CYTOGENETIC ACTION OF THE ANTITUMOR PHOTRIN IN CULTURES OF HUMAN LYMPHOCYTES

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Concentration curves of the cytogenetic action of the Soviet antitumor preparation photrin were studiedin 24-h cultures of human lymphocytes with an exposure of 1 h (concentrations from 10 to 70 μg/ml, interval 10 μg/ml). The percentage of aberrant metaphases at the minimal concentration was 19.0 and at the maximal 69.5. The relationship between the concentration of photrin and the number of damaged chromosomes per 100 cells within the range of concentrations studied was described by the equation

$$Y = 3.126 + 1.33\ c - 0.01156\ c^2,$$

where Y is the number of damaged chromosomes per 100 cells and c the concentration of photrin. The main types of chromosomal aberrations were single and paired fragments and chromatid exchanges. With respect to the type and frequency of the cytogenetic lesions induced by it, photrin resembles the known preparation thioTEPA and it is a typical alkylating mutagen.

KEY WORDS: alkylating mutagens; photrin; lymphocytes; cytogenetic injuries.

Considering the large number of possible medicaments and in the attempt to use those with the strongest therapeutic action, the assessment of their possible genetic effects has become particularly important [1, 5, 6].

The object of this investigation was to study the cytogenetic action of the new Soviet cytostatic photrin in cultures of human peripheral blood lymphocytes.

EXPERIMENTAL METHOD

Photrin (2,2,4,4,6-pentaethyleneimino-6-morpholinocyclotriphosphazatriene) is an original Soviet antitumor preparation; in its chemical structures it is an ethyleneimine derivative with 5 ethyleneimino groups.

Tests were carried out on human blood lymphocytes in microculture. Photrin was diluted in distilled water before use and added to the cultures for 1 h in various concentrations after growth for 24 h, and the cultures were then washed twice with 10 volumes of Hanks' solution. The medium was replaced by fresh in the original proportion but without phytohemagglutinin. Cells were fixed after 58 h in culture and preparations were obtained by the usual method.

EXPERIMENTAL RESULTS

The results of analysis of the cytogenetic action of photrin are given in Table 1. They show that in a concentration of 10 μg/ml photrin significantly increased the frequency of cells with aberrations com-

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TABLE 1. Frequency and Types of Aberrations Induced by Photrin in Cultures of Human Lymphocytes

Concn. of photrin (μg/ml)	No. of metaphases analyzed	% of aberrant metaphases	No. of aberrations per 100 cells		
			single fragments	paired fragments	exchanges
10	300	19,0	9,7	11,3	0
20	200	25,5	11,0	19,0	1,5
30	300	32,7	17,3	18,0	2,7
40	450	52,4	26,4	40 0	3,3
50	200	58,5	36,0	57,0	3,5
60	300	64,7	50,0	66,0	5,0
70	450	69,5	57,8	64,7	11,1
Control	500	1,4	1,6	1,0	0

TABLE 2. Experimental (X_e) and Probable (X_0) Values of the Number of Aberrant Chromosomes per 100 Cells

Concn. of photrin (μg/ml)	X_H	95% confidence limits	X_0
10	23,0	20—26	14,1
20	34,5	30—40	34,4
30	42,0	37—47	53,4
40	76,2	69—84	74,8
50	104,5	91—121	98,5
60	120,9	116—145	124,0
70	148,0	135—162	152,9
Control	2,0	1,8—2,2	3,1

pared with the control ($P < 10^{-10}$). With an increase in concentration the frequency of aberrant metaphases increased as a nonlinear function.

Among the types of chromosomal aberrations induced by photrin, most (94.3%) were single and paired fragment; their relative frequencies did not depend significantly on the photrin concentration ($P = 0.17$) and were 43.6 and 56.4%, respectively. The absolute frequency of single and paired fragments increased with an increase in the photrin concentration. The exchanges observed were mainly of the chromatid type, and their frequency also rose with an increase in the concentration of photrin. The relationship between the photrin concentration and the number of damaged chromosomes per 100 cells within the range of concentrations studied (Table 2) was described satisfactorily by the equation

$$Y = 3.126 + 1.33\,c + 0.01156\,c^2,$$

where Y is the number of damaged chromosomes per 100 cells and c the concentration of photrin.

Analysis of these results and of those obtained by other workers [2-4] who have studied the mutagenic action of cytostatic preparations in lymphocyte cultures suggests that the mechanism of action of photrin is similar to the cytogenetic action of the widely used preparation thioTEPA.

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