EFFECTS OF K^+ ON Ca^{2+} INFLUX AFTER DEPLETION OF INTRACELLULAR Ca^{2+} STORES IN ILEAL SMOOTH MUSCLE OF THE RAT

Mitsuyasu TABO

Laboratory of Pharmacology,
Department of Biomedical Sciences,
School of Veterinary Medicine,
Hokkaido University, Sapporo 060, Japan

1. The present experiment was performed to examine the effects of K^+ on a rise in intracellular Ca^{2+} level ($[Ca^{2+}]_i$) and a contraction induced by application of Ca^{2+} when intracellular Ca^{2+} stores were transiently or continuously depleted in fura-2-loaded longitudinal smooth muscle strips of the rat ileum.

2. After transient depletion of Ca^{2+} stores with carbachol (0.1 mM), application of Ca^{2+} caused a rise in $[Ca^{2+}]_i$ and a contraction, both of which were increased with increasing K^+ concentrations ($[K^+]_0$) applied simultaneously. The effect of K^+ was inhibited by methoxyverapamil (10 μM) and potentiated by Li^+ (10 mM).

3. After application of Ca^{2+} together with various concentrations of K^+ under Ca^{2+}-free conditions, carbachol caused a rise in $[Ca^{2+}]_i$ and a contraction, both of which increased ($[K^+]_0 < 40$ mM) or decreased (>40 mM) depending on the K^+ concentration used. The increasing effect of K^+ was inhibited by methoxyverapamil.

4. The intracellular Ca^{2+} stores were continuously depleted by pretreatment with thapsigargin or ryanodine. Under these conditions, the rise in $[Ca^{2+}]_i$ and contraction induced by application of Ca^{2+} were dose-dependently and markedly increased even in the presence of methoxyverapamil or nifedipine.

5. The rise in $[Ca^{2+}]_i$ and contraction induced by Ca^{2+} after treatment with thapsigargin or ryanodine were inhibited by the replacement of Na^+ with K^+. The inhibition by K^+ was attenuated by increasing the extracellular Ca^{2+} concentration.

6. The influx of Mn^{2+} was much greater in tissues pretreated with thapsigargin or ryanodine than in intact tissues. The enhanced Mn^{2+} influx was inhibited by the replacement of Na^+ with K^+.

7. These results suggest that the Ca^{2+} are replenished by Ca^{2+} stores passing through a voltage-dependent Ca^{2+} channel and another unknown pathway, when the intracellular Ca^{2+} stores are transiently depleted by an agonist in ileal smooth muscle of the rat. On the other hand, Ca^{2+} entry through another unknown pathway is markedly increased by continuous depletion of Ca^{2+} stores with thapsigargin or ryanodine, which is inhibited by increasing $[K^+]_0$. The inhibitory effect of K^+ on Ca^{2+} entry might be due to the reduction of the electrochemical gradient for Ca^{2+} across the plasma membrane.