## Action of Eledoisin on Isolated Vascular Strips[1]

Eledoisin[2] is a potent vasoactive peptide whose pharmacological action has been extensively investigated by ERSPAMER et al.[3,4]. Its basic effect on blood pressure is depressor, but in pithed or ganglion-blocked rats and chickens it is pressor, and is probably related to liberation of catecholamines by the peptide. In view of the different hemodynamic effects of the peptide, we undertook a study of its action on isolated vascular strips.

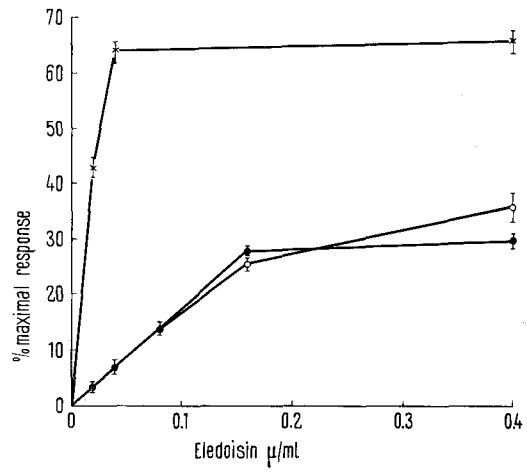
Spirally cut aortic and carotid artery strips from cats and rabbits were prepared according to FURCHGOTT and BHADRAKOM[5]. Vein strips from cat and rabbit inferior vena cavae were prepared in an identical way. Both arteries and veins were mounted in a muscle bath in Krebs' solution at 37 °C and aerated with 95% $O_2$, 5% $CO_2$. The dimensions of the strip and tension were kept constant in all experiments, and contractions were recorded isotonically. Myotropic agents and other drugs were added to the bath and kept in contact with the strip for 3 min. All results were expressed as % maximal shortening, which could be determined by adding an excess of a myotropic agent and measuring the response. One group of animals was reserpinized, using 2.5 mg/kg reserpine the first day, 5.0 mg/kg the second day, and preparing blood vessel strips on the third day.

*Results and discussion.* Eledoisin had no effect on isolated cat carotid artery and vein, and reserpine did not change these results. Both the artery and vein were very sensitive to angiotensin. The artery did not respond to bradykinin; the vein did, with a response as great as that to angiotensin.

On the other hand, eledoisin contracted isolated rabbit aortic strips. In comparison to the effect of angiotensin, eledoisin was twenty times less active on a weight basis; and, after washing away the peptide, a strip exposed to eledoisin took 30–45 min to relax, while a strip exposed to angiotensin relaxed in less than 15 min. A dose response curve (Figure) was obtained with eledoisin, and there was no tachyphylaxis. In comparison, isolated rabbit vein strips were also stimulated to contract with eledoisin, but very rapid tachyphylaxis developed, and fifty times more eledoisin was required to produce similar responses.

Neither phentolamine (5 $\mu$g/ml) nor dichloroisoproterenol (5 $\mu$g/ml) significantly changed the response of isolated rabbit aortic strip to eledoisin. One can thus conclude that the peptide does not act by means of adrenergic receptors. Metanephrine (1–2 $\mu$g/ml), however, potentiated the response to eledoisin. Eledoisin alone produced a contractile response of 36 $\pm$ 2.5% ($n = 6$), while in the presence of metanephrine the response was 60 $\pm$ 1.6% ($n = 4$). Reserpine-pretreated aortic strips also showed this potentiation (Figure). However, when re-equilibrated with norepinephrine (0.4 $\mu$g/ml) three times for 30 min each, to replenish the stores, the response to eledoisin returned to normal. On reserpinized veins, eledoisin was not potentiated.

These results indicate that the action of eledoisin on isolated rabbit aortic strips is somehow dependent upon norepinephrine stores. This effect is not mediated by the adrenergic receptors, since neither $\alpha$ nor $\beta$ adrenergic blocking agents block the effect of eledoisin. Neither does the peptide release storage norepinephrine, since reserpinized strips would then not respond. Instead, they respond with almost twice the contraction of normal strips. It has recently been shown that metanephrine potentiates the response of isolated aortic strips to angiotensin, vasopressin, and serotonin. It was postulated that metanephrine releases some storage norepinephrine, in low amounts, that remains intracellular and that facilitates the contractile machinery in the cell independent of the adrenergic receptor sites. On the other hand, intact norepinephrine stores may have an inhibitory action on muscle contraction. When released by either metanephrine or reserpine, the vasoactive peptides act maximally. What the relationships between these vasoactive polypeptides and norepinephrine stores are, are under investigation.




Dose response curves of aortic strips to eledoisin. —o— dose response curve of normal rabbit aortic strip (average of 5 experiments). —●— reserpine pretreated strip re-equilibrated with norepinephrine (average of 5 experiments). —x— reserpine pretreated aortic strip (average of 6 experiments). Cross bars represent standard error of mean. Between reserpine pretreated strip and normal strips the difference is significant ($p < 0.001$).

*Résumé.* Des bandelettes aortiques du lapin sont fortement stimulées par l'élédoisine. Après prétraitement du lapin à la réserpine, l'aorte devient deux fois plus sensible à l'élédoisine que normalement. Cette sensibilisation envers l'élédoisine diminue après incubation de l'aorte isolée avec la noradrénaline. Le même prétraitement à la réserpine n'a pas augmenté l'effet de l'élédoisine sur la veine isolée du lapin. Cette préparation par contre devient facilement tachyphylactique.

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