action on the contractions, indicating the absence of an alpha excitatory component in this phase. This was supported by the results of experiments with noradrenaline, oxymetazoline and phenylephrine in the absence or abolition of tone.

The relaxant component of the response to transmural stimulation was strongly inhibited by guanethidine, bethanidine, dimethylphenylpiperazinium and debrisoquin. Inhibition of this component was also obtained with Sotalol (5×10^{-8} g/ml.), but propranolol was less potent. The ratio of the EC50s with (—)-isoprenaline, (+)-isoprenaline, (—)-adrenaline, (—)-noradrenaline (1 : 33 : 300 : 1,150), together with the blockade of (—)-isoprenaline by Sotalol (5×10^{-7} g/ml.-10^{-5} g/ml.) support the conclusion that a β-receptor is responsible for the mediation of the inhibitory component in the bovine iris sphincter.

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Enhanced release of transmitter during sympathetic nerve stimulation in the presence of angiotensin

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Angiotensin can influence sympathetic function in such diverse ways as excitation of ganglia (Lewis & Reit, 1965; Farr & Grupp, 1967; Aiken & Reit, 1968), increased biosynthesis of noradrenaline (Boadle, Hughes & Roth, 1969) and potentiation of responses to sympathetic nerve stimulation (Bennelli, Della Bella & Gandini, 1964; Zimmerman & Gomez, 1965; Sjöstrand & Swedin, 1968). The potentiation of postganglionic sympathetic nerve stimulation by angiotensin could be explained by either a facilitation of noradrenaline (NA) release (Zimmerman & Gisslen, 1968), or by the inhibition of the re-uptake process for NA (Palaic & Khairallah, 1967); both these possibilities have now been investigated.

Uptake of ^{3}H-NA was studied in rat isolated hearts perfused with Krebs solution; ^{3}H-NA (5 ng/ml., specific activity 7–9 c/mM) was infused for 2, 5 and 10 min periods. Angiotensin II amide (Ciba, 100–1,000 ng/ml.) did not reduce the uptake of radioactivity at any of the time periods studied, indicating that the polypeptide does not exert cocaine-like effects, even at the highest concentration used.

The rabbit portal vein was used to study the release of transmitter during transmural stimulation of intramural sympathetic nerves (Hughes & Vane, 1967). The vein was preincubated with ^{3}H-NA (50 ng/ml., 0·25 mc) for 2–3 hr; it was then mounted in air surrounded by a water jacket maintained at 37° C. The vein was superfused with Krebs solution at a constant flow of 4 ml./min and contractions of the vein were detected with an isometric transducer coupled to a direct writing ink recorder. The superfusate was collected at timed intervals and the radioactivity determined by liquid scintillation spectrometry. NA and its metabolites were separated by alumina and Amberlite resin procedures (Roth & Stone, 1968).

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 μg/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.

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

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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