

A RECEPTOR RESERVE OF THE ALPHA-INHIBITORY RECEPTOR FOR ALPHA-ADRENOCEPTOR STIMULANTS IN THE TAENIA CAECUM OF GUINEA PIG

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Adrenoceptors were classified as α- and β-receptors by Ahlquist (1). The α-receptor is generally associated with the excitatory functions and the β-receptor with the inhibitory functions in various smooth muscles. Stimulation of the α- and β-receptors in intestinal smooth muscles produces a relaxation (2). Our knowledge of the receptor reserve of α-receptor for the α-adrenoceptor stimulants has been, however, obtained from data in the excitatory responses (3, 4). Little is known of the receptor reserve for the α-agonists in inhibitory mechanisms.

Male guinea pigs, weighing 300 to 400 g, were sacrificed by a blow on the neck and a piece (3 to 4 cm) of taenia was removed from the caecum and suspended in a 20 ml organ bath filled with Locke Ringer’s solution (NaCl 154, KCl 5.6, CaCl₂ 2.2, MgCl₂ 2.1, NaHCO₃ 5.9 and glucose 2.8 mM) kept at 37°C and bubbled with air. The physiological solution also contained propranolol hydrochloride (3 × 10⁻⁶ M) which blocks the β-adrenoceptor action of α-adrenergic stimulants. Norepinephrine hydrochloride, epinephrine bitartrate and phenylephrine hydrochloride were used as α-adrenoceptor stimulants and dibenamine
hydrochloride as an irreversible blocker of the α-adrenoceptor. The smooth muscle preparation was progressively incubated in dibenamine (3 × 10⁻⁷ M). The smooth muscle preparation after each incubation with dibenamine (3 × 10⁻⁷ M) was washed for 30 min in the bath fluid. Progressive incubation was carried out as follows. After control dose response curves of the test stimulants were made, the taenia caecum was incubated with dibenamine for 10 min. After washout, the dose response curves were again made using the same stimulants. The taenia caecum was incubated again with dibenamine for 10 min, and the curves were made. The third incubation was carried out for 20 min. Incubation times shown in Fig. 1 were expressed as the total time.

To determine the site of action of dibenamine, the following experiments were carried out. Phenylephrine (3 × 10⁻⁵ M) induced a maximal relaxation. After 40 min incubation

![Graph of Relaxation (%) vs. Log Dose (M)](image)

**Fig. 1.** Effects of progressive blockade by dibenamine (3 × 10⁻⁷ M) on dose response curves of norepinephrine (top), epinephrine (middle) and phenylephrine (bottom). The values are presented as mean with S.E. of 7 experiments. A: control, B: after 10 min incubation, C: after 20 min incubation, D: after 40 min incubation. Note the parallel shift which precedes a decline in the curves of the α-stimulants used.
with dibenamine \((3 \times 10^{-7} \text{ M})\) and washout for 30 min, the responses of the taenia caecum to phenylephrine \((3 \times 10^{-7} \text{ M})\) were \(22.5 \pm 2.8\%\) (means \(\pm\) S.E. of 5 experiments). When the taenia caecum was incubated with both dibenamine \((3 \times 10^{-7} \text{ M})\) and a high dose \((3 \times 10^{-4} \text{ M})\) of phenylephrine for 30 min, the responses to phenylephrine \((3 \times 10^{-5} \text{ M})\) were \(93.1 \pm 3.1\%\) (means \(\pm\) S.E. of 5 experiments). These values were statistically, significantly different. Thus, the site of action of dibenamine is probably the \(\alpha\)-adrenoceptor.

The progressive incubation of the taenia caecum with dibenamine \((3 \times 10^{-7} \text{ M})\) resulted in a parallel shift of the dose response curves of the \(\alpha\)-stimulants, followed by a decline, as shown in Fig. 1. The decline of the dose response curves of epinephrine and norepinephrine without a preceding shift has been reported in the case of rabbit aorta (3) and the rat vas deferens (4).

It is well known that the dose response curve of the agonist for which there are spare receptors shifts in parallel with application of an irreversible blocker of these receptors (5, 6). In this paper we observed parallel shifts in the dose response curves of all the \(\alpha\)-adrenoceptor stimulants after the progressive incubation of the guinea pig taenia caecum with dibenamine (Fig. 1). These results suggest that spare receptors are involved in the inhibitory adrenergic responses of the guinea pig taenia caecum to \(\alpha\)-adrenoceptor stimulants while there are no spare receptors involved in the excitatory \(\alpha\)-adrenergic responses of rabbit aorta (3) and rat vas deferens (4).

Furthermore, the parallel shift was least in the dose response curve of phenylephrine after progressive incubation with dibenamine, as shown in Fig. 1. These findings suggest that the spare receptors for phenylephrine were fewer than those for other stimulants used in this study. Since an irreversible block of \(\beta\)-adrenoceptors in the taenia caecum of guinea pig, by a photoaffinity labeling procedure shifted the isoprenaline dose response curve to the right, we conclude that there are a substantial number of spare receptors for isoprenaline in this tissue (7). Little is, however, known of the receptor reserve for the \(\alpha\)-adrenoceptor agonists in the inhibitory mechanisms. It is indicated in this paper that the \(\alpha\)-adrenoceptor stimulants have some spare receptors in the inhibitory \(\alpha\)-adrenergic mechanism of the guinea pig taenia caecum.

REFERENCES