An isolated vascular tissue preparation showing a specific relaxant effect of dopamine

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Dopamine produces hypotension and dilates certain vascular beds in dogs, cats, rabbits and man, an action that is suggested to be mediated by stimulation of specific receptor sites (Goldberg, 1972). In rabbits, dopamine increases blood flow in the coeliac artery and produces hypotension which is inhibited by bulbocapnine (Kullman, Rissing & Wasserman, 1978; Tseng & Walaszek, 1970). We have studied the vascular relaxation effect of dopamine *in vitro*, using the splenic branch of the coeliac artery of the rabbit.

Spirally cut strips of the splenic artery were suspended under 1.5 g isometric tension, in organ baths containing Krebs solution maintained at 37°C, bubbled with 95% O_2/5% CO_2, and to which had been added indomethacin (2 μg/ml). After stabilisation for 2 h, tissues were incubated with phenoxybenzamine (5×10^{-6} M) for 30 min, and then thoroughly washed prior to contraction with $PGF_{2\alpha}$ (10^{-7} to 10^{-5} M) to increase tension by 1400 ± 300 mg. When the tension was steady, doses of agonists were added cumulatively, 5 min after the previous dose or when the relaxation reached a maximum. After each agonist dose–response curve, maximum relaxation was determined by addition of papaverine (10^{-4} M). Tissues were equilibrated with antagonists for 30 min at the basal tension of 1.5 g.

Dopamine (3×10^{-8} to 3×10^{-5} M) caused dose-related relaxations in all tissues, while isoprenaline (3×10^{-9} to 10^{-6} M) caused relaxations in only one out of six tissues. After incubation with propranolol (10^{-6} M) isoprenaline responses were markedly attenuated and the dose–response curve shifted to the right by at least 1000, whereas dopamine responses were unchanged. Propranolol (10^{-6} M) was included in the Krebs solution throughout all subsequent experiments.

After equilibration of the tissues with bulbocapnine (10^{-6} to 3×10^{-5} M), relaxations to dopamine were antagonised. Analysis by the method of Arunlakshana & Schild (1959) gave a slope of unity and a PA_2 value of approximately 6.2. Bulbocapnine had no marked effect on the dose-related relaxations produced by sodium fluoride (0.03 to 3 mg/ml), histamine (10^{-7} to 10^{-4} M), prostaglandin E_2 (0.1 to 30 ng/ml), papaverine (10^{-7} to 10^{-4} M) and erythrityl tetranitrate (0.01 to 1 μg/ml).

The phenylethylamines epinine, noradrenaline and adrenaline, and the semi-rigid analogue of dopamine, 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (6,7-ADTN) each caused dose-related relaxations which were antagonised by bulbocapnine (10^{-5} M). The order of agonist potency was:

Epinine = 6,7-ADTN > Dopamine > Adrenaline > Noradrenaline

1 : 3 : 8 : 15.

These experiments demonstrate a specific vascular relaxant effect of dopamine which is selectively antagonised by bulbocapnine.

References

ARUNLAKSHANA, O. & SCHILD, H.O. (1959). Some quantitative uses of drug antagonists. *Br. J. Pharmac. Chemother.*, **14**, 48–58.

GOLDBERG, L.I. (1972). Cardiovascular and renal actions of dopamine: Potential clinical applications. *Pharmac. Rev.*, **24**, 1–29.

KULLMAN, R., RISSING, R. & WASSERMAN, K. (1978). Species differences of dopaminergic vasodilatation in the intestine. Proceedings of the Satellite Symposium to the 7th International Congress of Pharmacology: *Peripheral dopaminergic receptors*. Strasbourg, 1978.

TSENG, L.F. & WALASZEK, E.J. (1970). Blockade of the dopamine depressor response by bulbocapnine. *Fed. Proc.*, **29**, 741.

Comparison of plasma, erythrocyte and brain lithium concentrations in the guinea-pig and rat

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Lithium was first used clinically as an antimanic agent because of its reported sedative effect in guinea-pigs (Cade, 1949). Since, unlike in man and the rat, little subsequent work has been done in the original test animal (Smith, 1977), we initiated studies comparing lithium in the guinea-pig and rat.

Female rats (Wistar, 190–220 g) or guinea-pigs (Dunkin-Hartley, 380–420 g) were given oral LiCl either as a single dose (2 mmol/kg) or chronically for the maximum period which avoided intoxication at the high dose (10, 20 or 40 mmol/kg dry weight of diet for 18 d, 6 rats at each dosage; 1, 2 or 4