MECHANISM OF THE STIMULANT EFFECT OF OROTIC ACID ON PHAGOCYTIC ACTIVITY OF LEUKOCYTES

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The stimulant action of orotic acid on phagocytosis is inhibited by its antimetabolite 6-azauridine. It is considered that stimulation of phagocytosis by orotic acid is due to its participation in nucleic acid synthesis.

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Previous work in the authors' laboratory revealed the stimulant action of orotic acid on the phagocytic activity of leukocytes; experiments on guinea pigs and rats showed that if it is injected daily for 15 days in doses of 50 and, in particular, 100 mg/kg body weight, the phagocytic activity of the leukocytes is increased. In guinea pigs of the control group the maximum phagocytic activity of the leukocytes was 10 ± 2.1%, compared with 67 ± 7.8% in the experimental animals ($P < 0.001$). Orotic acid, in a dose of 5 mg/kg, had no effect on the phagocytic index [2]. Chukichev [3] found that this acid, in a dose of 10 mg/kg, increased the phagocytic activity of leukocytes by 2-3 times.

Having regard to the role of orotic acid in synthesis of protein and, in particular, of nucleic acids [1, 4-15], it may be considered that its stimulant action on phagocytic activity is due to its participation in nucleic acid synthesis and to the existence of a direct link between this acid and the phagocytic activity of the leukocytes.

To investigate this problem experiments were carried out to study the effect of the orotic acid antimetabolite 6-azauridine on the phagocytic activity of leukocytes in rats.

EXPERIMENTAL METHOD

The phagocytic activity of leukocytes was determined in peritoneal exudate by Perel'man's method. A 0.1% suspension of carmine in physiological saline was used as the object of phagocytosis.

Experiments were carried out on 47 laboratory rats weighing 90-100 g. Orotic acid and 6-azauridine were given to the animals daily by mouth for 14 days. Control group 1 included intact animals; the rats of group 2 received orotic acid in a dose of 100 mg/kg, the animals of group 3 received orotic acid (100 mg/kg) together with 6-azauridine (100 mg/kg); the rats of group 4 received 6-azauridine (100 mg/kg) only.

The number of leukocytes carrying out phagocytosis (in %), counted 45 min after injection of the carmine, was used as the index of phagocytic activity of the leukocytes.

TABLE 1. Number of Leukocytes Engaged in Phagocytosis (in %) 45 min after Injection of Carmine

Group of animals	n	$M \pm t$	P*
1-	12	11,0± 1,6	—
2-	10	39,2± 3,9	<0,001
3-	12	9,0± 2,9	>0,05
4-	13	2,3± 0,4	<0,01

*P given relative to control indices.

EXPERIMENTAL RESULTS

The results (Table 1) showed that the phagocytic activity of the leukocytes was highest in the rats of group 2; in the control animals (group 1) the proportion of leukocytes engaged in phagocytosis 45 min after injection of carmine was 11%, compared with 39.2% in the experimental animals ($P < 0.001$).

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In the rats of group 4 the number of leukocytes engaged in phagocytosis was extremely small—2.3% ($P < 0.01$),—and they were not found in all animals.

These experiments thus clearly revealed antagonistic relationships between orotic acid and 6-azauridine; the latter prevented the simulant action of orotic acid on phagocytosis.

It can be concluded from these results that the mechanism of the stimulant action of orotic acid on phagocytosis is connected with its direct participation in nuclei acid synthesis.

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