Short communications

Adrenoceptors in the guinea-pig colon

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Guinea-pig colon was shown to contain both α- and β-adrenoceptors. Isoprenaline-induced relaxation was mediated by β-adrenoceptors alone whilst that produced by phenylephrine was mediated by both α- and β-adrenoceptors.

Farmer & Levy (1969, 1970) reported that the relaxation produced by isoprenaline on guinea-pig colon was mediated mainly by α-adrenoceptors. In contrast, the work of Bartlet & Hassan (1969, 1970) showed that isoprenaline acted solely on β-adrenoceptors in this tissue. This paper reports the results of experiments on guinea-pig colon in which the antagonism of the actions of isoprenaline and phenylephrine by propranolol, phentolamine, thymoxamine and dibenamine was studied.

Methods.—Lengths of guinea-pig distal colon (2–3 cm) were set up in 20 ml tissue baths containing Krebs solution maintained at 32° C and bubbled with 5% CO_2 in O_2. Resting tension was adjusted to 4 g. Tension changes were measured using a force-displacement transducer and pen recorder.

Agonist contact time was 60 s at intervals of 6 min, the solution in the tissue bath being changed three times after each addition of agonist. The antagonists propranolol, phentolamine and thymoxamine were added to the Krebs solution and a 30 min equilibration period was allowed before responses to the agonist were re-examined in the presence of the antagonist. Experiments were conducted in the presence of 10^{-8}M, 10^{-7}M and 10^{-6}M concentrations of each antagonist.

The effect of increasing the concentration of antagonist on the responses of the tissue to the agonist was analysed by the method of Arunlakshana & Schild (1959). A graph of log (agonist concentration ratio —1) against —log (antagonist concentration) was plotted. From this graph, the values of —log (antagonist concentration) corresponding to 2-fold and 10-fold antagonism (the pA_2 and pA_{10} values respectively) were read off. The difference between these two values (pA_2–pA_{10}) was calculated and compared with the theoretical (pA_2–pA_{10}) value of 0·95 as a test of simple competitive antagonism.

The tissue was exposed to Krebs solution containing dibenamine for 30 minutes. After washing with Krebs solution for 30 min at 4 min intervals, agonist responses were re-examined in the absence of dibenamine.

Except where indicated, all measurements of variation stated are of standard errors derived from ten experiments.

Results.—Both isoprenaline and phenylephrine produced a concentration-dependent relaxation of the distal colon. The onset of relaxation was rapid for both agonists but the effect of isoprenaline was more persistent than that of phenylephrine.

The relaxation produced by isoprenaline was antagonized in the presence of propranolol (Fig. 1). The pA_2 was $8{\cdot}3 \pm 0{\cdot}6$ and the (pA_2–pA_{10}) was $0{\cdot}90 \pm 0{\cdot}9$. The value for (pA_2–pA_{10}) was not different from the value 0·95 ($P \frown 0{\cdot}6$). The action of isoprenaline was unaffected in the presence of phentolamine (Fig. 1) or thymoxamine. After exposure to dibenamine (6×10^{-7}M and 3×10^{-5}M) the response to isoprenaline was unaffected ($n=6$) but the maximum response was reduced by $31 \pm 9\%$ after exposure to dibenamine (10^{-4}M; $n=5$).

The relaxation produced by phenylephrine was antagonized by propranolol ($pA_2 = 7{\cdot}65 \pm 0{\cdot}9$; pA_2–$pA_{10} = 1{\cdot}30 \pm 0{\cdot}12$; Fig. 1), phentolamine ($pA_2 = 8{\cdot}35 \pm 0{\cdot}6$; pA_2–$pA_{10} = 1{\cdot}17 \pm 0{\cdot}09$; Fig. 1) and thymoxamine ($pA_2 = 7{\cdot}71 \pm 0{\cdot}5$; pA_2–$pA_{10} = 1{\cdot}25 \pm 0{\cdot}09$). These ($pA_2$–$pA_{10}$) values were each different from the value 0·95 ($P \leqslant 0{\cdot}05$).

After exposure to dibenamine (6×10^{-7}M, 3×10^{-5}M and 10^{-4}M; $n=6$), the phenylephrine log concentration : effect curve was shifted progressively to the right and the maximum response was gradually reduced. In the presence of dibenamine (10^{-4}M), the maximum response to phenylephrine was reduced by $48 \pm 9\%$.

Discussion.—The results indicate that the action of isoprenaline on guinea-pig colon is mediated by β-adrenoceptors.

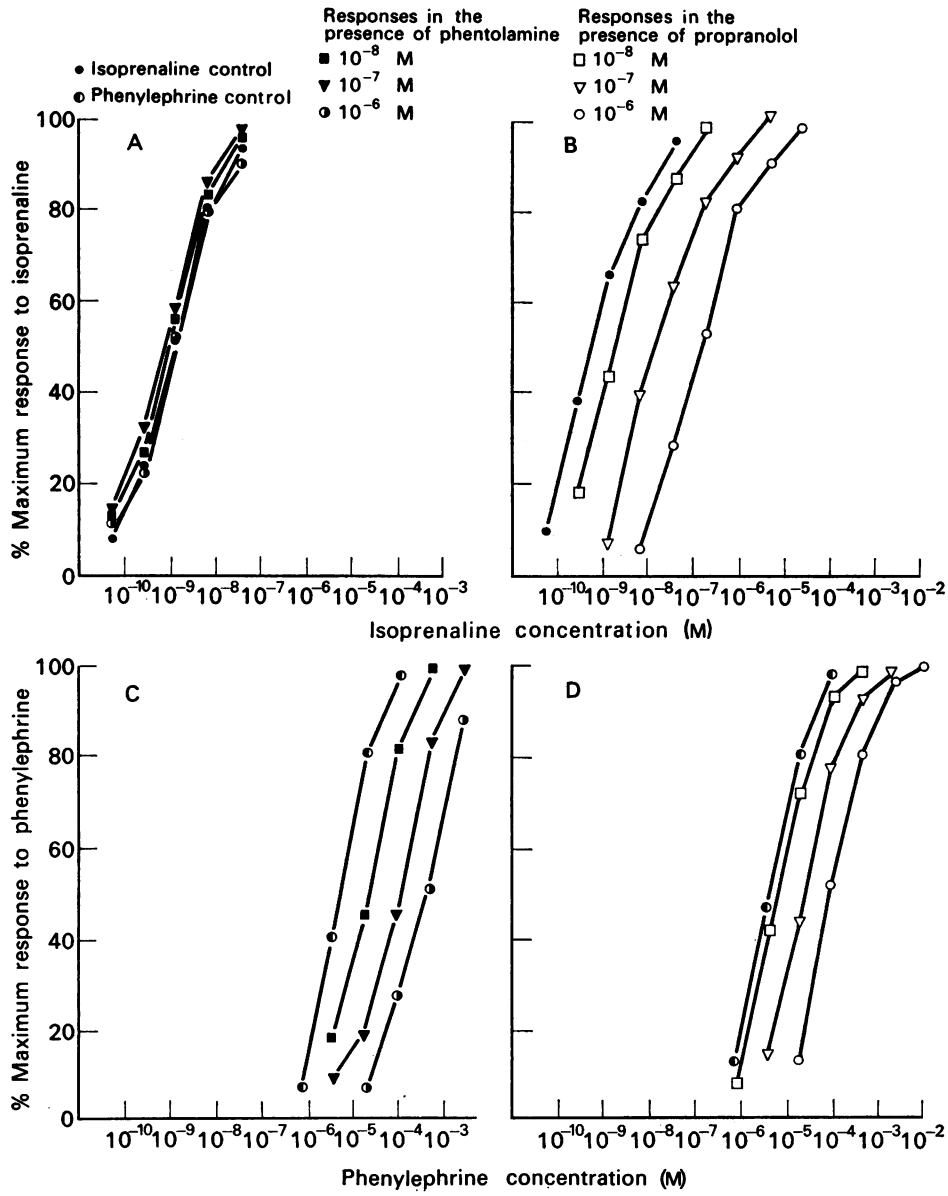

FIG. 1. Effects of phentolamine and propranolol on the relaxation of the guinea-pig colon produced by isoprenaline and phenylephrine. A and B, responses to isoprenaline; C and D, responses to phenylephrine. Each point is the mean of ten experiments.

This contrasts with the findings of Farmer & Levy (1969, 1970) but confirms the observations of Bartlet & Hassan (1969, 1970). The only evidence of α-adrenoceptor involvement was the reduction in the isoprenaline maximum response in the presence of high concentrations of dibenamine. This effect might, however, have been due to a non-specific action of the antagonist.

In the distal colon, the effects of phenylephrine can be explained in terms of an interaction with both α- and β-adrenoceptors. It is of interest that Bartlet & Hassan (1970) found no evidence of an interaction of phenylephrine with the β-

adrenoceptors in guinea-pig proximal colon in contrast to the chick rectum where most of the action of phenylephrine was mediated by β-adrenoceptors.

It appears from these results that a further investigation of the properties of β-adrenoceptors in lower intestinal tissues and their interaction with phenylephrine would be worthwhile.

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