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UTERINE RESPONSE TO DIHY-DROTHEELIN¹

It has been observed for many years that the estrogenic hormones from any source caused a considerable thickening in the epithelium of the vagina and the development of a cornified layer of epithelium in experimental animals. Stockard and Papanicolaou² noted this while working with guinea pigs in 1917. Allen and Doisy³ used this observation to develop a simple test for the estrus condition—namely, the vaginal smear method. Since then the method has been refined by various workers and is widely used. Fee, Mirian and Parkes,⁴ Zondek^{5, 6} and others have shown that estrogenic substances cause marked hypertrophy of the uterus and early vaginal introitus in immature females.

Dorfman, Gallagher and Koch⁷ have suggested that quantitative observations on the hypertrophy of the uterus be used to distinguish between the estrogenic compounds. Twenty-five day-old rats were injected daily for five days with the assayed estrogenic substance. They were then sacrificed, and weights of both the uteri and the ovaries were determined. The ratio of uterine weight (mg) to animal body weight (gm) less the gut was plotted against the dosage in rat units. Theelin and theelol compared in the same way showed a marked difference in their effects upon uterine growth.

Ralls and Jordan,⁸ D'Amour and Gustavson,⁹ Thayer, Jordan and Doisy¹⁰ and later MacCorquodale, Thayer and Doisy¹¹ have reported the presence of an estrogenic compound in the follicular fluid of the ovary. Using its properties as a basis of opinion the

¹ Contribution No. 221, Department of Chemistry, Kansas State College.

² C. R. Stockard and G. N. Papanicolaou, Am. Jour. Anat., 22: 225, 1917.

⁸ E. Allen and E. A. Doisy, Jour. Am. Med. Assoc., 81: 819, 1923.

⁴A. R. Fee, G. F. Mirrian and A. S. Parkes, *Jour. Physiol.*, 67: 377, 1929.

⁵ B. Zondek, Nature, 133: 209, 1934.

⁶ B. Zondek, Nature, 133: 494, 1934.

⁷ R. I. Dorfman, T. F. Gallagher and F. C. Koch, *Endocrin.*, 19: 33, 1935. ⁸ J. C. Ralls and C. N. Jordan, *Endocrin.*, 10: 273, 1926.

⁸ J. C. Ralls and C. N. Jordan, *Endocrin.*, 10: 273, 1926. ⁹ F. E. D'Amour and R. G. Gustavson, *Jour. Pharm. and Exp. Therap.*, 49: 141, 1935.

¹⁰ S. A. Thayer, C. N. Jordan and E. A. Doisy, *Jour. Biol. Chem.*, 79: 53, 1928.

¹¹ D. W. MacCorquodale, S. A. Thayer and E. A. Doisy, Proc. Soc. Exp. Biol. and Med., 32: 1185, 1935. latter named authors suggested that the reported compound was dihydrotheelin.

As was stated above, Dorfman, Gallagher and Koch,⁷ suggest that the uterine response is a good test method to distinguish between the various estrogenic compounds. It was decided to compare the standardized international theelin and dihydrotheelin in this respect. The technique used was that suggested by D'Amour and Gustavson,¹² theelin assayed 0.84 γ per rat unit; dihydrotheelin assayed 0.154 γ per rat unit. These preparations were incorporated in olive oil for injection. Olive oil was injected in controls. Litter mates were selected for each test. Dosages of .05, .1, .2, .3, .4, .5 and .6 rat units were used. The number of animals receiving dosage for each substance varied from three to ten.



FIG. 1. Uterine response to theelin and dihydrotheelin.

By reference to Fig. 1, it can be seen that dihydrotheelin had a much greater effect upon hypertrophy of the uterus than theelin did. This is considered reasonable upon the basis of relative activity of the two as reported by several workers.

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THE VITAMIN C CONTENT OF THE HUMAN TONSIL¹

THE tonsils of 54 persons, mostly children, were analyzed for vitamin C on the day of operation by the method used for foods by Birch, Harris and Ray.² Values ranged from 10.6 to 47.6 milligrams per 100

¹² F. E. D'Amour and R. G. Gustavson, *Jour. Pharm.* and *Exp. Therap.*, 40: 473, 1930. ¹ Preliminary report.

² T. W. Birch, L. J. Harris and S. N. Ray, *Biochem.* Jour., 27: 590, 1933.