NANOSCALE DRUG AND GENE DELIVERY SYSTEMS BASED ON NOVEL OLIGOELECTROLYTES AND NANOGELS

A. Zaichenko[1], N. Mitina[1], M. Moskvin[1], A. Ryabtseva[1], S. Trotsenko[1], L. Ivanitska[2], E. Filyak[2], N. Boiko[2], R. Stoika[2]

[1]Lviv Polytechnic National University, 12 S. Bandera Str., Lviv, 79013, Ukraine;
[2]Institute of Cell Biology of NASU, 14/16 Dragomanov Str. Lviv, 79005, Ukraine;

zaichenk@polynet.lviv.ua

Novel telechelic, block, comb-like and branched oligoelectrolytes including PEGylated ones of tailored molecular weight, narrow molecular weight distribution, and functionality possessing controlled solubility and surface activity were developed. The originality of the created approaches is based on the synthesis of functional surface-active oligomers containing end or side ditertiary peroxide fragments and their subsequent using for the obtaining block or graft oligoelectrolytes via radical solution polymerization. That provides molecular design and controlling the copolymer molecular structures, molecular weight characteristics and behavior in water media of various polarities, namely: conformational state and size of the micelle-like zones, rheology, pH and temperature responsivity, and biological compatibility or genuine physiological activity.

On the basis of such oligoelectrolytes biocompatible polymeric and polymer-mineral nanogels and nanoparticles with controlled size, porosity and functionality containing desired amount of radical forming ditertiary peroxide fragments were developed. Their synthesis is based on using surface-active mono – and poly functional unsaturated substances including peroxide monomers as well as coordinating metal complexes with functional oligoperoxide ligands as templates for nanogels and nanoparticle formation, curing and functionalization. Composite nanogels and nanoparticles comprise of polymeric (including fluorine containing ones) or siliceous, Fe_3O_4, Ni, Au, Ag core and functional reactive polymer shell.

There was shown by light scattering and SAXS techniques that size of the nanoscale drug delivery systems is in the range 20 – 100nm depending on oligoelectrolyte nature and content. Such novel functional oligoelectrolytes and nanoparticles possess ability to immobilize low molecular weight physiologically active substances (biocides, antibiotics including anticancer ones) via mechanisms of solubilization, formation of intermolecular complex, covalent binding etc and to form nanoscale water drug delivery systems. They can be labeled with luminescent, MRI and X-ray detectable markers. The availability of reactive functional fragments in their structures provides irreversible binding antibodies, lectins or saccharide-containing fragments possessing specific interaction with the cell membranes. The toxicity and genuine biological activity studied in the lab of Institute of Cell Biology witness their strong dependence on the molecular weight and molecular weight distribution as well as functionality and surface activity. Testing of oligoelectrolytes and nanoparticles *in vitro* and *in vivo* showed very low toxicity some of them and allowed to select the most promising ones as carriers for antimicrobial and anticancer drug delivery systems.

Water based nanoscale drug delivery systems consisting of novel oligoelectrolytes and nanogel carriers and immobilized chloramphenicol or ampicillins were successfully tested on microbial and fungi cultures. Study of anticancer drug (doxorubicin) delivery systems testified to their overcoming cell membranes and natural biological barriers and as a result high efficiency of the action on some tumor cells *in vitro* and *in vivo* and their low toxicity at the same time. This provides significant lowering the amount of anticancer drug. The study of the novel developed drug delivery systems is on the stage of the patenting.

References

[1] A. Zaichenko, N. Mitina, O. Shevchuk, O. Shapoval, N. Boiko, R. Bilyy, R. Stoika, A. Voloshinovskii, D. Horak // American Institute of Physics / Conference Proceedings. - 2010.; P.178-182.

[2] Bilyy R., Podhorodecki A., Nyk M., Stoika R., Zaichenko A.,Misiewicz J., Strek W. Physica E: Low-dimensional Systems and Nanostructures, 2008. V.40. P. 2096-2099.
[3] Zaichenko A., Mitina N., Shevchuk O., Rayevska K., Lobaz V.,Skorohoda T., Stoika R. Pure Applied Chemistry, 2008, V.80, N11. P.2309-2326.
[4] V.Novikov, A. Zaichenko, N. Mitina, O. Shevchuk, K. Rayevska, V. Lobaz, V. Lubenets. Yu. Lastukhin. Inorganic, polymeric and hybrid colloidal carriers with multi-layer reactive shell// In: Macromolecular Symposia. Reactive Polymer, Wiley-VCH, - 2004 -№ 210. - P. 193-202.

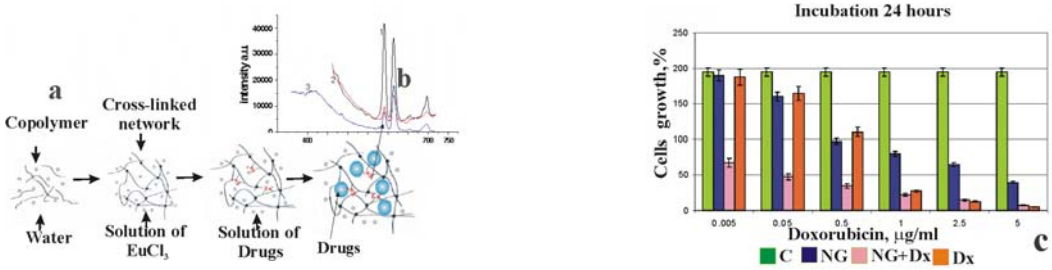

FIGURE. The scheme of nanogel formation and drug immobilization (a), the luminescence spectrum of nanogel labelled at different Eu^{3+} content (b) and diagram of mice leukemia L1210 cell treatment (c): C – control, NG – nanogel carrier, NG + Dx – immobilized drug, Dx – free doxorubicin