Inhibition of propranolol-induced bronchospasm by sodium cromoglycate

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We have previously reported to the Society that the bronchospasm induced by β-adrenoceptor blocking drugs in guinea-pigs and rats is unrelated to the blockade of β-adrenoceptors in the airway smooth muscle (Maclagan & Ney, 1977). In the present experiments the effects of several pharmacological antagonists on the bronchospasm induced by (±)- and (+)-propranolol were studied.

Guinea-pigs and rats were anaesthetised with urethane (1.25 g/kg^{-1}) and allowed to breathe spontaneously. Airway resistance (R_{aw}) and dynamic lung compliance ($C_{d,n}$) were measured using the subtractor method described by Green & Widdicombe (1966). Intravenous injections of mepyramine (2 mg/kg), cimetidine (2 mg/kg), methysergide (1 mg/kg), phenoxybenzamine (2 mg/kg) and atropine (1 mg/kg) did not affect the increase in airway resistance produced by propranolol or its isomer (+)-propranolol.

In contrast, intravenous injection of sodium cromoglycate (100 μg kg to 2 mg/kg) 15–20 min before (±)- or (+)-propranolol (6×10^{-7} mol/kg to 10^{-6} mol/kg) resulted in an approximately 50% reduction in the propranolol-induced bronchoconstriction.

Jackson & Richards (1977) have shown that sodium cromoglycate can cause a reduction in the reflex response to irritant receptor stimulation mediated via the parasympathetic nervous system. However, such a modification of the reflex control of airway smooth muscle is unlikely to explain the present results because pretreatment with atropine (1 mg/kg) did not alter the inhibitory effect of sodium cromoglycate on propranolol-induced bronchospasm in guinea-pigs and rats.

References

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Does the hypoglycaemic effect of 5-hydroxytryptophan involve insulin?

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5-Hydroxytryptophan (5HTP) but not 5-hydroxytryptamine (5HT) produces hypoglycaemia in mice pretreated with monoamine oxidase inhibitors (MAOI). (Lundquist, Ekholm & Ericson, 1971; Furman, 1974). In large doses 5-HTP can also produce hypoglycaemia in *normal* mice, the effect being augmented by pretreatment with MAOI or by the concurrent administration of drugs known to inhibit the neuronal uptake of 5HT (Furman & Wilson, 1978). Some evidence has been presented suggesting that the hypoglycaemic effect of 5-HTP is mediated at least in part through some central nervous system effect of 5-HT (Darwish & Furman, 1974). Although insulin does not appear to mediate the hypoglycaemic effect of 5-HTP administered in small doses to MAOI pretreated mice, its role in 5-HTP induced hypoglycaemia in *normal* mice has not been reported and this is the subject of the present communication.

All experiments were made using white, male CFLP mice (20–25 g) fasted for 18 hours. Plasma glucose (Beckman Glucose Analyzer) and plasma immunoreactive insulin (IRI) (Hales & Randle, 1963) were determined in blood samples obtained from the femoral vein after anaesthetizing the mice lightly with ether at the desired time after drug injection.

5-HTP (100–400 mg/kg i.v. 30′ or 60′ before blood sampling) produced a dose dependent decrease in the plasma glucose concentration of normal fasted mice. This hypoglycaemia was accompanied by marked increases in the plasma IRI concentration detectable at 5′ after drug injection (e.g. control 6 ± 1 μU/ml; 5-HTP 200 mg/kg 55 ± 9 μU/ml $P < 0.001$). In *niala-mide pretreated* mice 5-HTP produced hypoglycaemia in doses as low as 2–5 mg/kg i.v. but no change in the plasma IRI concentration was detectable at any time. Induction of diabetes using alloxan (80 mg/kg i.v. 2 days beforehand) prevented or markedly reduced the hypoglycaemic effect of 5-HTP (400