The Ionophore Nigericin Transports Pb^{2+} With High Activity and Selectivity: A comparison to monensin and ionomycin

Shawn A. Hamidinia*, Bo Tan‡, Warren L. Erdahl*, Clifford J. Chapman*,
Richard W. Taylor‡ and Douglas R. Pfeiffer*

From the Department of Molecular and Cellular Biochemistry*,
The Ohio State University, Columbus, Ohio 43210 and the Department of Chemistry and Biochemistry‡, University of Oklahoma, Norman, Oklahoma 73019

The K^+ ionophore nigericin is shown to be highly effective as an ionophore for Pb^{2+}, but not other divalent cations, including Cu^{2+}, Zn^{2+}, Cd^{2+}, Mn^{2+}, Co^{2+}, Ca^{2+}, Ni^{2+}, and Sr^{2+}. Among this group a minor activity for Cu^{2+} transport is seen, while for the others activity is near or below the limit of detection. The selectivity of nigericin for Pb^{2+} exceeds that of ionomycin or monensin and arises, at least in part, from the high stability of nigericin-Pb^{2+} complexes. Plots of log rate vs. log Pb^{2+} or log ionophore concentration (Fig.1), together with the pH dependency of transport and complexation (Fig. 2), indicate that nigericin transports Pb^{2+} via the species PbNigOH, and by a mechanism that is predominately electroneutral.

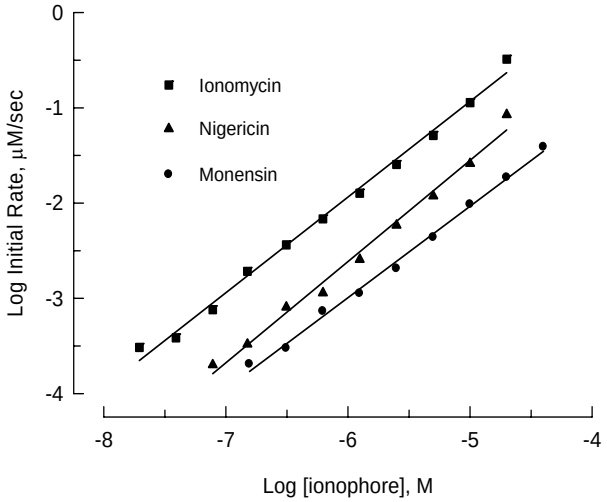

Figure 1. Relationships betweenl log ionophore concentration and log of the Pb^{2+}transport rate for ionomycin, nigericin, and monensin. Rates were determined using unilamellar POPC vesicles loaded with the chelating indicator Quin-2. The free Pb^{2+}concentration was buffered at 1.0×10^{-8} M, using citrate, and ionophore concentration was varied as shown. For further details see S. A. Hamidinia et.al. (2004) Biochemistry 43, 15956-15965.

As with monensin and ionomycin, a minor fraction of activity may be electrogenic, based upon a stimulation of rate that is produced by agents which prevent the formation of transmembrane electrical potentials. Nigericin catalyzed Pb^{2+} transport is not inhibited by physiological concentrations of Ca^{2+} or Mg^{2+} and is only modestly affected by K^+ and Na^+ concentrations in the range of 0-100 mM. These characteristics, together with higher selectivity and efficiency suggest that nigericin may be more useful than monensin in the treatment of Pb intoxication, although the toxicity of this compound might be a problem (see related poster by Steinbaugh et.al).

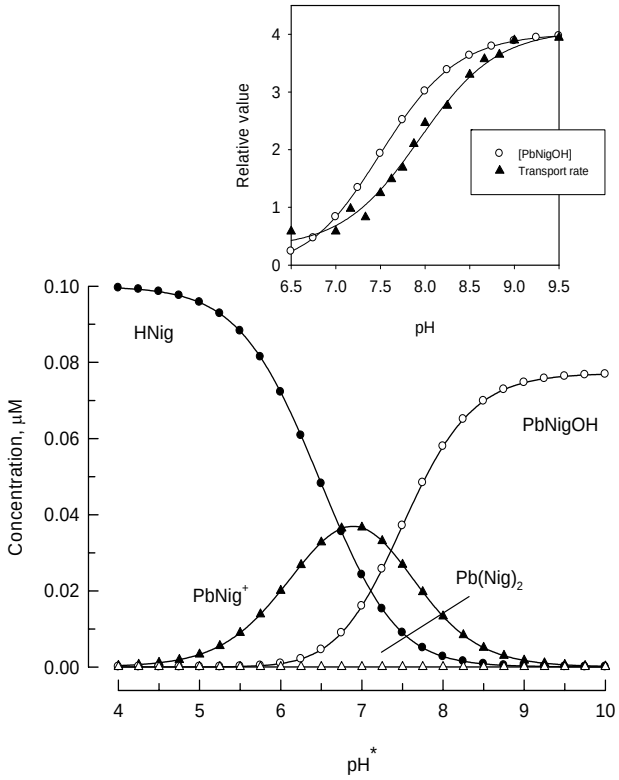

Figure 2. Species distribution diagram showing the prevalence of selected nigericin-Pb^{2+} species as a function of pH. Individual concentrations are calculated using equilibrium constants determined in 80% methanol-water solutions for nigericin and free Pb^{2+} concentrations of 1.0×10^{-7} M each. The inserted panel shows the correlation between transport rate and formation of PbNigOH as a function of pH.