

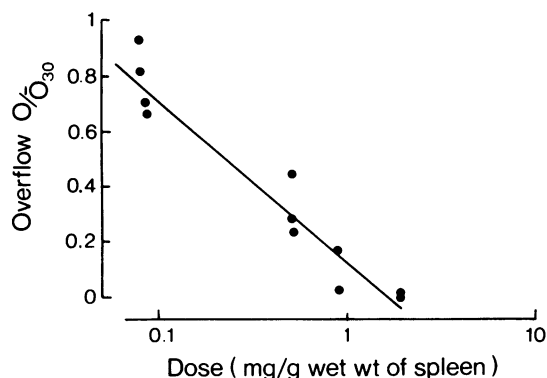
## The effects of L9394 on adrenergic transmission in the cat spleen

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L9394 (2-ethyl-3-(4- $\gamma$ -di-*n*-butylaminopropoxybenzoyl)-indolizine hydrochloride) has, in the dog, similar haemodynamic effects to amiodarone (Charlier, Bauthier & Richard, 1976). Amiodarone is known to produce a dose-dependent reduction in the overflow of transmitter from the isolated blood perfused cat spleen following nerve stimulation at 30 Hz yet has no effect on release induced by tyramine (Bacq, Blakeley & Summers, 1976). We have examined the effects of L9394 upon transmitter release and overflow in the isolated blood perfused cat spleen (for methods and experimental plan see Bacq *et al.*, 1976). Each dose of the drug was added to the blood perfusing the spleen and allowed to act for 30 minutes. L9394 produced a dose-dependent decrease in transmitter overflow from the spleen following trains of 200 stimuli at 30 Hz ( $r=0.97$  d.f.=9). The  $ED_{50}$  for this effect was 0.24 mg/g wet wt. of spleen ( $CL_{95}$  0.19–0.32). The response of the spleen to nerve stimulation was reduced in a parallel manner to the reduction in overflow. In direct contrast to this effect on stimulation evoked release of transmitter, L9394 (0.9 mg/g wet wt. spleen) had no effect on the release induced by tyramine of [ $^3$ H]-(-) noradrenaline pre-loaded into the spleen by infusion 30 min earlier. After L9394 the intra-arterial injection of tyramine (50  $\mu$ g) released 106.5% of the control release of label but stimulation-evoked release was reduced to 3.7% of control (1 experiment).

L9394 (0.5 mg/g wet wt. spleen) did not alter the ability of the spleen to take up [ $^3$ H]-(-) NA from an



**Figure 1** The effect of L9394 on overflow of transmitter following 200 stimuli at 30 Hz. Overflow (O) is expressed in terms of the mean pre-drug value ( $O_{30}$ ).

intra-arterial infusion at 345 ng/minute. At steady state control spleens took up  $45.5 \pm 1.6\%$  ( $n=20$ ) of the infusion compared with  $51.1 \pm 5.3\%$  ( $n=8$ ) for spleens treated with L9394.

L9394 therefore not only resembles amiodarone in its haemodynamic profile but has similar effects on adrenergic transmission in the spleen.

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### References

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