**STORE OPERATED Ca2+-CHANNEL BLOCKERS AS A POTENTIAL THERAPY FOR HYPERTENSION**

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**Background and Objectives:** Hypertension is invariably associated with elevated levels of intracellular Ca2+, which is determined by the functional status of both L-type Ca2+-channels and store-operated Ca2+channels as well as Na+-Ca2+ exchange system in the vascular smooth muscle. Although L-type Ca2+-antagonists such as verapamil are known to exert anti-hypertensive actions, the effects of store-operated blockers such as SKF-36365(SK) on blood pressure, [Ca2+]i in smooth cells and cell proliferation have not been examined.

**Methods:** The blood pressure in rats was measured by using microtip pressure transducer, changes in [Ca2+]iin rat aortic smooth cells were monitored by Fura-2 AM technique and cell proliferation was determined by thymidine incorporation in the cells.

**Results and Discussion:** In this study, SK was observed to reduce systolic and diastolic blood pressures in rats in a dose and time dependent manner. While SK showed no effect on basal [Ca2+]i in aortic smooth muscle cells, the increase in [Ca2+]i due to lysophosphatidic acid (LPA) or angiotensin II was depressed by this agent. On the other hand, norepinephrine- or the endothelin-induced increase in [Ca2+]i was not affected by SK. The cell proliferation, as determined by cell number as well as thymidine incorporation in the absence or presence of LPA, was reduced by SK. This agent was also observed to augment the verapamil-induced reduction in diastolic blood pressure without any effect on the verapamil-induced reduction in systolic blood pressure. In addition, verapamil was found to depress LPA-induced or ATP-induced increase in [Ca2+]i; these actions of verapamil were potentiated by SK.

**Conclusions:** The results suggest that store-operated Ca2+-channel blockers, which affect sites different from those for L-type Ca2+-channel antagonists, either alone or in combination, may be useful for the treatment of hypertension.