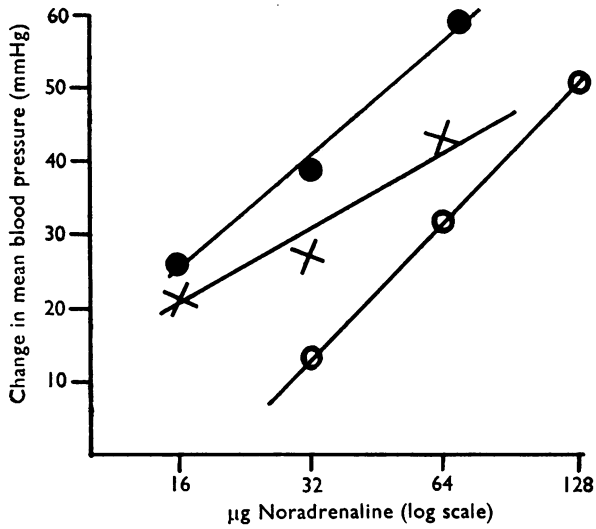

FIG. 1. Effect of indoramin on the pressor action of bolus injections of noradrenaline. The closed circles represent the change in mean blood pressure measured with a sphygmomanometer caused by noradrenaline before administration of indoramin, in three subjects. The open circles represent B.P. changes at 55 min and the crosses at 145 min after indoramin (20 mg. i.v.).

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Pharmacology of M & B 17803A in man and dog

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±-1-(2-acetyl-4-n-butyramidophenoxy)-2-hydroxy-3-isopropylaminopropane hydrochloride, M & B 17803A, is a new β-adrenoceptor blocking agent which in dog, cat and guinea-pig has a greater affinity for β_1 adrenoceptors than for β_2 receptors. There are no previous studies of its selectivity in man.

Selectivity has been assessed in three normal human volunteers by its effects on tachycardia and fall in diastolic B.P. evoked by intravenous doses of isoprenaline and on increase in forearm blood flow produced by isoprenaline given through a catheter in the left brachial artery. In similar studies performed on six anaesthetized mongrel dogs isoprenaline was given into the left femoral artery and flow was recorded with an electromagnetic flowmeter.

In man there was no evidence of significant cardioselectivity, isoprenaline tachycardia, or vasodilatation being blocked to a similar degree.

TABLE 1

Subject	Dose and route of administration	Time after dose (min)	Degree of blockade (dose ratio—1) Heart rate	Diastolic B.P.	dp/dt	Forearm flow
A	300 mg orally	100	13·0	12·9	40·3	
		165				29·6
		189	88·5	36·5	102·8	
B	300 mg orally	135	17·0	14·9	15·4	
		192				15·7
		212	15·4	12·4	10·1	
C	20 mg intravenously	46	4·8	4·0	6·7	
		73				17·2
		109	2·3	2·1	1·9	

Taking the blockade of heart rate as unity, the ratio of blockade of diastolic B.P. to heart rate was 0·81±S.E.M. 0·08 and forearm flow to heart rate was 2·19±1·44.

In two subjects given similar doses of practolol there was significant selectivity for the β_1 adrenoceptors; blockade of diastolic B.P. to heart rate (at maximum effect)= 0·26±0·11 and forearm flow to heart rate=0·18±0·03.

In the dog, however, after both intravenous and intraduodenal injections with M & B 17803A, isoprenaline vasodilatation was affected to a lesser degree than heart rate. In five dogs the blockade of diastolic B.P. to heart rate was 0·039±0·008 and femoral flow to heart rate was 0·058±0·016 indicating a 25·6 and 17·2-fold selectivity for the β_1 receptors respectively. In the sixth dog, there was no evidence of significant selectivity.

The explanation of these findings is not known; they may reflect either a species difference in receptor responses to M & B 17803A or, alternatively, variations in the pathways of its metabolism.

Effect of practolol on limb blood flow in anaesthetized patients with cardiac dysrhythmias

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The effect of practolol on limb blood flow was studied in four patients who developed cardiac ventricular dysrhythmias during an investigation of the peripheral vascular responses to anaesthesia. The patients were male volunteers between the ages of 40 and 65 years who were about to undergo elective surgery. After premedication with pethidine (1 mg/kg) and atropine (0·6 mg) intramuscularly, anaesthesia was induced with 2·5% thiopentone (5 mg/kg) given intravenously followed by suxamethonium (75 mg) to facilitate intubation. Before intubation the larynx was sprayed with 4% lignocaine hydrochloride (2 ml). Anaesthesia was maintained with a mixture of nitrous oxide and oxygen (6:3 l/min) administered through a Mapleson 'A' circuit and supplemented by halothane (1–4%) from a Dräger 'Vapor' calibrated vaporizer.

Forearm and calf blood flows were measured continuously by venous occlusion plethysmography using mercury-in-rubber strain gauges (Whitney, 1953) as the variable resistance of a bridge circuit. The outputs were transmitted from the operating room by telephone to an Elliott 903 digital computer where the blood flows were calculated in real time by a modification of a technique described previously (Hope, Carter, Horny & Wilcock, 1970). The analogue signals were also charted continuously on a Mingograf 81 recorder as were the ECG and B.P. records. The B.P. was measured