Metal-Nitrilotriacetate-Penicillamine Ternary Complexes-Ionophoretic Studies

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The complexation data involving essential metal ions and bioactive ligands - nitrilotriacetate and penicillamine - give insight into many physicochemical processes. Iron and chromium are essential and benificial metals respectively [1]. Iron is an important constituent of the blood and tissue of the animal body. Most of the iron in the body is present as iron porphyrin or heme proteins [2]. Chromium(III) is an essential element for man and animals, required as a part of the glucose tolerance factor (GTF) for the initiation of peripheral insulin action [3]. The immune system of the body provides protection against foreign substances and pathogenic organisms. Chromium ion is reported to mediate immune response [4].

Ionophoretic mobility has been used to study binary and ternary complexes [5]. The present work is an extension of the technique for study of the systems containing ligands - penicillamine and nitrilotriacetate - with metal ions like Fe(II) and Cr(III).

EXPERIMENTAL

Ionophoresis equipment of systronic make (Naroda, India) Model 604 has been used. It has a built-in power supply (a.c. -d.c.) which is directly fed to a paper electrophoretic tank.

The electric current running through paper strips generates heat which causes evaporation of background electrolyte leading to serious error. In order to eliminate it, two hollow metallic plates, coated externally with thin paper plastics, have been used for sandwitching paper strips and thermostated water (35°C) is circulated through them. Measurements were made with an Elico (Hyderabad, India) Model L_{1-10} pH meter using glass electrodes.

Iron (III) and Chromium(III) carbonates were precipitated from a 0.1M solution of sulphates of Fe(III) and Cr(III) with a solution of sodium carbonate (AR grade chemicals, BDH, Poole, UK). Solutions of iron(III) and chromium(III) metal perchorate were prepared from this sample of pure carbonate.

Stock solutions of 9.0M perchloric acid, 2.0M sodium hydroxide and 0.5M penicillamine were prepared from AR grade chemicals (BDH). A 0.01M NTA solutions was prepared from the compound obtained from Merck.

The background electrolytes used in the study of binary complexes were 0.1M perchloric acid and 0.01M penicillamine / NTA. For the study of ternary system the background electrolytes used were 0.1M perchloric acid, 0.01M NTA and varying concentrations of 0.01M penicillamine. The ternary system was maintained at pH 8.5 by the addition of sodium hydroxide.

At the end of paper electrophoresis, Fe(III) spots were detected on the paper using

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potassium ferrocyanide solution (BDH) and Cr(III) with 1-(2 pyridylazo)-2 napthol (PAN) (E.Merck, Darmstadt, Germany). A saturated aqueous solution (0.9 mL) of silver nitrate was diluted with acetone to 20 mL. Glucose was detected as a black spot by spraying this solution followed by 2% ethanolic sodium hydroxide.

RESULTS AND DISCUSSION

(i) Metal(M)-penicillamine binary system

The plot of overall electrophoretic mobility of metal spot against pH gives a curve with three plateaus shown in Fig.1A. In region

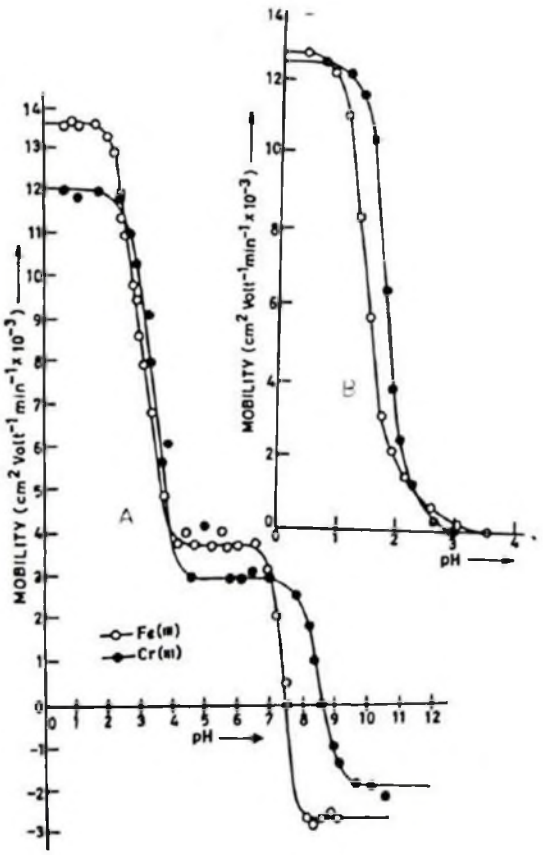


Fig 1 Mobility Curves vs pH
A Ligand - Penicillamine B Ligand NTA

of low pH (first plteau), concentration of $[(CH_3)_2\ C(SH)\ CH\ (NH^+_3)COOH]$ species of penicillamine is maximum and this species is non complexing. In the region of first plateau, metal ions are uncomplexed. Beyond this range, concentration of anionic species increases progressively with the increase of pH. Metal ion spots have progressively decreasing mobility. Complexation of metal ions should be taking place. Chemical literature indicates not much of liganding property to the zwitterion species [6,7]. It is therefore assumed that anionic species $[(CH_3)_2\ C(S^-)\ CH(NH_2)COO^-]$ of penicillamine has complexed with the metal ions to form complexes. Fig.1 reveals that first complex of Fe(III) and Cr(III) metal ions (second plateau) move towards negative electrode. This indicate cationic nature of (1:1) metal complex. Hence one $[(CH_3)_2\ C(S^-)\ CH(NH_2)COO^-]$ must have combined with metal ion to form $M[(CH_3)_2\ C(S)\ CH(NH_2)COO]^+$ complex cation.

With further increase of pH, mobility decreases giving rise to third plateau with negative mobility indicating anionic nature of metal complex. Two penicillamine anions must have combined with metal ions to give $[Fe[CH_3)_2\ C(S)\ CH(NH_2)COO]_2]^-$ and $[Cr[CH_3)_2\ C(S)\ CH(NH_2)COO]_2]^-$ for Fe(III) and Cr(III) respectively. Since there is no fourth plateau, 1:2 metal:ligand is the highest complex.

Stability constant (K values) of the complexes of metal ions with penicillamine ion is calculated using the relationship $K = 1/[L^{2-}]$ at the mean mobility betwen the plateaus. With the help of protonation constants of penicillamine ($pK_1 = 1.90$, $pK_2 = 7.85$, $pK_3 = 10.55$) [8,9] and pH at the mean mobility between two successive

plateaus, the concentration of penicillamine ion, $[L^{2-}]$ is determined at this pH and thus K can be calculated.

For calculating first stability constant K_1, the region between first and second plateau is partinent. The overall mobility is equal to the arithmatic mean of mobility of uncomplexed metal ion u_0 and that of first complex, u_1. Stability constant K_2 of second complex can be calculated by taking into consideration, the region between second and third plateau of mobility curve. These calculated values are given in Table 1.

Table 1

Stability Constants of Binary & Ternary Complexes

μ = 0.1 M; Temp. = 35°C;

NTA anion = $N(CH_2COO)_3^{3-}$;

Penicillamine anion (L) = $[(CH_3)_2C(S^-)CH(NH_2)COO^-]$

		logarithm of	
$K_1^{M}{}_{ML}$	$K_2^{M}{}_{ML2}$	$K_3^{M}{}_{M\,NTA}$	$K_4^{M\,NTA}{}_{M\,NTA\,L}$
Fe(III) complexes			
13.90	19.53	11.57	6.46
		16.33 [8]	
		15.90, 11.56 [9]	
		15.91, 16.25 [10]	
Cr(III) Complexes			
13.51	17.66	10.60	6.38
		8.74, 11.80 [8]	
		6.23 8.45 [9]	

(ii) Metal-nitrilotriacetate binary system

Fig. 1B shows the mobility curve of metal spots with nitrilotriacetate. The mobility of last plateau in each case is in zero region showing neutral nature of M(III)-nitrilotriacetate complexes. Only one NTA anion is assumed to combine with an trivalent metal ion to give 1:1 complexes. The complexation of metal ion with nitrilotriacetate may be represented as

$$M^{3+} + (N(CH_2COO)_3)^{3-} \xrightleftharpoons{K_3} [MN(CH_2COO)_3]$$

The stability constant K of binary complexes with NTA are calculated in the same manner as for amino acids. The calculated values are given in Table 1.

(iii) Metal-nitrilotriacetate-penicillamine system

The plot of mobility against log of concentration of added penicillamine gives a curve with two plateaus shown in Fig.2.

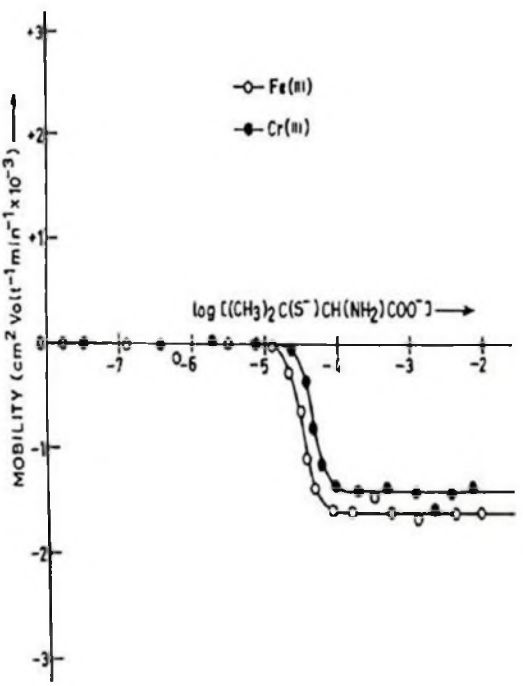


Fig.2 Mobility curves for the M-NTA-Penicillamine systems

It was observed from the study of M-penicillamine and M-nitrilotriacetate system that these complexes were formed at pH lower than 8.5. Thus, it would be proper to study the transformation of M(III)-NTA-penicillamine complex at pH 8.5 to avoid any side interaction. The mobility in last plateau does not agree wih the mobility of (1:1) and (1:2) M-penicillamine complex. It is inferred that the complex species corresponding to the last plateau is formed by the coordination of penicillamine anion with M-nitrilotriacetate moiety resulting in the formtion of (1:1:1) mixed complexes. This complexation is due to penicillamine ligand adding on to M-NTA binary complex. Hence overall mobility is given by

$$U = u_o f_{[M\text{-}NTA]} + u_1 f_{[M\text{-}NTA\text{-}L]}$$

where u_o, u_1 and $f_{[M\text{-}NTA]}$, $f_{[M\text{-}NTA\text{-}L}$ are mobilities and mole fractions of the [M-NTA] and [M-NTA-L] complexes respectively.

By substituting values of the mole fraction, above equation can be transferred into following useful form

$$U = \frac{u_o + u_1 K_4 [(CH_3)_2\ C(S^-)\ CH(NH_2)COO^-]}{1 + K_4\ [(CH_3)_2\ C(S^-)\ CH(NH_2)COO^-]}$$

The mixed stability constants K_4 is equal to $1/[(CH_3)_2\ C(S^-)\ CH(NH_2)COO^-]$ and the value of stability constants of mixed complexes are also include in Table 1.

CONCLUSION

It can be concluded from these studies that nitrilotriacetate and penicillamine can be used to reduce the level of Fe(III) and Cr(III) in living systems.

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