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Micronucleus test and assessment of changes in peripheral blood erythrocytes of dominant animal species in the Turkestan region

Abstract. *The article presents the results of a study of peripheral blood erythrocytes of dominant animal species in the Turkestan region. The relevance of this work is due to the construction of a nuclear power plant on the territory of Uzbekistan (Jizzakh region, Lake Tuzkan), since the areas of the Turkestan region fall under the potential influence of nuclear power plants and biota objects require monitoring at the 'zero stage' before the construction of a nuclear power plant. The data obtained are of great importance in assessing the impact of technogenic factors on biota. Given the location of uranium deposits in the Turkestan region, the uranium content was determined in samples (bones, soft tissues) of amphibians and fish. It has been established that the concentration of uranium in samples of biological objects is within the normal range. We have carried out work on the analysis of erythrocytes and micronuclei in the following biota representatives: desert lacerta (lat. Eremias intermedia), yellow ground squirrel (lat. Spermophilus or Citellus), lake frog (lat. Pelophylax ridibundus), rudd (lat. Redd pisces), snakehead (lat. Channa argus). According to the results of studies in the desert lacerta (lat. Eremias intermedia) and lake frog (lat. Pelophylax ridibundus), various pathological conditions of erythrocytes and micronuclei were observed in 11% of the total number of blood products studied.*

Keywords: *micronucleus test, erythrocytes, technogenic factors, monitoring, biota.*
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Introduction

The micronucleus test (MNT) is used for toxicological screening of potential genotoxic compounds. Currently, MNT is recognized as one of the successful and reliable tests for genotoxic carcinogens, which is based on the formation of the number of micronuclei in cells [1].

Depending on the number of detected formations, one can speak about the degree of pollution of the organism's habitat [2]. The appearance of micronuclei has a direct correlation with chromosome damage. There is a direct relationship between an increase in the number of chromosome aberrations and the activity of the mitosis process. This is due to the fact that the violation of mitotic division when exposed to toxic substances [3-4].

In recent years, micronucleus analysis has been used for biomonitoring in nuclear power plant workers [5-6]. In one of the most extensive studies, Tierens and colleagues evaluated various groups of workers in Belgian nuclear power plants and found a slight increase in the frequency of micronuclei [7].

The micronucleus test is widely used to assess cytogenetic damage caused by chemical or physical agents. Although most of the work published so far has performed this analysis on mammalian species (especially rodents), the micronucleus test has proven to be a useful tool for samples taken from other members of the biota. In particular, it makes it possible to reveal the genotoxic properties of compounds present in the aquatic environment. Both laboratory studies (to assess the genotoxicity of xenobiotics) and in situ studies (to assess water quality) included several species of invertebrates, amphibians, and teleosts [8-9].

The need for this study is explained by the fact that micronuclei in cells often appear as a result of the mutagenic effects of technogenic factors (heavy metals, radionuclides, pesticides, etc.) on

organisms. At the nuclear power plant under construction in Uzbekistan, it is planned to install a water-cooled power reactor VVER-1200 and, accordingly, water from Lake Tuzkan, which is located at a short distance from the Shardara reservoir and the Syrdarya River, will be used to cool the nuclear power plant. It should also be noted that uranium deposits are located in the Turkestan region. After the commissioning of nuclear power plants to monitor the state of environmental objects, an important role is played by the assessment of the degree of change in erythrocytes and micronuclei of biological objects (fish, amphibians, reptiles, rodents) in the study areas. Therefore, at the "zero stage" it is relevant to assess the real state of blood erythrocytes of biological objects living near the territory of the NPP.

Lake Tuzkan (Aydar-Arnasai system of lakes) in the Jizzakh region, is located about 40 km from the Turkestan region, the most densely populated region of Kazakhstan. Near Lake Tuzkan is the Shardara Reservoir, a portable water source and a strategic reservoir located on the transboundary Syrdarya River (Fig. 1). The specifics of the Tuzkan reservoirs and the chain of Aydarkul lakes, formed as a result of recharge and lenses of groundwater, is such that contamination of reservoirs with radionuclides can lead to their spread into underground lenses downstream [10]. The above specifics of the location of water arteries can become one of the factors of contamination with radionuclides, and pathological changes in erythrocytes of biological objects.

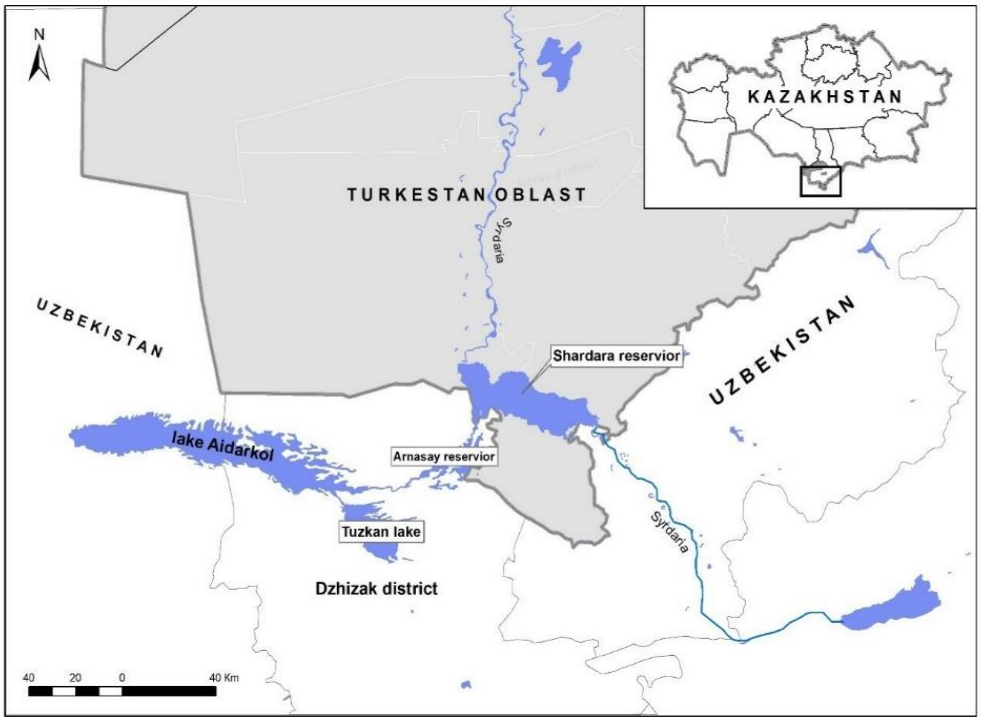

Figure 1. Characteristics of the location and correlation of Aidar - Arnasay system of lakes (Tuzkan Lake) in Uzbekistan and Shardara reservoir (Kazakhstan)

Since 2010, the Kazakhstan has become the world's largest supplier of uranium, topping the list of leading producers of natural uranium [11]. It is necessary to focus on the location of uranium ore deposits in relation to the studied territories - Sozak and Otyrar districts of Turkestan region (Zarechnoye uranium deposit).

Shu-Sarysu and Syrdarya uranium provinces are located in the sedimentary basins of the marginal part of Turan Plate [12]. The largest halos of fallow waters formed along these fronts; due to infiltration, they are unsuitable for drinking water supply due to anomalously high concentrations of natural radionuclides in them [13]. This fact also explains the need to control the uranium content in the

dominant biological objects of aquatic ecosystems in Turkestan region. This will allow assessing the impact of uranium mining on the biological objects of the aquatic ecosystems of Turkestan region (changes in erythrocytes, the appearance of micronuclei). And also to differentiate the causes of spontaneous changes in micronuclei at the 'zero stage'.

Methodology and materials of the study

The object of the study was blood preparations of the following biological objects: Desert lacertas (Lat. Eremias intermedia) – 21 slides, ground squirrel (Lat. Spermophilus *или* Citellus) – 27 slides. Peripheral blood preparations of the lake frog were taken for bioindication of aquatic ecosystems (Lat. Pelophylax ridibundus) – 20 slides, dominant fish species in water bodies of selected areas – Redeye (Lat. Rudd pisces) – 3 slides, Shakehead fish (Lat. Channa argus) – 18 slides.

Peripheral blood samples taken with a syringe from the tail vein of the dominant species of biological objects in the Turkestan region were fixed on a defatted glass slide. In fish, peripheral blood was taken from the caudal artery by cutting off the caudal peduncle. The resulting preparations in the amount of 65 pieces were dried in air and fixed with 96% ethyl alcohol. The work was carried out in the field.

At the laboratory stage, the slides were stained according to Romanovsky-Giemsa. Before staining the smears, the finished liquid dye is diluted at the rate of 1– 2 drops of the dye per 1 ml of distilled water. After rinsing with distilled water, it was dried on filter paper for 30 min. Anomalies of nuclei in blood erythrocytes and morphological analysis of changes in erythrocytes, micronuclei were evaluated on hematological preparations using an EX20-MSC-Company microscope (China) with an oil immersion objective - PLAN 100x/1.25 oil, ∞/0.17 (100-fold increase).

The content of uranium in the tissues of fish (Sander lucioperca, Cyprinus carpi), frogs (Pelophylax ridibundus) was determined by inductively coupled plasma mass spectrometry on an Agilent-7800 instrument using regulated analysis methods in an accredited testing laboratory of radiochemistry and radio spectrometry of the Institute of Radiobiology and Radiation Protection NJSC "Astana Medical University". Samples of biological objects (bones and soft tissues) were preliminarily dried in the laboratory for two weeks.

Statistical data processing was carried out by generally accepted methods, using a package of documents, Microsoft Excel and Statistica 6.0 programs.

Results and discussions

As an indicator of changes in mitotic processes and the pathological state of erythrocytes, micronuclei were found - these are the remains of a nuclear (chromatin) substance formed as a result of degradation of erythrocyte nuclei. They were rounded chromatin-containing formations 1.5–2 μm in size, mostly in a single amount per cell.

Comparative micronucleus analysis of spontaneous chromosomal instability revealed no correlation differences in the frequencies of micronuclei between different habitats of animals from the same species group found in the territory of the Turkestan region. Statistical processing did not reveal statistically significant differences (α 0.05). In addition, analysis of variance between groups (species of dominant animal species) was used to evaluate the results, where F=1.8. P=0.1 (no statistically significant differences between species were found). The exception was 1 specimen of the lake frog (lat. Pelophylax ridibundus), and 2 specimen s of the Desert lacertas (lat. Eremias intermedia), where single micronuclei were found. It has been established that in the peripheral blood of frogs and lizards, erythrocytes with attached and loose micronuclei were mainly found.

Guided by atlases of blood cells, pathomorphological changes in erythrocytes were determined [14,15,16]. For each individual, from 3 to 15 smears were made. On the preparation of each individual

type, blood cells were examined. A total of 62 preparations and 3053 cells were analyzed. Mature erythrocytes had an elongated shape, the nucleus was elongated. In the studied drugs, several types of pathological changes in erythrocytes were recorded:

1. Change in the shape of red blood cells (poikilocytosis).
2. Agglutination (clumping) of erythrocytes
3. Changes in the shape of nuclei
3.1 Displacement of nuclei to the periphery
3.2 Invagination of the nucleus
3.3 Nuclear shadows
4. Hypochromasia
5. Scalloped border

Poikilocytosis may be the result of a violation of intracellular metabolism or occur as a result of external physicochemical and immunological influences. Examining preparations of peripheral blood of frogs in 2 studied smears (sample names: L1, L2), the following transformations in the shape of erythrocytes were noticed (Fig. 1a, 1b, Fig. 3)

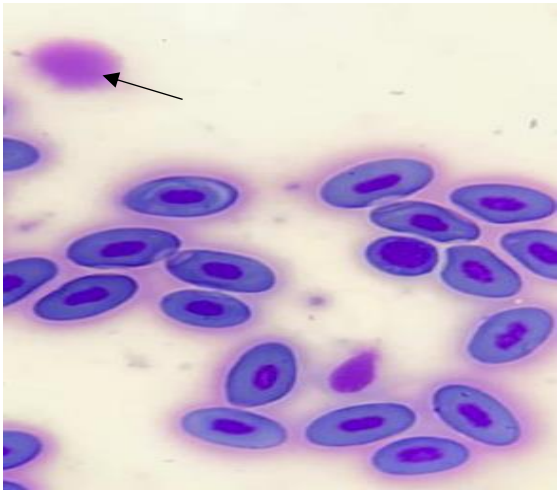

Figure 1a. Nuclear shadows in a smear of a lake frog (lat. Pelophylax ridibundus)

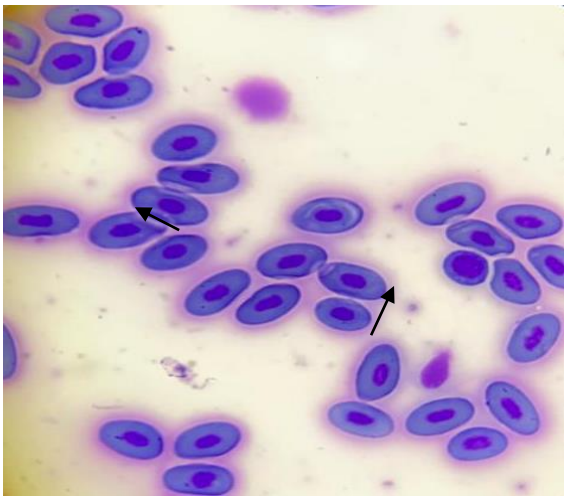

Figure 1b. Hypochromasia and agglutination of erythrocytes in a smear of a lake frog (lat. Pelophylax ridibundus)

All slides were coded prior to microscopic analysis. To exclude contaminating factors on peripheral blood preparations, a clear strategy for micronucleus differentiation was adopted. Micronuclei were taken into account only when the micronucleus was clearly separated from the main nucleus and had a rounded shape and color corresponding to the main nucleus. Erythrocytes with micronuclei were observed in the peripheral blood samples of Desert lacertas (Lat. Eremias intermedia) (Fig. 2a, 2b). The types of identified nuclear anomalies corresponded to the accepted morphological criteria of the micronucleus.

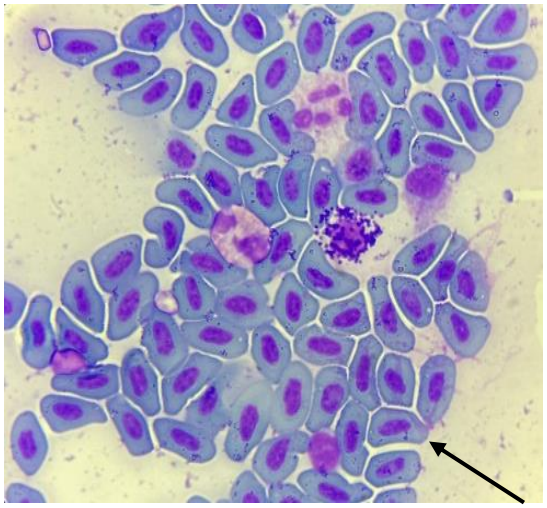

Figure 2a. Anomalous nucleus (micronucleus) in preparation № 2 of Desert lacertas (Lat. Eremias intermedia)

Figure 2b. Anomalous nucleus (micronucleus) in preparation № 1 of Desert lacertas (Lat. Eremias intermedia)

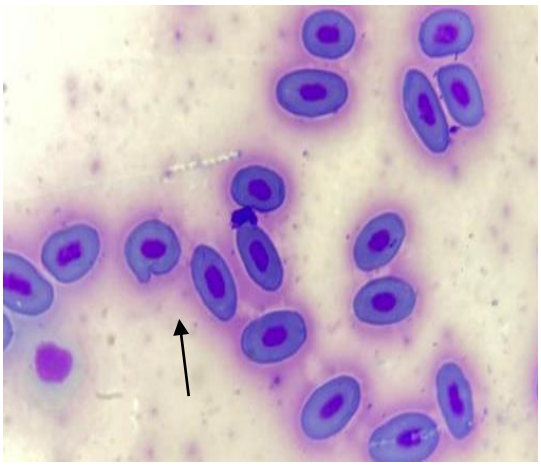

Figure 3. Scalloped edge of an erythrocyte of a lake frog (лат. Pelophylax ridibundus)

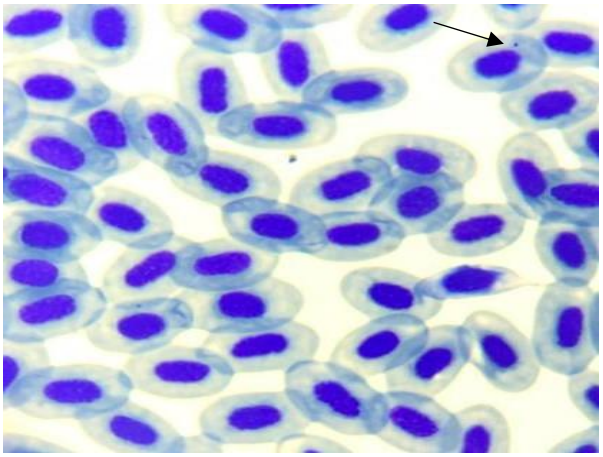

Figure 4. Anomalous nucleus (micronucleus) in preparation № 1 of lake frog (лат. Pelophylax ridibundus)

The study area includes the Shardara reservoir. This reservoir is an important economic and ecological object for the Turkestan region. The predominant fish species of the Shardara reservoir are carp and pike perch.

In the Shardara Reservoir, the dominant fish species are carp and zander (Sanderlucioperca, Cyprinuscarpi), whose bioassays were analyzed for uranium content. Judging by the reference source, uranium isotopes are unevenly distributed in fish organisms [17]. The highest concentration is observed in the body and head of fish, so tissue samples from the body of fish (Sanderlucioperca, Cyprinuscarpi) were analyzed for U content and the following results were obtained (Table 1).

Table 1

Uranium content in fish from Shardara reservoir

No.	Settlement	Product type	Uranium concentration (ng/l)	Uranium concentration (mkBq/kg)	Worldwide range* of U, μBq/kg
1	Shardara	fish-zander	bones-14.88 meat-1.92	bones-183.76	100000
				meat-23.71	
2	Shardara	fish- carp	bones-69 meat-6.54	bones-852.15	
				meat-80.769	

*UNSCEAR

According to *UNSCEAR 2000, the uranium content in fish samples (bones and soft tissues) from the Shardara reservoir corresponds to the background values.

Amphibians have thin skin that absorbs water well, thereby exposing them to radionuclides from the environment both internally and externally [18]. The obtained values are included in the calculated reference values of natural concentrations of uranium in the body of animals and humans (in terms of mgl/l-0.00033 for bones and 0.0001 per 0.0002 mgl/l of tissues) (Fig. 5).

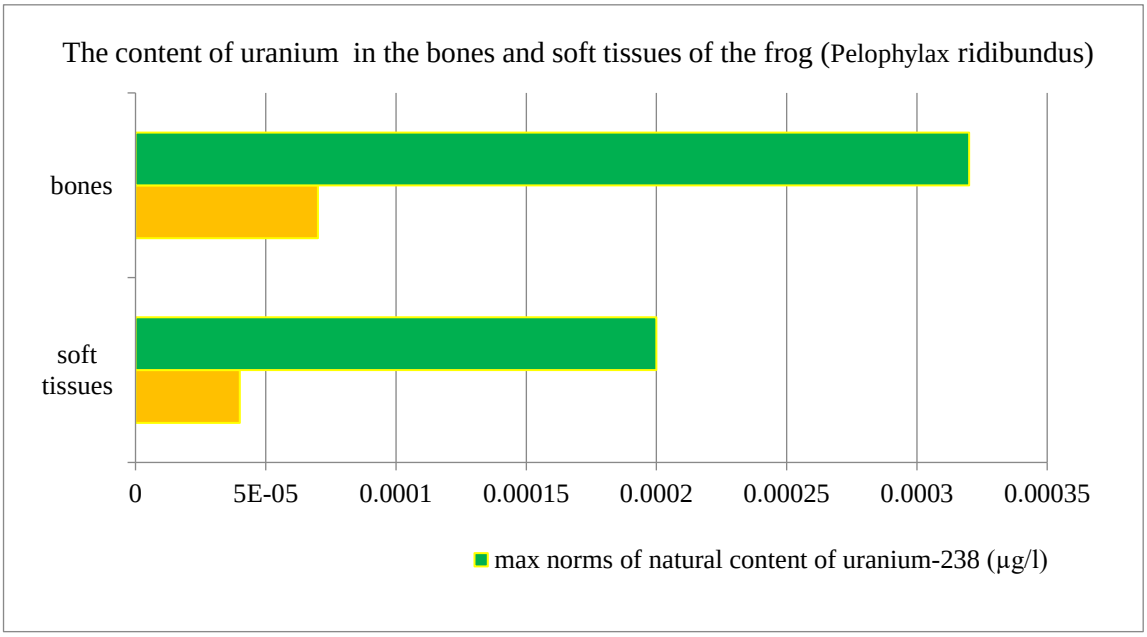

Figure 5. Uranium content in the bones and soft tissues of lake frog (Pelophylax ridibundus)

The lake frog (Pelophylax ridibundus) is one of the dominant amphibian species in the area of the Shardara Reservoir. This biological object is further proposed as a bioindicator for pollution control at various stages of NPP operation. Given the proximity of uranium mining facilities, it is advisable to take into account the laboratory-confirmed uranium content in the bones and soft tissues of the lake frog (Pelophylax ridibundus).

Conclusion

Our studies have shown that under the given environmental conditions of the Turkestan region (Zhetisay, Shardara and Maktaaral Districts), 5.88 ± 2.8% of the cells of the studied biota objects had pathologies associated with erythrocytes and micronuclei. Erythrocytes with any one type of pathology were found in 2.5±2.3% of marsh frogs. In the blood of 11.82± 2.7% of animals (out of the total number) there are 2 different types of disorders in the morphology of erythrocytes. Three types of pathologies of red blood cells were noted in 7.94±5.4% of Desert lacertas, and 4.76±3.9% of amphibians had 4 different types of pathologies of erythrocytes.

Regarding the formation of micronuclei, the following distribution was observed: among lizards, 0.41 ‰ of abnormal erythrocytes with micronuclei were found, among frogs, 0.32 ‰ of cells with micronuclei were found.

The formation of micronuclei is a consequence of the pathology of mitotic cell division, during which some chromosomes lag behind in metaphase and anaphase. During apoptosis, micronuclei of various sizes can occur, which is associated with fragmentation of the nucleus of the cell subject to this process. At this stage of research, a number of disorders of the nucleus and erythrocytes have been identified, which may indicate a possible adverse effect of environmental factors in their habitat. The practical application of this study is the development of a program for monitoring the state of the environment and biota at various stages of the construction of a nuclear power plant in Uzbekistan for the nearest areas of the Turkestan region. In addition, this study can serve as a basis for including the studied biological objects in the territory monitoring program at the stage preceding the construction of a nuclear power facility. In a particular case, it is recommended to include a block of research of biological objects as indicator factors of environmental change in the general monitoring program at the "zero stage of construction of the Uzbek NPP, and to monitor biological objects annually at each stage of construction and operation of a nuclear power plant in Uzbekistan.

Taking into account the ability of amphibians to absorb radioactive elements through the surface of the skin, as well as the proximity of uranium deposits in controlled areas, this study recommended: to include in the monitoring program the control of uranium content in the soft tissues of the dominant species of fish and frogs. This will make it possible to establish or eliminate the correlation between the presence of micronuclei, changes in the shape of erythrocytes, and the level of uranium content in soft tissues and bones. This study should be carried out at the "zero stage" and annually during the operation of nuclear power plants in Uzbekistan.

A differentiated count of micronuclei shows the need for comprehensive studies using the cytogenetic features of living organisms to obtain information about the ecological and genetic state of populations of organisms and their habitat at the zero stage.

A pilot study of the uranium content in amphibian tissues shows the need for further study of this topic in order to establish a connection between a possible increased content of uranium and the presence of micronuclei or other changes in erythrocytes.

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Түркістан облысындағы доминантты жануарлар түрлерінің перифериялық қанының эритроциттерінің өзгеруін микронуклеус сынағы және бағалау

Аңдатпа. Мақалада Түркістан облысындағы доминантты жануарлар түрлерінің шеткі қанындағы эритроциттерді зерттеу нәтижелері берілген. Бұл жұмыстың өзектілігі Өзбекстан аумағында (Жиззах облысы) атом электр станциясының салынуымен байланысты, сондықтан Түркістан облысының аймақтары АЭС потенциалды әсеріне ұшырайды және биоталас объектілері «нөлдік кезеңнен» бастап бақылауды талап етеді. Алынған мәліметтер биота үшін техногендік факторларды бағалауда үлкен маңызға ие. Біз биотаның келесі өкілдерінде эритроциттер мен микроядроларды талдау жұмыстарын жүргіздік: кесіртке ортасы (*лат.* Eremias intermedia), сары тиін (*лат.* Spermophilus немесе Citellus), көл бақасы (*лат.* Pelophylax ridibundus), руд. (*лат.* Rudd Pices), жыланбас балық (*лат.* Channa argus). Зерттеу нәтижелері бойынша микроядролар орта кесіртке (*лат.* Eremias intermedia) мен көл бақасында (*лат.* Pelophylax ridibundus) табылған. Зерттелетін қан препараттарының жалпы санының 11% -ында эритроциттер мен микронуклеустардың әртүрлі патологиялық жағдайлары байқалды. Қазақстанның оңтүстігіндегі уран аймақтарының біршама жақындығын ескере отырып, қосмекенділердің жұмсақ тіндерінде уран анықталды. Уран қосмекенділер мен балықтарда өздігінен микроядролардың түзілуіне және эритроциттердің өзгеруіне әсер етуі мүмкін.

Түйін сөздер: микроядро сынамасы, эритроциттер, техногендік факторлар, мониторинг, биота.

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Микроядерный тест и оценка изменений эритроцитов периферической крови доминантных видов животных Туркестанской области

Абстракт. В статье представлены результаты исследования эритроцитов периферической крови доминанатных видов животных Туркестанской области. Актуальность данной работы обусловлена строительством атомной электростанции на территории Узбекистана (Джизакская область, озеро Тузкан), так как районы Туркестанской области попадают под потенциальное влияние АЭС и объекты биоты требуют мониторинга на «нулевая стадия» перед строительством АЭС. Полученные данные имеют большое значение при оценке воздействия техногенных факторов на биоту. Учитывая расположение урановых месторождений в Туркестанской области, в образцах (кости, мягкие ткани) амфибий и рыб определили содержание урана. Установлено, что концентрация урана в образцах биообъектов находится в пределах нормы. Нами проведены работы по анализу эритроцитов и микроядер у следующих представителей биоты: пустынная *лацерта* (*лат.* Eremias intermedia), желтый суслик (*лат.* Spermophilus *или* Citellus), озерная *лягушка* (*лат.* Pelophylax ridibundus), краснопёрка (*лат.* Redd pisces), Змееголов (*лат.* Channa

argus). По результатам исследований у пустынной лацерты (лат. Eremias intermedia) и озерной лягушки (лат. Pelophylax ridibundus) различные патологические состояния эритроцитов и микроядер наблюдались в 11% от общего количества исследованных препаратов крови.

Ключевые слова: микроядерный тест, эритроциты, техногенные факторы, мониторинг, биота.

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