BIOLOGICAL ACTIVITY OF EPIDERMAL CHALONES IN THE PRESENCE OF BLOOD SERUM FROM PSORIASIS PATIENTS

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An interesting aspect of the study of the pathogenesis of psoriasis is the character of local tissue-specific regulation of cell proliferation in the epidermis which, in the modern view, is effected by epidermal chalones [5, 6]. Investigations have shown that the epidermis, affected by psoriasis, can respond to exogenous epidermal chalones [7, 8]. The level of this response was found to depend on the clinical stage of the disease [1, 3]. Addition of blood serum from patients with a progressive stage of psoriasis to the culture medium is known to reduce the ability of epidermal chalones to inhibit incorporation of [^{3}H]thymidine into DNA of epidermocytes of normal human skin [2].

The aim of this investigation was to study the mechanism of disappearance of biological activity of chalones under the influence of blood serum from psoriasis patients, depending on the clinical stage of the disease.

EXPERIMENTAL METHOD

Biopsy specimens of skin from 12 healthy persons (eight men and four women) aged from 19 to 26 years were subjected to short-term organ culture. Blood serum was obtained from 17 patients with psoriasis (10 men and 7 women) aged from 16 to 54 years, and not previously treated. A progressive stage of psoriasis was diagnosed in 11 of these patients, a stationary stage in three, and a regressive stage in three. A lyophilized alcoholic extract of rat skin, containing epidermal chalones G_1 and G_2, generously provided by the staff of the Laboratory of Experimental Histology, Research Institute of Experimental Medicine, Academy of Medical Sciences of the USSR (Leningrad), was used as the epidermal chalone. The use of rat chalones experimentally was justified by the absence of species-specificity of their action [5, 6]. After culture of the biopsy material from human skin for 8-10 h in medium 199 in the presence of [^{3}H]thymidine, the skin fragments were washed to remove unincorporated isotope and fixed in Bouin's fluid [4]. Liquid photographic emulsion was applied to sections 4 μ thick. Labeled cells were counted in 1000 cells from the basal layer of the epidermis. Statistical analysis was carried out by the Fisher-Student t test [1, 2, 4]. There were three series of experiments altogether. In the first two series organ culture of skin biopsy material from a healthy person was continued for 10 h. In the experiments of series I, after incubation for 2 h in the presence of 1 ml of blood serum from a psoriasis patient, chalones were added in concentrations of 1, 2, and 3 mg/ml medium. In series II, chalones were added for the first 2 h to the culture medium in the same concentrations as in series I, followed by blood serum from psoriasis patients. In both series of experiments pieces of skin incubated for 10 h in nutrient medium alone, without the addition of chalones and serum, served as the control.

In series III skin biopsy material from a healthy person was incubated for 8 h, and epidermal chalones in a concentration of 2 mg/ml and 1 ml of blood serum were added simultaneously to the culture medium. Blood serum from healthy persons and psoriasis patients, in whom progressive, stationary, and regressive stages of the disease had been diagnosed, was used. The positive control consisted of pieces of skin incubated in nutrient medium only or with the addition of epidermal chalones (2 mg/ml). In all series of experiments the total volume of nutrient medium for culture of one biopsy specimen was 5 ml.

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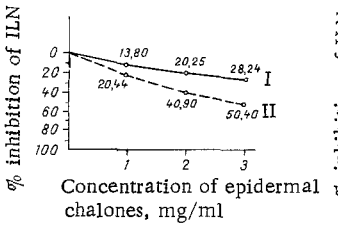

Fig. 1.

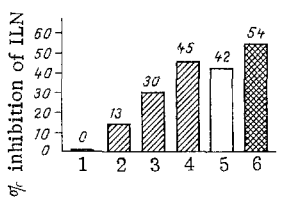

Fig. 2.

Fig. 1. Dependence of inhibitory activity of epidermal chalones on their concentration in presence of blood serum from patients with progressive stage of psoriasis, when added in different ways to culture medium. Abscissa, concentration of epidermal chalones (in mg/ml); ordinate, percentage inhibition of ILN. I) Experiments of series I, serum added before chalones, II) experiments of series II: chalones added before serum.

Fig. 2. Inhibitory activity of epidermal chalones in presence of blood serum from patients with different stages of psoriasis. Abscissa: 1) control (incubation without chalone or serum), 2, 3, 4) sera from psoriasis patients with progressive, stationary, and regressive stages of disease respectively, 5) healthy human serum, 6) chalone (incubation in presence of chalone only); ordinate, percentage of inhibition of ILN.

EXPERIMENTAL RESULTS

In the experiments of series I, when epidermal chalones were added to the medium 2 h after preincubation of the biopsy material in the presence of blood serum from patients with progressive psoriasis, no inhibitory activity of the epidermal chalones could be found. For instance, with chalones in a concentration of 1 mg/ml the index of labeled nuclei (ILN) was 89.1 ± 7.4 ($P > 0.05$), in a concentration of 2 mg/ml it was 82.8 ± 6.2 ($P < 0.01$), and in a concentration of 3 mg/ml it was 73.4 ± 4.5 ($P < 0.01$). ILN in the epidermis of the control skin fragments was 104.6 ± 5.4. Despite the small decrease observed in ILN under the influence of chalones, statistical analysis showed that the decrease was not significant.

In the experiments of series II, in which skin biopsy material was incubated for 2 h in the presence of chalones, after which serum from patients with progressive psoriasis was added, the inhibitory effect of the chalones was strong. With chalones in a concentration of 1 mg/ml, ILN was 100.3 ± 5.4 ($P < 0.001$), with a concentration of 2 mg/ml it was 74.5 ± 5.1 ($P < 0.001$), and in a concentration of 3 mg/ml it was 62.5 ± 4.3 ($P < 0.001$). In control samples ILN was 126.0 ± 6.5.

Dependence of activity of epidermal chalones on concentration in the presence of blood serum from patients with the progressive stage of psoriasis is shown in Fig. 1. In the experiments of series I, when psoriasis serum was added initially to the medium, followed by epidermal chalones, their inhibitory effect was much weaker (Fig. 1) than in series II, when chalones were added before psoriasis serum.

The results of the first two series of experiments thus showed that blood serum from patients with progressive psoriasis, if added to the medium before epidermal chalones, reduced the effectiveness of their action by a much greater degree than in experiments in which this same serum was added after the chalones. This fact can evidently be explained on the grounds that certain components of blood serum from psoriasis patients may perhaps prevent binding of chalone with surface receptors of epidermocytes or its penetration into the cytoplasm.

In the experiments in series III the inhibitory effect of epidermal chalones on DNA synthesis in the epidermocytes was exhibited to different degrees depending on the serum in which they were cultured. For instance, in the presence of serum from patients with progressive psoriasis ILN was 111.6 ± 8.9 ($P > 0.05$). If blood serum from patients with stationary psoriasis was added to the culture medium, ILN was 89.6 ± 8.0 ($P > 0.05$).

If serum from patients in whom the regressive stage of psoriasis was diagnosed was added to the medium, ILN did not exceed 71.6 ± 7.3 ($P < 0.01$), whereas on the addition of epidermal chalones alone in a concentration of 2 mg/ml, ILN in the absence of blood serum was 59 ± 8.1 ($P < 0.001$).

In the control, in which skin was cultured in medium 199 only, without the addition of either blood serum or chalones, ILN was 129.3 ± 10.5.

Data showing the inhibitory activity of epidermal chalones in the presence of blood sera from patients with different stages of psoriasis, and also of healthy human serum, are given in Fig. 2. They show that in the presence of serum from patients with progressive and stationary psoriasis, epidermal chalones inhibited DNA synthesis in the cells of the epidermis only slightly, and the percentage of inhibition did not exceed 30. Serum from patients with regressive psoriasis, like healthy human serum, has no significant effect on the inhibitory activity of epidermal chalones.

The ability of serum of patients with psoriasis to block the biological effect of epidermal chalones was thus exhibited to the greatest degree in the progressive stage of psoriasis. In the regressive stage of the disease, blood serum from patients with psoriasis had no blocking action of epidermal chalones.

The mechanism of action of blood serum from patients with progressive psoriasis on the effectiveness of inhibitory activity of epidermal chalones on DNA synthesis in epidermocytes of human skin is evidently that certain components of serum, binding with the epidermocyte membrane, prevent interaction between chalone and receptors or penetration of chalone into the cell. The results of these experiments indicate that blood serum from patients with progressive psoriasis contains the largest quantity of factors preventing the action of epidermal chalones.

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