always obtained from the same muscle and the strips were incubated with oxytocin for 5 min prior to the exposure to the agonists. The ^{45}Ca uptake of a fraction not removable by La^{3+} (2 mM) and ^{45}influx were measured as described by Van Breemen, Farinas, Gerba & McNaughton (1972) in a model SL-3000 Intertechnique liquid scintillation spectrometer.

The inhibitory effects of oxytocin (200–1000 μm/ml) on the contractile responses elicited by submaximal equipotent concentrations of noradrenaline (1 μM), serotonin (20 μM), potassium (80 mM) and barium (12 mM) were measured in isolated aortic strips. In all cases, prior exposure to oxytocin inhibited in a dose-dependent manner the contractile response to each of these agents. The inhibitory effect of oxytocin was readily reversed after replacement of the media with drug-free solution. In another experiment, aortic strips were suspended in Ca^{2+}-free solution containing EDTA (0.1 mM) for 2 hours. Then the solution was replaced with Ca^{2+}-free high-K^+ (80 mM) solution for 5 min and then Ca^{2+} (1–5 mM) was added in stepwise fashion over 45 minutes. Oxytocin (500 μm/ml) shifted the dose-response curve to Ca^{2+} downward and to the right and the maximum contractile response induced by addition of Ca^{2+} (5 mM) was significantly reduced ($P < 0.001$). Addition of oxytocin (500 and 1000 μm/ml) reduced the ^{45}Ca uptake and the ^{45}Ca influx in a sustained manner in rat aortic strips at all incubation time intervals (5, 10, 15 and 30 minutes).

Thus, it appears that oxytocin acts on: (a) the membrane to inhibit the influx of extracellular Ca^{2+}. The experiments performed on Ca^{2+}-free high-K^+ solution provided additional evidence for a membrane to inhibit the influx of extracellularCa^{2+}. Ca^{2+}, since oxytocin inhibits the noradrenaline-induced contractile responses.

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Diuretic and antidiuretic responses to oxytocin administration in the rat

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Although the renal saluretic response is well established, the effect of oxytocin on urine flow in rats has been variously described as diuretic or antidiuretic. Chan (1976) has related these effects of the hormone to its ability to interact with the vasopressin receptor. Accordingly the influence of oxytocin on urine flow rate in normal rats, and in rats congenitally lacking endogenous vasopressin (Brattleboro strain) has been investigated.

Male rats (300 g) anaesthetized with 5-ethyl-5(1, methylphenyl)-2-thiobarbiturate (0.11 g/kg, Inactin) were placed on a continuous jugular infusion of 0.45% NaCl at 150 μl/minute. Following a 3.5 h equilibration period 5 min urine collections were made for volume and osmolality measurements during both control periods and 20 min periods of oxytocin administration at 0.15 or 1.5 mu/minute. Values (means ± s.e. mean) are compared by paired *t* test.

In normal rats ($n = 7$) urine flow (μl/min) increased from 150 ± 12 to 175 ± 15 ($P < 0.02$) during administration of oxytocin at 0.15 mu/min, though urine osmolality was unchanged. Administration of oxytocin at 1.5 mu/min increased the peak flow rate further to 232 ± 17 μl/min ($P < 0.001$). Maximal urine flow was, however, delayed until 5–10 min after the end of oxytocin administration. Urinary osmolality (mosmol/kg) showed a diphasic change rising from 283 ± 11 to 357 ± 15 ($P < 0.01$) during oxytocin administration but falling to 195 ± 10 ($P < 0.01$) coincident with the delayed peak in urine flow. If the period of oxytocin administration was extended to 40 min the peak of urine flow was still delayed until 5–10 min after the period of administration.

In contrast the Brattleboro rat showed no significant change in urine flow when oxytocin was given at 0.15 mu/minute. However, a consistent antidiuresis, maximal in the first 10 min of hormone administration was observed when oxytocin was given at 1.5 mu/minute. Urine flow rate (μl/min) fell from 200 ± 15 ($n = 6$) to 151 ± 14 ($P < 0.02$) coincident with a rise in urine osmolality (mosmol/kg) from 175 ± 14 to 258 ± 21 ($P < 0.001$). A similar antidiuretic response to 1.5 mu/min oxytocin was produced in normal rats when the rate of 0.45% NaCl infusion was doubled to 300 μl/minute. In these rats in which endogenous vasopressin release might be expected to be largely suppressed urine flow rate (μl/min) decreased from 312 ± 44 ($n = 5$) to 244 ± 46 ($P < 0.01$) when oxytocin was given.

Thus when endogenous vasopressin is supressed or congenitally absent, oxytocin exhibits a weak antidiuretic action possibly as a consequence of its structural similarity to vasopressin. However, in the presence of vasopressin this action is masked and a diuretic action revealed perhaps due to the competitive displacement of the more potently antidiuretic vasopressin.

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Inhibition of angiotensin-induced drinking by ergot alkaloids

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Angiotensin, injected into the cerebral ventricles, causes water replete rats to drink (Fitzsimons, 1972). There is evidence that dopamine is involved in this response and the dipsogenic action of angiotensin is blocked by neuroleptic drugs (Fitzsimons & Setler, 1975). In the present study we have studied the effect of ergometrine and of other ergot alkaloids on the dipsogenic response to angiotensin and carbachol.

Drugs (in 2–4 µl of 0.9% NaCl) were injected unilaterally into the lateral ventricles of male Wistar rats via permanently-implanted cannulae and water intake was measured (Sumners, Woodruff, Poat & Munday, 1979).

Following angiotensin injections, the rats commenced drinking within 2 min of injection and drinking was usually completed within 20 minutes. The maximum response was produced by angiotensin (1 nmol); at this dose the mean amount of water drunk (ml) was 20.8 ± 0.9 (± s.e. mean, $n = 26$). A dose of 200 pmol angiotensin (the dose used in all antagonist studies) produced a drinking response of 9.4 ± 0.7 ml ($n = 37$). Ergometrine maleate, injected 5 min before the angiotensin, inhibited angiotensin-induced drinking in a dose-dependent manner. The threshold dose for ergometrine was 1 nmol which caused a 24.9 ± 4.0% ($n = 9$) inhibition of the angiotensin response. At a dose of 22 nmol ergometrine, angiotensin-induced drinking was inhibited by 76.1 ± 7.3% ($n = 10$). Other ergot alkaloid derivatives were less active, producing the following inhibitions of angiotensin-induced drinking: Lysergic acid diethylamide tartrate (31 nmol), 42.8 ± 1.9% ($n = 12$); methysergide bimaleate (21 nmol), 36.5 ± 7.1% ($n = 10$). BOL-148 (50 nmol) had no significant effect on the angiotensin response.

The dipsogen carbachol (1.1 nmol) caused a drinking response of 8.7 ± 0.8 ml ($n = 24$). This response was not significantly affected by ergometrine (1, 2 or 22 nmol).

These results further demonstrate that the dipsogenic action of angiotensin is produced by a different mechanism from that of carbachol. Ergometrine is known to act as an agonist or antagonist on dopamine receptors (Woodruff, 1978). Further experiments are required to determine whether the inhibition of angiotensin-induced drinking produced by ergometrine is related to the dopamine receptor-blocking activity of the latter.

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