Inhibition of the human epithelial calcium channel TRPV6 by 2-aminoethoxydiphenyl borate (2-APB).

Kovacs G, Montalbetti N, Simonin A, Danko T, Balazs B, Zsembery A, Hediger MA.

Institute of Biochemistry and Molecular Medicine, University of Bern, Bern, Switzerland; Swiss National Centre of Competence in Research, NCCR TransCure, University of Bern, Bern, Switzerland.

Abstract

TRPV6, a highly calcium-selective member of the transient receptor potential (TRP) channel superfamily, is a major pathway for calcium absorption in the fetal and adult body. It is expressed abundantly in the duodenum, the placenta and exocrine tissues. TRVP6 was postulated to contribute to store-operated calcium channel (SOC) activity in certain cell types such as exocrine cells. In this study, we tested 2-APB, a widely used SOC inhibitor on human TRPV6 (hTRPV6) activity using fluorescence imaging, patch clamp and radioactive tracer techniques in transiently and stably transfected HEK293 cells. We found that the basal calcium and cadmium influx was higher in HEK293 cells transfected with hTRPV6 than in non-transfected cells. 2-APB inhibited hTRPV6 activity in both transient and stably transfected cells. This effect was slightly sensitive toward extracellular calcium. The extracellular sodium concentration did not affect the inhibition of hTRPV6 by 2-APB. However, N-methyl-d-glucamine significantly diminished the inhibitory effect of 2-APB presumably through direct interaction with this compound. Furthermore, 2-APB inhibited the activity of TRPV6 orthologs but not human TRPV5. 2-APB may serve as a parental compound for the development of therapeutic strategies specifically targeting the hTRPV6 calcium channel.