Comparative Study of PolyAminoCarboxylicAcid Complexes of Essential and Biotoxic Metals

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Summary: Potentiometeric studies have been carried out on 1:1 ML mononuclear complexes, where Ca (II), Fe (III) and Zn (II) represent the essential metals whereas Pb (II), Cr (III, VI) and Ni (II) are the biotoxic metal ions. The ligands selected are the polyamino carboxylic acids(PAC)such as EDTA, DTPA and CDTA. pH titrations were performed in aqueous solutions at an ionic strength of 0.1M and temperature 30°C. Formation of above-mentioned metal-PAC complexes were studied and compared. DTPA was found comparatively a strong acid among the three PAC acids and suitable for complexation especially at the pH below 2.5 contrarily to CDTA and EDTA.

Introduction

Regarding the importance of trace metals in human, their improper limits might cause metabolic disturbance [1]. The toxic effects of Chromium, Nickel and Lead may be increased by interactions or a deficiency of nutritionally essential metals e.g. iron, zinc and calcium [2,3]. These deficiencies enhance the negative effects of lead. Iron deficiency increases the gastrointestinal absorption of cadmium, and cadmium competes with zinc for binding sites on metallo-thionein, This protein is important in the storage and transport of zinc during development [3]. Nickel may displace zinc in DNA polymerase, due to its different size it seems to increase the chance of non-required binding with nucleotide, thus resulting in the formation of DNA of a wrong consequence [4]. The potential polydentate ligands like polyaminocarboxylic acids (PAC), having large number of donor sites have been used as antidote compounds in heavy metal intoxication [5]. The solubilizing property of PAC acids accounts for the mobilization of heavy metals in the living system.

CDTA and DTPA can be used as newer chelating and sequestering agents in biological processes [6-8]. Both of these acids are known as better complexing agents than EDTA for heavy metals on the basis of increased basicity and co-ordination sites [9-11]. During chelation of metals, PAC acids have been reported as nonspecific toward metals, so deficiency of essential metals might occur [12]. PAC acids have been used to chelate toxic metal ion in a solution containing several species of essential metal ions. Since the stabilities of PAC acid complexes are pH dependent [13], it is assumed that chelation of PAC acids can be directed towards the desired metal ion only by selecting and controlling the pH of the system.

This study has been performed to compare the chelating ability of EDTA, CDTA and DTPA for essential as well as biotoxic metal ions. It might be helpful as it includes the discussion on the deprotonation and complex formation of PAC-Metal complexes at different pH.

Result sand Discussion

pH titrations of PAC acids (CDTA, DTPA and EDTA) with above mentioned toxic and essential metal ions, were performed to study the nature of complexation at different pH. Their stability constant values calculated from these graphs were compared with reported values (Table 1).

Table 1: Stability Constants (log K) [14]

Chelators	Ni^{2+}	Cr^{3+}	Fe^{3+}	Zn^{2+}	Ca^{2+}	Pb^{2+}
EDTA	18.56	-	25.1	16.26	10.7	18.3
CDTA	19.4	-	29.3	18.6	12.5	19.7
DTPA	20.2	-	27.3	18.8	10.7	18.7

From pH titration curves of PAC acids there effective pH range for metal complexation were studied (Fig 1). The initial flat portion of the DTPA curve indicate the deprotonation and complexation region of DTPA below pH 2.5, Therefore in alkaline medium it can completely engrave the metals. For CDTA and EDTA titration, a sharp rise in the titration curves observed at lower pH (Fig 1), showing no deprotonation. It means that these ligands are not available in dissociated state in acidic medium, and either weaker or no complex formation

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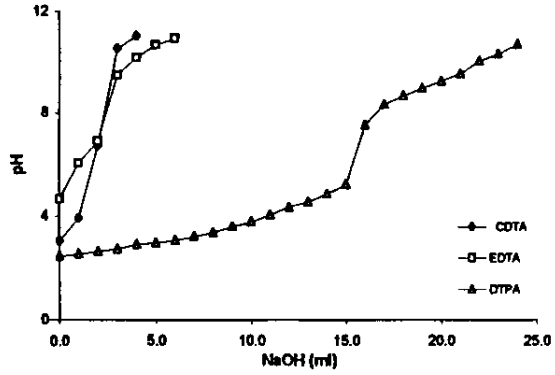

Fig 1: pH titrations of CDTA, DTPA and EDTA ligands against 0.10 M NaOH at 30 ±1°C

can take place below pH 5. From these observations, DTPA might be supposed as stronger chelating agent than EDTA as well as CDTA, following the order as DTPA>CDTA>EDTA.

In other titrations metal DTPA solution were titrated with base and it is found that DTPA form complex with Fe (III) at comparatively low pH (Fig 2), indicating that even if a little amount of dissociated ligand is available, FeDTPA complex will exist and it also explain the high stability constant of this complex. The stability of DTPA complex of iron (III) is 10^7 to 10^8 times greater than its complex with Pb (II) (Table 1). It can be presumed that in presence of Pb (II) in the solution of iron if pH < 2.5 iron remain fully complex while Pb (II) remain free in the mixture solution. When the pH of the mixture was increased by adding sodium hydroxide, due to increase in the available deprotonated ligand at specific concentration, DTPA start forms complex formation of Pb (II) also.

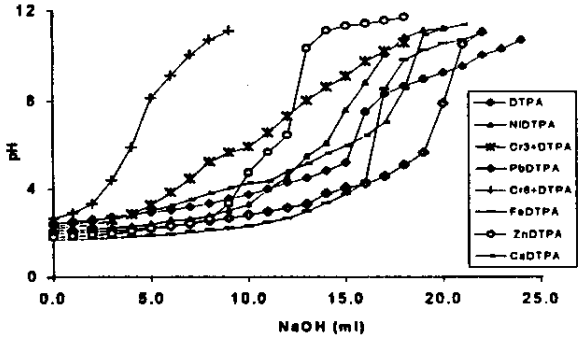

Fig 2: pH titrations of DTPA Metal Complexes against 0.1 M NaOH at 30 ±1°C

The titration curves with Zn(II) and Ca(II) showed that DTPA also chelate with these metals at pH below 2.5. In case of chromium, a weaker complexation was observed in trivalent form whereas in hexavalent state no complexation occur at pH 4. Ni(II) also showed complex formation at the similar pH.

From metal-CDTA curves (Fig 3) it has been found that Cr (III) formed considerable complex with CDTA somewhat more strongly than with DTPA, the titration curve shows complex formation in the lower region at the pH range above 4 as compared to that of Ca (II) and Zn (II) complexes. CDTA chelated Ni (II) in presence of Ca (II) at low pH. Whereas curve for the Pb (II) complex was in the lower region at pH below 4 and above 8 as compared to that of Ca (II).

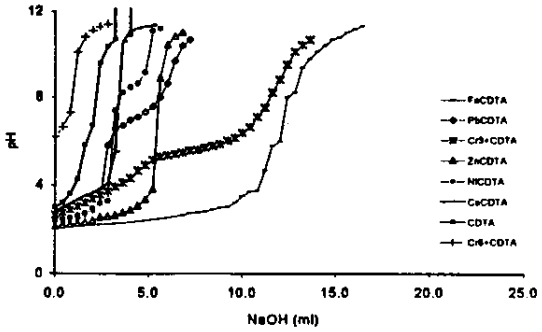

Fig 3: pH titrations of CDTA Metal Complexes against 0.1 M NaOH at 30 ±1°C

In Fig 4, the EDTA titration curves are shown. EDTA formed complex with Pb (II) in presence of Zn (II) as well as Ca (II) in the pH range below 4. It means that as compared to DTPA, the EDTA complexation is stronger with nickel than with Ca (II) in the range of pH below 4. EDTA formed its complex with trivalent chromium, at lower pH.

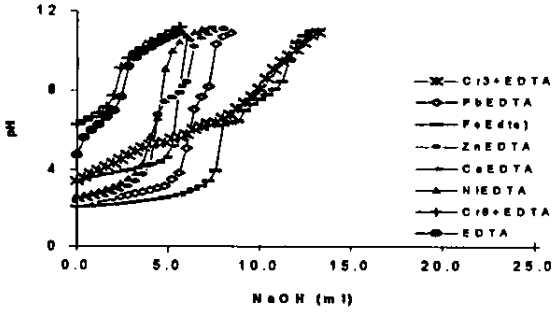

Fig 4: pH titrations of EDTA Metal Complexes against 0.1 M NaOH at 30 ±1°C

Experimental

Aqueous solution (1.5 x 10^{-2}M) of all the metal ions and PAC acids (CDTA, EDTA and DTPA) were prepared in deionized distilled water. Each metal solution was standardized with standard EDTA solution. Reaction mixtures were prepared by mixing equal volumes of standard metal ions and ligand solutions, in order to get 1:1 mole ratio. The concentration of metal and PAC acid were same in all cases, final volume (40.0 ml) and ionic strength (μ = 0.1M) was also kept constant. The solutions were individually titrated against standard alkali solution. The variation of pH was measured by a digital Orion pH meter Model SA-720 having resolution of ±0.01 pH with a glass electrode.

Conclusions

DTPA can chelate Pb (II), Zn (II) and Fe (III) below pH 2.5, whereas CDTA and EDTA do not form complexes with any metal ion at lower pH which infers that DTPA is a better chelating agent. It can chelate toxic metals in digestion track (e.g in stomach) at initial stage, if entering in the body by means of food. Therefore in presence of DTPA these toxic metals may not be available for absorption in the intestinal region where generally they are absorbed. Cr (VI) does not form complex with any of the PAC acids as it is obvious that chromium at higher oxidation state is not able to form complexes. Highest valances of metals can only form covalent molecules. For the complexation with Cr(VI) a ligand which also has reducing properties is required. In another set of experiments, reducing properties of these PAC acids are under observations. It is also observed that Ni(II), which shows weaker complexation in all cases, does not have an effective detoxification effect with these type of ligands. In case of DTPA, Fe (III) and Pb (II) chelate simultaneously below pH 4 so exchange can be studied.

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