Inhibition of Guinea-Pig Taenia Coli Mediated by α_1-, β_2-Adrenoceptors and ATP-Receptor Activation

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Abstract. The actions of α- and β-adrenoceptor agonists, antagonists and ATP were investigated on the smooth muscle of the guinea-pig taenia coli. Electrical and mechanical activities were recorded by means of the sucrose gap method. Noradrenaline, phenylephrine and methoxamine hyperpolarized the smooth muscle membrane, decreased the membrane resistance, reduced the size of phasic contractions, decreased the smooth muscle tone and supressed the spontaneous and evoked spike activities. Clonidine and ephedrine were inactive. The effects of agonists were abolished by α_1-adrenoceptor antagonists (carbidine and phenoxybenzamine) and $\alpha_{1,2}$-adrenoceptor antagonist (phentolamine) but were unchanged by α_2-adrenoceptor antagonist (yohimbine) and $\beta_{1,2}$-adrenoceptor antagonist (propranolol). Isoprenaline and salbutamol suppressed the spontaneous spike generation, reduced the smooth muscle tone, caused a small hyperpolarization of the membrane without any change in the membrane resistance. Tazolol was ineffective. The effects of isoprenaline were abolished by $\beta_{1,2}$-adrenoceptor antagonists (propranolol, metipranolol and pindolol) and only partially inhibited by a β_1-adrenoceptor antagonist (practolol). The actions of ATP were similar to those of α_1-adrenoceptor agonists but they were not inhibited by α- and β-adrenoceptor antagonists. It is suggested that the α_1- and β_2-adrenoceptors mediate the inhibitory action of adrenoceptor agonists in the taenia coli. The actions of ATP, which are very similar to those of α_1-adrenoceptor agonists, are not mediated by adrenoceptors, but the sequence of events induced by α_1-adrenoceptor and ATP-receptor activation could be very close.

Key words: Taenia coli — α_1-adrenoceptor — β_2-adrenoceptor — ATP-receptor

Introduction

It is well known that the inhibitory actions of catecholamines on the visceral smooth muscles can be mediated by α- and β-adrenoceptors (Ahlquist 1948). Lands et al. (1967) discovered that β-adrenoceptors are of two subtypes, β_1- and

β_2-receptors, which are characteristic of the heart and the vascular smooth muscle, respectively. Recently, evidence has accumulated which indicates that the adrenergic α-receptors are not of a single type, as well. Langer (1974) first proposed that the α-adrenoceptors should be classified as α_1- and α_2-adrenoceptors. The α_1-adrenoceptors were referred to as the postsynaptic α-receptors which initiate the response of the effector tissue, while the α_2-type constitutes the presynaptic α-receptor which regulates the transmitter release (Langer 1977; Starke et al. 1977). The subdivision of α-adrenoceptors is now widely accepted, but many data indicate that the two subtypes may not have an identical localization and may not exist as the only two homogenous populations. Starke and Langer (1979) proposed that the classification into α_1- and α_2-adrenoceptors should be based on the pharmacological differences in their relative affinities for specific agonists and antagonists disregarding either the location, or function of α-adrenoceptors exclusively.

The inhibitory action of catecholamines in the small intestine (Ahlquist and Levy 1959; Kosterlitz et al. 1970; Bauer 1981) and the taenia coli (Bülbring and Tomita 1969b; Watanabe 1976; Bauer and Zakhari 1977; Iwayama et al. 1979) was proposed to be mediated by α- and β-adrenoceptors. Burnstock (1972), moreover described the non-cholinergic, non-adrenergic inhibition of the intestinal smooth muscle, which was tentatively classified as a response mediated by the so called "purinergic" nerves. This assumption was based on the parallelism between the response induced by ATP and transmural stimulation (Jager 1974).

There are only a few data on α- and β-adrenoceptor subtypes in the guinea-pig taenia coli (Bauer and Zakhari 1977; Török and Vizi 1980). The present investigation has been undertaken, therefore, to characterize the adrenoceptors and ATP-receptor induced changes, as well as the α and β-adrenoceptor subtypes in ther guinea-pig taenia coli on the basis of their relative affinities for agonists and antagonists. Some of these results have been communicated to the Czechoslovak Pharmacological Society (Bauer 1978).

Material and Methods

Male guinea-pigs (250—400 g) were sacrificed by a blow on the neck. Fine strips of the taenia, about 0.5—0.7 mm in width and 20—40 mm in length were removed from the caecum. The preparations were inserted into a double sucrose-gap apparatus (Bülbring and Tomita 1969a) and exposed to the isotonic K_2SO_4 solution (77.5 mmol.l^{-1}), to the isotonic sucrose solution (270 mmol.l^{-1}, of specific resistance of at least 10^6 ohm.cm) and to the modified Krebs solution of the following composition (mmol.l^{-1}): Na^+ 136.6, K^+ 5.9, Ca^{++} 2.5, Mg^{++} 1.2, Cl^- 133.3, HCO_3^- 15.4, $H_2PO_4^-$ 1.2 and glucose 11.5. Approximately a 0.7—0.8 mm long section of the tissue was in the test solution. Any contact between the sucrose solutions and the electrolyte solutions flowing on either side was prevented by using latex membranes through which the taenia were threaded (Bauer and Zakhari 1977). The rate of flow of all the solutions was kept constant throughout the experiments. Constant current pulses of 0.1 — 4 μA intensity, 1.3 s duration and 0.07 Hz frequency, usually with alternating polarities were applied across one gap. The membrane potential and voltage changes evoked by square current pulses were measured

across the second gap. Calomel electrodes were used for stimulation and recording.

One end of the muscle was fixed and the other end was attached by a thread to a strain gauge system for isometric measurements.

The effect of adrenoceptor agonists and antagonists was analysed on the membrane potential, spike activity, membrane resistance and muscle activity. All parameters were displayed on an Elema Mingograph.

The following drugs were used: adrenaline hydrochloride (Spofa), carbidine hydrochloride (Inst. Pharmacol., Medical Acad. Sci., Moscow), clonidine hydrochloride (Boehringer, Ingelheim), ephedrine hydrochloride (Spofa), adenosine-5′-triphosphate disodium salt (ATP; Reanal), isoprenaline hydrochloride (Spofa), methoxamine hydrochloride (Welcome), metipranolol tartarate (Spofa), noradrenaline hydrogentartrate (Spofa), phenoxybenzamine hydrochloride (SKGF), phentolamine hydrochloride (Ciba-Geigy), phenylephrine hydrochloride (Boehringer, Ingelheim), pindol (Sandoz), practolol (ICI), propranolol hydrochloride (Galenika), salbutamol sulphate (Res. Inst. Pharmacol. Biochem., Prague), tazolol hydrochloride (Syntex Research), yohimbine hydrochloride (Spofa). Fresh drug solutions were prepared in a modified Krebs solution just before the experiments. All the drug concentrations are expressed as mol (base).l^{-1}. The Krebs and test solutions were gassed with a mixture of 95% O_2 and 5% CO_2 and the pH was maintained at 7.2—7.4.

A period of 30—40 min was allowed to elapse after mounting the preparation in the sucrose gap chamber to equilibrate the preparation. The agonists were left in contact with the preparation for 90 s and antagonists were applied 10—15 min before and were left during the contact of preparation with the agonists.

The results are expressed as arithmetic means with standard error of mean (SEM). Differences were tested by Students t-test for paired observations (Delaunois, 1973). Agonists dose-ratios were determined from the concentrations causing 50% of the maximum effect in the absence and the presence of each concentration of antagonists. The pA_2 values were determined by Schild plot analysis. The slopes and x-intercept of the Schild plot (mean and 95% fiducial limits) were determined by least-squares regression analysis (Tallarida et al. 1979).

Results

A. The effect of adrenoceptor agonists

The taenia coli of the guinea-pig at 30°C under the initial tension of 1.0 g exhibited a spontaneous activity. The threshold current intensity for the triggering spike and phasic contraction was 0.4 to 0.8 μA. Based on the amplitude of anelectrotonic potentials, applied current intensity and surface area of the tissue, calculated from the cell volume (65% of tissue volume; Bülbring and Tomita 1969a) and the volume-surface ratio (1.5×10^{-4} cm; Goodford and Hermansen 1961), the specific membrane resistance was calculated to be 56.1 ± 5.3 kohm.cm^2, which was of the same order of magnitude as that observed by other methods (Tomita 1966).

a. Changes in the membrane potential

Fig. 1 shows the effects of noradrenaline, adrenaline, isoprenaline (0.01—100 μmol.l^{-1}) and phenylephrine (0.1—100 μmol.l^{-1}) on the membrane potential. Methoxamine (n = 5) and salbutamol (n = 4)(0.1—100 μmol.l^{-1}) elicited also a concentration-dependent increase in the membrane potential. However,

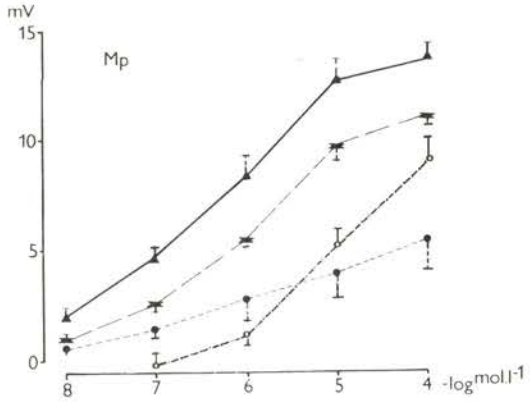

Fig. 1. Membrane hyperpolarization induced by noradrenaline (▲—▲), adrenaline (**X**— —**X**), isoprenaline (●----●) and phenylephrine (○— · —○) on the taenia coli of the guinea-pig. Each point represents the mean of at least seven trials, vertical lines show SEM. Ordinate: membrane hyperpolarization; abscissa: concentration of agonists.

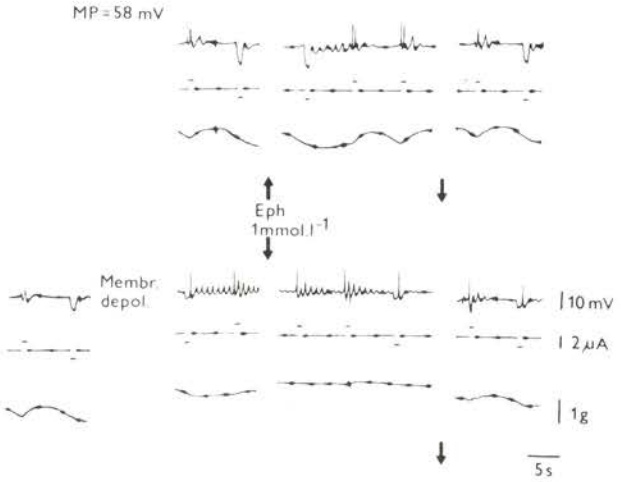

Fig. 2. Effect of ephedrine (Eph) on the taenia coli of the guinea-pig. Upper part: under control condition; and lower part: during the conditioning depolarization of the membrane. In both parts: upper trace is the membrane activity; middle trace is the applied current; lower trace is the muscle tone.

their affinity to the receptors was 10 and 100 times lower than that of phenylephrine (Table 1). The maximal hyperpolarization induced by noradrenaline, adrenaline, phenoxybenzamine and methoxamine reached 10—14 mV. Isoprenaline and salbutamol induced significant changes in the membrane potential only in concentrations higher than 1 and 10 µmol.l^{-1}, respectively and the maximal value

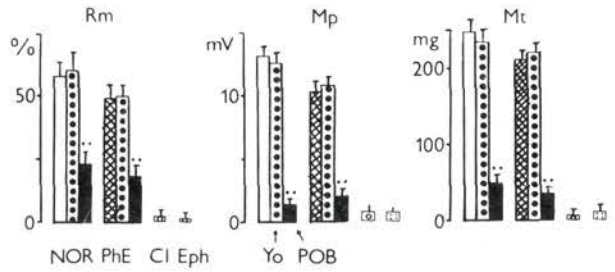

Fig. 3. Effect of noradrenaline (NOR, 1 μmol.l^{-1}, open columns), phenylephrine (PhE, 50 μmol.l^{-1}, hatched columns), clonidine (Cl, 0.5 mmol.l^{-1}, open circles) and ephedrine (Eph, 0.5 mmol.l^{-1}, stippled bars) on the membrane resistance (Rm), membrane potential (Mp) and muscle tone (Mt), before and after 15 min of yohimbine (Yo, 5 μmol.l^{-1}, filled circles) or phenoxybenzamine (POB, 0.5 μmol.l^{-1}, filled columns) treatment. Each column represents the mean of at least six determinations, vertical lines show SEM. Ordinates represent percentage of decrease in amplitude of anelectrotonic potential, membrane hyperpolarization and muscle relaxation, respectively. ... significantly different from the control response ($p<0.05$).

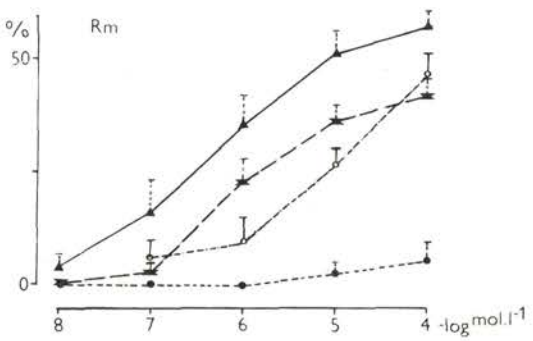

Fig. 4. Decrease in membrane resistance induced by noradrenaline (▲ – ▲), adrenaline (X – – X), isoprenaline (●----●) and phenylephrine (○ – · – ○) on the taenia coli of the guinea-pig. Each point represents the mean of at least seven trials, vertical lines show SEM. Ordinate: percentage of decrease in the amplitude of anelectrotonic potentials, abscissa: concentration of agonists.

hardly reached 5 mV. In contrast ephedrine, clonidine and tazolol, in concentrations up to 1 mmol.l^{-1} did not alter significantly the membrane potential and they remained ineffective in spite of the conditioning depolarization of the membrane as well, as shown in the Figure 2 in the case of ephedrine. The conditioning depolarization, however resulted in an increase in the action of noradrenaline, adrenaline, phenylephrine and ATP.

b. Changes in the membrane resistance

Ephedrine and clonidine (Fig. 2, 3) did not change the amplitude of the anelectrotonic potentials, like tazolol ($n=5$). Noradrenaline, adrenaline and

Table 1. EC_{50} values of adrenoceptor agonists and ATP on the guinea-pig taenia coli

Agonist	$EC_{50} \pm$ s. e. mean ($\mu mol.l^{-1}$)			
	Hyperpolarization	Muscle relaxation	Decrease in membrane resistance	Decrease in evoked spike amplitude
Noradrenaline	0.62 (0.45—0.86)	7.2 (2.6—19.9)	13.1 (7.2—21.3)	1.6 (1.2—2.05)
Phenylephrine	87.3° (46—163)	49.2° (31—76)	121.6° (119—374)	21.4° (12—37)
Methoxamine	905° (384—2010)	504° (360—705)	992° (573—1930)	340° (233—512)
Adrenaline	3.9* (2.7—5.6)	0,8 (0.31—2.4)	94.05 (39—225)	0.52 (0.43—0.63)
Isoprenaline	5495° (3236—9832)	5.8 (3.6—9.4)	>10 mmol.l^{-1}°	7.4* (6.1—8.95)
Salbutamol	8975° (5795—13903)	12.3 (8.5—16.9)	>10 mmol.l^{-1}°	13.5* (8.9—20.4)
ATP	720° (322—1420)	510° (244—1051)	1351° (708—2530)	420° (206—857)

Significantly different from the EC_{50} of Noradrenaline: *$p<0.05$; °$p<0.01$

phenylephrine reduced the size of anelectrotonic potentials, whereas isoprenaline (Fig. 4) and salbutamol (Table 1.) had no significant effect in concentrations up to 100 $\mu mol.l^{-1}$. Methoxamine and ATP had a similar effect to noradrenaline and increased the membrane conductance by 20 to 45% ($n=5$ and $n=6$, respectively). The current voltage relationship had a flatter slope in the anelectrotonic region and the rectification almost disappeared in the catelectrotonic region during the action of noradrenaline (5 $\mu mol.l^{-1}$), phenylephrine (0.1 $mmol.l^{-1}$) and ATP (0.1 $mmol.l^{-1}$) (Fig. 5).

c. Changes in the spike activity

The α- and β-adrenoceptor agonists (noradrenaline, adrenaline, phenylephrine and isoprenaline) decreased the frequency of the spontaneous action potentials and the amplitude of evoked spikes (Fig. 6, 7). Similar effects were apparent by using methoxamine, salbutamol and ATP (Table 1). The inhibition of the spontaneous spike frequency by isoprenaline and salbutamol was more pronounced than their

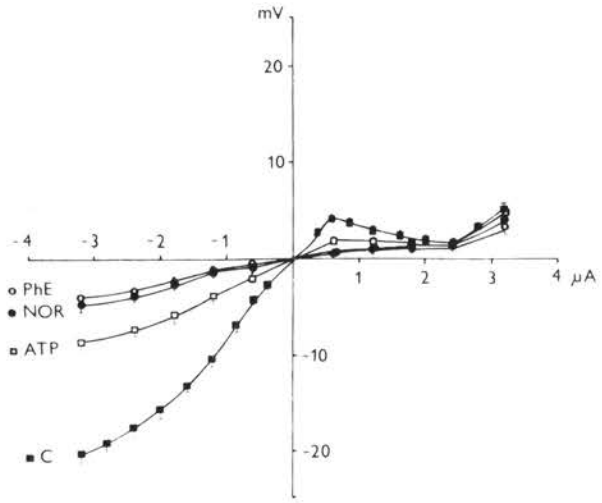

Fig. 5. Current-voltage relationship in the guinea-pig taenia coli, before (■, C) and during the action of noradrenaline (●,NOR 5 μmol.l^{-1}), phenylephrine (○, PhE 0.1 mmol.l^{-1}) and ATP (□, 0.1 mmol.l^{-1}). Each point represents the mean of at least six trials, vertical lines show s. e. mean.

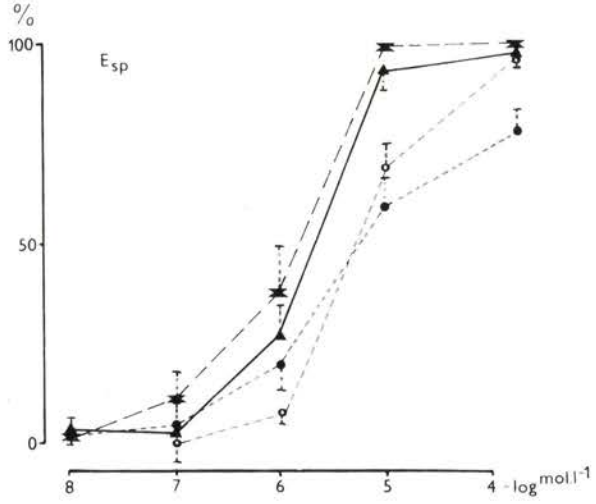

Fig. 6. Inhibition of spontaneous spike frequency by noradrenaline (▲−▲), adrenaline (**X**− −**X**), isoprenaline (●----●) and phenylephrine (○· −○) on the guinea-pig taenia coli. Each point represents the mean of at least seven trials, vertical lines show SEM. Ordinate: percentage of decrease in the spontaneous spike frequency; abscissa: concentration of agonists.

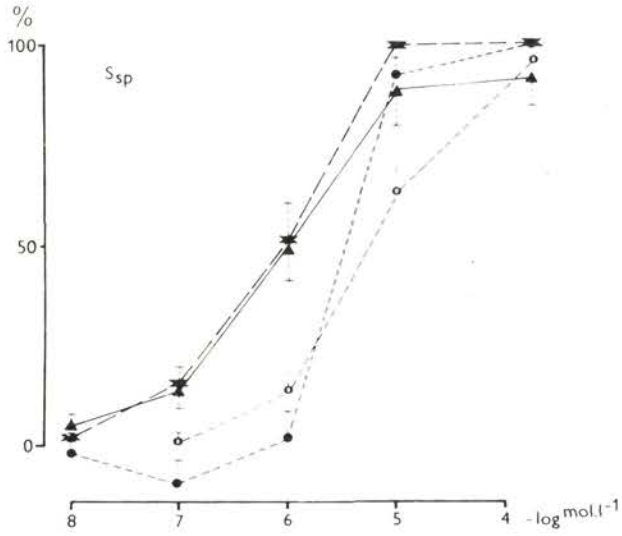

Fig. 7. Same as Fig. 6 for evoked spike amplitude. Here the ordinate is the percentage of decrease in amplitude of spikes induced by direct muscle stimulation.

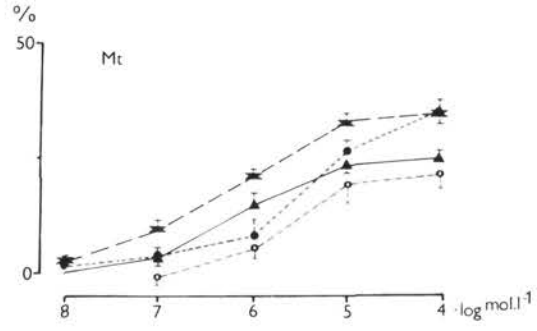

Fig. 8. Decrease in the muscle tone of the guinea-pig taenia coli induced by noradrenaline (▲ – ▲), adrenaline (**X** – – **X**), isoprenaline (●- - - -●) and phenylephrine (○ – – ○). Each point represents the mean of at least seven trials, vertical lines show SEM. Ordinate: percentage of decrease in the initial tone (1.0 g); abscissa: concentration of agonists.

effect on the evoked spikes. The other tested adrenoceptor agonists diminished the frequency of spontaneous and also the amplitude of evoked spikes to the same degree. Clonidine, ephedrine and tazolol, however, did not change the spike activity.

d. Changes in the muscle tone

Adrenaline was the most active in the smooth muscle relaxation and inhibition of the phasic contractions induced by electrical stimulation. Isoprenaline in the

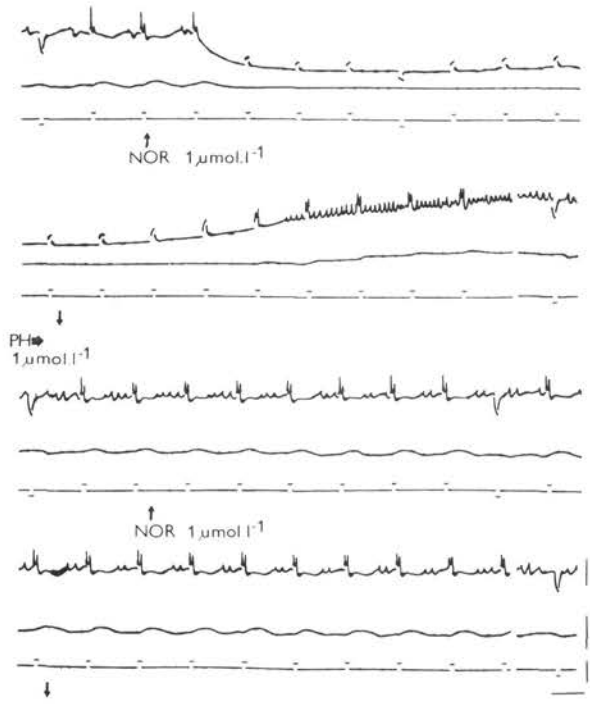

Fig. 9. Inhibition of the effect of the noradrenaline (NOR, 1 μmol.l^{-1}) by phentolamine (PH, 1 μmol.l^{-1}) treatment for 15 min on the guinea-pig taenia coli. Upper part: effect of noradrenaline before, lower part: 15 min after the application of phentolamine to the perfusion solution. Upper trace: membrane activity; middle trace: muscle tone; and lower trace: applied current. Vertical lines represent 10 mV, 2.0 g and 1 μA, respectively, and the horizontal line 10 s.

highest tested concentration induced comparable relaxation to adrenaline, whereas the maximal relaxation elicited by noradrenaline and phenylephrine were smaller (Fig. 8). Methoxamine and ATP had a similar activity to noradrenaline, but in about 70 times higher concentrations (Table 1). Ephedrine and clonidine, however, were almost inactive (Fig. 3). EC_{50} values were calculated in order to compare the effectiveness of α- and β-adrenoceptor agonists and ATP on the membrane potential, muscle tone, membrane resistance and spike activity (Table 1).

B. Interaction between the adrenoceptor agonists and antagonists

a. α-adrenoceptor antagonists

Phentolamine (0.5—5 μmol.l^{-1}), phenoxybenzamine (0.1—2 μmol.l^{-1}) and carbidine (1—50 μmol.l^{-1}) inhibited the actions of noradrenaline (1 μmol.l^{-1}) and phenylephrine (50 μmol.l^{-1}) on the membrane potential, membrane resistance and

Table 2. pA_2 values of α-adrenoceptor antagonists against noradrenaline on the guinea-pig taenia coli

Antagonist	$pA_2 \pm 95\%$ fiducial limits		
	Membrane potential	Muscle tone	Membrane resistance
Phenoxybenzamine+	8.312 (8.089—8.535)	7.925 (7.613—8.237)	8.152 (7.879—8425)
Phentolamine	7.761* (7.490—8.032)	7.346* (7.150—7.542)	7.823* (7.562—8.084)
Carbidine	6.958* (6.775—7.141)	6.739* (6.482—6.996)	6.914* (6.746—7.082)
Yohimbine	< 4.5*	< 4.5*	< 4.5*

+ pD_2'

* significantly different from the pA_2 of phenoxybenzamine ($p<0.05$)

smooth muscle tone (Fig. 3, 9 and Table 2). The inhibitory action of noradrenaline on the spontaneous spike frequency, however, partly remained. Only the membrane hyperpolarization induced by isoprenaline (10 $\mu mol.l^{-1}$) was decreased by α-adrenoceptor antagonists ($n=4$), and the actions of ATP (0.5 $mmol.l^{-1}$) were not changed at all ($n=5$). Yohimbine (0.5—5 $\mu mol.l^{-1}$) (Tab. 2) had no pronounced effect against α-adrenoceptor agonists. Similarly, propranolol (0.15 $\mu mol.l^{-1}$, $n=7$) was ineffective.

b. β-adrenoceptor antagonists

Propranolol (0.5—1 $\mu mol.l^{-1}$), metipranolol (0.5—10 $\mu mol.l^{-1}$), pindolol (0.5—10 $\mu mol.l^{-1}$) and practolol (5—30 $\mu mol.l^{-1}$) increased the spontaneous spike frequency, especially when the spontaneous activity was smaller at lower temperatures (27°C) of the bathing fluid.

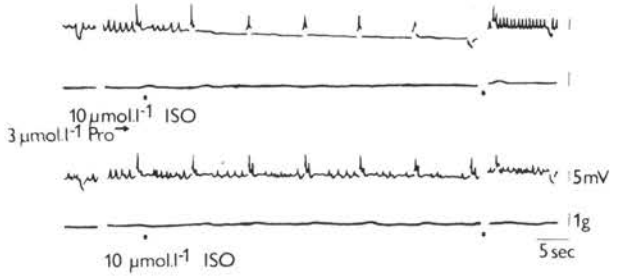

Fig. 10. Inhibition of the effect of isoprenaline (ISO, 10 $\mu mol.l^{-1}$) by propranolol (Pr, o 3 $\mu mol.l^{-1}$) treatment for 5 min of the guinea-pig taenia coli. Upper part: effect of isoprenaline before, lower part: 5 min after the application of propranolol to the perfusion solution. Upper trace: membrane activity; lower trace: muscle tone.

Table 3. pA_2 values of β-adrenoceptor antagonists against isoprenaline on the guinea-pig taenia coli

Antagonist	$pA_2 \pm 95\%$ fiducial limits		
	Membrane potential	Muscle tone	Spontaneous spike frequency
Practolol	4.458 (4.207—4.709)	4.728 (4.496—4.960)	5.263 (5.067—5.459)
Metipranolol	5.879* (5.682—6.076)	6.537* (6.378—6.796)	6.631* (6.493—6.769)
Propranolol	6.534*° (6.358—6.710)	7.039*° (6.852—7.226)	8.105*° (7.895—8.315)
Pindolol	6.336* (6.042—6.630)	7.012* (6.771—7.253)	7.928*° (7.749—8.107)

* significantly different from the pA_2 of practolol ($p<0.05$)
° significantly different from the pA_2 of metipranolol ($p<0.05$)

Propranolol (3 $\mu mol.l^{-1}$) antagonized predominantly the inhibition of the spike activity induced by isoprenaline (10 $\mu mol.l^{-1}$) and only partly its action on the membrane potential (Fig. 10). Similarly the other tested β-adrenoceptor antagonists were less effective against hyperpolarization induced by higher concentrations of isoprenaline and were more effective against the isoprenaline induced decrease in spontaneous spike activity. They shifted the isoprenaline concentration-response curves to the right. Based on the pA_2 values practolol, in taenia coli, was less active against the isoprenaline actions, by 1—2 orders, than the other β-adrenoceptor antagonists (Table 3). None of the studied β-antagonists changed significantly the actions of noradrenaline, phenylephrine and ATP on the membrane and muscle activities of the taenia coli.

Discussion

Noradrenaline, adrenaline, phenylephrine, methoxamine and ATP affect mainly the membrane potential and membrane resistance, whereas isoprenaline and salbutamol act predominantly on the spontaneous spike frequency of the guinea-pig taenia coli. Therefore, as previously suggested the stimulation of both α- and β-adrenoceptors and ATP-receptors could mediate the inhibition in the taenia coli of the guinea-pig (Jenkinson and Morton 1967; Andersson and Mohme Lundholm 1969; Bülbring and Tomita 1969a; Jager 1974; Bauer and Zakhari 1977).

The selectivity of α_1- and α_2-adrenoceptors has been determined for a variety of α-adrenoceptor antagonists (Drew, 1978; Starke et al. 1975, Wikberg 1978; Bauer 1979; 1980; 1981). As far as the agonists are concerned, it has been suggested that methoxamine and phenylephrine are α_1 selective and clonidine and

ephedrine are α_2 selective agonists, whereas adrenaline and noradrenaline have approximately an equal potency at both α_1- and α_2-adrenoceptors and are therefore nonselective α-adrenoceptor agonists (Berthelsen and Pettinger 1977; Bauer 1981). In the present study α-agonists (noradrenaline, adrenaline, phenylephrine and methoxamine) hyperpolarized the smooth muscle membrane, increased the membrane conductance, decreased the spike activity and smooth muscle tone. The selective α_2-adrenoceptor agonists ephedrine (Bauer 1981) and clonidine (Wikberg 1978; Starke et al. 1975) failed to change the membrane potential, membrane resistance, spike activity and smooth muscle tone not only under control conditions, but also during the conditioning depolarization of the membrane. Among the α-adrenoceptor antagonists phenoxybenzamine (Doxey et al 1977; Bauer 1980) and carbidine (Bauer 1980) are considered as α_1-selective; yohimbine (Doxey et al. 1977; Bauer 1980) as α_2-selective and phentolamine (Cavero et al. 1977) as non-selective α-adrenoceptor antagonist.

The fact that hyperpolarization, the increased membrane conductance and decreased smooth muscle tone induced by noradrenaline, phenylephrine and methoxamine were fully prevented by α-adrenoceptor antagonists phenoxybenzamine, carbidine and phentolamine and that they were not influenced by yonimbine indicates that the postsynaptic inhibitory α-adrenoceptors of the taenia coli are of α_1-type, different from those of pre- and postsynaptic inhibitory α-adrenoceptors present in the guinea-pig ileum (Bauer 1979; 1980).

It has been emphasised that the action of isoprenaline in the taenia coli resulted in the abolition of pacemaker activity, reduction in the size of phasic contraction, or smooth muscle tone with no appreciable changes in the membrane potential and the membrane resistance (Bülbring and Tomita 1969b). Later, however, Bauer and Zakhari (1977) and Bülbring and Den Hetog (1980) showed the data, as it was also seen in the present experiments, namely that isoprenaline and the β_2-adrenoceptor agonist salbutamol are able to elicit a small, concentration-dependent membrane hyperpolarization simultaneously with a decrease in the phasic contractions, of smooth muscle tone.

The inhibition of spike activity, muscle relaxation and partly membrane hyperpolarization induced by isoprenaline were antagonized predominantly by propranolol, metipranolol and pindolol, which block both β_1- and β_2-adrenoceptors (Shanks 1967; Karow et al. 1971; Zakhari 1974). Practolol, which is a specific β_1-adrenoceptor antagonist (Karow et al., 1971) was less active and the β_1-agonist tazolol was almost inactive in the taenia coli. Carlson et al. (1977) suggested that both β_1-and β_2-adrenoceptors could coexist in a single organ and radioligand studies support this concept (Minneman and Motinoff 1980). Based on the presented results, it could be concluded that in the guinea-pig taenia coli the majority of the β-adrenoceptors are represented by β_2-adrenoceptors, but β_1-adrenoceptors are also present in the taenia coli of the guinea-pig.

The effects of ATP were very similar to those of α_1-adrenoceptor agonists in the guinea-pig taenia coli. In contrast, however, the action of ATP was not inhibited by the α- and β-adrenoceptor antagonists like in the case of the non-cholinergic, non-adrenergic inhibitory junction potentials in this tissue (Jager 1974). It seems unlikely, therefore, that α- and β-adrenoceptors might be involved in the actions of ATP. Since the effect of α_1-adrenoceptor agonists and ATP on the membrane activities and smooth muscle tone are so similar, the activation of α_1-adrenoceptors and ATP-receptors might finally induce the same sequence of events mediated probably by common subreceptor units.

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