Potentiometeric Study of Binary Complexes of Triethylenetetraminehexaacetic Acid with Cd^{2+}, Co^{2+}, and Pb^{2+} Ions in Aqueous Solutions

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The interaction between triethylenetetraminehexaacetic acid, TTHA, and three divalent metal ions Cd(II), Co(II) and Pb(II) was investigated potentiometrically in two 1 : 1 and 2 : 1 metal to ligand mole ratio systems. The overall equilibrium formation constants were computed by the BEST program. The species distribution diagrams were also depicted using the SPE program. Eight protonation constants were obtained which were assigned for the protonation of nitrogen donors at first and carboxylic groups in continuation. For the 1 : 1 metal to ligand ratio, the main species in the middle pH region is MLH, the concentration of which decreases slowly on going to the basic region. The main complex at basic pH is ML, which becomes the sole species at pH above 10. In the 2 : 1 system, only the M_2L species remain intact in a broad range from pH = 4 to the basic region. Compared to EDTA, TTHA has a higher relative stability with cadmium and so, can potentially present as a suitable candidate for chelation therapy.

Key words: Potentiometry, Aminopolycarboxylic Acid, Formation Constant, Chelation Therapy

Introduction

Aminopolycarboxylic acids are higher homologues of ethylene diamine tetraacetic acid, EDTA, which have been extensively used as suitable ligands in many fields of applications because of their strong sequestering ability towards almost all metal ions (complexons). For analytical purposes they are used in quantitative complexometric titrations, ion selective electrodes, extraction *etc.* [1 – 3]. They are used in agriculture to protect plants from essential metal deficiency. Complexons are involved in many aspects of clinical biological practices such as contrasting agents, plant growth, and also in many industries as suppressors of unfavorable catalytic effects of metal ions, softening agents in treatment of water supplies, for prevention and removal of stains caused by iron compounds *etc.* [4 – 6]. The large number of applications justifies the intense interest of chemist in the binding ability of complexons in new fields such as chelation therapy for selective treatment of heavy metal poisoning and to remove metals that have built up in tissues as a result of increase in the world consumption of the metal such as Itai Itai disease [7]. The key rules in the understanding of the chemical reactions between such chelate and available metal ions in the body are the relative stability constants. Unfortunately, EDTA has similar affinity towards most transition metal ions. So, deficiency of some essential transition metal ions is an inevitable result of EDTA treatment.

It has been shown that extended EDTA structures such as diethylene triamine pentaacetic acid form considerably more stable metal chelates than EDTA, especially with more highly charged metal ions. The decadentate ligand triethylenetetraminehexaacetic acid, TTHA, is of interest because of the possibility of further increasing the affinity for metals of higher charge and also for the formation of polynuclear complexes with metals of lower charge [8]. The stability constants of metal complexes of this ligand have being investigated by many authors since Frost introduced TTHA [9 – 13].

Because of the large number of donor atoms, TTHA can be coordinated to two metal ions. So many authors tried to investigate the coordination of two different metal ions with different metal-ligand affinity [14 – 15]. As the individual stabilities of complexes are essential for such investigations, we studied the interaction between TTHA and three divalent metal ions Cd(II), Co(II) and Pb(II) in metal to ligand ratios 1 : 1

and 2 : 1. The equilibrium constants were determined using the BEST program [16] and are compared with the stabilities obtained in previous investigations [17]. The species distribution diagrams were depicted using the SPE program [16].

Results and Discussion

Protonation constants of TTHA

The protonation constants of the ligand were determined potentiometrically at 25 °C and in 0.1 M KNO_3 as supporting electrolyte. The pH data versus the volume of the KOH were listed as an input file for the computation using the BEST program. The resulting eight protonation constants are summarized in Table 1. The results of previous investigations are also listed for comparison [13, 18]. As Table 1 shows, a very good agreement can be observed between our results and results obtained previously. In our results, the value $K_{HL} = 10.42$ was obtained. Harris and Martell reported 10.40 for the same constant. Similarly, in our study, the values $K_{H_2L} = 9.56$, $K_{H_3L} = 6.22$ and $K_{H_4L} = 4.21$ were obtained which are very close [18], while the values of Anderegg and coworkers are different. In the other hand, Harris and Martell did not succeed in determining all eight protonation constants as Anderegg and coworkers have pointed out [13].

The species distribution diagram of the free ligand (Fig. 1) shows that the H_8L species is too unstable to be present in significant amounts even at pH 2. This species disappears completely at pH 2.5 and is converted to H_7L. The H_7L and H_6L species are present in maximum concentration of about 35% of the total

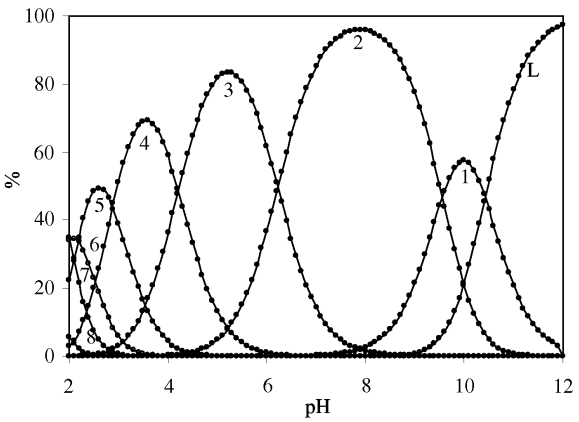


Fig 1. Species distribution diagram for TTHA (L), at 25 °C and ionic strength 0.1 M KNO_3. The numbers cited on the figures indicate the protons attached to the ligand.

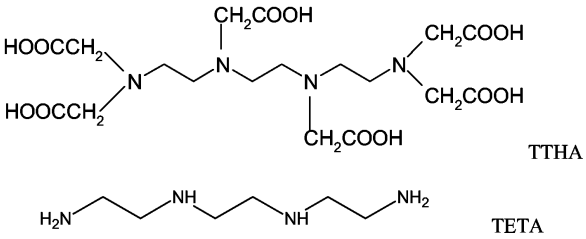
Table 1. Stepwise protonation constants of TTHA in 0.1 M KNO_3 at 25 °C ($\sigma_{fit} = 0.02$).

		Found	
	Calcd. ($\sigma_{fit} = 0.02$)	Ref [13]	Ref [18]
Log K_1	10.42	10.55	(10.40)
Log K_2	9.56	9.48	(9.50)
Log K_3	6.22	6.11	(6.19)
Log K_4	4.21	4.08	(4.10)
Log K_5	2.88	2.86	(2.81)
Log K_6	2.18	2.26	(2.30)
Log K_7	2.01	1.88	
Log K_8	1.21	1.30	

Table 2. Stability constants of 2 : 1 metal to ligand ratio systems at 25 °C and ionic strength 0.1 M KNO_3[a].

Log K	Co-L (2 : 1)	Pb-L (2 : 1)	Cd-L (2 : 1)
ML	16.39(16.55)	17.12(16.83)	17.87(17.98)
MLH	9.18(7.85)	8.98(8.82)	8.52(8.40)
MLH_2		3.32(4.04)	3.41(3.46)
MLH_3		2.07	2.14(2.37)
MLH_4			1.50(1.85)
M_2L	12.67(10.93)	11.56(11.49)	8.96(8.61)
M_2LH	3.36(3.22)	2.74(3.46)	
M_2LH_2	1.91(2.64)	1.50(1.80)	
	$\sigma_{fit} = 0.03$ (0.02)	$\sigma_{fit} = 0.02$ (0.02)	$\sigma_{fit} = 0.01$ (0.01)

[a] Values in parentheses are from 1 : 1 metal to ligand concentration ratio.



Scheme 1. Simplified structure of TTHA and TETA.

concentration of the ligand. Their concentrations decrease slowly and become insignificant at pH = 3.5. The H_5L species appears at pH = 2 and then its concentration increases on going to pH = 2.5 where it reaches a maximum and gradually disappears at pH = 4.5. The distribution of all of the species can be followed from Fig. 1. The first four protonation constants are comparable to the corresponding constants of triethylenetetramine [19], TETA, (Scheme 1).

Stability constants of TTHA complexes

The stability constants of the complexes of TTHA with Co(II), Pb(II), and Cd(II) were determined potentiometrically at 25 °C and in 0.1 M KNO_3 as supporting electrolyte and are summarized in Table 2. Species

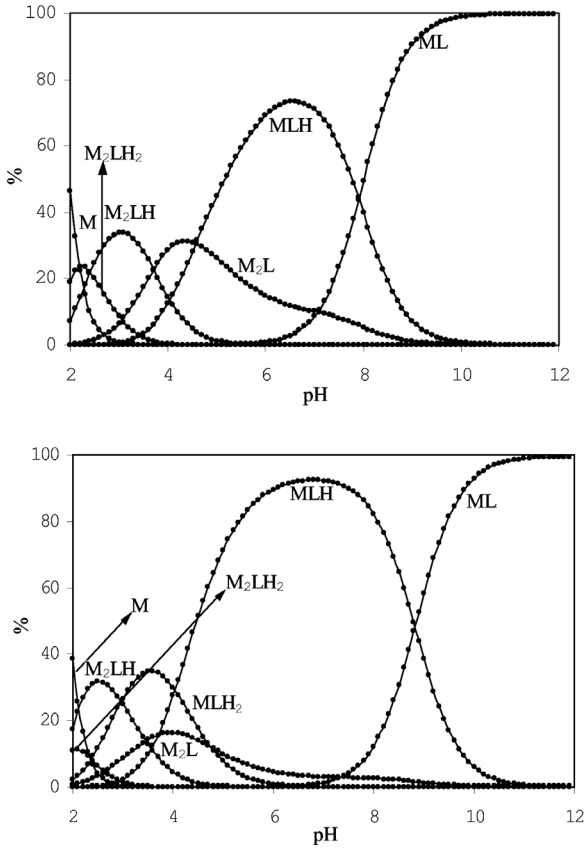


Fig 2. Species distribution diagram for 1 : 1 (top) and 1 : 2 (down) molar ratio of TTHA (L) to Co^{2+}(M) at 25 °C and ionic strength 0.1 M KNO_3.

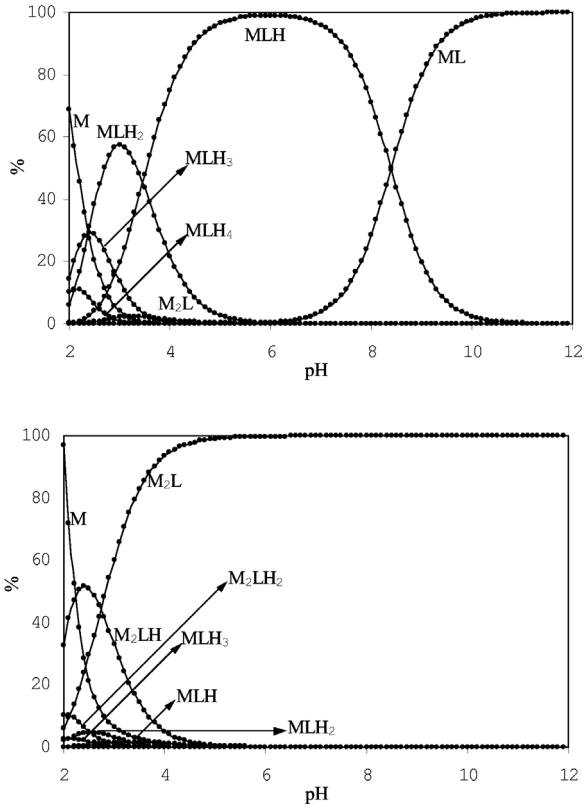


Fig 3. Species distribution diagram for 1 : 1 (top) and 1 : 2 (down) molar ratio of TTHA (L) to Pb^{2+}(M) at 25 °C and ionic strength 0.1 M KNO_3.

distribution curves of the complexes of TTHA with the metal ions in both 1 : 1 and 2 : 1 metal to ligand ratios were obtained using the SPE program and the resulting curves are shown in Figures 2 to 4.

In the Co-TTHA system (1 : 1), (Fig. 2a), the protonated binuclear complexes M_2LH and M_2LH_2 are observed at acidic pHs. At the initial pH, the M_2LH_2 species is formed, and its maximum concentration appears at pH = 2.5. When the pH of solution reaches to 4, this species has disappeared completely. M_2LH is formed at the initial pH and disappears at pH greater than 5. The maximum amounts of M_2LH_2 and M_2LH are about 25% and 35% of the total ligand concentration, respectively. Because of the absence of any metal-free ligand species even at initial pH, it may be suggested that metallation of the semi protonated species (observed in the species distribution diagrams of the free ligand at the same pH range) is followed by fast deprotonation, causing the formation of M_2LH_2 and M_2LH. These species gradually lose their acidic protons to form the species M_2L observed in the pH range of 2 – 8. The M_2L species reaches its maximum concentration of about 30% of the total ligand concentration at pH $\sim$ 4. The metallation reaction of LH or metallation of LH_n ($n > 1$) and deprotonation of the resulting complexes causes the formation of MLH to produce ML. Uninuclear complexes are dominant in this system. The maximum concentration of MLH appears at middle pH. The main species ML appears at middle pH and increases in concentration reaching a maximum of about 100% in the pH range 9 – 12.

Similarly, in the 1 : 1 Pb-TTHA metal to ligand ratio (Fig. 3a) the same pattern is observed, with the negligible exception that MLH is the main species in a wider pH range with a concentration of about 90% of the total ligand concentration.

The comparison of the distribution curve of Cd-TTHA (1 : 1) (Fig. 4a) with that of the previous systems shows that, not only the mononuclear complexes

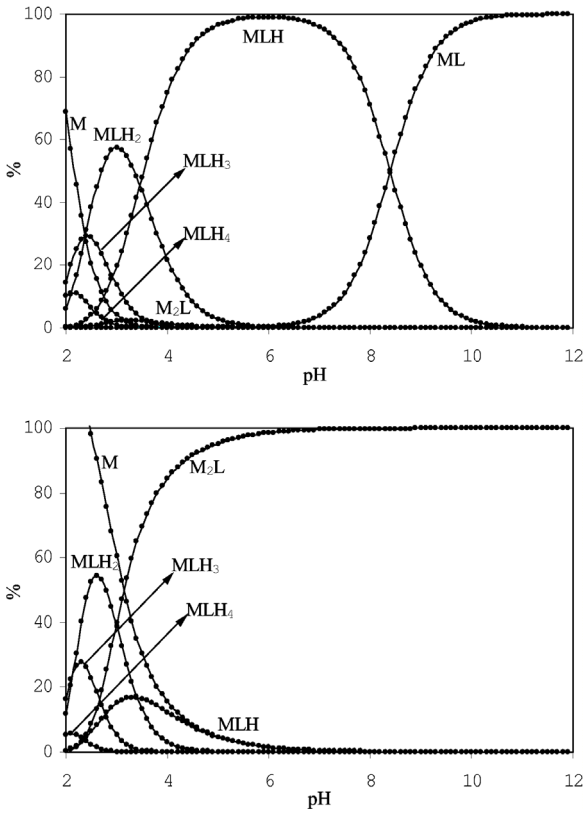


Fig 4. Species distribution diagram for 1 : 1 (top) and 1 : 2 (down) molar ratio of TTHA (L) to Cd^{2+}(M) at 25 °C and ionic strength 0.1 M KNO_3.

are dominant forms, confirming a pervious report [20], but also the formation of higher protonated mononuclear complexes such as MLH_3 and MLH_4 is possible. The appearance of MLH_2, MLH_3 and MLH_4 is initiated in the acidic region, while at pH higher than 5 deprotonation occurs and MLH and ML are produced.

In conclusion, in all the 1 : 1 systems, MLH is the main species at middle pH, while in the basic region, ML is the dominant form.

In all 2 : 1 M-TTHA systems mononuclear complexes and their protonated complexes and also binuclear protonated complexes appear in the acidic region. On going to the basic region, the only species that was observed is M_2L. In 2 : 1 Co-TTHA (Fig. 2b) and Pb-TTHA (Fig. 3b) systems the tendency of forming binuclear complexes, either protonated or deprotonated, is greater than that of mononuclear complexes, while this tendency is reversed in the case of the 2 : 1 Cd-TTHA system. In these binuclear complexes, the octahedral coordination sphere of each metal ion is likely to be completed with H_2O molecules forming species $M_2LH_m(H_2O)_n$, dissociating gradually at very low pH's. The first proton of M_2LH_2 is released at the initial pH and M_2LH is formed. The maximum concentration of this species occurs at about pH ~ 3. Consequently, the release of the remaining proton occurs at pH > 3, and finally $M_2L(H_2O)_n$ is formed as the main species at pH > 6. MLH_4 is the species that is observed only in both Cd-TTHA systems. The only binuclear complex that appears in this system (2 : 1) is M_2L. In the 2 : 1 Pb-TTHA and Co-TTHA systems binuclear complexes such as M_2LH_2, M_2LH and M_2L are dominant with respect to mononuclear complexes, while in the Cd-TTHA system only M_2L is formed.

Table 2 shows the stabilities of the TTHA complexes of Co(II), Pb(II), and Cd(II) species, and the distribution curves for the 1 : 1 and 2 : 1 of metal-to-ligand systems are shown in Figs 2 – 4. There is no significant difference between the stability obtained for 1 : 1 as compared to 2 : 1 metal to ligand ratios. This feature may be interpreted by the same coordination of the ligand to the metal ions independent of the concentration ratio of the system.

Experimental Section

The TTHA was purchased from Fluka and was used without any further purification. The concentrations of ligand in its stock solutions were determined by titration with KOH solution of known concentration. Metal ions were introduced as analytical grade nitrate salts (Merck Company) and the stock solutions were standardized complexometrically by EDTA titration [21]. KOH solution (0.06 M) was prepared with doubly distilled water and standardized against potassium hydrogen phthalate (KHP) with phenolphthalein as an indicator. The HNO_3 solution was standardized with standard KOH. The extent of carbonate accumulation ($< 0.5\%$) was checked periodically by titration with a standard HNO_3 solution.

Potentiometric titrations were performed by means of a Hana-pH 300 series Bench-Top pH meter equipped with a Metrohm piston buret (715 Dosimat) with a 5.0 ml exchange unit that was used for precise delivery of the standard KOH. The pH meter was calibrated to read the hydrogen ion concentration by titration of nitric acid solution with standard KOH solution at 25 ± 0.1 °C and 0.1 M of KNO_3 as supporting electrolyte, according to Gran's method [22]. All samples were titrated in a double–walled glass cell maintained at 25 ± 0.1 °C by circulating water and stirred magnetically under a continuous flow of purified nitrogen. The pH range for accurate measurements was considered to be 2 – 12. The concentrations of reactants in the experimental solution were in the order $1.6 \cdot 10^{-3}$ M for each component.

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