M^{-1}, obtained from the curves of the inhibition of [^{3}H]-mepyramine binding, were in good accord with values reported from organ bath studies.

The total number of H_1-receptors varied somewhat from preparation to preparation, the mean value being 124 pmol/g protein. This value is of the same order as that, 169 pmol/g protein, found in homogenates prepared in a similar way from the longitudinal muscle of guinea-pig intestine, although in that tissue, where measurements have been made over a longer period of time, it has become apparent that the number of H_1-receptors can vary widely (range 94–312 pmol/g protein).

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Comparison of the actions of central and peripheral administration of clonidine and BS 100-141 in the rabbit

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Clonidine is a potent antihypertensive drug that lowers blood pressure and heart rate, mainly by an action on central alpha adrenoceptors. However, rapid reversal of the hypotension on withdrawal and the central nervous side effect of sedation limit its usefulness. BS 100-141 (N-amidino-2-(2,6-dichlorophenyl)-acetamide hydrochloride) also appears to lower blood pressure by central mechanisms (Scholtysik, Lauener, Eichenberger, Bürki, Salzmann, Müller, Schweinitzer & Waite, 1975). We have compared the effects of these two drugs after central and peripheral injection.

Male New Zealand white rabbits (2.5–4 kg) had mean arterial pressure (MAP) recorded directly from the ear artery. Intravenous (i.v.) and intracerebroventricular (i.c.v.) injections were given to conscious animals and intracisternal (i.c.) injections after pentobarbitone anaesthesia.

Clonidine (3–100 μg/kg) and BS 100-141 (30–1000 μg/kg) i.v. had a biphasic effect on MAP, first causing a rise then a longer-lasting fall, together with bradycardia. The rise in MAP lasted 1 min after clonidine (30 μg/kg) and 90 min after BS 100-141 (300 μg/kg). These doses caused a similar hypotensive effect, although it was longer after BS 100-141 than clonidine (4 and 1.5 h respectively).

Clonidine (3 μg/kg) given i.c.v. caused a fall in MAP (14 ± 2 mm Hg) by 5 min which lasted for 90 minutes. There was a delay in the fall in MAP after i.c.v. BS 100-141 (12 μg/kg). MAP was not significantly reduced until 60 min (8 ± 3 mm Hg) and remained so at 6.5 hours. Heart rate did not significantly alter on either drug.

Clonidine (3 μg/kg i.c.) had a hypotensive effect (18 ± 5 mm Hg) apparent by 2 min and lasting for 60 minutes. Heart rate was reduced for 90 min only. The fall in MAP (10 ± 4 mm Hg) after BS 100-141 (12 μg/kg i.c.) occurred within 10 min and lasted for 150 minutes. Heart rate was significantly lowered at 90, 150 and 180 minutes ($P < 0.05$).

BS 100-141 has a similar profile of action to clonidine, however, it is less potent, having about one-tenth the potency after i.v. administration and about one-quarter the potency after central administration. The slow onset and longer duration of action of BS 100-141 after i.v. and i.c.v. administration may be due to delay in reaching its site of action in the central nervous system or a result of the prolonged hypertensive effect. The longer duration of action of BS 100-141 may be clinically relevant and permit oral administration to man as a single daily dose.

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