LETTER TO THE EDITOR

INHIBITION OF CALCIUM INDUCED SYSTOLIC CONTRACTURE OF THE PERFUSED FROG'S HEART BY PHENOXYBENZAMINE

Sir,

Positive inotropic action of acetylcholine on the frog heart perfused with excess of calcium is blocked by calcium antagonists as well as by phenoxybenzamine (7, 8). It is, therefore, of interest to know if phenoxybenzamine can also antagonise the action of calcium.

Frog's heart was perfused through inferior vena cava by the method of Bulbring as described by Burn (2). Ventricular contractions were recorded on the Encardiorite polygraph model 432, using 532 preamplifier and with FT_3 force transducer (Encardiorite).

Administration of 0.2 and 0.4 *ml* of 1% solution of $Cacl_2$ in the perfusion fluid caused an increase in the amplitude of contractions. 0.8 *ml* of $Cacl_2$ (1%) when administered into the perfusion fluid caused the systolic arrest of the heart to be followed by increase in amplitude. $4x10^{-6}$ *gm/ml* of phenoxybenzamine was added to the perfusion fluid. Doses of calcium chloride were repeated after perfusing the heart with phenoxybenzamine containing media for 30-40 min. 0.2 and 0.4 *ml* of 1% $Cacl_2$ solution when administered in the perfusion fluid increased the amplitude of contraction even in the presence of phenoxybenzamine. However, administration of 0.8 *ml* of 1% $Cacl_2$ failed to produce the typical systolic arrest of the heart (Fig.1).

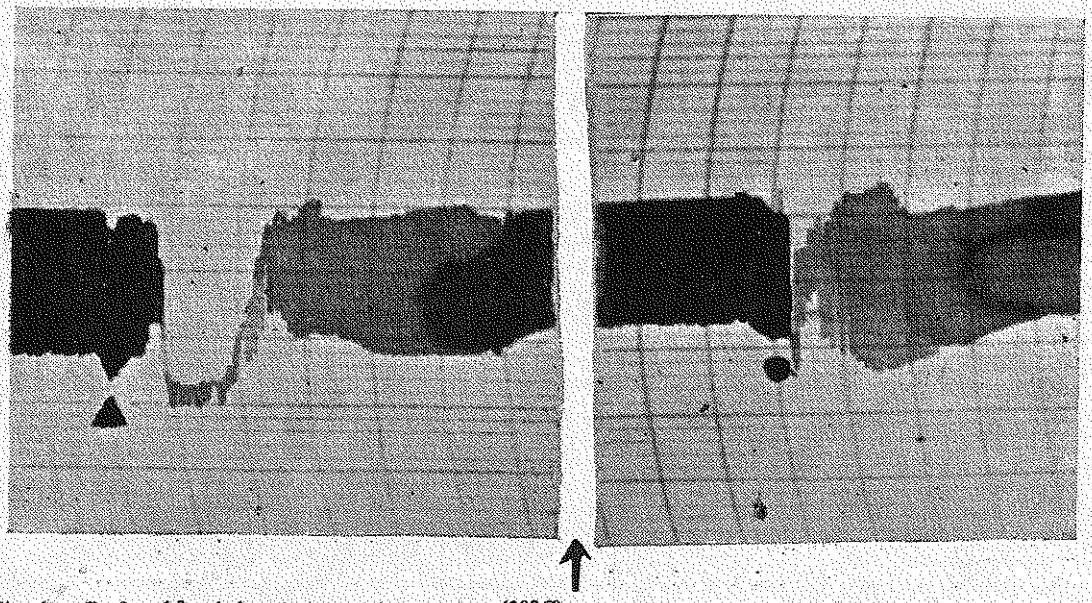

Fig. 1: Perfused frog's heart at room temperature (30°C).

- ▲ $Cacl_2$ 0.8 *m.* (1%). Injection of $Cacl_2$ caused systolic arrest of the heart. Fluid accumulated in the auricle. Bloated up auricle caused upward thrust on the tranducer resultng in downward movement of the writing pen.
- ● Cac'_2 0.8 *ml* (1%), 45 min after perfusing the heart with Phenoxybenzamine.
- ↑ Continuous infusion of 4×10^{-6} *gm/ml* of penoxybenzamine was started.

Phenoxybenzamine, thus, blocked the calcium induced systolic contracture of the heart but did not block the increase in the amplitude of contractions. Graham *et al.* (6) have observed by radioautographic studies that phenoxybenzamine is distributed intracellulary and none of the labelled phenoxybenzamine is found on the cell membrane. Thus it may be assumed that calcium produces systolic arrest of the heart by acting intracellularly and increases the amplitude of contraction by acting on the cell membrane.

Like local anaesthetics (4) phenoxybenzamine also inhibits the cabcium induced contractions of depolarised rat uterus (9). But unlike local anaesthetics (4) it does not interfere with the influx or efflux of calcium (9). It is interesting to note that phenoxybenzamine also inhibits 5-HT (5) and potassium (1) induced contractions of smooth muscles which are mediated through calcium 3.

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