MERCURY REVERSIBLY BLOCKS APICAL K CHANNELS IN THE URINARY BLADDER OF THE WINTER FLOUNDER, PSEUDOPLEURONECTES AMERICANUS.

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The isolated urinary bladder of the winter flounder actively secretes potassium and this net flow can be measured as a serosa to mucosa short circuit current (I_{sc}). Previous studies provided evidence that K secretion could be described by a model which included active K uptake across the basolateral membrane via a Na/K ATPase and passive K exit across the apical membrane via K channels which are reversibly blocked by the divalent cation, barium (Bull. M.D.I.B.L. 20:84, 1982). The aim of the present experiments was to test the effects of a heavy metal ion, Hg^{++}, on apical K channels. Our results were consistent with the notion that mercury is a potent, reversible blocker of apical K channels.

Portions of flounder urinary bladder were mounted as flat sheets in Ussing chambers as previously described (Bull. M.D.I.B.L. 19:46, 1981) and bathed on both sides by Ringer's solutions containing (in mM) Na: 147.5, Cl: 147.5, K: 2.5, Ca: 1.5, Mg: 1.0, glucose: 10.0, HEPES: 15.0. Mucosal and serosal solutions were stirred with air and the pH at room temperature was approximately 7.5. The serosal solution also contained verapamil (50 μM) to inhibit smooth muscle contractions. The short circuit current, I_{sc}, was measured as previously described and was recorded continuously on a strip chart recorder. Mercuric chloride ($HgCl_2$) and dithiothreitol (DTT) were added to the bathing solution in a small volume of concentrated aqueous solution.

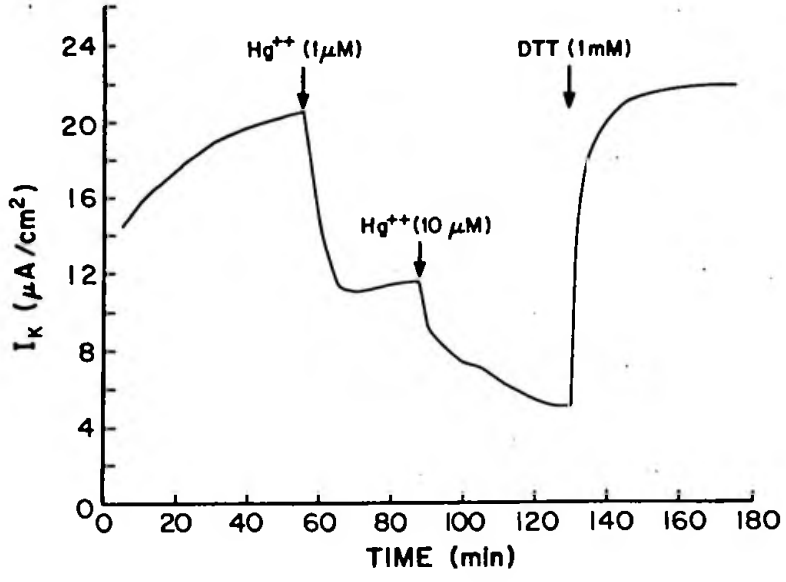

Figure 1 shows the results of a representative experiment. The addition of 1 uM $HgCl_2$ to the mucosal bath resulted in a rapid reduction in I_{sc} to about 50% of the original value. Raising the mucosal concentration of Hg to 10 uM further reduced I_{sc} to about 25% of the initial value. I_{sc} was restored to the control value by the addition of 1 mM dithiothreitol to the mucosal bath. The use of DTT was based on the presumption that the highly toxic Hg^{++} might react with K channel proteins by forming a covalent, Hg-S (mercaptide) bond. Subsequent experiments, however, (not shown) showed that simply washing the tissue was equally effective, suggesting that the Hg^{++}-membrane interaction did not involve the formation of a covalent bond. It seems likely that the reversal of inhibition by DTT was the result of a simple mass action effect due to the complexation of the Hg^{++} in the solution by DTT.

These results are consistent with the notion that inorganic mercury is a potent, reversible blocker of epithelial K channels. The fact that the inhibition is readily reversed simply by washing suggests that the ion is not interacting with SH groups to form a covalent bond. Rather, the action of the ion may be similar to that of barium which appears to block some K channels by entering and occluding the pore. This work was supported by grants from NIH (AM32901 and AM29786).