ACTION OF ESTRADIOL DIPROPRIONATE, ACTINOMYCIN D, AND THEIR COMBINATION ON ENZYMIC ACTIVITY IN THE RAT UTERUS

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The action of estradiol and actinomycin D on the activity of alanine and aspartate aminotransferases, fructose-1,6-diphosphate aldolase, and acid phosphatase in the uterus of sexually immature rats was investigated. The estrogen increases the activity of all these enzymes. In some cases actinomycin D modifies the action of estradiol.

Steroid hormones are of great importance in the regulation of homeostasis [3].

The object of the present investigation was to study the effect of estradiol dipropionate, actinomycin D, and a combination of both on the activity of alanine aminotransferase, aspartate aminotransferase, fructose-1,6-diphosphate aldolase, and acid phosphatase in the rat uterus.

EXPERIMENTAL METHOD

Noninbred sexually immature female rats weighing 25-35 g were used in the experiments. Estradiol was injected in a dose of 0.1 mg/100 g body weight. Actinomycin D was injected as a single dose of 0.25 μg/g or, in some series of experiments, in a dose of 0.25 μg/g at intervals of 24 h. When the combined action of the hormone and antibiotic was studied, estradiol was injected 30 min after actinomycin D. Activity of the enzyme was determined by colorimetric methods in an anuclear homogenate of the uterus, using reagents from the biochemical sets marketed by Boehringer–Mannheim (West Germany) as substrates.

EXPERIMENTAL RESULTS

An increase in the activity of all the enzymes studied was observed 24 h after injection of estradiol (Table 1). These results are in agreement with those in the literature [6-9] to the effect that estrogens stimulate protein biosynthesis and glycolysis in the rat uterus. The results now obtained, which show changes in the activity of acid phosphatase during the action of the estrogen and of actinomycin D, are indirectly confirmed by the results of an investigation [4] which showed that injection of testosterone into young rhesus monkeys leads to a rapid increase in the acid phosphatase level in the prostate gland up to values observed in adult animals, and also by data in the literature [2] reflecting increased activity of lysosomal enzymes as a result of the action of inhibitors of RNA synthesis.

The combined administration of estradiol and actinomycin D led to a decrease in the maximal effect of the hormone on the aminotransferase (Table 1). This suggests that RNA biosynthesis is concerned in the change in activity of these enzymes. However, the fact that the hormonal effect was not completely suppressed by the antibiotic prevents any definite conclusions being drawn regarding activation of operons responsible for aminotransferase formation in the genome of the uterine cells.

The possibility cannot be ruled out that the increase in the level of transamination enzymes taking place as a result of administration of estradiol may be due to substrate induction.

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TABLE 1. Effect of Estradiol Dipropionate and Actinomycin D on Activity of Enzymes (in % of control level) in Uterus of Sexually Immature Rats (M ± m)

Preparation	Dose	Alanine aminotransferase				Aspartate aminotransferase			
		time after administration of hormone (in h)							
		24	48	72	96	24	48	72	96
Estradiol	0,1 mg/100 g	169[1]±14,4	493[1]±21,2	214[1]±16,7	209[1]±11,4	118[1]±3,79	159[1]±3,12	140[1]±2,78	137[1]±3,27
Actinomycin D	0,25 μg/g	100±8,15	89±7,78	102±9,47	129[1]±6,24	93±4,3	111[1]±3,7	102±6,4	108±1,9
Actinomycin D	0,5 μg/g	89±6,5	96±5,5			96±6,0	92±6,3		
Actinomycin D + estradiol	0,1 mg/100 g	125±10,5	286[1]±18,0	277[1]±5,9	209[1]±18,2	128[1]±3,7	156[1]±4,3	145[1]±3,8	130[1]±3,6
Actinomycin D + estradiol	0,1 mg/100 g	99±11,7	201±19,5			129[1]±3,2	131[1]±3,2		

(continuation)

Preparation	Aldolase				Acid phosphatase (total activity)				Acid phosphatase (free activity as percent of total)			
	24	48	72	96	24	48	72	96	24	48	72	96
Estradiol	152[1]±3,16	218[1]±3,92	183[1]±3,61	159[1]±4,03	197[1]±6,18	185[1]±6,4	381[1]±13,2	850[1]±24,2	7±2,2	17±2,2	23[1]±2,8	41[1]±5,32
Actinomycin D	105±6,2	94±2,2	99±3,3	93±2,8	146[1]±10,5	331[1]±12,5	685[1]±70,7	562[1]±27,7	37[1]±7,6	39[1]±7,4	35[1]±5,3	38[1]±6,3
Actinomycin D	109±5,5	112±7,2			556[1]±28,8	649[1]±47,8			36[1]±4,2	38[1]±6,3		
Actinomycin D + estradiol	146[1]±5,6	217[1]±9,1	219[1]±8,9	209[1]±6,4	233[1]±19,6	719[1]±28,8	693[1]±53,5	740[1]±63,2	38[1]±6,7	48[1]±11,6	45[1]±12,6	49[1]±14,9
Actinomycin D + estradiol	158[1]±6,1	161[1]±7,3			491[1]±34,4	405[1]±43,8			23±4,7	41[1]±7,6		

[1]Differences statistically significant relative to control.

The results of these experiments show that the combined action of estradiol and actinomycin D causes some increase in the aldolase level in the uterus compared with that observed after administration of the steroid alone; so far as acid phosphatase was concerned, there was a tendency toward summation of the effect after 48 h (Table 1). Taken in conjunction with results showing swelling of the mitochondria after addition of lysosomal fraction to a cell culture [5],and demonstrating activation of lysosomal enzymes during hypoxia [1], the increased total acid phosphatase activity and the relative increase in free acid phosphatase activity as a percentage of the total after 48 h obtained in the present experiments (Table 1) can be attributed to a change in the functional state of the lysosomal membranes of the uterine cells.

In this case, the incomplete depression of the action of estradiol on the amino-transferases by the antibiotic and the increased aldolase activity at subsequent times may be explained by a possible compensatory increase in glycolysis.

It can accordingly be postulated on the basis of these results that, besides the action of estradiol and actinomycin D directly on the genetic apparatus of the cells of target organs, their action on biochemical systems connected with changes in the functional state of subcellular components of membrane structures cannot be ruled out.

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