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# TBAB A Cationic Surfactant Influence on Chemical Speciation of Nickel(Ii) Binary Complexes with Biologically Important Ligands L-Glutamine and Succinic Acid

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**KEYWORDS**
complex equilibria, speciation, L-glutamine, succinic acid, nickel, TBAB, MINIQUAD 75

**ABSTRACT:**
Tetrabutylammonium bromide(TBAB), a cationic surfactant influence on chemical speciation of Nickel(II) binary complexes with L-glutamine(Gln) and Succinic acid(Suc) have been studied with a Control Dynamics-APX 175E/CpH-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 the Nickel(II) are ML and MLH with Suc and that for Gln are $ML_2$ and $ML_2H$. 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.

## Introduction

Metalloenzymes or metal activated enzymes are catalyze most of the metabolic reactions[1] the activities of these enzymes are due to the metal-enzyme-substrate complexes[2]. Nickel performs number of biological activities[3] in the animals and humans. Urease is a Nickel dependent metalloenzyme [4], which is required in nucleic acid and lipid metabolism and iron absorption. The signs of nickel deprivation include depressed growth, reproductive performance and plasma glucose[5].Nickel deprivation also affects the distribution and proper functioning of other nutrients[5].

L-Glutamine(Gln) and succinic acid (Suc) are biologically important ligands[6]. Gln is conditionally essential during inflammatory conditions such as infection and injury under appropriate conditions. It can act as a respiratory fuel and it can enhance the stimulation of immune cells[7]. Gln in the diet increased survival to bacterial challenge[8]and is also required to support optimal lymphocyte proliferation[9], production of cytokines by lymphocytes and macrophages[10] and it is highly conserved outer sphere residue in the active site of Escherichia coli (E.Coli) manganese superoxide dismutase[11]. Suc can be used for manufacture of medicaments or nutritional supplements effective for treating of insulin resistance[12] in mammals.It is involving in citric acid or Tricarboxylic acid (TCA) cycle[13] and Glyoxalate cycle. In neurotransmission, GABA is inactivated by transamination to succinic semi-aldehyde andoxidises to succinate. The concentration of succinic acid in human blood plasma is 0.1-0.6 mg/dl. Succinate stimulates insulin secretion and pro-insulin biosynthesis[14].TBAB,Tetrabutylammoniumbromidei s a cationic surfactant and has a positively charged head group, which plays important role in modifying the behavior of aqueous media. It is a quaternary ammonium salt with a bromide counter ion commonly used as a phase transfer catalyst[15]. It is also used to prepare many other tetrabutylammonium salts via salt metathesis reactions[15].

Protonation and complexation equilibria of Gln and Suc in urea-water[16], dimethylformamide-water[16], ethylene glycol-water[17] acetonitrile-water[17] and TBAB-water[18] media have been studied to thoroughly understand the speciation of its complexes. The protonation constants of Glu and Suc are correlated[16] with the dielectric constant of the medium using various solvents. Similarly, effectsof urea[19] on nickel(II),TBAB[20] on zinc(II), influences

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of TBAB[21] on cobalt(II)and TBAB[22] on copper(II) complexes with Gln and Sucwere studied. No such study was reported for Ni(II) with TBAB in the literature, hence the authors have chosen TBABinfluence on chemical speciation ofnickel(II)binary complexes with Glu and Suc.

**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[18]. Models containing various numbers and combination of nickel with Gln and Suc are generated using an expert system package CEES[23]. These models were inputted to MINIQUAD75[24] along with the alkalimetric titration data and the best-fit model were obtained. The active forms of the Nickel(II) are ML and MLHfor Suc and $ML_2$ and $ML_2H$ for Gln are given in Tables 1 and 2 along with the statistical parameters. The skewness is between -1.67 to 2.14 for Suc and closeness to zero for Gln 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 nickel(II) complexes with 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$^{-3}$

| %w/v TBAB | Log$\beta_{mlh}$(SD) | | NP | Skew ness | Kurtosis | $\chi^2$ | Ucorr x $10^6$ | R- factor |
|---|---|---|---|---|---|---|---|---|
| | 110 | 111 | | | | | | |
| 0.0 | 2.96(7) | 7.83(2) | 108 | 2.14 | 3.16 | 62 | 3.96 | 0.0133 |
| 0.5 | 2.77(1) | 7.79(1) | 149 | 0.13 | 3.48 | 88.7 | 1.83 | 0.0196 |
| 1.0 | - | 7.75(2) | 126 | -0.09 | 2.99 | 19.54 | 2.38 | 0.0691 |
| 1.5 | - | 7.72(2) | 128 | -0.01 | 2.68 | 42.33 | 3.05 | 0.0764 |
| 2.0 | 2.24(1) | 7.68(1) | 127 | -1.15 | 3.15 | 21.7 | 2.57 | 0.0248 |
| 2.5 | 2.11(1) | 7.64(1) | 122 | -1.07 | 2.58 | 75.11 | 2.24 | 0.0233 |
| 3.0 | 2.06(2) | 7.62(2) | 70 | -1.67 | 3.83 | 51.45 | 2.13 | 0.0293 |

**Table 2:** Best fit chemical model of nickel(II) complexes with L-glutamine in 0 –3% w/vTBAB – water mixtures. No of titrations in each percentage is 6, temp = 303K, ionic strength = 0.16mol.dm$^{-3}$

| %w/v TBAB | Log$\beta_{mlh}$(SD) | | NP | Skew ness | Kurtosis | $\chi^2$ | Ucorr x$10^6$ | R- factor |
|---|---|---|---|---|---|---|---|---|
| | 120 | 121 | | | | | | |
| 0.0 | 20.46(1) | 23.81(2) | 79 | -0.22 | 2.27 | 16.27 | 1.16 | 0.0268 |
| 0.5 | 20.13(5) | 23.57(6) | 71 | -0.45 | 2.92 | 7.58 | 1.48 | 0.0332 |
| 1.0 | 19.69(6) | 23.44(2) | 58 | -0.09 | 2.17 | 7.70 | 1.17 | 0.0300 |
| 1.5 | - | 23.37(3) | 61 | -0.38 | 2.50 | 21.28 | 1.57 | 0.0333 |
| 2.0 | 18.84(1) | - | 45 | -0.17 | 3.34 | 7.24 | 6.45 | 0.0426 |
| 2.5 | 18.57(2) | 23.13(3) | 57 | -0.74 | 3.33 | 12.53 | 1.52 | 0.0388 |
| 3.0 | 18.38(9) | 23.09(9) | 46 | -0.59 | 3.22 | 1.05 | 1.79 | 0.0297 |

The linear variation of species with increasing %TBAB indicates that electrostatic forces are dominating the equilibrium process under the present experimental conditions. The decrease in formation constants with %TBAB indicate that the equilibrium process is destabilising due to interaction of metal ion with TBAB(Fig 1).

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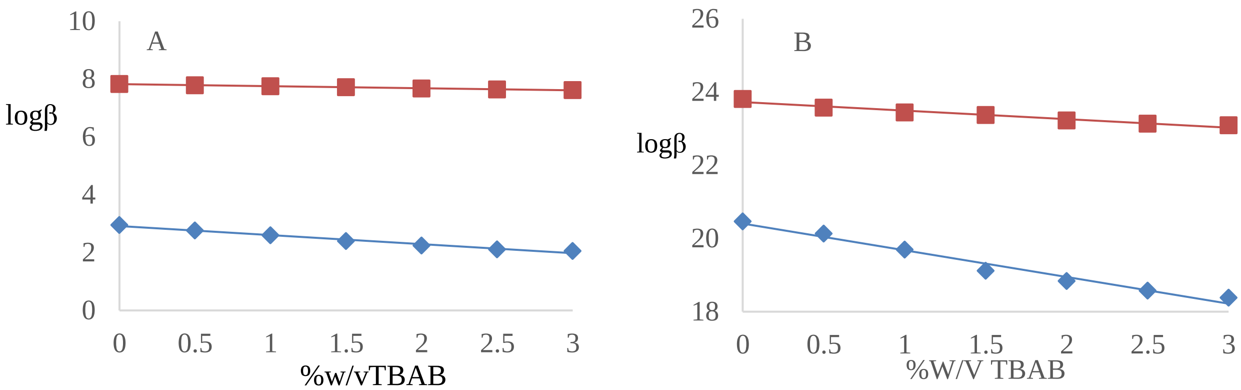


**Fig 1:** Variation of logβ with %w/v TBAB-water mixtures A)Ni(II) (♦) ML (■) MLH and B)Ni(II) (♦) $ML_2$ and (■)$ML_2H$

**Solute-solvent interactions**

TBAB acts as structure-breaker of water structure due to large hydrophobic group of TBAB and thus forming cages around itself, with empty spaces in the structure [25,26]. TBAB is a hydrotrope in presence of water [27] and CMC for TBAB is 0.2632mol/L at 303.16K in aqueous solutions [28]. The anisotropic water distribution within micellar structure causes non-uniform micropolarity, microviscosity and degree of hydration within the micellar media [29]. The degree of stability of complexes could be measured in terms of 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 viscosity is strongly influenced by the ability of the liquid to transport the mass within the liquid, which is immensely responsible for any changes in the chemical reactions. 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 [30]. The linear variation of species with increasing % of TBAB indicates that electrostatic forces are dominating the equilibrium process under the present experimental conditions.

In the present study, results of the stability constants were found to be linearly decreasing with increasing TBAB content for both Gln and Suc complexes with Ni(II). Dielectric constant(ε) is one of the most and prominent solvent properties that could be altered [31] by surfactants in the given titration mixtures. The dielectric constant of water is 78.4 and that for TBAB is 8.93 at 25ºC is much lower than [32,33] aqueous media, but no data in the literature for corresponding percentages. Hence, the authors are taken %w/v TBAB on the abscissa. The destabilization of the metal ligand complexes could be attributed mainly to the low dielectric constant of the surfactant mediated solvent compared to aqueous medium. Moreover, the destabilization effect of the low dielectric constant is synergized by the cationic surfactant TBAB.

**Distribution diagrams**

L-glutamine has amino, carboxyl and amido functional groups but only amino and carboxyl groups can associate with protons. Succinic acid has two carboxyl groups and both are protonated. The various forms of ligands exist in the pH range of study (2.0-10.0) are $LH_2^+$, LH and $L^-$ for Gln and $LH_2$, $LH^-$ and $L^{2-}$ for Suc. The zwitterionic form (LH) of Gln is present to an extent of 90% in the pH range 2.5-8.5,which are confirmed by MINIQUAD75. Perusal of the models indicates that the species MLH concentration is highly stable at pH 4and the species MLconcentration is stable at pH above 6 for Suc. The formed species $ML_2H$ is stable at pH below 3 and $ML_2$ is stable at pH above 3 for Gln (Fig 2).

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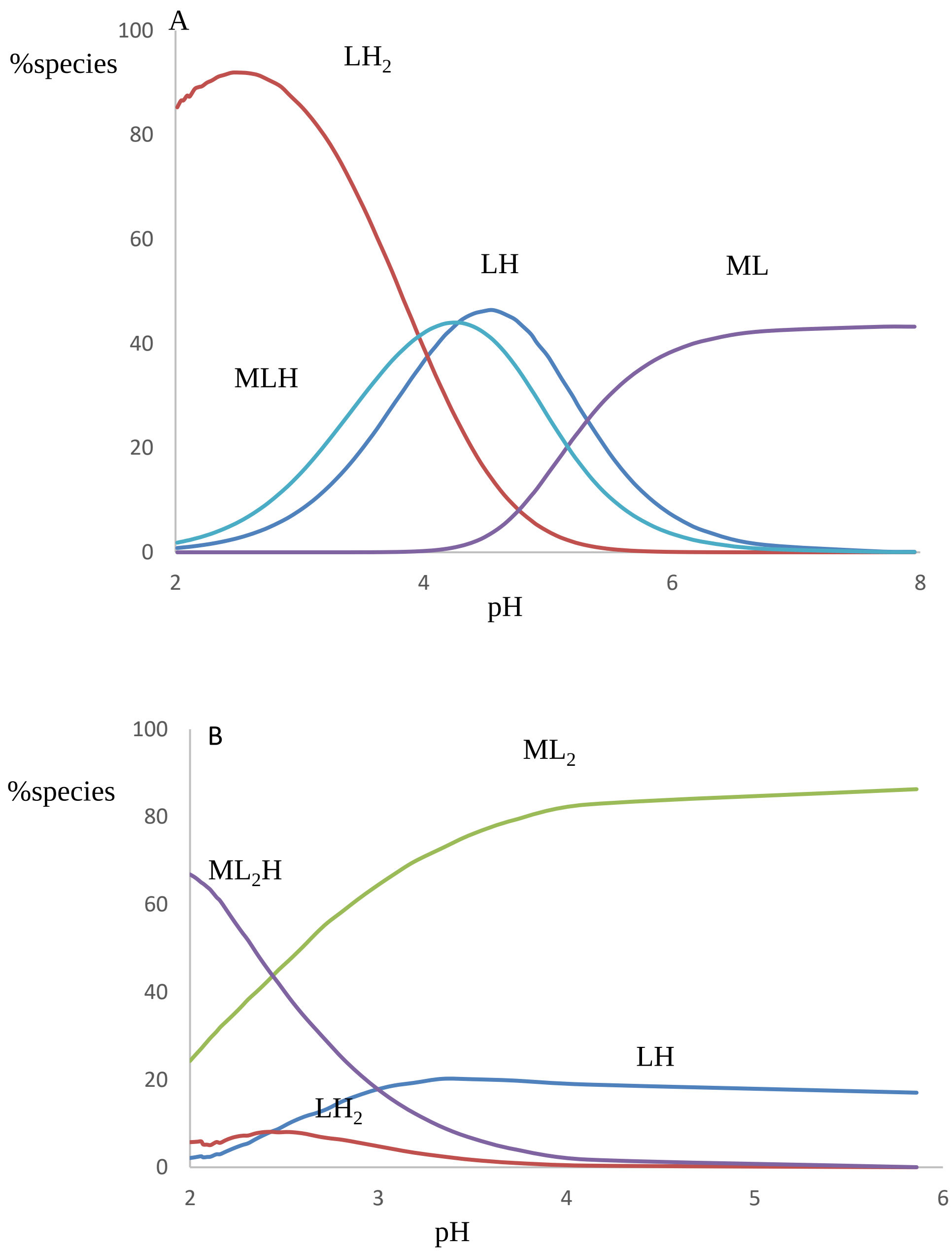


**Fig 2:** Distribution diagrams of (A) Ni(II)-Suc and (B) Ni(II)-Gln in 0.5%w/v TBAB-water mixtures.

The plausible formation equilibria for nickel(II)with L-glutamineand succinic acid are given below.

$M(II)+LH_2 \rightleftharpoons MLH + H^+$ ....(a)

$MLH \rightleftharpoons ML + H^+$ ....(b)

$M(II)+2LH_2 \rightleftharpoons ML_2H + H^+$ ....(c)

$ML_2H \rightleftharpoons ML_2 + H^+$ ....(d)

The charges of species are omitted for clarity. The formation of LH and $LH_2$ for both Gln and Suc are insignificant. The variation of species concentration with pH is shown in Fig. 2 for typical systems. Equations a and b represent the formation equilibriaofnickel with Sucand equations c and dare for nickel with Gln species.The speciesML concentration is highly stable at pH above 6 for Suc and $ML_2$ is readily converted from $ML_2H$(Eq.d). Plausible structures for the formation species are given in Figs 3 and 4.

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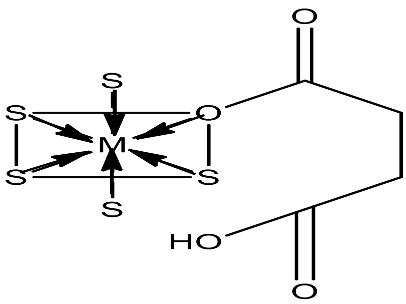
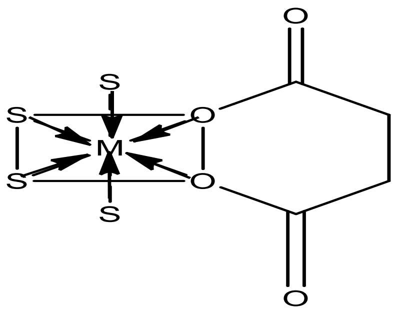
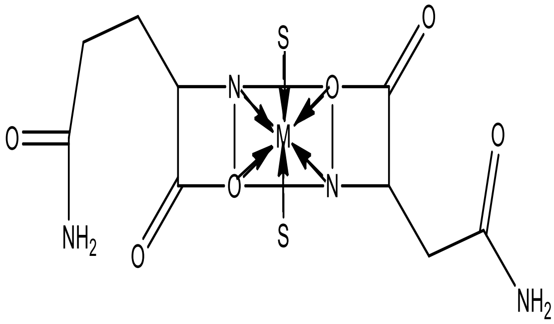
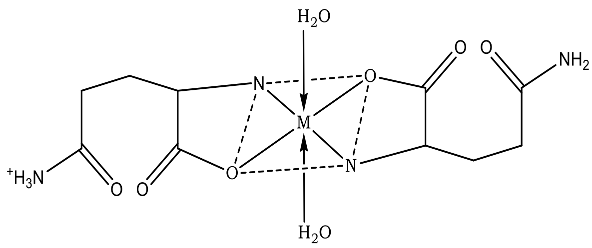



MLH ML

**Fig 3:** Plausible diagrams of Ni(II) binary complexes with Suc. (M is Ni(II), L is Suc., S is solvent/water)

$ML_2H$

$ML_2$

**Fig 4:** Plausible diagrams of Ni(II) binary complexes with Gln (M is Ni(II), L is Gln, S is solvent/water)

**MATERIAL AND METHODOLOGY**

Nickel chloride, L-glutamine and succinic acid (E.Merck, Germany) solutions were prepared in triple distilled water. A 99.5% pure TBAB (Sigma, Aldrich) was used without further purification. The data were subjected to ANOVA[34] to assess the errors that might have crept into the determination of the concentrations of above solutions.The strength of alkali (NaOH) was determined using the Gran plot method[35]. 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/CpH meter. The glass electrode was equilibrated in inert electrolyte. The correction factor, log F was determined using the computer program SCPHD[36]. Titrations with different ratios of metal to ligand (1:2 and 1:3) were carried out with 0.4 mol $dm^{-3}$ sodium hydroxide. Other experimental details are given elsewhere[34]. The approximate protonation constants were calculated using SCPHD. By following some heuristics[37] in the refinement of the stability constants and using the statistical parameters of the least squares residuals, the best-fit chemical models for each system were arrived at using the computer program MINIQUAD75.

**CONCLUSIONS**

The presence of cationic surfactant, TBAB in aqueous solution considerably decreases the dielectric constant and these solutions are expected to mimic the physiological conditions. The present study is useful to understand.

1. The role played by the active site cavities in biological molecules.
2. The bonding behaviour of the protein residues with the metal ion in further studies.
3. The species refined and their relative concentrations represent the possible forms of glutamine and succinate residues under the present experimental conditions.
4. The active forms of the Nickel(II) are MLand MLH for Suc and that for Gln are $ML_2$ and $ML_2H$
5. Tetra butyl ammonium bromide (TBAB) is a cationic surfactant and has a positively charged head group, which plays important role in modifying the behaviour of aqueous media. As a cumulative effect, the stabilities of the species decreased with increased TBAB content for both Suc and Gln.

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