Selective Transport of Pb^{2+} and Cd^{2+} Across a Bilayer Membrane by a Cyclohexanetricarboxylic Acid-Capped Crown Ether

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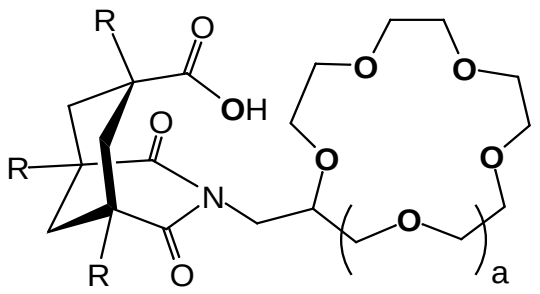
ABSTRACT. Recent studies have show that polyether carboxylic acid antibiotics such as monensin and nigericin have high transport activity and selectivity for Pb^{2+} relative to other divalent cations *(Hamidinia et al., J. Biol. Chem., 277, 38111-38120 (2002); Biochemistry, 43, 15959-15965 (2004)*. Because these natural products are difficult to modify, structure-activity studies require synthetic monocarboxylic acid ionophores that allow systematic variation of key structural and chemical properties such as the number of ether groups and hydrophobicity. A compound having these characteristics (see Figure 1) was prepared by the reaction of an equimolar mixture of 2-aminomethyl-15-crown-5 and *c i s,cis*-1,3,5-tripropyl-1,3,5-cyclohexanetricarboxylic acid to give the ionophore P3CTA-15C5 (a =1, R = *n*-C_3H_7).



a = 1, 2; R = H, CH_3, *n*-C_3H_7

Figure 1. General structure of crown ether based monocarboxylic acid ionophores.

Transport studies using phospholipid vesicles, shown in Figure 2, reveal that P3CTA-15C5 has high selectivity for Pb^{2+}, and to a lesser extent, for Cd^{2+} over other divalent cations. Based on the ratio of initial transport rates, the selectivity factors for Pb^{2+} and Cd^{2+} over Ca^{2+} are 280 and 70, respectively. Concentration studies show that the transport rate has a first-order dependence on ionophore concentration at fixed concentrations of Pb^{2+} and Cd^{2+}. The reaction order for $Pb^{2+}$and Cd^{2+} is more complex, going from second order to first order as the cation concentration is increased. The transport rate for Pb^{2+} goes through a maximum at pH ~6.5. In contrast to the behavior found for the naturally occurring antibiotics, P3CTA-15C5 transports $Pb^{2+}$and Cd^{2+} by an electrogenic mode.

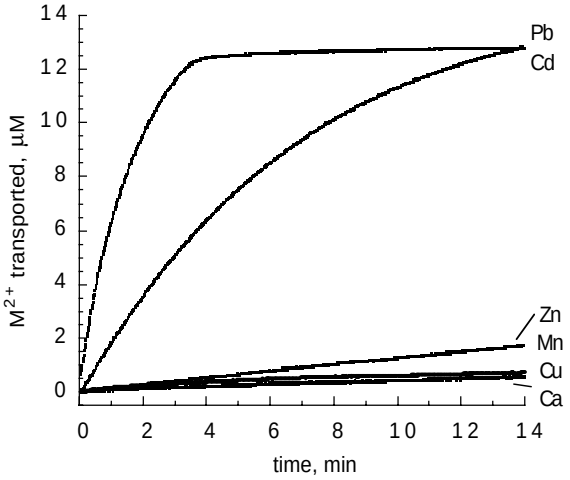


Figure 2. Relative efficiency of divalent cation transport into phospholipid vesicles at pH = 7.0

These results are consistent with a mechanism involving cation transport via a unipositive 1:1 complex (ML^+) with countertransport of H^+ (as HL) to complete the cycle.

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