Effect of methoxamine on the outflow of [^{3}H]-noradrenaline from rat vas deferens

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Methoxamine has very low affinity for neuronal uptake mechanism in the isolated rat heart (Burgen & Iversen, 1965) and cat nictitating membrane (Trendelenburg, Maxwell & Pluchino, 1970). These findings are not supported by the reports that the effect of methoxamine is potentiated by cocaine in the rabbit aorta (Kalsner & Nickerson, 1969) and guinea-pig vas deferens (Shah, Patel & Gulati, 1974). In the rat vas deferens, the mechanism of uptake seems to be different from that of other tissues; the effect of tyramine is not prevented by cocaine (Barnett, Staub & Symchowicz, 1969). In the present experiments, we used isolated rat vasa deferentia to study the mode of action of methoxamine. Pretreatment with reserpine (5 mg/kg and 2.5 mg/kg, i.p., 48 and 24 h before experiment respectively) had no significant effect on the response of the tissue to methoxamine (negative log molar ED_{50} 5.86 ± 0.11 control; 5.65 ± 0.77 reserpinized) while it potentiated significantly the effects of noradrenaline (5.34 ± 0.08 control, 6.17 ± 0.10 reserpinized) and carbamylcholine (4.19 ± 0.17 control, 5.11 ± 0.12 reserpinized). Vasa deferentia were loaded with [^{3}H]-noradrenaline and then washed at 10 min intervals for 90 minutes. Methoxamine (1.2×10^{-4} M) increased the rate of the outflow coefficient for [^{3}H]-noradrenaline by 84% (from 0.64 ± 0.09 to 1.18 ± 0.18, $n = 14$, $P < 0.05$ for paired samples). This effect of methoxamine was prevented by pretreatment of the tissue with cocaine (2.94 μM) or desipramine (1 μM). These results suggest that, in the rat vas deferens, methoxamine has a small indirect effect in addition to its main direct action.

References

BARNETT, A., STAUB, M. & SYMCHOWICZ, S. (1969). The effect of cocaine and imipramine on tyramine-induced release of noradrenaline-^{3}H from the rat vas deferens *in vitro*. *Br. J. Pharmac.*, **36**, 79–84.

BURGEN, A.S.V. & IVERSEN, L.L. (1965). The inhibition of noradrenaline uptake by sympathomimetic amines in the rat isolated heart. *Br. J. Pharmac.*, **25**, 34–49.

KALSNER, S. & NICKERSON, M. (1969). Mechanism of cocaine potentiation of responses to amines. *Br. J. Pharmac.*, **35**, 428–439.

SHAH, N.S., PATEL, S.R. & GULATI, O.D. (1974). Potentiation by 3,4-dimethoxyphenylethylamine (DMPEA) and cocaine of norepinephrine-induced contraction of guinea-pig vas deferens. *J. Pharmac. exp. Ther.*, **190**, 227–233.

TRENDELENBURG, U., MAXWELL, R.A. & PLUCHINO, S. (1970). Methoxamine as a tool to assess the importance of intraneuronal uptake of l-norepinephrine in the cat's nictitating membrane. *J. Pharmac. exp. Ther.*, **172**, 91–99.

Localisation of [^{3}H]-clonidine binding in guinea pig kidney

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[^{3}H]-Clonidine binds to membranes prepared from guinea pig kidney by a high affinity, saturable process. The binding is probably to renal α-adrenoceptors since it is readily displaced by α-adrenoceptor agonists or antagonists but not by drugs acting on histamine receptors, acetylcholine receptors, β-adrenoceptors, or by prostaglandins, angiotensin II or arginine vasopressin (Summers, Jarrott & Louis, 1978a, b). The present study investigates the localisation of the binding site within the kidney.

Kidneys were removed from male guinea pigs (600–800 g) and the renal cortex, medulla and papilla separated by dissection at 4°C. Membranes were prepared for each area by a modification of the method of U'Prichard, Greenberg & Snyder (1977). After incubation with [^{3}H]-clonidine (5.29 Ci/mmol) the membranes were rapidly filtered under vacuum at 4°C onto Whatman GF/B filters and washed with 3 × 5 ml of ice cold 50 mM Tris buffer pH 7.6 containing clonidine (1 μM). [^{3}H]-Clonidine remaining bound to the membranes was estimated by liquid scintillation counting. Non specific binding was measured in identical samples containing clonidine (1 μM).

Comparison of binding in membranes prepared from the three areas showed that of the total