Considering the effects of β-adrenoceptor blocking agents, it has been shown that in dioestrus propranolol converted the inhibitory effects of adrenaline, noradrenaline and hypogastric nerve stimulation to an excitatory response resembling that seen in oestrus. Conversely, the α-blocking agents tolazoline and phentolamine converted the effects seen in preparations from animals in oestrus to those resembling the responses of the uterus of the rat in dioestrus.

It is suggested that the number and/or the activity of the uterine α-adrenoceptors in the rat is increased in oestrus. An alternative interpretation of these results is that in oestrus the number and/or the activity of β-adrenoceptors is decreased, but it is considered that this is unlikely because the potency of isoprenaline in causing uterine inhibition was not appreciably different in the various stages of the oestrous cycle.

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REFERENCES

BELL, G. H. & ROBSON, J. M. (1937). The effect of certain hormones on the activity of the uterine muscle of the guinea-pig. *J. Physiol., Lond.*, **88**, 312–327.

DIAMOND, J. & BRODY, T. M. (1966). Hormonal alteration of the response of the rat uterus to catecholamines. *Life Sci., Oxford*, **5**, 2187–2193.

LEVY, B. & TOZZI, S. (1963). The adrenergic receptive mechanism of the rat uterus. *J. Pharmac. exp. Ther.*, **142**, 178–184.

MANN, MONICA (1949). Sympathin and the rat uterus. *J. Physiol., Lond.*, **110**, 11*P*.

RUDZIK, A. D. & MILLER, J. W. (1962). The mechanism of uterine inhibitory action of relaxin-containing extracts. *J. Pharmac. exp. Ther.*, **138**, 82–87.

TOTHILL, ANNE (1967). Investigation of adrenaline reversal in the rat uterus by the induction of resistance to isoprenaline. *Br. J. Pharmac. Chemother.*, **29**, 291–301.

Raspberry leaf tea: a new aspect to an old problem

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Therapeutic effects have been attributed to extracts of raspberry leaves at least since 1597 (Gerard, 1597). Despite this long practical experience the first scientific evaluations only took place in 1941 (Burn & Withell, 1941; Whitehouse, 1941). Beckett, Belthle, Fell & Lockett (1954) undertook an extensive chemical investigation in order to separate and establish the nature of the active constituents of raspberry leaves. They also carried out biological investigations, both in the whole animal and in isolated preparations. Since this time very little work has been done on the extract.

In the present study no attempt was made to separate the various fractions isolated by Beckett *et al.* (1954); instead 1 g of dried raspberry leaves was crushed and infused with 15 ml of saline at 95° C. The infusion was allowed to draw for 10 min and the mixture was filtered. The extract was applied to rat uteri in different stages of the cycle, uterine strips from pregnant rats, and strips from non-pregnant and pregnant human uteri.

The extract had little or no effect on uteri from non-pregnant rats, but inhibited the contractions of those from pregnant rats. A variable response was obtained in uteri in induced oestrus. Inhibition lasted 3–4 min and then intrinsic contractions were resumed. A second dose of extract again induced inhibition, so an adrenaline-

like resistance did not develop. The inhibitory effect was not prevented by propranolol (100 ng/ml).

In the concentration used, the raspberry leaf extract was without effect on the strips of human non-pregnant uterus, although this was difficult to evaluate since strips from non-pathological human uteri were not available. The extract contracted strips of normal human uteri at 10–16 weeks of pregnancy. The effect lasted for a few minutes and the intrinsic rhythm was then resumed.

In uteri in which a pharmacological effect was observed (pregnant human and rat uteri) the intrinsic rhythm observed over a 20 min period, while the extract remained in contact with the tissue, appeared to become more regular in most cases and contractions were less frequent.

Earlier writers have alleged that if pregnant women take raspberry leaf extract it has a beneficial effect on their subsequent labour, but the precise nature of this effect is never specified. A major problem in obstetrics is incoordination of uterine action, and it may be that raspberry leaf extract is able to modify the course of labour favourably by producing more coordinated uterine contractions.

REFERENCES

BECKETT, A. H., BELTHLE, F. W., FELL, K. R. & LOCKETT, M. F. (1954). The active constituents of raspberry leaves. *J. Pharm. Pharmac.*, **6**, 785–794.

BURN, J. H. & WITHELL, E. R. (1941). A principle in raspberry leaves which relaxes uterine muscle. *Lancet*, **2**, 1–3.

GERARD, J. (1597). The herbal, or a General History of Plants. London: E. Bollifant, for B. and J. Norton.

TOTHILL, A. (1967). Investigation of adrenaline reversal in the rat uterus by the induction of resistance to isoprenaline. *Br. J. Pharmac. Chemother.*, **29**, 291–301.

WHITEHOUSE, B. (1941). Fragarine: an inhibitor of uterine action. *Br. med. J.*, **2**, 370–371.

The effect of the interval between electrical stimuli on the acetylcholine output of the myenteric plexus-longitudinal muscle preparation of the guinea-pig ileum

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When the myenteric plexus-longitudinal muscle preparation of the guinea-pig ileum is stimulated supramaximally by electrical field stimulation with eserine and choline (20 μM) in the Krebs solution, the output of acetylcholine per stimulus is higher at a frequency of 0·1 Hz than at 1 Hz (Cowie, Kosterlitz & Watt, 1968; Paton & Zar, 1968). It has now been found that, when the stimulus frequency is reduced further, the output increases until a maximum of (250 ng/g)/stimulus is reached at a frequency of 0·016 Hz. This output is about 1% of the total acetylcholine content of the preparation.

With such large outputs it was possible to determine the output due to a single stimulus by removing the bath fluid for assay of acetylcholine 15 s after the application of the stimulus. When this output was compared with that obtained during a collection period of 4 min during which four stimuli were applied at a frequency of 0·016 Hz, it was found that there was no spontaneous transmitter release between stimuli; that is, the usual spontaneous output was depressed. Similarly, the output due to a single train of ten pulses at a frequency of 10 Hz was not different from that due to a single pulse. When the effect of a test pulse applied at varying intervals after a conditioning pulse was investigated the test pulse had no effect on acetyl-