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THE MECHANISM OF ACTION OF RADIOPROTECTORS AND COSMIC RADIATION ON MEMBRANE SYSTEMS AND THE WHOLE ORGANISM

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It is known that the radiobiological effect of high-intensity ionizing (γ - and UV-irradiation, hard cosmic rays) and non-ionizing (EMR) irradiation manifests itself in a strong effect on the electronic structure of DNA, in single- and double-strand DNA breaks, and initiation of lipid peroxidation processes (LPO), the formation of free radicals (SR) of lipids and proteins, peroxides and hydroperoxides of water, in changing the physical and chemical properties of biological molecules. We have shown that lipid peroxidation products, which are also formed during any pathological process, damage cell and mitochondrial membranes, erythrocyte and nerve cell membranes, reduce immunity, and reduce the activity of cell division processes and energy generation. Ionizing and non-ionizing radiation of low intensity induce the formation of extremely low concentrations of SR, but even a slight activation of chemical reactions in this case is sufficient for the manifestation of oxidative stress, changes in the redox potential of cells and tissues, initiation of chain chemical reactions, modification of covalent bonds of molecules, activation of enzyme systems, increasing the amount of biogenic amines in the body.

1. On membrane systems and the whole organism, we have developed a comprehensive biophysical express method (CBM) for studying the primary mechanisms of action of radiation and biologically active compounds (BAS) that exhibit radioprotective (RP) radiomimetic (RM) action, which are natural and synthetic compounds from the class and bioflavonoids (BF), benzimidazoles, ubiquinones, carotenoids, nitrofurans, organic carbon compounds of selenium, nanostructures (fullerenes),

salicylanilides, adaptogens (ginseng, eleutherococcus, etc.), steroid hormones, mono- and dibasic sulfur-containing acids. The method also includes methods for determining toxicity, stability of drugs over time, the nature of the effect of BAS on ecosystems, and the degree of environmental pollution.

2. It is shown that at the molecular-cellular level, the primary mechanisms of action of natural non-toxic substances (dihydroquercetin, catechins, anthocyanins, flavonols, hydrochalcones, gossypol, lycopene, echinochrome, adaptogens), which have a radioprotective therapeutic effect after irradiation of the body in various doses, are realized in their the ability to bind SR, increase the proton conductivity of membranes, increase the synthesis of macroergic compounds in mitochondrial membranes, and increase the activity of respiratory enzymes. In addition to the stimulating effect on bioenergetics, these drugs are able to regulate the passive transport of Ca^{2+} , K^{+} , Na^{+} , Cl^{-} ions, affect the structure of dipole water molecules and the synthesis of nucleic acids (DNA).
3. It has been shown that some of the drugs listed in paragraph 1 affect the state of transmembrane ion channels, receptors and the potential of excitable membranes, regulated by Na,K-ATPase, Na,Ca- and $\text{Na}^{+} / \text{H}^{+}$ - exchange pumps, as well as a combination of enzymes , included in the protein kinase A regulation system, including chemoreceptors, cAMP, c-GMP, phosphodiesterases, phospholipase A, calmodulin, and in the protein kinase C (PKC) system associated with the regulation of cell differentiation and division. The interaction of growth stimulants and hormones with cell membrane receptors leads to the activation of PCD through an increase in the concentration of such second messengers as diacylglycerol and calcium ions. 80%-85% of drugs known to date have a membranotropic effect. 4. At the physiological level, some of these drugs had a positive effect on the central and peripheral nervous systems, on the immune system, on cell proliferation and on hematopoietic

system, on the system of the epithelium of the small intestine, which, in general, led to an acceleration of metabolic processes, an increase in the body's resistance to pathologies and adverse external factors. For the prevention of lethal and super-lethal effects of high doses of radiation (7-16 Gy), we offer other, more effective compounds (code T-1, TCSD) with a different mechanism of action. 5. The main patterns of changes in the biological activity of BAS associated with the chemical structure of the preparations were experimentally established. Thus, plant BP and a number of other studied drugs exhibited antioxidant and radioprotective activity of different intensity during γ -irradiation of laboratory animals, depending on the presence of substituents Cl-, Br-, I-, NO_2 , NH, COOH, on the concentration and number of OH groups in benzene rings, which are a trap for SR.

Specific structural rearrangements and changes in the physicochemical properties of membranes that occur after irradiation were studied - with the introduction of known RP and RM, as well as newly synthesized and natural substances, the radioprotective effect of which was not studied. 6. With the help of KBM, among a large group of chemicals isolated from plants, microorganisms and marine animals of the Far Eastern flora and fauna, 4 drugs were selected (code MA, TA, Po, EC), which meet the therapeutic and prophylactic requirements for RP with high dose change factor index. The drugs can be used at nuclear power plants, nuclear submarines, proton and neutron accelerators, in long-term space flights (to Mars), for the rehabilitation of cancer patients after radiotherapy.

7. Theoretically generalized and experimentally studied the mechanisms of action of little-studied physical factors of the environment on various biological objects: microwave EMR of especially low intensity with complexly organized modulation, physical radiation from fundamentally new sources (high-energy pulsed electromagnetic effects - corona discharge fields), which cause destructive changes in supramembranous, membranous and

intracellular structures of tumor cells and pathogenic microorganisms, causing inhibition of their proliferative activity and death. Conducted a comprehensive physiological and biochemical study of the influence of high-energy pulsed discharges on the germination of various seeds, on the functional activity of the central nervous system and other organs of mammals. 8. Taking into account the hypotheses about the role of free-radical processes in the mechanisms of nonlinear biological effects of weak electromagnetic radiation in the radio frequency range, ideas about soliton effects in clusters of the liquid phase of water and the concept of the distance factor in radiation hormesis, it will be possible to largely clarify the mechanisms of action of weak electromagnetic radiation in various frequency ranges, radiation from mobile phones and various household appliances, secondary biogenic radiation from polaritons (changes in pH, microviscosity, electrical conductivity and the time of spin-spin and spin-lattice relaxation of water molecules), to outline ways to protect a person from these radiations by natural and synthetic RP identified by the method KBM, proposed by us. To enhance the effect of natural and synthetic RP, it is proposed to use them jointly with other complex therapeutic agents (licolam, lycoprofit, ginkgo biloba, phenotropil, mexidol, carbon nanostructures, bacteriorhodopsin, ADP and ATP, low molecular weight DNA) and with matrix applicators developed by the AIREIS Foundation investigated by us. In medical practice, other therapeutic properties of radioprotective drugs developed by us are also used. The following are used: 1) tegalide from the class of salicyllinylides as

fasciolocide, 2) bitionol from the class of dibasic acids - as an antibacterial and fasciolocidal drug, 3) dihydroquercetin (drug "Capillar") from the BF class with an antioxidant effect - as a capillary-strengthening agent and immunostimulant, 4) ubiquinone Q10 with an antioxidant and energy-stimulating effect (drug "Kudesan") - for the treatment of cardiovascular diseases, asthenic syndrome and as a cosmetic product, 5) BF gossypol (as part of the drug "Batridin") - as an antiviral, antibacterial and contraceptive drug, 6) echinochrome isolated from sea urchin cells) with antioxidant action - as a pacemaker, neuroprotector.