

EFFECT OF ESTROGEN-MEGESTROL AND NEUROTROPIC SUBSTANCES  
ON THE RNA CONTENT OF THE RAT ENDOMETRIUM

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The effect of the hormone-like estrogen-progestagenic preparation megestranol and of a combination of megestranol and spasmolytin on metabolic activity in the endometrium was studied in experiments on rats. The results of a cytochemical investigation showed that megestranol and the megestranol-spasmolytin combination alter the metabolism of the endometrium and lead to a decrease in the RNA content in the epithelial cells of the endometrial glands, thereby creating conditions that prevent normal implantation and development of the fertilized ovum.

**KEY WORDS:** *megestranol-spasmolytin combination; cytospectrophotometry; endometrium; contraception.*

Previous investigations [1-3] showed that one of the first hormonal preparations synthesized in the USSR, megestranol (containing an estrogenic component, 0.1 mg megestranol, and a progestagenic component, 5 mg megestrol acetate, ratio 1:50), is a highly effective contraceptive both when used by women and in experiments on animals. The mechanism of action of this preparation is to change the character of ovulation, principally by changing the secretion of luteinizing hormone.

Experimental investigations by the same workers showed that if cholinergic mediation is depressed, the contraceptive activity of megestranol is increased. The combined use of a noncontraceptive dose of megestranol with spasmolytin results in the highest contraceptive effect, accompanied by a more favorable change in the gonadotropin level.

The object of this investigation was to study the effect of megestranol and a combination of megestranol with spasmolytin on metabolic activity in the rat endometrium, or specifically, to study changes in the RNA content in the endometrium. RNA synthesis in the uterus is closely dependent on hormonal stimulation and the RNA content is an indicator of the functional state of the ovaries and endometrium [4, 5].

#### EXPERIMENTAL METHOD

Experiments were carried out on 30 noninbred female rats weighing 160-180 g with a 4-5-day estrous cycle. The animals were divided into five groups depending on the substance injected and the dose (Table 1). All substances were given by gastric tube in the course of 14 days as solutions or as a thin aqueous suspension. The rats were killed in the stage of diestrus. To determine the RNA content, the method of single-

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TABLE 1. RNA Content in Endometrium of Rats following Administration of Megestranol Alone and in Combination with Spasmolytin

Substance and dose (in mg/kg)	Contraceptive effect (in %)	P	RNA content (in pg)	P
Control	—		15,2±2,6	
Megestranol 1,5	—		13,1±1,6	
3	66	0,025	8,5±1,0	<0,01
Spasmolytin 30	—		11±1,4	
Megestranol 1,5 + spasmolytin 30	75	<0,01	8,8±1,2	<0,01

wave UV-cytospectrophotometry was used. The results are based on photometry of 900 epithelial cells of the endometrial glands and measurement of the volumes of cytoplasm of 750 cells.

#### EXPERIMENTAL RESULTS

The results are shown in Table 1.

The histochemical investigations showed that following administration of a contraceptive dose of megestranol and megestranol + spasmolytin, the RNA content in the rat endometrium fell. This points to changes in the metabolic activity in the mucous membrane. The RNA content in the endometrium of rats receiving a noncontraceptive dose of megestranol (1.5 mg/kg) and

spasmolytin in a dose of 30 mg/kg separately did not differ significantly from its content in the endometrium of the animals of the control group.

It can be concluded from the results of these experiments that the reduction in metabolic activity of the endometrium following administration of megestranol alone or in conjunction with spasmolytin to rats is one of the mechanisms of the pharmacological activity, including the contraceptive action, of these preparations. Megestranol in a contraceptive dose changes the metabolic activity of the uterine mucous membrane, with a consequent lowering of the RNA level in the epithelial cells of the endometrial glands of the rats, thus preventing normal implantation and development of the fertilized ovum. The combined use of a noncontraceptive dose of megestranol with spasmolytin in doses modifying the central regulation of hypothalamic-pituitary function leads to similar disturbances of metabolic activity.

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