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 \(\text{cis,cis-1,3,5-tripropyl-1,3,5-}\)cyclohexanetricarboxylic acid to give the ionophore P3CTA-15C5 (\(a=1, R=n-C_3H_7\)).

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 \(\sim 6.5\). 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.