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C_{60}-CONTAINING NANOCOMPOSITES AS CATALYTIC SYSTEM FOR REACTIVE AS CATALYTIC SYSTEM FOR REACTIVE OXYGEN SPECIES GENERATION IN CELLS

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Finding of a new nanopartical systems suitable for manipulation at cell molecular level is the urgent problem of bionanotechnology. The representatives of a new allotropic form of carbon – C_{60} fullerenes have potential for biological application. C_{60} molecule has a significant reduction potential and is able to scavenge free radicals, its surface could be easily modified by substituent, small size and hydrophobicity allows it to interact with biological molecules and to be inserted in cell membrane. Photoexcited C_{60} fullerenes is a highly efficient sensitisizer, potentially useful for photodynamic therapy of tumors, but the kind of reactive oxygen species produced in the medium as well as the mechanisms of damaging effect on structural components of the normal and transformed cells are still not clear. The aim of the study was to estimate the indexes of metabolic state of the normal (rat thymocytes) and oncotransformed (Erlich ascites carcinoma and leukemia L1210) cells under the action of photoexcited C_{60} fullerenes. Samples of C_{60} fullerenes colloidal solution ($2 \cdot 10^{-4}$M) were prepared as described in [1].

Biological application of C_{60} is strongly limited by its poor solubility and aggregation in aqueous medium. To provide a proportional distribution of C_{60} in the contact zone, to increase the contact area, prevent aggregation and optimize the specific interaction with the cell we performed C_{60} immobilization on the spherical nanoparticles of aminopropylaerosil. The surface of C_{60} fullerene as the constituent of the composite was minimally modified (because significant modification photoexcitation) – it was covalently sewed to aminogroups on the surface of the particle. Two types of nanoparticles were synthesized – C_{60}-aminopropylaerosyl (composite 1, Figure) and C_{60} – antracenaliminopropylaerosyl with antracenal antenna to increase photosensitization of C_{60} in the visible region. UV/Vis irradiation of C_{60}-containing composites in aqueous media was done by Hg- lamp in diapasone 320 – 580 nm. After introduction of photoexcited composite into cell suspension the C_{60} concentration was 10^{-5}M. Cells were incubated up to 24 h. Generation of reactive oxygen species in cell suspension was determined by EPR spectroscopy.

Photodynamic damage of oncotransformed cells by photoexcited $_{60}$ – composites was confirmed both at mitochondrial and nuclear level. The decrease of cell viability, enhanced content of terminal products of free-radical peroxidation, inhibition of mitochondrial respiratory activity, estimated by MTT test and intensification of DNA fragmentation was observed, more pronounced in suspension of Erlich ascites carcinoma cells than in L1210 cells. . No effects of photoexcited $_{60}$ – composites were detected in thymocytes suspension.

It is supposed that the different effects of photoexcited composites are connected with distinctions in membrane permeability and structure of the surface of the normal and oncotransformed cells. Data obtained testity to perspective utility of $_{60}$- composites for optimization of photodynamic therapy methods.

Reference

1. Golub A, Matyshevska O. Prylutska S, et all. Fullerenes immobilized at silica surface: topology, structure and bioactivity. J Mol Liq 2003; **105**: 141-7.

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THE SYNTHESIS OF THE NEW POLYMERIC DRUG FORM BASED ON HYDROPHILIC BLOCK-COPOLYURETHANE

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Polymeric materials play a significant role in the decision of some actual problems of medicine, in particular, for creation of polymeric medicinal forms, allowing directly to influence the damaged organ. Poly(N-vinyl pyrrolidone), poly(vinyl alcohol) and their copolymers are widely used in medicine for creation of depot of medicinal substance. Therefore, introduction in structure polyurethane elements of copolymer N-vinyl pyrrolidone and vinyl alcohol (NVP-co-VA) and reception on the basis of new hydrophilic carrier medicinal form of the prolonged action is quite proved.

The purpose of investigation is synthesis of the new polymeric medicinal form on the basis of the block copolyurethane, containing elements of NVP-co-VA in the backbone. As medicinal substance it is chosen amizonum (N-methyl-4-benzylcarbamidopyridiny iodide) which belongs to group non-narcotic analgetic and has interferonogenous, anti-inflammatory, antioxydative and immunomodulative actions.

Amizonum was immobilized on a polymeric carrier simultaneously with formation polyurethane matrix synthesized with the use of isocyanate prepolymer (on the basis of 2,4-2,6-toluene diisocyanate and polyoxypropylene glycol, average molecular weight 1000) and NVP-co-VA.

The possibility of chemical immobilization amizonum on a polyurethane carrier was investigated on example of model reaction amizonum wich phenylisocyanate. The structure of the product of model reaction was argued by elemental analysis, ^{1}H NMR- and IR-spectroscopy. Therefore, the possibility of chemical immobilization amizonum on a polyurethane carrier has been shown.

The structure of drug polymer is :