

A basal release of ^3H was detected throughout the superfusion; this consisted mainly of deaminated metabolites. Electrical stimulation at 1, 2, 5 and 10/sec caused increasing contractions of the vein and a rise in the efflux of radioactivity; the major portion of this increased radioactivity was associated with intact NA. Passive stretching of the vein did not increase the ^3H efflux. Angiotensin (10–1,000 ng/ml.) had no appreciable effects on either the contractility or the output of radioactivity; however, the contraction and ^3H -NA efflux associated with electrical stimulation (1–2/sec for 30–60 sec) were significantly enhanced in the presence of angiotensin. This effect was reproduced in ten preparations, and could be repeated with the same vein when the angiotensin infusion was stopped and then restarted after a rest period. Identical results were obtained in the presence of cocaine (2–4 $\mu\text{g}/\text{ml}$). Under these conditions the contraction and ^3H -NA efflux were markedly enhanced during nerve stimulation, and were further increased by angiotensin.

These results suggest that the potentiating effect of angiotensin-II is not due to an inhibition of the NA re-uptake process at the synaptic terminals, but is associated with an increased release of the transmitter.

This work was supported in part by a grant from the Connecticut Heart Association. J. H. is most grateful to the Wellcome Trust for a Travel Grant.

REFERENCES

- AIKEN, J. W. & REIT, E. (1968). Stimulation of the cat stellate ganglion by angiotensin. *J. Pharmac. exp. Ther.*, **159**, 107–114.
- BENELLI, G., DELLA BELLA, D. & GANDINI, A. (1964). Angiotensin and peripheral sympathetic nerve activity. *Br. J. Pharmac. Chemother.*, **22**, 211–219.
- BOADLE, M. C., HUGHES, J. & ROTH, R. H. (1969). Angiotensin accelerates catecholamine biosynthesis in sympathetically innervated tissue. *Nature, Lond.*, **222**, 937.
- FARR, W. & GRUPP, G. (1967). The mechanism of the positive inotropic and chronotropic effects of angiotensin. *Fedn Proc.*, **26**, 465.
- HUGHES, J. & VANE, J. R. (1967). An analysis of the responses of the isolated portal vein of the rabbit to electrical stimulation and to drugs. *Br. J. Pharmac. Chemother.*, **30**, 46–66.
- LEWIS, G. P. & REIT, E. (1965). The action of angiotensin and bradykinin on the superior cervical ganglion of the cat. *J. Physiol., Lond.*, **179**, 538–553.
- PALAIK, D. & KHAIRALLAH, P. A. (1967). Inhibition of noradrenaline uptake by angiotensin. *J. Pharm. Pharmac.*, **19**, 396–397.
- ROTH, R. H. & STONE, E. A. (1968). The action of reserpine on noradrenaline biosynthesis in sympathetic nerve tissue. *Biochem. Pharmac.*, **17**, 1581–1590.
- SJÖSTRAND, N. O. & SWEDIN, G. (1968). Potentiation by smooth muscle stimulants of the hypogastric nerve–vas deferens preparation from normal and castrated guinea-pigs. *Acta physiol. scand.*, **74**, 472–479.
- ZIMMERMAN, B. G. & GISSLEN, J. (1968). Pattern of renal vasoconstriction and transmitter release during sympathetic stimulation in presence of angiotensin and cocaine. *J. Pharmac. exp. Ther.*, **163**, 320–329.
- ZIMMERMAN, B. G. & GOMEZ, J. (1965). Increased response to sympathetic stimulation in the cutaneous vasculature in presence of angiotensin. *Int. J. Neuropharmac.*, **4**, 185–193.

Inhibition of angiotensin pressor responses with diethyl-dithiocarbamate (DDC)

M. D. DAY and D. A. A. OWEN*, *Pharmacological Laboratories, Department of Pharmacy, University of Aston, Birmingham 4*

Schwyzer (1963) found that angiotensin formed amorphous precipitates with Zn^{++} and Cu^{++} ions and postulated that this precipitate might be the active pressor form of angiotensin. This hypothesis was supported by the finding of Gascon & Walaszek

(1966) that osajin, an isoflavone derivative which also forms complexes with Zn^{++} and Cu^{++} ions, specifically antagonized the contractile action of angiotensin on the guinea-pig isolated ileum. Osajin, however, was subsequently shown to possess no *in vivo* anti-angiotensin activity (Walaszek, personal communication).

We have examined DDC, a substance known to chelate bivalent metal ions, as a potential antagonist of the pressor action of angiotensin in pithed rats and in anaesthetized cats. DDC administered intravenously in doses of 5–25 mg/kg in pithed rats and 10–50 mg/kg in anaesthetized cats usually caused an initial enhancement of the pressor responses to both angiotensin and noradrenaline. The enhancement was usually maximal after one hour and was followed by a slow decline in the responses to both pressor agents. In pithed rats the responses to angiotensin declined more rapidly than did those to noradrenaline such that 2–3 hr after DDC the angiotensin responses were often abolished while those to noradrenaline were either slightly enhanced, unaffected, or reduced by up to 50% of their control size.

In pithed rats pretreated with reserpine (5 mg/kg) 18 hr before the experiment, the initial enhancement and subsequent decline of the angiotensin responses following DDC administration were accelerated in onset. The effect of DDC on noradrenaline responses was not altered by reserpine.

In anaesthetized cats DDC enhanced but did not subsequently block angiotensin pressor responses. In acutely adrenalectomized cats the responses to angiotensin were similar to those in control animals but were markedly reduced by DDC treatment. In cats with intact adrenals DDC did not impair angiotensin responses even after the administration of a mixture of α - and β -receptor blocking agents sufficient to block the pressor responses to injected adrenaline and noradrenaline. Similarly, DDC was ineffective in cats pretreated with reserpine (0.25 mg/kg per day) for 3 days to deplete adrenal catecholamine stores.

Penicillamine, another chelator of bivalent metal ions, potentiated but did not impair the responses to angiotensin in both rats and cats.

It was concluded that DDC possesses anti-angiotensin activity in pithed rats and in adrenalectomized cats. The mode of action of DDC is not clear but the failure of penicillamine to affect angiotensin responses suggests that DDC acts by a mechanism other than chelation of bivalent metal ions.

REFERENCES

- GASCON, A. L. & WALASZEK, D. J. (1966). Inhibition of valyl⁵ angiotensinamide II by osajin. *J. Pharm. Pharmac.*, **18**, 478–479.
SCHWYZER, R. (1963). Chemical structure and biological activity in the field of polypeptide hormones. *Pure appl. Chem.*, **6**, 265–295.

The anaphylactic reaction in the longitudinal muscle strip of guinea-pig ileum

M. M. DALE and L. ZILLETTI*, *Department of Pharmacology, University College London, London W.C.1*

The longitudinal muscle strip (Ambache, 1954) provides a much simpler system than full-thickness ileum for investigation of the mechanisms involved in the Dale-Schultz reaction. The relation between response and antigen dosage was measured in both preparations and found to be reasonably similar. The total histamine content of the