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Pharmacology of the (fore)-stomach smooth muscles

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ABSTRACT
A short review is presented on the pharmacology of the (fore)-stomach smooth muscles. Detailed information is given on the smooth muscle pharmacology of the lower oesophageal sphincter, the oesophageal groove, the reticulum, the rumen, the omasum, the abomasum and the pylorus.

CONTRACTION OF SMOOTH MUSCLES
Smooth muscle membrane permeability changes usually affect membrane potential by allowing one or more ions to pass through the membrane more freely. Since none of the ions in smooth muscle cells is in equilibrium at a membrane potential of -50 to -60 mV, there will be a net flow of ions into and out of the cells, tending to move the membrane potential closer to equilibrium. Membrane depolarization usually results in a contraction, although a change in potential is not a prerequisite for induction of contraction in all smooth muscle cells. Contraction of smooth muscles can be initiated by changes in membrane permeability either after binding of agonists to their receptors or after exposure to high K+ concentrations. In either instance, electrical or chemical cell membrane signals indirectly activate contractile elements by releasing membrane-bound Ca2+, or increasing Ca2+ influx, or...
both. Three sources of Ca can be distinguished: the free Ca in the extracellular fluid, the Ca bound to the surface membrane and the intracellular Ca in endoplasmic reticulum and mitochondria. Ca influx during receptor activation seems to be different from Ca influx induced by membrane depolarization. Two pathways of transmembrane flux of Ca exist: a voltage-dependent Ca channel, activated by changes in membrane potential, and a receptor-linked channel, activated by binding of agonists to their receptors. The plasma membrane of vascular, intestinal and myometrial smooth muscle seems to be equipped with the exchange system to regulate intracellular Ca concentration. A (Ca-Mg)-ATPase was demonstrated in pig stomach muscle, which could be purified on a calmodulin affinity column and is calmodulin-dependent. This protein is able, when incorporated into lipid vesicles, to transport Ca in an uphill fashion if ATP is present in the medium.

Receptor agonists also induce contraction without changing membrane potential in smooth muscles that do not generate action potentials, or in depolarized smooth muscles. All eukaryotic cells contain inositol lipids. Phospholipase C catalyses the breakdown of phosphatidylinositol 4,5-biphosphate, a multiple-charged anion that has a very high affinity for Ca (greater than that of EDTA) and exhibits a rapid turnover in vivo. Its hydrophilic/hydrophobic solubility partition coefficient is markedly altered when Ca replaces monovalent phosphate counterions. The receptor-mediated breakdown of phospholipids is not mediated by an increase in cytosol Ca but is closely coupled to receptor occupation. Inositol triphosphate (IP) and also the lipid-soluble product of phosphatidylinositol 4,5-biphosphate breakdown, 1,2 diacylglycerol (DAG), act as second messengers in the cells. The phosphoryl groups, covalently attached to IP, turn over extremely rapidly. The rise in IP may be the means whereby the intracellular (non-mitochondrial) pools of calcium are mobilized. The less Ca bound to inositol