

No. 9631

The Relation of Chloride Channels and Cytoprotective Mechanism
in Gastrointestinal Cells.

Hideki Sakai, Akira Ikari, Noriaki Takeguchi

Faculty of Pharmaceutical Science, Toyama Medical and Pharmaceutical University

Summary

The membrane potential of rabbit gastric parietal cells is dominated by a chloride (Cl^-) channel with a subpicoSiemens single channel conductance in the basolateral membrane. The effect of ecabapide, a vasodilator, on the opening of this Cl^- channel, the cGMP content and the intracellular free Ca^{2+} concentration ($[\text{Ca}^{2+}]_i$) of parietal cells were investigated by patch-clamp technique, enzyme immunoassay and Fura 2-fluorescence measurement. Furthermore, we investigated cytoprotective function of this channel. Ecabapide stimulated the opening of the Cl^- channel as determined by the reversal potential. Both the basal and ecabapide-induced openings of the channel were inhibited by NPPB, a Cl^- channel blocker. The power spectra of the currents before and after the addition of ecabapide were analyzed. Both spectra contained only one Lorentzian ($1/f^2$) component. LY83583, which prevents activation of soluble guanylate cyclase, significantly inhibited both the basal and ecabapide-induced openings of the Cl^- channel. Ecabapide concentration-dependently elevated the cGMP content in the parietal cell-rich suspension. In single Fura 2-loaded parietal cells, ecabapide did not increase $[\text{Ca}^{2+}]_i$. Our results indicate that ecabapide stimulates an intracellular production of cGMP in the parietal cell without increasing $[\text{Ca}^{2+}]_i$, and leads to an activation of the housekeeping Cl^- channel. On the other hand, dibutyryl cGMP showed cytoprotective effect on the BCECF-loaded isolated parietal cell against ethanol. The cytoprotective effect of dibutyryl cGMP was abolished when the Cl^- channel was inhibited by NPPB. We suggest that ecabapide elevates the cGMP contents, resulting in the opening of the Cl^- channel in the basolateral membrane. Therefore, the Cl^- channel is the target of the cytoprotective mechanism in the parietal cell.