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EFFECTS OF CYCLIC AMP ON CONTRACTILE RESPONSES AND INTRACELLULAR Ca MOBILIZATION OF GASTRIC SMOOTH MUSCLE OF THE RAT

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This experiment was performed to study the effects of pertussis toxin or cholera toxin on the contraction induced by carbachol (CCh) and on the inhibitory action of VIP to CCh-induced contraction. The effects of dibutyryl cAMP (db-cAMP) on the intracellular Ca store in antral smooth muscles of the rat were also studied.

1. Pertussis toxin or cholera toxin did not affect contraction induced by CCh and the inhibitory action of VIP on CCh-induced contraction.
2. When the tissue was exposed to 2.5mM Ca and 150mM K solution in order to load Ca into the intracellular Ca store, a contractile response was evoked (Ca-contraction). After washing the tissue with Ca-free solution, application of CCh evoked a contraction in a dose-dependent manner and subsequent application of caffeine evoked a small contraction but CCh did not.
3. The Ca-contraction was developed in a K or Ca concentration-dependent manner and was blocked by nifedipine.
4. The contraction induced by caffeine was increased with increasing K or Ca concentrations during Ca-loading. The contraction was abolished by ryanodine.
5. Dibutyryl-cAMP inhibited Ca-contraction, but enhanced caffeine-induced contraction. The extent of the enhancement of the caffeine-induced contraction by db-cAMP depended on K or Ca concentration. However, when db-cAMP was applied after the period of Ca-loading, there was little influence on the caffeine-induced contraction.
6. In fura-2 loaded preparations, the Ca-contraction and the caffeine-induced contraction were accompanied by an increase in intracellular Ca level, $[Ca]_i$, in K or Ca concentration dependent manner during Ca-loading. Dibutyryl-cAMP inhibited the Ca-contraction, but not the increase in $[Ca]_i$. Furthermore, db-cAMP hardly affected the elevation of $[Ca]_i$ concomitant with the contraction induced by caffeine.
7. Ryanodine abolished the contraction and the increase in $[Ca]_i$ in response to caffeine. After ryanodine treatment, db-cAMP inhibited the Ca-contraction to the same extent as that of the untreated.
8. It is concluded that db-cAMP stimulates Ca uptake into the intracellular Ca store, without affecting Ca leakage from the store. The inhibition of the Ca-contraction by db-cAMP may result from decreased sensitivity of contractile machinery to $[Ca]_i$ in the gastric smooth muscle.