exudate cells, isolated from these animals, were shown to be well sensitized by challenge *in vitro* with antigen and assay of the histamine released, using a guinea-pig ileum. Using a preparation (Wan, 1977) of an isolated perfused stomach from a mouse sensitized similarly 3–4 weeks before, the addition of a solution of the antigen induced a profuse secretion of acid.

The response curve to doses of antigen or histamine shown in Figure 1 illustrates that acid secretion rate induced by antigen was comparable to that with histamine, except that the maximal acid secretion for histamine was higher. Antigen-induced acid secretion was inhibited by metiamide (5×10^{-5} M) or atropine (5×10^{-6} M) by about 50% and sodium cromoglycate (5×10^{-5} M) by about 33%, but not by the potent phosphodiesterase inhibitor ICI 63197 (10^{-4} M). Although the histamine concentration in the gastric effluent and the serosal solution bathing the sensitized mouse stomach did not correlate with antigen-induced acid secretion, the present evidence still suggests that endogenous histamine released in the anaphylactic mouse stomach is involved in gastric acid secretion. However, the possibility that antigen could also release gastrin and acetylcholine, which would induce acid secretion, should not be excluded.

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Influence of 2-2'-pyridylisatogen tosylate on responses produced by ATP and by neural stimulation on the rat gastric corpus

W.B. HUNT, D.G. PARSONS, A. WAHID & J. WILKINSON (introduced by B.C.L. WALKER)

Physiology and Pharmacology Academic Group, The Hatfield Polytechnic, Hatfield, Hertfordshire.

The ATP-induced relaxation of the isolated guinea-pig taenia caeci can be antagonized by 2,2'-pyridylisatogen tosylate (PIT) while a similar response to field stimulation remains unaffected (Spedding, Sweetman & Weetman, 1975). In the isolated guinea-pig terminal ileum, PIT potentiated contractile responses to applied ATP and to field stimulation (Kazic & Milosavljevic, 1977). Using the rat gastric corpus, we found that ATP produced a biphasic response consisting of a relaxation followed by a contraction. Vagal or field stimulation produced a similar reponse in the presence of atropine, The influence of PIT on these responses has been studied.

A strip of gastric corpus was bathed at 36°C in Krebs–Hensleit solution containing barium chloride (10^{-3} M), to elevate tone, and atropine sulphate (3×10^{-6} M). For most experiments a cumulative dosing technique was used for the application of ATP to the preparation. The contractions which are normally apparent after a single dose of ATP were absent. The relaxations produced by such applications of ATP (5×10^{-5} M to 5×10^{-2} M) were antagonized by incubating the tissue with PIT (5×10^{-5} M to 5×10^{-4} M) for 30 minutes. The extent of this antagonism was dependent upon the dose of PIT and the duration of its incubation with the tissue. After 90 min incubation the antagonism was apparently irreversible. When relaxations of the tissue were induced with either noradrenaline (10^{-7} M to 10^{-5} M) or isoprenaline (10^{-7} M to 10^{-5} M) PIT (10^{-4} M) was without antagonistic effect. Incubation periods of both 30 min and 2 h were used.

Sequential doses of ATP produced biphasic responses at concentrations $\leqslant 5 \times 10^{-4}$ M; higher doses produced relaxation only. Pre-incubation of the tissue with indomethacin (10^{-5} M) (a prostaglandin synthesis inhibitor, Vane, 1971) for 10 min antagonized the contractile part of the biphasic response to ATP while the relaxation was unaffected. Again relaxations produced by ATP could be antagonized by PIT (10^{-4} M, duration of incubation 30 min).

Cumulative frequency (0.5–20 Hz) response curves were produced to field stimulation (100 v, pulse width 2.0 ms). Relaxations produced by such stimulations were not antagonized by incubation with PIT (10^{-4} M) for either 30 min or 2 hours. Sequential stimulation of the vagi at 10 v and 30 v (pulse width 2.0 ms, 20 Hz for 90 s) produced a biphasic response which was not antagonized by incubation with either PIT (10^{-4} M) or indomethacin (10^{-5} M) for 30 min or 2 hours.

This study demonstrates differences between the response to applied ATP and neural stimulation and so does not support the view that ATP is the non-adrenergic, non-cholinergic inhibitory transmitter in the rat stomach (Burnstock, 1972). A biphasic response to applied ATP was observed. The selective effect of PIT on the phase of relaxation could be

accounted for by ATP interacting with more than one type of receptor. Furthermore the contractile effect of ATP may be mediated by prostaglandins.

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The effects of a benzotriazinium salt on ventricular fibrillation in the guinea-pig perfused isolated heart

A.McK. FRENCH & N.C. SCOTT

Pharmacology Section, Department of Pharmacy, Heriot-Watt University, Edinburgh.

It has been previously reported that a benzotriazinium salt, 2-*n*-propyl-4-*p*-tolylamino-1,2,3-benzotriazinium iodide (TnPBI) has effects on intracellularly recorded cardiac action potentials which suggest that the compound may have antiarrhythmic properties (French & Scott, 1977).

TnPBI has been compared with quinidine in its ability to raise the electrical threshold necessary to cause ventricular fibrillation (VFT) and also to reverse persistent ventricular fibrillation induced by high frequency stimulation in the presence of increased calcium concentration.

Guinea-pig hearts were perfused by the Langendorff technique with Locke solution, preoxygenated and prewarmed to 35°C, at a rate of 4–6 ml/minute. Electrocardiograms (ECG) were recorded between two silver wire electrodes, one placed between the atria, and the other on the left ventricular surface, and were displayed on an Advance OS4000 digital storage oscilloscope. Mechanical responses were measured with an Ether UF1 force transducer and recorded on a Devices M2 recorder. VFT values were determined by applying pulses of 1 ms duration at 25 Hz to the ventricular surface from a Grass S48 stimulator. The current intensity (estimated via the voltage drop across a 1 kΩ resistor) was increased until ventricular fibrillation was observed in the ECG and mechanical contractions became uncoordinated.

The VFT was increased in a dose-related manner when the perfusion fluid contained TnPBI at concentrations from 1×10^{-6} M to 1×10^{-5} M. Quinidine (6.25×10^{-6} M to 5×10^{-5} M) also increased the VFT values. All measurements were made after 10 min perfusion with each drug concentration. TnPBI was approximately six times more potent than quinidine on a molar concentration basis.

Both TnPBI and quinidine were capable of restoring sinus rhythm to hearts in which persistent ventricular fibrillation had been induced by a technique similar to that of Armitage, Burn & Gunning (1957). The Langendorff heart preparations were perfused with Locke solution containing twice the usual concentration of calcium (i.e. 4.16 mM). The ventricles were then stimulated with 1 ms pulses at 25 Hz for 1 minute. This resulted in ventricular fibrillation which persisted for at least 30 min after stimulation was stopped. Injection of TnPBI (250 μg) or quinidine (500 μg) into the side arm of the perfusion cannula reversed the fibrillation within 0.5–2 minutes.

When TnPBI was perfused through Langendorff preparations of spontaneously beating guinea-pig hearts, certain ECG changes were observed. Low concentrations (about 1×10^{-6} M) prolonged the Q-T interval, while increasing the concentration to 5×10^{-6} M caused a progressive increase in the P-R interval, with a further increase in the Q-T interval and a widening of the QRS complex. These changes are indicative of delayed conduction throughout the entire myocardium, while the initial prolongation of the Q-T interval indicates a delay in ventricular repolarization. This latter effect may be responsible, in part at least, for the depressant effects of TnPBI on ventricular fibrillation.

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