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EFFECT OF SIGETIN ON ANOVULATION IN RATS

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UDC 615.256.51.015.4:612.622.3

The effect of sigetin on anovulation was investigated in experiments on sexually mature female rats. Anovulation was induced experimentally by stress (keeping the rats under overcrowded conditions) and by unilateral ovariectomy (hemicastration). Treatment with sigetin in a dose of 10 mg/kg for 4-5 days restored normal ovulation. If large doses of sigetin (up to 30 mg/kg) were given for longer periods (2-3 weeks) no such effect was observed. The results of these experiments suggest that sigetin, in small doses, stimulates the secretion of luteinizing hormone.
KEY WORDS: hemicastration; stress; anovulation; sigetin.

Research is in progress in the Department of Pharmacology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, to obtain therapeutic preparations with a selective type of action on the hypothalamo-hypophyseo-ovarian system. One such compound is sigetin, the dipotassium salt of disulfomeso-3, 4-diphenylhexane, which is similar to dihydrostilbestrol but differs from it in chemical structure by replacement of two hydroxyl radicals by potassium sulfonate radicals. As a result sigetin has lost some of its properties as an estrogen (the peripheral proliferative action on tissues and organs) but has retained its ability to give a central inhibitory action on gonadotropic function [3, 5] and also some of its pharmacological properties as an estrogen, as a result of which sigetin can be used with success in obstretrics to improve the uterine and placental circulation and for the relief of intrauterine fetal asphyxia [2].

Nowadays, following investigations by Hungarian research obstetricians and gynecologists [4] and also experimental studies in the present writer's department, further information has been obtained of the mechanism of action of sigetin. In particular, it has been shown that by binding with specific estrogen-sensitive receptors, sigetin can prevent the action of estrogens on them [1, 4]. This property enables sigetin to be used in clinical obstetrics for the treatment of anovulation and sterility in patients with hyperestrogenemia [1].

The object of the present investigation was to study the action of sigetin on ovulation in rats when delayed by hypoluteinemia and a deficiency of ovarian hormones in the blood.

EXPERIMENTAL METHOD

Sexually mature female rats with experimentally induced anovulation were used. Anovulation was induced by stress (by keeping the rats in overcrowded cages). Various types of experimental stress are known to be effective and to cause inhibition of secretion of gonadotropins, especially luteinizing hormones, and to block ovulation. This inhibition of gonadotropic function is explained by activation of secretion of ACTH.

Department of Pharmacology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 83, No. 6, pp. 741-742, June, 1977. Original article submitted November 9, 1976.

TABLE 1. Effect of Sigetin and Diethylstilbestrol on Ovulation in Rats

Series of expts.	Experimental conditions	No. of experimental animals	No. of ovulations	Percentage of ovulations	No. of ova
I	Control	10	8	80	10
	Stress	10	1	10	9
	Stress + sigetin, 10 mg/kg daily for 4-5 days	10	6	60	10
II	Stress	10	2	20	8
	Stress + sigetin, 30 mg/kg daily for 20 days	13	3	23	7
III	Stress	10	2	20	7
	Stress + diethylstilbestrol, 0.5 μg daily for 10 days	13	5	38,5	9
IV	Hemicastration	10	1	10	10
	Hemicastration + sigetin, 10 mg/kg daily for 4-5 days	10	8	80	8

Anovulation was induced in the remaining animals by unilateral ovariectomy (hemicastration). The mechanism of anovulation in this case was evidently connected with the reduction in the level of sex hormones in the blood and a consequent disturbance of the secretion of luteinizing hormone.

EXPERIMENTAL RESULTS

The results of these experiments showed that overcrowding of the animals caused anovulatory cycles in the rats in 90% of cases. Administration of sigetin in small doses (10 mg/kg) for 4-5 days led to effective restoration of the ovulatory reaction in the rats: Ovulation was observed in 60% of cases (Table 1). After administration of sigetin in a dose of 30 mg/kg for 2-3 weeks no such action was observed. Hemicastration led to persistent anovulation in 90% of animals. After administration of sigetin in small doses (10 mg/kg) for 4-5 days, the disturbed ovulation in the rats was restored to normal. Estrogens are known to have a similar stimulating effect on ovulatory function. For instance, the present writer found experimentally that diethylstilbestrol, in a dose of 0.5 μg given daily to rats for 5-10 days, like sigetin induced partial recovery of ovulation.

The results of these experiments indicate that sigetin, in small doses, stimulates the secretion of gonadotropins and, in particular, of luteinizing hormone. They suggest that sigetin can be used in clinical practice for the treatment of sterility not only in the case of hyperestrogenemia, but also in the presence of hypoleutinemia and hypoestrogenemia.

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