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## THE CYTOTOXICITY OF CADMIUM IONS SMALL DOSES IN LONG-TERM CULTURE OF BONE MARROW CELLS

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**Introduction.** It is known that cadmium ions have the property to accumulate in cells, leading to disturbances in their metabolism. The effects associated with the long-term influence caused by small doses of cadmium ions have not been studied at all. The purpose of this work was to assess the cytotoxicity effects and degree of damage to bone marrow DNA in rats during prolonged cultivation in the medium containing small doses of cadmium ions – 0.1-10  $\mu\text{M}$ /liter of culture medium. The extent of cell adhesion and their morphology, culture density, cell membrane integrity, and the number of apoptotic cells were analyzed. The extent of DNA damage was assessed by the number of micronuclei, fragmentation of nuclear DNA and single-strand DNA concentration in cells.

**Methods.** Studies were carried out on a monolayer of bone marrow cell culture from the femur of a three-month-old Wistar rats. The cells were cultured in a storage medium with cadmium ions in concentrations of: 0.1; 0.5; 1.0; 10  $\mu\text{M}$ /l of culture medium. Studies were conducted every 48 hours for 30 days, before replacing the medium with fresh, containing  $\text{Cd}^{2+}$ . The number of cells in the early and late stages of apoptosis was determined by flow cytofluorome-

try (Millipore Guava Nexin Kit). Detection of micronuclei was carried out by fluorescence microscopy. To assess the extent of DNA fragmentation, comet analysis was performed, the DNA tracks were visualized with fluorescence microscopy and analyzed using CASPlab software. The single-strand DNA concentration was determined by Molecular Probes Qubit ssDNA Assay Kit.

**Results and Discussion.** It is shown that the degree of damage to DNA cells depends on the exposure time and the concentration of cadmium. Exposure to cadmium for 30 days at a concentration of 0.1 and 0.5  $\mu\text{M}$ /l leads to an increase in the number of cells in the early apoptosis stage, which is reversible and does not affect the fragmentation of nuclear DNA. Exposure to cadmium at a concentration of 1.0 and 10.0  $\mu\text{M}$  leads to a significant increase in the number of cells in the irreversible stage of late apoptosis, the fragmentation of nuclear DNA and ssDNA concentration by 30 days of observation.

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