CORRECTIONAL EFFECT OF THE EXTERNAL ELECTROMAGNETIC FIELD ON BIOLOGICAL OBJECTS: EXPERIMENTAL STUDY

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Abstract

The action of a device for correcting a functional state consisting of two elements with active layers of ferromagnets, constructed on the chirality principle has been studied on living systems. It was found that, the electromagnetic field, generated by the device, did not have a cytotoxic effect on eukaryotic cells and increased the killer potential of innate immunity cells against Candida albicans. Morphological analysis of tissue structure of animals target organs infected with C. albicans showed, that when receiving water charged with the device under test, less pronounced signs of toxic inflammation are observed, than in animals that did not take this water.

Key words: *electromagnetic field, chirality, superweak effect, stereoisometry, infection, immunity*

1. INTRODUCTION

Eukaryotic cells of the body are open complex thermodynamic living systems with various energy transformations and thermoelectrochemical processes in the cytoplasm. This causes the instantaneous transformation of cells in space in response to the impact of external signals. And in conditions of an unbalanced state, cells, like living systems, are more sensitive to the effects of various external factors (Sarpeshkar, 2012). In the excited state of the structure of bioobjects, in general, they obey the stochastic distribution, and the normalization of their functional status can be ensured by a minimum effect on the molecular-atomic level, for example, such as electromagnetic, dipole, spin or other (Dumont & Prakash, 2014, Lucia, 2015). Moreover, various devices that provide weak, non-thermal effects on living systems can achieve a more significant effect than the means that create a significant degree. It is shown that, in bacteria the interaction of a part of macromolecules is ensured by significant electrostatic repulsion between low- and large-molecular complexes of RNA, whereas between proteins and glycolytic enzymes, on the contrary, a weak attraction (Zhou et al., 1994, Baird et al., 2010, Gromiha, et al., 2010, Papoušková *et al*., 2013). This demonstrates the possibility of forming dynamic complexes with the help of the electromagnetic field for the rational distribution of substrate flows and improving the efficiency of multi-stage reactions, for example, such as glycolysis. Biological processes are based on the system of wave exchange of coupled vibrations (Shelly *et al*., 2006, Dillman & Beck, 2010). But frequency-phase interactions between natural oscillations in the system and external influences are most rational to consider from the position of nonlinear resonance synchronization of oscillations. A natural mechanism for realizing the effects and wave exchange between biosystems is the widespread use of scalar magnetic fields and associated longitudinal electromagnetic waves, which are bioinformation fields of living matter.

In the electromagnetic theory, the concept of spiral chirality plays an important role. The term chirality denotes the property of an object, not under any displacements and rotations may not coincide with its mapping in a flat mirror. This implies that, this property is possessed by only three-dimensional objects, which can exist in two forms: the object itself and its double, having the form of a mirror image, for example, the hands, the right and the left. Chiral properties are possessed by crystals, molecules of various substances, stereoisomers, oscillating electric and magnetic dipoles (Başar, *et al*., 2010, Pan *et al*., 2013). Artificial electromagnetic media are formed from chiral microelements, much smaller than the length of the electromagnetic wave of the spiral. Such a medium can be in the form of an ordered lattice structure or a chaotic mixture of chiral elements with a regular dielectric (Schäferling, *et al*., 2012, Mitamura *et al*., 2014). Also, the chirality property of the magnetic field lies

in the formation of an ordered three-dimensional structure that is variable in the material of the active layer of the element. The presence of chirality properties in the secondary information carrier comes out when these carriers influence on liquid media before and after polarization.

Devices for generating an external electromagnetic field (correctors of a functional state, CFS), created on the basis of chiral elements with intermediate layers of a dielectric, are dynamically resistant to external action (English *et al*., 2012). These are low-intensity generators of longitudinal waves that are able to purposefully change the functional state of the bio-object by small, constantly acting influences. Correctors do not shield external electromagnetic radiation, but change it into a spatio-temporal structure compatible with the structural organization of the biosystem. Wave carriers for CFS have a chiral purity and are capable of integrally affecting the acid-base balance, the equilibrium of oxidation-reduction processes, thereby supporting a complex hierarchy of body biorhythms. When creating the CFS, we concidered the property of biosystems to resonantly respond on biologically significant multifrequency effects of information character. In this case, the emerging scalar magnetic field and the accompanying longitudinal waves are the main mechanism of bioinformation exchange. Separate components of devices are made in passive resonators, prescribing images in the millimeter, decimeter and meter wavelengths simultaneously, which determine their properties as sources of influence on the bioobject in order to synchronize with the rhythms of the external field.

CFS adaptively reacts in the first place to a change in all external orientation bonds generated by spin, gravitational, electromagnetic interactions. It has been experimentally proved that the CFCs possess the property of contactless activation of liquid media. These devices are protected by RF patents, as a device for correcting the functional state of a bioobject, as a device for the activation of liquid media, as a device for correcting an external electromagnetic field that affects a living organism (Koltsov, 2003, Koltsov & Starikova, 2005). In the CFS, made according to the principle of a scalar magnetic field, the quanta of the electromagnetic field, entering its para- or ferromagnet, induce a magnetic field in it. In this case, the electrons are oriented along the lines of force of the magnetic field and amplify the external fields in a paramagnet or a ferromagnet.

Numerous studies of superweak effects on living systems show that in order to identify their mechanism, it is necessary to involve qualitatively different ideas. These perceptions differ from the understanding of direct external influence on certain biologically important systems of the body (Schwabl *et al*., 2013). The biological significance of ultraweak influences can be considered on the examples of their influence on the course of biochemical and physiological processes, which determines a fully justified phenomenological approach (Prato & Binhi, 2017, Maes & Verschaeve, 2016). Understanding whether superweak actions are an ordinary statistical unit or an information matrix of the course of biochemical processes is the starting point for clarifying the biological essence. The most accessible models for understanding the mechanism of superweak effect are such objects as prokaryotes (bacteria). In our study, we found it possible to study the effect of CFC on Candida, due to the high incidence of the population of the Earth. According to WHO, a fifth of the population suffers from various fungal diseases, of which candidiasis is the most common of systemic mycoses and diseases. About 40% of adults are carriers of Candida albicans, and any serious violation of local or general immunity can trigger the activation of these microorganisms (Poulain, 2015). In the structure of infectious pathology of the lower genitalia, the candida is 40-50%. C. albicans is considered the main causative agent of urogenital candidiasis. Mucous of the vagina of women is an ecological niche in which different types of bacteria, viruses, fungi are constantly inhabited, both in practically healthy and in patients. In recent years, certain interest is in the study of interaction between candida and factors of nonspecific protection of the mucous membranes, which include of innate immunity cells.

On the other hand, it is also necessary to identify the effect of CFS on models of eukaryotic cells, of which the elements of the body's defense system are of particular interest. According to the main biochemical parameters, phagocytic cells of innate immunity-monocytes / macrophages and neutrophils-have no fundamental differences from other cells, but a characteristic feature of their metabolism is the ability under the influence of various factors of exogenous and endogenous origin to instantaneous activation (Locati *et al*., 2013, Elliott *et al*., 2014). The ability of these cells to stimulate

systems reflects their "readiness" to perform basic functions, namely bactericidal, absorption and digestion of pathogens, which further provide antigen-presenting and immunoregulatory functions in protecting the body. Despite numerous studies of the role of local immunity in anticandinous protection, the mechanisms of interaction between candidiasis and neutrophilic granulocytes, which are the main cells of mucosal secretions, have not been sufficiently studied. In recent years, it has been shown, that under the action of bacteria neutrophils secret their DNA into the environment, forming neutrophilic extracellular traps that participate in the anti-infective protection of the mucous membranes (Pijanowski et al., 2013).

Proceeding from the above, the aim of the study is to develop a concept of the response of biological objects to the effect of the electromagnetic field, as one of the components of the ultraweak effect of the external environment on living systems.

2. MATERIALS AND METHODS

2.1. Object of study

The device for stimulation and / or correction of a functional state (CFS) includes two elements, each of which has an active layer of a material having the memory effect of a wide spectrum of external electromagnetic radiation. The contact surfaces of active layers of tightly fitting elements are polarized in the millimeter range of electromagnetic waves with the formation of a spectral analogue of the radiation of the initial action from biologically significant information carriers and with giving them chirality properties. As a standard of information, preparations of the homeopathic series and other objects of living and inanimate nature, including geometric patterns and applicators. The directions of the axes of the cascades of the magnetic concentrator are chosen experimentally depending on the size of the polarizable plates. The active layers are a magnetoelectric element based on a composite medium using spin-wave spintronics, in which one and zero are shifted by the phase shifts 0 and π, respectively, relative to some reference wave. In contrast to a spin-polarized current in which information about the original spin polarization persists in the dissemination in a ferromagnet for a length not exceeding a micrometer, spin waves at room temperatures can remain coherent at distances up to a millimeter (Park et al., 2017). In order to eliminate the damping of the wave amplitude in the external medium, due to magnon-phonon scattering, spin-wave amplifiers are inducted into the integrated circuits of the device.

The circuit of the device is shown in Fig. 1. It is a layered structure of two elements, each of which has an active layer of a ferromagnet (a material possessing the memory effect of a wide spectrum of external electromagnetic radiation), the layers of elements are connected directly or through a gasket of transparent material for electromagnetic radiation, in which spin waves distribute, as well as throug the piezoelectric layer. The contact surfaces of the active layers are preliminarily polarized prior to their connection by the radiation of an external identical electromagnetic field of the waves with the simultaneous recording onto the active layer of elements of a spectral analogue of radiation from biologically significant carriers of information. After polarization, one of the elements is rotated about an axis perpendicular to the axis of their coaxial or parallel coaxial arrangement in the direction of approach of their contact surfaces to a full abutment. This way, in the case of polarization, the elements are arranged in the same plane in a mirror-symmetrical fashion. In this case, it is necessary to strictly observe the mutual arrangement of the elements, since otherwise there appear noise frequencies that do not correspond to the information analogue, which can lead to the opposite effect.

2.2. Models of living systems

Animals. Study approval from the local Ethical Committee of the Pacific State Medical University (Vladivostok, Russia) was received under No. 2015-0102. Male C57BL/6J mice were purchased from a laboratory of the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry (Pushchino, RU). Mice in the age range of 8–12 week (20–25 gr.) were used in all experiments.

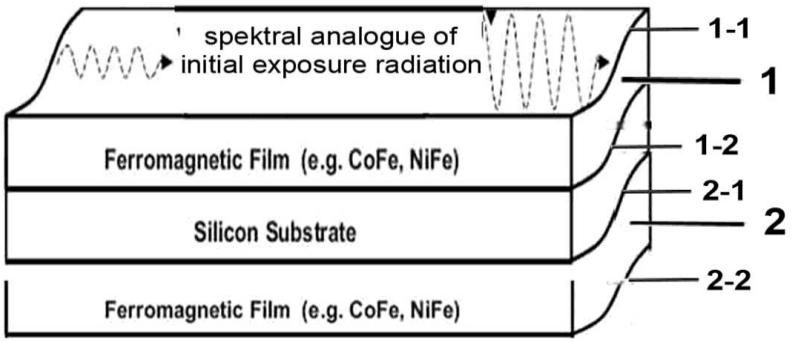

Fig. 1. Scheme of the corrector of the functional state. Two elements with active layers of ferromagnetic material (1, 2) and tight contact surfaces (1-1, 1-2, 2-1, 2-2) are presented. The outer surface of the plates is covered with a protective layer. In active layers 1 and 2, the chiral principle in each of the elements by means of polarization formed a spectral analogue of the radiation of the initial action from biologically significant carriers of information.

Neutrophils and macrophages cell culture. The cells were isolated from peritoneal cavity prepared from C57BL/6J mice. The cells were cultured in Dulbecco's modified Eagle's medium (Lonza, Belgium) with a high glucose concentration (4.500 g/ml) supplemented with 10 % heat-inactivated fetal bovine serum (HyClone, USA), 2 mM L-glutamine, and 1 mM sodium pyruvate at 37°C with 5 % CO^2. Cells were grown to confluence and then detached from the dishes, and $2X10^5$ cells were seeded into wells of 6-, 96-well tissue culture plates, and incubated overnight.

Microorganisms. The strain Candida albicans 601, isolated from a patient with chronic pneumonia, was deposited in the Russian State Scientific Research Institute for Control, Standardization and Certification of Veterinary Preparations and Feeds (RSSRIC). For the study, 48-hour cultures of C. albicans grown on a Saburo medium at 30 ° C were used. Determination of the adhesive properties of C. albicans was carried out on the model of adhesion of fungal cells on a nitrocellulose film with immobilized hemoglobin. The viability of microorganisms was determined by the number of colony forming units (CFU) when cultivated on Saburo's medium within 24 hours after exposure to CFS.

To determine the bacteriostatic effect, a suspension of C. albicans cells (106 mcd / ml) was placed near the FBS for 15, 30, 45 minutes and 1 hour, after which their viability by the number of colony forming units (CFU) was determined. In addition, under the influence of CFC, the bactericidal and functional activity of cells against C. albicans was studied. The cell concentration was adjusted to 2 × 10 6 cells / ml and the suspension was dispensed into wells of a flat-bottomed plate for immunological reactions of 100 µl per well, in triplets for each sample. The time of exposure to CFS was 30, 45 minutes, after which microorganisms were introduced at a rate of 1 phagocyte of 20 bacteria. As a control, cells without CFS.

To study the effects of CFC on the in vivo model, the animals were divided into groups: intact (group 1), animals taking daily saline-charged water for 10 minutes CFS water (group 2); animals infected with C. albicans, strain 601, at a dose of 104 cfu per mouse (1/2 LD50, group 3); animals infected with C. albicans and taking daily saline-charged water for 10 min CFS (group 4). The animals were withdrawn from the experiment after 10 days, were euthanized using carbon dioxide asphyxiation followed by cerebral dislocation as a secondary method, as approved by the MIT committee on animal care (National Institute of Health Guide for the Care and Use of Laboratory Animals, NIH Publications No. 80023, 1996).

2.3. Methods of determination of the cells functional activity

Cell viability was estimated at 18, 24, and 36 h using a mitochondrial colorimetric assay (MTT assay) by the percent of total succinate dehydrogenase (SDH) released. Briefly, in each well, 600 μL of culture medium was aspirated, leaving 400 μL, to which 40 μL of MTT solution (3-(4.5-dimethylthiazol 2-yl)-2.5-diphenyltetrazoliumbromide, Sigma) was added. The cells were incubated at 37 °C and 5 % CO^2 for 4 h. The upper medium was removed carefully, and the intracellular formazan was solubilized by adding 400 μL of dimethylsulfoxide to each well (Sigma-Aldrich, USA). Then, the contents of the wells were mixed thoroughly using a pipette. Two hundred microliters from each well were transferred into a separate well on a 96-well ELISA plate (Corning Costar, Lowell, MA, USA). The absorbance was measured at 570 nm. The results expressed as optical density (OD) were obtained for three different experiments from each surface modification.

Cells incubated with CFS and separate supernatant were frozen and stored at –20 °C. The disrupted cells were mixed with 100 μL of Griess reagent, which consisted of equal volumes of 0.1 % N (1 naphthyl) ethylenediamine dihydrochloride and 1% *n*-aminobenzene sulphanilamide (ICN, USA) in 2.5 % phosphoric acid solution. After incubation for 10 min, the absorbances were measured at 540 nm using a Multiscan Titertek Plus spectrophotometer (Flow lab, Finland).

Determination of the ATPase and 5' nucleotidase activity. We added 20 μl of substrate for ATPase (8 mg ATP on 1 ml of Tris HCl buffer (pH 7.8), which contained 87 mg of NaCl, 28.7 mg of KCl, and 52 mg of $MgCl_2$ 6 H_2O, ICN, USA) and 5' nucleotidase (4 mg of AMP per 1 ml of the same buffer containing 87 mg of NaCl and 70 mg of $MgCl_2$, ICN, USA) to the monolayer of cells; the samples were left for 30 and 60 min. The reaction was stopped by adding 100 μl mixture of ascorbic and molybdenum acids at a ratio of 1:1. After 20 min, the optical density of the substrates was measured on a spectrophotometer at a wavelength of 620 nm.

For the determination of the activity of lactate dehydrogenases (LDH), the Lloyd method in his own modification was used. 100 μl of substrate was added into wells of plate with adherent cells (2 mg/ml iodine nitro tetrazolium (Sigma-Aldrich, USA) on phosphate buffer pH 7.2 with 0.4% $MnCl_2$ (ICN)) and incubated at 37 °C for 30 min. Diformazana pellets were dissolved by adding 100 μl of isopropyl alcohol and acidified with 0.04 M HCl for 20 min. The optical density of the substrates was determined on a spectrophotometer at a wavelength of 650 nm.

Myeloperoxidase activity (MPO). 100 μL of OPD (*o*-phenylenediamine, ICN, USA) (4 mg per 10 mL) in phosphate citrate buffer (pH 5.0) supplemented with 500 μL of 0.33% hydrogen peroxide was added to well plates with fixed cells. The reaction was stopped by adding 100 μL of 10% sulfuric acid solution to each well. Absorbance of the reaction product was determined on a spectrophotometer at 492 nm.

The spectrophotometric results of optical density were evaluated as the simulation index (T), which was calculated as the ratio of the difference between the mean values of the optical density of the solutions containing reaction products of control and experimental cells, versus the mean value of optical density of intact cells (and expressed as per cents).

For histological examination, the material (heart, liver, kidney, spleen) was fixed in 10% formalin, buffered according to Lilly. Wiring and casting of the material into paraffin wax, dewaxing and staining of sections with hematoxylin-eosin according to conventional methods. The preparations were viewed in a light microscope "Olympus CX41" (Japan) with a digital camera "Olympus 4G". Morphometric data processing was performed in accordance with the principles of system quantitative analysis using the "CellSens Standard" image processing program (Olympus, Japan). The parameters were expressed as a percentage (%) of the relative density of the volume fraction of the structural components relative to the airspace area by 0.01 mm3 of tissue, in pixels, taking into account the correction for the thickness of the cut and the diameter of the nuclei, also counted the nucleated components in the field of view.

2.4. Statistical analysis

Data for the differentiation assay were analyzed by analysis of variance (anova) and the Mann–Whitney method for comparisons between groups. The levels of cytokines and cellular proliferation, as well as the fluorescence intensity of the mature DC, were also analyzed by 'anova' followed by the Newman–Keuls test to determine multiple comparisons. Values were considered significant when different at $P < 0.05$.

3. RESULTS

3.1. Morphology of bacteria

The culture of C. albicans was represented by microorganisms oval (2: 1) or almost circular shape with well-marked vacuoles with small cores. Under the influence of CFS No. 2 on the culture of yeast C. albicans, it was found that, the number of cells capable of multiplication decreased significantly after 5 hours of exposure, compared to the control culture (Fig. 2). Indicators of colony forming units were 1020 ± 172.6 and 1537 ± 125.0 CFU per 1 ml, respectively. When yeast was stained for viability with acridine orange, cells with a luminescence in the orange spectrum were detected, which indicated their death when exposed to CFS No. 2 (Fig. 2). When yeast was sown on the nutrient medium, a decrease in the number of colony-forming units was revealed (Fig. 1e, f).

During the entire observed period of exposure to CFS number 2 (5 hours), no morphological signs of death were found on the cells. Opposite, in comparison with the control, there was an improvement in the morphological state of the cells. So, after 15 minutes of exposure to CFS, neutrophils and macrophages were mostly detected in the activated state. As indicated by the change in the architectonics of the cell surface, which acquired folding, numerous pseudopodia were found along the periphery of the cells (Fig. 2A-D). The absence of the cytotoxic effect of CFC on cells was confirmed by our study of their apoptotic activity, as well as indices of necrosis of phagocytes. For intact cells, the apoptotic index was 12 ± 0.9%, then for cells after exposure to CFS, 13.6 ± 1.6; the necrosis index was 8.7 ± 0.7 and 9.4 ± 0.6%, respectively (Fig. 2F, G). So, we did not find cytotoxic and proapoptotic effects of CFS on cells.

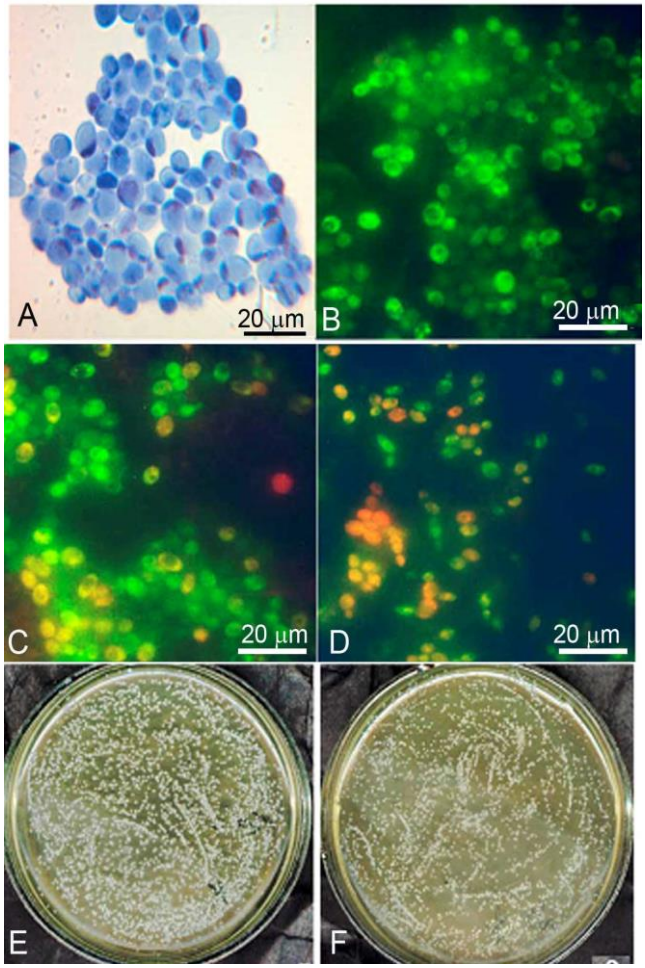

Fig. 2. Morphology of yeast cells C. albicans. a) cells of the initial culture, we can see a thin shell, a homogeneous, fine-grained cytoplasm, a color according to Nocht-Maximov; b) cells of the initial culture with brightly colored cores; c) yeast after exposure to CFS number 2 for 45 min, nonviable are colored in the orange spectrum; d) exposure to CFS for 5 hours, luminescent microscopy method, coloration with acridine orange. Colonies C. albicans: e) before exposure to CFS No. 2; e) after 5 hours of exposure to CFS No. 2.

3.2. Functional activity of cells

Adhesion of phagocytic cells to the substrate is one of the factors of the activation necessary for the implementation of subsequent events phagocytosis phagocyte from spreading on the surface of the target cell and ending with the digestion of killed target cells. When studying the adhesive ability of phagocytic blood cells, under the influence of CFS No. 2, its increase was established. Maximum adhesion activity indices were observed after 30 min and reached 20,7 ± 1,6%, the control (cells without exposure) hereinafter taken as 0. Defined increase the adhesive activity of the phagocytes under the action of CFS can be one of the possible mechanisms for activation of bactericidal activity cells.

When determining the SDG activity in the MTT test, an increase in the indices was found in comparison with intact cells, especially when exposed to CFS in the initial periods. After 15 min, the maximum values of 24.4 ± 1.6% of the intracellular content of this enzyme were noted, and over time its activity decreased. This indicated a stimulation of the functional activity of neutrophils and macrophages after exposure to CFS No. 2.

When calculating phagocytic parameters, it was found that after exposure to CFS No. 2, the cells were more actively absorbed by C. albicans. Without the effect of CFS, the percentage of cells that absorbed yeast in 30 minutes was 46 ± 5.2% and 2 hours 52 ± 4.8%. After exposure to CFS, it increased 1.3 times and was equal to 55.2 ± 4.7 and 61.7 ± 5.7%, respectively. The number of absorbed C. albicans without the action of the device after 30 min was 2.4 ± 1.6 and 2 h 3.2 ± 1.7, which indicated the reproduction of C. albicans in the cells. After exposure, this indicator was 3.2 ± 1.7 and 2.9 ± 1.5, respectively.

The utmost interests are the data obtained in the study of the activity of cell enzymes in the process of C. albicans infection. For cells with phage, pino, and exocytosis, a constant consumption (intereration) of the plasma membrane is typical, which is compensated by the permanent synthesis of its components. Determination of the activity of macrophage membrane ectoenzymes, which include ATP-ase, 5'-nucleotidase allows to estimate the degree of stimulation of these cells. Decrease in the level of these enzymes is considered as a manifestation of the biochemical processes accompanying the activation of phagocytes. Under the influence of CFS, we found a statistically significant decrease in the intracellular content of 5'-nucleotidase and ATP-ase in the initial terms to 1.5 contacts (Fig. 4A, B). To reflect the degree of activation of oxygen-dependent metabolism of phagocytes and the associated accumulation of free oxygen radicals, a cytochemical method is used with nitrosine tetrazolium (NST test). In the study of phagocytes after CFS exposure, a statistically significant decrease in the NST test was revealed. Also, when studying the activity of lactate dehydrogenase, which takes an active part in the initial transformation of the substrate for the formation of reactive oxygen species, a marked decrease in the activity of this enzyme in phagocytes under the influence of CFS was observed (Fig. 4C). Moreover, in cells infected with C. albicans, it was significantly higher than in phagocytes after CFS exposure. The antioxidant effect of CFS was indicated by the obtained data on the study of the content of myeloperoxidase in neutrophils, which was significantly lower in cells infected with C. albicans without prior CFS exposure (Fig. 4D).

3.3. Histological examination

The analysis of organs the intact and animals that drank the saline water charged by CFS No. 2 (10 min) daily for 3 days revealed no significant differences in the morphological pattern (Fig. 5). The cardiomyocytes of elongated form with dense secretory granules in the cytoplasm with an ordered system at the periphery of the myofibrilles location were defined in the heart (Fig. 5A). Morphological state of capillaries (their quantitative characteristics, spatial organization and structure of the walls) did not differ from the state of capillaries of muscle tissue of healthy animals. The liver tissue retained a typical beam structure with insignificant deposits of hemosiderin, the hepatocyte cytoplasm was observed without signs of vacuolization (Fig. 5B). In nuclei, chromatin was represented by fine-grained fractions with a uniform distribution over the area.

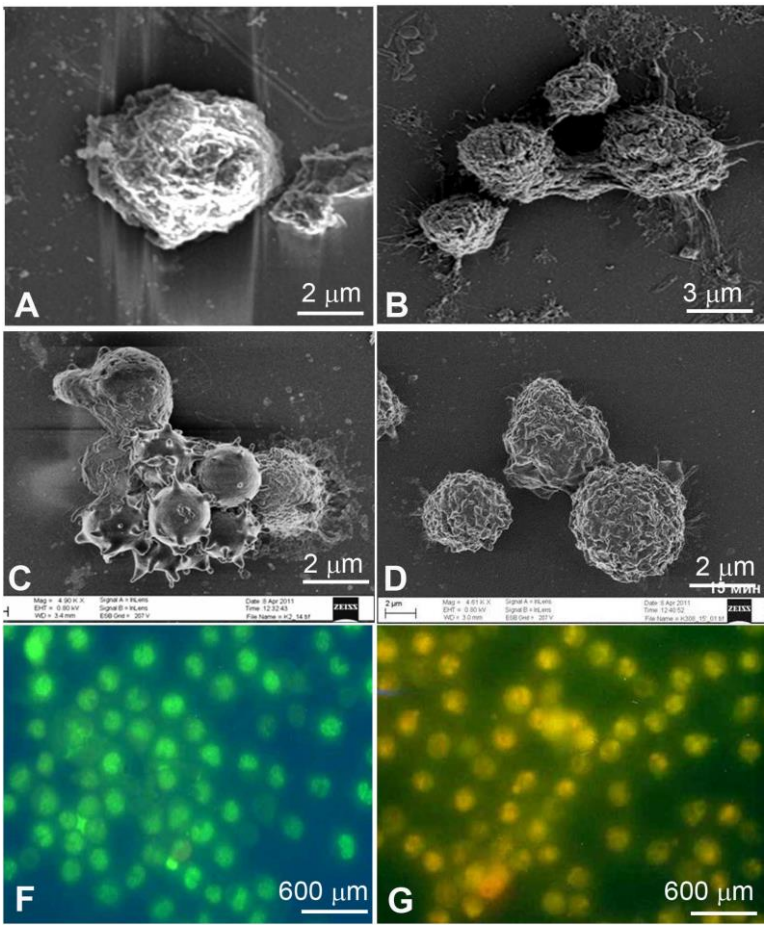

Fig. 3. Morphology of innate immunity cells.

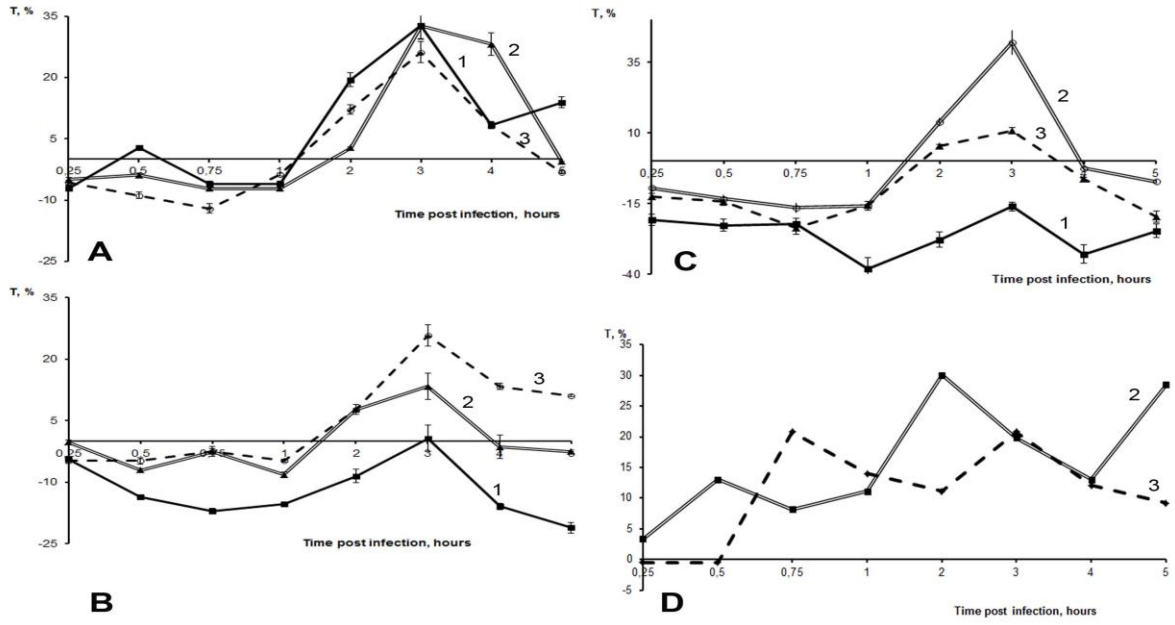

Fig. 4. Enzymatic activity of neutrophils and macrophages infected by yeast C. albicans.

Activity of 5'-nucleotidase (A); ATP-ase (B); lactate dehydrogenase (C) and myeloperoxidase (D). 1. after CFS impact; 2. cells infected with C. albicans without prior CFS exposure; 3. Cells infected with C. albicans, after a preliminary 30-min CFS exposure.

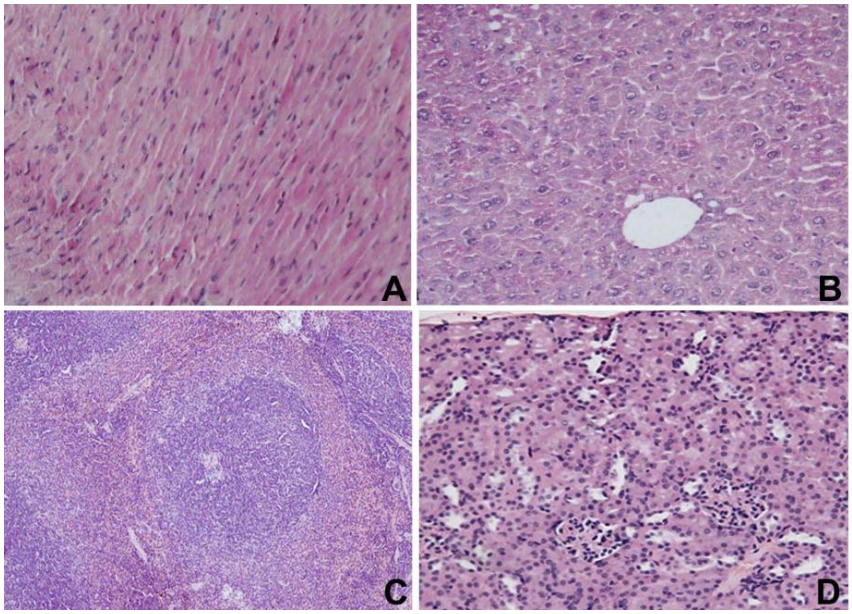

Fig. 5. Pathomorphological changes in the organs of animals infected with C. albicans (14 days): a) intracellular edema and vacuolization of cardiomyocytes in the perivascular region of the heart, focal colliquative necrosis, X200; b) toxic hepatic dystrophy, polymorphism of hepatocytes in size, shape and size of the nucleus, mosaic staining parenchyma, X200; c) a change in the ratio of the area of the red and white pulp of the spleen to the fusion of lymphoid follicles X100; d) rarefaction of the interfollicular space of white pulp, a small number of lymphocytes in the germinative center.

The spleen of the animals was also unchanged, a distinct contouring of the white pulp, represented by the lymphoid tissue forming the follicles, was noted. The periarterial zone of lymphatic follicles, smoothly turning into red pulp, is filled with cells (Fig. 5C). The mantle zone surrounding the germinal center contained a small number of macrophages and plasma cells. The red pulp was represented by the reticular tissue with blood cells, connective tissue and blood vessels of venule type, filled with erythrocytes and small clumps of hemosiderin. The kidney is without features, with a clear separation boundary (Fig. 5D). Renal corpuscles of rounded shape, a capsule cavity in the form of a narrow slit around the vascular glomerulus, consisting of blood capillaries.

In animals infected with C. albicans at a dose of 10^4 c.f.u. per mouse (1/2 LD50, 3), a sharp change in the morphology of the cardiomyocytes was defined (Fig. 6A). This way, in the presence of cardiomyocytes with normal morphology, clusters of cells of a rounded type with enlightened and vacuolated cytoplasm were observed. Intracellular edema and vacuolization of cardiomyocytes was noted mainly in the perivascular and subendothelial regions of the heart. These changes indicated the presence of focal colliquative necrosis, which develops as a result of impregnation of the myocardium with exudate from the blood vessels (Shkurupy, 2011). This process, as a rule, accompanies the presence of systemic inflammation, caused in this case by candidal infection (Gurin, 2009).

In the liver, clear phenomena of toxic dystrophy, especially in the central part of the hepatic lobules, were found, which was expressed in the polymorphism of hepatocytes in size, shape and size of the nucleus, mosaic staining of the parenchyma (Fig. 6B). There were also small necrotic lesions with polymorphic cell infiltration, vessels with fibrinoid necrosis of the wall and loose perivascular infiltration. In the kidneys, toxic changes were not expressed, small changes were noted in the size and shape of the vascular glomeruli. In the spleen, there was a change in the ratio of the area of red and white pulp with an increase in the latter, where fusion of lymphoid follicles was observed (Fig. 6C). In some animals, the white pulp lymphatic follicles were poorly visualized with a decrease in the cellularity of the interfollicular space in the white pulp. A violation of the stratification of layers in the follicles with an ineffective separation of the periarterial and mantle zones with a sharp decrease in the number of lymphocytes in the germinative center (Fig. 6D).

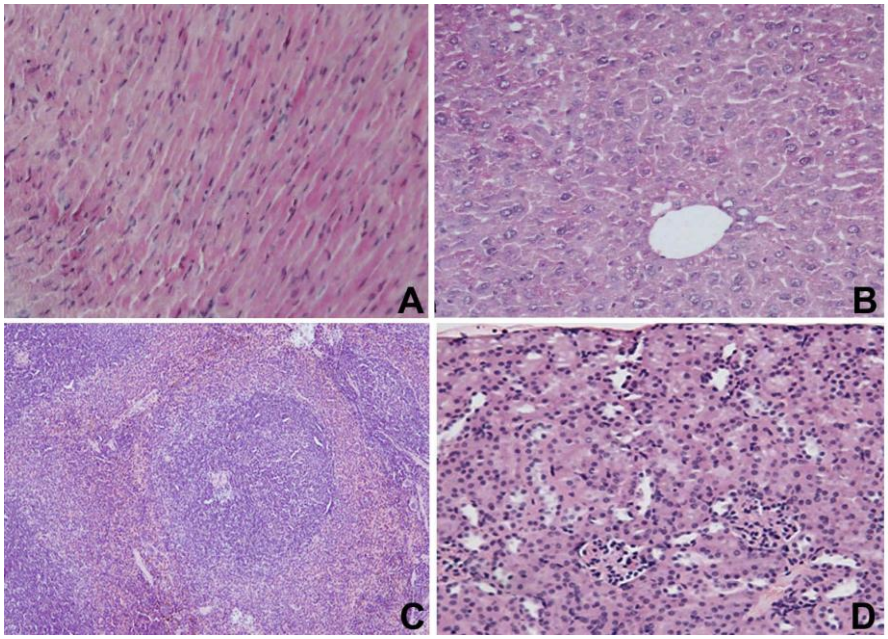

Fig. 6. Pathomorphological changes in the organs of animals infected with C. albicans (3 s): a) intracellular edema and vacuolization of cardiomyocytes in the perivascular region of the heart, focal collibatory necrosis, X200; b) toxic hepatic dystrophy, polymorphism of hepatocytes in size, shape and size of the nucleus, mosaic staining parenchyma, X200; c) a change in the ratio of the area of the red and white pulp of the spleen to the fusion of lymphoid follicles X100; d) rarefaction of the interfollicular space of white pulp, a small number of lymphocytes in the germinative center.

In the organs of animals infected with C. albicans and taking daily salted, charged CFS No. 2 water (10 min), the toxic effect of Candida was less expressed (Fig. 7). In the perivascular and subendothelial regions of the heart, there were no phenomena of intracellular edema and vacuolization of cardiomyocytes, which indicated the absence of focal colliquative necrosis (Fig. 7A). The predominantly cardiomyocytes were elongated with dense secretory granules in the cytoplasm. A typical beam structure with insignificant deposits of hemosiderin and small foci of lymphoid infiltration was observed in the liver. In the hepatocytes, a dense cytoplasm was observed, without signs of vacuolation (Fig. 7B). Along with the cores, where chromatin was represented by reticularly large-smoby zones localized either at the center of the cores or diffusely in the core lamina region, pycnotic cores were observed (supercompactization, Fig. C). In the spleen, there was a clear structuring of the lymphoid follicles with normal cellularity of the interfollicular space in the white pulp. In the mantle zone, a small number of macrophages were detected, the germinal center was filled with lymphocytes (Fig. 7C). Red pulp is represented by a reticular tissue with blood cells and small clusters of hemosiderin. Kidneys, same as in animals infected with candida, showed signs of changes characterizing inflammation (Fig. 7D). We identified the edema of subcapsular space, damage to vascular glomeruli with a decrease in their cellularity, vasoconstriction, small hemorrhages in surrounding tissues.

4. CONCLUSION

From the theory of modeling non-linear nonequilibrium systems subjected to the action of fluctuations, and this is precisely what happens in complex biosystems, it is known that, if several stable states are possible in a system, but under fluctuation emanates only one (Guerin & Kunkle, 2004). Any oscillating objects tend to synchronize with each other with a phase ratio of multiple integers, and the interaction force can be arbitrarily small.

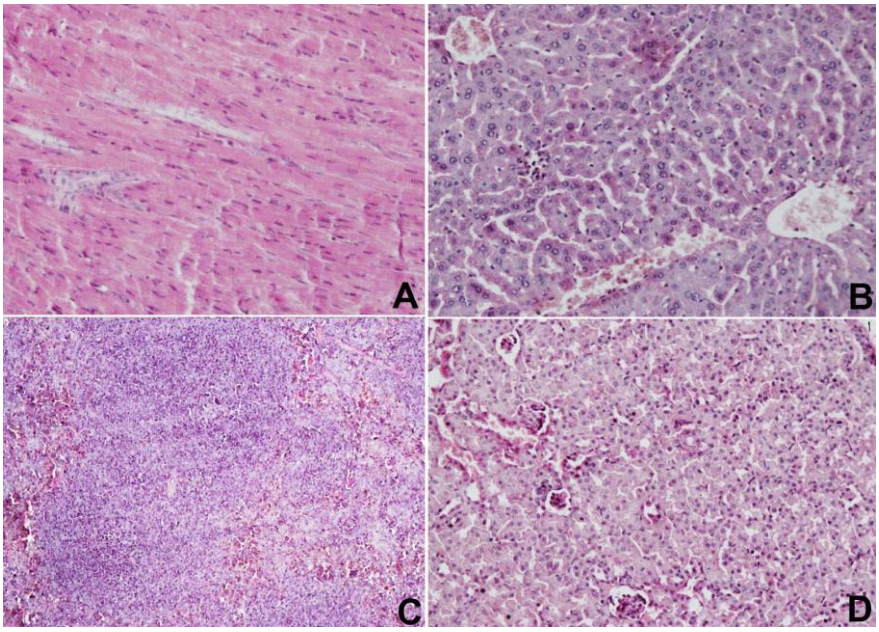

Fig. 7. Pathomorphological changes in the organs of animals infected with C. albicans (3 s) and taking daily salted and charged CFS No. 2 water: a) cardiac epicardial cardiomyocytes with tight secretory granules in the cytoplasm X200; b) a typical beam structure of the liver with insignificant deposits of hemosiderin and a small focus of lymphoid infiltration X200; c) a clear structuring of the lymphoid follicles of the spleen with normal cellularity of the interfollicular space in the white pulp, X100; d) inflammatory changes in the kidneys with edema of the subcapsular space, damage to the vascular glomeruli with reduced cellularity, vasoconstriction, X200. Hematoxylin eosin.

There are known devices for activating the fluid and the functional state of a biological object by force fields with a resonant electrical circuit in the form of a spiral (Chen et al., 2012). There are also secondary data carriers made in the form of an applicator on the basis of materials capable of forming a spectral analogue of the radiation of the initial action with the inclusion of the EHF-range (Jokela, 2000). With all the advantages, these devices are not protected from the influence of external electromagnetic fields, as a result of which the information recorded on the applicator remains for a very short time. Device - CFS, used in our study, has increased protection of recorded information from external electromagnetic fields. It contains two elements, each of which has an active layer of a material that has the memory effect of a wide spectrum of external electromagnetic radiation. The active layers of the elements are polarized in the millimeter range of electromagnetic waves, giving them chirality properties and forming a spectral analogue of the radiation of the initial action from biologically significant information carriers. This device allows, analogically to the double helix of a DNA molecule, to connect two polarized active layers that have a chirality property after polarization, which determines its stereospecific effect on macromolecules.

During natural evolution, living systems were formed as structures connected energetically and functionally with fluctuations of the external world. The macromolecules of living systems are preferably optically active substances that have the ability to equivalently rotate a plane-polarized light beam (Li et al., 2013). Moreover, biomolecules inherent property of chirality, incompatibility in space with its mirror image. For example, nucleic acids (DNA) preferentially deflect the plane of polarization of the beam to the right and are called dextrorotatory (D-isomers). The change in the spatial arrangement of the same groups of atoms in macromolecules can have as significant consequences as the change in the chemical nature of these groups (Wanapun et al., 2009). Biocatalysts - cell enzymes are constructed from chiral molecules of α-amino acids and are sensitive to interacting substrates with similar properties. Thus, the spatial structure of enzymes is associated with the stereospecificity of biochemical processes.

In our study, it is shown that the effect of CFS, which is inherent in the chirality of the magnetic field, consists in the formation of an ordered three-dimensional structure, variable in the material of its active layer of the element. This way, this device can produce a corrective electromagnetic effect by changing the stereochemical properties of the enzymes. It is known that, these enzymes participate in the production of reactive oxygen molecules that carry out bactericidal functions of phagocytes (Puchart, 2015). In it's turn, the phagocyte system is a rapid reaction unit, plays a crucial role not only in antibacterial, but also in antitumor protection of the body, as well as in allergic reactions of immediate hypersensitivity (Forman & Torres, 2002). At present, this system is considered as a set of immunocompetent and immunoregulatory cells participating in intercellular contacts and interactions forming immune homeostasis. The functional usefulness of these cells largely depends on the genesis, course and outcome of many pathological conditions (Levy, 2004). The pronounced stimulating effect of CFS No. 2 on these cells indicates a stereospecific property of the corrector. This property is determined by the effect of CFC on certain stereoisomers and the result of the cell's response is an increase in its protective potential against C. albicans.

While studying the effect of water, charged with CFS No. 2, on the pathogenesis of candidiasis infection, it was determined during the experiment, that in animals taking water, the signs of toxic inflammation were less expressed than in infected animals. So, in the perivascular and subendothelial areas of the heart, no signs of focal collisional necrosis were detected. In the liver, a decrease in signs of toxic dystrophy was observed, namely normalization and homogeneity of hepatocytes in size, shape and size of the cores, absence of necrotic foci with polymorphic cell infiltration and vessels with fibrinoid necrosis. In the spleen, in comparison with the spleen of animals infected with C. albicans, a clear structuring of the lymphoid follicles was observed in the normal cellularity of the interfollicular space in the white pulp and the filling of the germinal center with lymphocytes. Nevertheless, the morphological picture of the kidneys, same as in animals infected with C. albicans, showed signs of changes characterizing the inflammation. The edema of subcapsular space, damage to vascular glomeruli with a decrease in their cellularity, vasoconstriction, small hemorrhages in surrounding tissues were detected.

This way, we can make a conclusion that the water charged with CFS No. 2 influences mainly the antitoxic orientation, stimulates the cells to purify the body from C. albicans life activity products. This can be a decisive factor determining the perspective of its use as an additional to the main therapy of an immunostimulating agent, in particular, to increase the body's natural resistance to infectious agents of various infectious diseases, and also as a means of reducing the toxic effect of bacteria.

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