known choleretic agents acemoquinazone was generally more potent and had a longer duration of action.

Toxic doses cause a general vaso-dilatation, with prostration and weakness in the animals. The LD50s (mg/kg) in mice are 1155 (1016–1313) oral, 559 (433–721) intraperitoneal, 237 (206–273) intravenous. In rats, rabbits and dogs similar figures were found. Oral administration in rats daily for 6 months showed no evidence of toxic symptoms up to a dose of 62 mg/kg. In dogs, daily oral doses of 320 mg/kg were lethal after a few days administration ; 160 mg/kg were tolerated, with the exception of some sporadic signs of nervous excitement.

Clinical trials confirmed the choleretic activity of acemoquinazone and showed hypocholesterolemic effects, based probably on cholesterol depletion due to choleresis.

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The effect of cunaniol, a polyacetylenic alcohol isolated from the plant *Clibadium sylvestre*, on piscine behaviour

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The leaves of *Clibadium sylvestre* (Aubl.) Baill. are used by some South American Indians as a fish poison, known by them as " cunani." The effects of two compounds isolated from the leaves of this plant have been examined on goldfish *(Carassius auratus)* and guppies *(Lebistes reticulatus)*. These compounds appear to be a polyacetylenic tetrahydropyranyl alcohol, here referred to as " cunaniol," and its acetate. Both these compounds, and simple aqueous extracts of the plant leaves, had similar effects on goldfish or guppies, when these fish were placed in tapwater containing the material.

With cunaniol at 0.15 μg/ml. of tapwater, the fish rapidly became agitated and hyperactive. At higher concentrations (0.3 μg/ml.), these periods of increasingly violent activity were followed by loss of co-ordination, paralysis and finally death. Extremely rapid swimming round the perimeter of the beaker (" circuiting ") was a characteristic response to cunaniol and to some other drugs. It was used as an endpoint for EC50 estimations (the concentration inducing such behaviour in 50% of the fish) in guppies. The effects of picrotoxin, leptazol and strychnine were also examined. The concentrations used ranged from that which had no action to that at which most fish died. Goldfish were tested at one concentration for each drug, and always responded similarly to the guppies. Picrotoxin and leptazol induced piscine behavioural changes similar to those seen with cunaniol and its acetate.

An EC50 for cunaniol on guppies was 7.10×10^{-7}M (0.15 μg/ml.) with 95% confidence limits of $6.5–7.7 \times 10^{-7}$M ; for picrotoxin – 7.94×10^{-6}M ($7.3–8.7 \times 10^{-6}$

M); and for leptazol approximately 1.5×10^{-3}M. While " circuiting " was never seen with strychnine, a brief episode of uncoordinated violent activity was a characteristic effect of this drug, and was used as the strychnine endpoint EC50 (approximately 2.5×10^{-6}M). Cunaniol was the most potent of these compounds, and it was also the most rapid in its onset of action. Only cunaniol acetate, with an EC50 of 4.5×10^{-7}M ($4.2–4.8 \times 10^{-7}$M) was potent, and acted with similar rapidity to cunaniol.

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Selection of two strains of rats with inherited hypertension. Preliminary studies with some hypotensive drugs

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The inability to reproduce essential hypertension in animals is one of the difficulties in searching for a rational therapeutic approach to this disease. Most investigators suggest that hereditary factors are involved in human essential hypertension, so an attempt has been made to use the hereditary hypertension of rats as an experimental model for pharmacological investigations. We have developed two strains of rats with inherited hypertension, by means of selective inbreeding from CF stock of Wistar rats, following suggestions by Smirk & Hall (1958) and Dahl & Schackow (1964). One strain was fed with a high salt diet (NaCl, 8%) and the other with a normal diet.

In the strain on a normal diet, the average blood pressure increased from 134 (± 1.4) mm Hg in the first generation to 162 (± 1.8) mm Hg in the fifth generation, and remained at this level until the eighth generation. In rats fed with high salt diet average blood pressure increased progressively from 145 (± 1.6) mm Hg in the first generation to 166 (± 1.5) mm Hg in the eighth generation.

The main difficulties encountered in the selection of these strains were reduction of body weight and decrease in fertility, both related to the inbreeding procedure. In rats with the high salt diet the rate of sterile matings increased after the seventh generation, because of sterility of the males, as demonstrated by cross breeding experiments. The hereditability coefficient of hypertension in both strains was high: 0.39 for rats fed with the normal diet and 0.64 for rats fed with the high salt diet.

Preliminary histological studies of kidneys and adrenals from rats of up to 8 months in age, did not show any significant differences from normal animals. The absence of renal or adrenal lesions and the involvement of hereditary factors, are two aspects of this experimental hypertension which are also shared by human essential hypertension. Several other aspects have to be investigated to demonstrate the suitability of this animal as an experimental model of the human disease.

The hypotensive effects of hydralazine (1, 2 and 4 mg/kg); methyldopa (50 mg/kg), morphine 0.5 and 3 mg/kg), papaverine (30 mg/kg), guanethidine (10 mg/kg), mecamylamine (2 and 8 mg/kg), reserpine (0.25 and 1 mg/kg), chlorothiazide (50 mg/kg) and phenoxybenzamine (1–3 mg/kg) have been studied on the rats belonging