and the ability to inhibit dopamine-induced relaxations of the gastroesophageal junction. Similarly the selective α_1 adrenoceptor antagonist prazosin (Cambridge, Davey & Massingham, 1977), gave pA_2 values of 8.6 ± 0.2 and 9.0 ± 0.1 on the gastroesophageal junction and aorta respectively, indicating that the gastrointestinal effects of domperidone are more likely to be mediated by an interaction with α-adrenoceptors. The dopamine antagonists did not inhibit noradrenaline-induced relaxations of the gastroesophageal junction pointing to a difference in the mode of action of noradrenaline and dopamine on this tissue. This is an aspect of the study requiring further investigation.

C.E. is an SRC CASE award student.

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The effects of Cd^{2+} on the myogenic activity and the responsiveness of the rat portal vein to perimural stimulation, noradrenaline and potassium ions

Z. FADLOUN & G.D.H. LEACH

Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, BD7 1DP

Cd^{2+} have been shown to inhibit the responses of rat vas deferens and anococcygeus muscles preparations to noradrenaline (NA), tyramine, K^+ and perimural stimulation, NA being the least effected (Fadloun & Leach, 1979). In the present study the responses of the rat portal vein have been studied, since it possesses myogenic activity which is independent of its sympathetic innervation.

Rat portal veins were prepared using the method described by Johansson & Ljung (1967). Special tissue holders were used to allow adequate superfusion and perimural stimulation (Fadloun & Leach, 1978). The superfusion rate was 3 ml/min using Krebs solution at 37°C aerated with 95% O_2/5% CO_2. The stimulation parameters used were: 20 V, pulse width 0.1 ms, 1–25 Hz with a stimulation period of 1 minute. The effects of NA (10–160 ng) and K^+ (5–40 μM) were also tested.

The tissue responses to perimural stimulation were found to be biphasic. Cd^{2+} (0.5–2 μM) were shown to reduce the amplitude of the spontaneous phasic contractions Cd^{2+} (0.5 μM) increased the frequency of the phasic contractions by approximately 25%, whilst Cd^{2+} (2 μM) failed to change the frequency, but reduced the amplitude to approximately 50% of the control.

Cd^{2+} (0.5–2 μM) were also found to inhibit the responses to perimural stimulation, the first phase being more effected. Low frequencies (1–12 Hz) were more effected than the higher frequency (25 Hz). In addition, Cd^{2+} were also shown to inhibit the contractions caused by small doses of K^+ (5–20 μM). However, Cd^{2+} (0.5 μM) did not affect NA responses, but at 2 μM the inhibition ranged between 40% and 10% according to the dose tested (10 ng and 160 ng respectively).

Responses to perimural stimulation, K^+ and NA were reduced when the Ca^{2+} concentration of the Krebs solution was reduced (1.27 mM) and 0.635 mM). The responses to perimural stimulation and smallest doses of K^+ were most effected. No myogenic activity was seen at Ca^{2+} (0.635 mM).

The inhibitory effects of Ca^{2+} (1.27 mM) and Cd^{2+} (0.5 μM) were found to be synergistic to all three tests.

Cysteine (0.5 mM), administered when the effect of Cd^{2+} (2 μM) had been established, partially restored the responses inhibited by Cd^{2+}. Cysteine significantly increased the frequency of the phasic contractions but did not affect the amplitude; this was found to be similar to the effect of restoration to normal Krebs after using Ca^{2+} (0.635 mM). Yohimbine (10 ng/ml) potentiated the responses to perimural stimulation at all frequencies (1–25 Hz), but did not affect NA (10 ng–160 ng) responses at the same concentration.

The results obtained in the sympathetically innervated vascular muscle preparation are in close agreement with previous studies using non-vascular preparations (Fadloun & Leach, 1979), suggesting that Cd^{2+} possess a higher affinity towards presynaptic sites, possibly by interference with the intracellular Ca^{2+} mobilisation.

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Effect of verapamil on rhythmic contractions in isolated rat vasa deferentia

D.W.P. HAY & R.M. WADSWORTH

Department of Physiology and Pharmacology, University of Strathclyde

Both extracellular and intracellular sources of calcium have been shown to be involved in the contractile process in smooth muscle (Hurwitz & Suria, 1971). We have studied excitation-contraction coupling in the vas deferens using verapamil which is known to block selectively transmembrane calcium ion influx, causing electro-mechanical decoupling and inhibiting contraction (Haeusler, 1971; 1972).

Vasa deferentia from Wistar rats (250–450 g body weight) were suspended in Krebs-Henseleit solution (Na^+ = 143, K^+ = 5.6, HCO_3^- = 25, glucose = 11.1, Mg^{2+} = 1.2, $H_2PO_4^-$ = 1.2, Ca^{2+} = 2.5, SO_4^{2-} = 1.2 and Cl^- = 135.8 mM) at 36–37°C and contractions were recorded isometrically. Methoxamine HCl (2 μg/ml), 5-hydroxytryptamine creatinine SO_4 (50 μg/ml) and $BaCl_2$ (1 mM) each caused rhythmic contractile activity (frequency = 1.3–4.8/min, amplitude = 0.02–2.38 g tension). In Krebs-Henseleit from which $CaCl_2$ had been omitted, none of these drugs produced a response. As the $[Ca^{2+}]o$ was raised gradually, contractions were observed when the $[Ca^{2+}]o$ exceeded a threshold of 0.3 mM in different experiments. Both the amplitude and frequency of these contractions then increased dramatically in the range 0.5–1 mM over this threshold.

High concentrations of verapamil HCl were required to inhibit rhythmic contractions produced by methoxamine (Figure 1(a)), 5-HT or $BaCl_2$. The amplitude was reduced by 5–30 μg/ml, while the frequency was inhibited only with 50–100 μg/ml verapamil. In most experiments, there was a slight increase in frequency at concentrations of verapamil in the range 5–10 μg/ml.

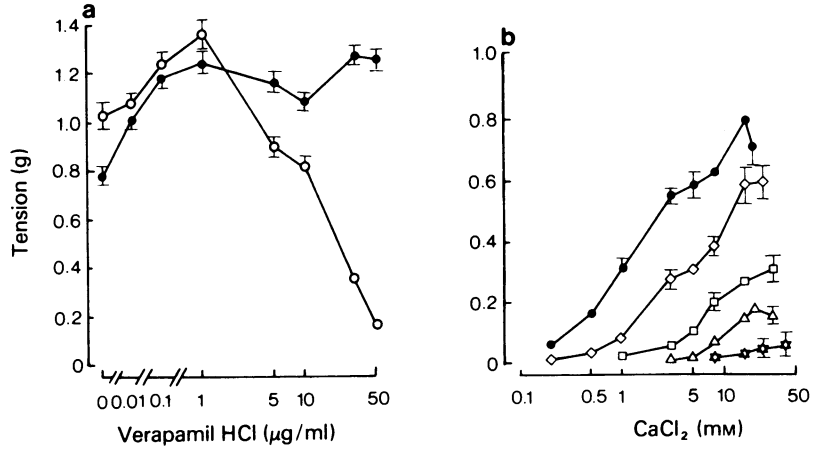

Figure 1 (a) Effect of cumulatively increasing concentrations of verapamil on rhythmic contractions induced by methoxamine HCl (2 μg/ml) in isolated rat vasa deferentia. One vas served as the control (●) while the contralateral vas received verapamil (○). Each point is the mean ± s.e. mean of 4 experiments. (b) Effect of verapamil on the dose-response curve for $CaCl_2$ on depolarized rat vasa deferentia. (●) control, (◇) 0.1 μg/ml verapamil, (□) 1 μg/ml verapamil. (△) 10 μg/ml verapamil, (✡) 50 μg/ml verapamil. Each point is the mean ± s.e. mean of 3 experiments.