We now have evidence of a very rapid and sustained effect of alloxan on the electrical properties of islet cells.

Segments of mouse pancreas were placed in a Perspex tissue bath and maintained at 37° C in oxygenated Krebs–Henseleit solution containing glucose (2.7 mM). The islets of Langerhans were exposed by micro-dissection and potassium-citrate filled glass micro-electrodes used to record the cellular transmembrane potentials by methods described previously (Matthews, 1967).

Islet cells had normally a membrane potential of -19.9 mV $\pm$ S.E. 1.1 mV ($n=620$ impalements). In the presence of alloxan (5 mM) the islet cells rapidly depolarized. After about 15 min exposure the membrane potential had fallen to -10 mV; it was not restored after washing out the alloxan for 60 min. In contrast, the membrane potential recorded from pancreatic acinar cells was unaffected by alloxan (5 mM) and remained stable at -38.8 mV $\pm$ S.E. 2.1 mV ($n=79$) throughout.

It has been reported that glutathione protects islet cells against the action of alloxan (Watkins, Cooperstein & Lazarow, 1964). Preincubation of the pancreatic tissue with glutathione (10 mM) for 10 min did not, however, prevent the depolarization of islet cells by alloxan. On the other hand, if the islets were pretreated for 10 min with glucose (16.6 mM), alloxan (5 mM) no longer caused depolarization. Another stimulant of insulin secretion, L-leucine (15 mM), in these conditions did not prevent the depolarization by alloxan. Thus the protection by 16.6 mM glucose against alloxan induced depolarization may indicate an action of the glucose molecule at the alloxan "receptor" rather than an effect on the acceleration of the insulin secretion mechanism.

Maske & Weinges (1957) have shown that guinea-pigs are resistant to the diabetogenic effect of alloxan. Guinea-pig islet cells had a membrane potential of -20.6 mV $\pm$ S.E. 1.7 mV ($n=123$). and did not depolarize even when the concentration of alloxan was increased to 15 mM.

There appears, therefore, good correlation between the electro-pharmacological effects and the remarkable susceptibility of islet β-cells to alloxan.

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Acemoquinazone, a new choleretic agent

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Acemoquinazone (1-morpholinoacetyl-3-phenyl-2,3-dihydro-4(1H)-quinazolinone), synthesized by Bonola, de Re, Massarani, Magistretti & Setnikar (1968) has a remarkable choleretic action, in rats, guinea-pigs, rabbits and dogs. This is a "true" choleretic activity, for the drug increases the excretion of dry residue and particularly of bilirubin and cholesterol. This activity was observed in all the species examined, at doses of 6–25 mg/kg, intraduodenally. In comparison with

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 ($7.3–8.7 \times 10^{-6}$