EFFECT OF CADMIUM ON SODIUM ALANINE COTRANSPORT IN RENAL BRUSH BORDER MEMBRANES ISOLATED FROM THE WINTER FLOUNDER (PSEUDOPLEURONECTES AMERICANUS): TIME DEPENDENCE, SENSITIVITY AND REVERSIBILITY

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In order to further elucidate the inhibitory action of cadmium on the sodium alanine cotransport system in flounder kidney (E. Kinne-Saffran et al., Bull. MDIBL 26:18-20, 1986) brush border membrane vesicles were isolated by differential calcium precipitation and alanine uptake was studied by a rapid filtration method (Eveloff et al., J. Comp. Physiol. 135:175-182, 1980).

Incubation of isolated membrane vesicles with 100 μM cadmium chloride led to a time dependent inhibition of sodium alanine cotransport. The inhibition of the sodium-dependent alanine uptake was 20% after 10 minutes, 48% after 30 minutes, and 67% after 60 minutes. Alanine uptake in the absence of sodium and sodium D-glucose cotransport remained constant, indicating a specific effect of Cd on the sodium alanine cotransport system. When uptake after 30 minutes of preincubation in various cadmium concentrations was determined half maximal inhibition was found at a nominal cadmium concentration of 150 μM (11.2 ppm), this concentration corresponds to a free cadmium activity of 15 μM (1.1 ppm), as measured by a cadmium-sensitive electrode.

In order to investigate the reversibility of the cadmium inhibition membranes were first incubated with 100 μM cadmium for 30 minutes and then exposed for 30 minutes to 1 mM EDTA. This treatment did not affect sodium alanine cotransport in control membranes nor in cadmium pretreated membranes, i.e. the inhibition of sodium alanine cotransport by cadmium was not reversed by EDTA. EDTA, however, drastically reduced the amount of cadmium bound to the membranes as well as the free cadmium concentration in the incubation medium.

These studies indicate that the apparent affinity of the sodium alanine cotransport system to cadmium in vitro lies in the range of the cadmium concentrations found in renal tissue in studies where acute effects of Cd on renal amino acid reabsorption in the rat were observed by Lindner and Foulkes (Env. Res. 36:241-247, 1985). The striking time dependence of the inhibition as well as the apparent irreversibility suggest that cadmium interacts with sites of the transporter either deeply embedded in the membrane or located at the inner surface of the membrane vesicles. Furthermore, chronic exposure to cadmium might have a much more detrimental effect on sodium alanine cotransport than acute exposure.

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