THE INHIBITORY EFFECTS OF CYCLIC NUCLEOTIDES ON THE CONTRACTILE RESPONSES OF THE GASTRIC SMOOTH MUSCLE OF THE RAT

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The inhibitory effects of forskolin, nitroprusside and membrane permeable cyclic nucleotides on contractions evoked by carbachol, caffeine and isotonic KCl were studied in antral smooth muscles of the rat stomach.

1. Nifedipine (10^{-6}M) blocked the contractions evoked by 40mM isotonic KCl and 10^{-6}M carbachol, but not those caused by 10^{-4}M carbachol and caffeine.
2. Db-cAMP and 8Br-cAMP inhibited 10^{-6}M carbachol-induced contraction, and had no effects on the 40mM isotonic KCl- and 3mM caffeine-induced ones. Forskolin inhibited carbachol-induced contraction and slightly suppressed isotonic KCl- and caffeine-induced ones.
3. Nitroprusside blocked carbachol-induced contractions and suppressed the isotonic KCl-induced one, but had no effect on the caffeine-induced one. 8Br-cGMP blocked carbachol-induced contractions and suppressed isotonic KCl- and caffeine-induced ones. Db-cGMP had little effect on these contractions.
4. Forskolin hyperpolarized the membrane potential. Nitroprusside and all membrane permeable cyclic nucleotides had no effects on the membrane potential. Db-cAMP suppressed carbachol-induced depolarization.
5. The inhibitory effects of db-cAMP and 8Br-cGMP on carbachol-induced contraction were accompanied by inhibition of the carbachol-induced incrase of the cytoplasmic Ca concentration.
6. Forskolin increased both cyclic AMP and cyclic GMP contents of the antral smooth muscles. Nitropursside increased only cyclic GMP content.
7. The intracellular Ca store was depleted by caffeine but not by carbachol.
8. Db-cAMP and 8Br-cGMP inhibited carbachol-induced Ca release, but not caffeine-induced Ca release from the intracellular Ca store.
9. It is concluded that cyclic AMP and cyclic GMP inhibit Ca influx and Ca release from intracelluler Ca stores in response to carbachol in the antral smooth muscle of the rat. The inhibitions of voltage-operated Ca channels is partly involved in the effect of cyclic GMP but not in that of cyclic AMP.