mg/kg) in *normal* mice although such treatment is known to have no effect on the hypoglycaemic effect of lower doses of 5-HTP in MAOI pretreated mice (Lundquist, *et al.*, 1971, Furman, 1974).

In *normal* mice the combination of a threshold hypoglycaemic dose of 5-HTP (100 mg/kg) with drugs known to inhibit the neuronal uptake of 5-HT (ORG6582 25 mg/kg; fenfluramine 20 mg/kg, fluoxetine 20 mg/kg, clomipramine 25 mg/kg, or mazindol 25 mg/kg) produced marked hypoglycaemic responses although these drugs were themselves without effect on plasma glucose in normal mice. These responses were accompanied by increases in the plasma IRI concentration but these increases were no greater than those produced by 5-HTP alone.

The results suggest that 5-HTP has a dual action on plasma glucose. One effect appears to be mediated by a stimulation of insulin secretion and is seen when large doses of 5-HTP are given to normal mice. The second does not involve stimulation of insulin secretion and is evident when lower doses of 5-HTP are administered to MAOI pretreated mice or to normal mice in combination with drugs known to inhibit the neuronal uptake of 5-HT.

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Pharmacological control of corticosterone secretion in the intact rat

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Corticotropin releasing factor (CRF) in the rat has been shown *in vitro* to be under cholinergic and serotoninergic facilitatory and noradrenergic inhibitory control (Buckingham & Hodges, 1977; Jones, Hillhouse & Burden, 1976). In intact male Sprague-Dawley rats weighing 150–210 g, plasma corticosterone (CS) levels have been assayed to give a measure of CRF and adrenocorticotrophic hormone activity. In most experiments, drugs were administered intraperitoneally and blood was always collected by decapitation and collection of trunk blood into heparinised tubes.

The muscarinic agonist oxotremorine (Oxo-T) produced a dose related rise in plasma CS 15 min after injection in the dosage range 0.01–0.05 mg/kg. This dose response curve was shifted significantly to the right by pretreatment with atropine (1 mg/kg s.c.i.) one hour before Oxo-T treatment.

5-Hydroxy-L-tryptophan (5-HTP, 1–20 mg/kg) also produced a rise in plasma CS levels 30 min after injection. Both Oxo-T and 5-HTP begin to raise the plasma CS level at dosages below those needed to induce peripheral or behavioural effects. A number of putative serotonin antagonists have been studied for their effect on the 5-HTP induced plasma CS rise. Of these, methergoline (5 mg/kg) and methysergide (10 mg/kg) produced no change. Cyproheptadine (10 mg/kg), (−)-propranolol (20 mg/kg) and cinanserin (10 mg/kg) produced a slight depression of the plasma CS response to 5-HTP. Only mianserin (10 mg/kg) given one hour before 5-HTP produced a statistically significant suppression of the CS response. Pretreatment with atropine (2 mg/kg s.c.i.) did not inhibit the CS response to 5-HTP. Mianserin did not decrease significantly the CS response to Oxo-T.

Rats given α-methyl-para-tyrosine methyl ester (αMpT, 400 mg/kg) decreased their hypothalamic noradrenaline levels by 50% after 14–16 hours. At the same time, such rats exhibited a rise in plasma CS levels. This rise was suppressed one hour after injection of clonidine (0.01–0.05 mg/kg). This suppression could be decreased by piperoxane (5 mg/kg) given 15 min prior to blood collection. Clonidine at this dosage has no effect on basal plasma CS levels in rats not pretreated with αMpT. Apomorphine (5 mg/kg) produced no change in plasma CS levels in rats treated with αMpT.

These results confirm *in vivo* that elevation of plasma CS levels and, by inference, CRF secretion are brought about by muscarinic and serotoninergic stimulation or by depletion of brain noradrenaline. The muscarinic and serotoninergic pathways in this model appear to be independent of each other. Inhibitory receptors appear to be of the α_2 type. Dopamine receptors appear not to be involved in the inhibition of CS secretion.

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The effect of cortisol on the response of the depolarized, calcium-free mouse uterus to calcium

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Several of the stimulatory effects of oestrogens on uterine metabolism can be inhibited by anti-inflammatory corticoids (Szego & Davis, 1969). These steroids can also affect the response of the potassium-depolarized, calcium-free uterus to calcium, when they are added directly to the tissue bath (Henry, Jackson & Knifton, 1973).

Virgin, Porton mice (20 g) were ovariectomised under ether anaesthesia. Seven days after ovariectomy the animals were injected i.p. with arachis oil (0.1 ml), oestradiol 17B (4 μg/100 g), cortisol (either 1.0 or 0.5 mg/100 g) or oestradiol (4 μg/100 g) and cortisol (either 1.0 or 0.5 mg/100 g). Cumulative log dose-response curves (DRC) to calcium were obtained on the mouse uterus with the technique described by Simonis, Ariens & Van den Broeke (1971). Contractions were recorded isotonically with a Washington transducer and MD400 pen recorder.

Some DRCs were plateau-shaped. The effect of oestrogen was to shift the DRC to the left of the vehicle-only control (i.e. arachis oil-treated) group. The mean DRC for the oestrogen group ($n = 12$) was significantly different ($P < 0.05$) from that of the control group (tested by anal. of var.). In both of the cortisol-treated groups the DRC was similar to that obtained with oestrogen and neither was statistically different from it. However, in both of the groups which received oestrogen plus cortisol the DRC was similar to that obtained from the control group. ($n = 10$ in all groups other than oestrogen-treated).

Kimura, Kimura & Maekawa (1978) observed a plateau-like DRC in similar experiments on rat uterus, which they attributed to an interaction between extracellular and membrane bound calcium. Since we observed this type of DRC in some groups, we support their claim that this is not an artifact. Our results suggest that cortisol alone has an oestrogen-like effect on the DRCs to calcium but that in the presence of oestrogen it is anti-oestrogenic.

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