(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 valyl[5] 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

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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

strip was $8 \pm 0{\cdot}98$ μg/g wet weight, compared with $20{\cdot}7 \pm 1{\cdot}63$ μg/g in the whole ileum segment. Histamine release with antigen was significantly greater in the strip, being approximately 10% of the total histamine content, as compared with about 2% in the full-thickness ileum preparation. As much as 36% of the total histamine was released by antigen in some strips.

The role of Auerbach's plexus in the anaphylactic response was investigated using tetrodotoxin. This substance in a concentration of 5×10^{-7} g/ml. eliminates the response to nicotine and DMPP in both strips and full-thickness loops, while leaving the histamine response unaffected. The anaphylactic dose response curve was unchanged in the presence of this concentration of tetrodotoxin in both strips and full thickness ileum. Some aspects of the role of the mast cells in the Dale–Schultz response were investigated using octylamine. The normal mast cell distribution was studied in spread strips and the dose-response curve for the disruption of mast cells with octylamine was assessed. Exposure of the strips to octylamine (10^{-3} g/ml.) for 1 min decreased the mast cell count by 95%, compared with control strips. The response of the muscle to small concentrations of histamine (10 ng/ml.) was still present after this treatment, but the anaphylactic response of the strips was eliminated entirely, while that of the full-thickness ileum was markedly reduced. The significance of these findings for the theory that part of the anaphylactic response is due to a direct antigen antibody reaction on muscle is discussed.

REFERENCE

AMBACHE, N. (1954). Separation of the longitudinal muscle of the rabbit's ileum as a broad sheet. *J. Physiol., Lond.*, **125**, 53-55*P*.

Pharmacological studies of cinanserin in human isolated smooth muscle

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Cinanserin hydrochloride is 2'-(3-dimethylaminopropylthio) cinnamanilide hydrochloride. It has been shown *in vitro* and *in vivo* to antagonize 5-hydroxytryptamine (5-HT) (Krapcho, Spitzmiller, Turk & Fried, 1964; Krapcho & Turk, 1966; Rubin, Piala, Burke & Craver, 1964). It has been used successfully in patients with carcinoid syndrome but not in schizophrenia (Gallant & Bishop, 1969; Costello, 1966; Mengel & Lotito, 1968).

The actions of cinanserin on isolated strips of human smooth muscle have been studied. Specimens were obtained from surgical operations and set up in an isolated organ bath in aerated Krebs-bicarbonate solution at 37° C as described previously (Coupar, Hedges, Metcalfe & Turner, 1969; Coupar & Turner, 1969). Responses were recorded by a frontal writing lever on a kymograph.

Cinanserin (0·02–100 μg/ml. for 5 min) did not contract or relax the tissues studied. When antagonizing responses to 5-HT for pA_2 determinations (Schild, 1947), an incubation period of 2 min with the antagonist was used before adding 5-HT for a 1 min contact period. The dose cycle was 15 min. The anti-5-HT properties of cinanserin were compared with methysergide, and their interactions with acetylcholine studied.