A Potentiometric Study of the Lead(II)–EDTA and Lead(II)–D-Penicillamine Systems

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Ethylenediaminetetraacetic acid (EDTA) and D-penicillamine (DPEN) have both been extensively used in the treatment of lead poisoning [1–4]. Their *modus operandi,* however, are distinctly different. EDTA complexes strongly with lead in plasma and is efficiently excreted. However, the highly charged $EDTA^{4-}$ species is unable to penetrate the cell membrane and mobilize lead held within the soft tissue. Conversely, DPEN forms a neutral complex, $PbDPEN^{0}$, intracellularly which can return to plasma once a favourable concentration gradient has been established.

Previous workers have employed computer simulations of *in vivo* equilibria [5] to explain medical observations arising from the treatment of cases of plumbism [2]. Such simulations are only as reliable as the formation constants used as computer input. Lead constants were not available at physiological conditions and so this note reports constants at 37 °C and with a background electrolyte of sodium chloride (150 mmol dm^{-3}). A more biologically relevant understanding of the Pb(II)–EDTA and Pb(II)–DPEN systems may thus prove useful in the treatment of lead poisoning.

Experimental

D-Penicillamine (Sigma Chemical Co.), was obtained as the anhydrous hydrochloride and stored under desiccation at 0–5 °C. (C, H, N *Anal.*: *Found,* C, 32.2; H, 6.60; N, 7.6%; *calcd* for $C_5ClH_{12}NO_2S$; C, 32.3; H, 6.51; N, 7.5%). D-Penicillamine solutions were freshly prepared each day.

Di-sodium ethylenediaminetetraacetic acid (BDH Chemicals) was prepared as a single stock solution and stored at room temperature. (C, H, N *Anal.*: *Found,* C, 32.0, H, 4.70, N. 7.30%; *calcd* for $C_{10}H_{18}N_2Na_2O_{10}$: C, 32.2; H, 4.87, N, 7.50%).

A standard stock solution of lead was prepared from the chloride (BDH Chemicals). Analysis for metal ion concentration was by complexometric EDTA titration [6] and for hydrogen ion concentration by Gran Plots [7]. All potentiometric titrations were carried out at 37 °C and I = 150 mmol dm^{-3} (sodium chloride).

Formation constants were evaluated from the titration data using the MAGEC [8], MINIQUAD [9] and ESTA [10] computer programs. ESTA was again employed to check the formation constants in a method similar to that of PSEUDOPLOT [11] used in previous work.

Results and Discussion

Lead(II)–D-Penicillamine

The proton–DPEN system, analysed by MAGEC and MINIQUAD cycling, gave three protonation constants in good agreement with previous workers [12, 13]. The pK values 10.64, 7.75 and 1.66, obtained from Table I, can be attributed to the –SH, $-NH_2$ and –COOH groups respectively.

TABLE I. Formation Constants for the Proton and Lead(II)–D-Penicillamine Interactions at 37 °C and I = 0.15 mmol dm^{-3} [NaCl].

$$\beta_{pqr} = \frac{[L_pM_qH_r]}{[L]^p[M]^q[H]^r}$$

p q r	$\log\beta_{pqr}$	Stnd. devn.	Sum of squares of residuals	MINIQUAD R Factor	n
1 0 1	10.64	0.004			
1 0 2	18.39	0.005	3.1×10^{-6}	0.003	280
1 0 3	20.05	0.007			
1 1 0	13.06	0.004			
1 1 1	16.28	0.033	5.5×10^{-7}	0.003	322
1 1 –1	7.33	0.067			

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TABLE II. Formation Constants for the Proton and Lead(II)–EDTA Interactions at 37 °C and I = 0.15 mmol dm^{-3} [NaCl].

p q r	$\log\beta_{pqr}$	Stnd. devn.	Sum of squares of residuals	MINIQUAD R Factor	n
1 0 1	9.14	0.002	5.7×10^{-6}	0.006	350
1 0 2	15.088	0.003			
1 1 0	18.62	0.014			
1 1 1	21.10	0.027	3.7×10^{-6}	0.006	325
1 1 2	23.03	0.018			

All titrations involving both metal and ligand were terminated at pH = 5.0 due to precipitation. MINIQUAD analysis of the titration data showed the 110 species to be predominant over the pH range covered (pH 2.0–5.0). Table I shows the final model to include the species 111 and 11 – 1. Formation of these two complexes was to a lesser extent than 110, however, their inclusion provided a better overall analysis of the system reflected in improved statistics. Comparison of the formation constant for 110 shows good agreement with previous workers [12–16], considering the different experimental conditions and techniques employed.

Corrie *et al.* [12] detected the bis-complexes 212, 211, 210 and 21 – 1 as well as 110 and 111 in their study. Formation constants for these complexes, with the exception of 210, were also evaluated from the present work but were not considered significant to the extent of inclusion into the final model (Table I).

Lead(II)–EDTA

Analysis of the proton-EDTA system revealed two constants (Table II) which are in good agreement with other workers [17–19]. EDTA is a strong complexing agent towards most metal ions, binding in a 1:1 ratio with the majority. Thus, analysis of the metal-ligand titration data resolved only three formation constants (Table II). The species 110 predominates throughout the titration, binding 60% of the total metal concentration by pH 3.0 and 100% by pH 5.0. The mono- and di-protonated species 111 and 112 are only significant at a pH < 4.0.

Numerous workers have studied the complexing ability of EDTA with metal ions, most notably G. Schwarzenbach and colleagues. A review of the formation constants of EDTA with Pb(II) and other metal ions has been compiled by G. Anderegg [20]. Although a direct comparison is not possible due to experimental variations, good agreement between the formation constant for 110 determined from this work, the tentative value proposed by Anderegg and the results of other workers [19, 21, 22] can be observed.

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