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Spermine Modulation of Maxi-K Channels in Gastric Smooth Muscle Cells

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Polyamines are polyvalent cations which are ubiquitously present in pro- and eukaryotic cells. In the present study we investigated the action mechanism of spermine^{+4} (C_{10}), a natural polyamine, on the large-conductance Ca^{2+}-activated K (maxi-K) channel using excised patches from the human gastric smooth muscle. Exposure of the cytoplasmic side of inside-out patches to spermine produced two different effects on maxi-K channel activity: (1) reduction of the unitary current amplitude (i), and (2) increase of the open probability (NP_o), in a dose-dependent manner. The reduction of unitary current amplitude showed voltage dependence (marked effect under positive voltages), indicating that spermine acts as the blocker which sense a fraction of the electrical field in the channel pore. Channel block was characterized by a voltage-dependent dissociation constant [$V_D(V)$] for the binding of spermine to a blocking site located a fraction of the distance across the membrane field (δ). The intracellular spermine binding site had a $K_D(0)$ of 53.1 mM (Hill number, 0.35 ~ 0.45) and an effective valency, $z\delta$ of 1.27 (δ=-0.32). From these values, it was deduced that the middle of spermine is flexible enough to allow it to bend double so as to let multiple charges enter the channel pore. Increase of channel open probability by the spermine showed weak voltage dependence. Elevating concentration of K^+ or impermeable Na^+ into the cytoplasmic side dose-dependently reduced spermine's effects on the i as well as the NP_o.