymes are due to the metal-enzyme-substrate complexes. Copper is one of the essential metal ions for various biological processes, including maintaining the skin's, blood vessels, epithelium, and connective tissue's strength throughout the body [1]. It aids in the formation of hemoglobin, myelin, and melanin and in the normal functioning of the thyroid gland also[1]. Copper is an antioxidant as well as a pro-oxidant. It acts as an antioxidant and neutralizes the free radicals, reducing the damage [2]. When copper serves as a pro-oxidant, it contributes to preventing Alzheimer's disease by promoting free radical damage [3,4]. It is critical to maintaining an adequate dietary intake of copper and other minerals such as zinc and manganese [5]. Copper stimulates and is critical for rapid wound healing [6]. It enters the bloodstream via the plasma protein ceruloplasmin (CP), which is metabolized and eliminated in bile [7]. Additionally, it functions as an enzyme, catalyzing the oxidation of minerals, most notably iron [8]. Copper deficiency causes Wilson's disease [9] and Menkes's illness [10]. Copper proteins play a variety of roles in biological electron and oxygen transport pathways that take advantage of the relatively facile inter-conversion of Cu(I) and Cu(II) [11]. Copper deficiency can express itself in various ways [12], including hernias, aneurysms, blood vessel rupture manifesting as bruising or nosebleeds, loss of colour, weakness, weariness, skin rashes, and impaired thyroid function [6]. Zinc is also one of the essential for all living organisms and is involved in numerous processes of cellular metabolism [13]. It was estimated that about 10% of human proteins potentially bind with zinc. It is required for the catalytic activity of more than 200 enzymes [14,15], and it plays a role in immune function [15,16], wound healing, protein synthesis, DNA synthesis, and cell division [17]. Zinc required for proper sense of taste and smell [18,19] and supports normal growth and development during pregnancy, childhood, and adolescence [20-23]. It possesses antioxidant properties, which protect against accelerated aging and help speed up the healing process after an injury [24].

L-Glutamine (Gln) and succinic acid (Suc) are biologically important ligands [25]. Gln is usually considered a non-essential amino acid, but recent studies have shown that glutamine may become "conditionally essential" during inflammatory conditions. Gln can act as a respiratory fuel, enhancing the stimulation of immune cells [26]. Gln in the diet increased survival to bacterial challenge [27]. It is required to support optimal lymphocyte proliferation [28], production of cytokines by lymphocytes and macrophages [29], and it is a highly conserved outer sphere residue in the active site of E. Coli manganese superoxide dismutase [30]. Suc can be used to manufacture medicaments or nutritional supplements effective for treating insulin resistance [31] in mammals. Suc is involved in the citric acid cycle [32] and the Glyoxalate cycle [33]. The concentration of Suc in human blood plasma is 0.1-0.6 mg/dL. Succinate stimulates insulin secretion and proinsulin biosynthesis [34]. Tetrabutylammoniumbromide (TBAB) is a cationic surfactant, and it is commonly used as a phase transfer catalyst [35]. It is used to prepare many other tetrabutylammonium salts via salt metathesis reactions [35].

Protonation and complexation equilibria of Gln and Suc in urea-water[36], dimethylformamide-water[36], ethylene glycol-water[37] acetonitrile-water[37] and TBAB-water[38] media have been studied to thoroughly understand the speciation of its complexes. Similarly, effects of urea [39] on nickel(II), TBAB [40] on zinc(II), influences of TBAB [41] on cobalt(II), TBAB [42] on manganese(II), and TBAB [43] on copper(II) complexes with Gln and Suc were studied. No such study was reported for Cu(II) and Zn(II) with TBAB in the literature, hence the authors have chosen TBAB influence on chemical speciation of Cu(II) and Zn(II) ternary complexes with Glu and Suc.

Experimental

Solutions of zinc and copper chlorides, L-glutamine, and succinic acid (E. Merck, Germany) were prepared in triple distilled water. A 99.5 % pure TBAB (Sigma-Aldrich) was used without further purification. The data were subjected to ANOVA [44] to assess the errors that might creep into determining the concentrations of the solutions. The strength of NaOH was determined using the Gran plot method [45]. The glass electrode was equilibrated in the TBAB solution. Alkalimetric titrations were carried out in the medium containing 0.0 – 3.0 %, w/v of TBAB in water at an ionic strength of 0.16 mol dm-3 with NaCl at 303.0±0.1 K using a Control Dynamics-APX 175E/C pH meter. The titrations were carried out in 1:2:2 and 1:2:3 metal-ligand-lgand ratios for both succinic acid and L-glutamine in the presence of metal ions.

The computer program SCPHD [46] is used to determine the correction factor, to correct the pH meter dial reading. Other experimental details are given elsewhere [44]. The approximate step-wise stability constants were calculated using SCPHD. By following some heuristics [47] in the refinement of the stability constants and using the statistical parameters of the least-squares residuals. Models containing various numbers and combination of nickel with Gln and Suc are generated using an expert system package CEES[48]. These models were inputted to MINIQUAD75[49] along with the alkalimetric titration data and the best-fit model were obtained.

Results and discussion

L-glutamine has amino and carboxyl groups of and Succinic acid has two carboxyl groups. Alkalimetric titration curves in TBAB-water mixture revealed that the active forms of Gln and Suc are in the pH ranges 2.0–10.0 and 2.0-7.0 respectively[50]. The active forms of the copper(II) and zinc(II) MLX, MLX_2 and MLXH are given in Tables 1 and 2 along with the statistical parameters. The skewness is between -1.06 to 1.36 for Cu(II) and 3.58 to 1.93 for Zn(II) indicates that the residuals follow Gaussian distribution and so least squares technique can be applied. The low standard deviation in the model parameters (log β) illustrates the adequacy of the models.

Table 1: Best fit chemical model of copper(II) complexes with L-glutamine and succinic acid in 0 – 3% w/v TBAB – water mixtures.No of titrations in each percentage is 6, temp = 303 K, ionic strength = 0.16mol. dm^{-3}

S. No	%w/v TBAB	$Log\beta_{mlxh}$ (SD)			NP	Skew ness	Kurtosis	χ^2	Ucorr x 10^6	R-factor
		1110	1120	1111						
1	0.0	15.18 (0.251)	18.83 (0.208)	20.73 (0.159)	191	1.36	3.21	10.3	6.89	0.0269
2	0.5	15.07 (0.361)	18.79 (0.385)	20.57 (0.424)	178	1.18	1.43	20.3	8.53	0.0331
3	1.0	rej	Rej	20.35 (0.299)	157	-1.06	1.63	16.8	1.0	0.0337
4	1.5	14.87 (0.143)	18.34 (0.173)	20.15 (0.240)	163	-0.26	2.97	33.4	4.86	0.0224
5	2.0	14.80 (0.371)	18.13 (0.156)	20.08 (0.515	68	-0.01	2.94	11.4	2.07	0.0623
6	2.5	14.75 (0.323)	17.96 (0.234)	20.03 (0.232)	172	-0.44	2.18	10.6	2.35	0.0175
7	3.0	14.69 (0.096)	Rej	19.65 (0.106)	87	-0.09	2.20	11.3	4.61	0.0099

Table 2: Best-fit chemical models of Zn^{II} complexes of L-glutamine and succinic acid in TBAB-water mixtures. No. of titrations in each percentage = 6, Temperature = 303K, Ionic strength = 0.16 $mol.dm^{-3}$

S.No	%w/v TBAB	$Log\beta_{mlxh}$ (SD)			NP	Skew ness	Kurtosis	χ^2	Ucorr x10^6	R- factor
		1110	1120	1111						
1	0.0	15.05 (0.295)	18.73 (0.228)	20.31 (0.349)	187	1.21	3.58	118.2	5.59	0.0246
2	0.5	14.97 (0.309)	18.77 (0.287)	20.24 (0.309)	178	1.17	1.93	108.2	7.02	0.0298
3	1.0	rej	Rej	19.96 (0.204)	154	-2.17	3.30	98.9	1.48	0.0424
4	1.5	14.81 (0.150)	18.61 (0.149)	19.72 (0.149)	156	0.15	3.40	8.51	1.15	0.0115
5	2.0	14.71 (0.133)	Rej	19.56 (0.021)	64	-0.02	3.44	56.75	1.90	0.0614
6	2.5	14.68 (0.504)	18.25 (0.423)	19.44 (0.448)	151	-0.09	2.06	89.77	2.36	0.0509
7	3.0	14.51 (0.025)	17.94 (0.445)	19.30 (0.019)	80	-0.15	3.34	25.85	1.12	0.0163

Influence of TBAB on the complex equilibria

TBAB acts as a structure-breaker of pure water due to a large hydrophobic group and forms cages around itself, with empty spaces in the structure [51, 52]. The critical micellar concentration (CMC)of TBAB is 0.2632 mol/L at 303.16 K in aqueous solutions [53]. The anisotropic water distribution within the micellar structure causes non-uniform micropolarity, microviscosity, and degree of hydration within the micellar media [54]. TBAB is a hydrotrope [55]. The degree of complex stability could be measured in terms of the magnitude of the overall stability constants of each species formed in metal-ligand dynamic equilibria. The linear and non-linear variations in the magnitude of the stability constants of metal-ligand complexes are due to electrostatic and non-electrostatic opposing factors, respectively. The high viscosity of the TBAB causes the limited mobility of species within, which in turn causes a low conversion of products, especially in enzymatic reactions [56]. In the present study, the stability constants were found to linearly decrease as the %w/v TBAB increased (Fig. 1). The linear variation indicates that electrostatic forces are dominating the equilibrium process under the present experimental conditions. The dielectric constant is one of the most prominent solvent properties that surfactants could alter [57]. The destabilization of the metal-ligand complexes could be attributed mainly to the low dielectric constant of the surfactant-mediated solvent compared to an aqueous medium. The dielectric constant(ε) of water is 78.4 Debye (D) and for TBAB is 8.93 D [58,59] at 25 °C, much lower than the aqueous medium. Moreover, the destabilization effect of the low dielectric constant is synergized [60] by the cationic TBAB surfactant, which causes the logβ values to decrease linearly.

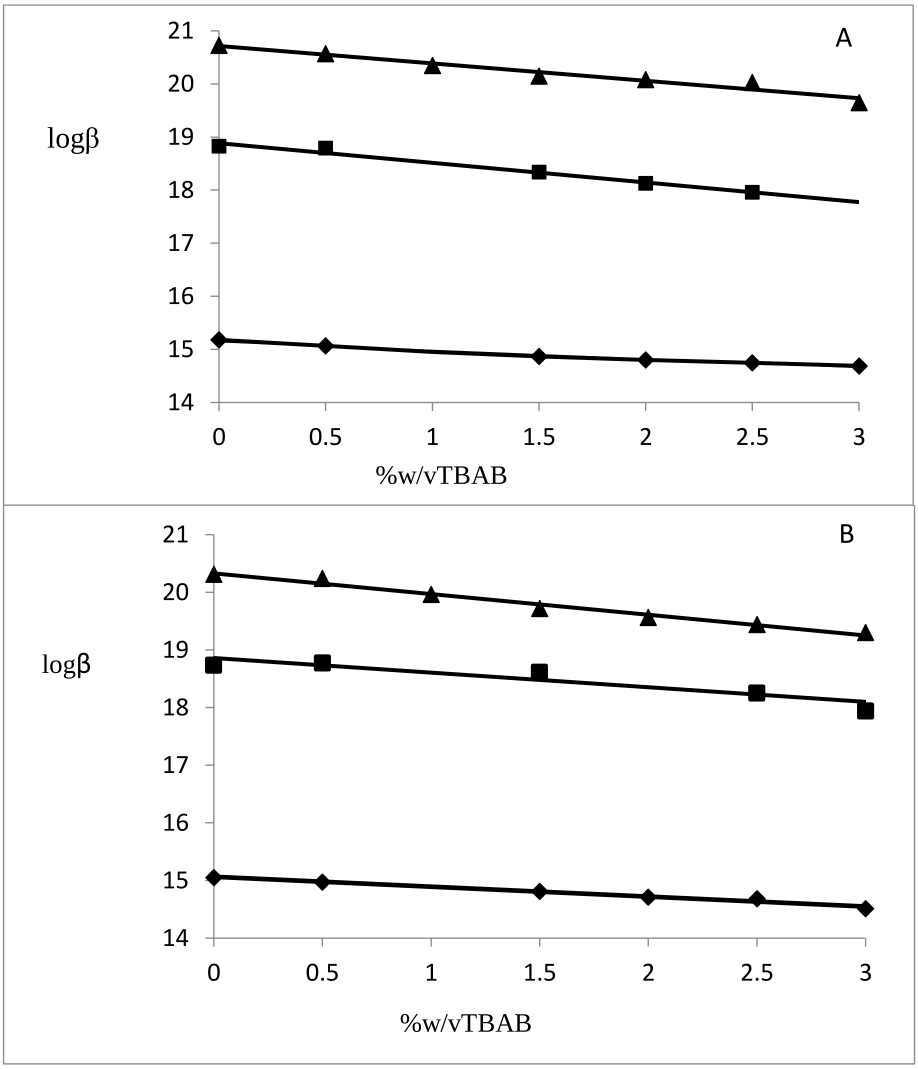

Fig. 1. Variation of log β with TBAB-water mixtures of (A)Cu-Gln-Suc: and (B) Zn-Gln-Suc. (▲) MLX, and (■)MLX_2 (♦) MLXH

It can be inferred that Cu(II) and Zn(II) systems have [MLXH], [MLX] and [MLX_2 in TBAB-water mixtures. The magnitudes of stability constants of Cu(II) are higher than Zn(II). This trend is in accordance with Irving-William's order. It is because Cu(II) has higher positive charge density and polarising power and hence the covalent character between Cu(II) and the ligands is more. Based on the above equilibria and the literature, the possible structures of the ternary complexes can be represented in Fig 3.

Distribution diagrams:

Succinic acid has two carboxyl groups, and both are protonated. L-glutamine has three functional groups (amino, carboxyl, and amido), but only amino and carboxyl groups can associate with protons. The various forms of ligands in the pH range of the study are LH_2^+, LH and L for Gln and LH_2, LH and L_2^- for Suc. The species MLXH concentration is maximum at pH 4, which forms MLX and MLX_2 for both Cu(II) and Zn(II) ions. MLX_2 is stable at pH above 6, which confirms MINIQUAD75. (Fig. 2)

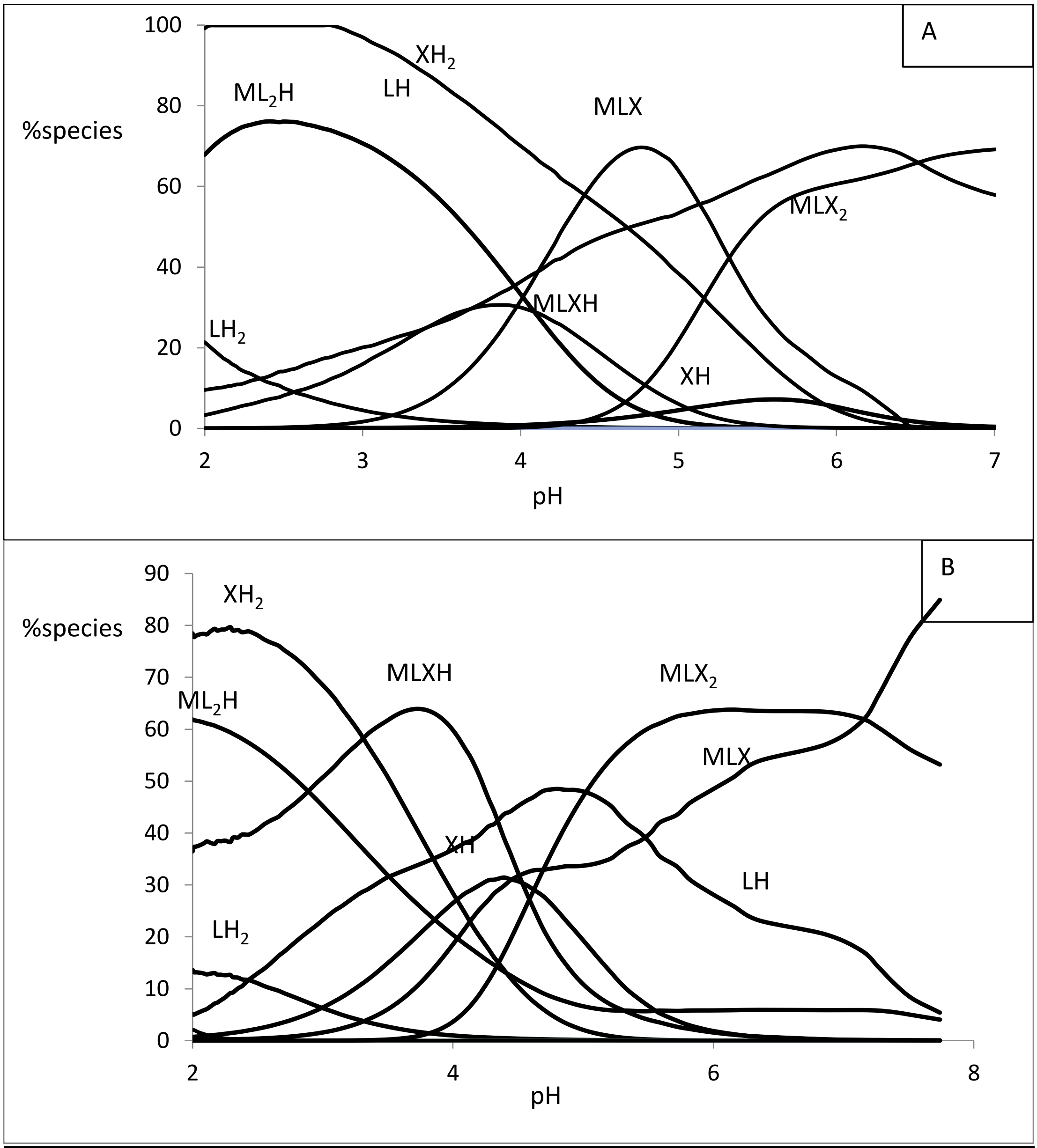

Fig. 2. Distribution diagrams of (A) Cu(II) and (B) complexes with L-glutamine and succinic acid in 0.5 %w/v TBAB-water mixture

The species MLXH can be represented as M(LH)(X) or M(L)(XH). L-glutamine can exit as XH in the pH range where the carboxylate protons are easily lost by succinic acid below a pH of 7.0. Even beyond a pH of 7.0, L-glutamine can exist as LH since its amino proton is lost beyond a pH of

9.0. Succinic acid cannot exist as XH in the pH range where L-glutamine does not exist as LH. Therefore the MLXH species shall be represented(b) only as M(LH)(X) but not as M(L)(XH). This species may be formed due to the following equilibrium.

$$M(LH)(XH) \rightleftharpoons M(LH)(X) + H^+$$

The possible equilibria for the formed species MLX and MLX_2 is given below.

(a) $M(II) + XH_2 \rightleftharpoons MXH_2$

(b) $MXH_2 + LH_2 \rightleftharpoons M(LH)(X) + 3H^+$ (major)

(c) $M(LH)(X) \rightleftharpoons MLX + H^+$

(d) $M(II) + LH_2 \rightleftharpoons MLH_2$ (minor)

(f) $MLX + XH_2 \rightleftharpoons MLX_2 + 2H^+$ (major)

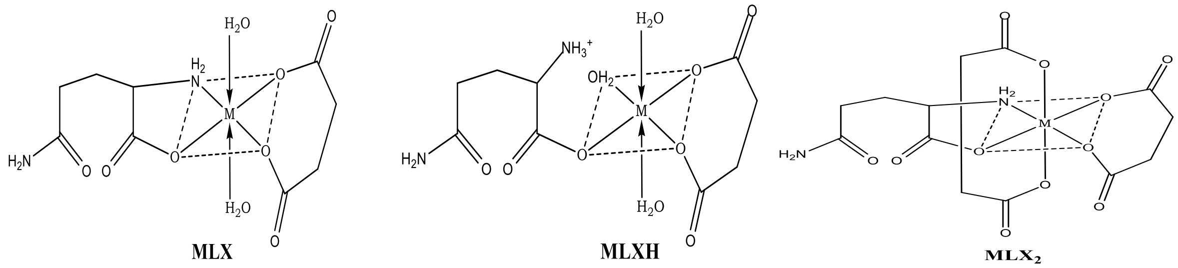

Fig. 3. Plausible diagrams of (A) Cu(II) and (B) complexes with L-glutamine and succinic acid in 0.5 %w/v TBAB-water mixture

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