ACTION OF EPIDERMAL CHALONE ON 17-β-ESTRADIOL-STIMULATED PROLIFERATION OF VAGINAL EPITHELIAL CELLS OF OVARIECTOMIZED MICE

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The vaginal epithelium, which is a tissue of epidermal type [2, 4], exhibits marked hormonal dependence on its proliferation, so that relations between the hormonal and chalone systems in maintaining the proliferative status of this tissue can be studied. The writers showed previously that injection of epidermal chalone into ovariectomized mice after an injection of estrogen [1] does not inhibit proliferation of vaginal epithelial cells. The effect of inhibition of proliferation was obtained after single and multiple injections of chalone, only before injection of the hormone.

The aim of this investigation was to study the duration of interaction between chalone and vaginal epithelial cells of castrated mice required to lower the level of estrogen-induced proliferation and also the duration of action of epidermal chalones when injected repeatedly. Particular attention was paid to the tissue specificity of effects induced by chalones.

EXPERIMENTAL METHOD

Experiments were carried out on 50 female mice weighing 18-20 g from the "Rappolovo" nursery, Academy of Medical Sciences of the USSR, which were ovariectomized in the diestrus stage of the estrous cycle. The animals were given a subcutaneous injection of 17-β-estradiol (from Organon, The Netherlands) in a dose of 0.1 μg per mouse 4-6 weeks after the operation. Epidermal chalone in a dose of 5 mg per mouse was given as a single intraperitoneal injection 8, 4, and 1 h before injection of the hormone. Some animals, used as the positive control, received three injections of chalone at the same time. The animals were killed by cervical dislocations 15 h after injection of the estrogen; [^{3}H]thymidine was injected intraperitoneally into all the animals 1 h before sacrifice. Material was taken after 24 and 48 h, in addition to the times specified above, in the experiment with three injections of chalones only.

Histoautoradiographs were obtained by covering the dewaxed sections with type M liquid photographic emulsion.

The mitotic coefficient (MC) and the index of labeled nuclei (ILN), in promille, were determined.

EXPERIMENTAL RESULTS

The experiments showed that the number of mitotically dividing and DNA-synthesizing cells after 15 h in response to injection of estrogen into the ovariectomized animals (control) reached a high level in both the vaginal and the uterine epithelium (Table 1). After three injections of epidermal chalone, inhibition of proliferation was observed in the vaginal epithelium, whereas in the uterine epithelium no fall in the level of proliferation took place.

It follows from these results that the inhibitory effect of epidermal chalones is manifested only in the vaginal epithelium, which, as was stated above, is a tissue of epidermal type, and not in the uterine epithelium.

In castrated animals 15 h after injection of 17-β-estradiol (control) ILN in the vaginal epithelium was found to be 318 ± 76%.

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TABLE 1. Changes in MC and ILN of Uterine and Vaginal Epithelial Cells after Three Injections of Epidermal Chalones

Source of epithelium	Ovariectomy + 17-β-estradiol		Ovariectomy + chalone + 17-β-estradiol	
	MC	ILN	MC	ILN
Uterus	20±6	562±69	18±6	440±82
Vagina	29±10	370±41	0,41±0,17*	144±20*

Legend. *P < 0.01 compared with control.

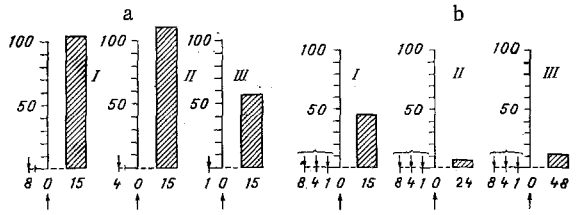

Fig. 1. ILN of vaginal epithelium of ovariectomized mice after injection of 17-β-estradiol. Absciasa, time (in h); ordinate, ILN (in % of control, taken as 100). a) Single injection of chalone 8 h (I), 4 h (II), and 1 h (III) before injection of hormone; b) three injections of chalone: I, II, III) 15, 24, and 48 h respectively after injection of hormone. Arrows pointing downward — injection of chalone, arrows pointing upward — injection of hormone.

In the next series of experiments a single injection 8 h or 4 h before injection of the hormone was found not to inhibit entry of the vaginal epithelial cells into the stage of DNA synthesis (Fig. 1).

The inhibitory action of chalone on the number of cells labeled with [^{3}H]thymidine was observed only if a single injection of epidermal chalone was given 1 h before injection of the estrogen (Fig. 1A). If three injections of epidermal chalone were given before injection of the hormone, stimulation of proliferation induced by estradiol in the vaginal epithelium was 55% lower than in the control (Fig. 1B). Later, 24 and 48 h after injection of the chalone, the level of DNA-synthesizing cells continued to fall.

Absence of the inhibitory effect when epidermal chalone was injected 8 h or 4 h before hormonal stimulation of proliferation and its presence if chalone was injected 1 h before the hormone indicate that binding of the chalone by vaginal epithelial cells is of short duration.

Consequently, the effect of three injections of chalone was mainly due to the last injection (1 h before injection of the hormone).

The decrease in the number of DNA-synthesizing cells observed after 24 and 48 h can be explained by the decrease in the concentration of exogenous estradiol by these times and the subsequent fall in the level of epithelial cell proliferation in the ovariectomized animals.

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