EFFECT OF MERCURY ON SODIUM ALANINE CO-TRANSPORT IN BASOLATERAL LIVER PLASMA MEMBRANES ISOLATED FROM RAJA ERINACEA

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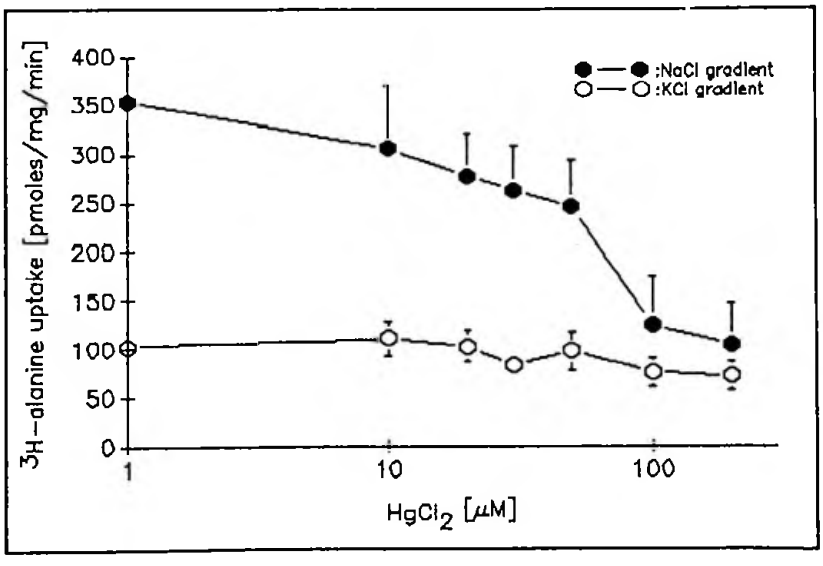
Alterations in electrolyte and substrate transport induced by mercury have been documented in various species and tissues (Rothstein,A. in Current Topics in Membranes and Transport, Bronner, F. & Kleinzeller, A. Eds., pp 135-176, Academic Press, New York. 1970; Kinter, W.B. & Pritchard, J.B., Handbook of Physiology-Reactions to Enviromental Agents, Lee, D.H.K., Ed. pp 563-576, Am. Physiol. Soc., 1977). The plasma membrane is clearly one target for these mercury induced alterations. However, it is difficult to distinguish primary effects of the heavy metal on the membrane from secondary or indirect effects due to inhibition of intracellular metabolic processes by mercurials (Clarkson, T.W. Ann. Rev. Pharmacol. 12: 375-406, 1972). In our previous study on isolated hepatocytes from Raja erinacea we have demonstrated several effects of mercurials on the transport properties of the plasma membrane including an inhibition of sodium dependent alanine uptake and Na^+,K^+-ATPase as well as an increase in K^+ permeability (Ballatori,N., Shi, C. & Boyer, J.L. Tox. Apppl. Pharmacol. 95: 279-291, 1988).

Because $HgCl_2$ could inhibit sodium alanine co-transport by secondary effects related to changes in the sodium gradient or the membrane potential rather than a direct effect on the carrier, we examined the effect of $HgCl_2$ on ^{3}H-alanine uptake into plasma membrane vesicles isolated from the liver of the little skate (Raja Erinacea), using a rapid filtration technique.

^{3}H-alanine uptake into liver plasma membrane vesicles was stimulated by an out to in sodium gradient, linear up to 2 minutes and saturable with increasing alanine concentrations. Initial rates of ^{3}H-alanine uptake in the presence of the out to in sodium gradient were significantly decreased when the vesicles were preincubated with 10-200 μM $HgCl_2$ for 5 minutes at 25 °C. In contrast, alanine uptake in the presence of an out to in potassium gradient was not changed (Fig.).



At high $HgCl_2$ concentrations (≥100 μM) intravesicular volume (as assessed by the intravesicular alanine content after 2 hrs.) was reduced and was then associated with a reduction in initial uptake rates in the absence of sodium.

To determine whether $HgCl_2$ inhibited sodium dependent alanine uptake by increasing sodium permeability (Will, P.C. & Hopfer, U., J. Biol. Chem. 254: 3806-3811, 1979), we examined the effect of 75 μM $HgCl_2$ on alanine, ^{3}H-alanine exchange with equilibrated ion concentrations of either NaCl or KCl. Preincubation of membrane vesicles with $HgCl_2$ for 5 minutes at 25 °C resulted in a 50 % inhibition of the initial rates of alanine, ^{3}H-alanine exchange in the presence of sodium. In contrast, alanine, ^{3}H-alanine exchange in the absence of sodium was significantly lower, but was not altered by preincubation with $HgCl_2$.

The present data suggest that $HgCl_2$ has a direct inhibitory effect on sodium alanine co-transport in liver plasma membranes. $HgCl_2$ may also effect alanine uptake by effects due to alterations in membrane permeability.

(Supported by NIH grants Dk 25636, DK 34989; NIEHS grant IS 03828; and DFG grant Se 481/1-2)