Inhibition of the longitudinal muscle of rabbit duodenum

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In some smooth muscle preparations which are inhibited by intramural nerve stimulation, there is growing evidence that transmission is neither adrenergic nor cholinergic (Campbell, 1970; Hughes & Vane, 1970). The longitudinal muscle of rabbit duodenum is convenient for further studies of this problem since changes in its mechanical activity can be measured (Weston, 1971) and its electrical activity recorded using the sucrose gap technique (Small & Weston, 1971).

Strips of longitudinal muscle were removed from rabbit duodenum together with the attached mesentery and mounted in electrodes which allowed the perivascular and intramural nerves to be stimulated separately. Mechanical activity was recorded isometrically.

In Krebs solution containing atropine (10 μM), perivascular nerve stimulation (0·5 ms; 4–64 Hz; 30 V; for up to 10 s) produced frequency dependent reduction in the amplitude of spontaneous tension waves which persisted for several seconds after stimulation had ceased. This inhibitory response was abolished by guanethidine (10 μM), phentolamine+propranolol (each 1 μM), was unaffected by hexamethonium (10 μM) and was absent in strips removed from rabbits pretreated with reserpine (2 mg/kg i.p.) on each of 2 days before the experiment.

Intramural nerve stimulation in the presence of atropine (0·5 ms; 1–64 Hz; 30 V; for up to 10 s) produced a frequency dependent, transient inhibition of mechanical activity. This inhibitory response was unaffected by guanethidine, phentolamine+propranolol, hexamethonium, or pretreatment with reserpine. On cessation of stimulation, mechanical activity increased for several seconds.

Phenylephrine (0·01–2·56 μM), adenosine and its mono-, di-, and tri-phosphates (AMP, ADP, ATP, each 0·1–10 μM) produced a concentration dependent, transient inhibition of mechanical activity. On washout, mechanical activity increased for several seconds. The effect of phenylephrine was antagonized by phentolamine (pA_{10}=6·7) but responses to adenosine, AMP, ADP, and ATP were unaffected by phentolamine (up to 2·5 μM) or propranolol (up to 5 μM).

Isoprenaline (0·01–2·56 μM) and papaverine (5–80 μM) each produced a concentration dependent inhibition of mechanical activity which developed slowly and was maintained. The effect of isoprenaline was antagonized by propranolol (pA_{10}=6·45) but neither phentolamine nor propranolol affected responses to papaverine.

In the sucrose gap, each spontaneous tension wave was associated with a slow wave of depolarization surmounted by a burst of spike activity (a multispike complex). Phenylephrine, isoprenaline, papaverine, adenosine, AMP, ADP, and ATP each produced a hyperpolarization and selectively abolished the spike component of the multispike complex with little effect on the slow waves. The increase in mechanical activity after washout of phenylephrine, adenosine, AMP, ADP and ATP was associated with increased spike frequency.

The results obtained using adenosine and its phosphates are relevant to the suggestion (Burnstock, Campbell, Satchell & Smythe, 1970) that the inhibitory transmitter released by intramural nerve stimulation is ATP.

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Effects of catecholamines on the electrical and mechanical activity of the guinea-pig ureter

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We have studied the activity of the isolated guinea-pig ureter by recording simultaneously the transmembrane potentials and the intraluminal pressure development. This pressure was a better measure for the mechanical activity of the ureter than the longitudinal tension development. The ureter, isolated from the pelvis, is not spontaneously active *in vitro* and was therefore stimulated electrically throughout the experiment at a rate of 1/minute. The normal action potential is characterized by an initial depolarization at a rate of 15 V/s and a plateau phase on which, in its initial part, about ten oscillations occur. This action potential is accompanied by an increase of the intraluminal pressure from the resting level of 3 cm water to about 50 cm.

Noradrenaline (2×10^{-7} to 10^{-6} M) induces spontaneous activity, increases the number and frequency of oscillations during the initial part of the plateau phase of the action potential and prolongs the total duration of the action potential by a factor of 1·3 to 2. The electrophysiological effect of adrenaline is similar but less pronounced. Moreover both catecholamines increase the active intraluminal pressure by a factor of 1·2 to 1·4. Isoproterenol (5×10^{-7} M) neither induces spontaneous activity nor modifies significantly the action potential. However, it reduces the intraluminal pressure development during an elicited action potential by a factor of 0·5.

We have tried to elucidate these actions of the different catecholamines by using adrenergic blocking agents. The α-adrenoceptor blocking agent phenoxybenzamine (10^{-6} M) exerts an action, which is similar to the action of noradrenaline. It induces spontaneous activity and increases the active intraluminal pressure. Phentolamine (10^{-6} M) does not induce spontaneous activity and causes only a small increase of the intraluminal pressure. Both drugs prolong the duration of the action potential to about 3 times the control value. Adding noradrenaline during exposure of the ureter to an α-adrenoceptor blocking agent slightly reduces the effect of these substances on the duration of the action potential and on the intraluminal pressure.

The β-adrenoceptor blocking agent, propranolol (10^{-6} M), causes a small prolongation of the action potential and decreases the number of its oscillations. This substance also prevents the decrease of tension caused by isoproterenol.

These experimental results indicate that sympathomimetic drugs and adrenoceptor blocking agents can affect the excitability and the excitation-contraction coupling in the isolated guinea-pig ureter. The significant modification of the action potential by some of these substances suggests that their action is not limited to adrenoceptors, but might also exert a direct action on the properties of the smooth muscle membrane.

This investigation is supported by research grant 1182 of the F.G.W.O. of Belgium.