(rate) but not β-1 type (force) of the atria. This result suggests that β-1 type receptors are not homogeneous. Orciprenaline is not selective and has equal but low activity on β-1 and β-2 type receptors. The activities described for these new compounds further substantiate the classification proposed by Lands and co-workers (1967) for β-receptors in cardiac and bronchial muscle.

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## The absence of a significant histamine receptor reserve in vascular smooth muscle

The existence of a receptor reserve was first postulated by Nickerson (1956) on the basis of the parallel shift in the dose response curve for histamine, produced by partial blockade with GD-131, an irreversible antagonist of the β-haloalkylamine class. This phenomenon, which was observed in the guinea-pig ileum preparation, can readily be explained by supposing that only a small fraction of the total number of available receptors need to interact with the agonist in order to elicit the maximum response. Such a receptor reserve has been observed in cholinergic systems (Ariens, van Rossum & Koopman, 1960) but appears to be absent or insignificant in adrenergic systems (Moran, May & others, 1967a, 1967b; Moran, Triggle & Triggle, 1969).

To determine whether this parallel shift of the dose-response curve after partial blockade with a β-haloalkylamine is a characteristic of other histamine receptor systems, the nature of the progressive blockade of the histamine-induced contractions of rabbit aortic strips has been observed, using phenoxybenzamine as the irreversible antagonist.

Rabbit aortic strips prepared as described by Furchgott & Bhadrakom (1953) were suspended in organ baths of 15 ml working volume and allowed to equilibrate at 37° for 3 h in Krebs bicarbonate solution containing 0·05 M glucose. The resting tension was maintained at 1 g. A cumulative dose response curve to histamine was then obtained; contractions were recorded by means of a force-displacement transducer (Grass FT03) connected to a Grass model 5P1 polygraph. The preparations were then washed with Krebs bicarbonate solution at frequent intervals until they had returned to the resting tension. Phenoxybenzamine hydrochloride was dissolved in normal saline containing 0·01 M hydrochloric acid and, after this solution had been kept at room temperature for 10 min, aliquots were added to the organ baths to achieve the required concentration. After 5 min exposure to phenoxybenzamine the tissues were washed twice and washed thereafter at 15 min intervals for 2½ h. A further cumulative dose-response curve to histamine was then obtained. Since this preparation is known to increase in sensitivity with time, the experiment was repeated

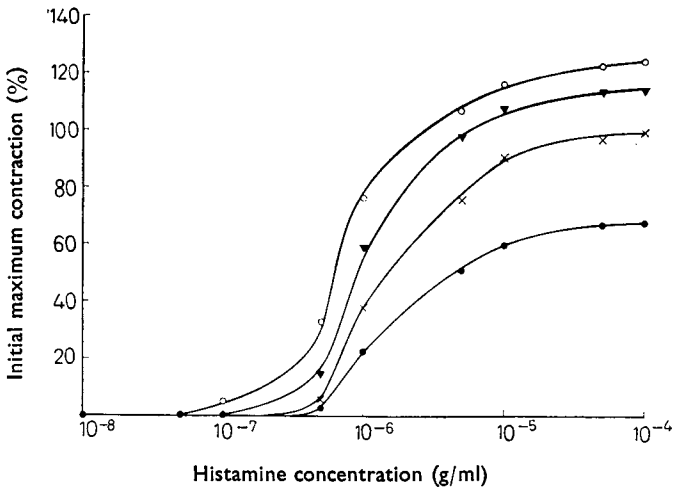


FIG. 1. Dose-response curves for histamine. ○——○ control, ▼——▼ after phenoxybenzamine ($10^{-8}$ g/ml), ×——× after phenoxybenzamine ($2{\cdot}5 \times 10^{-8}$ g/ml), ●——● after phenoxybenzamine ($5 \times 10^{-8}$ g/ml).

a number of times with the omission of the phenoxybenzamine blockade, such preparations being regarded as controls. The histamine phosphate used in these studies was obtained from Fisher Scientific and the phenoxybenzamine hydrochloride was generously donated by Smith Kline and French; drug concentrations are expressed as grams of the salt/ml of bathing medium.

The dose-response curves obtained from these experiments are shown in Fig. 1. The contractions are expressed as the percentage of the maximum response obtained initially, and each curve represents the mean of at least seven experiments. It can be seen that progressive blockade is not accompanied by a shift in the dose-response curve and both the maximum contraction and the slopes of the dose-response curves are depressed after blockade with phenoxybenzamine. This situation would be anticipated in the absence of a significant fraction of spare receptors and it is, therefore, concluded that there is no significant receptor reserve for histamine in rabbit aortic strip.

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