Some properties of 5-hydroxytryptamine receptors in the hindquarters of the rat

MARIE COOPER & J.H. WYLLIE

Department of Surgery, University College Hospital Medical School

Vascular reactions to 5-hydroxytryptamine (5HT) are complex and often biphasic in the whole animal; so we have attempted to study them in a preparation which eliminates effects arising from the brain, heart, lungs and other organs.

Wistar rats (mean wt 300 g) were decapitated and Krebs' solution warmed to 36°C was pumped at a constant rate of 10 ml/min into the distal aorta; the returning effluent escaped through a laceration of the interior vena cava. Perfusion pressure was recorded; 1-min infusions of 5HT, noradrenaline and some other substances provoked rapid, reproducible dose-related elevations in perfusion pressure. After constructing a dose-response curve to a particular agonist an antagonist was added to the perfusion medium and, after equilibration, a new dose-response curve was made; the antagonists studied could be washed out again with return of sensitivity to near the original value. Both methysergide and cyproheptadine showed a non-competitive type of block whereas phentolamine and a homologous series of phenothiazines produced parallel displacement of the dose-response curves compatible with competitive antagonism (Table 1). On this preparation 5HT never showed any vasodilator activity. Vasospasm produced by 5HT and noradrenaline was mediated by different receptors but no evidence was obtained of heterogeneity of the 5HT-receptors. Activity of the phenothiazines against 5HT-induced vascular spasm ran parallel with their potency as tranquillizers.

Table 1 pA_2 values in perfused hindquarters of rats

Agonist	*Antagonist (B)*	*No. of expts.*	*Mean slope of regression of log (DR-1) on log (B) & 95% conf. limits*	*Mean value of pA_2 and 95% conf. limits*
5HT	Promazine	12	1.08 (0.77–1.39)	7.72 (6.99–8.65)
5HT	Chlorpromazine	19	0.88 (0.65–1.11)	8.97 (7.94–10.23)
5HT	Triflupromazine	12	0.76 (0.48–1.04)	10.34 (9.19–12.17)
5HT	Phentolamine	9	0.76 (0.48–1.03)	6.62 (5.68–7.80)
Noradrenaline	Phentolamine	8	0.96 (0.86–1.06)	8.23 (7.92–8.57)
Tryptamine	Chlorpromazine	10	0.89 (0.63–1.15)	9.07 (8.43–9.92)
Tryptamine with Nialamide 0.1 mM	Chlorpromazine	7	1.01 (0.46–1.56)	9.15 (7.99–11.22)
5-Methyltryptamine with Nialamide 0.1 mM	Chlorpromazine	4	1.24 (0.66–1.83)	8.54 (7.98–9.64)
5-Methoxytryptamine with Nialamide 0.1 mM	Chlorpromazine	6	1.04 (0.81–1.27)	8.86 (8.38–9.43)

The effect of SQ 14225 on baroreceptor reflex sensitivity in conscious normotensive rabbits

D.J. HEAVEY & J.L. REID

Department of Clinical Pharmacology, Royal Postgraduate Medical School, London

SQ 14225 (2-D-methyl-3-mercaptopropanoyl-L-proline) is a new dipeptidase inhibitor which prevents angiotensin II formation and bradykinin inactivation (converting enzyme inhibitor, C.E.I.). It has been shown to have a hypotensive effect in essential and renovascular hypertension in man (Gavras, Brunner, Turini, Kershaw, Tifft, Cuttelod, Gavras, Vukovich & McKinstry, 1978), not significantly increasing heart rate in spite of significant falls in blood pressure. In the salt depleted dog another C.E.I. SQ 20881 was found to reduce the increase in cardiac output in response to a pressure fall (Conway, Hatton & Keddie, 1978). We have investigated the effects of intravenous