(0.1–100 ng/ml), (±)salbutamol (0.1–100 ng/ml) and (−)noradrenaline (1–10,000 ng/ml) caused concentration-dependent relaxations, the concentration-effect curves being similar in slope and maxima. Relative potencies are summarized in Table 1 which includes comparative data obtained on guinea-pig isolated tracheal and right and left atrial strips.

The rank order of potency of the catecholamines in causing relaxation of the rat mesovarium was isoprenaline > adrenaline ≫ noradrenaline. The potency of (±)salbutamol relative to (−)isoprenaline was similar to that on the guinea-pig isolated trachea; other β_2-stimulants such as (±)terbutaline (0.1–1000 ng/ml) and (±)fenoterol (0.01–100 ng/ml) were also potent agonists on the rat mesovarium. Propranolol was a potent antagonist of (−)isoprenaline-induced relaxations of rat mesovarium (pA_2 = 8.8); in contrast, practolol was only a weak antagonist (pA_2 = 5.0–5.3).

We conclude that rat mesovarian smooth muscle contains β-adrenoceptors and that these are of the β_2-subtype. It is possible therefore that the leiomyomas referred to above result from prolonged and intense activation of β_2-adrenoceptors in mesovarian smooth muscle.

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Experimental atherosclerosis in the Wistar rat

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The search for a laboratory model to study potential anti-atherosclerotic compounds has been well documented (Constantinides, 1965; Kritchevsky, 1974). The rat has received little attention and is generally considered to be resistant to the induction of atheromatous lesions. However, following the reports of Altman (1972) and Testa, Canestrini & Oldani (1975) a short-term induction of atherosclerosis in the rat seemed possible using large doses of vitamin D_2 and cholesterol. We have undertaken a series of experiments to investigate this methodology.

Groups of male Biorex Wistar rats were used and treated orally (Table 1) with vitamin D_2 suspension (Duphasol, Duphar, 1000 iu/mg, 4 ml/kg in distilled water) and cholesterol (BDH, 2 ml/kg in olive oil experiments 1 and 2, 1.2 ml/kg in isopropyl myristate experiment 3). At termination the animals were exsanguinated under ether anaesthesia, serum collected and stored at −21°C for cholesterol assay. The aortas were dissected out from the heart to the bifurcation and weighed. Liver weights were also recorded.

Experiment 1

The higher dose of vitamin D_2 (480,000 iu/kg) and cholesterol (60 mg/kg) produced almost a 3-fold increase in aorta weight and a 57% increase in plasma cholesterol levels but resulted in a mortality rate of 83%. The lower dose regimen over 5 and 7 days produced similar increases but the aorta weights were not significantly different from controls.

Experiment 2

A reduced vitamin D_2 treatment resulted in decreased mortality. Aorta weights and plasma cholesterol levels were increased significantly.

Experiment 3

Reducing the vitamin D_2 treatment to 1 day prevented mortalities, did not alter aorta weights but did increase plasma cholesterol levels ($P < 0.01$).

Toxic doses of vitamin D_2 and high cholesterol intake will produce lipid deposition and hyperlipidaemia in the rat but when this is severe enough to enable treatment for screening purposes undue mortality is encountered, not reported by Altman (1972) and Testa *et al.* (1975), making the method unsuitable for drug evaluation.

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Table 1 The effect of oral treatment with vitamin D_2 and cholesterol on, aorta and liver weights and serum cholesterol levels in Biorex Wistar rats

	Vitamin D_2 iu/kg ($\times 10^4$)	*Days*	*Cholesterol (mg/kg)*	*Days*	*Bodyweight (g)*	*No. of rats*	*Mortality (%)*	*Aorta wet weight (mg)*	*Liver weight (g)*	*Serum cholesterol (mg/dl)*
(1)	0	—	0	—	292 ±9	12	0	9.7 ±0.8	12.1 ±0.4	71 ±4
	48	5	60	5	239	12	83	24.0	8.8	125
	24	5	30	5	212 ±5	12	41	11.2 ±0.5	9.0(2) ±0.8	113(2) ±12
	24	7	30	7	217 ±12	12	50	10.1 ±1.0	8.4 ±0.2	151(2) ±26
(2)	0	—	0	—	281 ±6	10	0	10.3 ±0.3	11.3 ±0.3	55 ±3
	48	2	60	7	215 ±12	10	40	12.6(1) ±0.8	8.2(2) ±0.7	73 ±9
	48	3	60	7	254 ±5	10	70	12.9(3) ±0.3	9.1(2) ±0.4	81(2) ±5
(3)	0	—	0	—	246 ±10	10	0	10.7 ±0.3	9.7 ±0.6	58 ±2
	48	1	0	—	259 ±4	10	0	11.8(1) ±0.3	11.2(1) ±0.3	58 ±3
	48	1	60	7	253 ±4	10	0	11.0 ±0.7	10.6 ±0.3	70(2) ±3
	0	—	60	7	246 ±7	10	0	10.3 ±0.7	9.3 ±0.5	58 ±2

Means are given ±s.e. mean where sufficient numbers allow. (1) $P < 0.05$, (2) $P < 0.01$, (3) $P < 0.001$. Student t test.

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