A STUDY OF THE ACTIONS OF ETILEFRINE ON
SYMPATHETICALLY INNERVATED BLOOD VESSELS

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by

BARRY RAYMOND FROST
(B.Sc. Hons)

Department of Clinical and Experimental Pharmacology,
The University of Adelaide,
South Australia.

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1. The aim of this study was to examine the effects of etilefrine on blood vessels and to compare its actions on vascular smooth muscle with those of other sympathomimetic amines. In particular, it was proposed to determine the mode of action of etilefrine and to ascertain whether it interacted with other substances which modified noradrenaline disposition via neuronal and extraneuronal mechanisms.

2. The vascular model used in this study was the ventral caudal artery of the rat tail. This artery was used "in situ" and also as an isolated preparation. In some parts of this investigation the isolated rabbit ear artery was also used.

3. Etilefrine was found to exert a vasoconstrictor action on the ventral tail artery "in situ", which was in part mediated by noradrenaline release from sympathetic nerve endings in the vessel. The response of etilefrine was enhanced by pretreatment of the artery with noradrenaline or cocaine and abolished by phentolamine. The sympatholytic agents reserpine, guanethidine and 6-hydroxydopamine decreased the response of the artery to etilefrine. The potency of etilefrine on this vessel was less than that of noradrenaline, adrenaline and phenylephrine but similar to metaraminol.

4. In the isolated tail artery similar findings were observed as in the tail artery "in situ". Pretreatment with reserpine or guanethidine decreased the response to etilefrine and this paralleled the decrease in tissue catecholamines observed. Pretreatment with the monoamine oxidase inhibitor iproniazid elevated tissue catecholamine levels but paradoxically decreased the etilefrine response.
5. The response to etilefrine in the rabbit ear artery was analogous to that observed in the ventral tail artery. Surgical denervation of the ear artery decreased the response to etilefrine but did not alter the response to noradrenaline. Treatment of the artery with 9-alpha-fluorohydrocortisone did not affect the etilefrine response.

6. When the ventral tail artery was incubated with tritiated noradrenaline, etilefrine was found to enhance the efflux of radio-label from this vessel. This enhanced efflux was comparable with that of ephedrine but less than that induced by tyramine.

7. The metabolite content of the enhanced efflux from the ventral tail artery was also assessed. The sympathomimetic amines etilefrine, ephedrine, tyramine and REN-293 were found to increase the efflux of tritiated noradrenaline and dihydroxy-phenylglycol to different degrees. These results provided good evidence that etilefrine has an indirect sympathomimetic component to its action.

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