Between 77·5 and 96·8% of the estimated dose was recovered in the urine in 48 hours. Urine radioactivity consisted of an unidentified metabolite (46·4–60%) and unchanged salbutamol.

Improvement in lung function occurred within 5 min of inhalation of salbutamol and did not correlate with drug plasma concentrations.

The pattern of metabolism following oral administration of salbutamol is very similar, suggesting that most of the aerosol dose was in fact swallowed as has been reported for isoprenaline (Blackwell, Conolly, Davis & Dollery, 1970; Evans, Richards, Walker & Paterson, 1971).

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Human pharmacology of indoramin

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The effects of indoramin, a new hypotensive drug with competitive α-adrenoceptor blocking properties (Alps, Hill, Johnson & Wilson, 1970) have been studied in healthy human adult volunteers.

In a double blind investigation of six subjects indoramin (20 mg) orally produced a marked fall in blood pressure and a rise in heart rate at high exercise loads when compared with placebo. One hypertensive volunteer was studied under identical circumstances and demonstrated marked falls of resting supine and erect blood pressures as well as those after exercise. He did not suffer from symptoms referable to exercise-induced hypotension.

The effect on erect blood pressure, critical flicker frequency (CFF) (Turner, 1968), histamine skin wheal and phenylephrine-induced mydriasis was studied in a further six subjects following the double blind random administration of placebo and indoramin (20 mg and 40 mg). A dose related reduction in blood pressure and rise in heart rate was demonstrated but there was no significant effect on CFF. A dose related reduction in the size of histamine-induced skin wheals was observed (Hedges, Hill, Maclay, Newman-Taylor & Turner, 1971). There was a reduction of phenylephrine-induced mydriasis (Turner & Sneddon, 1968) followed by a dose related meiosis.

The pressor response to intravenous noradrenaline in three subjects was shifted to the right after the intravenous administration of 20 mg indoramin as shown in Fig. 1.

Indoramin (20 mg) orally twice daily for 2 weeks to four subjects reduced erect and supine blood pressures with no effect on pulse rate. Estimations of plasma concentrations of indoramin showed no evidence of accumulation. In no investigation was there any drug-related effect on liver function tests, haematology, or urea and electrolytes.

These studies in man confirm some of the pharmacological actions of indoramin found in experimental animals (Alps, Hill, Johnson & Wilson, 1970).

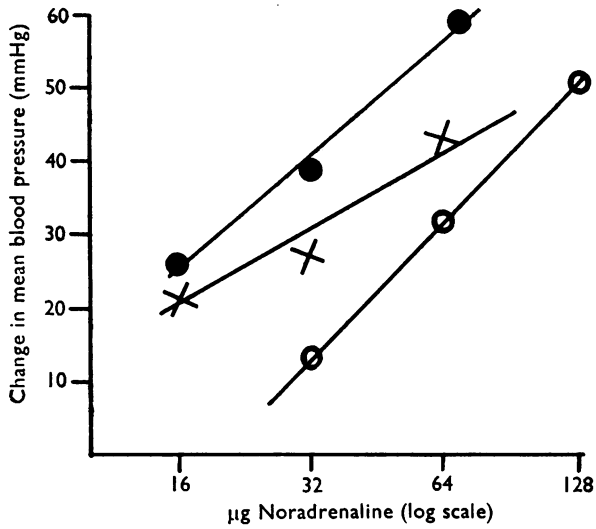

FIG. 1. Effect of indoramin on the pressor action of bolus injections of noradrenaline. The closed circles represent the change in mean blood pressure measured with a sphygmomanometer caused by noradrenaline before administration of indoramin, in three subjects. The open circles represent B.P. changes 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.