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TOXIC EFFECTS OF POTENTIAL AGENTS FOR BORNEUTRON CAPTURE THERAPY

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ANNOTATION

The aim of the investigation was to study the cytotoxicity of boron-containing compounds intended for boron neutron capture therapy of oncopathology. The studies were performed on human cell cultures.

The results obtained indicate a low toxic effect of the GL-57 sample as compared to the GL-63 sample.

Key words: boron neutron capture therapy, cell line.

Modern approaches in the treatment of oncological diseases necessitate the creation of methods that would ensure the directed destruction of transformed cells without damage to neighboring tissues and the body as a whole. Such an effect is achieved by boron neutron capture therapy (BNCT), which is already used in medical centers in Sweden, the Czech Republic and the United States, research continues in Japan, Argentina, England, Italy, Israel, and begins in Russia. The uniqueness of the technique lies in the selective death of tumor cells, while normal cells in the immediate vicinity remain intact.

As a result of neutron irradiation, stable B-10 captures thermal neutrons, forming an excited B-11 nucleus. Removal of the excitation of the formed nucleus occurs almost immediately through its disintegration into particles with a short linear path, which leads to an explosive destruction of cells.

BNCT preparations should have low toxicity, selective penetration and accumulation in tumor cells. Since the selection of such substances requires the analysis of a large number of boron-containing molecules, it is necessary to use the fastest methods to determine both the amount of a substance that accumulates in normal and transformed cells and the concentration that has a minimal toxic effect. In this regard, studies on cultured human cells are considered the most effective.

Materials and methods

We used a culture of human dermal fibroblasts (7-12 passages). Dermal fibroblast culture was obtained from a skin explant of a healthy 58-year-old male donor after signing a voluntary informed consent. Disaggregation of tissue was carried out by an enzymatic method according to the original technique [1].

The cells were cultured at 37 ° C, 5% CO2, 95% in a humidity incubator (Sanyo, Japan) with daily macro- and microscopic control using an Olympus CX41 inverted microscope at x40, x200. The medium was changed every 3 days for 60% of the total volume.

To determine the cytotoxic effect, the cultured cells of the fibroblastic diferon were planted in an adhesive coated Petri dish (Sarstedt). Determination of the minimum toxic dose was carried out in 3 stages with a wide range of concentrations and a gradual identification of the border between toxic and pre-toxic doses. To obtain reliable data, 3 replicates were used in each group. The control group was represented by intact fibroblasts. In accordance with the recommendations of the International Nomenclature Committee for the classification of cell death [3], the assessment of the cytotoxic effect was based on morphological criteria. After 24 and 48 hours, the cultured cells were stained according to the Romanovsky method. Objects were visualized using an Olympus CX41 microscope at x100, x400, x1000.

The GL-63 and GL-57 samples provided for evaluation were transferred by the Department of Organic and Biomolecular Chemistry of the Chemical-Technological Institute of the Ural Federal University. To introduce substances into the culture, they were preliminarily dissolved in the culture medium used when working with the studied cell line.

Results and discussion

The cytograms of the cultures of the control group are represented by fibroblasts of varying degrees of differentiation. There is a predominance of process cells with pronounced cell contacts and a well-contoured nucleus.

Sample GL-63 had a pronounced toxic effect on human fibroblast culture when using concentrations above 1 μg / ml. There was a deterioration in cell adhesion, an increase in the number of cells with signs of cell death: vacuolization of the cytoplasm, disturbances in the structure of the cell membrane, pycnosis of the nucleus. The increase in the concentration of the substance was accompanied by the predominance of mature cells of the fibroblastic differon. Thus, the test substance can be used at a maximum concentration of 1 μg / ml with an exposure of no more than 48 h. The results are shown in Figure 1.

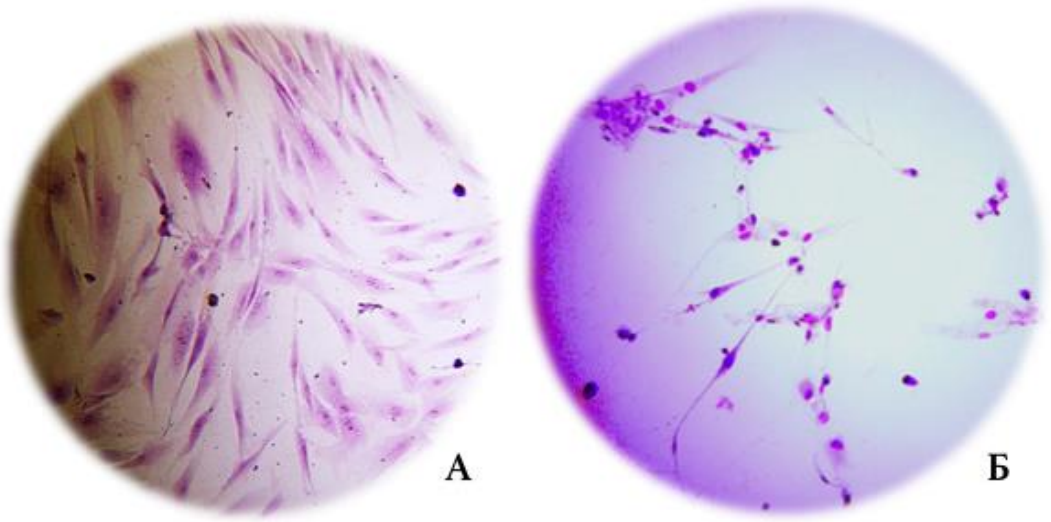

Figure: 1. Culture of human fibroblasts 24 hours after injection of the GL-63 sample. A - concentration 1 μg / ml, B - concentration 10 μg / ml. Magnification 100.

When the GL-57 sample was introduced into the fibroblast culture, a pronounced cytotoxic effect was observed when using concentrations of the substance above 15 μg / ml, which was expressed in the deterioration of cell adhesion, predominance of mature fibroblasts, elongation of cell pseudopodia, pycnosis of the nuclear apparatus, which is shown in Figure 2.

The study made it possible to work out an algorithm for the primary assessment of the cytotoxicity of the incoming substances, including the morphological analysis of the samples, the establishment of a barrier between the pre-toxic and toxic concentrations and the acceptable time range for each concentration.

The results obtained indicate a low toxic effect of the GL-57 sample as compared to the GL-63 sample, which may be due to the different structure of the studied molecules, including the spatial arrangement of chemical groups relative to each other. Probably, the relatively high toxicity of substances is associated with the use of cesium in the synthesis of samples in order to increase the aqueous solubility of substances.

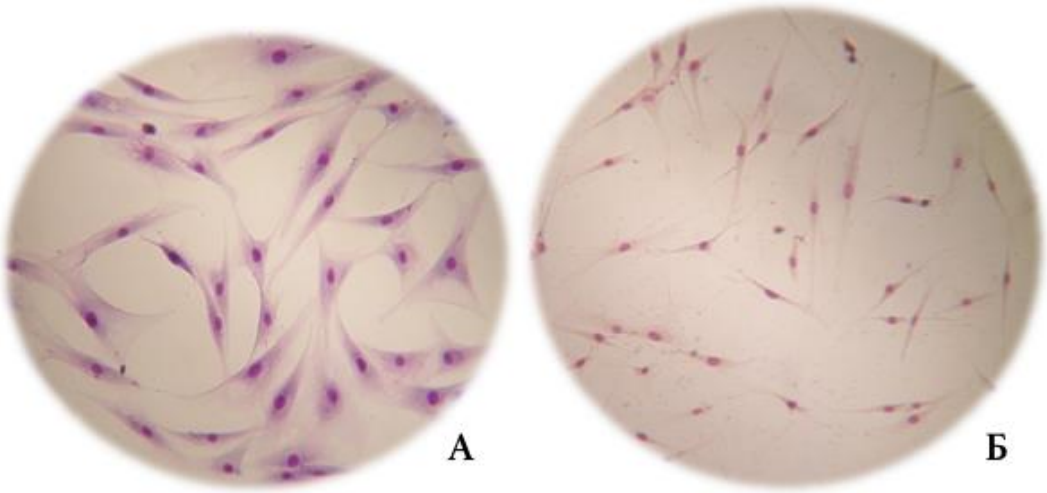

Figure: 2. Culture of human fibroblasts 24 hours after injection of the GL-57 sample. A - concentration 15 μg / ml, B - concentration 20 μg / ml. Magnification 100.

Cconclusions

1. The algorithm determined in the course of the work allows obtaining reliable data in a relatively short time, revealing the degree of toxicity of the substances under study and identifying the directions for further research.

2. The use of the GL-63 sample at a concentration of 1 μg / ml and the GL-57 sample at a concentration of 15 μg / ml with an exposure of no more than 48 hours is permissible on human cell lines. The data obtained will make it possible to shorten the duration of the LD50 detection in a series of experiments on animals, as well as to establish the accumulation of the studied substances in normal and tumor cells.

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ЭКОЛОГИЧЕСКИЕ ГРУППЫ ВОДНЫХ ЖЕСТКОКРЫЛЫХ (INSECTA, COLEOPTERA) СЕМЕЙСТВА DYTISCIDAE В ТУВЕ.

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ECOLOGICAL GROUPS OF WATER BEETLES (INSECTA, COLEOPTERA) OF THE FAMILY DYTISCIDAE IN THE TUVA REPUBLIC.

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РЕЗЮМЕ

В бассейнах рек и озер Тувы было найдено 91 вид водных жесткокрылых из семейства Dytiscidae. Все виды из семейства Dytiscidae были сгруппированы в различные экологические группы впервые для Тувы по отношению к основным факторам водной среды: проточности, температуре, солёности и типу грунта.

ABSTRACT

In the basins of rivers and lakes of Tuva, 91 species of water beetles from the Dytiscidae family were found. All species from the Dytiscidae family were grouped into different ecological groups for the first time in Tuva Republic in relation to the main factors of the aquatic environment: flow rate, temperature, salinity and ground type.

Ключевые слова: Coleoptera, Dytiscidae, проточность, температура, соленость, тип грунта, Тува.

Key words: Coleoptera, Dytiscidae, flow, temperature, salinity, ground type, Tuva Republic.