

Possible thiol group involvement in intracellular pH effect on low- conductance Ca²⁺-dependent K⁺ channels

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We have studied the effect of intracellular pH (pH(i)) shifts on the activity of Ca²⁺-dependent, inwardly rectifying K⁺ channels of HeLa cells. Recordings of macroscopic currents in symmetrical 145 mM K⁺ and internal pH of 7.4 gave moderate inward rectification of the current. At pH 6.4, inward rectification was more marked, whereas it switched to outward rectification at pH 8.2. In excised inside-out membrane patches, similar changes in pHi did not affect the single-channel conductance of the channels underlying the Ca²⁺-dependent K⁺ currents. At neutral pH, the open state probability (P₀) was independent of voltage in the range from -70 to 70 mV. At alkaline pH, P₀ became voltage dependent, decreasing at negative potentials and increasing with depolarization compared with pH 7.4. These changes accounted for the pH-dependent changes in rectification of the macroscopic current. The possibility that voltage dependence might arise from the ionization of a thiol group was tested by using