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

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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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