Overflow of [^{14}C]-practolol and [^{14}C]-racemic propranolol from the isolated rat vas deferens

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It has been suggested that propranolol is taken up into noradrenergic neurones via an uptake process and that it releases endogenous noradrenaline (Dollery, Lewis, Myers & Reid, 1974). This present investigation was performed to test and extend this hypothesis.

Twelve male Wistar rats of 250-300 g were killed by cervical dislocation, the vasa deferentia removed, the mesentery stripped, and the organ immersed in cold Holman solution containing ascorbic acid (20 μg/ml) and EDTA (10 μg/ml) to prevent oxidation of the noradrenaline (NA). After 15 min the tissues were blotted, weighed and incubated in Holman's solution containing one of the following drugs: (1) [^{3}H]-(−)-NA (1 μg/ml, 23.3 n Ci/ml); (2) [^{14}C]-sorbitol (2.6 μg/ml containing 50 nCi/ml 6.5 mg/ml); (3) [^{14}C]-practolol (8.4 μg/ml, 100 nCi/ml); (4) [^{14}C]±-propranolol (4.48 ng/ml, 65.6 nCi/ml). Six vasa were used for each incubation. Each vasa was mounted in a 5 ml Perspex bath between 2 cm longitudinal platinum electrodes and allowed to equilibrate, for 30 min after [^{3}H]-NA and 10 min after the other drugs, at a tension of 0.3 g, the bath fluid being changed every 5 minutes. After equilibration 0.5 ml of the bath solution was transferred to scintillation vials, the fluid changed and supramaximal field stimulation applied 10 s later (biphasic pulses 150 V, 25 Hz, 1 ms for 10 seconds). Contractions were recorded with a force displacement strain gauge. After 5 min samples of bath fluid were collected as before, the bath changed and 5 min periods with no stimulation alternated with 5 min periods containing 10 s stimulation, repeated four times. Each sample was counted using standard scintillation technique.

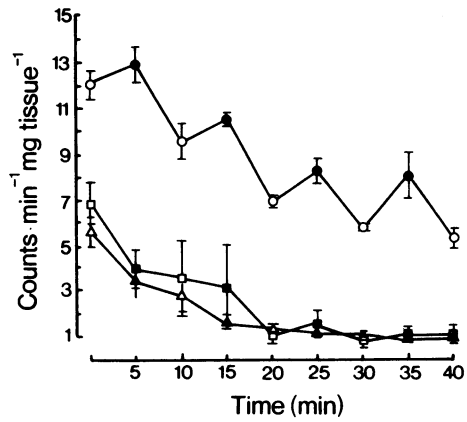

Fig. 1 Overflow pattern of [^{3}H]-(-)-NA (○, ●); [^{14}C]-practolol (□, ■) and [^{14}C]-propranolol (△, ▲) from the rat isolated vas deferens following transmural stimulation (closed symbols) and at rest (open symbols).

Tritium overflow following transmural stimulation of the isolated rat vas preincubated with [^{3}H]-(−)-NA, was significantly greater than the non-stimulated overflow. This was not so after incubating with [^{14}C]-sorbitol, [^{14}C]-practolol or [^{14}C]-propranolol. Figure 1 shows the results obtained with [^{14}C]-practolol, [^{14}C]-propranolol and [^{3}H]-(−)-NA.

D-sorbitol is distributed extracellularly whereas NA is known to be taken up by adrenergic neurones. The overflow of [^{14}C]-practolol and propranolol resembled that of sorbitol rather than that of NA.

Reference

DOLLERY, C.T., LEWIS, P.J., MYERS, M.G. & REID, J.L. (1974). Mechanism of the early pressor effect of centrally administered propranolol in the conscious rabbit. *Br. J. Pharmac.* (in press).