Effects of Ca^{2+} withdrawal and verapamil on excitation-contraction coupling in rabbit pulmonary vascular smooth muscle

I.W. RODGER

Department of Physiology and Pharmacology, University of Strathclyde, Glasgow G1 1XW

In many vascular preparations concentrated KCl solutions induce contraction principally by utilising Ca^{2+} from low affinity, extracellular stores with more sequestered Ca^{2+} sources being used in the maintenance of contractile tone. In contrast pharmacological agonists use these Ca^{2+} sources in the opposite manner (for references see Weiss, 1977). The present study is designed to evaluate the processes operating in smooth muscle cells of the rabbit pulmonary artery.

Transverse strips of rabbit extrapulmonary arteries were suspended in Krebs–Henseleit solution (KHS) at 37°C and gassed with 5% CO_2 in O_2. The strips were contracted almost maximally using 60 mM KCl (high K^+) solution or an equieffective concentration of either 5-hydroxytryptamine (5-HT; 2×10^{-6} M) or phenylephrine (1×10^{-5} M).

Incubation in Ca^{2+}-free KHS for periods up to 10 min caused a marked reduction in the response to KCl (60 mM), the response after 10 min being reduced by approximately 90%. Longer incubations (up to 60 min) produced little further reduction. Replotting these data in the form of a Ca^{2+} efflux curve (Hurwitz & Joiner, 1970) revealed that the decline in tension could be described by two exponentials; a fast component ($T_{1/2}$ = 1.65 min) and a slow component ($T_{1/2}$ = 158 min).

Phasic contractions to either phenylephrine or 5-HT were elicited after 10 min incubation in Ca^{2+}-free KHS. At the peak of the phasic response Ca^{2+} (2.5 mM) was added to the bath thereby initiating the slower (tonic) contraction. Verapamil (1×10^{-8} M to 1×10^{-3} M) caused a concentration-dependent inhibition of high K^+ contractions and of both phasic and tonic elements of the 5-HT and phenylephrine contractions. The rank order of sensitivity to inhibition by verapamil was high K^+ = 5-HT (phasic) > 5-HT (tonic) > phenylephrine (phasic) > phenylephrine (tonic). The separation of phasic and tonic components for each agonist was 3–4 fold. Times to peak tension of the phasic ontractions were unaltered by verapamil whereas times to peak tension of the tonic responses and of high K^+ contractions were prolonged.

It can be concluded that in this preparation 5-HT, phenylephrine and high K^+ solutions induce contraction by utilising extracellular Ca^{2+} sources. The stores activated by high K^+ must bind Ca^{2+} with low affinity. Furthermore, the results are consistent with the hypothesis (Rodger, Gillespie & Diamond, 1978) that KCl and pharmacological agonists may modulate membrane translocation of Ca^{2+} via separate calcium channels.

References

HURWITZ, L. & JOINER, P.D. (1970). Mobilisation of cellular calcium for contraction in intestinal smooth muscle. *Am. J. Physiol.*, **218**, 12–19.

RODGER, I.W., GILLESPIE, M.N. & DIAMOND, L. (1978). Differentiation of calcium channels in pulmonary vascular smooth muscle. *Pharmacologist*, **20**, 227.

WEISS, G.B. (1977). Calcium and contractility in vascular smooth muscle. In *Advances in General and Cellular Pharmacology*, Vol. II, eds. Narahashi, T. & Bianchi, C.P. pp. 71–154. New York, Plenum.