Normal DNA sedimentation profiles were obtained for CBA mouse cells 24 h after removal of the mustine (Fig. 1: D, 3): mol. wt.$_{1/2}$ was $(1.14 \pm 0.06) \cdot 10^8$ and $(1.29 \pm 0.07) \cdot 10^8$ for the experiment and control respectively ($P > 0.05$, $n = 3$). It can accordingly be concluded that repair of DNA injuries induced by mustine in CBA cells is complete after 24 h of incubation. The sedimentation profiles of fibroblast DNA from 101/H mice point to intensive fragmentation of DNA (Fig. 1: B, 3), indicating that integrity of the DNA strand is not restored in cells of this line of mice. The reason may be insufficiency of the last stage of excision repair, namely the ligase reaction, or the uncoordinated character of the endonuclease and ligase reactions. The results are evidence of the defective repair of DNA lesions induced by mustine in 101 H mouse cells.

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EFFECT OF WIDELY USED DRUGS ON FREQUENCY OF SISTER CHROMATID EXCHANGES IN CULTURED HUMAN LYMPHOCYTES

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As the number and variety of chemicals used by man increase, so also does the number of reports of undesirable effects of some of them and, in particular, of the mutagenic activity of drugs [1, 11]. The development of methods of differential staining of sister chromatids has made it possible to test chemical compounds for mutagenicity by analysis of sister chromatid exchanges [5, 6]. In some cases this method proved to be more sensitive than analysis of chromosomal aberrations or the micronuclear test [4, 9]. The cytogenetic action of several chemical agents has already been studied by analysis of the frequency of sister chromatid exchanges [7, 8, 10]. However, widely used drugs exhibiting weak mutagenic activity, or not exhibiting it at all in other tests, have been investigated very rarely.

The object of this investigation was to determine the frequency of sister chromatid exchanges (SCE) in cultures of human peripheral blood lymphocytes under the influence of widely used drugs.

EXPERIMENTAL METHOD

Five drugs were studied: dibazol*, diphenhydramine, caffeine sodium benzoate, magnesium sulfate, and procaine. These drugs are widely used in medical practice, available for the

*2-Benzylbenzimidazole hydrochloride.

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TABLE 1. Frequency of Sister Chromatid Exchanges under the Influence of Various Concentrations of Drugs (M ± m)

Preparation	Concentration of drug, μg/ml				
	62,5	125,0	250,0	500,0	1000,0
Dibazol	5,68±0,32	5,78±0,39	6,00±0,37	5,83±0,32	7,33±0,36
Diphenhydramine	7,05±0,32	6,65±0,29	7,10±0,30	7,68±0,30	7,53±0,33
Caffeine sodium benzoate	6,90±0,47	7,43±0,46	7,38±0,38	7,23±0,28	7,70±0,41
Magnesium sulfate	6,28±0,42	5,95±0,32	7,08±0,51	6,95±0,35	7,25±0,28
Procaine	6,33±0,39	6,40±0,25	6,90±0,29	6,73±0,37	7,10±0,34

general public, readily soluble in water, and differ in their chemical structure. Preparations dispensed in ampuls were used: dibazol 1% — 5.0 ml, diphenhydramine 1% solution — 1.0 ml, caffeine sodium benzoate 20% solution — 1.0 ml, magnesium sulfate 25% solution — 2.0 ml, and procaine hydrochloride, 2% solution — 10.0 ml. The tests were carried out on cultures of lymphocytes from one clinically healthy donor. Blood was cultured by a micromethod for 96 h. 5-bromodeoxyuridine was added to the culture mixture 30 h before fixation, in a final concentration of 10 μg/ml. The drugs were diluted in Hanks' solution and added to the culture 24 h before fixation. Subsequent incubation was carried out without washing off. The concentrations of drugs tested were deliberately chosen to be in excess of the highest therapeutic doses per kg body weight, and amounted to 62.5, 125, 250, 500, and 1000 μg/ml. Sister chromatids were differentially stained by a modified method suggested by Chebotarev et al. [2]. At each experimental point and in the corresponding control 40 metaphases of the second mitosis were analyzed, according to the recommendations of Yakovenko and Platonova [3]. SCE were counted in metaphases with 45 and 46 chromosomes.

EXPERIMENTAL RESULTS

The mean number of SCE in the control was 6.20 ± 0.43 (Table 1). Statistical analysis of the experimental data by Student's t test showed that the frequency of SCE under the influence of all doses of dibazol, diphenhydramine, caffeine sodium benzoate, magnesium sulfate, and procaine tested did not differ significantly from the control ($P > 0.05$).

Since the concentrations of drugs investigated were 30 to 50 times higher than the real therapeutic doses, it can be concluded that dibazol, diphenhydramine, caffeine sodium benzoate, magnesium sulfate, and procaine hydrochloride have no mutagenic effect when studied by the SCE test.

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