Experiments are currently being performed to determine whether prostaglandin release by bradykinin could be responsible at least for the slowly developing contractile response.

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Inhibitory effect of propranolol on insulin secretion

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Inhibition of glucose-stimulated insulin secretion by propranolol occurs in man (Cerasi, Luft & Efendić, 1972) but the mechanism involved is unknown.

Fasted male rats were anaesthetized with pentobarbitone sodium (60 mg/kg I.P.), and a femoral artery and vein were cannulated for blood sampling and drug administration respectively. The animals were heparinized (100 u I.V.). Plasma glucose was determined by a glucose oxidase method (Beckman glucose analyser) and plasma immunoreactive insulin (IRI) was determined by the method of Hales and Randle (1963).

(±)-Propranolol (0·5 mg/kg I.V., 15 min prior to glucose administration) caused a significant reduction in both plasma glucose and plasma IRI concentrations following glucose injection (0·5 g/kg I.V.). The increase in IRI concentrations caused by sulphonylurea administration (glibenclamide 2 mg/kg or tolbutamide 200 mg/kg I.V.) was similarly reduced although their hypoglycaemic effect was not significantly altered. The hyperglycaemia and increase in IRI concentrations produced by isoprenaline administration (175 μg/kg by slow I.V. injection) were completely prevented by (±)-propranolol (0·5 mg/kg) as was isoprenaline-induced tachycardia. (+)-Propranolol (0·25 mg/kg I.V.) exerted similar effects on the plasma glucose and plasma insulin changes caused by each of the above agents but did not modify isoprenaline tachycardia.

(±)-Propranolol (0·5 μg/ml; $1{\cdot}7\times10^{-6}$ M) caused a marked suppression of the increased IRI secretion stimulated by glucose (3 mg/ml: $1{\cdot}7\times10^{-2}$ M) or tolbutamide (200 μg/ml; $7{\cdot}4\times10^{-4}$ M) from pieces of chopped pancreas incubated *in vitro* according to the method of Coore and Randle (1964).

(±)-Propranolol up to 20 μg/ml ($2{\cdot}8\times10^{-5}$ M) did not affect the determination of human insulin in protein buffer solutions, suggesting that inhibition of IRI secretion by the drug is a real effect and is not due to interference of the drug with the assay system.

We conclude that the inhibitory effect of propranolol on IRI secretion is exerted directly on the islets of Langerhans and is not meditated through primary effects on plasma glucose or on pancreatic blood flow. The lack of specificity of the inhibitory effect of (±)-propranolol to any of the three agents tested, together with the similar effects of (+)-propranolol, suggests that the effect may not be mediated by β-adrenoceptor blockade. The effect may be meditated through the membrane stabilizing action of propranolol or by an action on some other component of the insulin secretory mechanism common to the insulinotropic effect of all three agents.

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