BIONANOTOX 2018

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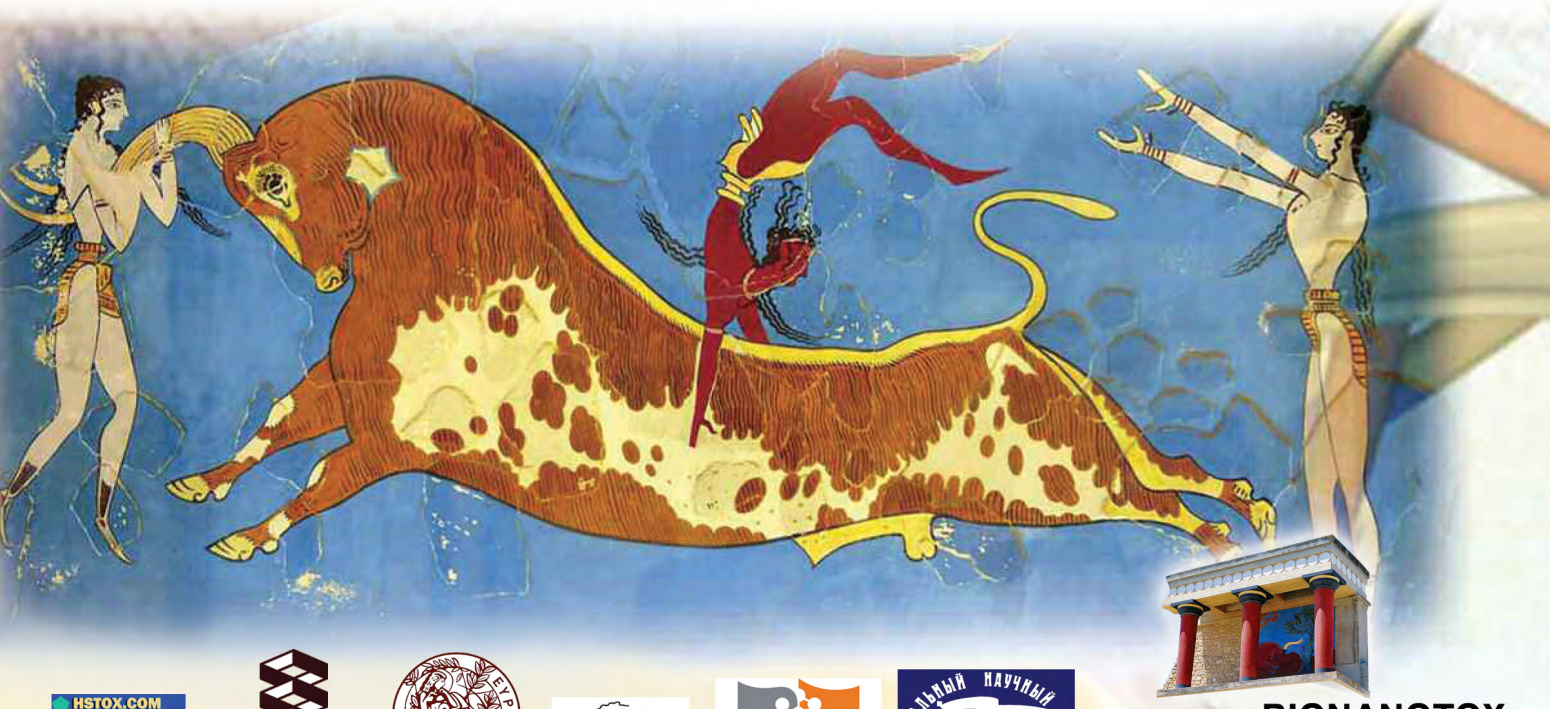
9th INTERNATIONAL CONFERENCE

"BIOMATERIALS AND NANOBIOMATERIALS:

Recent Advances Safety-Toxicology And Ecology Issues

Including Russian-Hellenic Workshop And School Of Young Scientists

06-13 MAY, 2018, AGAPI BEACH, HERAKLION, CRETE - GREECE



HELLENIC SOCIETY OF TOXICOLOGY

M. SHEMYAKIN AND YU. OVCHINNIKOV INSTITUTE OF BIOORGANIC CHEMISTRY

UNIVERSITY OF CRETE

EUROTOX

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INVITATION LETTER

On behalf of the organizing committee of 9th International Congress "Biomaterials and Nano-biomaterials: Recent Advances Safety - Toxicology and Ecology Issues" Including Russian-Hellenic Workshop and School of Young Scientists and Symposium of Nano-toxicology, we are privileged to invite you to grace with your presence and participation the works of the Congress, which is to be held in Heraklion, in the beautiful island of Crete, in May 2018.

Crete is one of Europe's most popular holiday destinations. The island's historic importance as Knossos, Phaistos and Gortys is evidenced by thousands of visitors to these sites each year. Heraklion is located almost in the centre of Crete.

The theme of the Symposium, Bio Nano-toxicology, lie at the interface of many disciplines, from biology to chemistry, toxicology, computational science chemistry, nanotechnology and biotechnology. The Symposium is a continuation of a long term co-operation between Russian and Hellenic scientists in this field that has been ongoing for the last 20 years, in the frame of the bilateral scientific state programs.

It is anticipated that scientists from the Russian Academy of Science, the most prominent Universities as well as Technological Institutes and Companies and distinguished field specialists coming form many countries will attend the symposium. Very low package fees including registration, accommodation, lunch meals and congress material have been secured for participants, in order to enable more young scientists to attend the Symposium.

At this symposium the attendee will have the chance to meet important representatives of research in the field, discuss with them and exchange ideas. This will accomplish the aim of the symposium, which is the generation of new and vigorous interactions between the different aforementioned disciplines, which will have enormous positive effects in our societies.

Co-Chairmen of the Organizing Committee

Aristidis Tsatsakis, PhD, DSc, ERT

Mikhail Shtilman, PhD, DSc

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Kabanov Alexander Professor, Director of Center for Drug Delivery and Nanomedicine, University of Nebraska, Omaha, USA

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Syed F. Ali Ph.D., Fellow ATS, National Center for Toxicological Research/USFDA, USA

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Varfolomeev Sergey Corresponding member of RAS, Director of N. Emanuel Institute of Biochemical Physics of RAS, Moscow, Russian Federation

Vladimirov Yurii A Academician RAMS, Moscow State University

Volova Tatiana G. Professor, Director of Department of Biotechnology, Siberian Federal University, Krasnoyarsk, Russian Federation

COMMITTEES

Organizing Committee

Co-President of the Congress

Tsatsakis Aristidis	Professor, Director of Forensic Sciences & Toxicology Dep., University of Crete, Iraklion, Greece
Shtilman Mikhail	Professor, Head of Center "Biomaterials", D.Mendeleyev University of Chemical Technology of Russia, Moscow, Russian Federation

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Markvicheva Elena	Professor, M.Shemyakin-Yu.Ovchinikov Institute of Bioorganic Chemistry, Moscow, Russian Federation
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Tsakalof Andreas	Professor, Medical Chem. Dep., University of Thessaly, Larissa, Greece
Tzatzarakis Manolis	PhD, Assistant Professor, University of Crete, Iraklion, Greece
Velonia Kelly	Associate Professor, Department of Materials Science and Technology, University of Crete, Greece

Sunday, May 6, 2018

ARRIVAL - REGISTRATION

20.00 **Welcome Cocktail**

Monday, May 7, 2018

08.00-09.30 **BREAKFAST**

10.00 **OPENING CEREMONY**

10.00-10.10 **WELCOME ADDRESS**
Aristidis M. Tsatsakis, Co-head of Organizing Committee
University of Crete, Iraklion, Crete, Greece

10.10-10.20 **ABOUT SYMPOSIUM PROGRAM**
Mikhail I. Shtilman, Co-head of Organizing Committee
D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russian Federation

10.20-11.00 **RECENT DEVELOPMENTS IN LIPOSOMAL NANOPREPARATIONS AGAINST CANCER**
Vladimir P. Torchilin, President of Conference
Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, Boston, MA 02115, USA

11.00-11.30 **COFFEE BREAK - POSTER SESSION**

11.30-12.30 **MORNING SESSION**

Chairmen: Prof. V.P. Torchilin, Prof. R. Katsarava

11.30-12.00 **THE ROLE OF NON-HEME IRON IN CHAIN LIPID PEROXIDATION IN INTRACELLULAR MEMBRANES AND IRON-DEPENDENT PROGRAMMED CELL DEATH (FERROPTOSIS)**
Yu.A. Vladimirov
Lomonosov Moscow State University, Moscow, Russian Federation
Shubnikov Institute of Crystallography of Federal Scientific Research Centre "Crystallography and Photonics" of Russian Academy of Sciences, Moscow, Russian Federation

12.00-12.30 **IMPACT OF MAGNETIC FIELD SPATIAL AND TEMPORAL CHARACTERISTICS ON ACTUATION MECHANISMS OF BIOCHEMICAL SYSTEMS BY MAGNETIC NANOPARTICLES**
Y.I. Golovin[1,2], A.O. Zhigachev[2], M.V. Efremova[1,4], K.Y. Vlasova[1], M.M. Veselov[1], A.G. Majouga[3,4,1], A.V. Kabanov[1,5], N.L. Klyachko[1,5]
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[2] Nanocenter, G.R. Derzhavin Tambov State University, Tambov, Russian Federation
[3]D. Mendeleev University of Chemical Technology of Russia, Moscow, Russian Federation
[4] National University of Science and Technology MISIS, Moscow, Russian Federation
[5]Center for Nanotechnology in Drug Delivery, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

12.30-13.00 **CHOLESTEROL-LOWERING THERAPY AND NATURAL LIPID TRANSPORTING NANOSTRUCTURES OF BLOOD PLASMA (LOW DENSITY LIPOPROTEINS) FREE RADICAL PEROXIDATION**
V.Z. Lankin, A.K. Tikhaze
National Medical Research Center of Cardiology, Ministry of Health of Russia, Moscow, Russian Federation

13.00-14.00 **LUNCH**

14.00-16.30 **BREAK**

16.30-18.00 EVENING SESSION

Chairmen: Prof. E.A. Markvicheva, Prof. N.L. Klyachko

16.30-16.50 MOLECULAR AND CELLULAR MECHANISMS IN ATHEROSCLEROSIS DEVELOPMENT

A.V. Balatskiy[1,2], V.A. Tkachuk[1,3]
[1]*Faculty of Medicine, Lomonosov Moscow State University, Moscow, Russian Federation*
[2]*Medical scientific and Educational Centre, Lomonosov Moscow State University, Moscow, Russian Federation*
[3]*Institute of Regenerative Medicine, Lomonosov Moscow State University, Moscow, Russian Federation*

16.50-17.20 GLYCOSYLPHOSPHATIDYLINOSITOL-ANCHORED PROTEINS: HOW TO STUDY AND USE

M.N. Balatskaya[1], G.V. Sharonov[2], V.A. Tkachuk[1]
[1]*Lomonosov Moscow State University, Moscow, Russian Federation*
[2]*Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Moscow, Russian Federation*

17.20-17.40 IN VITRO UPTAKE STUDY OF NANOPARTICLES BASED ON AMPHIPHILIC N-VINYLPYRROLIDONE
BY DIFFERENT TYPES OF CELL CULTURES

A.L. Luss[1], P.P. Kulikov[1], A.V. Goryachay[1], A.N. Kuskov[2], L. Gurevich[3], C.P. Pennisi[4], M.I. Shtilman[1], Ya.O. Mezhuev[1]
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[2]*Department "Chembiotech", Moscow Polytechnic University, Moscow, Russian Federation*
[3]*Department of Physics and Nanotechnology, Aalborg University, Aalborg, Denmark*
[4]*Department of Health Science and Technology, Aalborg University, Aalborg, Denmark*

17.40-18.00 BREAK

18.00-18.20 PHYSICOCHEMICAL PROPERTIES OF MULTICOMPONENT POLYHYDROXYALKANOATES: NOVEL ASPECTS

E.G. Kiselev[1,2], N.O. Zhila[1,2], T.G. Volova[1,2]
[1]*Siberian Federal University, 79 Svobodny av., Krasnoyarsk, Russian Federation*
[2]*Institute of Biophysics of Siberian Branch of Russian Academy of Sciences Krasnoyarsk, Russian Federation*

18.20-18.40 FORMATION AND MOLECULAR STRUCTURE OF NATURAL POLYSACCHARIDES BASED THIN FILMS

I.V. Zhuikova[1], D.V. Kurek[2], V.P. Varlamov[1]
[1]*Institute of Bioengineering, Research Center of Biotechnology RAS, Moscow, Russian Federation*
[2]*"Future Biotech", Moscow, Russian Federation*

18.40-19.00 NOVEL METHOD FOR RAPID TOXICITY SCREENING WITH ELECTROCHEMICHAL NANOPROBES FOR SINGLE CELL ANALYSIS

A. Erofeev[1,2], P. Gorelkin[3], P. Actis[4], A. Alova[2], A. Garanina[1], C. Edwards[4], Y. Korchev[4], A. Majouga[1,2,5]
[1]*National University of Science and Technology "MISIS", Moscow, Russian Federation*
[2]*Department of Chemistry, Lomonosov Moscow State University, Moscow, Russian Federation*
[3]*Medical Nanotechnology LLC, Moscow, Russian Federation*
[4]*Department of Medicine, Imperial College London, London, United Kingdom*
[5]*D. Mendeleev University of Chemical Technology of Russia, Moscow, Russian Federation*

19.00-20.00 DINNER

Tuesday, May 8, 2018

08.00-09.15 **BREAKFAST**

09.30-13.00 **MORNING SESSION**

Chairmen: Prof. S.D. Varfolomeev, Prof. M.A. Ostrovskii

09.30-10.00 **STRUCTURE AND PROPERTIES OF NEW THERMOPLASTIC COMPOSITIONS ON THE BASE OF POLYETHYLENE AND POLYLACTIDE**

S.Z. Rogovina, Ch.V. Alexanyan, A.A. Berlin

Semenov Institute of Chemical Physics, Russian Academy of Sciences, Russian Federation

10.00-10.30 **CONTENTS OF OMEGA-3 POLYUNSATURATED FATTY ACIDS VS HEAVY METALS IN SEVEN SMOKED FISH SPECIES FROM SIBERIA (RUSSIA): BENEFIT-RISK RATIO**

Gladyshev M.I.[1,2], Anishchenko O.V.[2], Sushchik N.N.[1,2], Makhutova O.N.[1,2], Kalachova G.S.[2], Gribovskaya I.V.[2], Morgun V.N.[1,3]

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[2]Institute of Biophysics SB RAS, Krasnoyarsk, Russian Federation

[3]Federal Center for Standardization, Metrology and Testing in the Krasnoyarsk Region, Krasnoyarsk, Russian Federation

10.30-11.00 **REVERSIBLE ENZYMATIC REACTIONS. HOW TO INCREASE THE YIELD OF THE TARGET NUCLEOSIDES AND NUCLEIC BASIS**

S.N. Mikhailov

Engelhardt Institute of Molecular Biology of the Russian Academy of Sciences, Moscow, Russian Federation

11.00-11.30 **COFFEE BREAK - POSTER SESSION**

Chairmen: Prof. N.P. Kildeeva, Prof. S.N. Mikhailov

11.30-12.00 **POROUS BIOPOLYMERIC MATERIALS FOR BIOMEDICAL APPLICATIONS**

N.R. Kildeeva[1], M.A. Kurinova[1], Y.N. Filatov[2]

[1]A.N. Kosygin Russian State University, Moscow, Sadovnicheskaya Str. 33, Russian Federation

[2]Karpov Scientific Research Institute of Physics and Chemistry, Russian Federation

12.00-12.30 **MOLECULAR PHYSIOLOGY AND PATHOLOGY (CATARACT) OF THE LENS OF THE EYE: α-CRYSTALLIN AS A CHAPERONE LIKE DRUGS**

M. Ostrovsky

Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, Moscow, Lomonosov Moscow State University Department of Molecular Physiology, Biological Faculty, Russian Federation

12.30-13.00 **ASTROBIOLOGY: THE PRIMARY PROCESSES**

S. Varfolomeev

Moscow State University, Institute of Biochemical Physics, Russian Academy of Sciences, Moscow, Russian Federation

13.00-14.00 **LUNCH**

14.00-19.00 **BREAK**

16.30-18.00 EVENING SESSION

Chairmen: Prof N.L. Klyachko, Prof. S.A. Eremin

16.30-16.50 ENHANCING NANOPARTICLE-BASED APPROACHES FOR ULTRASENSITIVE IMMUNOASSAYS

I.V. Safenkova, V.G. Panferov, A.V. Zherdev, and B.B. Dzantiev
A.N. Bach Institute of Biochemistry, Federal Research Centre "Fundamentals of Biotechnology" of the Russian Academy of Sciences, Moscow, Russian Federation

16.50-17.20 CHITOSAN COATED SUPEROXIDE DISMUTASE NANOPARTICLES FOR ANTI-INFLAMATORY OPHTHALMIC APPLICATIONS

A.N. Vaneev[1,5,7], A.D. Aleksashkin[1], T.O. Abakumova[2,6], O.A. Kost[1], N.B. Chesnokova[4], O.V Beznos[4], P.V. Gorelkin[5,6], A.S. Erofeev[5,7], N.L. Eremeev[1], A.V. Kabanov[1,3], N.L. Klyachko[1,3]
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[3] University of North Carolina at Chapell Hill, USA
[4] Helmholtz Institute of Ophthalmology, Moscow, Russian Federation
[5] Medical Nanotechnology, Skolkovo innovation center, Moscow, Russian Federation
[6] Skolkovo Institute of Science and Technology, Moscow, Russian Federation
[7] Nanoprofiling, Skolkovo innovation center, Moscow, Russian Federation

17.20-17.40 NOVEL PHYSICAL TECHNIQUE FOR MACROSCOPIC LOCALIZATION OF MAGNETO-NANO-MECHANICAL ACTUATION OF MAGNETIC NANOPARTICLES IN VIVO

A.O. Zhigachev[1], Y.I. Golovin[1,2], A.G. Majouga[3,4,1], A.V. Kabanov[2,5], N.L. Klyachko[2,5]
[1] Nanocenter, G.R. Derzhavin Tambov State University, Tambov, Russian Federation
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[4] National University of Science and Technology MISIS, Moscow, Russian Federation
[5] Center for Nanotechnology in Drug Delivery, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

17.40-18.00 BREAK

18.00-18.20 NEW HYBRID MATERIALS BASED ON GOLD AND MAGNETITE NANOPARTICLES, MODIFIED BY BIFUNCTIONAL ORGANIC LIGANDS: SYNTHESIS, PROPERTIES, APPLICATION

P.G. Rudakovskaya[1,2], M.V. Efremova[3], O.M. Metelkina[3], N.L. Klyachko[3], U.I. Golovin[4], I.A. Ananieva[3], A.G. Majouga[2,3]
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[2]D. Mendeleev University of Chemical Technology of Russia, Russian Federation
[3]M.V. Lomonosov Moscow State University, Chemistry Department, Russian Federation
[4]Derzhavin Tambov State University, Russian Federation

18.20-18.40 INFLUENCE OF RECOMBINANT INTERLEUKIN-1 BETA ON BLOOD- BRAIN BARRIER PERMEABILITY IN EXPERIMENTAL GLIOMA MODELS

I.I. Kuznetsov[1,2], M.P. Valikhov[1], P.A. Melnikov[1], T.O. Abakumova[3], A.S. Semkina[1,4], D.A. Vishnevskiy[4], N.F. Grinenko[1], A.S. Simbircev[5], V.P. Chekhonin[1], N.L. Klyachko[2,3]
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[2]Department of Chemistry, Lomonosov Moscow State University, Moscow, Russian Federation
[3]Skolkovo Institute of Science and Technology, Moscow, Russian Federation
[4]Medicobiologic faculty, Pirogov Russian National Research Medical University, Moscow, Russian Federation
[5]Research Institute of Highly Pure Biopreparations, St. Petersburg, Russian Federation

Tuesday, May 8, 2018

18.40-19.00 **ANALYSIS OF CARBOHYDRATES-LINKED LIGANDS MOLECULAR INTERACTIONS WITH HUMAN LIVER ASIALOGLYCOPROTEIN RECEPTOR IN VITRO USING SPR SPECTROSCOPY**

A.V. Lopukhov[1], I.I. Kuznetsov[1,2], P.V. Binevski[1], S.Y. Maklakova[1], R.A. Petrov[1], I.V. Uporov[1], A.G. Majouga[4,5,1], N.L. Klyachko[1]

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19.00-20.00 **DINNER**

Wednesday, May 9, 2018

08.00-09.30 **BREAKFAST**

09.30-13.00 **MORNING SESSION**

Chairmen: Prof. V.Z. Lankin, Prof. V.N. Rakitskii

09.30-10.00 **CAFFEINE AFFECTS BREAST CANCER CELL ADHESION INDEPENDELY OF THEIR ESTROGEN RECEPTOR EXPRESSION STATUS**

Ei. Giatagana, K. Voudouri, S. Ftika, A. Berdiaki, D. Nikitovic, G.N. Tzanakakis

Laboratory of Anatomy-Histology-Embryology, Faculty of Medicine, University of Crete, Heraklion, Greece

10.00-10.30 **NEW 1,2,3-TRIAZOLE CONTAINING POLYMERS VIA CLICK STEP- GROWTH POLYMERIZATION**

R. Katsarava, Teng. Kantaria, Tem. Kantaria, N. Zavradashvili, D. Tugushi

Institute of Chemistry and Molecular Engineering, Agricultural University of Georgia, Georgia

10.30-11.00 **ANTIMICROBIAL (NANO)MATERIALS: USE, EFFICIENCY AND SAFETY ASPECTS**

A. Kahru[1,2], A. Ivask[1], O. Bondarenko[1], K. Kasemets[1], M. Ahonen[3]

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[2]Academy of Sciences, Kohtu 6, Tallinn, Estonia

[3]Faculty of Technology, Satakunta University of Applied Sciences, P.O. Box 211, FI-26101 Rauma, Finland

11.00-11.30 **NANOTOXICOLOGY IN BELARUS. ACHIEVEMENTS, PROBLEMS**

S.I. Sychyk, I.I. Ilyukova

Republican Unitary Enterprise "Scientific and Practical Center for Hygiene", Minsk, Republic of Belarus

11.30-12.00 **COFFEE BREAK - POSTER SESSION**

Wednesday, May 9, 2018

Chairmen: Prof. Yu.A. Vladimirov, Prof. M.I. Gladyshev

12.00-12.30 **ORGANIZATIONAL ASPECTS OF PREPAREDNESS TO EMERGENCY MEDICAL RESPONSE IN CHEMICAL ACCIDENTS**

G. Prostakishin, S. Sarmanaev

ARCDM "Zaschita" Moscow, Russian Federation

12.30-13.00 **EFFICENECY AND SAFETY OF NANO-ENABLED TEXTILES FOR ANTIMICROBIAL APPLICATION**

K. Kasemets[1], I. Perelshtein[2], A. Gedanken[2], J. Wang[3,4], P. Mantecca[5]

[1]Labortory of Environmental Toxicology, National Institute of Chemical Physics and Biophysics, Estonia
[2]Department of Chemistry and Nanomaterials, Bar-Ilan University, Israeli
[3]Laboratory for Advanced Analytical Technologies, Empa, Dübendorf, Switzerland
[4]Institute of Environmental Engineering, ETH Zurich, Switzerland
[5]Department of Earth and Environmental Sciences, University of Milano- Bicocca, Italy

INVESTIGATION OF THE MECHANISM OF PEROXIDASE REACTIONS CATALYZED BY THE COMPLEX OF CYTOCHROME C WITH CARDIOLIPIN BY MEANS OF KINETIC CHEMILUMINESCENCE

G.K. Vladimirov

Shubnikov Institute of Crystallography of Federal Scientific Research Centre "Crystallography and Photonics" of Russian Academy of Sciences, Moscow, Russian Federation

13.00-14.00 **LUNCH**

14.00-19.00 **BREAK**

19.00-20.00 **DINNER**

Thursday, May 10, 2018

08.00-09.00 **BREAKFAST**

10.00-13.00 **MORNING SESSION**

Chairmen: Prof. Y.I. Golovin, Prof. V.Z. Lankin

09.30-10.00 **ELECTROSPINNING OF POLYHYDROXYALKANOATE FIBROUS SCAFFOLDS: EFFECTS OF ELECTROSPINNING PARAMETERS ON STRUCTURE AND PROPERTIES**

E. Shishatskaya[1,2], D. Goncharov[2], T. Volova[1,2]

[1]Siberian Federal University, Krasnoyarsk, Russian Federation
[2]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Akademgorodok, Krasnoyarsk, Russian Federation

10.00-10.30 **POLYVINYL ALCOHOL MACROPOROUS HYDROGELS AS NEW MATERIALS FOR MEDICINE**

A.A. Artyukhov[1], M.I. Shtilman[1], A.I. Piskareva[1], D.E. Lisovyy[1], S.M. Chudnykh[2]

[1]Mendeleyev University of ChemicalTechnology of Russia, Moscow, Russian Federation
[2]Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation

Thursday, May 10, 2018

10.30-11.00 **DEVELOPMENT OF SELF-ASSEMBLED AMPHIPHILIC POLY-N- VINYLPYRROLIDONE NANOPARTICLES AS A STABLE DRUG DELIVERY SYSTEM**

A.N. Kuskov, P.P. Kulikov, A.L. Luss, A.V. Goryachaya, M.I. Shtilman
Department of Biomaterials, D.Mendeleev University of Chemical Technology of Russia, Miusskaya sq 9, Moscow, Russian Federation

11.00-11.30 **DEVELOPMENT OF SELF-ASSEMBLED AMPHIPHILIC POLY-N- SCANNOING ION CONDUCTANCE MICROSCOPY AS A NEW METHOD FOR NANOPARTICLE RESEARCH**

P.V. Gorelkin[1], A.S. Erofeev[2,6], A.V. Komarova[1,2], A.S. Garanina[2,6], M.A. Abakumov[6], A.O. Prelovskaya[1,6], A.A. Nikitin[1,6], E.V. Dubrovin[2], T.O. Abakumova[2,6], N.L. Klyachko[1,2], A.G. Majouga[2], P. Novak[3], A.I. Shevchuk[4], C. Edwards[5], Y.E. Korchev[4]
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[4]Imperial College London, United Kingdom
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[6]The National University of Science and Technology "MISiS", Moscow, Russian Federation

11.30-12.00 **COFFEE BREAK - POSTER SESSION**

12.00-12.30 **MULTIFUNCTIONAL MAGNETIC NANOPARTICLES IN TUMOR TERAPY AND DIAGNOSTICS**

M. Abakumov[1,2], A. Majouga[2,3,5], A. Kabanov[3,4], V. Chekhonin[1]
[1] Department of Medical Nanobiotechnology, Russian National Research Medical University, Moscow, Russian Federation
[2] Laboratory "Biomedical Nanomateials", NUST "MISiS", Moscow, Russian Federation
[3] Chemistry Department, MSU, Moscow, Russian Federation
[4] Eshelmal School of Pharmacy, University of North Carolina, Chapel Hill, USA
[5] D.Mendeleyev University of Chemical Technology of Russia, Moscow, Russian Federation

12.30-13.00 **ASSESSMENT OF PEGYLATED CdSe/ZnS QUANTUM DOTS CYTOTOXICITY IN VITRO**

S.V. Bozrova[1], M.A. Baryshnikova[1,2], Z.A. Sokolova[1,2], I.R. Nabiev[1,3] and A.V. Sukhanova[1,3]
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13.00-14.00 **LUNCH**

14.00-19.00 **BREAK**

19.00-20.00 **DINNER**

Friday, May 11, 2018

08.00-09.00	**BREAKFAST**
09.30-11.30	**MORNING SESSION**
	Chairmen: Prof. M.I. Shtilman, Prof. E.A. Markvicheva
09.30-10.00	**OXIDATIVE POLYMERIZATION IN NANOSIZED SYSTEMS** Ya.O. Mezhuev, S.E. Pokhil, I.V. Plyuschiy, A.L. Luss, Yu.V. Korshak, M.I. Shtilman *D. Mendeleev University of Chemical Technology of Russia, Moscow, Russian Federation*
10.00-10.30	**PPREPARATION OF CARBON QUANTUM DOTS FOR FLUORESCENCE DETECTION OF CU(2+) IONS** S.A. Eremin, A.S. Yakusheva, D.V. Kuznetsov *National Research Technical University "MISiS", Leninsky Prospekt 4, Moscow, Russian Federation*
10.30-11.00	**NANOCARRIERS FOR ANTICANCER DRUG DELIVERY: PREPARATION AND EVALUATION IN 3D IN VITRO MODEL** E. Markvicheva, A. Gileva, A. Akasov *Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Rus Acad Sci., Moscow, Russian Federation*
11.00-11.30	**TOLL LIKE RECEPTOR 4 (TLR4) AFFECTS HYALYURONAL METAMOLISM IN CONTACT ALLERGY** R.M. Kavasi, G. Fanouraki, A. Berdiaki, I. Spyridaki, G.N. Tzanakakis, D. Nikitovic *Laboratory of Anatomy-Histology-Embryology, Faculty of Medicine, University of Crete, Heraklion, Greece*
11.00-11.30	**BREAK**
	CLOSING CEREMONY **Farewell Address – Closing Remarks**
13.00-14.00	**LUNCH**
19.00-22.00	**FAREWELL DINNER**

Saturday, May 12, 2018

08.00-09.00	**BREAKFAST**
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08.00-09.00	**BREAKFAST**
	Departure of Participants

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M. Tawfik[1], L. Grigartzik[1], M.V. Sokolov[1], P. Kulikov[2,3], M.I. Shtilman[2,3], A. Tsatsakis[3], B.A. Sabel[1], P. Henrich-Noack[1]
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P 02 IN VIVO IMAGING OF BLOOD BRAIN BARIER PASSAGE OF MOIETY LABELLED POLYMERIC NANOPARTICLES

M. Tawfik[1], M. Sokolov[1], L. Grigartzik1, P. Kulikov[2], A. Kuskov[2], M. Shtilman[2], B.A. Sabel[1], P. Henrich-Noack[1]
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P 03 IN VIVO BRAIN DISTRIBUTION PATTERN OF COUMARIN6-SIGNAL AFTER INJECTION INTO RODENTS IN A PLGA-NANOPARTICLE FORMULATION

E. Zhang[1], L. Grigartzik[1], M.V. Sokolov[1], N. Osipova[2], V. Zhukova[2], O. Maksimenko[2], S. Gelperina[2], A. Tsatsakis[3], B.A. Sabel[1], P. Henrich-Noack[1]
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[3]ToxPlus SA, Heraklion, Greece

P 04 INFLUENCE OF MILD TRAUMATIC OPTIC NERVE INJURY ON BLOOD-BRAIN BARRIER PASSAGE OF PVP-NANOPARTICLES

M. Tawfik[1], L. Grigartzik[1], M.V. Sokolov[1], P. Kulikov[2], M.I. Shtilman[2], A. Tsatsakis[3], B.A. Sabel[1], P. Henrich-Noack[1]
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P 05 ELABORATION OF BIODEGRADABLE POLY(ESTER AMIDE) NANOPARTICLES FOR OCULAR DRUG DELIVERY AND IN VIVO PRELIMINARY STUDY OF THEIR PERMEABILITY INTO THE OCULAR BARRIERS

D. Tugushi[1], Tem. Kantaria[1], Teng. Kantaria[1], S. Kobauri[1], A. Kezeli[1], G. Chichua[1], W. Zhang[2], N. Eter[2], P. Heiduschka[2], R. Katsarava[1]
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Acknowledgement: This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) [FR17_102, Elaboration of Biodegradable Nanocarriers for Ocular Drug Delivery]

P 06 PRODUCTION AND CHARACTERIZATION OF PHA FROM BIODIESEL-GLYCEROL BY CUPRIAVIDUS EUTROPHUS B10646

A. Demidenko[1,2], E. Kiselev[1,2], T. Volova[1,2]
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P 07 PROPERTIES OF PHA BI-, TER-, AND QUARTER-POLYMERS CONTAINING 4-HYDROXYBUTYRATE MONOMER UNITS

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P 08 SPHEROIDIZED GLASS-BASED MATERIALS FOR TARGETED DELIVERY OF DRUGS AND RADIOPHARMACEUTICALS

V.N. Sigaev, G.Yu. Shakhgildyan, V.I. Savinkov, E.E. Stroganova
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N.S. Markvichev[1], E.E. Savelyeva[1], E.E. Dosadina[2], A.A. Khanafina[1], A.A. Vaniushenkova[1], L.L. Brkich[3], V.I. Panfilov[1], A.A.Belov[1]

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P 10 LIPOAMINO ACID-BASED CERASOMES FOR ANTICANCER DRUG DELIVERY: PREPARATION AND EVALUATION IN 3D IN VITRO MODEL

A. Gileva[1], G. Sarychev[2], U. Kondrya[2], M. Mironova[2], U. Budanova[2], Yu. Sebyakin[2], E. Markvicheva[1]

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P 11 POLYMERIC NANOPARTICLES BASED ON AMPHYPHILIC DERIVATIVES OF N-VINYL-2- PYRROLIDONE CONJUGATED WITH ANTITUMOR CYTOKINE TRAIL DR5-B

A.V. Yagolovich[1], P.P. Kulikov[2], A.N. Kuskov[2], E.A. Markvicheva[1]

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P 12 MACROPOROUS HYDROGELS BASED ON GRAFT COPOLYMERS OF CHITOSAN WITH OLIGO (L, L- / L, D-LSCTIDES) FOR REGENERATIVE MEDICINE

T.V. Balabanova[1,2], M.A. Stroilova[1,2], M.G. Drozdova[1], T.S. Demina[3], Yu.S. Sotnikova[3], A.V. Istomin[3], T.A. Akopova[3], E.A. Markvicheva[1]

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P 13 PREPARATION OF 3D-SCAFFOLDS BASED ON CHITOSAN MODIFIED BY CHEMICAL CROSS-LINKING

N.A. Sazhnev[1], M.G. Drozdova[2], N.R. Kildeeva[1], E.A. Markvicheva[2], V.I. Lozinsky[3]

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Usvaliev A.D.[1], Nikitin A.V.[1,2], Rudakovskaya P.G.[5], Gribanovsky S.L.[3], Ghigachev A.O.[3], Legotsky S.A.[1], M.M. Veselov[1], A.V. Lapankova[1], K.A. Miroshnikov[4], E.A. Zaitseva[1], A.G. Majouga[5,2,1], Yu.I. Golovin[1,3], A.V. Kabanov[1,6], N.L. Klyachko[1,6]

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The work was supported by RSF-14-13-00731П and RFBR 17-54-33027 ОНКО_а grants.

P 15 STAPHYLOCOCCUS AUREUS LYTIC ENZYMES KINETICS STUDIES

G.P. Emelyanov[1], L.Y. Filatova[1], D.M. Donovan[2], V.G. Pugachev[3], N.L. Klyachko[1,4]

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A. Sapach[1,2], A. Gileva[2], E. Shmendel[3], O. Koloskova[3], E. Markvicheva[2]

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P 17 POLY(N-VINYLPYRROLIDONE) NANOPARTICLES LOADED WITH DNA PLASMIDS ENCODING GLYCOPROTEINS AGAINST RVF VIRUS

O. Selina[1], A. Kuskov[2], P. Kulikov[2], V. Balysheva[3], M. Shtilman[2], E. Markvicheva[1]

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P 18 COMPOSITE CROSS-LINKED HYDROGELS BASED ON POLYSACCHARIDES AND FIBROIN FOR REGENERATIVE MEDICINE

M. Stroilova[1,2], T. Balabanova[1,2], M. Drozdova[2], M. Chernogortseva[3], N. Sazhnev[3], T. Demina[4], S. Uspensky[4], N. Kildeeva[3], E. Markvicheva[2]

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P 19 CYTOTOXICITY OF NEW BEXAROTENE DERIVATIVES FOR RAT GLIOMA C6 AND HUMAN GLIOMA U-87MG CELLS

A.M. Ashba[1], M.G. Akimov[1], R.A. Akasov[1,2], N.M. Gretskaya[1], V.V. Bezuglov[1], E.A. Markvicheva[1]

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P 20 ENCAPSULATION OF P140 PEPTIDE-HYALURONIC ACID COMPLEX FOR LUPUS ERYTHEMATOSUS TREATMENT

A. Khovankina[1,2], C. Amine[1], E. Markvicheva[2], D. Poncelet[1]

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P 21 DIHYDROQUERCETIN POLYMERIZATION USING MULTICOPPER OXIDASES

M.E. Khlupova[1], I.S. Vasileva[1], G.P. Shumakovich[1], O.V. Morozova[1], E.A. Zaitseva[2], V.A. Chertkov[3], A.K. Shestakova[1], A.V. Kisin[4], K.V. Lisitskaya[1], A.I. Yaropolov[1]

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P 22 EXPERIENCE OF THE STUDY ON THE EXPERIMENTAL MODELS IN VITRO TOXIC PROPERTIES OF NANOMATERIALS IN BELARUS

M.V. Anisovich, I.I. lyukova

Republican Unitary Enterprise "Scientific and Practical Center of Hygiene", Minsk, Republic of Belarus
The aim of the study was to develop methodological approaches for assessment of nanosafety in Belarus

P 23 STUDY OF TOXICOLOGICAL PROPERTIES OF MICROFERTILIZERS "NANOPLANT" IN EXPERIMENTS IN VITRO

E.S. Yurkevich[1], M.V. Anisovich[1], S.G. Azizbekyan[2]

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P 24 ECOTOXICOLOGICAL RESEARCH OF MICROWAVES "NANOPLANT"

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P 25 STUDY OF THE TOXICOLOGICAL PROPERTIES OF MICROFERTILIZER "NANOPLANT" IN EXPERIENCE IN VIVO

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M. Veselov[1], M.A. Tagirova[1], M.V. Efremova[1,2], I.A. Barakovskaya[2], F. Secundo[3], A.G. Majouga[4,2,1], Yu.I. Golovin[1,5], N.L. Klyachko[1]

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P 27 HEAT-RRESISTANT COMPOSITION

N. Ormotsadze[1], M. Meskhishvili[1], D. Bibileishvili[2]

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P 28 pH-SENSITIVE LIPOSOMAL NANOCONTAINERS

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P 29 THERMO-INDUCED SHRINKING OF POLYMER MULTILAYER CAPSULES MODIFIED WITH MAGNETIC NANOPARTICLES

A.S. Burova[1,2], D.B. Trushina[2,3,4], T.V. Bukreeva[2,4], T.N. Borodina[2,3]

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P 30 SYNTHESIS AND PROPERTIES OF AMPHIPHILIC POLYMERS OF ACRYLIC ACID

O.Yu. Sizova, A.L. Luss, V.T. Dzhedzheia, M.I. Shtilman, D. Borozdina, Yu.V. Korshak, Ya.O. Mezhuev

D. Mendeleev University of Chemical Technology of Russia, Moscow, Russian Federation

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M.V. Stenkina, S.V. Osadchenko, M.I. Shtilman, A.L. Luss, Ya.O. Mezhuev

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M.I. Shtilman[1], A.N. Kuskov[1], A.V. Goryachaya[1], G.I. Kandelaki[1], Ya.O. Mezhuev[1], V.T. Dzhedzheya[1], A.M. Tsatsakis[2], V.N. Rakitskii[3]

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A.V. Varankin, Ya.O. Mezhuev, M.I. Shtilman, Yu.V. Korshak

D. Mendeleev University of Chemical Technology of Russia, Moscow, Russian Federation

P 34 POLYMERIC MACROPOROUS POLYVINYL ALCOHOL HYDROGELS FOR MICROSURGICAL RECONSTRUCTION OF THE SPINAL CORD

A. Dekopov[1], A. Artyukhov[2], E. Salova[1], A. Piskareva[2], L. Bryukhanov[2], K. Kushneryov[2], A. Tomskiy[1], M. Shtilman[2]

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M. Rodin[1,2], A. Artyukhov[1], N. Mustafaev[1], V. Muravieva[3], T. Priputnevich[3], M. Shtilman[1]

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P 36 POLYMER CATHETERS WITH AN ANTIMICROBIAL SURFACE

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A.L. Luss[1], P.P. Kulikov[1], M.I. Shtilman[1], P.G. Tzanakakis[2], Ya.O. Mezhuev[1], A.M. Tsatsakis[2]

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V. N. Rakitskii

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P 39 CULTIVATION OF MESENCHYMAL STEM CELLS WITH LIF AND FGF

I.S. Kashapova, G.Yu. Kosovsky

Federal State Budget Scientific Institutie "Scientific Research Institute of Fur-Bearing Animal and Rabbit Breeding Industries n.a. V.A. Afanasyev" (FSBSI NIIPZK)

P 40 ENZYMATIC DESTRUCTION OF THE CAPSULES BASED ON POLYELECTROLYTE COMPLEX "POLYPEPTIDE / POLYSACCHARIDE"

D.A. Shepelenko[1,2], D.B. Trushina[2,3,4], T.V. Bukreeva[2,4], T.N. Borodina[2,3]

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T.M. Razheva[1], E.A. Podorozhko[2]
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M.N. Chernikova[1], O.V. Zaborova[2]
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E.O. Batyrbekov[1], A.E.Borisova[2]
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[2]*Kazakh-British Technical University, Almaty, Kazakhstan*

P 44 FUNCTIONAL MATERIALS BASED ON BIOPOLYMERS FOR MEDICAL APPLICATIONS
E.N. Glazacheva, M.V. Uspenskaya, N.D. Pastukhova, R.O. Olekhnovich, P.P. Snetkov
ITMO University, Saint-Petersburg, Russian Federation

P 45 CROSSLINKED CHITOSAN/PVA FILM BASED ON 5- FLUOROURACIL
A.B. Ismailova[1,2], E.O. Batyrbekov[2], A.T. Zamanbekova[1]
[1] *Kazakh Leading Academy of Architecture and Civil Engineering, Almaty, Kazakhstan*
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P 46 POLYMER INFLUENCE ON THE CATALYTIC ACTIVITY OF SUPPORTED POLYMER- PROTECTED NICKEL CATALYSTS FOR THE HYDROGENATION PROCESS OF ACETYLENE ALCOHOLS
A. Zharmagambetova[1], A.T. Zamanbekova[1,2], A.B. Ismailova[2]
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P 47 DEPOSITION OF CHITOSAN ONTO POLYLACTIDE FILMS USING VARIOUS METHODS
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P 48 DIFFERENTLY FUNCTIONALIZED CUO NANOPARTICLES: EFFICIENT ANTIMICROBIALS OR THE POISON TO HUMAN MACROPHAGES
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O 01

RECENT DEVELOPMENTS IN LIPOSOMAL NANOPREPARATIONS AGAINST CANCER

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Liposomal formulations of various anti-cancer drugs are still causing great interest from pharmaceutical scientists. Both, non-targeted and targeted liposomal dosage forms are under development. Some of those will be discussed here.
Glioblastomas (GBMs) are highly aggressive brain tumors with a very grim prognosis even after multi-modal therapeutic regimens. Resveratrol (RES), a natural polyphenol with pleiotropic health benefits, has proven chemopreventive effects in all the stages of cancer including initiation, promotion and progression. However, the poor physico-chemical properties of RES severely limit its use as a free drug. To counter its drawbacks as a free drug, RES was loaded into PEGylated liposomes (RES-L). Since transferrin receptors (TfRs) are up-regulated in GBM, the liposome surface was modified with transferrin moieties (Tf-RES-L) to make them cancer cell-specific. The RES-L were stable, had a good drug-loading capacity, prolonged drug-release in vitro and were easily scalable. As shown by flow cytometry and confocal microscopy with U-87 MG cells, the Tf-RES-Ls were significantly more cytotoxic and induced higher levels of apoptosis accompanied by activation of caspases 3/7 in GBM cells compared to free RES or RES-L. The ability of RES to arrest cells in the S-phase of the cell cycle, and selectively induce production of reactive oxygen species in cancer cells are responsible for its cytotoxic effects. In a subcutaneous xenograft mouse model of GBM, a tumor growth inhibition study and a modified survival study showed that Tf-RES-Ls were more effective than other treatments in their ability to inhibit tumor growth and improve survival in mice.
Among many approaches for active tumor-targeting, arginine-rich cell penetrating peptides (such as octaarginine, R8) and ligands specific to target over-expressed receptors on cancer- cell surfaces, are popular. We have prepared doxorubicin(DOX)-loaded liposomes, surface- modified with, R8 and transferrin (Tf) (Dual DOX-L), to improve targeting of A2780 ovarian carcinoma cells via the over-expressed transferrin receptors (TfRs) with the subsequent R8- mediated intracellular DOX delivery. Flow cytometry analysis with fluorescently-labelled DualL showed 2-fold higher cancer-cell association than other treatments after 4 h treatment. Blocking entry pathways of R8 (macropinocytosis) and Tf (receptor-mediated endocytosis, RME) resulted in a decreased cancer-cell association of DualL. Confocal microscopy confirmed involvement of both entry pathways and cytoplasmic liposome accumulation with nuclear DOX delivery for Dual DOX-L. Dual DOX-L exhibited enhanced cytotoxicity *in vitro* and was most effective in controlling tumor growth in vivo in an A2780 ovarian xenograft model compared to other treatments.

O 02

THE ROLE OF NON-HEME IRON IN CHAIN LIPID PEROXIDATION IN INTRACELLULAR MEMBRANES AND IRON-DEPENDENT PROGRAMMED CELL DEATH (FERROPTOSIS)

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In a long series of experiments, we showed that Fe^{2+} initiate chain lipid peroxidation in mitochondrial, microsomal, and phospholipid membranes in reaction of chain branching, in which the substrate is the phospholipid hydroperoxide LOOH, and lipid free radical $LOO^{\bullet}$ is the product. The reaction kinetics was investigated by measuring weak chemiluminescence (CL) associated with interaction of two $LOO^{\bullet}$ radicals. Later we used several coumarine derivatives that enhanced the CL emission quantum yield in order to measure more accurately the CL kinetics. The length of the chain was determined in mitochondrial and microsomal membranes; it reached several dozens of coins, depending on the Fe^{2+} concentration and other antioxidants. It was also shown that both Fe^{2+} and Fe^{3+} present in cytoplasm at low concentrations, sufficient for prooxidant action of iron ions. The possibility of interaction of Fe^{2+} with a polar group attached to different carbon atoms of fatty acid chains in the lipid bilayer was demonstrated and explained by the transmembrane diffusional motion of the chains resulted in collision of surface- bound Fe^{2+} with the group.
In view of these data, the molecular mechanism of iron-dependent programmed cell death (ferroptosis) is essentially the total lipid peroxidation in any intracellular membrane where (1) some amount of free Fe^{2+} does occur and (2) a trace quantity of lipid hydroperoxide appear as a result of insufficient activity of phospholipid glutathione peroxidase-GSH system. All other known factors affecting ferroptosis perform their action via disbalance between Fe^{2+} and GSH in this locus.

O 03

MOLECULAR PHYSIOLOGY AND PATHOLOGY (CATARACT) OF THE LENS OF THE EYE: α-CRYSTALLIN AS A CHAPERONE LIKE DRUGS

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The major lens protein α-crystallin together with ß- and γ-crystallins ensures transparency of the lens. The clouding of the lens (cataract) is due to aggregation of crystallins, mainly ß- and γ- crystallins. The ability of crystallins to aggregation, for example to UV-induced aggregation, is rises in a row: γ-crystallins > ß-crystallin > > α-crystallin [1, 2]. In case of age-related modification, the ability of crystallins to aggregation is increased. We have demonstrated such increasing of N-terminal extension truncated recombinant ßA3-crystallin to

UV light-induced photo-aggregation [3].
α-Crystallin belongs to the small heat shock protein family. As a chaperone-like protein, it prevents age clouding of the lens (cataract) by preventing the aggregation of the proteins damaged by post-translational modifications, for example by UV-irradiation [2], temperature increasing [4], etc.
Mechanism of chaperone-like activity of α-crystallin is far from understanding.
We have used UV-damaged $ß_L$-crystallin as a target protein for the chaperone-like activity study of α-crystallin [6,7]. Mixture of α-crystallin and UV$ß_L$-crystallin (5:1, mol/mol) was incubated at 37° C for 0.33, 2, 24, and 72 hours and studied using SEC, SDS PAGE, AUC, and DSC. We have shown that α-crystallin and UV$ß_L$-crystallin form dynamic complexes with a mass of 75 to several thousand kDa. Mass of complexes grows with time of incubation. The content of UV$ß_L$-crystallin in in complex increases with a mass of complex. Complexes containing more than 10% UV$ß_L$-crystallin were prone to precipitation whereas complexes containing less than 10% target protein is relatively stable. Refolding of denatured UV$ß_L$-crystallin was not observed under incubation with α-crystallin.
The results clearly demonstrate that UV$ß_L$-crystallin forms the low molecular weight complex with monomer of α-crystallin. We suppose that α-crystallin dissociation is a result of interaction with a large amount of target protein in the incubation mixture *in vitro*. However, in the lens in- vivo the ratio of the number of damaged molecules to b-crystallin is unlikely to reach the value. That is why there is not α-crystallin oligomer dissociation in vivo since there is not interaction of α-crystallin oligomer with a large amount of target protein in vivo. We suggest that in the lens the rare damaged molecules (ß-, and γ- crystallins mainly) form the complexes with the α- crystallin oligomer by collision. The formed complex will be rearranged due to the exchange of subunits within the α-crystallin oligomer. As a result, the target protein will be surrounded by the chaperone monomers and will be in the center of the complex. As a result, the transparency of the optical medium of the lens *in-vivo* is maintained.
We have also shown that a mixture of peptides (N-acetylcarozine and D-pantetine) enhances the chaperone-like effect of α-crystallin. So, this mixture of peptides can be considered as potential chaperone-like anticataract drugs [8, 9].

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O 04

ASTROBIOLOGY: THE PRIMARY PROCESSES

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The physical and chemical grounds for primary synthesis and evolution of macromolecules as the basis of life origin at different conditions are discussed. The thermocycling with reactions of polycondensation of monomers and hydrolysis of the unstable structures is the physical basis for evolutionary combinatorics and selection.
The problems under consideration:
The temperature limits of life from the point of view of polymer chemistry and stability of polymers.
Limits of rates under different conditions.
Co-existence of three polymeric worlds: protopeptides, protoRNA and protoRNA.
Catalysis and kinetic principles of primary evolution. The basis of exponential growth.
Hirality: the kinetic exploration.
Exthermophilic forms of life on Earth.
Several aspects of discussed problems are illustrated by experimental data. So, the basic conditions for origin of life and evolution to biological forms are:
The existence of three functional monomers with part of molecules "recognizing" each other by supramolecular interactions.
Thermocycling as basis for synthesis and evolutionary combinatorics.
Several types of co-existing macromolecules with catalytic and proliferational properties.
Catalysis by polymeric molecules as basis for rapid and exponential growth of selected macromolecules.
If these three conditions take place, the origin of polymeric proliferation systems (life origin) is determinated and the development of "life system" is the problem of time. The "life system" can be constructed from the absolutely different "chemical bricks" if we compare these systems with the life on Earth.

O 05

CHOLESTEROL - LOWERING THERAPY AND NATURAL LIPID TRANSPORTING NANOSTRUCTURES OF BLOOD PLASMA (LOW DENSITY LIPOPROTEINS) FREE RADICAL PEROXIDATION

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Objectives. To study the effect of therapy of patients with coronary artery disease by statins or protein convertase subtilisin/kexin tipe 9 (PCSK9) inhibitor on the level of oxidatively modified low-density lipoprotein (LDL) from blood plasma (or concentration lipohydroperoxides in LDL) and the activity of erythrocyte Se-containing glutathione peroxidase (GSH-Px).
Subjects and methods. Patients with coronary artery disease (10 men per group) were included in the study, who underwent therapy for a 6-month period including statins - 40 mg/day of pravastatin (group 1) or 0.4 mg/day of cerivastatin (group 2), as well as therapy with the inclusion of the inhibitor PCSK9 - 420 mg/month evolocoumab (group 3) for 1 year. The level of lipohydroperoxides in LDL (LOOH-LDL) was measured in groups 1 and 2 by a modified method using the Fe-xylenolorange reagent; the content of oxidatively modified LDL (ox-LDL) in group 3using the immunochemical method by Mercodia Oxidized LDL ELISA (Sweden). GSH-Px activity in all groups was determined by a modified method with glutathione reductase system using tert-butyl hydroperoxide as a substrate.
Results. Simultaneously with the decrease in LDL cholesterol (LDL-C) in groups 1 and 2 was significantly increased (group 2 - in 6-7 times after 3-6 months of therapy) LOOH-LDL level. In group 2 there was a sharp drop in GSH-Px activity, starting from the 3rd month of therapy. In group 3, when there was a decrease in the concentration of LDL-c, a significant decrease in the level of ox-LDL was observed in the absence of changes in GSH-Px activity.
Conclusion. Statins, while effectively reducing the level of LDL-C, simultaneously induce oxidative atherogenic modification of LDL and decrease activity of antioxidant enzyme GSH-Px. PCSK9 inhibitor not only effectively reduces the level of LDL-C but also reduces the content of ox-LDL without decreasing in GSH-Px activity.
The work was carried out with financial support of Russian Science Foundation grant No. 14-15- 00245P.
Main publications: Lankin V. et al., in: Handbook of Lipoprotein Res. 2010, Nova Sci.Pub., 85-107; Lankin VZ et al., Mol Cell Biochem 2014, 395(1-2): 241-252; Lankin VZ et al., J.Diabetes 2015, 8(3): 398-404; Lankin VZ, Tikhaze AK. Curr Aging Sci. 2017, 10(1): 18-25.

O 06

ORGANIZATIONAL ASPECTS OF PREPAREDNESS TO EMERGENCY MEDICAL RESPONSE IN CHEMICAL ACCIDENTS

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Appropriate information on the accidents risks, assessment of probable accident scale and value of health response is the basis for preparedness of medical institutions and out-staff units to emergency medical response. This information is necessary to provide preparedness of man power and resources to acute chemical trauma medical response.
It is necessary to develop plans to deliver emergency health care.
We developed and approved official methodical materials to arrange and deliver care in acute chemical trauma health response. These documents present modern ideas to appropriate health care in chemical accidents, identify parameters of chemicals toxicity, requirements to chemical pollution monitoring, protective measures, decontamination, medical triage, poisoning and antidote therapy etc.
During accidents one of the most urgent issues is prompt identification of chemical agent and degree of its exposure, which is necessary to know to take optimum decisions to deliver medical care.
Emergency medical care to the injured is delivered in two stages: pre-hospital and hospital. Prehospital stage is the most difficult for emergency health procedures and it is realized by mobile medical units.
Inpatient treatment of patients with acute chemical trauma is given in the special centres for acute poisoning treatment. However, these centres have different status (from independent specialized institutions to departments in city hospitals).
In lack of clinical toxicologists very often emergency medical care is delivered by therapists and resuscitators-anesthesiologists. That is why post-graduate training of medical personnel in toxicology is so important.

O 07

NEW 1,2,3-TRIAZOLE CONTAINING POLYMERS VIA CLICK STEP-GROWTH POLYMERIZATION

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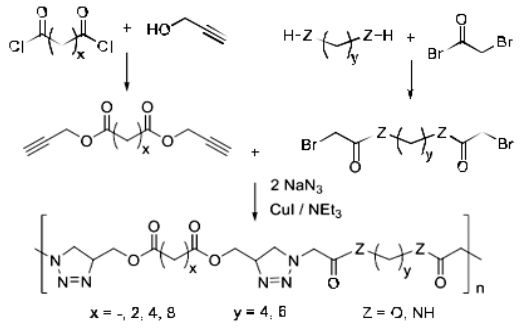
AA-BB-type aliphatic polyesters were synthesized via Cu(I)-catalyzed click step-growth polymerization (SGP) following a new synthetic strategy. The synthesis was performed between diyne and diazide monomers in an organic solvent as one pot process using three components and two stages. The di-propargyl esters of dicarboxylic acids (component 1) were used as diyne monomers, di-(bromoacetic acid)-alkylene diesters (component 2) were used as precursors of diazide monomers, and sodium azide (component 3) was used for generating diazide monomers. The SGP was carried out in two steps: at the Step-1 di-bromoacetates interacted with two moles of sodium azide resulting in diazide monomers which interacted *in situ* with diyne monomers at the Step-2 in the presence of Cu(I) catalyst. A systematic study was done for optimizing the multiparameter click SGP in terms of the solvent, duration of the both Step- 1 and Step-2, solution concentration, catalyst concentration, catalyst and catalyst activator (ligand) nature, catalyst/ligand mole ratio, temperature of the both steps of the click SGP. As a result, high-molecular-weight (MW up to 74 kDa) elastic film-forming click polyesters and poly(ester



Scheme 1. Synthesis of 1,2,3-triazole cycles-containing polyesters and poly(ester amide)s

amide)s (Scheme 1) were obtained. The "clicking" polymers revealed improved thermal properties compared to their regular analogues. The new polyesters are promising for practical applications in medicine, agriculture, food industry as biodegradable (bioresorbable) materials, as environmentally friendly polymers, etc. One of the important advantages of the obtained 1,2,3-triazole-containing polyesters is the possibility of quaternization of 1,2,3-triazole cycles that opens a way to cationic polymers – both water soluble ones and cross-linked cationic hydrogels promising for numerous biomedical applications. The new polymers were also found suitable for fabricating biodegradable nanoparticles, including positively charged ones, promising as drug delivery containers in nanotherapy, e.g. for ocular drug delivery, etc.

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O 08

ANTIMICROBIAL (NANO)MATERIALS: USE, EFFICIENCY AND SAFETY ASPECTS

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Hospital-aquired infections and spreading of infectious diseases are continuous threat to human health and important challenges worldwide. Nanoparticles (NPs), e.g., silver, copper and zinc NPs are increasingly used in antimicrobial coatings (AMCs) in bandages, face masks, privacy curtains, bed-sheets etc., due to their antimicrobial efficiency. As the above mentioned chemicals/materials are inherently toxic, the application of (nano-enabled) antimicrobials, e.g. in surface coatings may also cause harm in addition to benefits. Indeed, in the various stages of their Life Cycle (production, transportation, usage, wear and tear, cleaning and/or disposal of AMCs) these materials will inevitably reach the environment, mostly via various waste streams originating e.g., from the production, applications. Therefore, in parallel to cutting down the spread of potentially infectious microbes, antimicrobial materials may induce (eco) toxicological hazard and antimicrobial resistance.

We have collected and databased the antimicrobial efficiency (MIC and MBC values) and toxicity information (EC50 values for various environmental species) for various, mostly metal- based, biocidal materials. These data provide the basis for analysis of the antimicrobial efficiency versus environmental safety aspects of antimicrobial (nano)materials. By comparing the MIC and MBC values published in scientific literature, it was obvious that the zinc, copper and silver compounds were much more toxic to 'non-target' organisms of studied antimicrobial compounds (key aquatic organism groups such as algae, daphnids, fish) than to target organisms, i.e. bacteria. Also, the comparison of the data of soluble salts of zinc, copper and silver with these of ZnO, CuO and nanosilver showed that the above mentioned nanomaterials perform their biocidal action via dissolved Zn-, Cu- and Ag-ions. That information is valuable in design of more efficient and safer antimicrobial compounds.

Concluding, AMCs can be a double-edge sward: in addition to inhibition/killing of noxious microbes adverse effects to environmental organisms can occur via various waste-streams of AMCs. Thus, the risk assessment of AMCs over the entire life cycle into different environmental compartments is needed for the sustainable application of AMCs. Currently there are some data available for hazard evaluation of AgNPs – the antimicrobial nanomaterial that has been most efficiently studied - but not yet enough to conduct a detailed risk-benefit assessment. The data gaps are even more severe for other (nano)antimicrobials that have remarkably less available information.

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O 09

REVERSIBLE ENZYMATIC REACTIONS. HOW TO INCREASE THE YIELD OF THE TARGET NUCLEOSIDES AND NUCLEIC BASIS

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An enzymatic transglycosylation reactions, a transfer of the carbohydrate residue from one heterocyclic base to another, is being actively developed and applied for the synthesis of practically important nucleosides. These reactions are catalyzed by nucleoside phosphorylases that perform reversible phosphorolysis of nucleoside to yield the corresponding heterocyclic base and monosaccharide 1-phosphate. The equilibrium of these reactions is shifted towards nucleosides, especially in the case of purine nucleoside phosphorylase (PNP, EC 2.4.2.1), which is widely used in labs and industry for the synthesis of modified nucleosides.

$$\text{Nuc1} + \text{pi} \leftrightarrow \text{Sug-p} + \text{Base1} \qquad \text{Sug-p} + \text{Base2} \leftrightarrow \text{Nuc2} + \text{Base1} + \text{pi}$$

The analysis of these reactions shows that the highest yield of Nuc2 may be expected when the equilibrium of step 1 is shifted towards the formation of Sug-p, and the equilibrium of step 2 is shifted towards the target nucleoside Nuc2. 7-methyl-2′-deoxyguanosine hydroiodide

(1) was shown for the first time to be a valuable source of 2′-deoxyribose in the enzymatic synthesis of deoxynucleosides. Phosphorolysis of 1 proceeds quantitatively with the formation of Sug-p and the yield of Nuc2 was substantially increased [1].

Bacterial PNPs have rather broad substrate specificity utilizing a wide range of purines with different substituents to form corresponding nucleosides. To shift the reaction in the opposite direction we have used arsenolysis instead of phosphorolysis. This reaction is irreversible due to the hydrolysis of the formed α-D-ribose-1-arsenate. As a result, heterocyclic bases are produced in quantitative yields and can be easily isolated [2].

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O 10

POROUS BIOPOLYMERIC MATERIALS FOR BIOMEDICAL APPLICATIONS

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The main directions of biomedical application of porous polymeric materials are [1,2]:

- tissue engineering (biopolymer scaffolds);
- wound dressings for the treatment of skin and soft tissue injuries;
- controlled release systems;
- immobilized enzymes (heterogeneous biocatalysts, analytical test systems, monitoring systems);
- protective equipment and clothing for medical personnel and patients in hospitals;
- biosensors and filtering systems in devices "artificial kidney" and "artificial lungs

The report discusses the two main methods of obtaining porous polymeric materials: a method of phase separation and electrospinning. The method of phase separation is considered on the example of a system of biodegradable polyesters: polyhydroxybutyrate and polycaprolactone. From molding compositions of a blend of polymers dissolved in chloroform, fibers with a bimodal fiber distribution over the thickness were formed by electroforming from the free surface of the solution on a NS-LAB 200 Nanospider. The bimodal distribution of the thickness of the fibers obtained from a mixed solution of PHB and PCL is the result of phase separation in the polymer-polymer-solvent system during the evaporation of chloroform, resulting in the formation of an isolated phase-matrix structure. The effect of an electric field on a system containing deformable particles of an isolated phase leads to the formation of fine fibers. This structure is optimal for creating biodegradable matrices for tissue engineering: thin fibers provide the attachment of cells to the polymer matrix, and thicker fibers create opportunities for cell growth and proliferation due to large volumes of space between fibers [3,4]. Mixed solutions of polyesters in chloroform received composite film with different pore size and composition, as well as the repetition of nanofibers with antimicrobial and proteolytic activity. Highly porous biosorbent for selection of radionuclides produced by electrospinning of chitosan in the presence of cross-linking reagents.

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O 11

IMPACT OF MAGNETIC FIELD SPATIAL AND TEMPORAL CHARACTERISTICS ON ACTUATION MECHANISMS OF BIOCHEMICAL SYSTEMS BY MAGNETIC NANOPARTICLES

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Magnetic nanoparticles (MNPs) are one of the most prominent candidates for the role of remotely controlled nanomachines in regard to the future nanomedicine technologies due to their high biocompatibility and multimodal sensitivity to the external magnetic fields penetrating deep through the body. MNPs can be magnetically guided through the blood vessel system and specifically anchored to the specific cellular or even molecular targets by means of biochemical functionalization. Recently emerged magneto-nano-mechanical approach (MMA) to control function of native and artificial biochemical structures has shown its efficiency in vivo as well as in vitro experiments. However, theoretical basis of MMA is still relatively weakly developed. At present time, a lot of work has been done to develop new materials or find the most useful MNPs shape that would allow one to achieve best cellular manipulation in the lower magnetic fields. At the same time, there are only few articles aiming magnetic field spatial and temporal structure optimization. Comprehensive overview and comparative analysis of articles conducted using various types of magnetic fields is presented. Possible

MNPs dynamics specificity and alterations in biochemical effects in oscillating, rotating, chaotic, uniform, gradient, heating and non-heating, continuous and interrupting ones magnetic fields are to be discussed.

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O 12

CONTENTS OF OMEGA-3 POLYUNSATURATED FATTY ACIDS VS HEAVY METALS IN SEVEN SMOKED FISH SPECIES FROM SIBERIA (RUSSIA): BENEFIT-RISK RATIO

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In seven local smoked fish species of genus Coregonus, common for markets of Krasnoyarsk Region (Siberia, Russia), contents of fatty acids and heavy metals were measured. The highest content of sum of long-chain polyunsaturated fatty acids of omega-3 family (LC-PUFA), namely eicosapentaenoic (20:5n-3, EPA) and docosahexaenoic (22:6n-3, DHA) fatty acids, 6.53±0.78 mg/g wet mass, was characteristic of tugun *Coregonus tugun*. Thus, to obtain a daily personal doze of EPA+DHA of 1 g, recommended by World Health Organization, for prevention of cardiovascular diseases, one needs to consume 153 g of the smoked tugun. The analysis of metals revealed, that their contents did not exceed standards for fish meat established by Russian Federal standards, except Pb in sardine cisco *Coregonus sardinella*. Accordingly, values of hazard quotients, which estimate benefit-risk ratio of fish intake, indicate that most of the smoked fish species are safe product for human nutrition, except sardine cisco regarding its Pb content.

O 13

ELECTROSPINNING OF POLYHYDROXYALKANOATE FIBROUS SCAFFOLDS: EFFECTS OF ELECTROSPINNING PARAMETERS ON STRUCTURE AND PROPERTIES

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In this study, electrospinning was used to prepare fibers from PHAs with different chemical compositions: P(3HB) and copolymers: P(3HB-*co*-4HB), P(3HB-*co*-3HV), and P(3HB-*co*-3HHx). The main process parameters that influence fiber diameter and properties (polymer concentration, solution feeding rate, working distance, and applied voltage) have been investigated and their effects evaluated. Mechanical strength of aligned fibers prepared from different PHAs is higher than that of randomly oriented ones; no significant effect of fiber orientation on surface properties has been found. The study revealed electrospinning parameters for the production of high-quality fibers and determined which parameters should be varied to tailor the properties of the products. This study is the first to compare biological and physical-mechanical parameters of PHAs with different chemical compositions as dependent upon the fractions of monomers constituting the polymers and fiber orientation. None of the nanofibrous mats electrospun from PHAs had any adverse effects on attachment, growth, and viability of NIH 3T3 mouse fibroblast cells, and all of them were found to be suitable for tissue engineering applications.

The research was supported by the Russian Science Foundation (grant No. 17-15-01352).

O 14

STRUCTURE AND PROPERTIES OF NEW THERMOPLASTIC COMPOSITIONS ON THE BASE OF POLYETHYLENE AND POLYLACTIDE

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The creation of compositions of synthetic polymers with natural ones and polymers produced on the base of natural row attracts a great interest of investigators, as it promotes a decrease in the dependence from oil, which is the basic source of hydrocarbons.

In this connection the production of compositions of a wide-spread synthetic polymer – low density polyethylene (LDPE) with polylactide (PLA), which is a polymer synthesized from lactic acid forming under fermentation of the agriculture wastes, is one of the promising lines in this field. PLA is biodegradable polymer, which is degradable in compost and sea water, but in the same time it is rather expensive that decreases its competition as compared to synthetic polymers. The production of materials from LDPE and PLA allows one both to utilize synthetic polymers and to reduce the price of materials based on PLA. Thus, the compositions with a complex of new properties including the capacity to biodegradation that distinguish them from the existing LDPE compositions with synthetic polymers would be produced.

The PLA-LDPE blends were obtained under conditions of shear deformation in a rotor disperser at different components ratios. Using numerous mechanical, thermophysical and spectral methods of analysis, the influence of components ratio on the structure and

properties of the resulting composites were studied. The analysis of the data obtained by DSC showed that LDPE and PLA are not compatible confirmed by the character of melting and crystallization curves. An increase in the LDPE content in blend leads to an enhancement of the mechanical parameters. The study of the sample structure by X-ray and DSC methods demonstrated that with the rise in the LDPE content, the degree of crystallization increases. On the base of the data obtained, the mechanism of the mutual influence of components on the structure formation processes is discussed. By gel permeation chromatography and by determination fungi growth resistance, the biodegradation of the materials was established that makes them promising for different applications.

O 15

NANOCARRIERS FOR ANTICANCER DRUG DELIVERY: PREPARATION AND EVALUATION IN 3D IN VITRO MODEL

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Stability is one of the most important parameters of passive targeted drug delivery systems (PDDS). Cerasomes are hybrid organic-inorganic nanoparticles that could be considered as liposomes with rather durable silicon shell. Recently, we have synthesized structural blocks for formation of stable cerasome-forming lipoamino acids (CFLA). The aim of the current study was to obtain several types of doxorubicin(DOX)-loaded cerasomes which differed in lipid composition, and to study their accumulation and cytotoxicity effects both in monolayer cell culture (2D model) and in multicellular tumor spheroids (3D model). For this purpose, "pure" cerasomes containing only CFLA, as well as "mixed" cerasomes composed from a mixture of CFLA with a disintegrating lipid dipalmitoylphosphatidylcholine (DPPC) were obtained. The cerasomes were characterized in terms of their stability and efficiency as PDDS. The cerasome properties and in vitro behavior were found to be easily changed by varying their lipid composition. Physical-chemical parameters, such as mean diameter, ζ-potential, morphology and stability of "pure" and "mixed" as well as neutral and cationic cerasomes were evaluated. Human breast adenocarcinoma cells (MCF-7) were used as a model in the current study. Cerasome accumulation in the cells was studied by flow cytometry and confocal microscopy both in 2D (monolayer culture) and 3D (multicellular tumor spheroids) models. Cytotoxicity effects were estimated by MTT-test. The highest accumulation efficiency, as well as cytotoxicity effects were found for the "mixed" cationic DOX-loaded cerasomes, while the "pure" cerasomes demonstrated sustained drug release. Thus, the cerasomes are supposed to be able to overcome limitations of conventional drug delivery systems and are promising as rather stable and universal PDDS.

This study was supported by Russian Foundation for Basic Research (grant 18-34-00919 in part of cerasomes, and grant 18-04-01087 in part of 3D tumor spheroids).

O 16

POLYVINYL ALCOHOL MACROPOROUS HYDROGELS AS NEW MATERIALS FOR MEDICINE

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The present-day development of medicine and other sciences and technologies connected with human health requires creation of new highly-effective and harmless materials which allow to broaden possibilities of surgical, therapeutic and bio-analytical methods and systems.

In this study novel method of creation of macromolecular materials for medical application on the basis polyvinyl alcohol macroporous hydrogels is proposed. Polyvinyl alcohol finds wide application for medicine, hydrogels on the basis of polyvinyl alcohol also attracts great attention. However, easily prepared physical gels of polyvinyl alcohol formed by freezing of its aqueous solutions are unstable and readily turn reversibly into solution. Suggested novel method of preparation of polyvinyl alcohol hydrogels consists in formation of polymeric net by cross-linking of unsaturated derivatives of this polymer. Such method allows to form macroporous systems with broad set of pores of dozens and hundreds micrometers size, and stands out due to their high stability and good swelling capacity in water and salt solutions. It is also very important that obtained cross-linked products were made on the basis of beforehand synthesized and characterized polymers and that is why did not contain residua of monomers and other toxic agents.

Investigation of the influence of reaction conditions on the formation of porous gels allowed revealing of the conditions which provides reproducible preparation of the final product with high yield and adjusted overall porosity, pores size, polymer cross-linking degree.

Investigation of interaction of synthesized hydrogels with living organism tissues showed that introduction of developed preparation do not provoke inflammatory reaction on the initial stages of traumatic process and during the long-term contact novel hydrogels biodegrades fully with their substitution by conjunctive tissue. High biocompatibility. biodegradation with adjusted speed, good mechanical properties, stability under the conditions of application of standard sterilization methods, ability to sorb considerable amounts of liquids including salt solutions without changing of volume characteristics, availability of parent substances and of preparation methods allowed to propose obtained materials for medical application, especially in thoracic surgery, for treating of trophic ulcers and burns, in cosmetic surgery, for creation of therapeutic systems with controlled release of active substance and in several other areas.

O 17

DEVELOPMENT OF SELF-ASSEMBLED AMPHIPHILIC POLY-N-VINYLPYRROLIDONE NANOPARTICLES AS A STABLE DRUG DELIVERY SYSTEM

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Nanoparticles can experience numerous impacts during storage or after intravenous administration resulting in disassembly and/or drug leakage and affecting their efficiency as drug delivery systems.

In order to address the extremely important issue of creating stable, biocompatible, and effective nano-scaled carriers for different hydrophobic drugs and biologically active substances, we developed polymeric self-assembled nanoparticles prepared of biocompatible amphiphilic poly-N-vinylpyrrolidone derivatives (Amph-PVP) via self-assembly process in aqueous media. All polymers were found to exhibit low critical aggregation concentration values and could therefore form stable nano-scaled spherical architectures. It was further demonstrated that such monodispersed nanoparticles could effectively entrap the fluorescent probe pyrene and curcumin used in this study as a model hydrophobic substance. It is worth noting that the poor solubility of pyrene and curcumin in water and low bioavailability are to-date the major obstacles for their use in medical and biotechnological applications.

Studies concerning the thermodynamic and kinetic stability of the nanoparticles as well as their stability during long-term storage confirmed that the nanoparticles keep their structures intact upon dilution with body liquids and can therefore protect encapsulated drugs for long periods of time until reaching their target site. Systematic investigation showed that the ratio between the hydrophilic and hydrophobic part of the polymer has large impact on nanoparticles size, stability, biocompatibility, and hydrophobic drug entrapment efficiency. The study of the physicochemical properties of the nano-scaled carriers (i.e., surface charge, particle size, size distribution) together with their established stability in blood serum and lack of hemolytic effect indicate that the Amph-PVP nanoparticles can be tested for intravenous administration at a wide range of concentrations.

Thus, our studies support the use of Amph-PVP nanoparticles as drug carriers for application in sustained-release injectable delivery systems for poorly soluble and insoluble drugs. Although these results are very promising, further investigations will be necessary to determine the balance between an amphiphilic polymers' ability to form stable nanoparticles and entrap hydrophobic drugs, and the respective biocompatibility.

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O 18

POLYMERIC BIOMATERIALS - IMPORTANT DIRECTION OF BIOMEDICAL TECHNOLOGIES

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The main approaches to the use of polymers as materials for the creation of implants, components of biologically active systems, systems used in cellular, tissue and genetic engineering, materials for sorption and membrane separation devices and bioanalytical systems, as artificial bicatalytic materials, biodegradable materials of general purpose are considered.

The list of requirements for polymers used in these areas, and products and preparations based on them is extremely wide. Among them - strength indexes, for a particular application, solubility or insolubility in water, ability or inability to swell in water and the required level of gas permeability, biocompatibility, including hemocompatibility for products functioning in contact with blood, ability or resistance to biodegradation. A necessary characteristic of such materials and products from them is the ability to undergo sterilization without losing the required properties. Finally, their important characteristics are availability in production and competitiveness.

O 19

INVESTIGATION OF THE MECHANISM OF PEROXIDASE REACTIONS CATALYZED BY THE COMPLEX OF CYTOCHROME C WITH CARDIOLIPIN BY MEANS OF KINETIC CHEMILUMINESCENCE

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The complex of mitochondrial protein cytochrome c (CytC) with anionic phospholipid cardiolipin (CL) plays a crucial role in the initiation of apoptosis by catalyzing lipid peroxidation in mitochondrial membranes.

In our recent experiments we have shown that this complex is a nanosphere consisting of a cytochrome c globule in a partially molten state covered by a monolayer of cardiolipin molecules. The physico-chemical properties of the nanosphere were investigated in water solutions and in organic solvents and in sedimented microcrystals. But the catalytic action of those nanospheres was not properly clarified.

To clarify it, we used the kinetic chemiluminescence method: registration of the coumarin- activated chemiluminescence kinetics of the lipid peroxidation reactions catalyzed by the cytochrome c/cardiolipin complex and the mathematical modelling of the obtained kinetics. Mathematical modelling was performed with Kinetic Analyzer software. It was shown, that the observed kinetics of

the chemiluminescence correspond to the following reaction scheme:

$HOOH + Cyt^{3+} \rightarrow {}^{\bullet}Cyt^{4+}=O$

${}^{\bullet}Cyt^{4+}=O + LH \rightarrow {}^{\bullet}Cyt^{3+} + L^{\bullet}$

${}^{\bullet}Cyt^{3+} + LH \rightarrow Cyt^{3+} + L^{\bullet}$

$L^{\bullet} + O_2 \rightarrow LOO^{\bullet}$,

where Cyt^{3+} – complex of cytochrome c with anionic lipids (Cyt-CL),

$\bullet Cyt^{3+}$ is the product of one-electron oxidation of cytochrome c (Compound II)

$\bullet Cyt^{4+}=O$ – product of two-electron oxidation of cytochrome c (Compound I),

LOOH – PUFA hydroperoxide, LO• – alkoxy-PUFA radical,

L• – alkyl-PUFA radical, LOO• – dioxide (peroxyl) radical of PUFA. Rate constants of these reactions were also calculated.

These reactions of lipid oxidation in the mitochondrial membrane lead to the damage of the VDAC (Voltage Dependent Anion Channel)-ANT (adenine nucleotide translocase) complex, that in turn leads to reduction of the barrier property of the internal mitochondrial membrane, swelling of the mitochondrial matrix, appearance of megapores in the outer mitochondrial membrane, and finally to the release of CytC into cytoplasm that finally leads to launching of the apoptotic cascade.

O 20

OXIDATIVE POLYMERIZATION IN NANOSIZED SYSTEMS

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The kinetics of the polymerization of pyrrole, 2-methoxyaniline and N-phenylglycine in aqueous solutions of polyvinyl alcohol and polyethylene glycol has been studied. The possibility of formation of dispersions with particle sizes from 200 to 1000 nm has been shown. It has been established that the oxidative polymerization of pyrrole and 2-methoxyaniline proceeds autocatalytically, while the polymerization of N-phenylglycine proceeds without autocatalysis. The studies of infra-red spectrum of the dispersed phase particles have shown that the fixation of stabilizer is achieved by the formation of hydrogen bonds with the polar groups of the electrically conductive polymers. It has been found that the particles of the disperse phase have almost spherical shape and contain volumetric hydrated shells. It is supposed that the mechanism of stabilization of the particles of the electrically conductive polymers in aqueous media is connected with the inclusion of chains of polyvinyl alcohol and polyethylene glycol in the complex with electrically conductive polymers. In this case, the chains of polyethylene glycol and polyvinyl alcohol, located near the surface of the particles of the dispersed phase, are considered to be found in the aqueous medium, where they are hydrated due to the formation of hydrogen bonds. As can be seen from the above, the possibility of obtaining of the stable dispersions of the electrically conductive polymers is associated with steric stabilization.

t has been established that the appending of polymer stabilizers increases the activation energy of the catalytic stage, that can be due to the screening of catalytically active oxidative sections of chains of electrically conductive polymers by chains of polyvinyl alcohol and polyethylene glycol. At the same time, the introduction of polymer stabilizers does not significantly affect on the activation energy of the non-catalytic stage.

It has been shown that the particles of the dispersed phase are active in ion exchange processes, that offers broa d options for immobilization of biologically active substances including phytohormones.

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O 21

NANOTOXICOLOGY IN BELARUS. ACHIEVEMENTS, PROBLEMS

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There is no doubt that nanomaterials require special control, regulation and legislation, but the main problem is that there is no legislative base for nanomaterials in the Republic of Belarus. But this problem is a consequence of other problems, namely:

- the lack of a clear scheme for studying the effects of nanomaterials, taking into account their specific properties;
- the lack of rationing of nanomaterials, criteria for the rationing of nanomaterials with regard to their specific properties have not yet been developed;
- the lack of clear scientific conclusions on the issue of nanosafety, the use of nanomaterials, and as a result, there is no common position on the part of the world community;
- the lack of informing the public and government about the problem. It's very important for making any decisions.

More long-term, although difficult to achieve, are the following goals and actions:

- development of a clear methodology for studying the effects of nanomaterials, taking into account their specific properties
- harmonization of laboratory studies on the safety of nanomaterials at the global level (development of OECD methods). Studies conducted by OECD methods would be easier to publish and submit for discussion by the world community.
- development of laboratory validated methods for controlling the content of nanomaterials in the air of the work area and in products.

- the creation of a global scientific database of nanomaterials containing a description of nanomaterials, including the description of their specific effects, classification, labeling requirements, general conclusions, recommendations for production and use (some nanomaterials might well be used even if their negative effects are proven, but with appropriate restrictions in production and use).

- development of recommendations for the utilization of wastes containing nanomaterials (the Basel Convention could possibly be responsible for such a development)

- creation of a common information platform on nanomaterials in the our region, which should be harmonized with the global information platform.

- launching projects that raise awareness of the public and government in the region about nanomaterials and the problems asso ciated with them.

This will facilitate the tasks of informing the population and representatives of the authorities and their implementation in national legislation.

No less important is the creation of a scientifically sound mechanism for assessing the safety of nanomaterials, a scientific base and a broad scientific platform for the exchange of experience.

O 22

MOLECULAR AND CELLULAR MECHANISMS IN DEVELOPMENT

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Atherosclerosis is an important medical and social problem. Cardiovascular diseases have become one of the leading causes of death and disability worldwide. Many of them, including ischemic stroke, myocardial infarction and sudden cardiac death are consequences of atherosclerosis development in major arteries.

Atherogenesis includes several stages – accumulation of lipids in the vascular wall, inflammation and development of necrotic plaques with thin or thick fibrous cap. Despite intensive study, the initial phases of atherosclerotic plaque formation are poorly understood. It is well known fact that atherosclerosis usually develops in typical sites – curvatures and bifurcations of arteries, but the reasons for this have not been fully clarified. Atherogenic factors (age, obesity, dyslipidemia, hypertension, smoking) act systemically, so there must be a special mechanism of local atherogenesis induction. Shear stress plays a great role in this process, leading to changes in endothelial permeability and expression of different genes. However, there are relatively straight sections of vessels in humans in which atherosclerosis frequently occurs. Using immunohistochemistry and transgenic animals we showed possible cellular mechanisms of atherosclerosis mosaicism. Understanding of these mechanisms is extremely important for the creation of drugs that are effective at the initial stages of atherogenesis before the development of serious complications.

Advanced atherosclerotic lesions are much more dangerous and therefore better studied. A sudden rupture of a plaque leads to thrombosis and the development of myocardial infarction or stroke, so the main goal in the treatment of atherosclerosis is to prevent such ruptures. Using a genetic approach, we identified key proteins whose activity leads to the rupture of an atherosclerotic plaque.

Thus, our data not only contribute to a better understanding of atherogenesis but also can be used to create new generations of anti-atherosclerotic drugs.

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O 23

GLYCOSYLPHOSPHATIDYLINOSITOL-ANCHORED PROTEINS: HOW TO STUDY AND USE

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Many eukaryotic membrane proteins are anchored to the outer leaflet of cell plasma membrane by glycosylphosphatidylinositol (GPI) anchor. In humans, there are more than 130 GPI- anchored proteins (GPI-AP). GPI-AP are functionally diverse proteins: enzymes, adhesion molecules, navigation receptors, growth factors receptors, receptors participating in formation of immune complexes and some others. C-termini of all these proteins are modified with GPI- anchor that includes a phosphoethanolamine linker, glycan core, and phospholipid tail. GPI-AP have been used for modification of cell membranes in gene therapy, immune therapy, tumor therapy and vaccination. GPI-AP are released from the cell surface by cleavage of the GPI anchor or by release with vesicles (virus particles, microparticles and exosomes). This feature can be use in bioengineering.

It is believed that GPI-AP are associated with lipid rafts, membrane microdomains enriched in sphingolipids, cholesterol, and certain types of lipidated proteins. Clusterization of GPI-AP and their immobilization promote the formation of lipid rafts and the activation of cell signalling. Lifetime of dimer/oligomer GPI-AP is less than few seconds and their size is less than 200 nm usually. Such spatio-temporal dimerization dynamics of GPI-AP in biological membranes of living cells makes it difficult to study. We have developed methods based on detection of Förster resonance energy transfer (FRET) for measure the distance between two molecules (within 1- 10 nm). At first, we optimized the method of selective covalent fluorescent labelling of GPI- anchored T-cadherin in living cells. Then,

we developed protocols for FRET measuring by confocal microscopy and flow cytometry. Our data have shown that different natural ligands of T-cadherin promote formation of dimers with different lifetime and different cell signalling. We suggest that the signalling and physiological difference between two ligands can be explained by formation of different rafts. Methods developed in this work can be used to study GPI-AP in order to clarify their biological functions and to use them in biomedical applications.

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O 24

ASSESSMENT OF PEGYLATED CdSe/ZnS QUANTUM DOTS CYTOTOXICITY IN VITRO

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Highly fluorescent inorganic semiconductor nanocrystals "quantum dots" (QDs) have unique optical characteristics, including high quantum yields, broad emission spectra, narrow excitation spectra, and high chemical and photo-stabilities. Another advantage of QDs is that they can be excited at a wavelength which is far from their emission band and different QDs can be excited at the same wavelength but emit light of different colors, depending on their size. QDs are considered as promising tools for imaging of cellular processes and immunodetection and have proved to be useful for developing sensitive multiplexed cancer diagnostic systems.

Here, we have synthesized CdSe/ZnS core/shell QDs with an emission maximum at 591 nm and transferred them through the reaction of ligand exchange to the water using the multifunctional thiol-PEG derivative. The size, surface charge, optical properties and stability of water-soluble QDs at 37°C and at room temperature were analyzed. The size and charge of QDs were found to be 15.29±1.032 nm and –10.4±1.44 mV, respectively. Solubilized QDs were stable in a buffer, with a homogenous size disriburion, at both temperatures for 7 days. This proved that QDs are extremely stable and could be used for *in vitro* cytotoxicity analysis.

The QDs were further tested on SK-BR-3 human breast adenocarcinoma cells to assess their cytotoxicity by the MTT test. The data showed that, at concentrations from 1.2 to 3.7 μg/ml, QDs exhibited a very low cytotoxicity with the cells survival rate varied from 80 to 100%. At concentrations higher than 3.7 μg/ml, QDs became very cytotoxic, with cell survival rates of 20% or less. This data allow us to establish the range of concentrations were QDs are non-toxic and can be used as safe agents in *in vitro* live cells model.

An *in vitro* model using monocytes freshly isolated from whole human blood was further used to study interactions between QDs and live cells. The experiment with monocyte cell cultures showed that, after 48 h of cell incubation in the presence of 2 μg/ml of QDs, the nanoparticles penetrated the cells. It is noteworthy that the fluorescent properties of QDs were preserved in the primary monocyte culture. The vital activity of the monocytes was also unaffected.

Obtained data pave the way to development of safe *in vitro* and *in vivo* models for future investigations of QDs and development of QD-based diagnostic tools.

O 25

ENHANCING NANOPARTICLE-BASED APPROACHES FOR ULTRASENSITIVE IMMUNOASSAYS

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Progress in hazard protection causes new demands for highly sensitive analytical techniques, resulting in the need for new immunoassays. Colored nanoparticles are the most commonly used labels for non-laboratory immunoassays, and the primary means of improving these assays are through the formation of nanoparticle complexes and through coloration enhancement via additional reactions. This report provides a comparative assessment of the enhancing nanoparticle-based approaches and a presentation of the new techniques that we have developed and successfully applied in practice. The proposed approaches were applied to immunochemical test systems for the control of viral and bacterial pathogens of the potato.

First, we have proposed a new scheme for lateral flow immunoassay enhancement, which is based on the combination of magnetic nanoparticles (MNPs) and gold nanoparticles (GNPs). It integrates two types of amplification: (1) concentration of analytes in the samples using conjugates of MNPs with specific antibodies and (2) increased label visibility using heteroaggregates of MNPs and GNPs. This approach was applied to the detection of potato virus X and was found to be 32 times more sensitive than the common immunoassay. The combination of functionalized MNPs and GNPs shows significant potential as a universal approach for increased sensitivity of new lateral flow immunoassays.

Second, we found that the combination of two (specific and enhancing) GNP conjugates and alkaline phosphatase makes reaching a high sensitivity for a lateral flow immunoassay possible. The insoluble, precipitated dark-violet diformazan produced by the phosphatase significantly increased the intensity of the registered coloration. The limit of detection was 27 times lower than that of a non-amplified immunoassay.

The aforementioned easy-to-use approaches do not require additional preparatory procedures or washing steps, and they may be used by untrained persons in resource-limited settings. They are highly promising for the routine lateral flow immunoassay of different compounds.

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O 26

FORMATION AND MOLECULAR STRUCTURE OF NATURAL POLYSACCHARIDES BASED THIN FILMS

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Natural biodegradable and biocompatible polymers were used to form thin nanostructured films, their molecular structure was considered. The ability to control material parameters by assembling such materials at the nanoscale was demonstrated. Herewith, consideration of polymers structure, elements size and shape had a great importance. The study of molecular architecture at the nanoscale allows finding the interrelation between the microstructure of the

coatings and its parameters that enables efficient application of nanostructured coatings for different areas of biotechnology and medicine. Natural polymers with functional groups that contain an opposite charges were used to create thin nanostructured films by layer-by-layer deposition technique. Chitosan is natural cationic polysaccharide that can be obtained by the deacetylation of chitin. Its structure contains amino groups with high reactivity. Such biopolymers as pectin, that formed by partially ethoxylated D-galacturonic acid, κ-carrageenan, that contains sulfate groups and heparin with sulfate and carboxyl groups, have negative charges, and can be used to design thin coatings.

The influence of the chitosan deacetylation degree (DD) and molecular weight (MM) on the thin films structure was analyzed by atomic force microscopy (AFM). Various properties of coatings are demonstrated with variation of the main characteristics of the investigated chitosan samples. It was shown that with a decrease in the DD for samples with MM 14 kDa and 200 kDa, the filling degree of the substrate with a film decreases. The molecular weight of chitosan significantly influences the structure of the chitosan coating.

Using QCM-D method, film compactness and strength were studied, the viscoelastic characteristics of the polymer layers were determined. Based on the AFM data, models of interaction of two polymers in bilayer compositions are proposed. AFM spectroscopy method was used to study the rigidity and adhesion forces.

Biological compatibility of multilayer films on various substrates was evaluated by cultivation on their surface of fibroblast-like cells. It is shown that the modification of the substrate to improve adhesion is most effective with films of 4-6 layers of chitosan and κ-carrageenan. Covering the titanium-based material with such a nanostructured polymer coating results in improved surface biocompatibility. It demonstrates the possibility of using natural polysaccharides based thin films in tissue engineering.

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O 27

MULTIFUNCTIONAL MAGNETIC NANOPARTICLES IN TUMOR TERAPY AND DIAGNOSTICS

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In few past decades a lot of attention was paid to magnetic nanoparticles (MNP) as a novel materials for nanomedicine. Due to unique properties, such as high magnetization, superparamagnetism, high surface area and biocompatibility this materials were widely used as MRI contrast agents, drug delivery systems and cancer hyperthermia treatment. However many different approaches in synthesis, surface functionalization, drug loading and release lead to situation when for each application special design have to be created. In our work we have created multimodal system, that contains MNP, human serum albumin (HAS) and PEG, that allows loading of different types of drugs, fictionalization of surface by targeted ligands and MRI guided delivery to tumor tissue.

Bare iron oxide crystals were obtained by thermal decomposition of iron (III) acetylacetonate. To provide high colloidal stability in water suspensions further adsorption of serum albumin was carried out with following crosslinking by glutaric dialdehyde with formation of stable 3D coating. Obtained nanoparticles were characterized by different techniques, including HRTEM, DLS, AFM, XRD, TGA and others.

To provide therapeutic modality we have developed methods of loading of 3 different antitumor drugs: doxorubicin, cisplatin and bacteriochlorine a derivatives, used as photosensitizers. For each drud loading capacity was calculated and was equal to 8, 20 and up to 40% correspondingly. In vitro tests on cancer cell cultures have shown that after loading all three drugs have retained their cytotoxic potential. I.v. injection of MNP in animals bearing experimental tumors with following MRI in T2 weighted sequences have shown that MNP are effectively delivered to tumor region and visualize tumor mass and microvasculature.

Decoration of MNP surface by anti VEGF antibodies allows specific delivery to areas of active neoangiogenesis in tumors, that was confirmed by MRI. On the other hand MNP, loaded with doxorubicin and decorated by anti-VEGF antibodies have shown high therapeutic potential in treatment of murine 4T1 breast cancer tumor model. We have observed increase in median survival from 26 to 39 days.

Taken together this data allows us to postulate that our method synthesis of MNP can create biocompatible multimodal system for drug delivery and tumor diagnostics.

The study was supported by the Russian Science Foundation (grant No. 17-74- 10169) and NUST MISiS (K2-2018-008).

O 28

IN VITRO UPTAKE STUDY OF NANOPARTICLES BASED ON AMPHIPHILIC N- VINYLPYRROLIDONE BY DIFFERENT TYPES OF CELL CULTURES

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Nanoparticles were obtain on basis of amphiphilic poly-N-vinylpyrrolidone with thiooctadecil end-group and molecular weight 6 kDa. There are a lot works devoted to this polymer in present time. It proved itself like safe and non-toxic polymer, that can be used in medical purposes. Nanocarriers were obtained by self-organization of micelles at the interface the chloroform in water emulsion with following sonication. An average hydrodynamic diameter was measured by NTA and was 200 nm. It is shown that nanocarriers based on synthesized amphiphilic polymers are able to include biologically active substances of various nature with high efficiency. Fluorescent dye DiI was used as water-insoluble model substance to trace the particles uptake by cell cultures. For in vitro test were used human primary glioblastoma (U87), human skin fibroblast (CRL 2429), human embryonic kidney 293(HEK 293) and epidermoid carcinoma (A431) cell lines. As inhibitors of endocytosis were used dynasore, which blocks dynamin- dependent endocytosis by scission of endocytic vesicles and Wortmannin, the inhibitor of the receptor-mediated endocytosis of the cellular phosphatidylinositol 3-kinase (PI3-K). Hoechst 33258 was used as fluorescent DNA-binding dye. The DiI loaded micelles were used for the in vitro administration to cells. When the nanocarriers produced by the emulsion method were introduced into the cell cultures under study in the absence of endocytosis inhibitors, a slow increase in the relative fluorescence intensity of DiI with time was observed whereas in the presence of Dynasore it remained constant. Since the nanoparticle carriers used in the present study did not possess any specific receptor-targeting moieties, no inhibitory effect was expected in the presence of Wortmannin, which blocks the receptor-mediated endocytosis. These observations clearly indicate that the uptake of DiI-loaded nanocarriers produced by the emulsion approach mainly proceeds through dynamin-dependent mechanisms of endocytosis. This is also confirmed by the presence of a significant amount of endosomes in cells. It should be noted that the obtained micrographs indicate the presence of the nanocarriers in the interior cytosolic compartments of the cells while the nuclei show no emission in the DiI channel and are therefore not permeable by these nanocarriers. It was found that the nanocarriers produced by the emulsification method penetrate the cells via dynamin-dependent endocytosis and cannot enter the nucleus.

O 29

SCANNOING ION CONDUCTANCE MICROSCOPY AS A NEW METHOD FOR NANOPARTICLE RESEARCH

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Recently we have developed the new system for nanopipette navigation with feedback control. The ability to precisely move the nanopipette and to measure simultaneously an ion current allows an unprecedented level of nanoscale imaging of living cells – scanning ion conductance microscopy (SICM). The speed of data acquisition positions this as a technology which may be suited to relatively high-speed scanning of cell membrane during various biological processes in real time. This nanopipette navigation system can be used in combination with other techniques such as confocal and fluorescence microscopy, microinjection, electrochemical measurement, and patch-clamp recording. This has the potential to open new horizons in medicine and biology and could be of particular value to the pharmaceutical industry.

We have demonstrated unique application of SICM and nanopipette biosensing as new methods to study action mechanism of magnetic hyperthermia. It was shown that mechanical properties of cancer cell membrane were increased after incubation with cobalt ferrite nanoparticles and decrease after incubation with the same nanoparticles in altering magnetic field (figure 1). This fact proves a supposed acting mechanism that an apoptosis followed by destruction of an intracellular machinery during magnetic hyperthermia. Intracellular level of ROS was measured by nanopipette based biosensors for cancer cells incubated with cobalt ferrite nanoparticles in in altering magnetic field.

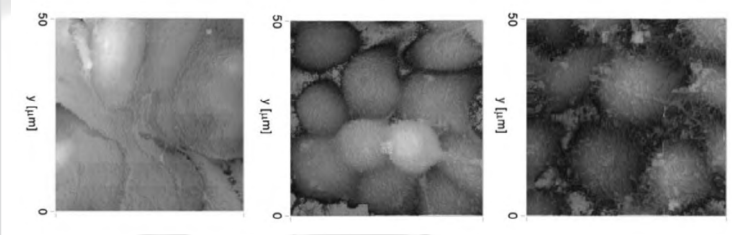

Figure 1. SICM tomography of 4T1 cells:
a) without magnetic nanoparticles (control);
b) incubated with magnetic nanoparticles;
c) after incubation with magnetic nanoparticles in alternating magnetic field.

We have demonstrated other examples of nanopipette techniques implementations for in vitro drug discovery which prove a good potential of these methods.

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O 30

PHYSICOCHEMICAL PROPERTIES OF MULTICOMPONENT POLYHYDROXYALKANOATES: NOVEL ASPECTS

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The physicochemical properties such as the degree of crystallinity and temperature and molecularmass characteristics of a number of polyhydroxyalkanoates of various chemical composition synthesized on a complex carbon substrate by bacteria *Cupriavidus eutrophus B10646* have been investigated. Two-, three-, and four-component copolymer samples have different sets and ratios of monomers with various lengths of carbon chains: 3-hydroxybutyrate (3HB), 4-hydroxybutyrate (4HB), 3-hydroxyvalerate (3HV), 3-hydroxyhexanoate (3HH), 3- hydroxy-4-methyl valerate (3H4MV), and diethylene glycol (DEG). It has been shown that weight-average molar mass *M*w and polydispersity vary in a wide range with no correlation existing with the composition of copolymer PHA and that thermal stability is preserved in the temperature interval between the melting temperature and the thermal degradation temperature from 100 to 120–140° C. The composition and ratio of monomers most notably affect the degree of crystallinity of polymers. Significant differences between the degrees of crystallinity of three- and four-component polyhydroxyalkanoates have been found for the first time. The degree of crystallinity for different polymers is from 9–22% to 50-80%. All of the types of copolymer samples, regardless of the monomer ratio, show an increase in elongation at break against the background of a decrease in tensile stress and Young's modulus, with these effects being pronounced to different extents. On the whole, the properties of multicomponent polyhydroxyalkanoates differ appreciably.

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O 31

CHITOSAN COATED SUPEROXIDE DISMUTASE NANOPARTICLES FOR ANTI-INFLAMATORY OPHTHALMIC APPLICATIONS

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Currently, an active search for new drugs to treat inflammatory ocular diseases occurs. Oxidative stress plays an important role in the pathogenesis of inflammatory diseases, and injection of antioxidants may be effective. Antioxidant enzymes, such as superoxide dismutase (SOD) and catalase, have much more efficiency in comparison with small molecular antioxidants. However, administering native enzymes to the eye in the form of eye drops is ineffective due to their rapid clearance. Therefore, it is important to create a drug delivery system that will possess long time of circulation and low immunogenicity.

To achieve this goal, SOD nanoparticles covered with chitosan were synthesized. Polymeric shell was used to decrease immunogenicity; chitosan was used to increase time of circulation.

Briefly, SOD nanoparticles were synthesized by mixing of SOD solution with protamine and PLE-PEG solutions sequentially after that glutaraldehyde was added. Byproducts were removed by centrifugation through centrifugal filters. Nanoparticles of 50 nm in diameter with negative charge were obtained.

The release experiments were conducted using a dialysis container (100 kDa). SOD had being released from nanoparticles more slowly than the native SOD.

Thus, 90% SOD had released after 24 hours from the solution with the native enzyme, for the same time 30% SOD had released from the solution with nanoparticles. This demonstrates that SOD is connected with the polymers strongly and the particles may have a large circulation time as opposed to the native enzyme.

Both nanoparticles and nanoparticles covered with chitosan were internalized by cells whereas SOD was not. SOD nanoparticles show therapeutic efficacy in the preclinical trial on the model of uveitis and alkaline burn in rabbits. Chitosan covered SOD nanoparticles did not show any irritating effect when applied as eye instillations. Thus, superoxide dismutase nanoparticles covered with chitosan seem to be perspective therapeutic agent due to improved stability and ability to internalize into cells.

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O 32

NOVEL PHYSICAL TECHNIQUE FOR MACROSCOPIC LOCALIZATION OF MAGNETO- NANO-MECHANICAL ACTUATION OF MAGNETIC NANOPARTICLES IN VIVO

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The new approach of magnetic nanoparticles (MNPs) control by means of external non-heating alternating magnetic field (AMF) with frequency below 1 kHz is described. Presented analytical models show that rod-like magnetite MNPs (diameter a. 20 nm and length a. 100 nm) can cause change of cell membrane structure and properties, can trigger ionic channels, mechanosensitive receptors due to their deformations under local mechanical load created by MNPs rotational oscillations. Estimations show that properties and functions of ionic channels and mechanosensitive receptors can be affected in weak magnetic fields below 10 kA/m, bioactive membrane structures can be changed in AMF about 100 kA/m. Higher fields 100-1500 kA/m can cause irreversible change in membrane structure.

The novel technique for magneto-nano-mechanical impact macroscopic localization based on application of additional gradient magnetic field with zero field point is presented. Under external activating AMF only MNPs in the small spot around zero field point where AMF amplitude is lower than gradient field would perform rotational oscillations. It is shown that localization spot size can be as small as 1-2 mm excluding another MNPs captured by liver, kidneys and other internal organs during in vivo applications thus minimizing undesired side-effects. Also it is illustrated that localization spot can be easily positioned in space by means of additional uniform magnetic fields.

Presented results and localization technique propose that MNPs can be safely used for such biomedical applications as drug release, regenerative medicine, tissue engineering and drugless cancer therapy via mechanotransduction triggering apoptosis in malignant cells.

The work was supported by Russian Science Foundation grant 14-13-00731 and Russian Foundation for Basic Research grants 17-54-33027 and 17-42-680803.

O 33

NOVEL METHOD FOR RAPID TOXICITY SCREENING WITH ELECTROCHEMICHAL NANOPROBES FOR SINGLE CELL ANALYSIS

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Nanopipettes have been used in different applications with integration into Scanning Ion Conductance Microscopy (SICM): high resolution topographical imaging of living cells, quantitative delivery of molecules to the surface of living cells. Additionally, nanopipette probes still hold great promises as intracellular biosensors.

Here we describe the fabrication, characterization, and tailoring of carbon nanoelectrodes based on nanopipette for intracellular electrochemical recordings. We demonstrate the fabrication of disk-shaped nanoelectrodes whose radius can be precisely tuned within the range 5-200 nm. The functionalization of the nanoelectrode with platinum allowed the monitoring of oxygen consumption outside and inside of melanoma cell.

We applied the nanoelectrode to perform intracellular measurement in cultured melanoma cells, HEK293 and LNCap cancer cell. Upon penetration of the cells the anodic current quickly increases followed by equilibration to a level above the one measured in the cell media. A cell can withstand multiple penetrations and we measured a substantial difference between the electrochemical signal measured inside and outside the cell. We believe these results show the potential of functional nanoelectrode to probe endogenous species into cells and with further improvements they may allow the study of oxidative stress under influence of different drugs. Our results show a significant difference for intracellular levels of ROS measured in cancer cells before and after exposure to nm size iron oxide NP.

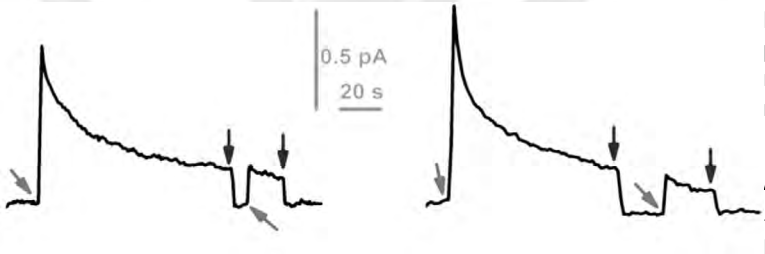

Figure 1. Representative current traces of a nanoelectrode polarized at +850 vs Ag/AgCl inside and outside a melanoma cell in culture. Red and blue arrows indicated respectively the moment of penetration and retraction

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O 34

INFLUENCE OF RECOMBINANT INTERLEUKIN-1 BETA ON BLOOD-BRAIN BARRIER PERMEABILITY IN EXPERIMENTAL GLIOMA MODELS

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The blood-brain barrier (BBB) plays an important role in the body, isolating cells and brain tissue from exposure of harmful substances. However, in diseases of the central nervous system, including gliomas, there is the necessity of drug use and targeted delivery to brain pathological lesions. One way to solve this issue is controlled increase of BBB permeability by administration of biologically active substances, such as interleukin-1 beta (IL-1ß). Combination of transient BBB breakdown and application of targeted nanocontainer systems could be a good strategy for brain diseases treatment.

The goal of this work was to study the influence of recombinant IL-1ß on permeability of BBB for low- and high-molecular substances, as well as nanocontainer drug formulations, on experimental glioma models.

IL-1ß was produced by recombinant gene technology from *E. coli* C600 by Research Institute of Highly Pure Biopreparations (St. Petersburg, Russia). Biological activity of IL-1ß was confirmed on adenocarcinoma cells (A549). The influence of recombinant IL-1ß on BBB permeability was studied on rat C6 and mouse M6 glioma models by intravital microscopy and confocal microscopy of brain sections. Doxorubicin, FITC-BCA, fluorescent-labeled monoclonal anti- GFAP and anti-VEGF antibodies and liposomes were chosen as testing substances. The synthesis of liposomes was carried out by emulsification of lipid film consisting from the mixture of L-α-phosphatidylcholine, cholesterol, DSPE-PEG2000 and fluorescent label Dil (or DiD) in phosphate-buffered saline. The action of IL-1ß was investigated in dose- and route-dependent manner (intratumoral, intraperitoneal and intranasal administrations).

Intravital microscopy of mice showed, that intraperitoneally injection of IL-1ß allowed low- molecular substances (doxorubicin, FITC-BSA) to overcome the vascular wall of the cerebral cortex. In case of glioma M6 mice, intraperitoneally injection of IL-1ß (≥ 1 μg) let liposomes to penetrate vascular wall of glioblastoma and accumulate in tumor stroma outside the vascular wall. Four hours after injection of IL-1ß (100 ng) into rat glioma C6, BBB became permeable to intravenously administered liposomes that was confirmed by confocal microscopy of brain sections.

This work was supported by Skolkovo Institute of Science and Technology (Master Research Agreement No 182-MRA).

O 35

NEW HYBRID MATERIALS BASED ON GOLD AND MAGNETITE NANOPARTICLES, MODIFIED BY BIFUNCTIONAL ORGANIC LIGANDS: SYNTHESIS, PROPERTIES, APPLICATION

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Magnetic nanoparticles based on iron oxides are promising materials for the biomedicine and pharmacology due to the high specific magnetization and the possibility of functionalization of the surface. Iron Oxide nanoparticles can be offered as drugs, such as a tumor - selective MRI contrast agents. Various materials based on magnetic nanoparticles may be used to the targeted delivery of anticancer drugs and to local hyperthermia therapy method. However, the use of magnetite nanoparticles in pharmacology has some problems such as toxicity, tendency to aggregate, the complexity functionalization. Using different kinds of bio neutral inorganic coatings, like gold, silica, carbon, and magnetite nanoparticles as the core material for the forming core-shell nanoparticles can significantly reduce or even eliminate problems described above. Herein we report the synthesis, functionalization process and characterization of superparamagnetic and ferrimagnetic iron oxide nanoparticles with different shape and size. Special attention in this paper devoted to covalent stabilization of magnetite nanoparticles by polymer, such as silane-polyethylene glycol (Peg-silane). The major advantage of modified by polymer magnetic nanoparticles is low toxicity and possibility for post functionalization. Iron oxide nanoparticles with different morphology (spheres, cubes, rods) were obtained by coprecipitation or redox methods. Iron oxide suspensions were reacted with aqueous PEG- silane to perform phase transfer functionalization.

Another part of our work is devoted to design and characterization of silica gel decorated with gold nanoparticles for application in chromatography. We demonstrate the adsorption of gold nanoparticles onto the unfunctionalized silica gel surface and silica gel functionalized with 3- aminopropyltrimethoxysilane and 3-mercaptopropylthrimethoxysilane. The surface of gold nanoparticles was stabilized by L-cysteine. It is shown that preliminary functionalization of the silica gel surface with NH2 or SH groups had a profound influence over the coverage of gold nanoparticles and clusters. TEM, SEM, UV-Vis DRS and AAS were used for characterizing the structure of the synthesized sorbents and the extent of gold nanoparticles adherence to the support. The possibility of using the synthesized sorbents as stationary phases in the normal- phase mode of HPLC for the separation of mixtures of aminopyridines was investigated.

This work was supported by grant of the president of the Russian Federation (grant MK- 925.2017.3)

O 36

PPREPARATION OF CARBON QUANTUM DOTS FOR FLUORESCENCE DETECTION OF CU(2+) IONS

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Carbon quantum dots (CQDs) with different surface modification have been synthesized by hydrothermal treatment and microwave assisted preparation. The CQDs were synthesized from salicylic acid and , ethylenediaminetetraacetic acid in two steps method. The CDQs were applied for sensitive and selective fluorescence detection of cupper ions. The measurements of Intensity and Polarization of Fluorescence were made by portable FP instrument Sentry-100.

The developed method was successfully applied for quick and simple quantities detection of Cu(2+) in drain waters.

The research is supported by grant K3-2017-073 "New methods for express analysis of liquid media for medicine, ecology and food industry based on nanoparticles of semiconductors and metals and substances with special optical properties".

O 37

EFFICENECY AND SAFETY OF NANO-ENABLED TEXTILES FOR ANTIMICROBIAL APPLICATION

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Metal oxide nanoparticles (Ag, CuO, and ZnO NPs) coated textiles have been proven efficient towards health-care associated pathogenic bacteria. Regarding the promising use of nano- enabled fabrics for antibacterial application (e.g., bandages, bed sheets etc), their health effects are still under the investigation.

In this study cytotoxicity of sonochemically synthesized ZnO and CuO NPs to human lung epithelial cells A549 and macrophage-like THP-1 cells was studied. Those NPs are reported to have ROS-mediated antibacterial properties towards *Escherichia coli*, and *Staphylococcus aureus* (including MRSA) and intended to use for the fabrication of textiles for biomedical application.

ZnO and CuO NPs effect on the lung and immune cells viability was evaluated after 24 h exposure by MTT assay. For the mechanistic study, pro-inflammatory and oxidative stress response (interleukins release or oxidative stress-response enzymes activity, respectively), and apoptosis (by flow cytometry of Annexin V/propidium iodide (PI) stained cells) were evaluated. NPs-cell interactions and internalization were studied by SEM and laser-confocal scanning microscopy. To assess the real exposure concentrations, sonochemically fabricated textiles were subjected to the abrasion test, and the released airborne particles were measured.

Results showed that that ZnO and CuO NPs were not toxic to the lung and immune cells up to the concentration ~20 μg/mL. Differently form ZnO NPs, CuO NPs induced interleukin IL-8 release already at subtoxic concentration (~0.1 μg/mL) in the lung epithelial cells but not in the immune cells. Abrasion test showed that very small amount of sonochemically fabricated CuO and ZnO NPs were released (less than the pro-inflammatory response inducing concentration). Role of oxidative stress and particle-cell interactions will be discussed.

This work was supported by Fondazione Cariplo (OverNanotox 2013-0987) and IUT23-5.

O 38

ANALYSIS OF CARBOHYDRATES-LINKED LIGANDS MOLECULAR INTERACTIONS WITH HUMAN LIVER ASIALOGLYCOPROTEIN RECEPTOR IN VITRO USING SPR SPECTROSCOPY

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Human asialoglycoprotein receptor (ASGPR) is an integral membrane protein and is responsible for the clearance of desialylated, galactose-terminal glycoproteins from the circulation by receptor-mediated endocytosis. This mechanism could be used for targeted drug delivery using small ligands as homing devices.

Analysis of the molecular interaction of a number of ligands with human liver asialoglycoprotein receptors using surface plasmon resonance spectroscopy was performed. Protein receptor was immobilized on the SPR sensor chip via amine coupling.

Dissociation constants for ligands of different types of structure were determined, numbers are given. Ligands can be divided into groups based on dissociation constants. Best affinity was shown by the group of ligands based on paclitaxel (PTX) structure with constants

in nanomolar range (0.1 - 0.2 nmol). For carbohydrate-connected ligands, the roles of linker length, linker type, and a number of carbohydrates attached were shown and explanations based on PDB ASGPR structure given. For different ligands various (effective and ineffective) binding patterns were proposed that lead to differences in their internalization efficiency.

This work was supported by Skolkovo Institute of Science and Technology (Master Research Agreement No 182-MRA).

O 39

TOLL LIKE RECEPTOR 4 (TLR4) AFFECTS HYALYURONAL METAMOLISM IN CONTACT ALLERGY

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Background: Allergic contact dermatitis (ACD) is an important occupational and environmental disease caused by topical exposure to chemical allergens. ACD therefore, presents as an inflammatory response to small molecules and involves both skin resident cells and activated skin infiltrating T cells. Skin inflammation is mediated, among others, by the transmembrane receptor Toll like receptor 4 (TLR4). Low Molecular Weight Hyaluronan (LMWHA) in its' role as a danger associated molecular pattern (DAMP) is able to bind to and activate TLR4. It has been strongly postulated that the onset of "sterile inflammatory diseases", including contact dermatitis, can be attenuated by modifying the ability of DAMPS to trigger inflammation.

Aim: The aim of this study was to examine the putative interactions of TLR4 and HA.

Methods: Human keratinocyte NCTC2544 cell line was utilized as an epidermis model system. The downregulation of TLR4 expression was achieved by transfecting cells with siRNA specific for the TLR4 gene. Levels of interleukin-18 (IL-18), a biomarker of keratinocyte activation were measured by an in house ELISA. Protein expression was determined by Real-time PCR and western blot.

Results: Treatment with contact sensitizers 2,4-dinitrochlorobenzene (DNCB) and PPD increased keratinocyte TLR4 expression at both mRNA and protein level, in a concentration dependent manner. Keratinocyte activation, at contact allergen concentrations utilized, was verified by increased IL-18 production. Transfecting keratinocytes with siTLR4 resulted in a strong downregulation of TLR4 expression at both the mRNA and protein level, 63% and 55% respectively. siTLR4 deficient cells had decreased Synthase 1 (HAS1) expression ($p < 0,01$).

Conclusions: Contact allergens upregulate TLR4 expression. TLR4- deficient keratinocytes exhibit changes in HA metabolism. Interactions of TLR4 and HA might contribute to processes of keratinocyte activation by contact allergens.

O 40

CAFFEINE AFFECTS BREAST CANCER CELL ADHESION INDEPENDELY OF THEIR ESTROGEN RECEPTOR EXPRESSION STATUS

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Background: Caffeine, a substance widely used daily by millions of people has been associated with breast cancer (BC) pathogenesis. However, despite the abundance of epidemiological studies on coffee consumption and its possible relationship to the development of cancer there is not much information about its biological action in BC cells. Our previous study demonstrated that the IGF-IR receptor is crucial in modulating BC cell adhesion and is a conduit point for IGF- I / EGF and E2 downstream signaling.

Aim: The aim of the present study, was to examine the role of caffeine on proliferation and fibronectin-dependent adhesion of BC cells with different expression profile of estrogen receptors. Fibronectin is a large glycoprotein abundantly expressed in BC extracellular matrices, postulated to be a marker of aggressiveness during cancer pathogenesis.

Methods: BC cells utilized were MCF-7 cells following stable transfection with shRNA for the ERα gene (SP10, ERα-deficient cells) and MCF-7 cells transfected with negative shRNA (control sh). Proliferation and adhesion were assessed by fluorescence based assays whereas, protein expression was determined by Real-time PCR and western blot.

Results: Caffeine did not affect SP10 and sh cell proliferation regardless of their estrogen receptor status. On the other hand, in cells expressing ERα receptor, caffeine treatment increased adhesion at 0.01mM and 0.03mM ($p \leq 0.01$), while no effect was observed at a concentration of 0.05mM and above. In sp10 cells, which do not express competent levels of ERα, caffeine treatment at 0.01 mM modestly enhanced these cells' adhesion ($p \leq 0.05$). Caffeine activated IGF-IR and increased its expression in ERα(+) cells at 0.01mM and 0.03mM ($p \leq 0.05$ and $p \leq 0.01$ respectively), and appeared to cause an increase this receptor activation in cells deficient in ERα ($p \leq 0.05$).

Conclusion: Caffeine increases the adhesion of BC cells, regardless of their ERα expression profile. In addition, caffeine increases the expression/activation of IGF-IR and is likely to use this receptor to induce its effect on adhesion.

P 01

ACUTE EFFECTS OF OPTIC NERVE CRUSH ON DISTRIBUTION OF FLUORESCENT LABLLED PVP NANOPARTICLES AT THE BLOOD RETINA BARRIER

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Objectives Polymeric nanoparticles (NPs) are developed as drug carriers and especially for delivery of compounds across the blood-brain barrier (BBB). However,so far, these carrieirs have been tested mainly under most physiological conditions. In the current animal study we therefore tested fluorescent-labelled polyvinylpyrrolidone NPs in vivo in a model of mild traumatic axonal injury and followed the distribution of the nano-carriers.

Methods Optic nerve crush (ONC) was performed as a model of mild optic nerve crush in rats. To this end, a lateral canthotomy was made from the orbita following an incision of the conjunctiva lateral to the cornea. The retractor bulbi muscles were separated, and the optic nerve was exposed by blunt dissection. To crush the nerve, a calibrated forceps was used for 30 s at a distance of 2–3 mm from the eye. After the surgery, the anaesthetized rats were transferred to the vivo Confocal Neuroimaging (ICON) set-up, fluorescent labelled PVP-NPs were injected via the tail vein (i.v.) and real time monitoring of the bio-distribution of fluorescent NPs at the blood- retina barrier (which is virtually the same as the BBB) was performed for 1-2 hrs. Subsequent ex-vivo wholemount preparation allowed imaging of the retina vessels with higher magnification. Rats without ONC and rats with ONC and i.v. injection of the standard marker FITC-dextran served as controls.

Results Within a time-window of 1-2 hrs after ONC we did not detect any difference between lesioned and healthy animals. After injection of the fluorescent PVP-NP we observed labelling of the vessels within minutes. This distribution of the fluorescent signal remained stable within the vascular system and without detectable leakage until the end of the in vivo experiment. Interestingly, higher magnification imaging of the retina vessels in the ex vivo wholemount preparation showed more variable results, which awaits further investigation. The in vivo imaging result was in line with the findings after injection of the standard marker FITC-dextran post ONC, which also did not leak out of the vascular system at this early time point after mild traumatic injury.

Conclusions After mild traumatic injury the transport mechanisms at the BBB regarding PVP-NPs do not seem to be impaired and nano-carriers cannot reach the parenchyma just by leaking through the retinal vessels. However, it will be of interest to investigate this question at later post-lesion time points and with more severe models of damage.

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P 02

IN VIVO IMAGING OF BLOOD BRAIN BARIER PASSAGE OF MOIETY LABELLED POLYMERIC NANOPARTICLES

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Aim In-vivo Confocal Neuroimaging of the retina (ICON) is a valuable tool for investigating the passage of fluorescent nanoparticles (NPs) across the blood-brain barrier (BBB) in living rats. However, the resolution of ICON is not high enough to detect (sub-) cellular structures. Therefore, in addition, we utilized an ex-vivo whole mount retina preparation. Our aim was to characterize the distribution of polyvinylpyrrolidone NPs in the retina.

Methods Three different fluorescent-labelled PVP NPs, (PVP-FITC), (PVP-DIL), and (PVP-DIL-FITC) were injected into the tail vein of Lister-Hooded rats after the anaesthetized rats had been fixed on a stage of a laser scanning microscope with the eye beneath the objective. We determined whether the distribution of the fluorescent signal indicated a vascular and/or parenchymal distribution. Afterwards the rats' eyes were enucleated and whole mount retina was prepared.

Results We detected with this combined in-vivo / ex-vivo protocol that the vessel walls were regularly labeled by (PVP-FITC) and by (PVP-DIL) NPs. In (PVP-DIL-FITC) NPs' case, however, the signal accumulated in retinal tissues 10 min after injection.

Conclusion The (PVP-DIL) and (PVP-FITC) NPs have shown a stable staining for blood vessels walls without crossing the BBB and without blood cells staining, probably due to the hydrophilic shell of the NPs. The (PVP-DIL-FITC) accumulated in retina tissues, with faster clearance and blood cells staining, probably due to hydrophobic FITC attached to hydrophilic shell which may be the main key for passing the BBB.

This work was supported by Era.Net.Rus.Plus initiative (project "NABUCO"; ID#169)

P 03

IN VIVO BRAIN DISTRIBUTION PATTERN OF COUMARIN6-SIGNAL AFTER INJECTION INTO RODENTS IN A PLGA-NANOPARTICLE FORMULATION

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Objectives Blood-brain barrier (BBB) passage is an important issue in health and disease: under physiological conditions the BBB serves as a shield against unwanted invasion of harmful substance, in cases of brain damage and diseases, however, transport of potential protective compounds across the BBB into parenchyma is a major concern for drug development. Furthermore, importantly, crossing the BBB is not the finish line in neuropharmacology: the compounds also need to distribute within the parenchyma to reach their target. In the current study we demonstrate in vivo the distribution of the fluorescent dye Coumarin6 transported in a nanoparticulate carrier system and passing the BBB.

Methods In vivo Confocal Neuroimaging (ICON) was used for real time monitoring of the bio-distribution of Coumarin6-labelled poly(lactic-co-glycolic acid) (PLGA) NPs at the blood-retina barrier (which is virtually the same as the BBB). To this end, rats were anaesthetised and fluorescence-labeled NPs were injected into the tail vein. The retina was imaged with a confocal laser scanning microscope via the eye before and after application of the NPs. ICON was followed by retina wholemount preparation. After decapitation, eyes were enucleated and placed in cold HEPES buffer. The retina was prepared, separated from the pigment epithelium and flattened on a membrane. For fixation 4% paraformaldehyde solution was applied for 10 minutes. Retina was washed and then Hoechst 33342 (0.005 mg/ml) was added to counterstain the nuclei.

Results Within one minute after NP injection the retina vessels were strongly fluorescent. However, the signal within the vessel declined already substantially 3 min post injection. Interestingly, the pattern distribution of fluorescence in the parenchyma further developed in the following 10-15 min. While at early time points a defined, rather structured fluorescent lining of the vessels could be detected, images taken 15 min post injection revealed a very diffuse, uniform Coumarin6 labelling of the parenchyma, but with still some intensified signal along the vessels. Ex vivo wholemount preparation demonstrated a uniformly distributed fluorescent signal in the parenchyma, but excluding the nuclei.

Conclusions In a nanoparticulate formulation, the very hydrophobic compound Coumarin6 can be injected in high concentrations and accumulate in the brain. The microscopic in vivo images indicate that the dye first concentrates along the vessels before further distribution in the tissue. This is in line with the hypothesis that after BBB passage the dye is distributed via the glymphatic system.

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P 04

INFLUENCE OF MILD TRAUMATIC OPTIC NERVE INJURY ON BLOOD-BRAIN BARRIER PASSAGE OF PVP-NANOPARTICLES

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Objectives Nanoparticles (NPs) are of interest as carrier systems for delivery of drugs across the blood- brain barrier (BBB). However, most BBB models provide results about the ability of nanoparticulate carriers to cross this barrier under physiological conditions. In the current animal study we therefore tested fluorescent-labelled polyvinylpyrrolidone NPs in vivo to demonstrate the influence of mild traumatic injury on the ability of these particles to pass the BBB.

Methods Optic nerve crush (ONC) was performed as a model of mild traumatic injury in rats. To this end, a lateral canthotomy was made from the orbita following an incision of the conjunctiva lateral to the cornea. The retractor bulbi muscles were separated, and the optic nerve was exposed by blunt dissection. To crush the nerve, a calibrated forceps was used for 30 s at a distance of 2–3 mm from the eye. After the surgery, the anaesthetized rats were transferred to the vivo Confocal Neuroimaging (ICON) set-up, DiI-labelled PVP-NPs were injected via the tail vein (i.v.) and real time monitoring of the bio-distribution of fluorescent NPs at the blood-retina barrier (which is virtually the same as the BBB) was performed for 1-2 hrs. Subsequent ex-vivo wholemount preparation allowed imaging of the retina vessels with higher magnification. Rats without ONC and rats with ONC and i.v. injection of the standard marker FITC-dextran served as controls.

Results Within a time-window of 1-2 hrs after ONC we did not detect any leakage through the BBB. After injection of the fluorescent PVP-NP we observed labelling of the vessels within minutes. This distribution of the fluorescent signal remained stable within the vascular system until the end of the in vivo experiment and no difference was detectable in comparison to the not-lesioned control animals. Also higher magnification imaging of the retina vessels in the ex vivo wholemount preparation did not reveal any fluorescent signal in the parenchyma. This result was in line with the findings after the post-lesion injection of the standard marker FITC-dextran, which also did not leak out of the vascular system at this early post-ONC time point.

Conclusions After mild traumatic injury the transport mechanisms at the BBB regarding PVP-NPs do not seem to be impaired and nano-carriers cannot reach the parenchyma just by leaking through the blood (or retinal?) vessels vessels.

This work was supported by Era.Net.Rus.Plus initiative (project "NABUCO"; ID#169)

P 05

ELABORATION OF BIODEGRADABLE POLY (ESTER AMIDE) NANOPARTICLES FOR OCULAR DRUG DELIVERY AND IN VIVO PRELIMINARY STUDY OF THEIR PERMEABILITY INTO THE OCULAR BARRIERS

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Drug delivery used to treat ocular disease still poses a challenge to modern ophthalmology. Well-established intravitreal injections imply

discomfort to the patients and risk of ocular complications. Therefore, opportunities to deliver drugs by topical administration are investigated thoroughly. Despite its seemingly easy accessibility, the eye is well protected by efficient mechanisms that rapidly remove drugs after instillation on the eye surface. Physical- biological barriers such as the cornea prevent drugs from intraocular penetration. Hence, eye drops are less effective for the treatment of various diseases, which necessitates a risk- containing procedure of intravitreal injection.

One of the rational ways to overcome the problem is the application of drug-loaded polymeric nanoparticles (NPs) that are able to penetrate through the ocular barriers when administered topically. Pseudo-proteins (PPs) - amino acid-based biodegradable poly(ester amide)s (PEAs) are one of the most promising for the design of NPs and will be cleared from the body after the fulfillment of their function.

We have prepared biodegradable NPs of various types by nanoprecipitation of the PP-PEA composed of L-leucine, 1,6-hexanediol and sebacic acid (8L6). The originally designed arginine-based cationic PEA and comb-like PEA containing lateral PEG-2000 chains along with 8L6 anchoring fragments in the backbones were used to construct positively charged and PEGylated NPs.The NPs were loaded with fluorescein diacetate (FDA) as a fluorescent probe to detect if the NP penetrated into the cells. A preliminary *in vivo* study on intraocular infiltration of the NPs has been done using wild-type C57BL/6 mice. After penetrating into the cellular lysosomes, FDA probes became visible due to the hydrolysis of the diacetate groups, thus allowing for the detection of the NPs as tiny fluorescent spots inside the tissues. One day after administration, fluorescent dots were found at various sites - always in the peripheral cornea and the sclera, and in different layers of the outer retina depending on the type of NPs used. Four days after administration, fluorescent dots were still visible in the peripheral cornea and the sclera with some of the NPs.

These results show that the new type of NPs infiltrate the ocular tissues after topical administration and are taken up by the cells. Afterwards, the NPs release their cargo, which becomes visible by the appearance of fluorescence dots that are also detectable after a long period of time. This raises hope that the NPs may be useful for ocular delivery of therapeutic agents.

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P 06

PRODUCTION AND CHARACTERIZATION OF PHA FROM BIODIESEL-GLYCEROL BY CUPRIAVIDUS EUTROPHUS B10646

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The current prominence on sustainability, eco-efficiency, and green chemistry has generated tremendous search for materials that are renewable and environmentally friendly. Polyhydroxyalkanoates (PHAs) are one of the versatile classes of biodegradable polymers which constitute a group of microbial biopolyesters with important ecosystem functions and high biotechnological potentials. Exploring the utilization of waste materials in PHA production is a good attempt of reducing the substrate cost by eliminating the necessity of supplementing with the more expensive carbon source. The large scale production of biodiesel, as an alternative and renew- able energy source, already results in a surplus of glycerol. This side carbon compound could be the ideal source for industrial production of PHAs. *C. eutrophus* B10646 grew and synthesized poly(3-hydroxybutyrate) (P3HB) from glycerol concentrations ranging from 10 to 60 g/L. The fermentation was successfully scaled up to 30 and 150 L for polymer production and the yield of dry biomass and P3HB were 100-110 g/L and 75-80% respectively during 60 h. Integrating PHA production in existing oilseed-based biodiesel plants could enhance the viability and sustainability of this first generation biorefinery.

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P 07

PROPERTIES OF PHA BI-, TER-, AND QUARTER-POLYMERS CONTAINING 4-HYDROXYBUTYRATE MONOMER UNITS

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The present study investigates physicochemical, mechanical, and biological properties of polyhydroxyalkanoate (PHA) copolymers containing 4-hydroxybutyrate (4HB) synthesized in Cupriavidus eutrophus B10646 culture. In poly(3-hydroxybutyrate/4-hydroxybutyrate) [P(3HB/4HB)] bipolymers, 4HB varied between 10.4 and 75.0mol%; in poly(3- hydroxybutyrate/3-hydroxyvalerate/4-hydroxybutyrate) terpolymers, 4HB constituted 28.7–55.6 mol%; and in poly(3-hydroxybutyrate/3-hydroxyvalerate/4-hydroxybutyrate/3-hydroxyhexanoate) quaterpolymers, 4HB varied between 9.3 and 13.3mol%. The degree of crystallinity of P(3HB/4HB) copolymers decreased consistently with an increase in 4HB content, reaching 38%. The incorporation of 3-hydroxyvalerate and 3-hydroxyhexanoate into copolymers enhanced that effect. The effect of 4HB monomer units on temperature properties of copolymers was exhibited as lowering of the melting temperature and crystallization temperature, which improved the processing-related properties of the copolymers. All copolymers containing 4HB showed enhanced elongation at break compared to poly(3- hydroxybutyrate). Polymer films prepared from PHAs with different chemical composition had similar microstructure and porosity and had no toxic effect on mouse fibroblast NIH 3 T3 cells, proving their high biocompatibility.

Study was financially supported by mega-grant (Agreement No 14.Y26.31.0023) in accordance with Resolution No 220 of the Government of the Russian Federation.

P 08

SPHEROIDIZED GLASS-BASED MATERIALS FOR TARGETED DELIVERY OF DRUGS AND RADIOPHARMACEUTICALS

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The development of biotechnology, genomics and combinatorial chemistry contributes to the creation of more advanced and differentially effective drugs, the use of which often prevents by low solubility, high chemical activity, radioactivity, instability in the body environment, etc. To overcome these problems, it is necessary to develop technological and safe methods of targeted delivery and controlled release of biologically active substances, therapeutic agents and radiopharmaceuticals to organs and parts of the body. Targeted delivery of drugs makes it possible to systematically and purposefully introduce the required dose of the drug, which is important in the treatment of chronic diseases and in particular radiotherapy of tumors. Moreover, the selection of the optimal drug carrier material allows varying the rate of prolonged release of the active substance, which makes it possible to control this process.

In this concern, the use of glass-based materials as carriers of drugs is of interest because of the possibility of a smooth change in the composition of the glasses and, as a consequence, smooth variation within a wide range of their properties. At the Glass Technology Department of Mendeleev University of Chemical Technology, we conduct extensive research and development of glass-based spheroidized materials for targeted delivery of radiopharmaceuticals and drugs in various configurations such: yttrium-aluminosilicate microspheres for the Y^{90} liver brachytherapy with visualization of treatment process in a gamma chamber [1-3]; nanoporous glass microspheres with ~ 2 to 100 nm controlled pore size and calcium phosphate glass microspheres with controlled rate of resorption for impregnation of drugs and substitution of bone tissue deficiency [4].

We plan to create a range of functional materials in the form of monolithic and porous microspheres, as well as hollow microspheres from glasses with different levels of resorption that could be used in various fields of medicine. Precise control of the microspheres size and their pore structure with a pore size from a few nanometers to microns opens the possibility of their saturation with a variety of drugs.

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P 09

DRESSING POLYSACCHARIDE PREPARATIONS CONTAINING ENZYMES FOR WOUND HEALING

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It has established by means of numerous studies that the current wound-healing agent must offer the following properties: sorb the purulent discharge and the products of its destruction, have purifying properties (usually due to the introduced proteolytic enzyme), possess biocidal properties, and include an antioxidant (especially for the treatment of long-term diseases).

Based on the periodate oxidized cellulose and chitosan, various dressings were developed. The influence on the biological activity of the developed preparations as interaction with each other, the method of preparation, and drying, storage, sterilization method and behavior under model conditions was studied. The effective rate constants of inactivation in the process of production, drying and storage, as well as thermal inactivation in the model liquid medium was calculated.

Dialdehyde cellulose is capable of degradation by oxidized links as a result of non-enzymatic hydrolysis. The low molecular weight fragments of the matrix disproportionate and accumulate in the solution in the form of low-molecular compounds (including carboxylic acids) over time. For immobilized drugs the change in the amount of reducing substances is not observed for 72 hours. This fact is related to the interaction of aldehyde groups of the oxidized cellulose carrier with the amino groups of chitosan which prevents the decay of the matrix and, correspondingly, the reduction in the number of reducing groups.

The conclusions are also confirmed by the study of the change in the zeta potential of solutions into which cellulose carriers were placed. The decrease in the value of the zeta potential for all the samples studied confirms the conclusion about the decay of cellulosic carriers under the conditions studied. Acute and chronic toxicity of extracts from solutions into which cellulose carriers were placed was studied in mice. Analysis of the results of the examination of animals in the determination of acute and chronic toxicity did not show any difference between the experimental and control groups in none of the observed tests.

The absence of toxic free aldehydes as products of hydrolytic degradation of cellulose carriers was also confirmed in the experiment on the study of activity.

It has been shown that low-molecular aldehydes (formaldehyde) capable of binding, apparently, to the amino groups of the active center of the enzyme, significantly reducing its activity, and at high concentrations completely inactivating it. At the same time, solutions (pH = 6.2) weighed cellulose carriers of different degrees of oxidation, as well as with immobilized chitosan at 37 ° C for 2 and 24 hours, do not inhibit

the enzymatic activity of the drugs studied, but increase the activity with time.

The mechanism of obtaining and working in the liquid medium of the developed compositions was proposed.

P 10

LIPOAMINO ACID-BASED CERASOMES FOR ANTICANCER DRUG DELIVERY: PREPARATION AND EVALUATION IN 3D IN VITRO MODEL

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Stability is one of the most important parameters of passive targeted drug delivery systems (PDDS). Cerasomes are hybrid organic-inorganic nanoparticles that could be considered as liposomes with rather durable silicon shell. Recently, we have synthesized structural blocks for formation of stable cerasome-forming lipoamino acids (CFLA). The aim of the current study was to obtain several types of doxorubicin(DOX)-loaded cerasomes which differed in lipid composition, and to study their accumulation and cytotoxicity effects both in monolayer cell culture (2D model) and in multicellular tumor spheroids (3D model). For this purpose, "pure" cerasomes containing only CFLA, as well as "mixed" cerasomes composed from a mixture of CFLA with a disintegrating lipid dipalmitoylphosphatidylcholine (DPPC) were obtained. The cerasomes were characterized in terms of their stability and efficiency as PDDS. The cerasome properties and in vitro behavior were found to be easily changed by varying their lipid composition. Physical-chemical parameters, such as mean diameter, ζ-potential, morphology and stability of "pure" and "mixed" as well as neutral and cationic cerasomes were evaluated. Human breast adenocarcinoma cells (MCF-7) were used as a model in the current study. Cerasome accumulation in the cells was studied by flow cytometry and confocal microscopy both in 2D (monolayer culture) and 3D (multicellular tumor spheroids) models. Cytotoxicity effects were estimated by MTT-test. The highest accumulation efficiency, as well as cytotoxicity effects were found for the "mixed" cationic DOX-loaded cerasomes, while the "pure" cerasomes demonstrated sustained drug release. Thus, the cerasomes are supposed to be able to overcome limitations of conventional drug delivery systems and are promising as rather stable and universal PDDS.

This study was supported by n Foundation for Basic Research (grant 18-34-00919 in part of cerasomes, and grant 18-04-01087 in part of 3D tumor spheroids).

P 11

POLYMERIC NANOPARTICLES BASED ON AMPHYPHILIC DERIVATIVES OF N-VINYL-2- PYRROLIDONE CONJUGATED WITH ANTITUMOR CYTOKINE TRAIL DR5-B

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Polymers based on amphiphilic derivatives of N-vinylpyrrolidone are able to form nanoparticles in water solutions and to immobilize water insoluble drugs. Chemically linking of the antitumor receptor-selective variant TRAIL DR5-B to the polymer-based nanoparticles will increase the protein stability and support the hypothesis that increase of the cytokine local concentration enhances the clustering of the DR5 death receptor on the surface of tumor cells and improves the efficiency of the apoptotic signal.

Amphiphilic copolymers of N-vinyl-2-pyrrolidone and acrylic acid (the content of acrylic units is 5 mol%) were synthesized by a one-stage method by polymerizing monomers of N-vinyl-2- pyrrolidone and acrylic acid in the presence of the initiator of radical polymerization (azobisisobutylonitrile), transmitter and regulator of chain growth (octadecylmercaptan). TRAIL DR5-B protein was produced in *E. coli* cells and purified on the affinity sorbent Ni-NTA followed by cation-exchange sorbent SP Sepharose. The TRAIL DR5-B protein was linked to the amphiphilic copolymer by the selective covalent interaction of the protein amino groups with activated carboxyl groups of the amphiphilic copolymer. Resulting conjugates were purified by gel filtration on a Sephadex sorbent using FPLC. Obtained polymers were characterized by the following parameters: the average size of the particles, ζ-potential, and the amount of the attached protein.

As a result, we obtained polymeric nanoparticles with a hydrophobic core and a hydrophilic surface based on amphiphilic N-vinyl-2-pyrrolidone, and developed optimal conditions for its conjugation with antitumor cytokine TRAIL DR5-B.

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P 12

MACROPOROUS HYDROGELS BASED ON GRAFT COPOLYMERS OF CHITOSAN WITH OLIGO (L, L- / L, D-LSCTIDES) FOR REGENERATIVE MEDICINE

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Chitosan is a biocompatible and biodegradable polymer with antibacterial and bioadhesive properties. Hydrogels based on chitosan are promising matrices for regenerative medicine.The modification of chitosan chemical structure is of great interest, since it allows regulating

biodegradation rate and physical and mechanical properties, as well as biological activity of the based materials.

The aim of this work was to obtain macroporous hydrogels based on graft copolymers of chitosan with oligo (L, L- / L, D-lactides), to study their structure and physicochemical properties and to evaluate cell growth in these 3D matricesin vitro model.

Copolymers of chitosan (MM60kDa, DD 0.9) with amorphous-crystalline oligo (L, L-lactide) and amorphous oligo (L, D-lactide) with MM 5kDa were previously obtained by the solid-phase synthesis technique. The hydrogels were prepared by freeze-drying of 4% solutions of the copolymers in 2% acetic acid, followed by heating (1500C, 3 h).

The effect of the chemical structure of chitosan derivatives on the hydrogels structure was evaluated by scanning electron and confocal laser microscopy. Swelling and biodegradability of the hydrogels were also studied. The cytotoxicity of the hydrogels was studied in extraction test using mouse fibroblasts cell lineL929 as a model. Using MTT-test, it was shown that hydrogels supported adhesion, growth and proliferation of fibroblastsat long-term cultivationfor 7 days.

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P 13

PREPARATION OF 3D-SCAFFOLDS BASED ON CHITOSAN MODIFIED BY CHEMICAL CROSS-LINKING

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An influence of conditions for the preparation of geniin-crosslinked chitosan cryostructures on their porous morphology, physico-chemical properties as well as their use as 3D-scaffolds for tissue engineering was studied. These chitosan cryostructures were fabricated by lyophilization of a chitosan acetate solution followed by the treatment of the obtained sponge with in order to transform polyaminosaccharide from a salt into a chitosan-base and further polymer cross- linking with genipin (at molar ratios of genipin to the number of chitosan amino groups equal to 0.05, 0.033 и 0.02, respectively). The pore sizes, water-retaining capacity and biodegradation in vitro were shown to depend on such ratio. Properties of the prepared chitosan cryostructures and hydrogels formed by chitosan cross-linking with genipin at room temperature, as well as films cast from chitosan solutions containing genipin were studied and compared after the solvent evaporation. Biocompatibility of the obtained macroporous sponge materials was demonstrated using mouse fibroblasts L-929. The cells were found to successfully distribute within the 3D–scaffolds, as well as the cells grow and proliferate upon the long-term cultivation for 7 days.

It is shown that the properties, functional characteristics (swelling degree, biodegradation rate) and porous morphology of the obtained materials depend on the ratio of functional groups in the chitosan acetate–cross-linking reagent system.

The developed method for obtaining a hydrogel scaffolds based on water solutions of chitosan acetate in the presence genipin in cryogenic conditions, which ensure the formation of macroporous structures necessary for cell growth.

This work was supported by the Russian Science Foundation (grant No. 18-33-00324).

P 14

FUNCTIONALYZED MAGNETIC NANOPARTICALS FOR ENZYMATIC LYSIS OF E.COLI CELL WALL UNDER ULTRA LOW FREQUENCY MAGNETIC FIELD

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Currently, the bacterial etiology infectious diseases still remain a global health problem. Most of them are caused by gram-negative pathogenic microorganisms. The traditional method of infectious diseases treatment is based on the use of antibiotics. However, the rapid development of the resistance of pathogenic microorganisms to existing antibiotics forces to seek alternatives to traditional therapy. One of such alternatives is the therapy with bacteriophage endolysins - bacteriolytic enzymes capable of destroying the bacterial cell wall by hydrolyzing of peptidoglycan. Endolysins are highly specific for certain pathogens. The main limitation of their use towards gram-negative bacteria is the presence of an outer membrane in the latter preventing the penetration of lytic enzyme to its substrate. The effectiveness of endolysin penetration can be increased by destabilizing the outer membrane of gram-negative bacteria.

In this study, bacteriophage S394 endolysin and rod-like (40 x 10 nm) dopamine functionalized magnetic nanoparticles (MNPs) were used. It was shown that application of ultra-low frequency (50 Hz) alternating magnetic field (AMF) in the presence of MNPs leads to the destabilization of the outer membrane of *E.coli* cells. Electrostatic interactions take place between positively charged amino groups of dopamine and negatively charged phosphate groups of membrane phospholipids. Complex oscillating motions and membrane deformations with normal and lateral components occur under AMF application. Such deformations lead to the increase of the enzyme penetration to its substrate (peptidoglycan) enhancing the rate of *E.coli* cells lysis.

AMF membrane destabilizing effect was confirmed by β-lactamase release from *E.coli* cell periplasm as well as significant decrease of the hydrophobic dye Nile Red intensity. Next, we were trying to determine the optimal magnetic properties of MNPs and their synthesis conditions. For this purpose, non-magnetic rod-like nanoparticles of akaganeite (β-FeOOH) were prepared by aqueous hydrolysis of ferric chloride in acid medium, followed by modification with dopamine and reduction with hydrazine hydrate in a microwave reactor. Magnetic properties and stability of MNPs can be altered significantly by varying dopamine and reducing agent concentrations enabling to have different ratios between magnetic and non-magnetic phases.

Experimental data of MNP optimal compositions for enzymatic lysis of *E.coli* cell wall are discussed.

The work was supported by RSF-14-13-00731П and RFBR 17-54-33027 ОНКО_а grants.

P 15

STAPHYLOCOCCUS AUREUS LYTIC ENZYMES KINETICS STUDIES

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Staphylococcus aureus is one of the most dangerous bacterium for humans and animals. It is a cause of human organs and tissues infections. The treatment of staphylococcal infections is difficult because of 90% of its strains are resistant to antibiotics. Lytic enzymes of bacteriophages can be considered as promising alternative to conventional antibiotic therapy.

The stability (residual activity dependence on the incubation time) of the lysins of phages 8161, K, and chimeric enzyme K-L (LysK CHAP endopeptidase and amidase domains, and the entire mature lysostaphin protein) was investigated at the physiologically relevant conditions (37°C, human serum, enzyme concentration of 0,2-0,4 mg/mL). Activity of the enzymes was measured in a turbidity reduction assay from time-dependent turbidity changes in a suspension of S. *aureus* cells (A_{600} = 0,6, 37°C, C_{NaCl} 137 mM, C_{KCl} 2,7 mM, $C_{Na2HPO4}$ 10 mM, C_{KH2PO4} 1,76 mM, pH 7,4).

The stability of lysin of phage 8161 depends on the enzyme concentration. Increase of the enzyme concentration from 0.2 to 0.4 mg/mL leads to the enzyme stability decrease. It can be concluded that intermolecular interactions (aggregation) is likely the main reason of the enzyme inactivation. At high concentration of phage 8161 lysin (0,4 mg/mL) two linear parts are presented on the dependence of residual activity logarithm versus incubation time. Such dependence corresponds to two different inactivation stages.

The rate of chimeric enzyme K-L inactivation does not depend on its concentration and is described by the first order equation. Both inactivation constant and half-inactivation time were calculated (k ~ $3{,}33\times10^{-5}$ s^{-1} τ1/2 ~ 347 min).

The inactivation rate of phage K lysin depends on its concentration. Increase of the enzyme concentration from 0.2 to 0.4 mg/mL (inactivation curve with fracture) leads to the enzyme stability increase. Such dependences correspond to dissociative mechanism of the enzyme inactivation.

It can be concluded that 8161 lysin inactivation has aggregative mechanism, chimeric enzyme inactivation has denaturation mechanism and phage K lysin inactivation has dissociative mechanism.

P 16

CATIONIC LIPOSOMES MODIFIED WITH FOLIC ACID FOR ACTIVE TARGETED ANTITUMOR DRUG DELIVERY

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Liposomes loaded with antitumor drugs are known to be delivered into cancer cells by so-called Enhanced Permeability and Retention (EPR) effect (passive delivery) as well as by ligand molecules which can bind only with specific cancer cell receptors (active delivery). Targeted delivery is a promising approach to anticancer treatment.

The aim of the study was to obtain doxorubicin(DOX)-loaded folate-associated cationic liposomes (FLPs) and to study their cytotoxicity *in vitro*. Cationic liposomes are supposed to have faster penetration into tumor cells compared to neutral and anionic ones due to their high positive membrane charge. The FLPs surface was modified with folic acid residues to provide their specific interaction with folate receptors. These receptors are known to be an attractive target for active drug delivery systems, since they are located mainly on the membrane of tumor cells.

To prepare FLPs, two types of lipid compositions were used as bases, namely cationic lipopeptide (1) and a mixture of polycationic amphiphile (2) with 1,2-Dioleoyl-sn-glycero-3- phosphoethanolamine (DOPE). Both bases were combined with two different folate ligands: (3) and (4). Thus, four types of DOX-loaded liposomal dispersions were obtained (Table 1). Physical-chemical FLPs parameters, such as mean diameter, ζ-potential and stability were measured. MTT-test was used for cytotoxicity assay with HeLa (a human cervical cancer), MCF-7 (a human breast adenocarcinoma), U-87 MG (human brain glioma) and C6 (rat brain glioma) cell lines which are known to differ in the folate receptors amount. The FLPs accumulation and localization in the cells and multicellular tumor spheroids was evaluated by confocal microscopy and flow cytometry.

Table. 1. Physical-chemical parameters of the obtained liposomal dispersions

Lipid composition, % w/w	D, nm	PI, %	ζ- potential, mV
(1) + (3) 98:2	254	87	+47
(1) + (4) 98:2	135	93	+51
(2) + DOPE + (3) 32,5:65,5:2	238	94	+16
(2)+ DOPE + (4) 32,5:65,5:2	270	98	+28

This study was supported by Russian Foundation for Basic Research (grant 18-34-00919 in part of liposomes, grants 17-54-33027 and 18-04-01087 in part of 3D tumor spheroids).

P 17

POLY(N-VINYLPYRROLIDONE) NANOPARTICLES LOADED WITH DNA PLASMIDS ENCODING GLYCOPROTEINS AGAINST RVF VIRUS

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Rift Valley Fever (RVF) is a peracute transmissible and zooanthroponotic viral infection which is characterized by fever, hemorrhagic diathesis, damage of central nervous system, necrotizing hepatitis and/or gastroenteritis. Sheep, goats, cattle, horses, antelopes, monkeys as well as humans are susceptible to this infection. Presently, there is no licensed or commercially available vaccines neither for humans nor for veterinary. Therefore development of vaccines is of great importance. Entrapment of DNA plasmids in polymer nanoparticles (NPs) could provide:

(1) DNA protection from cleavage by nucleases; (2) an increased DNA delivery to cells; (3) an easy binding specific ligand(s) to the nanocarrier which allows targeted delivery via interaction with cell receptors; (4) preparation of a polyvalent vaccine containing several DNA plasmids or a mixture a DNA plasmid with a protein (antigen).

The aim of this study was to develop new formulation based on polymer NPs loaded with DNA plasmids encoding Gn и Gc proteins of RVF virus and to evaluate these NPs in vivo using a mouse model. Two amino acid derivatives of amphiphilic poly-N-vinylpyrrolidone (PVP), namely ß-alanine containing polymer Ala-PVP-OD3500 and glycine-containing polymer Gly-PVP- OD3500 were synthesized and characterized as candidates for DNA plasmids biocompatible nano-scaled carriers. Both copolymers had molecular weight of 3500 Da. The introduction of amino acid groups into amphiphilic polymer structure provided tight binding and entrapment of DNA molecules in self-assembled NPs. The mean NPs diameter was 200 nm, spherical morphology was confirmed by transmission electron microscopy and scanning probe microscopy. Cytotoxicity of the NPs was estimated by MTT-test using mouse fibroblasts cells (L929). To study immunogenicity of the DNA-loaded NPs, immunization of BALB/c mice of two experimental and 1 control group (10 animals in each group) was carried out. The experimental group 1 was intramuscularly immunized with a single dose of native pCI-neo/Gc/3 and pCI- neo/Gn/1 plasmids (25 μg of each plasmid/mouse). The group 2 was administered with NPs loaded with DNA plasmids (25 μg of each plasmid/mouse), and group 3 was injected with blank NPs. Neutralizing antibodies against RVF virus were determined by ELISA of blood sera samples in 7, 14, 25 and 40 days after immunization. Entrapment of plasmids into NPs resulted in enhancement of antibody titres, in particular from 1:250 (in case of native plasmids) to 1:250-1:750 (for plasmids in NPs) on day 14. Thus, entrapment of DNA plasmids into PVP-based NPs by self-assembly is a promising approach for development of novel nano-encapsulated DNA vaccines.

P 18

COMPOSITE CROSS-LINKED HYDROGELS BASED ON POLYSACCHARIDES AND FIBROIN FOR REGENERATIVE MEDICINE

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Macroporous hydrogels based on natural biodegradable polysaccharide chitosan (Chit) and hyaluronic acid (HA) are promising biomaterials for tissue engineering. Chit has antibacterial and bioadhesive activity, while HA is a main extracellular component of a connective tissue being involved in growth, proliferation and differentiation processes. In order to improve mechanical properties of the hydrogels, a silk protein fibroin (Fb) could be proposed.

The work was aimed to obtain composite covalent cross-linked hydrogels based on Chit, HA and fibroin (Fb), to study structure and properties of these hydrogels, as well as their ability to support cell growth *in vitro.*

Hydrogels were produced by covalent cross-linking of Chit (MM 320 kDa), Fb and HA (30 kDa). HA was introduced to hydrogel composition in two ways: before and after cross-linking. Genipin was used as a cross-linking agent. When HA was introduced before Chit cross-linking: solutions of Chit, Fb and HA were mixed and cross-linked for 24 hs. In this case HA macromolecules were distributed mostly within the hydrogel volume. When HA was introduced after Chit cross- linking, the obtained cross-linked Chit hydrogel, containing Fb, was incubated in HA solution (2 mass. %) for 2 hs. As a result, the HA macromolecules were distributed mostly on the hydrogel surface. The structure of the hydrogels was studied by confocal laser microscopy. The cytotoxicity of hydrogels was evaluated by extract-test using mouse fibroblasts L929. Cultivation of the cells in the hydrogels was carried out in DMEM (10% FBS) for 7 days. Distribution, adhesion, and cell growth in the hydrogels were evaluated qualitatively by confocal microscopy, while the number of viable cells was determined by MTT-test. It was shown that the structure of the hydrogels changed with Fb introduction. The hydrogels were found to support adhesion, growth and proliferation of fibroblasts during their long-term cultivation.

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P 19

CYTOTOXICITY OF NEW BEXAROTENE DERIVATIVES FOR RAT GLIOMA C6 AND HUMAN GLIOMA U-87MG CELLS

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Glioblastoma is one of the most aggressive and lethal forms of brain tumors due to a lack of effective chemotherapy agents and high metastasis capacity. Recently, bexarotene (BXR), a retinoid X receptor (RXR) agonist, has been demonstrated as a drug candidate for glioblastoma treatment. However, BXR cytotoxicity was found to be limited. To enhance it, we modified BXR with dopamine and NO donor nitroethanolamine, which are known to induce NO-dependent cell death for various tumor cell lines.

The aim of the study was to evaluate the cytotoxicity of two novel bexarotene derivatives, namely bexarotene dopamine (Bxr-DA) and nitroethanol (Bxr-NEA) amides, using monolayer cell culture and multicellular tumor spheroids.

In this study, rat glioma C6 and human glioma U-87MG cell lines were used as tumor cells, while human fibroblasts BJ-5ta were proposed as model normal cells. Tumor spheroids, which are considered as 3D *in vitro* model of tumors *in vivo*, were obtained by RGD-induced cell assembly, as described earlier [Akasov et al, Int J Pharm. 2016; 506(1-2):148-57]. Both Bxr-DA and Bxr-NEA were found to be more toxic for glioma cells than BXR. Thus, after 24 h incubation of C6 cells(monolayer culture) with drugs, IC_{50} values were 31.41±1 μM, 23.36±1 μM, and 121.9±2 μM for Bxr-DA, Bxr-NEA, and BXR, respectively, Cell death occurred via apoptosis pathway that was demonstrated using annexin and propidium iodide staining. Tumor spheroids demonstrated higher resistance to treatment, and the IC_{50} values for C6 cells in spheroids after 24 h incubation were 50,65±2 μM, 40,28±2 μM, and 147,7±3 μM for Bxr-DA, Bxr-NEA, and BXR, respectively. The bexarotene modification effect on cytotoxicity for normal and tumor cells was of non-equal magnitude. Thus, a selectivity index of the compounds increased from 1.3-1.5 for Bxr to 1.7-3.1 for Bxr-DA.

In summary, BXR modification with NO donors and NO inducers is promising to increase the drug cytotoxicity, while Bxr-DA and Bxr-NEA derivatives could be proposed for glioblastoma treatment.

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P 20

ENCAPSULATION OF P140 PEPTIDE-HYALURONIC ACID COMPLEX FOR LUPUS ERYTHEMATOSUS TREATMENT

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Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease which is characterized by inflammation and severe damage of various tissues. Phosphorylated P140 peptide, an analogue of small nuclear ribonucleoparticle protein U1-70K has been proved to decrease symptoms in mice by injection [2]. For repeated human administration, a non-invasive route has to be developed. To provide proper delivery via the oral route, the P140 peptide has to be protected during gastric transit, released in the intestine in a form promoting uptake through the intestinal epithelium barrier.

Frère et al. have developed a method [1], consisting in the entrapment of P140-hyaluronic acid coacervate (< 500 nm) in small alginate beads (<150 μm). However, the method was involving many steps and was not easily reproducible. The coacervate production has been shown delicate operation very sensible to operating parameter. The production of alginate beads through an emulsion-internal gelation was complicated and requires important purification to extract alginate beads from the oil.

In collaboration with the above groups, the objective of this project was to optimize and simplify P140 encapsulation technique. It involved two main developments: 1) a better control of the P140-hyaluronic acid coacervation using a new approach for determining the optimum conditions; 2) the microfluidics for the coacervate production. The second step included a dripping-external alginate gelation using the nozzle resonance technology to entrap the coacervate. This study was mainly focused on the first development.

For this purpose, HA/P140 conditions of interaction were screened as a function of pH, agitation mode, mixing ratio, and ionic strength. The complex was characterized using dynamic light scattering and spectrophotometry. Size distribution and morphology of particles were studied using electron microscopy. Particle size can be tuned by pH variation: a complex size increases when pH decreases. No complex formation was observed in buffers with ionic strength above 25 mM what highlighted that interaction between HA and P140 was primarily driven by electrostatic interactions.

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P 21

DIHYDROQUERCETIN POLYMERIZATION USING MULTICOPPER OXIDASES

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Dihydroquercetin (taxifolin, DHQ) belongs to natural flavonoids and has a wide range of pharmacological effects, in particular antioxidant, angioprotective, hepatoprotective, antitumor and others. Furthermore, DHQ also shows regulatory properties and can control DNA reparation, apoptosis, and mitochondrial biogenesis, as well as it can regulate the activity of certain enzymes. It is known that many flavonoids including DHQ decompose rather quickly *in vivo* while their relatively high molecular weight derivatives have a longer lifespan. These data show promise for the synthesis of novel DHQ derivatives.

In this work a new method for dihydroquercitin oxidative polymerization has been proposed. Multicopper oxidases, namely, bilirubin oxidase (BOD) from *Myrothecium verrucaria* and laccase (LC) from the basidial fungus *Trametes hirsuta* were used as catalysts. The selected conditions enabled good yields of DHQ oligomers, which were then analyzed using UV-vis, FTIR, ^{1}H and ^{13}C NMR spectroscopy. DHQ oligomers synthesized using both enzymes demonstrated higher thermostability as compared with the monomer. Depending on the enzyme used, the products of DHQ polymerization differed in physico-chemical properties, and as shown by NMR studies, had different structures.

To estimate antioxidant properties the DHQ oligomers were tested for their DPPH (1,1-diphenyl- 2-picrylhydrazyl) radical scavenging activity. The significant increase of antioxidant activity (more than 2.5 times) was observed for BOD synthesized DHQ oligomers in comparison with antioxidant activity of DHQ monomer.

In order to improve the efficiency of DHQ polymerization process a fungal laccase (LC) was immobilized in hydrophobic ionic liquid (IL). It was found that the enzyme included into IL can be reused. The physicochemical characteristics of DHQ oligomers synthesized using LC/IL did not differ from the characteristics of the oligomers obtained with native laccase.

Comparative study of the antioxidant activity of monomer and DHQ oligomers was conducted on dog kidney cell culture (MDCK 1). 2'7'-dihlorofluorestsein diacetate (DHFD) was applied to detect free radicals. It was found that the DHQ oligomers obtained by enzymatic synthesis with immobilized into IL laccases also possess stronger antioxidant properties as compared with the monomer.

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P 22

EXPERIENCE OF THE STUDY ON THE EXPERIMENTAL MODELS *IN VITRO* TOXIC PROPERTIES OF NANOMATERIALS IN BELARUS

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The aim of the study was to develop methodological approaches for assessment of nanosafety in Belarus

Single-walled carbon nanotubes and silver nanoparticles were chosen as the objects of the research.

For the study of nanomaterials effects on different cell types, used a number of methods to determine the cytotoxicity, mutagenicity, the ability of nanomaterials to cause oxidative stress. Methods: method of investigation of metabolic activity in MTT assay, method of assessing cell viability using the trypan blue, method assessing the viability of cells in culture by analysis of lactate dehydrogenase activity, method for study the effect on the proliferative potential, method for studying the induction of reactive oxygen species (fluorescein diacetate staining), flow cytometry methods (study the effect on cell cycle, apoptosis, micronuclei formation).

The study was conducted in several cell lines (the culture of human lung carcinoma A549, human amnion FL, human neuroblastoma SH, the primary culture of human lymphocytes, the primary culture of cardiomyocytes from rats SHR line, the primary culture of mouse embryonic fibroblasts).

The study found that the most sensitive to the nanoparticles by the results of tests for cytotoxicity were tumor cells lines and human amnion cell line, rather than the primary cultures. This is probably due to a higher rate of division of transformed cells and amnion cells, as well as the intensity of metabolism.

In an experiment on viability using human lymphocytes, it was shown that the toxicity of carbon nanotubes (inhibitory concentration, IC50 = 20 μg / ml) is five times higher compared to silver nanoparticles (IC50 = 100 μg / ml).

The number of micronuclei under the action of silver nanoparticles increased by a factor of 10 compared to the control. To interpret the obtained data as evidence of a mutagenic potential, it is necessary to establish the nature of micronuclei.

Based on the results of experiments using silver nanoparticles and single-walled carbon nanotubes, the proposed methods for determining the toxicity of nanomaterials that encompass actions on viability, the determination of intracellular metabolic changes, the study of the effect on the formation of active oxygen species and apoptosis processes. The obtained data made it possible to develop algorithms for studying the toxicity of the produced nanoparticles.

P 23

STUDY OF TOXICOLOGICAL PROPERTIES OF MICROFERTILIZERS “NANOPLANT” IN EXPERIMENTS IN VITRO

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The aim of the study was to carry out toxicological studies of microfertilizer “Nanoplant” on the basis of micronutrient nanoparticles in experimental models *in vitro*.

Research objects: microfertilizers "Nanoplant" of the brands "Nanoplant-Co, Mn, Cu, Fe, Zn, Cr" (sample 1), "Nanoplant-Co, Mn, Cu, Fe" (sample 2), "Nanoplant-Cu, Fe" (Sample 3), based on biopolymer-stabilized colloidal solutions of micronutrient nanoparticles, developed by the institutions of the National Academy of Sciences of Belarus.

To conduct a toxicological assessment, human lung cancer cell lines (A549) and primary culture of human lymphocytes were used. From the presented samples, working solutions were prepared with a sample concentration of 0.35 ml / l in a nutrient medium (introduced in volumes of 10-100%).

The following methods for studying cytotoxicity and mutagenicity were used: a method for studying metabolic activity in the MTT assay, a method for assessing the viability of cells and the integrity of the cell membrane by determining lactate dehydrogenase activity, a method of intravital study of the effect on the proliferative potential.

The study found that samples of microfertilizers 1, 2 in concentrations of working solution of 10- 50% and sample 3 in a concentration of 10-70% did not affect the viability of cells (24 hours exposure) on the more sensitive A549 cell line. When the concentration of samples increased, the metabolic activity of the cells was dose-dependent, IC50 (inhibitory concentration) of sample 1 was 70%, sample 2 - 75%, and sample 3 - 100%.

When assessing the proliferative potential (14 days exposure on the A549), cell division was suppressed from 2 days of the experiment for concentrations greater than 60% (samples 1,2), more than 70% (sample 3). Complete suppression of cell division and growth were not observed in any experimental group. Perhaps suppression is associated with a purely mechanical effect of nanoparticles. The particles settle on the bottom of the plate and interfere with the growth and division of cells in the culture.

Thus, the study of the toxicological properties of microfertilizer "Nanoplant" in experimental models *in vitro* has a dose-dependent effect on the viability of cells without manifestation of any specific properties.

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ECOTOXICOLOGICAL RESEARCH OF MICROWAVES "NANOPLANT"

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Objective: To conduct ecotoxicological studies of microfertilizer «Nanoplant» with an assessment of the toxic effect on soil strains of microorganisms, the study of phytotoxic effects and the evaluation of long-term effects on aquatic organisms.

Research objects: microfertilizers «Nanoplant» of the brands «Nanoplant-Co, Mn, Cu, Fe, Zn, Cr», «Nanoplant-Co, Mn, Cu, Fe», «Nanoplant-Cu, Fe», «Nanoplant-Se», «Nanoplant-Mo»,

«Nanoplant-Co, Mn, Cu, Fe-Active», «Nanoplant-Ag» based on biopolymer-stabilized colloidal solutions of micronutrient nanoparticles developed by the National Academy of Sciences of Belarus.

Subject matter: mutagenic properties, toxicity for soil and water strains of microorganisms, phytotoxic effect.

Methods of research: toxicological, physiological, statistical. Results:

- when studying the mutagenic activity in the micronuclear test on L.STAGNALIS, the experimental groups of animal death were not observed and the level of cells with micronuclei did not exceed the control values, therefore, the studied microfuel «Nanoplant» brands do not exert a genotoxic effect on the cells of the mantle liquid of mollusks, hydrobionts;

- The toxicity of the declared microfertilizer «Nanoplant» brands was studied in the acute *Tetrahymena pyriformis* test object in acute, subacute and chronic experiments and it was established that the samples under study are related to acute toxicity (LD_{50}), cumulation factor, biological and toxic effect in a chronic experiment toxicity class (low toxicity substance);

- in the test for germination of seeds and in the test for growth and development of rootlets of seedlings of test plants, the test samples in working concentrations do not have phytotoxic effect, but exert a statistically significant stimulating effect on the germination of seeds of radish, cucumbers and oats.

Conclusions: on the basis of ecotoxicological studies conducted on specific and highly sensitive test systems of various hierarchical levels of living organisms (mutagenic properties in a micronuclear test, assessment of toxic effects on soil strains of microorganisms, study of phytotoxic effects, evaluation of long-term effects on aquatic organisms) «Nanoplant» on the studied indicators and test systems is not established.

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STUDY OF THE TOXICOLOGICAL PROPERTIES OF MICROFERTILIZER "NANOPLANT" IN EXPERIENCE IN VIVO

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Objective: To determine the toxicometry parameters of microfertilizer «Nanoplant» in the acute toxicological experiment with the establishment of a hazard class for intragastric intake and the ability to exert an irritating and sensitizing effect on experimental animals, as well as the ability to accumulate in the body upon repeated administration in a subchronic 30-day experiment.

Research objects: microfertilizers «Nanoplant» of the brands «Nanoplant-Co, Mn, Cu, Fe, Zn, Cr», «Nanoplant-Co, Mn, Cu, Fe», «Nanoplant-Cu,

Fe», «Nanoplant-Se», «Nanoplant-Mo»,

«Nanoplant-Co, Mn, Cu, Fe-Active», «Nanoplant-Ag» based on biopolymer-stabilized colloidal solutions of micronutrient nanoparticles developed by the National Academy of Sciences of Belarus.

Methods of research: toxicological, physiological, hematological, biochemical and statistical.

Results:

- On the parameters of acute toxicity with a single intragastric administration, the studied brands of microfertilizer «Nanoplant» refer to the IV hazard class according to GOST 12.1.007-76;
- with a single exposure to the mucous membranes of rabbit eyes, the studied brands of microfertilizer «Nanoplant» do not have an irritant effect (grade 4);
- a single epicutaneous effect of the studied brands of microfertilizer «Nanoplant» does not have a local irritant effect (grade 4);
- the studied brands of microfertilizer «Nanoplant» in the mouse paw swelling test (TOLM) do not lead to the development of edematoproliferative reaction of the mouse paw tissue (grade 4);
- with repeated intragastric administration of the studied brands of microfertilizer "Nanoplant" there was a statistically significant decrease in relative mass coefficients of the liver, an increase in the heart OKM; in the blood serum of animals in the experimental groups, the activity of AcAt and ALAT, urea, chloride and protein reduction statistically increased; in the urine of the animals the chloride content was statistically significantly increased in comparison with control. In this case, repeated intragastric administration of the studied samples is characterized by the absence of nonspecific functional effects in experimental animals, which indicates a weak capacity for material and functional cumulation.

Conclusions: Based on the conducted toxicological studies on laboratory animals, the studied microfertilizer «Nanoplant» brands have no negative effect on the morphometric, biochemical, hematological parameters of the organs and systems of warm-blooded animals studied.

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EFFECT OF ULTRALOW-FREQUENCY MAGNETIC FIELD ON IMMOBILIZED ON CORE@SHELL FE_3O_4@AU MAGNETIC NANOPARTICLES PHENYLACETONE MONOOXIGENASE

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Recently, new directions in the use of nanomaterials in biotechnology have been actively developed, and, therefore, many researchers focus on the study of new approaches to the immobilization of protein molecules on nanosized carriers.The use of nanomaterials, such as metal nanoparticles and quantum dots, gels and matrices, as carriers for enzyme immobilization, makes it possible to use their unique properties (magnetic, dimensional, optical) to create new types of biocatalysts. Thus, the use of single-domain magnetic nanoparticles in an alternating magnetic field (AMF) as mediators for local deformations of surrounding macromolecules allows the remote regulation of their structure and, accordingly, functions [1-3]. In this paper, we present the results on the effect of low-frequency AMF on the enzymatic activity of phenylacetone monooxygenase (PAMO) immobilized on magnetic nanoparticles of the core @ shell type Fe3O4 @ Au. As an enzyme for immobilization, we have chosen PAMO from the family of Baeyer-Villiger monooxygenases, which catalyzes the oxidation of non-cyclic and cyclic ketones to esters and lactones, respectively, and is the most stable representative of this group of enzymes [4]. This enzyme is of great interest for its use as a catalyst for obtaining important substances for industry. The enzyme was immobilized due to the formation of the S-Au bond between the cysteine residues 65 and 73 and the gold surface of the nanoparticles. The resulting preparation was active and characterized by the methods of NTA, DLS and TEM. To study the effect of low-frequency AMF on immobilized on magnetic Fe3O4 @ Au nanoparticles PAMO catalytic activity, kinetic measurements were carried out. The PAMO catalyzed product, NADPH, formation was followed spectrophotometrically by an absorbance increase at 340 nm. Under the action of ultralow-frequency magnetic field at 50, 110 and 250 Hz, an increase in the catalytic activity of the immobilized enzyme was observed achieving the maximal value at 250 Hz. As found, the enzyme catalytic activity was 2-2.5 times higher under the action of AMF at 50 and 110 Hz in comparison with the same samples with no field application and at 250 Hz the PAMO catalytic activity become exceeding 6 times the initial one. The possible reasons (one of the hypotheses we put forward is about the nanomechanical effect of nanoparticles on the structure of immobilized PAMO under the influence of AMF) and further applications of the phenomenon observed are discussed.

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HEAT-RRESISTANT COMPOSITION

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Step-by-step process may be among efficient decisions associated with elaboration of the method for preparation of pressmaterials on the basis of polynaphtoilenebenzimidazoles (PNBI) practically insoluble in organic solvents in the conditions of the reactions of thermal polycondensation providing the potential possibility for increase of their processing to the products.

The essence of proposed elaboration involves performing of the synthesis of polymeric binder – PNBI by the method of thermal polycondensation of bis(o-phenylendiamines) with bis (naphtalic dianhydrides) in the composite - inhomogenous medium – in carbon filler – at presscomposite formation. For this purpose the fine-dispersed equimolar mixture of initial monomers – bis(o- phenylendiamine) (3,3-diaminobenzidine or 3,3,4,4-tetraaminodiphenylenoxide) and dianhydride of naphthalene-1,4,5,8-tetracarbon acid was coated on carbon filler. Oligomer synthesis was performed immediately on the filler surface at $T_{reac}<T_{m.p}$ of tetraamine component - 1st step; hereafter in the conditions of thermal pressing the formation of coal plastic was carried out (pressure – 15 kgf·cm^{-2}, maximum pressing tempetature comprises 673K, rate of temperature increase – 5°min^{-1}). Elaborated method of preparation of structural coal plastics on the basis of PNBI was approved and was positively estimated.

Elaboration of new method for preparation of coal plastic allowed at first to produce the mentioned materials on the basis of PNBI. It should be noted that although prepared coal plastics for the present are inferior to coal plastics, based on polyimides, by absolute values of physical-mechanical characteristics, but outperform them by the level of conservation of strength properties in the conditions of high temperatures (preservation of bending strength comprises 90% at 573K).

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pH-SENSITIVE LIPOSOMAL NANOCONTAINERS

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In modern science, a very important role is given to the creation of systems for effective delivery of medicines to the place of their action in the body. One of the last achievements in this area is the creation of pH-sensitive liposomal containers capable to release loaded drugs when got to the environment with the characteristic pH value. To do this, lipid-like substances, "molecular conformation switches", capable of changing their hydrocarbon chains conformation depending on pH value, are embedded into lipid membranes, which leads to a violation of the packing of the hydrophobic part of the bilayer and to the release of the liposome internal content into the environment.

In this paper, we propose to use a switch of a different type - the production of bile acid (lithocholic acid (LC)), containing a hydrophobic steroid nucleus and pH-sensitive functional groups. LC was embedded into the membrane of electro-neutral liposomes formed from phosphatidylcholine or dipalmitoylphosphatidylcholine. The mass fraction of LC in the membrane was 2-5%. The liposome charge was evaluated by measuring the electrophoretic mobility (EPM) of the particles at different pH values using the corresponding buffer solutions. It was shown that in acidic medium liposomes possess positive charge, since the triazole group contained in the LC is protonated, and in the alkaline medium liposomes have negative charge, since LC carboxylic group dissociation is carried out.

By the dynamic light scattering method it was found that the LC molecules are located in the outer monolayer of the lipid membrane. To do this, oppositely charged polyelectrolyte was added to liposomes and amount of polymer, needed for complete neutralization of the liposome charge was monitored. Changing the pH of the environment, we can influence on the surface charge of liposomes. The substance embedded in the membrane, thus, appears to be changing its orientation in the lipid bilayer, seeking for the arrangement that will provide relevant charged group to be in contact with the external buffer medium. This reorientation of LC molecules can lead to the disorder of the bilayer and release of the substance entrapped in the internal volume of the liposomes. The results obtained in this study can be used for further development of pH- sensitive liposomal nano-scaled containers.

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THERMO-INDUCED SHRINKING OF POLYMER MULTILAYER CAPSULES MODIFIED WITH MAGNETIC NANOPARTICLES

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One of the promising directions of targeted drug delivery technologies is the production of polyelectrolyte capsules, which shell is modified by magnetic nanoparticles. Magnetically controlled drug formulations can accumulate in the desired area of the body under the influence of the applied magnetic field, providing targeted delivery of encapsulated substances.

In this paper, the polyelectrolyte capsules modified by magnetite nanoparticles were obtained by the method of electrostatic Layer-by-Layer

adsorption. Poly-L-arginine (PArg) and dextran sulfate (DS) were used as the polymers forming the capsule shell, and calcium carbonate particles were used as core templates. In order to study the possibility to reduce the capsule size, their thermo-induced shrinkage was carried out (90 ° C, 60 minutes). As a result, the capsule's size decreased from 5 μm to 2 μm.

The capsule morphology before and after the thermo-induced shrinkage was studied by scanning electron microscopy. The model fluorescent dye (rhodamine) was entrapped into the developed systems to show the possibility for future encapsulation. The rhodamine-loaded capsules were examined by scanning electron microscopy, the encapsulation efficacy was studied by spectrophotometry.

The obtained results demonstrate that the proposed capsules modified by magnetic nanoparticles can be thermo-induced shrink and applied for encapsulation of various compounds for further delivery.

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SYNTHESIS AND PROPERTIES OF AMPHIPHILIC POLYMERS OF ACRYLIC ACID

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A series of amphiphilic polymers was synthesized by radical polymerization of acrylic acid in the presence of thiols as transmitters of chain. It was studied, that amphiphilic polymers of acrylic acid are capable of micellization in aqueous medium, and the critical concentration of micellization is determined by the pH of the reaction medium and by the ratio of the lengths of the hydrophilic and hydrophobic fragments. The resulting micelles of amphiphilic polyacrylic acid have a narrow particle size distribution with an average diameter of 6 to 8 nm. It is shown, that when AIBN are the initiator of the radical polymerization of acrylic acid, the interaction of its thermal decomposition products with thiols occurs faster, than the initiation of polymerization of acrylic acid. This is confirmed by analysis the structure of the obtained polymers using 1 H NMR, 13 C NMR and IR spectroscopy. According to the data obtained, the terminal nitrile group is absent, although it should be present if the initiation occurs under the action of the AIBN radical decay products.

According to the analysis of the kinetic data of the polymerization of acrylic acid, chain growth in the 1,4-dioxane medium occurs with the participation of non-associated forms of the monomer and associates of acrylic acid stabilized by hydrogen bonds. It is likely that the participation of acrylic acid associates in the process of chain growth is the cause of the observed anomalously high order in the monomer concentration, which is 1.6. In this case, the order of concentration of the initiator is 0.5, this point out to a break in the chain by bimolecular interaction of the radicals. Amphiphilic polymers of acrylic acid are capable of solubilizing some water-insoluble hydrophobic substances, including plant growth regulators of the cytokinin series. The work was supported by Mendeleev University of Chemical Technology of Russia. Project Number 006- 2018.

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NEW ASPECTS OF THE KINETICS OF THE MODIFICATION OF POLYVINYL ALCOHOL WITH EPICHLOROHYDRIN IN AN ALKALINE MEDIUM AND THE PREPARATION OF HEMOCOMPATIBLE HYDROGELS BASED ON BRANCHED POLYVINYL ALCOHOL

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Despite of works devoted to the synthesis of branched polyvinyl alcohol hydrogels, the kinetic aspects of the interaction of polyvinyl alcohol with epichlorohydrin have not been studied to date. The main hindrance to the quantitative description of the kinetics of the interaction of polyvinyl alcohol with epichlorohydrin is the realization of a number of side reactions, including the hydrolysis of epoxy groups like epichlorohydrin and the products of its interaction with polyvinyl alcohol. At the same time, studies of the kinetics of hydrolysis of model epoxide- containing compounds, as well as the determination of the current concentration of epoxy groups bound to a polyvinyl alcohol chain, made it possible to calculate the rate constants of all the main stages. It is shown that the total concentration of epoxide groups in the system decreases, while the concentration of epoxy groups immobilized by chains of polyvinyl alcohol passing through the maximum reaches its kvazistationary value.

It was found that the interaction of polyvinyl alcohol with epichlorohydrin is controlled by diffusion and a description of the dependence of the reaction rate on the molecular weight and the concentration of polyvinyl alcohol in the system is given. A method is proposed for the preparation of hydrogels based on branched polyvinyl alcohol having both hemocompatibility and significant mechanical strength.

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PHYTOACTIVE SYSTEMS ON THE BASE OF NANOSIZED COMPOSITE CARRIERS

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Polymeric derivatives of plant growth regulators (phytoactive polymers) have significant advantages over low-molecular regulators

- prolonged action, low doses, reduced susceptibility to phytotoxicity, a given level of solubility.

Phytoactive polymers can be used in any technology of processing plants and planting material. It is essential that the use of phytoactive polymers does not require the use of adhesives, lyophilizers, surfactants and other co-components.

Wide trials of phytoactive polymers carried out in various regions have shown that they increase the yield of various agricultural and industrial crops, including under stressful environmental conditions - under the influence of negative and elevated temperatures, moisture deficit, salinization of soils.

At the same time, the use of phytoactive polymers is hampered by rather complicated methods for their synthesis. The aim of the proposed project is to develop fundamental approaches to a The new method for immobilizing low-molecular plant growth regulators by incorporating them into composite nanosized carriers, which makes it possible to create phytoactive systems with the optimal release rate of the active substance is observed. Such previously not described systems can be obtained by simple technologically available methods.

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THE STUDY OF KINETIC REGULARITIES AND THE INFLUENCE OF VARIOUS FACTORS ON THE PROCESS OF OXIDATIVE POLYMERIZATION OF DOPAMINE, AS WELL AS THE SYNTHESIS OF DOPAMINE-CONTAINING ADHESIVES

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A study of the specific features of the process of oxidative polymerization of dopamine was carried out in the presence of known oxidizing agents - ammonium persulfate, sodium periodate, air oxygen in the Tris-buffer solution, and also in the presence of sodium tetraborate as a blocking agent of dopamine hydroxyl groups. The structure of the substances obtained during the experiments was analyzed by nuclear magnetic resonance, ultraviolet and infrared spectroscopy. By the method of potentiometric analysis, it was possible to establish the kinetic regularities of the oxidation of dopamine in the presence of ammonium persulfate and sodium periodate. The study showed that the oxidation reaction of dopamine has the second order, and the rate of this process and the chemical equilibrium in the presence of these oxidants strongly depend on the pH of the environment. It has also been found that in the presence of sodium tetraborate, the oxidation of dopamine stops at the stage of formation of 5,6-dihydroxyindole without further oligomerization to form polydopamine, which was confirmed by nuclear magnetic resonance and UV spectroscopy.

Dopamine-containing biocompatible copolymers based on vinylpyrrolidone with allyl glycidyl ether and glycidyl methacrylate, containing up to 10 molar percent of dopamine in the macromolecule, have also been synthesized. The study showed that under the influence of oxidants, dopamine-containing macromolecules have high adhesion to a variety of surfaces, including soft tissues of living organisms, and the adhesive strength increases with increasing dopamine content in the copolymer molecule. Thu s, the considered systems can be used as a Tissue adhesive.

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POLYMERIC MACROPOROUS POLYVINYL ALCOHOL HYDROGELS FOR MICROSURGICAL RECONSTRUCTION OF THE SPINAL CORD

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Severe spinal injury, complicated by damage of the spinal cord such as its compression, crushing, partial or complete rupture, remains one of the urgent medical and social problems of modern medicine, since it leads to profound disability of the victims.

It is advisable to use various polymeric materials as a growth direction "guide" for nerve fibers in the reconstruction of the spinal cord, specifically such a class of materials as porous hydrogels based on biocompatible polymers. Provided a number of technological conditions are met, the structure of such materials can contain a system of uniaxially oriented pores, which can act as growth pathways in the growth of axons.

In the current work, such hydrogels were obtained by cross-linking of solutions of unsaturated derivatives of polyvinyl alcohol in the cryogenic conditions. The uniaxial orientation of the pores was achieved by creating a temperature gradient during freezing.

The method of microsurgical reconstruction of the spinal cord using hydrogel was developed on animal material (cats).

Surgical access to the lower thoracic region of the spinal cord was carried out, laminectomy of the Th10-Th12 arch was performed. Further, the dura mater was opened and a microsurgical hemisection of the spinal cord was performed at the lower thoracic level with the formation of 10 mm diastase between the distal and proximal ends. After that, a fragment of the hydrogel was implanted in the defect area.

Dynamic monitoring of animals lasted for 16 weeks. After 8 weeks after the intervention, separate movements in the affected limb were noted.

By the period of 10-11 weeks after the operation there was a restoration of strength to the level of 3 points (the possibility of leaning upon the affected limb).

After the end of the observation period, euthanasia of the animal and collection of material for histochemical studies were carried out, which showed the germination of myelin fibers through the hydrogel.

Thus, the use of macroporous polymeric hydrogels based on PVA allows us to achieve the main objective for the reconstruction of the spinal cord - the germination of myelin fibers through the hydrogel patch and consequently of the clinical effect in represented by restoration of muscular strength in the limbs to 3 points within 10-11 weeks after the operation.

The results obtained on this experimental animal model will make it possible to apply this technique in clinical practice in the reconstruction of the spinal cord in humans.

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NOVEL VENTRICULAR CATHETERS WITH ANTIMICROBIAL ACTIVITY

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At present, new high-performance materials intended for use in medical practice attract great attention. These include materials for medical products with antimicrobial activity, among which a large part is occupied by catheters used to access large blood vessels. This is justified by the significantly increased risk of infection f the patient during the catheterization of the bloodstream due to the direct access of bacteria into the vessel through the catheter from the outside.

With the annual growth of catheterization of large blood vessels, the number of serious complications, a significant proportion of which are catheter-associated blood flow infections, also grows. This pathology leads not only to an increase in the period of stay of patients in the hospital and, consequently, to an increase in the cost of treatment, but also to an increase in mortality, especially in critically ill patients.

We have studied the possibility of obtaining catheters containing rifampicin as an antimicrobial agent. Two methods of drug administration were considered - at the stage of product formation and impregnation by incubation in an antibiotic solution. In the case of direct administration of the preparation, its amount was in the range of 1 to 3% by weight, in the case of impregnation, the preparation was administered by means of solutions in chloroform at concentrations of 1 to 30 mg / ml. The dynamics of drug release and the antimicrobial activity of the catheters with the antibiotic introduced was studied. It was found that, although both in the case of direct antibiotic administration and in the case of its impregnation, it was possible to achieve high antimicrobial activity of the catheter (suppression of growth of staphylococcus aureus and staphylococcus epidermidis at 2 months), the second method is more preferable. Since direct administration of the preparation showed a significant thermal degradation of the drug administered during the mixing of silicone rubber.

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POLYMER CATHETERS WITH AN ANTIMICROBIAL SURFACE

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Widespread introduction of the methods of intensive and invasive therapy into health practice is inextricably linked with the necessity to provide vascular access, which is most often realized with the help of catheterization of blood vessels.

The use of catheters allows to carry out a wide range of manipulations, intended to increase the effectiveness and safety of treatment of patients.

Meanwhile, in spite of a number of obvious advantages that occur with the use of catheters, the problems associated with the necessity to prevent catheter-associated bloodstream infections accompanying catheterization of vessels remain unresolved.

Currently, the frequency of this type of complications in developed countries is about 1.0 -2.5 per 1000 days of use.

One of the most promising ways to overcome this problem is the development of polymer catheters with an antimicrobial surface.

We have developed new intravascular catheters containing the glycopeptide group antibiotic, vancomycin. The antibiotic was inserted into the catheter wall at the stage of product formation. Vulcanization was carried out at a temperature of less than 120 ° C, which made it possible to avoid thermal degradation of the injected preparation. The amount of the drug administered was in the range of 1.5 to 6% by weight. The dynamics of antibiotic isolation was studied and the high antimicrobial activity of the developed catheters, suppressing the growth of the golden and epidermal staphylococcus in the model experiment, was confirmed, depending on the amount of antibiotic administered, for no more than 7 days.

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SOME ASPECTS OF CARRIERS SUNTHESIS BASED ON AMPHIPHILIC POLY-N- VINYLPYRROLIDONE FOR THE INCORPORATION OF HYDROPHOBIC SUBSTANCES

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There was produced a series of amphiphilic polymers capable of forming aggregates in aqueous media by radical polymerization of N-vinylpyrrolidone. A number of mercaptans containing 6 to 18 carbon atoms were used as chain transmitters. All obtained polymers of N- vinylpyrrolidone contain thioalkyl end-group, which cause the ability to form aggregates. The structure of endcapped polymers obtained was characterized by ^{1}H NMR, ^{13}C NMR and IR spectroscopy. Spectral data indicate the the absence of isobutyric acid nitrile residues at the end of the chain, that is characteristic of radical polymerization products initiated by AIBN. Thus, the interaction of AIBN decomposition radical products with thiols occurs more rapidly than the direct initiation of radical polymerization of N-vinylpyrrolidone by it. It has been established that the critical concentrations of aggregation change regularly as the lengths of the hydrophilic and hydrophobic fragments of the synthesized oligomers are varied. Comparison of the data on the determination of the number average degree of polymerization by osmometry and end group analysis showed that only one thioalkyl group is on one chain, and the molecular weight of amphiphilic polymers is determined by the ratio of monomer and mercaptan concentrations in the initial system. The resulting polymers are capable of

incorporating a number of hydrophobic substances, which makes it possible to achieve their high conjugated solubility in aqueous media. In particular, systems with incorporated fat-soluble vitamins of groups A and E were obtained. Amphiphilic polymers of N-vinylpyrrolidone may be of interest for the inclusion of other biologically active substances, since their toxicity is low.

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GENERAL TRENDS OF GROWTH-REGULATING IMPACTS ON PLANT AND ENDOTHERMIC ORGANISMS

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The dose-effect trends of the influence of herbicides on plant and warm-blooded organisms were studied. As an example: herbicide 2,4-D was demonstrated to have a stimulating effect in minimal doses, no effect in large doses, and a herbicidal (deadly) effect in even greater doses when applied to sensitive plant objects. Experiments on warm-blooded animals showed, that changes in the direction of the effect can be observed in sensitive (pathogenetic) markers of intoxication.

Thus, the general biological trend for change in the direction of the effect depending on the dose of the exposure was established.

P 39

CULTIVATION OF MESENCHYMAL STEM CELLS WITH LIF AND FGF

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At present, factors that regulate proliferation and differentiation of mesenchymal stem cells (MSCs) are not revealed and it's unclear how they affect cells, cultivated under different conditions. These studies are very important to develop new experimental techniques to enhance the genetic stability of MSCs and to create differentiated tissue with necessary properties in vitro (Межевикина Л.М., Кашапова И.С. Влияние регуляторных белков LIF, FGF и IL-2 на пролиферацию мезенхимных стволовых клеток костного мозга крупного рогатого скота in vitro // ВЕТЕРИНАРИЯ, ЗООТЕХНИЯ И БИОТЕХНОЛОГИЯ. 2017. №5. С. 92-99.).

We conducted our experiments in February 2018. The aim of the study was to investigate how Leukemia Inhibitory Factor (LIF) (Sigma, USA) and Fibroblast Growing Factor (FGF) (Sigma, USA) affect proliferation and osteogenic differentiation of bone marrow (BM) rat MSCs (5 passage) or they do not affect it.

There were three groups of cells: I - control (MSCs without factors in growth medium); II - MSCs with 10ng/ml of LIF in growth medium; III - MSCs with 10ng/ml of FGF in a growth medium. Initial cell concentration in culture was 50000 per one milliliter of growth medium in each group. We cultured cells in DMEM (PanEco, Russia) + 10% FBS (HyClone, USA) under conditions of 5% CO2 in the atmosphere and at temperature of 37°C, and changed the medium every other day. Control cells achieved a monolayer after 5 days, in group II – on day 3, in group III - after 48 hours. When cells achieved a monolayer, we supplemented 1 mcM/ml of dexamethasone,

0.2 mM/ml of ascorbic acid and 1 мМ/ml of glycerol phosphate in growth medium to stimulate osteogenic differentiation and cultivated for another 10 days.

After 10 days, cells were fixed with 70% ethanol and stained with Alizarin Red (Sigma, USA).In control cells acquired osteogenic differentiation morphology. Small foci of calcification were found there. In group II differentiation didn't start, morphologically cells were similar to fibroblasts. In group III we saw large calcification foci, which in total occupied more than half of the whole surface under the culture.

Conclusions: LIF and FGF increase proliferation rate. LIF almost doesn't influence on osteogenic differentiation, FGF stimulates this process well.

P 40

ENZYMATIC DESTRUCTION OF THE CAPSULES BASED ON POLYELECTROLYTE COMPLEX «POLYPEPTIDE/POLYSACCHARIDE»

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Microencapsulation of biologically active substances (BAS) allows to provide a prolonged release of encapsulated material, to protect it against oxidation under influence of the external environment, separate interacting bioactive components in one formulation.

Various techniques applied to obtain the microcapsules, but not all of them could be used for encapsulation of bioactive compounds due to the high temperatures and toxic agents that reduce the activity of BAS. In this case, the technology of Layer-by-Layer (LbL) adsorption of oppositely charged polymers on inorganic templates is promising approach. The LbL method allows to carry out the process of the capsule formation under physiological conditions.

We prepare the capsules based on the polyelectrolyte complex of polypeptide and polysaccharide (poly-L-arginine and dextran sulfate) with encapsulated DNA as a model compound. We studied the influence of the nonspecific enzyme pronase on biodegradation of the capsules. Because one of the components of the shell is a polypeptide, we assume that pronase will drive the process of the capsules enzymatic

destruction followed by release of encapsulated DNA from them.

The morphology of the capsules was studied by optical and scanning electron microscopy. We demonstrate the possibility of the DNA release rate regulation by varying the concentration of the enzyme. The results could be used for development of drug delivery systems with controlled release of active component.

This research was supported by the Federal Agency of Scientific Organizations (Agreement No 007- Г3 / Ч 3363/26) in part of capsule formation and enzymatic degradation and by the Russian Science Foundation (Project No. 17-33-80141 mol_ev_a) in part of capsule analysis.

This work was performed using the equipment of the Shared Research Center FSRC "Crystallography and Photonics" RAS and was supported by the Russian Ministry of Education and Science".

P 41

POLY(VINYL ALCOHOL) COMPOSITE CRYOGELS FILLED WITH BACTERIAL NANOCELLULOSE

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Cryogels of poly(vinyl alcohol) (PVA) are the macroporous physical gels of crystallization type formed as a result of cryogenic processing, i.e. freezing, incubation in a frozen state and thawing of concentrated PVA solutions. Nowadays, the interest to such systems in medicine and biotechnology is very high, because the PVA cryogels are biocompatible and non-toxic.

The main ways to regulate the physicochemical properties of such gels are: varying the concentration of PVA in the feed solution, changing the parameters of low-temperature exposure, the number of freeze-thaw cycles, and incorporation of various modifiers, both soluble and insoluble. One of the developing areas of application of composite PVA cryogels is the creation of bone tissue implants possessing high physico-mechanical characteristics and biocompatibility.

In this work, the properties and morphology of composite PVA physical cryogels filled with the particles of bacterial nanocellulose (BNC) was studied. Such nano-filler serves as a reinforcing component, which can significantly increase the rigidity and the heat endurance of the composites. It was shown that a single freeze-thaw cycle of the PVA-BNC dispersion resulted in the composite cryogel which had the four times higher compression modulus of elasticity than the equi-concentrated filler-free PVA cryogel, and the fusion temperature of the composite was by 5°C higher. It has also been found that the number of freeze-thaw cycles significantly influenced on the rigidity of filled cryogels. Over the employed range of cellulose nanofiber concentrations (0.26-1.1%) the dependence of the strength characteristics of composites after cyclic cryogenic treatments on the filler concentration was not proportional, so further increase in the content of BNC in the composite turned out to be impractical.

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NONDESTRUCTIVE ELECTROSTATIC ADSORPTION OF LIPOSOMES ON ANIONIC LATEXES

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Liposomes are vesicles of spherical shape ranging in size from 20 nm to several micrometers. They are prepared from natural and synthetic lipids. Because of their size and hydrophobic- hydrophilic character, liposomes are the one of the perspective systems for delivery of biologically active substances and drugs.

Currently, there is a huge amount of medical preparations based on the use of liposomal carriers being investigated or introduced to the market. But the approach currently used for liposomal products creation has several shortcomings. First, most of the developed liposomal carriers have low internal volume, and secondly, such liposomal containers have low stability to mechanical influences, temperature, destabilizing agents and internal organism media.

Modification of liposome membranes with different polyelectrolytes allows eliminating partially these shortcomings, but often the formation of the polymer / liposome complex leads to undesirable aggregation of the obtained colloid system. In addition, adsorption of polyelectrolytes on vesicles causes a number of structural reorganizations in the lipid membrane which can lead to a disruption in the integrity of liposomes and, as a consequence, to impossibility of use of such systems for drug delivery. At concoction of liposomes on a surface, it is possible to control quantity of the liposomes adsorbed on it, but partial destruction of liposomes at contact with a surface is usually observed.

One of the most successful approaches for concentrating of liposomes is electrostatic adsorption of anionic liposomes on the colloidal particles representing a polystyrene kernel with the linear polycations imparted on his surface. This method allows effective concentrating liposomes without their destruction. However, this approach assumes existence of a "soft" layer between a liposome and a surface, which introduces its limitations on the nature of the carrier surface.

As modification of a surface of firm particles is rather difficult task, the purpose of this work is the research of a possibility of transferring of a "soft" layer from a surface on a liposome. For this, a lipid modified with polyethylene glycol (PEG) was included in the liposome composition. The mole fraction (v) of the PEGylated lipid in liposomes was varied in the range from 0 to 0.1. Anionic latex particles with a size of 350 nm were being used as the model surface. For a possibility of electrostatic adsorption of liposomes on the surface of latex spheres, cationic (mole fraction of cationic lipid, $v_+ = 0.1$) and zwitterionic liposomes ($v_+ = v_- = 0.1$) were used. It has been shown that unmodified PEG liposomes disrupted while adsorbed to the latex surface. The addition of PEG does not change the basic physical and chemical characteristics of the interaction of liposomes with latex (extent of binding, stability at physiological values of ionic force), but prevents the destruction of liposomes at adsorption.

P 43

DEVELOPMENT OF POLYMERIC FILMS FOR CONTROLLED RELEASE OF LOCAL ANESTHETICS

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The medical films containing various drugs were widely applied in dental therapy. The prolonged effect in such films is reached by the immobilization of drugs on various polymeric carriers. The purpose of present work is development of novel dosage forms with the controlled action by immobilization of local anesthetics on polymeric films. Local anesthetics lidocaine and novocaine are used as drugs. Polymeric films are received from the corresponding solutions of polymer and drug by water evaporation. The amount of PVA is filled with distilled water and maintained on magnetic mixer at temperature 80-90°C before full dissolution. The calculated amount of drug added to cooling at room temperature homogeneous solution of PVA. After stirring the received solution poured out in glass established horizontally and dried in at room temperature up to constant weight. The received medicinal form had an appearance of thin elastic transparent film from which by means stamp cut out squares 0,2-0,5 mm thick. Calculation of dose of drug was carried out from criterion of the minimum dose. The release behaviour of drug from polymeric samples was examined by means of immersing the disc- shaped samples of 0,3-0,5 mm thickness and 10,0 mm diameter in a Ringer-Lock solution at 37°C. The amount of drug released was determined by UV-spectrometry by measuring the absorption maximum. It is shown that the drug which has been evenly dispersed in polymer is released on model solution on the diffusion mechanism with rate reduction. Process of diffusion is described by Fick's law and occurs according to kinetics of the first order. It is established that release process of lidocaine from films in environment consists of three main stages: 1) water sorption by polymeric film and its swelling; 2) diffusion of drug in film on phases polymeric system - environment; 3) diffusion of drug in solvent volume. Drugs almost completely diffused from PVA-films within 6-8 hours, without undergoing any changes. With increase in thickness of film the process of diffusion of drug is slowed down. The increase in loading of drug leads to delay of lidocaine diffusion rate from the film. All the release data show the typical pattern for a matrix controlled mechanism. The cumulative amount of drug released from films was linearly related to the square root of the time and the release rate decreased with time. Duration of drug release from monolithic therapeutic systems considerably depends on the swelling of polymeric matrix. Dependence swelling degree of PVA-films from thickness of samples shown that the most optimum properties films 0,4-0,6 mm thick possessed. Such materials swelled for 55-60% within initial 1,5-2,0 hours with the subsequent achievement of the maximum value of 80% in 6 h, thicker films very slowly swelled for 45-50% within 1,5-2 h that didn't conform to medical requirements. Release of drug is limited by the rate of swelling and thickness of polymeric matrix. Clinical observations on patients with periodontal disease inflammatory and inflammatory-destructive nature showed significant advantages of using polymer film forms of lidocaine. Clinical efficacy was confirmed in statistically significant reduction of terms of treatment of patients with generalized periodontal disease, improvements of the test of Kulagina, gingival index of Loe, hygienic condition of the mouth, a higher percentage of remission of the disease in the early and late periods.

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FUNCTIONAL MATERIALS BASED ON BIOPOLYMERS FOR MEDICAL APPLICATIONS

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At present many biopolymers are used in biomedical applications due to their important properties such as non-toxicity, biodegradability and biocompatibility. Polyhydroxybutyrate (PHB) is one of the natural polymers that intensively studied for use in tissue engineering. This material is biodegradable polymer and biocompatible with the human body. However, polyhydroxybutyrate has disadvantage in use as medical materials - low rate of degradation. Besides, this polymer has highly degree of cristallinity that provides good mechanical properties, but brittleness and low elasticity. One of the methods to overcome the disadvantages of PHB is combining it with other materials by preparing of polymer blends. For these purposes polysaccharide chitosan has potential due to its relatively quick rate of degradation, good elastic characteristics, non-toxicity and biocompatibility. Moreover, this biopolymer has high antimicrobial activity. Since tissue engineering materials should have porous structure it is necessary to produce a polymer network. Direct method is chemical cross-linking by the formation of covalent chemical bonds between the polymeric chains.

This work is focused on development and investigation of a polymer composition based on the biopolymers - polyhydroxybutyrate and chitosan for use in tissue engineering. Described in this work method of film preparation involves casting a dissolved polymer mixture on plastic dish, drying and solidifying of the polymers. The investigation of compatibility of the polymers in the composition demonstrates that the content of polyhydroxybutyrate in the composition should not exceed 60% weight. It's can be explained by significant phase separation of the composition, because polyhydroxybutyrate is a hydrophobic polymer and chitosan is hydrophilic. The combination of biopolymers allows to reduce the terms of biodegradation and improves the mechanical characteristics of biomaterial. With increase of chitosan content in the blend the composition becomes amorphous, the degree of crystallinity of polyhydroxybutyrate decreases. The material was chemically cross-linked using calcium chloride to form a polymer network. The influence of the cross-linker content from 0 to 9% on the mechanical and thermal properties of the developed biopolymer material was investigated. The increase in content of the cross-linker up to 5% improves the mechanical properties of the composition. Thus calcium chloride is a suitable non-toxic material for cross-linking biopolymers, allowing them to make their structure stronger. The results of the thermal study and IR-spectra of biopolymer blends also confirm the occurrence of cross-linking between the polymer components.

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CROSSLINKED CHITOSAN/PVA FILM BASED ON 5- FLUOROURACIL

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5-Fluorouracil (5-FU)-loaded chitosan (Ch) film for chemotherapy were prepared applying a superhydrophobic surface-based encapsulation technology. The aim of this study was to develop polymeric film with glutaraldehyde (GA) of con-trolled drug delivery systems for 5 – fluorouracil (FU) as a model drug for the treatment of proliferative vitreoretinopathy. Polymer film of chitosan and polyvinyl alcohol (PVA in 75:25 ratios were prepared and treated with GA. FTIR spectra of 5-FU, Ch/5-FU and Ch/PVA film loaded 5-FU were studied. Physical characteristics such as thickness and swelling coefficient of the film were performed. It was established that the release consisted of three main stages: water sorption by a film and its swelling, the drug diffusion in a film at the phase inter-face "polymer system-environment" and the drug diffusion in the solvent volume. To determine the influence of drug loading on its release kinetics, polymer films were loaded with 250 mg/g and 500 mg/g of 5-FU. Compared with 250 mg/g to 500 mg/g of 5-FU, there was no significant effect on cumulative release of drug. Obtained results showed that the drug was diffused practically completely into Ringer-Locke solution within 60-70 h. A novel Ch/PVA film treated with GA was prepared by direct blend process and solution casting method. This investigation studied the properties of the crosslinked Ch/PVA films loaded 5-FU in amounts of 250 mg/g (0,05 ml) and 500 mg/g (0,1 ml). The effects of stock Ch/PVA concentration, the treatment of GA on the structure and thermal property of Ch/PVA films were characterized with FTIR and TGA. The FTIR analysis confirmed the successful introduction of 5-

FU in film. From the results it was concluded the thermal stability of the films in-creases with the treatment of GA. The evaluation of the permeation of 5-FU through the chitosan was conducted in this study. In vitro drug release could be resulted that the drug was diffused from of the crosslinked Ch/PVA films after 70 h. According to results of morphological research, toxic action from intravitreal injection of chitosan film, saturated with 5-FU (0,05 and 0,1 ml) in experiment wasn't observed. Some proliferative activity was revealed after implantation of the chitosan film saturated with 0,05 ml 5-FU.

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POLYMER INFLUENCE ON THE CATALYTIC ACTIVITY OF SUPPORTED POLYMER- PROTECTED NICKEL CATALYSTS FOR THE HYDROGENATION PROCESS OF ACETYLENE ALCOHOLS

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It is known that the nature of the polymer has a significant effect on the formation of nanosize metal particles, preventing their elution from the carrier surface and reducing the degree of their agglomeration. We have studied the catalytic activity of nickel nanocomposites in the hydrogenation reactions 3,7,11,15-tetramethylhexadecyn-1-ol-3 (acetylene alcohol C20). Results on the activity, selectivity and stability of 0.7% nickel catalysts supported on ZnO, not modified with the polymer, as well as modified with polyethylene glycol (PEG), in the hydrogenation of C20 acetylene alcohol are shown in the Table 1. It was shown that in the presence of PEG the process proceeds at a high rate of 2.1 * 10-2 mol / s, in contrast to a catalyst prepared without a polymer, the activity of which was 1.4 * 10-2 mol / s.

Table 1. Hydrogenation of 3,7,11,15-tetramethylhexadecyne-1-ol-3 on 0.7%Ni-polymer/oxide and 0.7%Ni/oxide catalysts

Reaction conditions: T = 40°C, PH2 = 1 atm., mcat = 0,05 g, solvent is C2H5OH

Catalysts	$W*10^{-2}$ mol/s	S, %	TON
Ni-PEG/ZnO	2.1	79.0	1200.0
Ni/ZnO	1.3	62.0	600.0

High selectivity to olefinic alcohol (79%) and stability expressed in TON (the number of catalytic cycles per gram atom of metal) (TON = 1200) is observed using Ni-PEG/ZnO catalyst. Less selective and stable is a catalyst that does not contain a polymer.

The TEM and SEM data of 0.7% Ni-PEG / ZnO catalyst are presented in Figures 1 and 2. The entire surface of zinc oxide is covered with small coils (30-40 nm), which in some cases are combined into larger aggregates of fine particles, interconnected, possibly of hydrophobic interactions (Fig. 2). Possibly, it is these coils that are polymetallic complexes (PMC), inside which PMCs are formed with sizes from 3-5 nm, which are fixed by the TEM (Fig. 1).

Thus, the low percentage polymer modified nickel catalyst immobilized on supports has been developed. The Ni-PEG/ZnO catalyst has shown the high activity, selectivity and stability in the hydrogenation of acetylene alcohol under mild conditions (atmosphere pressure hydrogen and temperature 400C).

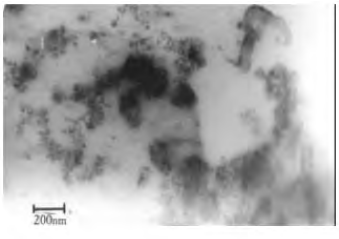

Figure 1. Micrograph (TEM) of 0.7% Ni-PEG/ZnO catalyst

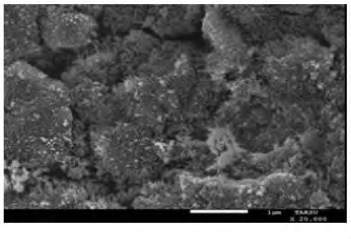

Figure 2. Micrograph (SEM) 0.7% of Ni- PEG/ZnO catalyst

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DEPOSITION OF CHITOSAN ONTO POLYLACTIDE FILMS USING VARIOUS METHODS

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Deposition of bioactive coatings onto surfaces of various scaffolds is an important issue of tissue engineering. Polylactide is biodegradable polymer having a number of properties desired for tissue engineering application, but it has a lack of specific sites for adhesion and growth of cells onto its hydrophobic surface. To overcome this drawback, a polylactide surface could be modified or coated by bioactive components, such as proteins, polysaccharides, etc. This work is aimed to coat polylactide films by chitosan using various methods, i.e. chemical entrapment, vacuum deposition by electron beam sputtering and electrospray deposition. Coating of polylactide films by chitosan using methods of electron beam sputtering and electrospray deposition led to increase of surface hydrophilicity, while contact angles of wettability of film coated by chitosan using chemical entrapment approach were similar to native polylactide films. Scanning electron and atomic force microscopy showed that electron beam sputtering allowed us to create more homogenous and thin coating, then electrostatic deposition method. X-ray photoelectron spectroscopy revealed that the highest content of nitrogen was in the case of the electrostatic deposition and lowest one for chitosan chemical entrapment approach. Visualization of chitosan amino groups by fluorescein isothiocyanate as well as FTIR- microscopy showed a high heterogeneity of polylactide films coated by chitosan using electrostatic deposition method in terms of surface chemical composition. Creation of chitosan coatings onto surfaces of polylactide scaffolds could be a promising approach to improvement of their biocompatibility.

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DIFFERENTLY FUNCTIONALIZED CUO NANOPARTICLES: EFFICIENT ANTIMICROBIALS OR THE POISON TO HUMAN MACROPHAGES

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Abstract CuO nanoparticles (CuO NPs, 1-100 nm) are already used in industrial and consumer products due to their antibacterial properties. When CuO NPs are applied in the health-care settings, wound-healing products or implants they can get into the direct contact with human cells. Human macrophages, a class of phagocytic immune cells, are one of the first cells that interact with NPs introduced into the bloodstream. Thus, the macrophage-NP interaction is highly important for the distribution and toxicological profile of NPs.

Here we studied the efficiency and safety of four CuO NPs with primary sizes about 30 nm and different surface functionalizations (coatings): uncoated CuO, CuO functionalized with amino group (CuO-NH_2), CuO functionalized with carboxyl group (CuO-COOH) and CuO functionalized with polyethylene glycol (CuO-PEG). *Escherichia coli* was selected as model bacteria to test antibacterial effects of CuO NPs. Human immune cells, macrophages differentiated from THP-1 cells *in vitro,* were selected as a model for immunotoxicity testing. Differently from all the previous studies, antibacterial and immunotoxicity tests were performed in the same conditions (test medium, temperature). Alamar blue assay was used as the toxicity endpoint in all cases. In parallel, dissolution of CuO NPs in these test conditions and the toxicity of ionic Cu (as $CuSO_4$) as a control for solubility were measured. Toxicity was expressed as EC_{50} values adjusted to the Cu content.

All tested CuO NPs and $CuSO_4$ were toxic to bacteria. The antibacterial toxicity (24 h EC_{50}) varied from 19 mg Cu/l (CuO-PEG) to 42 mg Cu/l (uncoated CuO) and the EC_{50} values increased in the order CuO-PEG<CuO-NH2<CuO-COOH<$CuSO_4$<uncoated CuO. In case of macrophages, the toxicity (24 h EC_{50}) varied from 15 mg Cu/l (CuO-NH_2) to >40 mg Cu/l (CuO- PEG) and the EC_{50} values increased in the order CuO-NH_2<uncoated CuO<$CuSO_4$<CuO-COOH<CuO-PEG. Thus, CuO-PEG could be the most suitable antibacterial as these NPs were the most toxic to *E. coli* cells and not toxic to human immune cells *in vitro.* In contrast, CuO-NH_2 was significantly more toxic to THP-1 cells then to *E. coli* cells and is the least favorable as the antibacterial.

Summarizing, we showed that the toxic effects of CuO NPs can be significantly tuned with the surface functionalization, and the effect of the coating is different for bacteria and human cells. This knowledge can be used for the synthesis of more efficient and safe antimicrobials.

This work was supported by Estonian Research Council grants IUT23-5 and PUT1015.

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