

LETTERS TO THE EDITOR

The Estimation of Ergometrine on the Rat Uterus

SIR,—Studies of the metabolism of ergometrine in these laboratories (Slaytor, Pennefather and Wright, 1959) prompted a search for a means of estimating its oxytocic activity by a method more sensitive than that of Vos (1943). The rat oestrous uterus has been used successfully for the estimation of 5-hydroxytryptamine (Erspamer, 1953) and oxytocin, but it has not been applied to the estimation of ergometrine; I have now found it suitable for this purpose.

Virgin female rats (180 g.) were treated with an intramuscular injection of stilboestrol (100 μ g. in peanut oil). Uteri were removed 30 hr. later, and one

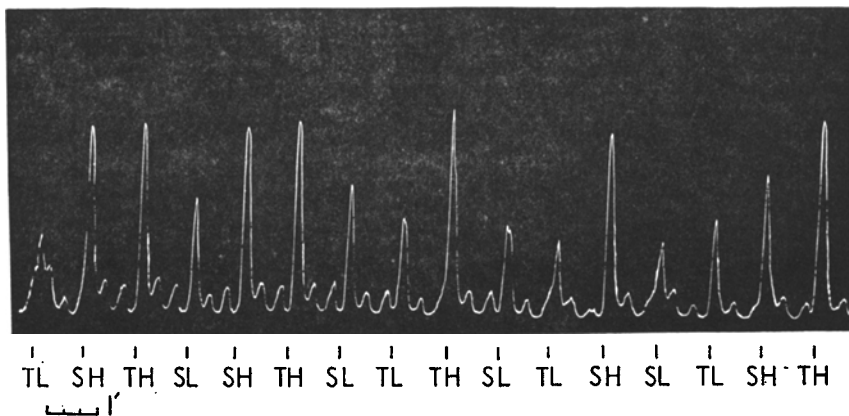


FIG. 1. Record showing contractions elicited by ergometrine on an isolated rat oestrous uterus. SH = 20 ng., SL = 10 ng. TH = 0.2 ml. of a solution of ergometrine of assumed strength 100 ng./ml. TL = 0.1 ml. of the same solution. Doses were given in a 4×4 Latin Square sequence.

horn suspended in a 10 ml. organ bath containing the solution described by Gaddum, Peart and Vogt (1949), maintained at 29° and oxygenated, and isotonic contractions recorded.

The assay design for ergometrine maleate solutions was similar to that described in the B.P. 1958 for the assay of Oxytocin Injection. If certain precautions were always followed, the height of contraction could be taken as the response, and tachyphylaxis rarely developed. Uteri were relatively refractory to the first few applications of ergometrine; at this stage, and throughout the assay, it was important not to use doses exceeding 200 ng. to avoid the possibility of prolonged insensitivity to subsequent doses. When responses were obtained, the drug was washed out of the bath as soon as each contraction reached its maximum. This precaution lessened the possibility of tachyphylaxis, and reproducible responses were produced by doses as low as 10 ng. Doses were given at 3 to 4 min. intervals.

Estimates within 5 per cent of actual strength were obtained with three of the four test solutions of ergometrine. The estimate of the strength of the fourth solution was within 8 per cent of the actual strength. The percentage limits of error ($P=0.95$) for all assays were within 85 and 120 per cent of actual strength. The precision of an estimate could be increased by combining results obtained

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in several assays in the manner described in the B.P. 1958. Fig. 1 is a record of an assay.

This method of estimation has three advantages. Firstly, it is sensitive enough to permit the assay of concentrations of ergometrine as low as 100 ng./ml. Secondly, the use of height of contraction as the response rather than latency as in earlier methods (Vos, 1943; Foster and Stewart, 1948) increases the accuracy of measurement. Finally, the absence of tachyphylaxis permits the use of a standard assay design and consequently simplifies calculation of results.

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Modification of Histamine Sensitivity after 48/80 Treatment

SIR,—Feldberg and Talesnik (1953) and Parratt and West (1957) have shown that in the rat treatment with the histamine liberator, compound 48/80 causes a prolonged fall in the levels of histamine in tissues.

Female rats were treated with a single intraperitoneal dose of 48/80 (2 mg./kg. found to be the LD33). They were killed after the times shown in Table I. Histamine sensitivity was determined on the isolated oestrous uterus which was stimulated electrically by a method similar to that described by Csapo and Corner (1952) for the rabbit uterus. Stimulation and recording characteristics were constant throughout the course of these experiments.

TABLE I
DOSES OF HISTAMINE ($\mu\text{G.}/10 \text{ ML.}$) PRODUCING 20 PER CENT INHIBITION
OF UTERINE CONTRACTIONS IN 48/80 TREATED RATS

Time after 48/80 (days)	Dose of histamine	Mean dose
0.25	100, 100, 120	107
1	20, 20, 40	27
2	2, 5	4
4	4	4
6	2, 5, 10	6
8	4, 5, 8, 8	6
12	4, 6, 8, 8	7
20	2, 2	2
28	5, 7	6
40	20, 20	20
50	20, 20	20

As on the spontaneously contracting rat uterus, the action of histamine against electrically-induced contractions was inhibitory. The doses of histamine which when added to the organ bath (10 ml. capacity) produced 20 per cent inhibition of the height of contraction was taken as the index of sensitivity.