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Characterization of postsynaptic α-adrenoceptors in the arteries supplying the oviduct

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1 *In vitro* experiments were designed to characterize postjunctional α-adrenoceptor subtypes in ring segments (1 mm length; outer diameter 300–500 μm) from arteries supplying the oviduct of the heifer.

2 Noradrenaline, adrenaline and phenylephrine evoked concentration-dependent contractile responses. The pD_2 values were 5.67, 5.89 and 5.93, respectively. Medetomidine, clonidine and B-HT 920 (2-amino-6-allyl-5,6,7,8-tetra-hydro-4H-(thiazo)-4,5-d-azepine) were ineffective.

3 The α-adrenoceptor selective antagonists, prazosin (1 nM–0.1 μM) and rauwolscine (0.1–10 μM) competitively antagonized the response to noradrenaline. The pA_2 values were 9.38 and 6.83, respectively.

4 The dissociation constant (K_D) for noradrenaline calculated by use of the irreversible antagonist, dibenamine, was 3.95 (2.09–5.81) μM. The occupancy-response relationship was non-linear. Half-maximal response to noradrenaline was obtained with 22% receptor occupancy while maximal response required 100% occupancy.

5 B-HT 920 evoked a biphasic contractile concentration-dependent response in preparations incubated in a physiological solution containing 20 mM K^+, 0.1 μM prazosin and 1 μM propranolol. Rauwolscine 0.1 μM significantly ($P < 0.01$) blocked the first component of the B-HT 920 concentration-response curve with an apparent pA_2 value of 8.52 (7.86–9.18).

6 These results strongly suggest that α-adrenoceptors in oviductal arteries are mainly of the α_1 subtype, although a possible role for α_2-adrenoceptors cannot be excluded.

Keywords: α-Adrenoceptors; vascular smooth muscle; oviductal arteries

Introduction

The oviduct and arteries which supply it (i.e. oviductal arteries) are richly innervated by sympathetic nerves (Brunding *et al.*, 1969; Black, 1974). It is well established that the sympathetic nervous system is involved in the control of the contractile activity of the oviduct (Howe & Black, 1973; Rodriguez-Martinez, 1984; Samuelson & Sjöstrand, 1986; Isla *et al.*, 1989). This control is also related to the hormonal status through the oestrous cycle, which could influence the catecholamine concentration as well as the receptor predominance (Samuelson & Sjöstrand, 1986; Juorio *et al.*, 1989).

The role of the sympathetic nervous system in non-contractile processes that take place in the oviduct, such as oviduct fluid formation, is yet to be elucidated (Forman *et al.*, 1986). It has been suggested that the sympathetic nervous system could be involved in regulating this process through a control of the blood supply to the oviduct, so that its agents would be expected to inhibit oviduct fluid formation (Leese, 1988).

Limited information exists on the effects of noradrenergic agents on the arteries supplying the oviduct. It is known that noradrenaline evokes a concentration-dependent contractile response in human isolated oviductal arteries (Forman *et al.*, 1985); however, the α-adrenoceptor subtypes involved in this response, have not yet been determined.

Selective receptor agonists and antagonists have shown to be useful tools in the pharmacological characterization of receptors (Kenakin, 1987). Irreversible antagonists such as dibenamine, partially inactivate the α-adrenoceptor population so that the fraction of receptor occupied at each concentration of agonist can be calculated (Furchgott & Bursztyn, 1967).

Since the importance of the sympathetic nervous system in the oviduct vascular bed is still rather unknown, the present investigation was undertaken to characterize the α-adrenoceptor subtypes involved in the contractile activity of isolated oviductal arteries. The dissociation constant and the receptor reserve for noradrenaline-induced responses were also determined. Oviductal arteries from immature heifers, in which an influence of the sex hormones can be ruled out, were used in this study.

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Methods

Vascular preparations

Genital tracts from immature heifers with ovaries macroscopically quiescent were collected daily from the slaughterhouse, placed in ice-cold physiological salt solution (PSS) (composition in mM: NaCl 119, KCl 4.6, $CaCl_2$ 1.5, $MgCl_2$ 1.2, $NaHCO_3$ 15, NaH_2PO_4 1.2, glucose 11 and EDTA 0.01 at pH 7.4) and transported to the laboratory.

The oviduct and a small portion of the tip of the uterine horn were separated from the rest of the genital tract and fixed in a Petri dish filled with ice cold PSS. The uterine branch of the ovarian artery was identified and segments of its secondary branches (300–500 μm outer diameter) supplying the oviductal isthmus were carefully dissected free from the mesosalpinx and surrounding tissue with the aid of micro-scissors and a stereomicroscope (Nikon SMZ 2B). Ring preparations of approximately 1 mm in length were obtained and transferred to 5 ml organ baths containing PSS at 37°C bubbled with 95% O_2 and 5% CO_2. The preparations were gently slid onto parallel stainless steel legs (75 μm diameter) of two L-shaped steel hooks (Högestätt *et al.*, 1983). One of the hooks was attached to a displacement unit allowing the fine adjustment of tension and the other was connected to a force-displacement transducer (GRASS FT O3C). Isometric wall tension was recorded on a GRASS model 7B polygraph. Preparations were allowed to equilibrate for about 1 h in PSS. During this period the organ baths were washed with fresh (37°C) PSS every 15 min and the passive tension was set at

1.75 mN mm^{-1} in length by stepwise stretching of the rings. This tension was obtained in previous experiments in which the level of passive tension was correlated to the maximum response elicited by K-PSS (PSS with 119 mM KCl substituted for NaCl). In brief, arterial ring segments ($n = 7$) were exposed every 30 min to K-PSS and the passive tension (resulting tension after washout in PSS) was increased stepwise until a maximal contraction to K-PSS was obtained in all vessel segments.

Experimental procedure

After the equilibration period, rings were contracted two or three times with K-PSS at 30 min intervals. Potassium depolarization served as a control of reproducibility of the contractions and as an internal standard for each vessel ring (Fallgren & Edvinsson, 1986).

The integrity of the endothelium was tested by applying acetylcholine (ACh) (1 μM) to vessels constricted with increasing concentrations of noradrenaline until the level of tension was approximately 50–60% of the response induced by K-PSS. Preparations with intact endothelium relaxed well (80–100% of the noradrenaline response) in the presence of ACh, whereas in the absence of endothelium, ACh had either no effect or even contracted rings.

Contractile concentration-response curves to the different α-adrenoceptor agonists were obtained by adding increasing concentrations of the agonists to the bath in half log unit steps, when the previous concentration had produced its equilibrium response, or after 5 min if no response was obtained (Van Rossum, 1963).

In the experiments where the effects of cocaine, propranolol, prazosin and rauwolscine were investigated, the preparations were incubated for 45 min with the drug before a second concentration-response curve to the agonist was obtained. In order to determine the dissociation constant (K_D) to noradrenaline, the irreversible α-blocker, dibenamine, was used. After determination of the concentration-response curve to noradrenaline, rings were exposed to dibenamine (50 nM) for 10 min and then rinsed at 5 min intervals for the next 60 min. After this period, reproducible concentration-response curves to noradrenaline were obtained which were depressed and shifted to the right with respect to the control. In all the experiments, at least one vessel ring that received no antagonist was run in parallel with the experimental rings. These control experiments showed no change in either the maximum effect or sensitivity after five applications of noradrenaline. In experiments involving α-adrenoceptor antagonists, tissues were pretreated with iproniazid (0.36 mM) for 45 min at the beginning of the experiment to block monoamine oxidase (MAO) and the bath solution contained propranolol (1 μM) to block β-adrenoceptors, corticosterone (10 μM) and cocaine (10 μM) to inhibit the extraneuronal and neuronal uptake mechanisms and tropolone (10 μM) to inhibit catechol-*O*-methyltransferase (COMT).

In order to investigate the α_2-adrenoceptor-mediated contractile activity in pre-depolarized arteries the following experiments were performed. Vascular rings were incubated for 45 min in a K-PSS (20 mM K^+) containing propranolol (1 μM) and prazosin (0.1 μM) to block β- and α_1-adrenoceptors, respectively. After this treatment, concentration-response curves to B-HT 920 (2-amino-6-allyl-5,6,7,8-tetra-hydro-4H-(thiazo)-4,5-d-azepine) in the absence and in the presence of 0.1 μM rauwolscine were established.

Calculations and statistics

The contractile response induced by each concentration of agonist was expressed in mN of tension developed above basal levels and used in the construction of the concentration-response curves. The concentration of each agonist eliciting 50% of its own maximum response (EC_{50}) was determined graphically for each curve by linear interpolation. The relative potencies of the agonists were calculated by the method of the 2 and 2 dose assay (Tallarida & Murray, 1987). The pA_2 values for prazosin and rauwolscine were determined from a Schild plot (Arunlakshana & Schild, 1959) using noradrenaline as the agonist. The concentration ratio (CR) produced by the antagonist (i.e., the ratio of concentrations of noradrenaline giving an equal response in the presence and in the absence of the competitive antagonist: always measured as the EC_{50} value) was determined for various concentrations of antagonist. The apparent pA_2 of rauwolscine in pre-depolarized preparations was determined with only one concentration of the antagonist and B-HT 920 as the agonist. K_B was calculated using the equation (Furchgott, 1972):

$$K_B = \frac{[\text{antagonist}]}{(\text{CR}-1)}$$

where CR is the concentration-ratio (i.e., the ratio of concentrations of B-HT 920 giving 50% of the control maximum response in the presence and in the absence of rauwolscine, 0.1 μM). The control maximum response was established at 10 μM B-HT 920.

The noradrenaline dissociation constant (K_D) was calculated according to the procedure described by Furchgott & Bursztyn (1967); after partial receptor inactivation by an irreversible antagonist, equieffective concentrations of noradrenaline before ([A]) and after ([A']) treatment were compared using the equation (Furchgott, 1966):

$$\frac{1}{[A]} = \frac{1}{q[A']} + \frac{1-q}{qK_D}$$

where K_D is the functional equilibrium dissociation constant for the agonist and q is the fraction of the active receptors remaining after partial irreversible blockade. A plot of 1/[A] against 1/[A'] was constructed. The slope of the regression line and y-intercept were used to calculate K_D from the equation:

$$K_D = \frac{(\text{Slope} - 1)}{\text{Intercept}}$$

The fraction of receptors occupied (RA/RT) in control tissues at each concentration of agonist [A] was calculated from the following equation (Furchgott & Bursztyn, 1967):

$$\frac{[RA]}{[RT]} = \frac{[A]}{K_D + [A]}$$

The control response for noradrenaline was then replotted as a function of the fractional receptor occupation and appropriate curves were constructed. Estimates of the receptor reserve were made from K_D/ED_{50} (Ruffolo, 1982; Kenakin, 1987).

Results are expressed as means ± s.e.mean or as mean values with 95% confidence intervals. One-way analysis of variance (ANOVA) was used when more than two groups were analysed. Statistical differences between two means were determined by Student's t test for paired or unpaired observations where appropriate. A value of $P < 0.05$ was considered to be statistically significant. The least squares method was used for calculating linear regressions. For the Schild plot, differences between the slope and unity were tested with Student's t test, under a null hypothesis (slope = 1). n denotes the number of animals from which vessels were taken.

Drugs

The following drugs were used: (±)-noradrenaline HCl and (−)-adrenaline (Serva, Germany); B-HT 920 (2-amino-6-allyl-5,6,7,8-tetra-hydro-4H-(thiazo)-4,5-d-azepine) (Boehringer Ingelheim, Spain); prazosin HCl (Pfizer, U.S.A.); rauwolscine HCl (Carl Roth, Germany); dibenamine HCl (Smith Kline & French, U.K.); medetomidine HCl (Farmos Group, Finland);

phenylephrine HCl, clonidine HCl, propranolol HCl, cocaine HCl, corticosterone, tropolone and iproniazid (Sigma, U.S.A.). Prazosin was dissolved in warm water (50°C) at pH 4–5 by constant agitation. Dibenamine and corticosterone were prepared in 99% ethanol and adrenaline in 0.25 N HCl and further diluted in water containing ascorbic acid (1 mM). Previous experiments showed that the solvents used had no effect on preparations. Stock solutions of drugs were stored at −20°C and fresh dilutions were made daily except for dibenamine which was prepared immediately before use for each experiment. All drugs were added directly to the bath in volumes of 5–50 μl and the concentrations given are the calculated final concentration in the bath solution.

Results

The α-adrenoceptor agonists adrenaline, noradrenaline and phenylephrine induced concentration-dependent contractions in the arteries supplying the oviduct of the heifer (Figure 1), whereas clonidine, B-HT 920 and medetomidine were ineffective in all vessels tested. The maximum contractile effect to these agonists as well as the sensitivity, expressed as pD_2, were not significantly different. The order of potency, was noradrenaline = phenylephrine = adrenaline (Table 1).

The maximum contractile response (E_{max}) and the EC_{50} (expressed as pD_2) to noradrenaline (E_{max} = 7.40 ± 1.52 mN, pD_2 = 5.87 ± 0.18, n = 5) were unaffected by the addition to the bath of 1 μM cocaine (E_{max} = 7.30 ± 1.46 mN, pD_2 = 5.63 ± 0.27, n = 5) or 10 μM cocaine (E_{max} = 7.30 ± 0.06 mN, pD_2 = 5.61 ± 0.03, n = 5). On the other hand, the concentration-response curves to noradrenaline (E_{max} = 6.50 ± 0.74 mN, pD_2 = 5.84 ± 0.18, n = 5) and adrenaline (E_{max} = 5.95 ± 0.34 mN, pD_2 = 5.91 ± 0.07, n = 7) were not significantly affected by 1 μM propranolol (E_{max} = 6.80 ± 2.20 mN, pD_2 = 5.88 ± 0.24, n = 5 for noradrenaline and E_{max} = 5.91 ± 0.37 mN, pD_2 = 5.88 ± 0.11, n = 7 for adrenaline).

The selective α_1-adrenoceptor antagonist, prazosin (1–100 nM), produced parallel shifts to the right in the noradrenaline concentration-response curve (Figure 2a). A significant antagonism was observed even at concentrations as low as 1 nM. The Schild plot constructed for prazosin against noradrenaline yielded a straight line with a slope not significantly different from unity and an intercept with the abscissa (pA_2) of 9.57 (Figure 2b). Concentration-response curves to noradrenaline were unaffected by 0.1 μM rauwolscine, whereas, increasing the concentration to 1–10 μM rauwolscine, significantly ($P < 0.001$) shifted the concentration-response curves to noradrenaline to the right (Figure 3a). The Schild plot demonstrating the effects of rauwolscine appeared also to fit in well with a single straight regression line close to unity and gave a pA_2 value of 6.83 (Figure 3b). Although some reduction in the maximal response to noradrenaline was seen at the high prazosin and rauwolscine concentrations, the antagonism can be considered competitive, since the concentration-response curves before and after the antagonist were parallel and construction of a Schild plot gave straight lines with slopes not significantly different from unity.

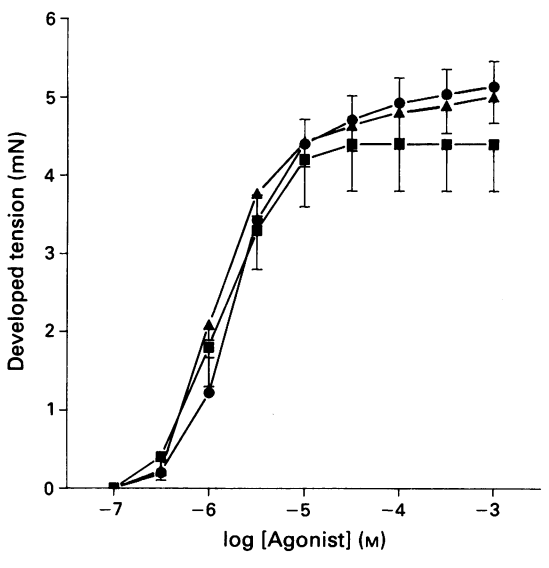

Figure 1 Concentration-response curves in heifer oviductal arteries to noradrenaline (●, n = 12), adrenaline (▲, n = 13) and phenylephrine (■, n = 8). Each point represents mean and vertical lines show s.e.mean.

Table 1 Comparative properties of adrenoceptor agonists on the heifer oviductal arteries

Agonist	n	E_{max} (mN)	pD_2	*Relative potency*
Noradrenaline	12	5.14 ± 0.32	5.67 ± 0.05	1
Adrenaline	13	5.01 ± 0.34	5.89 ± 0.05	0.71
Phenylephrine	8	4.40 ± 0.60	5.93 ± 0.08	0.87

E_{max} values reflect the maximum contractile effects, expressed as the maximal developed tension.
Relative potency obtained by the 2 and 2 dose assay method (Tallarida & Murray, 1987).
pD_2 = −log EC_{50}. Data shown are means ± s.e.mean. n = number of animals.

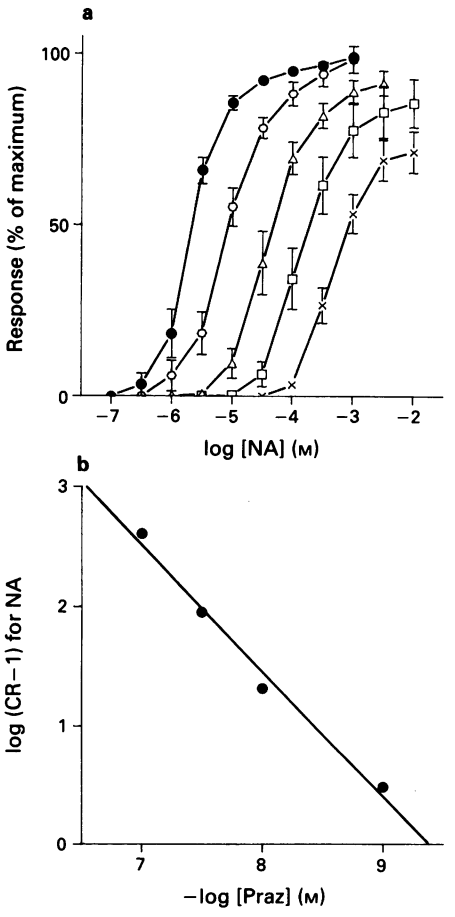

Figure 2 (a) Concentration-response curves for noradrenaline (NA) in the absence (●) and presence of various concentrations of prazosin (Praz): (○) 1 nM, (△) 10 nM, (□) 30 nM, (×) 100 nM. Each point represents the mean and vertical lines show s.e.mean (n = 11). (b) Schild plot of log [CR-1] against −log [antagonist] for Praz-NA antagonism on isolated ring segments of oviductal arteries from heifers. The intercept on the abscissa scale gives the pA_2 value. $y = -1.06x + 9.95$; $r = 0.99$; $pA_2 = 9.38$.

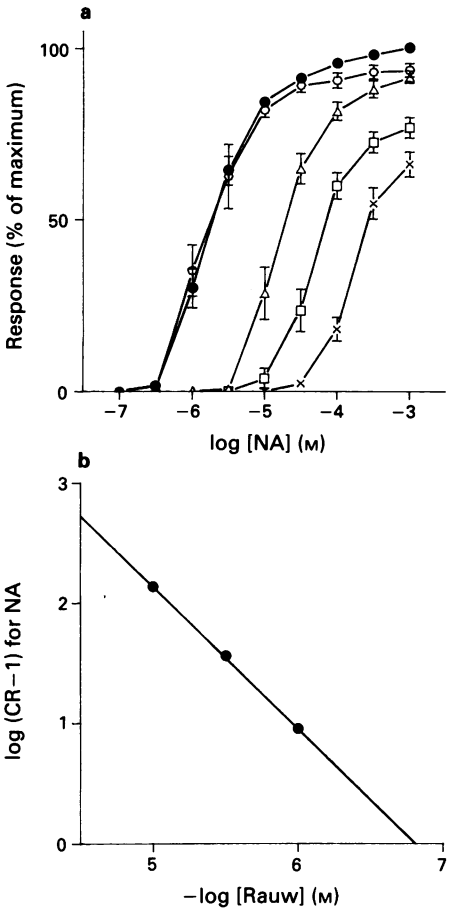

Figure 3 (a) Concentration-response curves for noradrenaline (NA) in the absence (●) and presence of various concentrations of rauwolscine (Rauw): (○) 0.1 μM, (△) 1 μM, (□) 3 μM, (×) 10 μM. Each point represents the mean and vertical lines show s.e.mean ($n = 12$). (b) Schild plot of log [CR-1] against −log [antagonist] for Rauw-NA antagonism on isolated ring segments of oviductal arteries from heifers. The intercept on the abscissa scale gives the pA_2 value. $y = -17x + 8.01$; $r = 0.99$; $pA_2 = 6.83$.

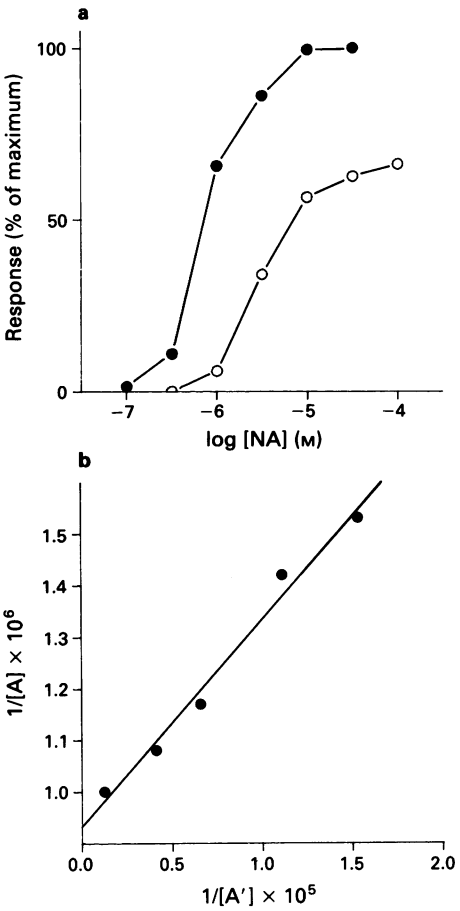

Figure 4 Typical experiment to determine the dissociation constant (K_D) for noradrenaline (NA) in the oviductal arteries of the heifer. (a) NA concentration-response curves before (●) and after (○) exposure of the preparation to dibenamine (50 nM for 10 min). (b) Plot of reciprocals of equiactive concentrations before (1/[A]) and after (1/[A']) treatment with dibenamine from which K_D was calculated as described under 'Methods'. $y = 4.04x + 933962.6$; $K_D = 3.26\,\mu$M.

The dissociation constant (K_D) for noradrenaline was determined by the method of partial alkylation of the α-adrenoceptor population with the irreversible antagonist, dibenamine. An example of these experiments is presented in Figure 4. The mean K_D value was calculated to be 3.95 (2.09–5.81) μM ($n = 11$). The concentration-response relationship for noradrenaline (Figure 5a) was replotted as a function of the receptor occupancy using the calculated K_D mean value (see Methods) and is shown in Figure 5b. A non-linear stimulus-response relationship was obtained, since the maximal response to noradrenaline needed 100% receptor occupancy, whereas the half maximal response was obtained with only 22% of the available receptors. The receptor reserve expressed as K_D/EC_{50} was 2.86.

In preparations pre-depolarized with K-PSS (20 mM K^+) and in the presence of propranolol (1 μM) and prazosin (0.1 μM), B-HT 920 evoked a biphasic concentration-response relationship with an initial small contractile component observed at concentrations up to 10 μM and a second component showing a greater contractile response at higher concentrations. Rauwolscine (0.1 μM) significantly ($P < 0.01$) blocked the first contractile component with an apparent pA_2 (−log K_B) value of 8.52 (9.18 − 7.86) ($n = 9$), whereas the second was unaffected (Figure 6).

Discussion

The results obtained in the present investigations suggest that responses to α-adrenoceptor agonists are mediated predominantly by α_1-adrenoceptors, although the presence of α_2-adrenoceptors cannot be excluded.

The contractile responses obtained with the endogenous agonists noradrenaline and adrenaline, which exhibit mixed α_1- and α_2-adrenoceptor activity (Timmermans & Van Zwieten, 1981), indicate the presence of α-adrenoceptors in the oviductal arteries of the heifer. The lack of effect of propranolol, a β-adrenoceptor antagonist, on the response to noradrenaline and adrenaline suggest that β-adrenoceptor activation is not involved in their effects.

Cocaine, which inhibits neuronal catechol uptake mechanisms and thus, increases the agonist concentration in the neuroeffector junction, had no effect on the noradrenaline-induced contraction, suggesting that no neuronal uptake occurs in the oviductal arteries of the heifer. This is in agreement with the results obtained in uterine arteries from the guinea-pig (Fallgren & Edvinsson, 1986) and ewe (Isla & Dyer, 1990).

Phenylephrine, a selective α_1-adrenoceptor agonist (Starke & Docherty, 1982) seems to behave as a full agonist since its maximum contractile effect was not significantly different from that obtained with the endogenous agonists adrenaline and noradrenaline. Phenylephrine was shown to be equipotent with noradrenaline and adrenaline suggesting the predominance of α_1-adrenoceptor activation by these agonists. Furthermore, the fact that the selective α_2-adrenoceptor agonists B-HT 920 (Timmermans & Van Zwieten, 1982) and medetomidine (Scheinin *et al.*, 1987) failed to contract oviductal arteries argues in favour of the α-adrenoceptors being of the α_1-subtype.

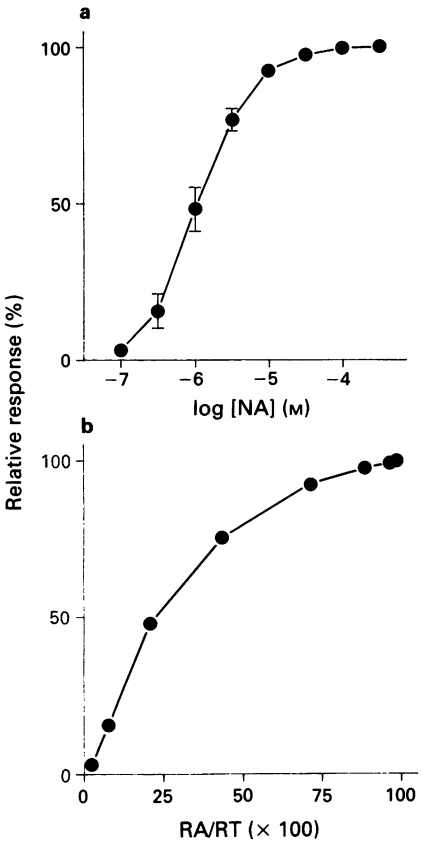

Figure 5 Relationship of the relative response to the log concentration and the fraction of receptors occupied in the noradrenaline (NA) stimulation. (a) Concentration-response curve for the contractile effects of NA in heifer oviductal arteries. Responses are expressed as a percentage of the maximum contractile response elicited by NA. Each point represents the mean and vertical lines show s.e.mean ($n = 15$). (b) Replot of data from (a) showing the relative response as a function of receptors occupied by NA. The fraction of receptors occupied was calculated employing the average K_D value for NA (3.95 μM).

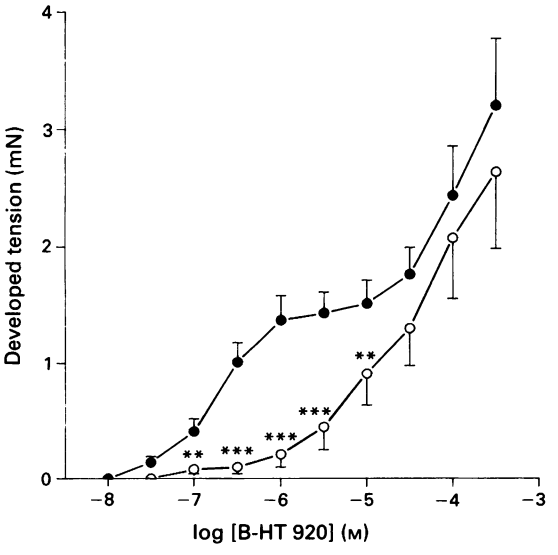

Figure 6 Concentration-response curve for B-HT 920 in the absence (●) and presence of 0.1 μM rauwolscine (○). The bath solution contained 20 mM K^+, propranolol (1 μM) and prazosin (0.1 μM). Tissues were exposed to rauwolscine for 45 min. Each point represents the mean and vertical lines show s.e.mean ($n = 9$). $^{**}P < 0.01$; $^{***}P < 0.001$.

It is generally held that antagonists are better tools than agonists for classifying receptors. This is mainly due to differences in efficacies between agonists, which may seriously hamper the interpretation of the results (Starke, 1981). Prazosin and rauwolscine are generally believed to be among the most selective antagonists for α_1- and α_2-adrenoceptors, respectively (Starke, 1981). The pA_2 value for an antagonist in blocking the response to an agonist should be an accurate indication of its affinity for binding to the receptor site if appropriate precautions are taken and certain criteria fulfilled (Furchgott, 1972; Ruffolo, 1982; Kenakin, 1984; 1987). In the present study, the experiments with prazosin and rauwolscine were carried out in the presence of blockers of neuronal and extraneuronal noradrenaline uptake, β-adrenoceptors, MAO and COMT. Furthermore, in order to maintain the functional integrity of the vessels, care was taken not to remove the endothelium.

The slope of the Schild plot for prazosin in this study was not different from unity indicating that the antagonism is caused in a competitive manner and therefore that the obtained pA_2 value can be assimilated as the $-\log K_B$ value (Arunlakshana & Schild, 1959). According to Furchgott (1972), the K_B value for a specific antagonist acting on the same type of receptor in different preparations should be the same. The pA_2 value of prazosin obtained in the present study (9.38) indicates a high affinity for this α_1-adrenoceptor and is within the range reported for α_1-adrenoceptor blockade (Agrawal *et al.*, 1984; Skärby & Larsson, 1987). However, the Schild plot for rauwolscine gave a slope which was not significantly different from unity and a pA_2 value of 6.83. According to Andersson *et al.* (1984), concentrations of rauwolscine around 10 nM selectively interact with α_2-adrenoceptors; however, concentrations higher than 0.3 μM have been reported to be non-selective for α_2-adrenoceptors, interacting in addition with α_1-adrenoceptors (Skärby & Larsson, 1987). Representative pA_2 values for the interaction of rauwolscine with α_1-adrenoceptors have been shown to be in the range 5.1 to 5.9 (Andersson *et al.*, 1984; Högestätt & Andersson, 1984). Although the rauwolscine pA_2 value in oviductal arteries was higher than this range, the high prazosin/rauwolscine affinity ratio (> 500) and the high rauwolscine concentration needed to obtain a significant inhibition of contraction indicates that rauwolscine is acting non-selectively on α_1-adrenoceptors in oviductal arteries of the heifer.

The obtained K_D value for noradrenaline is in the range reported for K_D in other vascular beds in which a predominance of α_1-adrenoceptors exists (Oriowo *et al.*, 1989; Isla & Dyer, 1990).

Partial receptor alkylation of α-adrenoceptors with dibenamine revealed a non-linear relationship between contraction and percentage receptor occupancy for noradrenaline. Noradrenaline evoked a half maximal contractile response by occupying only 22% of the α-adrenoceptors but maximal response required 100% occupancy. As originally defined, the receptor reserve is the fraction of the total receptor pool not required for a maximal tissue response. From our results, it can be seen that virtually all the receptors are required for maximal response (no receptor reserve as originally defined). The quantification of the receptor reserve by the ratio K_D/EC_{50} better expresses the efficiency of coupling (Ruffolo, 1982; Kenakin, 1987). In oviductal arteries, this ratio was higher than unity suggesting that noradrenaline behaves as a full agonist and that a receptor reserve for the half maximal response exists. However, this ratio is low compared to other vascular beds in which a receptor reserve exists. Thus, in the rabbit aorta, K_D was 21 fold higher than the EC_{50} value (Ruffolo, 1982). This may indicate that in the oviductal arteries of the heifer the coupling between stimulus and response is inefficient.

The results discussed here correlate well with the suggestion of an exclusive population of α-adrenoceptors of the α_1-subtype in oviductal arteries of the heifer. However, it has been noticed that agents causing an elevation of intracellular

calcium concentration such as KCl (Harker et al., 1990), prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) (Furuta, 1988), arginine vasopressin (Templeton et al., 1989), Bay K 8644 (Sulpizio & Hieble, 1987) and endothelin-1 (MacLean & McGrath, 1990) are able to 'unmask' or increase the expression of α_2-adrenoceptor activity. In this sense, contractions evoked by α_2-adrenoceptor stimulants are shown to rely more heavily on the influx of extracellular calcium than those caused by α_1-adrenoceptor activation (Cavero et al., 1983; Van Zwieten & Timmermans, 1987). It is most likely that this influx occurs through voltage-dependent calcium channels (Cavero et al., 1983) and would therefore be sensitive to any alteration in membrane potential. In oviductal arteries partially depolarized with KCl in the presence of prazosin, the α_2-adrenoceptor agonist B-HT 920 evoked a biphasic contractile concentration-dependent curve. This pattern of contractile behaviour has been previously shown with noradrenaline and could reflect the action of receptors other than α-adrenoceptors (Bevan, 1981). From our results, we can speculate that the slight initial contractile component to B-HT 920 could be related to the expression of α_2-adrenoceptor activity, whereas the more marked second component could reflect non-α-adrenoceptor activation or a nonspecific action of this compound. Thus, rauwolscine had a significant blocking effect on the first component with a pA_2 value (8.52) consistent with an interaction with α_2-adrenoceptors (Andersson et al., 1984; Skärby & Larsson, 1987), while the second component was not affected. The physiological significance of this α_2-population is not clear. Ford et al. (1989) have suggested that in uterine arteries, α_2-adrenoceptors could be involved in maintaining the vascular tone rather than in evoking contraction. However, further studies are necessary to ascertain the functional role of this α_2-adrenoceptor population.

In conclusion, we suggest that the α-adrenoceptors involved in the contractile activity of the oviductal arteries are predominantly of the α_1-subtype, without excluding a possible role for α_2-adrenoceptors. A receptor reserve for α-adrenoceptors exists in this tissue although a less efficacious stimulus-response coupling seems to operate compared to other noradrenergically innervated vascular smooth muscles.

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