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Title	EFFECTS OF TYROSINE KINASE INHIBITORS AND NON-SELECTIVE CATION CHANNEL BLOCKERS ON CAPACITATIVE Ca <sup>2+</sup> ENTRY IN RAT ILEAL SMOOTH MUSCLES
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greatly potentiated by Bay K 8644.

7. These results suggest that CA secretion evoked by  $\text{Ca}^{2+}$ -reintroduction, high  $\text{K}^+$  and the removal of extracellular  $\text{Na}^+$  and  $\text{Ca}^{2+}$  is mainly

mediated by  $\text{Ca}^{2+}$  entered through L-type voltage dependent  $\text{Ca}^{2+}$  channels in adrenal chromaffin cells.

## EFFECTS OF TYROSINE KINASE INHIBITORS AND NON-SELECTIVE CATION CHANNEL BLOCKERS ON CAPACITATIVE $\text{Ca}^{2+}$ ENTRY IN RAT ILEAL SMOOTH MUSCLES

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1. The present experiment was performed to examine the involvement of tyrosine kinase and non-selective cation channels in capacitative  $\text{Ca}^{2+}$  entry (CCE) in the rat ileal smooth muscles. The effects of tyrosine kinase inhibitors (genistein and tyrphostin 47), an inactive analogue of genistein (daidzein), non-selective cation channel blocker (SK & F96365) and  $\text{Ca}^{2+}$  entry blocker (tetrandrine) were examined in the presence of methoxyverapamil.

2. In the presence of external  $\text{Ca}^{2+}$ , carbachol-induced sustained contractions were dose-dependently inhibited by genistein, daidzein, tyrphostin 47, SK & F96365 and tetrandrine.

3. Under  $\text{Ca}^{2+}$ -free conditions, after the depletion of stored  $\text{Ca}^{2+}$  by carbachol or caffeine, the application of  $\text{Ca}^{2+}$  evoked transient contractions due to CCE. These contractions were inhibited by genistein, daidzein, tyrphostin 47, SK & F96365 and tetrandrine. The inhibitory potency of genistein was greater than that of daidzein. The application of  $\text{Ca}^{2+}$  evoked sustained contractions due to CCE after the depletion of stored

$\text{Ca}^{2+}$  with the treatment of thapsigargin. These five drugs also inhibited the contraction, but the potency of daidzein was greater than that of genistein.

4. SK & F96365 produced no inhibitory effects on the carbachol- and caffeine-induced contractions due to  $\text{Ca}^{2+}$  released from  $\text{Ca}^{2+}$  store. Genistein, daidzein and tyrphostin 47 inhibited these contractions. However, these drugs were less effective in inhibiting the contraction evoked by  $\text{Ca}^{2+}$  release than that by CCE. Tetrandrine inhibited contraction induced by carbachol but not caffeine.

5. Genistein slightly suppressed  $\text{Ca}^{2+}$ -induced contractions in  $\beta$ -escine treated skinned fibers.

6. These results suggest that CCE induced by carbachol and caffeine may be mediated by tyrosine kinase and this pathway is sensitive to SK & F96365 and tetrandrine. However, the inhibitory effects on CCE were produced by not only genistein but also daidzein, indicating that further studies are necessary to evaluate this hypothesis.