Erythropoietic Activity of Preparations Containing Receptors and Antibodies to Erythropoietin in Ultralow Doses

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We compared the erythropoiesis-stimulating effects of ultralow doses of erythropoietin receptors and antibodies to erythropoietin in intact mice. Antibodies to erythropoietin, but not erythropoietin receptors, possessed considerable erythropoiesis-activating properties.

Key Words: *erythropoietin; antibodies; ultralow doses; erythropoiesis; receptors*

Despite much recent progress in the search for effective antianemic preparations, elaboration of new stimulators of erythropoiesis for safe long-term treatment remains an actual problem. Various medicinal preparations, including recombinant erythropoietin derivatives, activate the erythroid hemopoietic stem, but often cause side effects (hypertension, hemostasis disturbances, and plasma iron deficiency) [3,5,6].

Preparations containing ultralow doses of active substances and producing no complications hold promise for long-term therapy of patients with anemia. Here we studied erythropoietic activity of preparations containing homeopathically potentiated erythropoietin receptors (ER) and antibodies to erythropoietin (ABE) and synthesized at the "Materia Medica Holding" Research-and-Production Company.

MATERIALS AND METHODS

Preparations of ER and ABE contained receptors or antibodies in homeopathic dilutions of C12, C30, and C200 (equivalent concentration 10^{-24} wt %). Specific activity of these preparations was studied on 78 female CBA/CaLac mice aged 2 months and weighing 18-20 g. The animals were obtained from the nursery of the Institute of Pharmacology. The test preparations were administered through a gastric tube in a daily dose of 0.2 ml for 10 days. Intact mice served as the control. The animals were killed by cervical dislocation under ether anesthesia on days 5-10 of the experiment. The total cellularity of the bone marrow and the count of leukocytes, erythrocytes, and reticulocytes in the peripheral blood were evaluated using routine techniques. Myelogram and hemogram were studied on bone marrow and blood smears, respectively, after staining with azure II and eosin.

The results were analyzed by Student's *t* test.

RESULTS

The test preparations stimulated bone marrow erythropoiesis. ABE markedly activated the erythroid bone marrow stem on day 6 of treatment (the count of bone marrow erythrokaryocytes surpassed the control by 54.7%) but then the intensity of erythropoiesis returned to normal. The stimulating effect of ER on the count of bone marrow erythroid cells was less significant and delayed by 1 day (compared to treatment with ABE, Fig. 1).

Ultralow doses of ER did not affect the count of peripheral blood erythrocytes. Only on day 8 after ER administration the number of peripheral blood erythrocytes surpassed that in mice receiving ABE and intact animals (by 20.5%, $p<0.05$, Fig. 1). These changes were probably associated with the increase in the count of erythrokaryocytes in the hemopoietic tissue of mice receiving ER. However, at later terms the number of circulating erythrocytes decreased because of the absence of enhanced migration of erythrocytes from the bone marrow.

In animals receiving ultralow doses of ER the count of peripheral blood reticulocytes did not increase, but even decreased compared to the control and mice treated with ABE. By contrast, in mice re-

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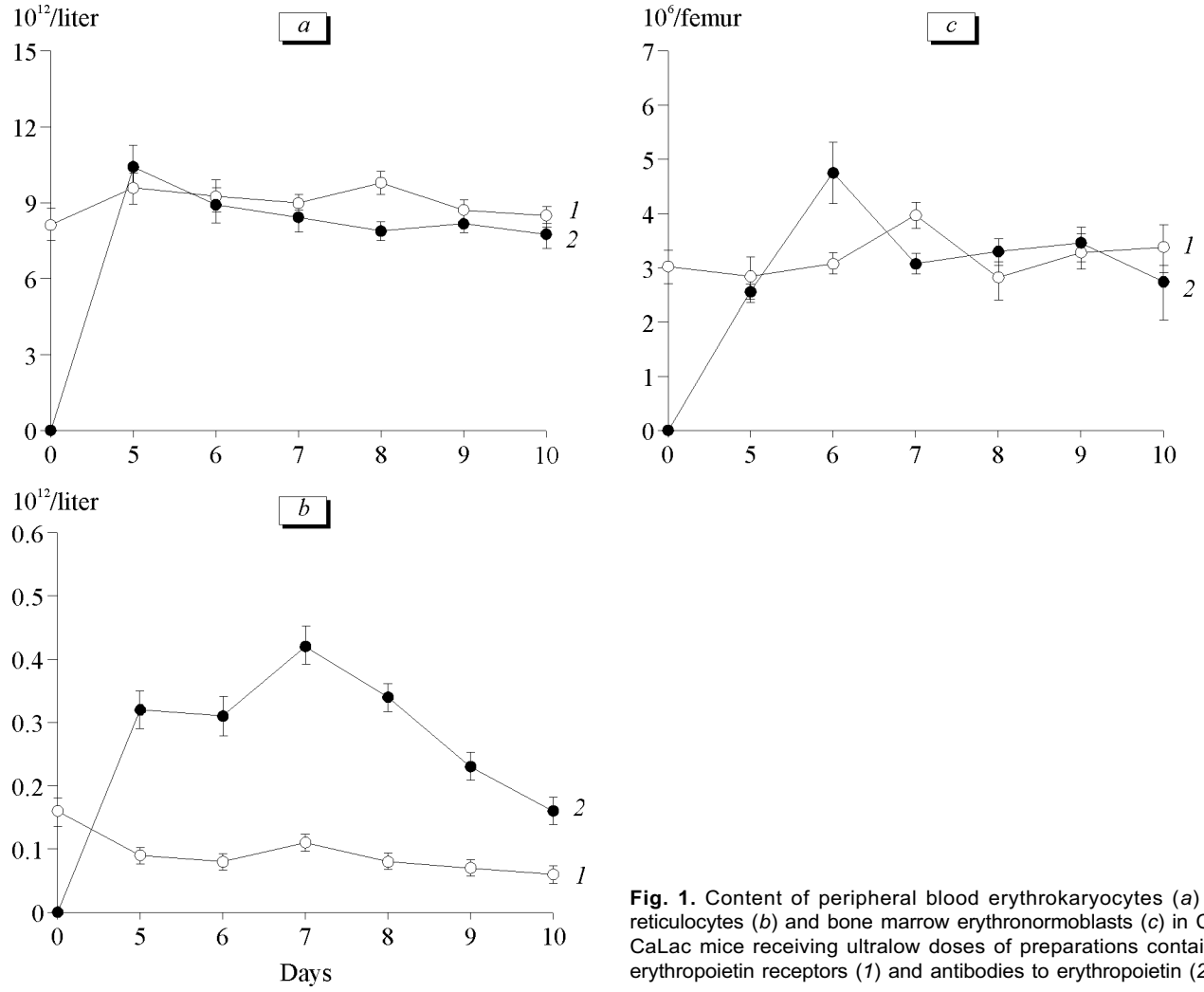

Fig. 1. Content of peripheral blood erythrokaryocytes (*a*) and reticulocytes (*b*) and bone marrow erythronormoblasts (*c*) in CBA/CaLac mice receiving ultralow doses of preparations containing erythropoietin receptors (*1*) and antibodies to erythropoietin (*2*).

ceiving ABE the number of circulating reticulocytes increased more than by 2.5 times on day 7 and markedly surpassed that in intact animals (days 5-9, Fig. 1).

Thus, homeopathic preparation containing ER was ineffective, while homeopathic preparation containing ABE displayed considerable erythropoiesis-stimulating activity. This preparation stimulated central and peripheral components of the erythroid hemopoietic stem. Taking into account the requirements for substances with hemopoiesis-stimulating activity [2], our results indicate that ABE in ultralow doses hold much promise as the stimulator of erythropoiesis.

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