Atrial contractions were increased by 50% with 0·1–0·3 μg/ml histamine, 0·3–1·0 μg/ml β-phenylethylamine, 3–10 μg/ml tyramine, 10–30 μg/ml isoamylamine and 300–1,000 μg/ml ethanolamine but were slightly reduced by 100–300 μg/ml cadaverine and by 100–300 μg/ml putrescine.

We conclude that histamine, which was found in the alcohol-soluble extract at a concentration of 1 μg/mg of extract, accounts for much of the activity observed on the atrial and ileal preparations. The contributions of the other amines cannot be assessed without knowing their concentrations in the spleen extract and this may vary.

REFERENCES

COBBIN, L. B. & THORP, R. H. (1957). Occurrence of a cardioactive principle in spleen. *Nature, Lond.*, **180**, 242.

COBBIN, L. B. & THORP, R. H. (1959). The cardio-active principle in spleen. *Br. J. Pharmac. Chemother.*, **14**, 392–400.

COBBIN, L. B. & THORP, R. H. (1960). Absence of catecholamines in cardioactive acetone extracts of ox spleen. *Nature, Lond.*, **186**, 473.

JACKSON, D. M., TEMPLE, D. M., CASSIMATIS, N., HORNE, M., MARMOT, M. & SNOW, D. (1969). The distribution of a cardiotonic factor, splenitransin, in mammalian tissues. *Comp. Biochem. Physiol.*, **30**, 419–432.

JACKSON, D. M. & TEMPLE, D. M. (1970). β-Phenylethylamine as a cardiotonic constituent of tissue extracts. *Comp. Gen. Pharmac.*, **1**, 155–159.

TEMPLE, D. M., THORP, R. H. & GILLESPIE, R. (1966). The purification and chemical properties of the cardiotonic factor in spleen. *Comp. Biochem. Physiol.*, **17**, 1089–1101.

Effect of dihydroergotamine (DHG) on the capacitance, resistance and precapillary sphincter vessels of denervated cat skeletal muscle

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Mellander & Nordenfelt (1970) have reported that, in the vascular bed of both human and cat skeletal muscle, the constrictor effect of DHE is mainly confined to the capacitance vessels. These authors used one dose of DHE in each species (10 and 15 μg/kg for human and cat studies respectively). We have now confirmed and extended their observations using the denervated vascular bed in calf muscles of the cat.

Forty male cats were anaesthetized with chloralose (40 mg/kg) and urethane (500 mg/kg) intramuscularly and prepared according to the method of Mellander (1966). The experimental findings were interpreted following the principles described by Mellander (1960).

DHG methanesulphonate was administered by close intra-arterial injection to the calf muscles over the following dose range (base): 1·67–405 μg/kg of muscle; one dose only/animal. The constrictor effect of DHG on the capacitance and resistance vessels is shown in Table 1. The threshold dose for constriction of the capacitance vessels was about 5 μg/kg and a dose-response relationship existed up to a dose of 405 μg/kg. Maximal capacitance responses were of similar magnitude to the capacitance response during supramaximal sympathetic nerve stimulation. On the arterial side no significant constriction was observed in doses of less than 45 μg/kg and even at the highest dose the mean constriction never exceeded 9% of the response during supramaximal sympathetic nerve stimulation. In none of the experiments was DHG found to change the capillary filtration coefficient. DHG does not, therefore, influence the tone of the precapillary sphincters.

TABLE 1. *Effect of DHG on the resistance and capacitance vessels in the denervated vascular bed of cat skeletal muscle (calf)*

Dose of DHG μg/kg intra-arterially	Capacitance response expressed as a % of the response to supramaximal sympathetic nerve stimulation*	Mean ± S.E.	Resistance response expressed as a % of the response to supramaximal sympathetic nerve stimulation†	Mean ± S.E.
1·67	0, 0, 0, 0, 0	0± 0	−1, 2, 0, 0, −1	0±0·5
5	65, 0, 0, 0, 0	13±13	1, 2, 1, 0, 0	1±0·5
15	76, 51, 58, 51, 40	55± 6	−1, 0, 2, 1, 1	1±0·5
45	54, 91, 43, 94, 62	69±10	5, 2, 2, 2, 2	3±0·5
135	101, 112, 76, 120, 83	98± 8	7, 17, 5, 6, 6	8±2
405	94, 109, 167, 60, 91	104±18	15, 6, 16, 5, 3	9±2·5

*100% capacitance response to supramaximal sympathetic nerve stimulation mobilization of 27·6% of tissue blood content.

†100% resistance response to sympathetic nerve stimulation 643% increase in resistance.

The results reported here confirm the findings of Mellander & Nordenfelt (1970) and establish the reported selectivity of DHG for the capacitance vessels over a wide dose range in which there is a straight line dose-response relationship.

REFERENCES

MELLANDER, S. (1960). Comparative studies on the adrenergic neuro-humoral control of resistance and capacitance vessels in the cat. *Acta physiol. scand.*, **50**, suppl. 176.

MELLANDER, S. (1966). Comparative effects of acetylcholine, butan-norsynephrine (Vasculat), noradrenaline and ethyl-adrianol (Effortil) on resistance, capacitance, and pre-capillary sphincter vessels and capillary filtration in cat skeletal muscle. *Angiology*, **3**, 77–99.

MELLANDER, S. & NORDENFELT, I. (1970). Comparative effects of dihydroergotamine and noradrenaline on resistance, exchange and capacitance functions in the peripheral circulation. *Clin. Sci.*, **39**, 183–201.

Transmission from cholinergic neurones to circular smooth muscle obtained from the rabbit caecum

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The rabbit caecum has a spirally arranged constriction which denotes the position of a fold of the mucous layer known as the spiral valve. In this region there is a thickening of the circular smooth muscle layer. The electrical and mechanical properties of preparations of circular smooth muscle from this region have been studied using the sucrose gap technique of Bülbring & Burnstock (1960).

When bathed by Krebs solution at 37·5°C most preparations were quiescent, both electrically and mechanically. Single pulses of 50V (0·5 ms duration) delivered via two ring electrodes around the live side of the tissue elicited depolarization, a burst of spike activity and the development of tension. The first indication of depolarization followed the stimulus artifact after a latent period of 176±8 ms (mean±standard error, n=30). This relatively long latent period was unaffected by stimulus strength and is comparable to that observed at other cholinergic neuro-effector junctions (Burnstock, Campbell, Bennett & Holman, 1964; Ohashi & Ohga, 1967; Creed & Wilson, 1969).

A train of stimuli was applied for 1 s every 100 seconds. The tension response increased with stimulation frequency up to a maximum at 64 Hz. The effects of increasing the stimulation frequency upon the electrical response were complex but generally included an increase in spike activity or a more prolonged period of depolarization.

Atropine (100 ng/ml) abolished the mechanical response of the tissue to stimulation and the electrical response was reversed in sign. Single pulses in the presence of atropine generated small hyperpolarizations which summated at frequencies over 4 Hz.