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Chlorpromazine Inhibits Store-operated Calcium Entry and Subsequent Norepinephrine Secretion in PC12 Cells

[1]Se-Young Choi*, [1]Yong-Hyun Kim, [2]Yong-Kyu Lee, and [1]Kyong-Tai Kim

[1]Department of Life Science, Pohang University of Science and Technology, Pohang, Republic of Korea. [2]Department of Food Engineering, Dongseo University, Pusan, Republic of Korea

The effect of chlorpromazine on the store-operated Ca^{2+} entry subsequently activated via the phospholipase C signaling pathway was investigated in PC12 cells. Chlorpromazine caused a rapid decline of the bradykinin-induced Ca^{2+} increase to basal level without attenuating the peak level. However, chlorpromazine did not inhibit bradykinin-induced inositol 1,4,5-trisphosphate production. Chlorpromazine inhibited the bradykinin-induced norepinephrine secretion in a concentration-dependent manner. The inhibition overlapped the inhibitory action of SK&F96365, an inhibitor of store-operated Ca^{2+} entry (SOCE). To test for a direct effect of chlorpromazine on SOCE, thapsigargin, an inhibitor of microsomal Ca^{2+}-ATPase, was used to induce SOCE in PC12 cells. Chlorpromazine reduced the thapsigargin-induced sustained Ca^{2+} level, and the inhibition also overlapped the inhibitory action of SK&F96365. The results suggest that chlorpromazine negatively modulates SOCE activated subsequent to PLC activation.