of re-uptake (Packham, Guccione, Chang & Mustard, 1973; Weiss, Rogers & Brand, 1973). The reasons for this will be discussed. Our results support the concept that collagen induces platelet aggregation by releasing platelet constituents (Haslam, 1967). We suggest that the initial release is associated with platelet-collagen adhesion; both processes occur rapidly and are independent of extracellular calcium.

A.H.D. is an M.R.C. scholar.

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Receptors for 5-hydroxytryptamine and noradrenaline in rabbit aorta and central ear artery

EIRA APPERLEY, P.P.A. HUMPHREY* & G.P. LEVY

Department of Pharmacology, Allen & Hanburys Research Ltd, Ware, Herts

There is considerable evidence implicating 5-hydroxytryptamine (5-HT) in the vascular disturbances associated with migraine (Lance, Anthony & Hinterberger, 1970). As part of a study into the pharmacology of drugs used in the treatment of migraine we have examined the characteristics of 5-HT receptors in vascular smooth muscle from rabbit aorta and ear artery. In addition, the pharmacological characteristics of the α-adrenoceptors in these two tissues were examined.

Preparations were obtained from New Zealand white rabbits anaesthetized with pentobarbitone sodium (36 mg/kg i.v.). Isolated aortic strips and central ear arteries were set up as described by Furchgott & Bhadrakom (1953) and de la Lande & Rand (1965) respectively. Tissues were maintained in Krebs solution gassed with 5% CO_2 in O_2 at

Table 1 Interactions between agonists and antagonists in rabbit vascular smooth muscle

		pA_2 (30 min) against				
Artery	*Antagonist*	*5-HT*	*Methysergide*	*Noradrenaline*	*KCl*	*Vasopressin*
Aorta	Methysergide	8.49 (7.85-9.14)	–	5.29 (4.95-5.63)	<4.6	–
Aorta	Phentolamine	6.21 (5.52-6.90)	–	7.96 (7.76-8.16)	<4.6	–
Central ear	Pizotifen	6.79 (6.39-7.18)	6.95 (6.48-7.42)	6.57 (6.15-6.98)	–	<5.4
Central ear	Phentolamine	8.41 (7.99-8.83)	8.25 (7.96-8.54)	8.09 (7.54-8.64)	–	<7.3

In the aortic strip both agonists and antagonists were added to the bathing solution. In the ear artery the agonists were administered as a bolus injection close to the artery and antagonists added directly to the perfusion reservoir.

The primary and secondary responses to 5-HT in the central ear artery were antagonized to the same extent by pizotifen and phentolamine. The results for the primary phase are presented in Table 1 In the case of methysergide the primary phase was often poorly defined and only the secondary phase was examined.

Each value quoted is the mean (95% confidence limits) of 4-8 separate estimates.

37°C. Agonist-antagonist interactions were examined using the method of Arunlakshana & Schild (1959). Control preparations were used in each experiment so that allowances for changes in sensitivity could be made.

In the aortic strip both noradrenaline (NA) and 5HT caused contractions in the same concentration range ($1.0 \times 10^{-8} - 2.5 \times 10^{-5}$ mol/l). In the ear artery NA ($1.0 \times 10^{-11} - 2.0 \times 10^{-9}$ mol) and 5-HT ($1.0 \times 10^{-8} - 2.5 \times 10^{-6}$ mol) produced vasoconstrictor responses at different doses. In the case of 5-HT the response was biphasic at submaximal doses. Methysergide ($1.0 \times 10^{-8} - 1.0 \times 10^{-6}$ mol) also produced biphasic contractile responses in the ear artery and was similar in potency to 5-HT. Both phases of the response to methysergide and 5-HT were still evident in arteries removed from animals treated with reserpine (1 mg/kg 18-24 h previously. The interactions between agonists and antagonists are summarized in Table 1.

The results suggest that in the aorta 5-HT and NA combine with different receptors whereas in the ear artery they appear to combine with the same receptor which can also be activated by methysergide. The profile of action of methysergide in these two preparations once again raises the question of whether its therapeutic action is mediated through 5-HT-receptor activation or antagonism.

We are grateful for a sample of pizotifen from Sandoz Ltd.

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A comparison of the accumulation of noradrenaline and 5-hydroxytryptamine into arterial smooth muscle

P. BUCHAN*, A.J. LEWIS & M.F. SUGRUE

Department of Pharmacology, Organon Scientific Development Group, Newhouse, Lanarkshire ML1 5SH

5-Hydroxytryptamine (5-HT) is capable of being taken up into both central (Shaskin & Snyder, 1970) and peripheral (Thoa, Eccleston & Axelrod, 1969) adrenergic neurones. In addition to its neuronal uptake, noradrenaline (NA) is extraneuronally accumulated (Gillespie, 1973). The objective of this study was to determine, first, if 5-HT like NA, is accumulated by arterial smooth muscle and secondly, if the accumulation characteristics of 5-HT are similar to those of NA.

Isolated segments of rabbit ear artery were incubated with either NA or 5-HT in 5 ml of Krebs-bicarbonate medium containing ascorbic acid (0.2 mg/ml), EDTA (0.05 mg/ml) and pargyline (0.025 mg/ml) at 37°C under an atmosphere of 95% oxygen and 5% carbon dioxide. Incubation was terminated by removing and washing the tissue in ice-cold Krebs-bicarbonate for 20 minutes. The effect of drugs on amine accumulation was studied by pre-incubating the tissue for 30 min with drug prior to the addition of either NA or 5-HT (3×10^{-3} M for 10 minutes). Segments of artery were subjected to the fluorescence procedure of Falck, Hillarp, Thieme & Torp (1962) and the fluorescence in arterial smooth muscle due to amine was measured photometrically in 7 μm transerve sections.

Histochemical examination of segments of rabbit ear artery incubated with 5-HT revealed an intense yellow-green fluorescence in the smooth muscle cells thus indicating an accumulation of 5-HT. The accumulation characteristics of NA and 5-HT were similar. Above a threshold concentration (3×10^{-5} M) accumulation of NA and 5-HT was concentration-dependent up to 10^{-2} M. The amount of amine accumulated rose rapidly over the first 10 min of incubation and reached a maximum after 20 minutes. Amine fluorescence was decreased in arterial smooth muscle when the incubation was continued in amine-free medium at 37°C (washout $t\frac{1}{2}$ for both amines was 8-12 min) but not after incubation in ice-cold Krebs bicarbonate.

Accumulation of both NA and 5-HT into rabbit ear artery smooth muscle was decreased in a concentration-dependent manner by oestradiol., phenoxybenzamine and normetanephrine. The accumulation of 5-HT was less susceptible to inhibition by these drugs than that of NA. 5-HT accumulation was unaltered by methysergide (10^{-4} M). Following a pre-incubation period of