BIONANOTOX 2014

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5th International Congress

"Biomaterials and Nanobiomaterials: Recent Advances Safety-Toxicology and Ecology Issues"

Including Russian-Hellenic Workshop and School of Young Scientists and Symposium of Nanotoxicology

4-11 MAY, 2014 Heraklion, Crete, Greece

HELLENIC SOCIETY OF TOXICOLOGY

M.SHEMYAKIN AND YU.OVCHINNIKOV INSTITUTE OF BIOORGANIC CHEMISTRY

UNIVERSITY OF CRETE

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BIONANOTOX CONGRESSES

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M. LOMONOSOV MOSCOW STATE UNIVERSITY

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Final Program/Abstract Book

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Welcome Letter

On behalf of the organizing committee of the 5th International Conference "Biomaterials and Nanobiomaterials: Recent Advances Safety – Toxicology and Ecology Issues" Including Russian-Hellenic Workshop and School of Young Scientists and Symposium of Nanotoxicology, we are privileged to invite you to grace with your presence and participation the works of the Symposium, which is to be held in Heraklion, in the beautiful island of Crete, in May 2014.

Crete is an island with numerous coves, bays, peninsulas, and sandy beaches along the beautifully blue Mediterranean Sea. After all, it's among the finest in the world and has established Crete as one of Europe's most popular holiday destinations. And, of course, the island's historic importance in today's world as Knossos, Phaistos and Gortys, is evidenced by the tens of thousands of visitors to these sites each year. Located almost in the centre of Crete, Heraklion has since the early years played a significant part in the history of the island.

The theme of the Symposium concerns one of the most progressing directions of science and technology. BioNanoToxicology Issues lie at the interface of many disciplines, ranging 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 from many countries will attend the symposium. Very low package fees including registration, accommodation, lunch meals and congress material have been secured for participants. Reduced registration rates will be provided, 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.

We invite you all to participate to our Symposium. Crete will welcome you with its smiling Cretan sun, the sounds of the Cretan lyre, the scents of orange blossom and jasmine, a slice of cool red watermelon and a glass of iced raki.

Co-Chairmen of the Organizing Committee

Aristidis Tsatsakis, PhD, DSc, ERT

Mikhail Shtilman, PhD, DSc

Committees

International Advisory Board

Honorary Chairman	Torchilin Vladimir	Professor, Director of Center of Pharm. Biotech & Nanomedicine, Northeastern University, Boston, USA
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	Kabanov Alexander	Professor, Director of Center for Drug Delivery and Nanomedicine, University of Nebraska, Omaha, USA
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	Neufeld Ron	Professor, Queen's University, Kingston, Ontario, Canada
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	Panarin Eugenie	Corresponding member of RAS, Director of Institute Macromolecular Compounds of RAS, St. Petersburg, Russia
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	Poncelet Denis	Professor, ONIRIS, UMR CNRS GEPEA 6144, Nantes, France
	Tkachuk Vsevolod	Academician of RAS and RAMS, Dean of Faculty of Fundamental Medicine, M. Lomonosov Moscow State University, Moscow, Russia
	Kouretas Demetrios	Professor, Vice Rector, University of Thessaly, Larissa, Greece
	Varfolomeev Sergey	Corresponding member of RAS, Director of N. Emanuel Institute of Biochemical Physics of RAS, Moscow, Russia
	Vladimirov Yurii A.	Academician RAMS, Moscow State University
	Ulbrich Karel	Professor, Head of Dept. of Biomedicinal Polymers, Institute of Macromolecular Chemistry, Pregue, Czech Republic
	Zezin Alexander	Corresponding member of RAS, Head of Chair, M. Lomonosov Moscow State University, Moscow, Russia

Organizing Committee

Co- Chairmen 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, Russia
	Eremin Sergey	Professor, M. Lomonosov Moscow State University, Moscow, Russia
	Klyachko Natalia	Professor, M. Lomonosov Moscow State University, Moscow, Russia
	Khalidya Khamidulina	PhD, Director of the Russian Register of Potentially Hazardous Chemical and Biological Substances,Moscow, Russia
	Markvicheva Elena	Professor, M. Shemyakin-Yu. Ovchinikov Institute of Bioorganic Chemistry, Moscow,Russia
	Rizos Apostolos	Professor, Department of Chemistry, University of Crete, Iraklion, Greece
	Shashkova Irina	PhD, Senior Research Scientist, D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
	Tsakalof Andreas	Professor, Medical Chem. Dep., University of Thessaly, Larissa, Greece
	Shishatskaya Ekaterina	Professor, Head of Chair Medical Biology, Siberian Federal University, Krasnoyarsk, Russia
	Stivaktakis Polychronis	PhD, Research Scientist, University of Crete, Iraklion, Greece
	Tzatzarakis Manolis	PhD, Assistant Professor, University of Crete, Iraklion, Greece
	Vamvakaki Maria	Associate Professor, Department of Materials Science and Technology, University of Crete
	Velonia Kelly	Associate Professor, Department of Materials Science and Technology, University of Crete
	Vynias Dionysios	PhD, Research Scientist, University of Crete, Iraklion, Greece

Scientific program

Sunday, May 4, 2014

Arrival - Registration

20.00 **Welcome Cocktail**

Monday, May 5, 2014

08.00-09.30 **Breakfast**

10.00 **OPENING CEREMONY**

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

10.10-10.25 **ABOUT SYMPOSIUM PROGRAM**
M. I. Shtilman, Co-head of Organizing Committee
D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia

10.25-11.05 **OPENING LECTURE**
STIMULI-SENSITIVE COMBINATION NANOPREPARATIONS OF siRNA AND CHEMOTHERAPEUTIC DRUGS TO TREAT MULTIDRUG RESISTANT CANCER
V. P. Torchilin, Honorary Chairman of Symposium
Northeastern University, Boston, USA

11.05-11.30 **Coffee break, Poster session**

11.30-12.30 ***MORNING SESSION***

Chairmen: Prof. V. P. Torchilin, Prof. M. I. Shtilman

11.30-12.00 **NEW ENERGETICAL TECHNOLOGY – NEW ECONOMICAL CHALENGES**
S. D. Varfolomeev
N. Emanuel Institute of Biochemical Physics, Moscow, Russia

12.00-12.30 **LONG TERM RELEASE OF INSULIN FROM MICROPARTICULATE POLYMERIC CARRIERS EMBEDDED IN A HYDROGEL DRESSING MATRIX IS DESIGNED TO PROMOTE WOUND HEALING**
M. T. Hrynyk[1], R. J. Neufeld[1], M. Martins-Green[2], Y. Liu[2], A. Barron[3]
[1]Queen's University, Kingston, Ontario, Canada
[2]University of California, Riverside, CA
[3]Stanford University, Stanford, CA

12.30-13.00 **ADVANCES OF CHROMATOGRAPHY BASED TECHNIQUES IN ENVIRONMENTAL AND CLINICAL TOXICOLOGY**
A. K. Tsakalof
University of Thessaly, Faculty of Medicine, Greece

13.00-14.00 **Lunch**

14.00-16.00 **Break**

16.00-18.00 ***EVENING SESSION - Young Scientists Session***

Chairmen: Prof. N. Klyachko, Prof. Yu. Golovin

16.00-16.15 **NOVEL ANTIOXIDANT NANOZYMES FOR SPINAL CORD INJURY TREATMENT**
A. D. Aleksashkin[1], T. O. Abakumova[2], E. A. Kirzhanova[1], D. S. Manickam[3], V. P. Chekhonin[2], N. L. Klyachko[1], N. V. Nukolova[1,2], A. V. Kabanov[1,3]
[1]Lomonosov Moscow State University
[2]The Serbsky State Scientific Center for Social and Forensic Psychiatry
[3]University of North Carolina at Chapel Hill

16.15-16.30 **OSTEOPLASTIC IMPLANTS BASED ON RESORBABLE POLYESTERS FOR RECONSTRUCTIVE SURGERY**
A. A. Shumilova[1], E. D. Nikolaeva[2], E. I. Shishatskaya[1,2]
[1]Siberian Federal University, Krasnoyarsk, Russia
[2]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia

16.30-16.45 **SYNTHESIS OF MAGNETIC AND MAGNETIC@GOLD FOR BIOMEDICAL APPLICATION**
P. G. Rudakovskaya, A. G. Majouga, M. V. Efremova, A. V. Barulin, M. M. Veselov, A. E. Machulkin, O. M. Metelkina, N. L. Klyachko, A. V. Kabanov
M. V. Lomonosov Moscow State University, Moscow, Russia

16.45-17.00 **TARGETED CONTRAST AGENTS FOR MRI DIAGNOSTICS OF MULTIPLE SCLEROSIS**
T. O. Abakumova[1,2], A. A. Kuzkina[3], D. A. Pozdeeva[3], M. A. Abakumov[4], D. A. Bychkov[2], N. V. Nukolova[1,2], V. P. Chekhonin[1,4]
[1]The Serbsky State Scientific Center for Social and Forensic Psychiatry, Moscow, Russia
[2]Lomonosov Moscow State University, Moscow, Russia
[3]I.M. Sechenov First Moscow State Medical University, Moscow, Russia
[4] Russian National Research Medical University, Moscow, Russia

17.00-17.15 **DEVELOPMENT OF POLIMERIC MICELLES FOR CURCUMIN DELIVERY**
R. Akasov[1,3], M. Chiper[1], S. Burov[2], T. Vandamme[1], E. Markvicheva[3]
[1] University of Strasbourg, France
[2]Institute of Macromolecular Compounds, St-Petersburg, Russia
[3]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia

17.15-19.00 **Break**

19.00-20.00 **Dinner**

Tuesday, May 6, 2014

08.00-09.30 **Breakfast**

10.00-12.30 ***MORNING SESSION***

Chairmen: Prof. S. D. Varfolomeev, Prof. V. P. Varlamov

10.00-10.30 **FUNCTIONAL NANOSYSTEMS FOR PHARMACOLOGY AND MEDICINE**

N. L. Klyachko[1], E. N. Efremenko[1], I. V. Lyagin[1], E. A. Zaitseva[1], O. A. Kost[1], P. V. Bineski[1], N. B. Chesnokova[2], I. I. Nikolskaya[1], N. V. Nukolova[3,1], A. D. Aleksashkin[1], I. V. Gachok[1], L.Yu. Filatova[1], A. D. Priyma [1], A. B. Belova[1], S. A. Legotsky[1], K. A. Miroshnikov[4], A. V. Kabanov[5,1]

[1]M. V. Lomonosov Moscow State University, Moscow, Russia, [2]Helmholtz Institute for Eye Disease, Moscow, Russia,[3]Center for Social and Forensic Psychiatry, Moscow, Russia, Russian State Medical University, Moscow, Russia, [4]M.M. Shemyakin and Yu. A. Ovchinnikov Institute of bioorganic chemistry RAS, *Moscow, Russia, [5] Eshelman School of Pharmacy, University of North Carolina-Chapel Hill, Chapel Hill, USA*

10.30-11.00 **MODERN BIOMATERIALS: WORLD TRENDS, PLACE AND POTENTIAL OF MICROBIAL POLYHYDROXYALKANOATES (PHAS)**

T. G. Volova[1,2]

[1]Siberian Federal University, Krasnoyarsk, Russia

[2]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia

11.00-11.30 **QUANTUM DOTS AS LABELS IN IMMUNOASSAYS**

S. A. Eremin

Department of Chemical Enzymology, Faculty of Chemistry, M.V. Lomonosov Moscow State University, Moscow, 119991, Russia

11.30-12.00 **Coffee break, Poster session**

Chairmen: Prof. T. G. Volova, Prof. M. I. Gladyshev

12.00-12.30 **TO UNDERSTANDING TOXICITY OF EXOGENOUS ANTIOXIDANTS USED TO COMBAT FREE-RADICAL DISEASES**

I. Juranek[1], D. Nikitovic[2], D. Kouretas[3], A. W. Hayes[4], A. M. Tsatsakis[2]

[1]Slovak Academy of Sciences Institute of Experimental Pharmacology & Toxicology, Bratislava, Slovakia [2]University of Crete Medical School, Heraklion, Greece [3]University of Thessaly School of Health Sciences, Volos, Greece [4]Harvard School of Public Health, Boston, USA

12.30-13.00 **RAPID AND MULTIPLEX BIOANALYTICAL TECHNIQUES ON THE BASE OF QUANTUM DOTS**

B. B. Dzantiev

Institute of Biochemistry Russian Academy of Sciences, Moscow, Russia

13.00-14.00 **Lunch**

14.00-19.00 **Break**

19.00-20.00 **Dinner**

Wednesday, May 7, 2014

08.00-09.30 **Breakfast**

10.00-13.00 ***MORNING SESSION***

Chairmen: Prof. B. B. Dzantiev, Prof. R. J. Neufeld

9.30-10.00 **BIODEGRADABLE FIBERS AND MICROCARRIERS AS PROMISING MATRICES FOR REGENERATIVE MEDICINE**

E. Markvicheva[1], M. Drozdova[1], T. Demina[2], A. Artyukhov[3], M. Shtilman[3], T. Akopova[2], G. Vikhoreva[4], Ch. Grandfils[5]

[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chem., Rus. Acad. Sci., Miklukho-Maklaya Str 16/10, 117997, Moscow, Russia, [2]Enikolopov Institute of Synthetic Polymer Materials, Rus Acad. Sci., Profsoyuznaya Str., 70, 117393 Moscow, Russia, [3]Mendeleev University of Chemical Technology of Russia, Miusskaya Sq., 9 125047 Moscow, Russia, [4]Moscow State University of Design and Technology, Sadovnicheskaya Str, 33, 117997 Moscow, Russia, [5]Interfacultary Research Centre on Biomaterials (CEIB), University of Liège, Chemistry Institute, B6C, B-4000 Liège (Sart-Tilman), Belgium.

10.00-10.30 **PROPERTIES OF POLY AZOLIDINE AMMONIUM MODIFIED BY HYDRATE HALOGEN IONS AND BIOLOGICAL PRODUCTS ON ITS BASIS**

E. I. Tikhomirova, O. V. Nechaeva, D. A. Zayarsky, M. M. Vakaraeva

Yuri Gagarin State Technical University of Saratov, Russia

10.30-11.00 **PRODUCTION OF HIGHLY OF UNSATURED FATTY ACIDS, ESSETIAL FOR HUMANS, IN AQUATIC ECOSYSTEMS**

M. I. Gladyshev

Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Akademgorodok, Krasnoyarsk, 660036, Russia, Siberian Federal University, Svobodny av. 79, Krasnoyarsk, 660041, Russia

11.00-11.30 **SURFACE MODIFICATION OF POLYHYDROXYALKANOATES FOR BIOMEDICAL PURPOSES**

A. N. Boyandin[1,2], E. D. Nikolaeva[1], R. A. Surmenev[3], V. V. Slabko[4], T. G. Volova[1,2]

[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia, [2]Siberian Federal University, Krasnoyarsk, Russia, [3]National Research Tomsk Polytechnic University, Tomsk, Russia, [4]L. V. Kirensky Institute of Physics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia

11.30-12.00 **Coffee break, Poster session**

Chairmen: Prof. S. A. Eremin, Prof. A. K. Tsakalof

12.00-12.30 **SINGLE-CELL KINETICS APPROACH TO STUDY NON-SPECIFIC REJECTION OF TOXINS BY CELLS**

S. N. Krylov, V. Koshkin

Department of Chemistry, York University, Toronto, Ontario, M3J 1P3, Canada

12.30-13.00 **SURGICAL DRESSINGS WITH ANTIMICROBIAL CARACTERISTICS OF MULTILAYER NONWOWEN**

S. K. Lopandina, Z. J. Kozinda, T. A. Podgaevskaya, O. O. Erofeev, T. V. Moreva

Central Research Studies Institute of Clothing Industry, Moscow, Russia

13.00-14.00 **Lunch**

14.00-16.00 **Break**

16.00-18.00 ***EVENING SESSION***

Chairmen: Prof. V. P. Torchilin, Prof. A. M. Tsatsakis

16.00-16.35 ***KEYNOTE LECTURE***
PUBLISHING IN BIOMEDICAL SCIENCES
D. Spandidos
University of Crete, Medical School, Heraklion, Greece

16.35-17.00 **SUBMITTING HORISONT PROPOSALS**
D. Vynias
ToxPlus S. A., Heraklion, Greece

19.00-20.00 **Dinner**

Thursday, May 8, 2014

08.00-09.00 **Breakfast**

10.00-13.00 ***MORNING SESSION***

Chairmen: Prof. S. Eremin, Prof. B. B. Dzantiev

10.00-10.30 **TRIBOLOGICAL STUDY OF MULTIWALLED CARBON NANOTUBES (MWCNT)/ALUMINA (Al_2O_3) REINFORCED ULTRA HIGH MOLECULAR WEIGHT POLYETHYLENE (UHMWPE) BIOCOMPOSITES FOR BIOMEDICAL APPLICATIONS**
A. K. Patel, K. Balani
Biomaterials Processing and Characterization Laboratory, Department of Materials Science and Engineering, Indian Institute of Technology, Kanpur 208016, India

10.30-11.00 **METHODS OF COMPLEX ASSESSMENT OF CYTO-, GENO-, AND EMBRYOTOXICITY OF NANOPARTICLES IN EXPERIMENTS IN VITRO**
G. A. Protasova, V. B. Popov, L. V. Shabasheva, I. V. Strekalovskii
Research Institute of Hygiene, Occupational Pathology, and Human Ecology Federal State Unitary Enterprise, Federal Medical Biological Agency, St.Petersburg, Russia

11.00-11.30 **FLUORESCENT DYE ENCAPSULATION FOR THE VISUALIZATION OF POLYELECTROLYTE CAPSULES PHARMACOKINETICS**
T. V. Bukreeva[1,2], O. D. Smirnova[1], A. A. Kochetkov[1], I. V. Kalashnikova[1], I. V. Marchenko[1,2], M. A. Vantsyan[1]
[1]National Research Centre "Kurchatov Institute", Moscow, Russia
[2]A.V. Shubnikov Institute of Crystallography of RAS, Moscow, Russia

11.30-12.00 **Coffee break, Poster session**

Chairmen: Prof. S. Eremin, Prof. B. B. Dzantiev

12.00-12.30 **DNA APTAMERS AS AFINITY PROBES AND INHIBITORS OF 2OG/Fe(II)-DEPENDED OXIGENASES**
S. M. Krylova
Department of Chemistry, York University, Toronto, Ontario, M3J 1P3, Canada

12.30-13.00 **IL-18 RESPONSE IN KERATINOCYTES SENSITIZED BY DNCB AND PPD IS REGULATED BY HYALURONAN DEPOSITION**

D. Nikitovic[1], A. Berdiaki[1], V. Galbiati[2], A. Papale[2], R. -M. Kavasi[1], A. Tsatsakis[3], G. N. Tzanakakis[1], E. Corsini[2]

[1]Laboratory of Anatomy-Histology-Embryology, School of Medicine, University of Crete, Heraklion, Greece, [2]Department of Forensic Sciences and Toxicology, University of Crete, Heraklion, Greece, [3]Laboratory of Toxicology, DiSFeB, Università degli Studi di Milano, Italy

13.00-13.30 **RELEASE OF HYDROPHOBIC MOLECULES FROM POLYMER MICELLES INTO CELL MEMBRANES.**

P. P. Kulikov[1], L. Gyrevich[2], A. N. Kuskov[1], A. Goryachaya[1], M. I. Shtilman[1]

[1]Mendeleyev University of Chemical Technology of Russia, 125047 Moscow, Russia
[2]Aalborg University, Aalburg, Danmark

13.30-14.00 **Lunch**

14.00-19.00 **Break**

19.00-20.00 **Dinner**

Friday, May 9, 2014

08.00-09.00 **Breakfast**

10.00-12.30 ***MORNING SESSION - Young Scientists Session***

Chairmen: Prof. E. Markvicheva, E. I. Tikhomirova

10.00-10.15 **KINETICS AND MECHANISM OF THE OXIDATIVE POLYMERIZATION OF AROMATIC AMINES AND PYRROLES IN AQUEOUS MEDIUMS**

Ya. O. Mezhuev, I. V. Solovyova, M. I. Shtilman, Yu. V. Korshak, S. V. Osadchenko, I. S. Strakhov, S. E. Pokhil

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

10.15-10.30 **APPLICATION OF 4f- AND 4d-COMPLEXES IN FLUORESCENT DETECTION OF FLUOROQUINOLONE ANTIBIOTICS.**

A. Mustafina[1], S. Eremin[2], M. Sokolov[3], V. Fedin[3], R. Zairov[1], N. Davydov[1], J. Elistratova[1], A. Konovalov[1]

[1]A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan, Russia, [2]M. V. Lomonosov Moscow State University, Moscow Russia, [3]Nikolaev Institute of Inorganic Chemistry, Novosibirsk, Russia

10.30-10.45 **TOXICITY AND HAEMOCOMPATIBILITY OF CHITOSAN-BASED NANOSYSTEMS**

A. A. Zubareva[1], T. S. Shcherbinina[1], E. V Svirshchevskaya[2], V. P. Varlamov[1]

[1]Centre «Bioengineering», RAS, Moscow, Russia, [2]Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, RAS, Moscow, Russia

10.45-11.00 **PROCESSES, OCCURRED DURING EXPOSURES OF AC MAGNETIC FIELD ON ENZYMME LOADED MAGNETIC NANOPARTICLES CLUSTERS**

K. Yu. Vlasova[1], H. Wishwarsao[2], M. A. Abakumov[1], M. Sokolsky[3], Y. I. Golovin[1,4], N. L. Klyachko[1], A. V. Kabanov[1,3]

[1]Lomonosov Moscow State University, Moscow, Russia, [2]University of Nebraska Medical Center, Omaha, USA, [3]University of North Carolina at Chapel Hill, Chapel Hill, USA, [4]Derzhavin Tambov State University, Tambov, Russia

11.00-11.45 **Coffee break, Poster session**

11.45-12.00 **EFFECT OF SIZE OF MAGNETIC CORE ON ENZYMATIC REACTION RATE OF MAGNETIC NANO SUSPENSION UNDER IMPACT OF LOW-FREQUENCY NON-HEATING MAGNETIC FIELD**

M. M. Veselov[1], P. G. Rudakovskaya[1], A. G. Majuga[1], A. Machulkin[1], M. V. Efremova[1], I. V. Uporov[1], Y. I. Golovin[2,1], N. L. Klyachko[1], A. V. Kabanov[3,1]

[1]Lomonosov Moscow State University, Faculty of Chemistry, Moscow, Russia, [2]G. R. Derzhavin Tambov State University, Tambov, Russia, [3]Eshelman School of Pharmacy, University of North Carolina-Chapel Hill, Chapel Hill, USA

12.00-12.15 **EXOSOMES AS NOVEL CLASS OF DRUG DELIVERY SYSTEM: PROGRESS AND PERSPECTIVES**

E. D. Plotnikova[1], M. J. Haney[2], Y. Zhao[2], A. V. Kabanov[1,2], E. V. Batrakova[2], N.L. Klyachko[1,2]

[1]Department of Chemical Enzymology, Lomonosov Moscow State University, Moscow, Russia
[2]Eshelman School of Pharmacy, University of North Carolina-Chapel Hill, Chapel Hill, USA

12.15-12.30 **MACROPOROUS HYDROGEL-BASED SCAFFOLDS WITH MODIFIED SURFACE TO ENHANCE CELL GROWTH: PREPARATION AND APPLICATION IN TISSUE ENGINEERING**

M. Drozdova[1], R. Akasov[1], D. Zaytseva-Zotova[1], A. Golunova[2], A. Artyukhov[2], E. Andreeva[3], M. Shtilman[2], E. Markvicheva[1]

[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia
[2]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
[3]Institute of Bio-Medical Problems RAS, Moscow, Russia

CLOSING CEREMONY

12.45-13.15 **Farewell Address – Closing Remarks**

13.15-14.00 **Lunch**

19.00-22.00 **Farewell Dinner**

Saturday, May 10, 2014

08.00-09.00	**Breakfast**
10.00-13.00	**Excursion**
13.00-14.00	**Lunch**
19.00-22.00	**Dinner**

Sunday, May 11, 2014

08.00-09.00	**Breakfast**
	Departure of Participants

List of Posters

P01
LOADING OF ANTIFUNGAL DRUG IN MODIFIED SURFACES WITH ERGOSTEROL AND OLEIC ACID, ON DIFFERENT SILICONE RUBBER GRAFT COPOLYMERS
G. Burillo[1], T. Segura[1], X. Rivera[1], A. Concheiro[2], C. Alvarez-Lorenzo[2]
[1] Instituto de Ciencias Nucleares, Universidad Nacional Autonoma de México, México 04510 D.F.
[2]Departamento de Farmacia y Tecnología Farmacéutica, Facultad de Farmacia, Universidad de Santiago de Compostela, 15782-Santiago de Compostela, España

P02
ANTIMICROBIAL POLIMERIC COATINGS FOR VENOUS CATHETERS
B. L. Biber[1], E. E. Zhukova[1], M. I. Shtilman[2], A. V. Gorshkov[1], A. L. Iordanski[3]
[1]CSC "MedSil", Mytishchi, Russia; [2]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia; [3]Semenov Institute of Chemical Physics, Moscow, Russia

P03
POLYMERIC MATERIALS BASED ON AMINo-CONTAINING POLYMERS FOR CONTROLLED DRUG RELEASE
M. A. Kasatkina[1], L. M. Simanenkova[1], T. A. Cherdynceva[2], N. R. Kildeeva[1]
[1]Moscow State University of Design and Technology, Moscow, Russia
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Abstract Book

LONG TERM RELEASE OF INSULIN FROM MICROPARTICULATE POLYMERIC CARRIERS EMBEDDED IN A HYDROGEL DRESSING MATRIX IS DESIGNED TO PROMOTE WOUND HEALING

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At previous BIONANOTOX congresses, I have had the privilege of presenting our research around the oral delivery of insulin from nanoparticulate carriers. This research led to a fruitful collaboration with groups working in biomaterials (Prof. Barron) and burn wound healing (Prof. Martins-Green). The objective of the collaboration was to achieve extended term delivery (1 month) of stable bioactive insulin from nano or microparticulate carriers, embedded within a natural polymeric matrix to be used as a therapeutic wound dressing material. Like oral delivery of insulin, long term sustained delivery of a protein therapeutic to a wound site, can be considered as an extreme controlled release challenge.
The optimal microparticulate formulation consisted of crystalline-stabilized human recombinant insulin within poly(lactic-co-glycolic acid) microparticles (PLGA). Sustained release of insulin was demonstrated over a period of weeks, and shown to be continuously bioactive through phosphorylation of AKT in L6 myoblasts, and through stimulation of human keratinocyte migration in a simulated scratch assay.
A wound dressing was then formulated, by dispersion of insulin-PLGA microparticles throughout a flexible alginate sponge matrix forming a fabric like material. Hydrated material formed a hydrogel dressing, and insulin release was demonstrated for a period a weeks, along with favorable wound exudate handling and physical properties conducive to wound healing. Dressings containing 0.04 mg/cm^2 insulin demonstrated continuous and steady dosing of bioactive insulin in simulations, and preliminary *in vivo* trials improved the time of burn wound healing by 25%, in comparison to controls where an identical dressing was applied, but lacking insulin.
Presently, wound dressing materials do not contain therapeutic additives, thus this research opens the possibility in the use of insulin and/or other growth factors, and antimicrobials into the design of next generation wound dressings.

ADVANCES OF CHROMATOGRAPHY BASED TECHNIQUES IN ENVIRONMENTAL AND CLINICAL TOXICOLOGY

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The chromatography based techniques are nowadays principal tools in toxicology research and practice. Reference methods for many applications are based on these techniques and these methods are very often referred as "gold standards" due to their distinguished selectivity and sensitivity. Recent developments in chromatography and chromatography mass spectrometry are intended to amplify their analytical capabilities and at the same time to overcome some "bottlenecks" in the laboratory applications of these techniques. These developments include in particular automation of sample preparation with on-line sample treatment, introduction of new ionization sources in LC-MS and new hyphenated instrument platforms with substantial increase in mass resolution and mass accuracy, shift from HPLC to UHPLC with also dramatic increase in separation efficiency. These achievements in chromatography based techniques will be presented and the advantages of their applications in environmental and clinical toxicology will be demonstrated.

NOVEL ANTIOXIDANT NANOZYMES FOR SPINAL CORD INJURY TREATMENT

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The use of antioxidant enzymes as therapeutics agents is a popular approach for biomedical applications. There are several enzymes, superoxide dismutase (SOD) and catalase among them that catalyze reactions to neutralize free radicals and reactive oxygen species (ROS), which can damage neurons. SOD catalyzes the breakdown of the superoxide anion into oxygen and hydrogen peroxide; catalase transforms hydrogen peroxide to oxygen and water. Introduction of optimal amount of antioxidant enzymes into the site of spinal cord injury may provide the neutralization of toxic effect of ROS. However, the use of native SOD and catalase is extremely ineffective approach because of their instability under physiological conditions. Therefore, it is important to develop the delivery system, which includes SOD (or other enzymes). To transfer this technology to manufacturing, this system should be scalable with good reproducibility, easy to synthesize, have low polydispersity of nanoparticles and high yield of enzyme specific activity. Moreover, therapeutic effect should be significant. The goal of this work was to develop the system of suitable SOD1 nanoparticles.
Our approach was based on formation of ionomer complexes between SOD1 and oppositely charged polymers. Briefly, SOD was mixed with polyarginine (MW 9600) for 30 min, after that poly (ethylene glycol)–block–poly(L-glutamic acid) (MW 12500) was added. Glutaraldehyde was used to stabilize particles. Further, nanoparticles were purified (gel-filtration chromatography, ultracentrifugation) and analyzed by: BCA assay (to evaluate the reaction yield), pyrogallol assay (specific enzymatic activity), chromatography (composition of reaction mixture), dynamic light scattering (size and charge of obtained nanoparticles).
SOD nanoparticles with diameter 40 ± 2 nm and low PDI (less than 0.05) were obtained (diameter of native SOD is 7 nm). In this

method, SOD retained 100 % of specific activity. In case of cross-linked approach, the SOD nanoparticles were 50-100 nm, PDI ≤ 0.2 (depended on conditions), with specific activity of 40-60%. SOD nanoparticles showed extremely high therapeutic efficiency in spinal cord injury model in rats.
Finally, scalable synthesis of active SOD nanoparticles was developed.
This work was supported by grant from the Ministry of Education and Science 11G34.31.0004 from 30.11.2010 and by grant from Foundation for assistance to small innovative enterprises in science and technology under the program "UMNIK".

OSTEOPLASTIC IMPLANTS BASED ON RESORBABLE POLYESTERS FOR RECONSTRUCTIVE SURGERY

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Reconstructive surgery seriously needs in biocompatible materials which are required for closing of bone defects resulting from surgical trauma. Polyhydroxyalkanoates (PHAs) are among the most interest materials which are developed and studied for solving these problems. PHA alone can function as osteoplastic material and implants, as well as used in combination (composition) with different materials, drugs and cells to improve their biocompatibility and physico-mechanical properties. In this work we proved the ability of scaffolds from poly-3-hydroxybutyrate (P3HB) support cell growth and differentiation of bone marrow cells osteoblastic series. Activity of alkaline phosphatase, osteopontin production and the presence of extracellular calcium precipitates were the markers of differentiation MMSCs. Osteoplastic properties of P3HB and their compositions with hydroxylapatite (HAP) as implants were studied on in vivo model of segmental osteotomy in comparison with commercial material Bio-Oss. It is shown that the reconstructive bone formation occurs more actively with using all types of implants containing P3HB as a main component. The results allow us to recommend these polymer matrices for the reconstruction of bone defects.
The study was supported by the project initiated by the Government of the Russian Federation (Decree No. 220 of 09.04.2010) for governmental support of scientific research conducted under the guidance of leading scientists at Russian institutions of higher learning (Agreement No. 11.G34.31.0013).

SYNTHESIS OF MAGNETIC AND MAGNETIC@GOLD FOR BIOMEDICAL 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.
In this work we synthesized and investigated the properties of magnetic nanoparticles with different morphology. Using different size and shape of magnetic nanoparticles can allow to vary the magnetic and biomedical properties. In this paper magnetite nanoparticles were synthesized by chemical methods with a spherical shape and size: 8 ± 2 nm and 24 ± 4 nm , and the magnetite nanorods 10 (± 3) x 50 (± 10) nm. Spherical magnetite nanoparticles with an average size of 8 nm were synthesized by coprecipitation of salts of iron (II, III) with ammonia, with a size of 24 nm - oxidation of iron (II) with hydrogen peroxide in alkaline medium. The nanorods were obtained by reduction of iron (III) salt in the presence of dopamine as a stabilizing ligand.
The use of gold as the shell provides their colloidal stability, ease of functionalization and biocompatibility. In this work we synthesized and investigated the properties of hybrid magnetite nanoparticles coated with gold shell. Firstly magnetite was obtained by coprecipitation of salts of iron (II, III), and then chloroauric acid was reduced with sodium citrate. Hybrid nanoparticles has core-shell structure. Varying concentrations of the reactants and reaction conditions allow to get nanoparticles with different size.
Gold shell allows easy functionalization of nanoparticle surface by thiol ligands. Prepared nanoparticles were consistently modified by thiolated carboxylic ligands, and then modified by enzymes. Resulted nanohybrid materiales were studied under the influence of non-heating magnetic fields. We have demonstrated that super low-frequency non-heating magnetic field can effect on the kinetics of chemical reactions catalyzed by the enzymes immobilized on nanoscale magnetic nanoparticles aggregates and core-shell magnetic nanoparticles.

TARGETED CONTRAST AGENTS FOR MRI DIAGNOSTICS OF MULTIPLE SCLEROSIS

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Introduction
Multiple sclerosis (MS) is a progressive neurodegenerative disease. More than 2 million people suffer from MS in the world. Magnetic resonance imaging is a standard necessary tool for diagnosis of MS. T1 and T2 contrast agents are used to enhance the vi-

sualization of demyelination by MRI. T1 contrast agent based on Gd-DTPA complex is the most popular agent, although it has some limitations: high toxicity, low T1-relaxivity and non-specific visualization. To improve the properties of Gd-DTPA and selective visualization of demyelination by MRI we developed targeted macromolecular contrast agent based on poly-L-lysine and monoclonal antibodies to glial fibrilar acid protein (mAb anti-GFAP).

Methods

Poly-L-lysine (PLL) were modified by chelating agents - diethylenetriaminepentaacetic acid (DTPA) or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) - using carbodiimide chemistry and loaded with Gd(III) ions. Unbound chelate complexes were removed by gel-filtration chromatography using PD-10 columns (Sephadex G-25). Then polymers (PLL-DTPA-Gd or PLL-DOTA-Gd) were conjugated with mAb anti-GFAP and activity of mAbs were determined by ELISA assay. Non-specific IgG-conjugated contrast agent was used as a control. Cytotoxicity of targeted agents was analyzed by MTT-test on human embryonic kidney cells (HEK293). T1-relaxivity was measured on 7T MR-tomograph ClinScan (Bruker).

Results

During synthesis the immunochemical activity of conjugated mAbs was preserved up to 85% in comparison with added mAbs. Maximal non-toxic concentration of contrast agents was 0,5 mg/ml. Important, that obtained contrast agents had higher T1-relaxivity value (5,5 and 7 $mM^{-1}s^{-1}$ for DTPA and DOTA chelating motif) in comparison with commercial available agent Magnevist (4,2 $mM^{-1}s^{-1}$).

Summary

Targeted T1-contrast agent for MRI diagnostics of multiple sclerosis based on polylysine and specific monoclonal antibody was successfully synthesized and characterized.

This work supported by RFBR grant №13-04-01383 and program «UMNIC» of Foundation for Assistance to Small Innovative Tnterprises

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DEVELOPMENT OF POLIMERIC MICELLES FOR CURCUMIN DELIVERY

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The limited solubility of many anti-tumor drugs in water leads to poor bioavailability in living cells conditions. For that reason, the improvement of drug solubility is one of the main tasks for anticancer drug delivery. Nano-sized systems based on nanoemulsions, liposomes, solid particles and micelles are widely used for this purpose. Moreover, these nano-systems stand out due to the possibility to control drug release and ability to be accumulated in tumors as a result of EPR (enhanced permeability and retention) effect.

Curcumin (CUR) is a natural antitumor compound extracted from Curcuma longa. Being used in traditional medicine, CUR is characterized by strong therapeutic activity against several types of cancer. One of the main drawbacks of CUR is the very low solubility in aqueous solution, which limits its large utilization in cancer therapy. Thus, different strategies need to be studied, in order to improve CUR solubility and delivery to the target.

The aim of this study was to develop nanosized micelles loaded with CUR and subsequently to study their cytotoxicity on two in vitro models: monolayer culture (2D) and multicellular tumor spheroids (MTS) which can be considered as 3D model. In order to protect CUR from degradation and to provide its targeted delivery and controlled release, the drug, was covalently attached to Tetronic® used as a drug nanocarrier. The functionalized block-copolymer is able to self-assembly in solution into micelles with different sizes in function of the concentration and working temperature.

The efficacy of the proposed delivery system was studied on several tumor cell lines, namely human breast carcinoma MCF-7, human glioblastoma U87MG and human cervix carcinoma HeLa, in monolayer (2D) conditions. Also we obtained MTS based on U87MG cells by adding RGD-peptides which contained arginine - glycine - aspartic acid in their structure.

Both 2D and 3D systems showed that free CUR was more effective compared to the CUR-micelles. However, this difference was maximum after 24 hours of incubation and comparatively small after 72 hours. Thus, for U87MG cells IC50 of free CUR and CUR-micelles after 24 hours was 44 and 150 μM, respectively. However, after 72 hours it decreased to 32 and 55 μM, respectively, which could be considered as the time-release effect for CUR-micelles. In the case of spheroids based on U87MG cells compared to 2D model, higher doses were needed to achieve a similar effect.

FUNCTIONAL NANOSYSTEMS FOR PHARMACOLOGY AND MEDICINE

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Current studies based on the technology "NanoZYME" are directed to the creation of enzyme-containing polymer nano-systems intended for the treatment of several diseases (diseases of the central nervous system, brain, neurotoxic injury, eye inflammations, bacterial infections).

With the use of "NanoZYME" technology based on organophosphate hydrolase enzyme (OPH), series of original biomaterials (hydrolytic nanozyme) that catalyze the decomposition of organophosphorus compounds (POS) were developed. The nanoformulation effect on chemical warfare agents and pesticides was studied *in vivo* using different ways of administration into the body:

intravenously, intramuscularly, intraperitoneally and buccally.
As revealed, it is possible to use these formulations as effective antidotes in cases of intoxication by high concentrations organophosphorus agents (up 6xLD50), survival rate is 100%. It was also demonstrated for the first time ever that it is possible to use these formulations as protectants (the same 100% survival rate), if they are administrated into the body a few hours (from 2 to 15 h) prior to intoxication by high-dose of organophosphorus agents (up 8xLD50). The hydrolytic nanozyme samples can be stored up to 500 days at room temperature without losing the enzyme activity. The absence of cytotoxicity and immunogenicity was shown. As found, the dosage of these formulations can be lowered be dozens of times comparing to the conventional antidotes used worldwide.
The properties and new formulations composed of SOD-containing polymeric nanocomplexes and conjugates were investigated. Significant improvement in the course of the disease of immunogenic uveitis (an inflammatory disease of the eye) at a local drip containing superoxide dismutase (SOD1-nanozyme) nanozyme solutions, in the eyes of rabbits was shown. Histological studies have proved the clinical and biochemical data. These results demonstrate high potential therapeutic efficacy of SOD1 nanozyme to treat a wide range of inflammatory diseases in the eye.
Nanoparticles of SOD1-polycation are safe in terms of survival rate for animals with spinal cord injury, and their administration improves recovery dynamics of rat's voluntary movements. Novel bionanomaterials based on nanoparticles bilayer composition SOD1-polycation-polyanion were developed. Significant increase of the yield of incorporation of the protein (from 20% to 70%) and the efficiency of the enzyme (up to 70%) were observed together with drug cytotoxicity reduction.
Bacteriolytic nanozymes effective against Gram-positive and Gram-negative bacteria were prepared and used as antibacterial agents. As an example, nanocompositions of enzymes from bacteriophage phi 11 and K with block-copolymers, effectively lysing of antibiotic resistant strains of Staphylococcus aureus, having high stability and decreased (2-10 times) toxicity, were investigated and characterized.
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MODERN BIOMATERIALS: WORLD TRENDS, PLACE AND POTENTIAL OF MICROBIAL POLYHYDROXYALKANOATES (PHAs)

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Development of environmentally friendly materials that could be involved in the biospheric cycling is one of the key issues of the present time due to both environmental hazard caused by accumulation of synthetic materials in the biosphere and the needs of modern biomedical technologies. The study analyzes the state of the art and current international trends in biomaterials research and the position and role of degradable bioplastics synthesized by microorganisms (polyhydroxyalkanoates, PHAs). The data are reported on the processes and production of this class of polymers by world's leading companies; potentials for the development of commercial production of degradable PHAs in Russia are investigated. The IBP SB RAS and SFU have developed the technologies of the synthesis of PHAs with different chemical structure, exhibiting properties of high-crystallinity thermoplasts and construction elastomers, and used them in pilot production of these polymers. The researchers have constructed 2D and 3D polymer devices, implants, prostheses, biocompatible coatings, microcarriers of drugs and functioning cells as nanoparticles and ultrafine fibers; preclinical trials have been performed and clinical trials started. PHAs have been studied as material for packaging, for constructing fertilizer formulations and plant protectants; studies have been performed to investigate PHA behavior and kinetics of their biodegradation by soil and aquatic microbial communities in nature. Technical and economic parameters of different substrate scenarios of PHA synthesis technologies, using individual and complex substrates, have been assessed.
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QUANTUM DOTS AS LABELS IN IMMUNOASSAYS

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New trend in immunoassays - the development of different types of inorganic nanoparticles (NPs) to be used as labels in immunoassays instead of fluorophores or organic particles. Fluorescence has been used most as the detection mode for immunoassays. The inorganic NPs are characterized by their high photostability and high quantum yield. The inorganic NPs studied most have been silica NPs, quantum dots (QDs), noble metals, metal nanoshells and lanthanide oxides.
Quantum Dots (QDs) is luminescent inorganic nanocrystals. The emission wavelength is a function of the crystal size - crystals of the same chemistry can have the emission maxima in a wide range. The CdTe nanocrystals are most widely used as QDs. Usually QDs coated with -COOH groups and can be easily used for labeling purposes for chemical and biological applications. The QDs have growing attention because of their good stability, excellent optical and electrochemical properties, resistance to photobleaching and to organic solvents. The recent advances in the preparation and the properties of QDs and their applications in environmental and biological areas will be discussed. In addition, the future development of QDs will be suggested.
Acknowledgement
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TO UNDERSTANDING TOXICITY OF EXOGENOUS ANTIOXIDANTS USED TO COMBAT FREE-RADICAL DISEASES

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An increasing number of findings on oxidative alterations of essential biomacromolecules, including lipids, proteins and nucleic acids, and their involvement in tissue injury had prompted the formulation of theory of free (oxygen) radical mediated diseases over decades ago. This traditional concept is based on understanding that increased formation of free oxygen radicals (correctly referred to as reactive oxygen species, ROS) results in *oxidative stress* that may ultimately lead to cell death and, in a massive scale, to tissue injury resulting in organ dysfunction and thus manifested as *free-radical disease*. Consequently, compounds with antioxidant properties were then suggested to prevent and treat these specific pathologies. However, despite the effective protection of macromolecules from oxidative damage *in vitro*, antioxidants often fail to do so *in vivo*. In fact, a significant number of clinical trials reported no benefit of exogenous antioxidant administration when combating free-radical diseases, and, in contrary, severe complications often developed.
The present paper provides an overview of important mechanisms where fluctuations in ROS concentration are inevitable for normal cellular functioning. They are of particular importance since exogenous antioxidants if applied in excess may dysfunction these physiological mechanisms. Under pathological conditions, particularly during the tissue injury, an increase in ROS production may actually happen as a consequence of the primary insult. Under such circumstances, ROS do not play a causal role in tissue injury. Right in contrary, increased ROS may readily participate in counteracting actions of the tissue directed against injurious processes. This concept is in a certain contradiction to traditional understanding of ROS as deleterious agents. On the other hand, it is in a good agreement with some recent findings indicating that ROS play, similarly to other cellular and tissue mediators, an important role in intracellular and intercellular signaling. Moreover, the concept provides a background for understanding of ineffectiveness of exogenous antioxidants in treating free radical diseases and, in particular, also a possible explanation of their undesired toxic effects that may in fact aggravate the condition treated.
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RAPID AND MULTIPLEX BIOANALYTICAL TECHNIQUES ON THE BASE OF QUANTUM DOTS

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Unique optical properties of semiconducting nanoparticles quantum dots (QDs) define wide possibilities of their analytical applications. The report presents state of the art of techniques, particularly immunotechniques, for detection of various biologically active and toxic compounds with the use of QDs. Immobilization of antibodies and other biorecepting molecules on the surface of nanoparticles and analytical application of these intermolecular conjugates is characterized. The development of analytical systems based on energy transfer processes (FRET and CRET-effects) with participation of QDs is discussed; the most successful examples of high sensitive methods are presented. QDs are compared with conventional markers (including non-fluorescent coloured nanoparticles) as tools to detect immune complexes in various analytical formats. The existing portable emitting/detecting de-

vices for on-site (point-of-care) monitoring of QDs as labels are presented.
Results of the development of QDs-based membrane test systems (immunochromatographic test strips) are discussed. On the example of competitive immunoassay of antibiotic chloramphenicol QDs are compared with colloidal gold labels. Tenfold decrease of the detection limit was reached by substitution of colorimetric assay by fluorometric one. Registered levels of the emission intensity at binding zones of test strips allow to quantify the target antigen content with accuracy not more than 10%. Specific features of direct QDs-based immunoassays of high molecular weight antigens such as immunoglobulin E are discussed. The application of a row of QDs with different emission spectra for «traffic-light» multiparametric immunoassay is demonstrated on the example of antibiotics control in foodstuffs. The application of QDs for assays in different matrixes (blood, milk, etc.) is discussed with the demonstration of the proposed solutions for samples pre-treatment.
Priority fields for further application of QDs-based assays in medical diagnosis, environmental monitoring and quality/safety control of foodstuffs and consumer products are discussed.
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BIODEGRADABLE FIBERS AND MICROCARRIERS AS PROMISING MATRICES FOR REGENERATIVE MEDICINE

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Various natural and synthetic polymer-based micro- and nanocarriers, with exciting properties have been developed for tissue regeneration, including bone, cartilage, nerve, blood vessels, and skin. Nano- and microfibers as well as microcarriers (microbeads 150-250 μm) are the most promising scaffolds in tissue engineering, since they are easily injectable delivery systems and can provide 3D cell growth. More over, they can be loaded with various drugs, growth factors and other bioactive molecules.
The aim of the study was to get a set of novel biodegradable nano- and microfibers and microcarriers and to evaluate cell behaviour in function of polymer matrix composition and surface characteristics. All scaffolds were fabricated from biocompatible synthetic and natural materials, such as natural polysaccharide chitosan, biodegradable synthetic polylactides, namely PLLA, poly(D,L-lactide (PDLLA), and polyvinyl alcohol (PVA). Mouse fibroblast L929 were used as model cells. To enhance cell adhesion, spreading and proliferation the PLLA and PDLLA microbeads were coated with polycations (chitosan, chitosan–g-PVA, chitosan-gelatin-PLA copolymers, poly(2-dimethylamino ethylmethacrylate) (PDMAEMA). Composite PVA-chitosan nanofibers (mean size 200 nm) were fabricated by electrospinning, and heat treated in autoclave (120 C, 30 min), in order to make them water insoluble and to sterilize at the same time. Then so-called extract- and contact tests with L929 cells were carried out to test nanofiber cytotoxicity. Optical, laser confocal microscopy and SEM were used to observe cell growth. Cell viability was determined by MTT-test on day 2. 4, and 7 of cultivation. Cell attachment, spreading, growth and proliferating were found to greatly depend upon polymer composition. The scaffolds will be loaded with bioactive peptides/proteins (for example, thrombin receptor agonist peptide TRAP-6), and their effect on cell growth will be studied in the nearest future.

PROPERTIES OF POLY AZOLIDINE AMMONIUM MODIFIED BY HYDRATE HALOGEN IONS AND BIOLOGICAL PRODUCTS ON ITS BASIS

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We studied antimicrobial properties and toxicity of poly azolidine ammonium modified by hydrate halogen ions (PAAHH), and core-shell structured biological preparations derived from it.
PAAHH is a biocompatible linear polymer with a molecular mass of about 100-200 kDa with sucrose molecules attached to both ends. PAAHH has unlimited solubility and toxicity class IV. To create the core-shell structure, we conducted sequential adsorption of 1% PAAHH on the surface of hydrophobic heterocyclic compound A-2 of enamine group (Nechaeva et al. 2009) and nano-aggregated flavonoids derived from propolis (Zayarsky et al.: the Patent of the Russian Federation No. 2446852; Zayarsky 2012). Antimicrobial properties were studied using serial dilutions until minimum inhibitory concentrations (MIC) for reference strains of bacteria, microscopic fungi, and clinical isolates of staphylococci were reached. We discovered dependence of PAAHH antimicrobial effect page from iodine hydrate ion concentrations. With the increase of their concentration from 100 to 500 (mcg/ml), MIC decreased from 64 to 8 (mcg/ml). For A-2 compound, MIC was 25-50 mcg/ml for reference strains and clinical isolates of bacteria. Nano-aggregated flavonoids did not display antimicrobial activity. Investigation of the core-shell structure with A-2 as a core and polyelectrolytes as a shell confirmed 62, 16, and 2 times increase in antimicrobial properties against staphylococci, bacilli, and other bacteria, correspondingly. The core-shell structure of nano-aggregated flavonoids (core), covered with PAAHH (shell) showed antimicrobial properties similar to PAAHH alone. We conducted the evaluation of PAAHH wound healing action in laboratory mice. We estimated daily reduction in would area (%) following the standard technique (Kuzin, Kostyuchenok 1990, Gul et al. 2008). When treated with the biological preparation, wounds underwent area reduction from the 2nd day, and were completely gone on the 8th day. When treated with nano-aggregated flavonoids, wounds healed on the 11th day. In control animals, wound healing took place on the 14th day. All the differences were statistically significant. When assessing morphological changes in wounds, we revealed an acceleration of healing by stimulating reparative processes and strengthening skin protective function. Therefore, the core - shell structures on the basis of nano-aggregated flavonoids, covered with a polymer PAAHH shell, have antimicrobial properties that can be used for the development of an innovative medication for treating uncomplicated and purulent wounds.

PRODUCTION OF HIGHLY OF UNSATURED FATTY ACIDS, ESSETIAL FOR HUMANS, IN AQUATIC ECOSYSTEMS

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Humans and other omnivorous animals, must get the physiologically important polyunsaturated fatty acids (PUFA), such as eicosapentaenoic acid, (EPA) and docosahexaenoic acid (DHA) from food. Only some taxa of microalgae, rather than higher plants can synthesize de novo high amounts of EPA and DHA. Once synthesized by microalgae, PUFA are transferred through trophic chain to organisms of higher levels. Thus, aquatic ecosystems play the unique role in the Biosphere as the principal source of EPA and DHA for most omnivorous animals, including inhabitants of terrestrial ecosystems. PUFA are transferred from aquatic to terrestrial ecosystems through riparian predators, emergence of amphibiotic insects and through water birds (432 10^6 kg y^{-1}). The essential PUFA are transferred through trophic chains with about twice higher efficiency than bulk carbon. Thereby, PUFA are accumulated, rather than diluted in biomass of organisms of higher trophic levels, e.g., in fish.
Man withdraws from aquatic ecosystems through fishery ~180 10^6 kg y^{-1} of EPA+DHA. However, global average personal daily consumption of EPA+DHA is only about 0.1 g. Thus, mankind is faced with a severe deficiency of the physiologically important long-chain PUFA in diet. Aquatic ecosystems should be protected from anthropogenic impacts, such as eutrophication, pollution and warming, which reduce PUFA production.
Besides the essential nutrients, PUFA, toxic materials, such as heavy metals and pesticides can be transferred through aquatic food chains and accumulated in organisms of higher trophic levels, namely in fish. Various fish species from diverse locations have different contents of PUFA, as well as different concentrations of toxic compounds. Thus, a quantitative estimation of risks versus benefits of fish intake for human health is very desirable. A formula for calculation of the risk-benefit ratio is suggested. Data are given on quantity of various fish products to be consumed for obtaining the recommended appropriate intake of EPA+DHA for humans.

SURFACE MODIFICATION OF POLYHYDROXYALKANOATES FOR BIOMEDICAL PURPOSES

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Surface properties of polymer materials are among the main characteristics of cell scaffolds used in tissue engineering as they significantly influence cell attachment and proliferation. Different physicochemical techniques are used to treat polymer surface in order to enhance its hydrophilic and adhesive properties; these include the use of high energies and chemicals causing hydrolysis and redox reactions.
One of the fundamental parameters for studying surface properties of polymer materials is surface free energy (SFE). This study investigated the effects of treatments with oxygen and peroxide plasma, laser beams, and chemical reagents on poly-3-hydroxybutyrate films prepared by evaporation from a chloroform solution. Changes in the SFE and its dispersive and polar components were evaluated from measurements of contact angles of water and diiodomethane drops, using the Owens, Wendt, Rabel and Kaelble method.
The greatest increase in the SFE was obtained by treating the films in pure oxygen plasma at 50 W for 5-15 min because of the polar component. Treatment with H_2O_2 plasma performed in a Sterrad NX medical sterilizer under standard conditions (for 0.5 h at 45°C) caused much less significant changes in film surface properties as only the polar component of the SFE increased.
The treatment using a CO_2 laser produced film surfaces with significantly increased dispersive and polar components of the SFE. The optimal spectrum of laser radiation for effective influence on electron molecular bonds of the PHA was found in a theoretical study, which showed that the vacuum laser should be used at wavelength 160 nm. Films with modified surfaces, varying from rough to perforated, were produced using laser treatment at 3.0 to 30.0 W. The microstructure and properties of the film surface were studied as dependent on the type of radiation, and conditions were found that caused a considerable increase in the SFE compared with the initial films.
Among the chemical reagents, a NaOH solution showed the highest activity: it increased the SFE considerably after 10 min of treatment, mainly due to the increase in the polar component. A longer (more than 20 min) treatment with NaOH made the films thinner and, later, caused them to dissolve, forming mainly sodium salt of crotonic acid.
Films were maintained in other chemical reagents for 30 min. A significant increase in the SFE was recorded in the experiment with the H_2O_2 solution: both the dispersive and the polar components increased. In H_2SO_4 treatments, only the polar component of the SFE increased, and that increase was insignificant. By contrast, the treatment with a concentrated HCl solution caused a decrease in the SFE due to a decrease in its dispersive component. No significant differences were found between the SFE of the films treated with HNO_3 and NH_3 and the SFE of the control films.
Biocompatibility of the polymer films with modified surfaces was evaluated in the culture of fibroblast NIH 3T3 cells.
Thus, a theoretical study and experimental treatments of poly-3-hydroxybutyrate films with physical agents and chemical reagents revealed the approaches that can be used to improve the surface properties without destroying the structure of the material.
The study was supported by the Government of the Russian Federation (Agreement No. 11.G34.31.0013 in accordance with Resolution No. 220 of April 9, 2010).

SINGLE-CELL KINETICS APPROACH TO STUDY NON-SPECIFIC REJECTION OF TOXINS BY CELLS

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Non-specific toxins' rejection driven by their active efflux from the cells by ABC transporters is one of the protection mechanisms from cytotoxicity. Understanding the nature of such rejection requires the comparison of the efflux rate between different subpopulations of cells. Here we describe a single-cell-kinetics approach for such a comparison. In essence, the entire cell population is loaded with a suitable fluorescent substrate for rejection-associated membrane transporters. The kinetics of substrate efflux from individual cells is followed by time-lapse confocal fluorescence microscopy and analyzed at the single-cell level. Microscopy is also used to assign cells to different subpopulations based on differences in morphology or level of staining by molecular probes. The kinetic parameters obtained for individual cells are then averaged for different cell subpopulations and the mean values of these parameters are finally compared between subpopulations. To test our single-cell-kinetics approach, we studied the efflux for two subpopulations of cultured breast cancer cells: cells in 2N and 4N phases of the cell cycle. The assignment of cells to 2N and 4N subpopulations was done by fluorescent DNA staining after the completion of efflux. By using the single-cell-kinetics approach we were able to prove for the first time that the rates of efflux differ in 2N and 4N phases of the cell cycle. We further studied the efflux in tumor-initiating cells and discovered 3 previously unknown subpopulations with distinct kinetics of the efflux. We foresee that this approach will be an important tool in studies of cell protection from cytotoxins.

SURGICAL DRESSINGS WITH ANTIMICROBIAL CARACTERISTICS OF MULTILAYER NONWOWEN

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Currently, in orthognatic surgery sterile gauze pads are used as surgical dressings, which become fixed on the wound surface by using Hippocrates' cap and plaster.
The institute scientists have developed a fundamentally new surgical dressings consisting of antimicrobial multilayer nonwovens (biologically active pack) for orthognatic surgery and special products to fix them on the maxillo-facial area. The developed nonwovens and products are working environment made and after packaging and sterilization are tested in the surgery department of the University of Medicine and Dentistry.
Medical and clinical studies have shown that the developed surgical dressings have highly absorption capacity and antibacterial activity – they absorb and hold the exudate, even by intensive exudates, and almost completely eliminate bacterial content of the wound surface.
The treatment of postoperative wound should be divided into two phases: profuse and moderate exudation. The nonwovens with high absorption properties should be used in the first phase of treatment, in the second - with the conventional properties.
Bacterial content of the wound surface of patients with phlegmons and abscesses was reduced by 90-99 % (in the control group by using gauze pads - 60-70%) in 5-7 days by using of the surgical dressings consisting of antimicrobial multilayer nonwovens in the treatment.
The application of the new surgical dressings in orthognatic surgery ensures a pronounced therapeutic effect, does not interrupt the blood circulation, does not provoke allergic reactions and due to minimal adhesion does not damage the wound edges and the surrounding skin integuments.
The special developed product for fixing keeps the biologically active pack on the wound surface and creates conditions for a comfortable, painless and quick bandage. Medical and clinical studies have shown that the sorption of the exudate occurs in 1-5 days of the treatment. At the same period of time the antimicrobial agent desorbs in the wound chamber.
Consequently, the surgical dressings made of the developed antimicrobial multilayer nonwovens containing of viscose fibers in outer layer, which is treated with cefazolin, and highly absorbent fiber in the inner layer are recommended for the postoperative care of surgical wounds in orthognatic surgery in the first phase of treatment. For the second phase of treatment the nonwovens without highly absorbent fiber are recommended.

TRIBOLOGICAL STUDY OF MULTIWALLED CARBON NANOTUBES (MWCNT)/ALUMINA (Al_2O_3) REINFORCED ULTRA HIGH MOLECULAR WEIGHT POLYETHYLENE (UHMWPE) BIOCOMPOSITES FOR BIOMEDICAL APPLICATIONS

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Tribomotion is well known contact degradation phenomenon in an aqueous media including body fluids. This is a most studied critical issue in the design of orthopedic implants like THP (Total hip) and TKR (Total knee). Since UHMWPE biopolymer has been widely used as an acetabular cup liner in total hip and total knee prostheses as a bearing surface against hard metal or ceramics femoral head as an articulating surfaces due to its better tribological properties but, generation of wear debris leads to aseptic loosening that limits the lifespan of implant and requires a revision of orthopedics surgery. So there is a highly need of such materials which have longer life span in vivo as well as in vitro applications. In this study to decrease the wear debris formation, carbon nanotubes [MWCNT] were modified by silane and synergistically reinforced with Al_2O_3 in UHMWPE matrix. The composites were processed by compression molding method. The Phases, chemical and microstructure of the nanocomposites based on synergistic reinforced with Al_2O_3 and MWCNTs were studied by the methods of X-ray diffraction analysis, FT-IR spectroscopy. The effects of the silane-modified MWCNTs on its reinforced composite were studied for their tribological properties. The results sh-

owed that the tribological properties of the composites were also improved due to better interaction of the MWCNTs with UHMWPE polymer matrix. It was observed that due to reinforcements of functionalized MWCNTs and Al_2O_3 that were embedded in polymer matrix, leaching out of MWCNT was restricted and tribological performance of composites were enhanced by 29.41% with respect to neat polymer. Cytocompatibility test was performed for L929, Mouse fibroblast cell line and found good biocompatibility without any cytotoxicity. It may conclude that UHMWPE-Al_2O_3-MWCNT based biocomposite might be a good material for orthopedic applications.

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METHODS OF COMPLEX ASSESSMENT OF CYTO-, GENO-, AND EMBRYOTOXICITY OF NANOPARTICLES IN EXPERIMENTS IN VITRO

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Objectives: A complex of express methods for assessing cyto-, geno-, and embryotoxicity of nanoparticles, including concurrent use of three models: pre- and post-implantation embryos of mice (blastocyst division-formation, 1-5 days of development) and rats (head process formation, 30 somite pairs, 9.5-11.5 days of development), as well as human peripheral blood lymphocyte cultures. The main objective was to assess the cyto-, geno-, and embryotoxicity of SiO_2 nanoparticles in experiments *in vitro*.
Methods: Silica nanoparticles 12 nm in size (Sigma-Aldrich) were used in the *in vitro* experiments. To prevent agglomeration, an aqueous suspension of nanoparticles was untrasonicated, after which bovine serum albumin was added to a final concentration of 15.0 μg/ml. The nanoparticles were introduced into the cultural medium at concentrations of 20, 100, and 200 μg/ml. Dividing mouse embryos were cultured from the 2-blastomer stage in droplets of the medium containing nanoparticles under a layer of paraffin oil (20 embryos per droplet) in a multigas incubator for 72 h. Post-implantation rat embryos were cultures in an incubator for 24 h from the 2-4 to 30 somite pair stage. Human peripheral blood lymphocytes were cultured for 72 h under cytokinesis-block conditions (in the presence of cytochalasin d), which allowed simultaneous assessment of the cyto- and genotoxicity of nanoparticles. The development of animal embryos and human blood lymphocytes was assessed by the embryolethal and teratogenic (dismorphogenesis) effects, dynamic morphofunctional disorders, and cytotoxic (cytostatic) and genotoxic effects.
Results: Direct addition of SiO_2 nanoparticles at concentrations of 100 and 200 μg/ml into the pre-implantation embryo culture lead to single embryo deaths and retardation of blastomer division, the total cell mass was reduced against control by a factor of 1.3. Silica nanoparticles at a concentration of 20 μg/ml had no effect of the development of dividing embryos. Upon culturing of embryos at an early organogenesis stage in a medium containing SiO_2 nanoparticles at the same concentrations, no embryolethal effect was observed, but the concentration 200 μg/ml caused some structural and dynamic pathologies. General retardation of embryonic morphogenesis was noted (retarded somitogenesis, reduced craniocaudal size). The SiO_2 nanoparticle concentrations of 100 and 200 μg/ml induced no cyto- and genotoxic effects in human peripheral blood lymphocyte cultures: the proliferative activity of cells, picnosis and apoptosis rates, and micronucleus count did not differ from control).
Conclusions: Complex assessment of the effects of SiO_2 nanoparticles revealed their embryotoxicity at concentrations of 100 and 200 μg/ml at pre- and post-implantation stages of embryonic development. Experiments with human peripheral blood lymphocyte cultures gave no evidence for any cyto- and genotoxic effects of the nanoparticles.

FLUORESCENT DYE ENCAPSULATION FOR THE VISUALIZATION OF POLYELECTROLYTE CAPSULES PHARMACOKINETICS

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Polyelectrolyte capsules are very promising for biomedical applications due to their unique properties such as monodispersity, wide range of the materials for capsule wall creation, and possibility to control the permeability of capsule shell. On one hand, fluorescent dyes encapsulation attracts a lot of attention due to the application for visualization, while, on the other hand, the dyes may be used as functional content, for example in photodynamic therapy.
In the present work the embedding of porous spherical microparticles of calcium carbonate (polyelectrolyte capsule cores) by fluorescent dyes rhodamine 6G and photoditazine was performed. The amount of absorbed dye was determined by spectrophotometry. Desorption of the substances in water and saline solution has been measured *in vitro*. It was found that increase in the ionic strength of the solution leads to the raise of desorption degree. In case of rhodamine 6G the dye is released due to $CaCO_3$ particles recrystallization.
Microcapsules formed by up to 8 layers of oppositely charged polyelectrolytes chitosan and dextran sulfate have been obtained by layer-by-layer technique using calcium carbonate particles as capsule cores. The capsule size was from 1 to 10 mkm. Chitosan/dextran sulfate capsules were stable in saline solution and aqueous solution with pH 4-8. Capsules destruction was observed in a highly acidic media (pH 2) during 20 min, while in a weakly alkaline medium (pH 9) the capsule shells were only deformed.
Pharmacokinetics of chitosan/dextran sulfate microcapsules labeled by the fluorescent dyes was investigated *in vivo* by the means

of noninvasive fluorescence diagnostics (Laser Diagnostic Complex LAKK M, M.F. Vladimirskiy Moscow Regional Research Clinical Institute) using experimental mice groups. The optimal route of microcapsules administration and the regularities of their distribution and degradation were determined. It was shown that there were no acute toxic effects and behavioral disorders in the general case. Fluorescent signal of the capsules with photoditazine was observed during 7-10 days opposite 3-4 days for free photoditazine solution. For capsules with rhodamine 6G this signal was observed during 6-7 weeks in contrast to 2-3 weeks for free dye solution.
The study was supported by the Russian Foundation for Basic Research, projects 13-03-00913, 14-03-00979.

DNA APTAMERS AS AFINITY PROBES AND INHIBITORS OF 2OG/Fe(II)-DEPENDED OXIGENASES

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The 2OG/Fe(II)-dependent oxygenases are the enzymes, that demethylase DNA and RNA in response to alkylating agents from the environment or generated during cellular metabolism.
Methylating agents are widely used in anti-cancer chemotherapy treatments, therefore, inhibition of nucleotide repair enzymes can be beneficial for enhancement of chemotherapeutic treatment. The use of such inhibitors in conjunction with anti-cancer alkylating agents may reduce their cytotoxic effects, allowing dose reduction and improving efficiency of chemotherapy.
The biological significance of human 2-oxoglutarate-dependent oxygenases is also linked to neurological disorders and obesity development in humans. Therefore, there is a high demand for both regulators of the activity of these oxygenases and reliable affinity probes, allowing measurements the expression level of enzymes in complex biological matrixes. Here, we report one of the applications of our Non-Equilibrium Capillary Electrophoresis of Equilibrium Mixtures (NECEEM) methodology offering rapid selection of strong binders of oxygenases via systematic evolution of ligands by exponential enrichment from large libraries of random-sequence ssDNA. Furthermore, the Capillary Electrophoresis - based enzyme activity assay of 2OG/Fe(II)-dependent oxygenases was developed for screening and characterization of inhibitors of human oxygenases. These bio-analytical tools allowed to establish the inhibition mechanisms and constants of inhibition reaction of the enzymes. A panel of DNA aptamers for both E.coli and human 2OG/Fe(II)-dependent oxygenases with a range a range of K_d values between 5 and 500 nM was selected and reported to be effective non-competitive inhibitors of nucleotide repair enzymes. Finally, NECEEM was applied as a general tool for a quantitative detection of oxygenases in an affinity analysis using aptamers over a wide range of protein concentrations from 1 to 1000 nM. The selected aptamers can be considered as a valuable model to test their conjugation with different types of nanoparticles. Such modification could (i) prevent aptamers from degradation by nucleases during their delivery into cells and (ii) allow aptamers to diffuse freely inside the cells. The CE-based technology can support high-throughput measurements of aptamer concentration in order to monitor their delivery and metabolism.

IL-18 RESPONSE IN KERATINOCYTES SENSITIZED BY DNCB AND PPD IS REGULATED BY HYALURONAN DEPOSITION

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IL-18 has been shown to play a key proximal role in the induction of allergic contact sensitization. LMWHA, an endogenous molecule, and a member of the so-called damage associated molecular patterns (DAMPs), has been suggested to elicit immune-stimulatory effects. The aim of this study was to investigate the correlation of HA-metabolism with IL-18 production of keratinocytes (KC) stimulated by contact sensitizers like 2,4,6-trinitrochlorobenzene (TNCB) and PPD. NCTC 2544 keratinocytes were utilized as a model system. Analysis of the HA deposition in PPD (30μg/mL) and DNCB (2μg/mL) treated KC by immunocytofluorescence, with the utilization of the HA-binding protein (HABP) and estimated as intensity of stain, suggested that both contact sensitizers inhibit HA deposition by 30% ($p \leq 0,05$) and 45% ($p \leq 0,01$) respectively, as compared to control. RT-PCR demonstrated that PPD and DNCB increase hyaluronidase (HYAL) expression by 11% and 22% ($p \leq 0,05$) for HYAL1 compared to DMSO control, and by 26% ($p \leq 0,001$) and 20% ($p \leq 0,05$) for HYAL2. Treatment with aristolochic acid, a HYAL inhibitor, resulted in increased deposition of HA at the KC pericellular matrix as visualized with immunocytofluorescence ($p \leq 0,01$). Increased HA deposition significantly inhibited both PPD and DNCB induced IL-18 secretion as determined by ELISA ($p \leq 0,01$). In addition, NCTC 2544 sensitized with the abovementioned reagents in the presence of DPI, an antioxidant, had increased HA deposition levels and decreased IL-18 production. The results demonstrate a direct involvement of HA metabolism on the evoked by chemical allergens KC IL-18 response.

RELEASE OF HYDROPHOBIC MOLECULES FROM POLYMER MICELLES INTO CELL MEMBRANES.

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It is generally assumed that polymeric micelles carry drug molecules until they are taken up into cells followed by intracellular release. In this work we investigated the interaction of the micelles with the cells (in particular, the interaction with the cells membranes). We observed that hydrophobic DiI (a fluorescent dye) escaped from micelles and entered the cells (fibriblasts) separately On the other hand, polymer micelle-forming does not penetrate through the cell membrane.
These results show that micelles exhibit membrane-mediated transportation of hydrophobic agents to cells.

KINETICS AND MECHANISM OF THE OXIDATIVE POLYMERIZATION OF AROMATIC AMINES AND PYRROLES IN AQUEOUS MEDIUMS

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Aniline oxidative polymerization mechanism explaining autocatalysis by slow formation of complex with charge-transfer between monomer and quinonediimines aniline n-mers agregates fragments in the absorption layer followed by its peroxydisulfate ion rapid oxidation was suggested. With due account for process heterogeneous nature and given mechanism theoretical analysis was carried out of experimental aniline oxidative polymerization kinetics; previously established semi-empirical oxidative polymerization kinetics quantitative relationships were substantiated theoretically. The oxidation of 2,4,6-trimethylaniline incapable to oxidative polymerization was shown to proceed without autocatalysis indicating the additional steps presence, except electron transfer step, determining the aniline oxidative polymerization rate.N-phenyl-1,4-phenylenediamine oxidation was indicated to proceed without autocatalysis which indicates the growth of polyaniline chain exclusively by recombination of n-mers radical cations with aniline monomer radical cations.
The complexing order change with the first to the second during the oxidative polymerization of aniline in aqueous solutions of polyethylene glycol and poly-(N-vinylpyrrolidone) was determined. The existence of critical polyethylene glycol molecular weight led to the complexing order change was shown. The activation energy of electron transfer from monomer molecule to peroxydisulphate ion in aqueous solutions of poly-(N-vinylpyrrolidone) significant decrease was determined.

APPLICATION OF 4f- AND 4d-COMPLEXES IN FLUORESCENT DETECTION OF FLUOROQUINOLONE ANTIBIOTICS

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Complexes of 4f- and 4d- metals are promising for sensing and imaging due to their unique photophysical properties and their potential responsibility to any changes in both inner- and outer-sphere environment of a metal ion. Many well known analytes, such as fluoroquinolone antibiotics, can be recognized through the fluorescent response of 4f- and 4d-complexes in organic solvents. The present report introduces the possible routes to gain in water solubility of luminescent 4f- and 4d-complexes, and the energy transfer from the fluoroquinolones to metal-centered excited states as the reason of the fluorescent detection of the antibiotics in aqueous solutions.
The reprecipitation from organic to aqueous solutions with further incapsulation into the polyelectrolyte capsules is introduced as rather universe route to obtain hydrophilic luminescent nanoparticles with high colloid stability on the basis of any luminescent f-complexes. The successful synthesis of polyelectrolyte coated nanoparticles on the basis of Eu(III) and Tb(III) complexes with various ligand environment confirms the efficiency of the developed route. The self-assembly with triblock copolymers represent another route to gain in a water solubility. This way was successfully applied for hexamolybdenum halide clusters. The structure of the triblock copolymers is highlighted as the main factor affecting both water solubility and photophysical properties of the hexamolybdenum iodine clusters in aqueous solutions.
The inner- and outer-sphere coordination of fluoroquinolones with 4f- and 4d-complexes is revealed as the origin of their fluorescent response on fluoroquinolone antibiotics. The impact of the structure of polyelectrolytes or triblock copolymers in the fluorescent response of 4f- or 4d-based sensors is highlighted as another factor affecting their sensing ability. The lower detection limits and linearity of the fluorescent response of 4f- or 4d-based sensors on the fluoroquinolones are also discussed.

TOXICITY AND HAEMOCOMPATIBILITY OF CHITOSAN-BASED NANOSYSTEMS

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Chitosan and its derivatives are widely used to develop delivery systems for different therapeutic agents (antitumor drugs, protein/peptides, antibiotics). Most of them are prepared for biomedical applications and thus the safety of this material is of primary impotence.
The aim of our study was to investigate toxicity and haemocompatibility of chitosan-based nanosystems (CBN). Positively charged (zeta-potential 25-40 mV) hexanoyl–chitosan nanoparticles (HCNPs) and negatively charged (zeta-potential -20 to -25 mV) succinoyl-chitosan nanoparticles (SCNPs) were used as model CBNs. The diameter of both CBNs was about 150-250 nm.
Average toxicity was studied by MTT assay using a panel of cell lines (HEK293, Colo-357, HaCaT). We found no toxicity of CBNs in a wide concentration range (100-0.01 ug/ml). To analyze biocompatibility with donor blood, red blood cells (RBC), lymphocytes and platelets.were purified and incubated with different CBN for 1 hr. Using colorimetric assay we found no lysis of RBC in both cultures. Positively charged HCNPs induced lymphocyte aggregation while negatively charged SCNPs did not as was visualized by light microscopy. Activation of platelets was studied by flow cytometry using anti-CD36-FITC and CD62-PE antbodies. We demonstrated that again HCNPs but not SCNPs activated platelets.
Taken collectively our results demonstrateda better blood compatibility of SCNPs than of HCNPs. However more precise investigation of CBN interaction with blood components is required.

PROCESSES, OCCURRED DURING EXPOSURES OF AC MAGNETIC FIELD ON ENZYMME LOADED MAGNETIC NANOPARTICLES CLUSTERS

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Introduction. Magnetic nanoparticles (MNPs) are widely used in nanomedicine and biotechnology. One of its applications is hyperthermia based on induction of orientation relaxation of single domain particle magnetic moments after AC magnetic field (MF) exposures and, as a result, heat dissipation. Magnetic hyperthermia aims to generate large amounts of heat to raise the temperature of the surrounding tissues and induce cells (mainly cancer cells) apoptosis and death. However, the heat generation is proportional to the frequency of MF and requires high MNPs concentration. Furthermore, high frequencies required heating generation cause unspecific heating, which can result in unspecific tissue damage. Contrary to high frequencies, super low frequency AC MF induces mechanical rotation of the particles, which can be translated to biologically relevant response. The aim of this study is to synthesize biopolymers coated MNPs nanoclusters and investigate the effect of super low frequency MF on immobilized biomolecules.
Methods. We have synthesized 7-12 nm MNPs. The MNPs were coated with block-copolymer polylysine-polyethylene glycol. The clusters were characterized using dynamic light scattering, thermogravimetric analysis, inductively coupled plasma mass spectrometry (ICP-MS), and transmission electron microscopy (TEM). Superoxide dismutase 1 (SOD1) was electrostatically adsorbed on the surface of the clusters. SOD activity was measured by inhibition of pyrogallol autoxidation.
Results. Polylysine coated MNPs formed nanosized clusters (as observed by TEM) with intensity average diameter of 86±5 nm and zeta potential 45±3 mV. After low frequency AC MF exposure we observed change of immobilized enzyme activity and hydrodynamic size of clusters. We posit that the SOD1 is released from the MNPs surface followed by additional aggregation of complexes in the MF medium. Centrifugation of the nanosuspension after AC MF exposures showed an increase of the positive charge of clusters and change in enzyme concentration in comparison with the control sample without MF exposure further confirming the desorption of negatively charged SOD1 from the positively charged surface of MNPs.
Conclusion. We describe a new application and mode of remote control of MNP and its application in drug delivery.
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EFFECT OF SIZE OF MAGNETIC CORE ON ENZYMATIC REACTION RATE OF MAGNETIC NANO SUSPENSION UNDER IMPACT OF LOW-FREQUENCY NON-HEATING MAGNETIC FIELD

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Magnetic nanoparticles can be used for nanomechanical control of biochemical properties of macromolecules via low-frequency non-heating magnetic field. In this idea, magnetic nanoparticles convert energy of alternating magnetic field to conformational changes in macromolecules immobilized on their surface. If macromolecule fixed between two magnetic nanoparticles, it may undergo deformation such as stretching, compression and torsion. This deformation may occur due to Brownian relaxation of single domain magnetic nanoparticles, which means that expose of external magnetic field to nanosuspension will be turning the particle together with its magnetic moment vector. According to alternative mechanism of magnetization, known as Neel relaxation, only the turn of magnetic moment of magnetic nanoparticle occurs. Thus, to implement the approach of nanomechanical control of biochemical properties of macromolecules via low-frequency non-heating magnetic field, Brownian relaxation is necessary. In general, the mode of relation which is faster at the conditions chosen will be dominating the whole process of relaxation. One of the parameters important for the experiment (which one of the mechanisms will be dominating) is R_M (radius of magnetic core). Neel relaxation occurs at small R_M, and Brownian - at bigger one. Thus, the aim of this paper was to compare the effect of low-frequency non-heating magnetic field on the? catalytic activity of chymotrypsin immobilized on core-shell Fe_3O_4@Au magnetic nanoparticles with different R_M. Nanoparticle's surface was covered by short linkers containing amino-groups, and chymotrypsin was immobilized using EDC and S-NHS method. Further the sample was purified via centrifugal filters units with pore diameter 300 kDa. Nanosuspension was analyzed by Transmission electron microscopy and nanoparticles trajectory analysis. Effect of low-frequency non-heating magnetic field was studied on custom installation TOR 01/12 at frequencies 30-540 Hz.
According to TEM measurements, diameters of magnetic core for two types of particles were 11-12 nm and 19-23 nm. Hydrodynamic radii of core-shell particles covered by amino linkers were 73 nm and 78 nm before, and 159 nm and 147 nm, after modification with chymotrypsin. The effect of low-frequency non-heating magnetic field on the catalytic activity of chymotrypsin/magnetic nanoparticles complex with diameter of magnetic core 19-23 nm was found maximal at frequencies 50-160 Hz (the loss of enzyme activity exceeded 50-60% at MF frequency 160 Hz). It should be noted that at 540 Hz, there was almost no effect of MF on the enzyme activity. It was found that chymotrypsin immobilized on magnetic nanoparticles with bigger size of magnetic core was 20% more sensitive to the MF influence than with smaller ones.
Finally, the effect of low-frequency non-heating magnetic field on chymotrypsin/magnetic nanoparticles conjugate with different size of magnetic core was studied.
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EXOSOMES AS NOVEL CLASS OF DRUG DELIVERY SYSTEM: PROGRESS AND PERSPECTIVES

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Exosomes are 30-100 nm cell-derived microvesicles that are present in the most of all biological fluids, including blood, urine, saliva, and cultured medium of cell cultures. Exosomes possess a cell-type-specific lipid-bilayer membrane containing proteins. The main functions of exosomes are intercellular communication, involvement in proteins secretion and immune response, etc. Exosomes are naturally adapted for the transport and targeted intracellular delivery of proteins and nucleic acids. [1,2]
Exosomes obtained from various types of cells have different protein and lipid content that allow them to interact with definite target cell. There are three types of therapy in which exosomes could be involved, immune therapy, RNA-based therapy (siRNA, mRNA, miRNA and others), and drug therapy. [3-5]
Exosome-based drug delivery systems may provide unique advantages over other systems such as liposomes, including limited or no undesired immunogenicity when self-derived exosomes are used, greater stability in the blood due to evasion of complement and coagulation factors, efficient delivery of cargo into the cytosol of the target cell, and possibly fewer off-target effects due to the natural tendency of exosomes to act on specific target cells. Drug substances are placed inside exosomes or on their membrane that facilitates targeted delivery to the cell, allowing penetration across blood–brain barrier and minimize drug degradation [6].
There is no general way for drug encapsulation into exosomes. For macromolecules (proteins and RNA) both electroporation and formation pores with surfactants, such as saponins, are widely used methods [1-3]. For incorporation of small drug molecules extrusion could be used [4]. It should be mentioned that encapsulation of substances into exosomes is still problematic, and investigation of new ways of incorporation of drugs, e. g. proteins, is an actual problem. In some cases it is also necessary to achieve drug release from nanocarries at certain moment.
In our laboratory, a new way of macromolecule encapsulation with low frequency magnetic field is developed. In the work presented, catalase, antioxidant enzyme, was used as a model protein. It was shown that ultrasonication and magnetic field treatment, both lead to the protein inclusion with no loss in enzyme activity. Furthermore, the enzyme entrapped with both methods could be released with magnetic field.
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MACROPOROUS HYDROGEL-BASED SCAFFOLDS WITH MODIFIED SURFACE TO ENHANCE CELL GROWTH: PREPARATION AND APPLICATION IN TISSUE ENGINEERING

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Hydrogels based on poly(vinyl alcohol) (PVA) are promising systems for biomedical applications, in particular for tissue engineering due to their biocompatibility and high water content, which is close to that of human tissue. A porous structure of hydrogels enables rapid nutrient and oxygen transfer while providing a 3D microenvironment for the cells, high surface for cell attachment and growth as well as vascularization. However, intrinsically pure PVA-based matrices have rather low cell affinity because of extremely hydrophilic polymer nature, and therefore they cannot provide good cell adhesion and spreading. On the other hand, as well known, cell adhesion and spreading are highly influenced by surface chemistry, namely surface charge and hydrophilic/hydrophobic properties. In order to enhance cell attachment and spreading on the support, PVA matrix could be modified either by introduction of various charged and hydrophobic monomers, or by entrapment of RGD peptide.
In the present research we aimed to prepare PVA hydrogel-based scaffolds with modified surface and to study cell behavior in these matrices *in vitro*. To modify hydrogels, positively charged N,N-diethylaminoethyl methacrylate (DEAEMA), negatively charged acrylic acid (AA), hydrophobic 2-hydroxyethyl methacrylate (HEMA) and RGD peptide were used.
The hydrogel structure, pore size distribution was studied using confocal microscopy. The cytotoxicity of the obtained hydrogels was studied using extraction and direct contact tests. Mouse fibroblasts L929 were used as model cells while their viability was measured by MTT-test. For the extraction test, the hydrogels were incubated with cell cultivation media for 24 hs. Then cells were cultivated in the obtained extracts, and cell viability was measured in 1 and 2 days. For the direct contact test, the hydrogels were kept in contact with the cell monolayer for 24 hs, and then cell viability was determined.
In order to study cell proliferation on modified PVA hydrogel-based scaffolds fibroblasts L929 and mesenchymal stromal cells (MSC) from human adipose tissue were cultured directly on the hydrogels. Relative cell viability was measured by MTT assay. Cell morphology and distribution within the matrices was studied by confocal microscopy. In order to visualize cells, they were treated with vital Calcein-AM dye staining living cells in green, while cell nuclei and hydrogel structure were stained with DAPI in blue.
The results of MTT-assay confirmed that modification of hydrogels didn't lead to any significant cytotoxicity and promoted cell growth and proliferation. Cell viability of fibroblasts increased with increase of HEMA content within a range of 10-90 % in the polymer matrix. Cell growth was found to depend on the type of cells. Thus, maximum viability of fibroblasts and MSC was observed on PVA-AA matrices modified with 2.5 and 12.5% of AA, respectively. More over, confocal microscopy observations con-

firmed that PVA modification with charged monomers promoted cell adhesion and spreading. Thus, the modification of macroporous PVA hydrogels allowed to enhance cell growth and proliferation, and therefore could be considered as promising scaffolds for tissue engineering.

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Posters

P01

LOADING OF ANTIFUNGAL DRUG IN MODIFIED SURFACES WITH ERGOSTEROL AND OLEIC ACID, ON DIFFERENT SILICONE RUBBER GRAFT COPOLYMERS

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Objectives. Due to the risks of contamination and biofilm formation on common objects used in hospital or on medical devices to be inserted, there is still a need for finding functional groups able to create surfaces with high affinity for antifungal agents. The aim of this work was to synthesize and modify four different graft copolymers. To carry out this work the monomers glycidylmethacrylate (GMA), methacrylic acid (MMA), hydroxyethylmethacrylate (HEMA) and binary HEMA/4-vinylpyridine (4VP) were grafted to silicone rubber (SR) via a gamma-radiation method. The new graft copolymers were modified either with ergosterol or with oleic and tested to load an antifungal drug.
Method. SR was pre-irradiated in presence of air by gamma rays from a source of Co^{60}, to form peroxides and hydroxyperoxides. Pre-irradiated silicone rubber was placed in contact with GMA in methanol solution, MMA in toluene solution and HEMA in toluene. The mixture of reaction was heated at different time periods in absence of oxygen. To the bynary graft, the grafting of HEMA onto silicone rubber was put in contact with 4VP in methanol/toluene solution and then the mixture of reaction was heated at 60°C for different time periods.
Ergosterol was covalently immobilized to the graft copolymers (SR-g-GMA and SR-g-MMA) and the oleic acid to the SR-g-HEMA and to the binary grafting.
Antifungal loading**.** The graft copolymers containing ergosterol or oleic acid were immersed in an aqueous solution containing the antifungal drug. To quantify the amount of antifungal drug loaded, the aquous solution absorbance was measured at 321nm, at pre-established times.
Results and conclusions
The SR-g-GMA modified with ergosterol was the best system for the uptake of the antifungal drug. Grafting with low amounts of ergosterol enabled the uptake of a greater amount of antifungal drug.
The graft copolymers modified with oleic acid showed a very limited ability to uptake the antifungal drug.
Acknowledgements. The authors thanks to M. Cruz and L. Diaz from ICN UNAM for technical support and Conacyt CNPq project 174378 for economical support, and CYTED for the support of RIMADEL network.

P02

ANTIMICROBIAL POLIMERIC COATINGS FOR VENOUS CATHETERS

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New high efficiency materials intended for use in medical practice have been given significant importance recently. They include materials for medical devices having antimicrobial activity, mostly catheters providing access to large vessels.
The present study reviews a method of manufacturing of catheters having antimicrobial properties, by means of applying a coating containing biocide on the catheter surface.
Composition based on segmented polyurethane and chlorhexidine for the coating application was developed. The analysis of the dynamics of biocide educing from the pattern segmented polyurethane films shows that chlorhexidine introduced into the coating is contained there in two forms, one of them educing according to the mechanism of diffusion, the other being stronger immobilized and having no remarkable biocide effect.
By means of spin probe method it was revealed that external action on the structure of polymeric films (significant increase of elongation, temperature, ozone treatment) resulted in macromolecular chains mobility reduction and could influence the rate of biocide release.
The analysis of antimicrobial effect of pattern films and catheter elements with antimicrobial coating on Staphylococcus Aureus and Staphylococcus Epidermidis determined the optimal values of biocide quantities introduced into the material and the thickness of the applied coating.
The optimal parameters of the technological process of the biocide-containing coating application on the catheters were found.

P03

POLYMERIC MATERIALS BASED ON AMINo-CONTAINING POLYMERS FOR CONTROLLED DRUG RELEASE

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Natural and synthetic amino-containing polymers are widely used in the creation of materials for biomedical application: modern dosage forms, biologically active suture filaments and wound dressings, biosorbents etc. The most abundant natural polymer, which is used to create hydrogel materials for medicine, is chitosan. Blending of biocompatible aminopolysaccharide chitosan and flexible-chain synthetic polymers can be a new implement for materials properties control and the basis for the creation of new polymer products.
The aim of the study was investigation of polymeric systems based on blends of chitosan and synthetic amino-containing copolymers for medical application, which are known under the trade name Eudragit® (Evonik, Germany) and production on their base fibrous and film materials for controlled drug release. The presence of tertiary amines in the structure of copolymers Eudragit E allowed to obtain polymeric materials from mixture of chitosan and amino-containing copolyacrylmethacrylate with common solvent – aqueous acetic acid, and to adjust their properties by using covalent or ionic cross-linking reagents.
Therapeutic systems on the basis of hydrogel films or fibrous materials are used in modern technique of wound healing. Water-insoluble films with high swelling ability, based on common solutions of chitosan and Eudragit E, cross-linked by sodium tripolyphosphate (TPP) and glutaraldehyde (GA) were obtained in this study. Anesthetic lidocaine and antimicrobial agent miramistin as biologically active compounds were used to impart an antimicrobial activity and analgesic action to films. The moisture-retaining capacity of films increased from 60% up to 1000% and drug release from 30 minutes up to 24 hours, depending on the polymers ratio, the film thickness and cross-linking conditions by TPP or GA. The antimicrobial activity of obtained films was investigated in relation to a number of pathogenic germs. The results showed that their activity was maintained at a high level during 2 hours of holding in physiological solution to all investigated strains: *Staphylococcus aureus, Eschrichia coli* and *Pseudomonus aeruginosa*.

P04

REVIEW ON THE APPROACH OF THE EUROPEAN UNION LAW REGARDING THE USE OF NANOMATERIALS IN COSMETICS

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Since July 2013 the (EC) Regulation 1223/2009 on cosmetic products has been into full implementation. Based on Article 2 Paragraph 1(k) the definition that the European Law assigns on nanomaterials is '*an insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm*'.
The most common raw materials that are used in cosmetics and are of concern regarding their particle size are; Titanium Dioxide (Cas no. 13463-67-7), Zinc Oxide (Cas no. 1314-13-2), Carbon Black (CI 77266, Cas no. 1333-86-4), Silica (Cas nos. 7631-86-9 / 112945-52-5 / 60676-86-0), Hydrated Silica (Cas no. 10279-57-9 / 1343-98-2 / 7631-86-9 / 112926-00-8 / 63231-67-4), Silica Silylate (Cas no.-)and Silica Dimethyl Silylate (Cas no. 68611-44-9).
The SCCS (Scientific Committee on Consumer Safety) that provides opinions on health and safety risks of non-food consumer products has issued fairly recently opinions on nanomaterials and their presence in cosmetics (SCCS/1484/12- Guidance on the Safety Assessment of Nanomaterials in Cosmetics, SCCS/1516/13- Opinion on Titanium Dioxide (nano form) COLIPA n° S75, SCCS/1518/13- Addendum to the Opinion SCCS/1489/12 on Zinc Oxide (nano form) COLIPA S76, SCCS/1515/13- Opinion on Carbon Black (nano-form)) and it is due to issue an opinion regarding the safety of Silica, Hydrated Silica, Silica Silylate and Silica Dimethyl Silylate after the Committee's Working Groups meetings this year.
It is apparent that there is a high demand from the Industry for the use of nanomaterials in consumer products generally and cosmetics in particular. This demand has raised concerns to the European Union's Working Groups regarding the safety and the presence of nanomaterials in everyday products.

P05

POLYETHYLENIMINE BASED POLYMERS AS HIGHLY EFFICIENT ANTIMICROBIAL AGENTS

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Infections by pathogenic microorganisms are of great concern in many fields, particularly in medical applications. In general there are two ways to prevent infecting humans or deteriorating materials—disinfection and antimicrobial surfaces. The polymeric antimicrobial agents have certain advantages such as long-termed service and hindered development of microbial resistance.
In the present work the series of quaternized polyethylenimine based polymers were synthesized using conventional and microwave assistant techniques using polyethylenimine as starting material. We used ethylene glycol derivatives and alkyl halides as alkylating agents. Quaternization was carried out using dimethyl sulfate or methyl iodide. All synthesized compounds were characterized

by IR, UV-Vis, NMR spectroscopy and thermogravimetry. These polymeric materials showed significant bactericidal activity against *E.coli* and *S.aureus* (log 3-6 colony forming unit reduction). Also it was determined that there was no release of antimicrobial agent from surface and the antimicrobial agent was stable up to 220°C. Thus the antimicrobial polymeric agent based on polyethylenimine derivative could be very useful in many applications such as preparation of packing material, implants and filters.

P06

POLYETHYLENIMINE BASED THERMOPLASTIC COMPOUNDS FOR PREPARATION OF ANTIMICROBIAL MATERIALS FOR MEDICAL USES

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Antimicrobial polymers are the up and coming new class of biocides, which can be used as an alternative to antibiotics in some cases. The main advantage of polymers is ability to exert antimicrobial activity without losing their biological activity, which enables the design of surfaces that kill microbes without releasing biocides. Antimicrobial polymers have been known since 1965 and a large number of different classes of macromolecules are known to date.
In the present work we synthesized a series of quaternized polyethylenimines as efficient antimicrobial agents. It was shown that quaternized polyethylenimines could be used as effective additive to common commercially available materials such as polystyrene and poly(methyl methacrylate) to produce antimicrobial properties of films, so the addition of 5% polyethylenimine based polymer to polystyrene matrix ensured total kill of pathogenic microorganisms at the surface. The films were also analyzed by UV-Vis, IR spectroscopy, optical and electronic microscopy. It was discovered that the character of antimicrobial polymer distribution is largely depends on polymeric matrix. We believe that antimicrobial coatings on implants for osteosynthesis would be very useful for preventing complications in orthopedic surgery.

P07

TOXIC EFFECTS OF INGESTION OF NANOSIZED MANGANESE OXIDE

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Currently nanosized manganese oxide is regarded as a promising material for use in portable power sources, solar panels, electrical, catalysts and sorption elements. This compound may be a danger to the health of workers involved in the manufacturing and consumer products. This leads to the study of the toxic effects of relevance in its various ways receipt in an organism.
Objectives. In our work presents the results of the first phase devoted to the evaluation of toxic effects, which are formed by oral prolonged intake of nanodispersed manganese oxide. Test manganese oxide particles have an acicular shape, size of the axes is less than 34-39 nm (this dimension is set at 97% of the total particles).
Methods. During the study Wistar rats orally administered for 90 days through intragastric gavage an aqueous suspension of the substance in the doses of 5.2, 10.3, 51.5 mg / kg body weight. Evaluated the change of biochemical and hematological parameters, as well as histological evaluation was performed morphological changes in tissues of internal organs. Comparative evaluation of the toxic effects made with microfine analogue.
Results of the study revealed that the introduction of nanodispersed manganese oxide at a dose of 10.3 mg / kg in animals formed nervous system disorders in the form of reducing the activity of dopamine, increase the activity of glutamate, presence of the centers of demyelination of nerve fibers. Established the presence of hepatocyte cytolysis, characterized by an increase in ALT activity, malondialdehyde, protein dystrophy hepatocytes; inflammatory effect in the form of moderate limfomakrofagalnoy infiltration predominantly in the submucosal layer of the gastric fundus. With an increase of dose the severity of the established toxic effects increases. With the introduction of microfine manganese oxide at a dose of 10.3 mg / kg in animals installed only inflammatory effect, characterized by mild limfomakrofagalnoy infiltration in the submucosal layer of the gastric fundus. When administered to animals microfine and nanodispersed manganese oxide at a dose of 5.2 mg / kg toxic effects not established.

P08

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

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Electrospinning is a promising technique that can be used for fabricating micro and ultrafine fibers and fibrous scaffolds and membranes, which are candidates to be used as scaffolds for in vitro cell cultures and as medical devices for surgical reconstruction.
Polyhydroxyalkanoates (PHAs) are a class of polymers of microbial origin with different chemical structure and diverse physicochemical properties. Numerous studies have shown that PHAs are suitable materials for fabricating medical devices and can be

effectively used in reconstructive medicine.
The purpose of this study was to produce electrospun ultrafine fibers differing in their physicochemical properties using PHAs with dissimilar chemical structures and to investigate the influence of electrospinning parameters and PHA chemical composition on the morphology of ultrafine fibers and physical-mechanical and biological properties of fibrous scaffolds.
To determine optimal conditions for the production of ultrafine fibers and fibrous scaffolds, we studied the effects of electrospinning parameters on morphology and physical-mechanical and biological properties of electrospun products.
The experiment showed that the process characteristics such as voltage, working distance, the feed rate and concentration of the solution have a significant effect on fiber diameter, and their mechanical properties.
The PHA samples with different chemical compositions had dissimilar degrees of crystallinity, which varied from 35 to 75%. These dissimilarities may be accounted for by differences in the micromolecular structure of polymer chains and crystallization processes of PHAs with different chemical compositions.
The effects of the parameters investigated in this study on physicalmechanical properties of electrospun fibers can be ranked from strongest to weakest as follows: fiber orientation – PHA chemical composition – polymer solution density. The factor that has the strongest effect on fiber diameter and morphology is polymer solution density, while the effect of PHA chemical composition is less significant. Thus, by using different types of PHAs and different collectors, one can prepare electrospun products with tailored strength and elasticity.
Spherical cells prevailed on all types of scaffolds; cell infiltration between fibers was observed. Greater deposits of extracellular matrix protein were recorded on randomly oriented scaffolds. Thus, all PHA scaffolds tested in this study were biocompatible and facilitated attachment and proliferation of fibroblast cells.
This study was 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 fibrous scaffolds produced from PHAs by electrospinning 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.

P09

MOLECULAR AND GENETIC MECHANISMS OF INDIVIDUAL SENSITIVITY TO ENDOCRINE DISRUPTORS, USING VALPROIC ACID AS A MODEL SUBSTANCE.

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BACKGROUND: In recent years, much attention is paid to the study of "endocrine disruptors" (ED). These include, in particular, synthetic derivatives of free fatty acids (FFA), such as perfluorooctanoic acid (*PFOA*), methoxyacetic acid, etc. Human exposure to FFA derivatives can occur through different ways and can lead to weight gain, hyperandrogenism and polycystic ovary syndrome. Some recent scientific studies show evidence of non-monotonic ED dose response, meaning that the response may be greater at lower doses than at higher doses. Sustained FFA load is known to affect transcription level of the enzyme proprotein convertase subtilisin/kexin type 1 (PCKS1), which converts proinsulin into insulin and proglucagon into glucagon-like peptide. Change in expression level results in hyperinsulinemia, insulin resistance and weight gain.
OBJECTIVES: We examined the problem of individual sensitivity to the FFA derivatives using pharmacological drug valproic acid as a reference substance and PCKS1 (Ser690Thr) polymorphism.
METHODS: We examined DNA samples from 83 patients who fulfilled the diagnostic criteria for VPA-treatment and were taking the drug in a monotherapy for at least 1 year. Genetic polymorphism PCKS1 (Ser690Thr) (rs6235) was investigated by PCR with subsequent restriction fragment length polymorphism (RFLP) analysis. Gender-specific association with insulin resistance (IR) level and weight gain were analyzed.
RESULTS: We found strong association of PCKS1 (Ser690Thr) polymorphism with the insulin level and weight gain in women taking VPA. For women with Ser/Ser genotype who gain weight, the average insulin level was 25,5 ± 3,7 uU/ml compared to 4.9 ± 2,3 uU/ml for combined Ser/Thr + Thr/Thr genotypes without weight gain (ANOVA, $p < 0,05$). For men, no association was found.
CONCLUSION: These results strongly suggest that PCKS1 (Ser690Thr) single nucleotide polymorphism is associated with the increase of insulin level and weight gain in women taking VPA, while this mechanism is not relevant for men. This observation should be considered in the development of safe exposure levels of fatty-acids-like substances.

P10

THE ASSESSMENT OF PESTICIDE POLLUTION OF ABIOTIC COMPONENTS OF THE AZOV SEA ECOSYSTEM IN 2013

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A broad application of various pesticides in agriculture is a real menace of their penetration through surface and subsoil waters into the ecosystem of the Azov Sea. Being toxic, the pesticides can affect negatively the hydrobionts of all kinds, including the fish (Lukyanenko, 1987; Sokolov et al., 2001). The aim of our work was to study the level of pesticide accumulation in the hydrobionts' environment. The water of the Azov Sea was sampled in the coastal regions in different seasons of 2013. The HPLC

method allowed us to make the quantitative assessment of active ingredients of pesticides in the water.
Our studies have revealed nine pesticides in the coastal zone of the Taganrog Bay and the eastern Azov Sea. The most frequently occurred pollutants were the following pre-emergence pesticides: Imazethapyr, Diflufenican (60% of samples) and Ethofumesate (40% of samples). Imazalil was found in 26% of samples. The other active ingredients of pesticides were observed in no more than 10% of samples.
In the summer of 2013 we found six pesticides in the coastal waters of the Taganrog Bay, namely, Diflufenican, Imidakloprid, Iprodione, Pencycuron, Quizalophop-p-ethyl and Ethofumesate. Diflufenican occurred in 42% of all the samples and Iprodione was found in 28% of samples.
Thirteen pesticides were found in autumn in the coastal Taganrog Bay and eastern Azov Sea. The post-emergence pesticide Quizalophop-p-ethyl was most frequently observed, it occurred in 58% of samples.The active ingredients Diflufenican, Imazalil, Iprodione and Ethofumesate occurred in 25%. The other pesticides were single.
The average concentrations of most pesticides registered in spring and autumn of 2013 were compared to the averaged long-term data (2008-2012) and, in most cases, appeared to be lower. The spring Imazethapyr and Ethofumesate were an exception. In autumn the concentrations of five pollutants found in the current year exceeded the average multi-year concentrations.
The analysis of the ecological and toxicological situation in the Azov Sea Basin in regard to the content of pesticides in different seasons of 2013 has shown that the habitat and hydrobionts experienced the greatest load in autumn. During the whole period of observations we have found no increase in the maximum permissible concentrations of the pesticides in the waterbody in question.

P11

STUDY OF THE ASSOTIATION OF CONCENTRATIONS AND CHEMICAL COMPOSITION OF $PM_{2.5}$ WITH MORTALITY RATE

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Several epidemiologic studies provide evidence of an association between mortality and daily concentrations of $PM_{2.5}$. Little is known, however, about which components of the particulate mixture are most dangerous to human health. In this study it was investigated the short term effects of fine particulate matter with aerodynamic diameter <1μg/m³ (PM_1), and of selected components of particulate matter with aerodynamic diameter <2.5μg/m³ ($PM_{2.5}$) on total, cardiovascular and respiratory mortality for all ages as well as for those above and below 75 years of age in Athens, Greece during the hot season in 2007-2009.
As concentrations of PM_1 and $PM_{2.5}$ ionic and carbonaceous components were available only for 1/3/2008 – 5/8/2008, prediction models were applied. The models included the measurements from the fixed monitoring sites for $PM_{2.5}$, $PM_{2.5-10}$, NO_2 and O_3, day of the week and month indicators, as well as meteorological parameters to estimate the concentrations for the corresponding periods in 2007 and 2009.
Aiming to connect the suspended particulate matter on human health, it has been applied generalized linear models Poisson. Specifically, using a case-crossover allowing for overdispersion, controlling for seasonality, weather, day of the week, and holiday effects, the relation of concentration and the chemical constituents of the aerosols ($PM_{2.5}$) with total, cardiovascular and respiratory mortality was investigated.
It was found that a 11.5 μg/m³ increase in $PM_{2.5}$ same day levels was associated with a 2.76% increase (95% confidence interval (CI): 0.16-5.42) in the number of cardiovascular mortality under 75 years, as well as a 6.2 μg/m³ increase in PM_1 was associated with a 2.30% increase ((CI): 0.25%, 4.38%) in the number of daily deaths. This percentage increased to 3.01% (95% (CI): 1.15%, 4.90%) when two days of exposure were considered. Increases in two days concentration of sulfate, ammonium, elemental and organic carbon were associated with statistically significant increases in mortality. The highest increase in mortality over 75 years, 5.00% (95%CI: 1.58%, 8.53%) for an interquartile increase, was associated with elemental carbon concentrations. The results for those under 75 years tented to be slightly smaller.
In this time series analysis of PM for the wider area of Athens, the concentrations of particles and their components were correlated strongly with all categories of mortality. Elemental carbon seems to be the most dangerous component of $PM_{2.5}$, which heavily influences the respiratory and cardiovascular mortality. On the scales of dangerousness, sulphate, ammonium ions and PM_1 follow.

P12

ROLE OF DEFECTS IN THE PHYSIOLOGICAL FATE OF CARBON NANOMATERIALS

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Charged defects play an important role in not only materials properties [1] but also in the determination of how materials interact at the nano-bio interface. Recently, it was shown that any physiological response, and hence the fate of carbon nanotubes

(CNTs) in biological media, is dictated by the formation of protein-corona. Accordingly, we explored how defects in CNTs influence the biological interactions and protein corona formation using micro-Raman spectroscopy, electrochemistry, photoluminescence, and infrared absorption spectroscopy. Our results show that the interaction of CNTs and proteins (albumin, fibrinogen, and fetal bovine serum) is strongly influenced by charge-transfer between defects and proteins ensuing in protein-unfolding which leads to a gain in conformational entropy.

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P13

PHYSICOCHEMICAL AND PREDICTIVE TOXICOLOGICAL PROPERTIES OF OXIDE METALS NANOPOWDER

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The study of physical and chemical behavior of nanoparticles in physiological solutions is of high relevance to predict nanoparticles toxicity. Metal nanopowders of Cu (24.66 m^2/g, particles size 27 nm) and Zn (13.58 m^2/g, particles size 62 nm), produced with the electrical explosion of wires, and nanostructured powders of Al_2O_3 (54.75 m^2/g) and ZrO_2 (8.10 m^2/g), obtained with plasma-chemical method, have been used in the work. Phosphate buffering saline, aqueous solution of glucose and synthetic alveolar fluid were used as physiological media. Aggregation stability of nanoparticles was demonstrated to depend on the powders composition (disperse phase) as well as physiological media composition (dispersion phase). Experiments included the help of laser diffraction method, electro-acoustic measuring, and transmission electron microscopy. It was figured out that in dispersions, based on nanopowders and physiological media, double dispersions had been formed: unstable suspensions with dispersoid size ~ 10^{-5}-10^{-4} m, and lyosol's being stable to aggregation during more than 60 hours (particles size ~ 10^{-7}-10^{-6}).
The experimental data have shown that nanoparticles can form stable dispersions in physiological liquid media. Being stable in the environment nanoparticles can migrate though living organism ignoring the most physiological barriers, that significantly increases their penetration capacity, and finally, their toxicity.
These assumptions have been approved by the helpf of *in vivo* testing of nanopowders ZnO and CuO

P14

EVALUATION OF INTRACELLULAR DISTRIBUTION OF LIPOSOMES USING SELECTIVE FLUORESCENT PROBES

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Creation of targeted liposomal delivery systems of biologically active substances to the tissues, cells and organelles is one of the topical problems of pharmacology. These studies require solving the problem of detection of the precise localization of substances delivered with liposomes. Complexity of this problem is associated with invisibility of liposomes in the light microscope because of the small size, lack of colour and autoluminescence. A possible way of solving this problem is to visualize the liposomes by including in their composition fluorescent dyes. In order to visualize intracellular organelles, dyes for differential staining are used. Fluorescent or confocal microscopy allow defining the colocalization of liposomal dyes and dyes for differential staining of intracellular organelles, which may serve as evidence of the presence of liposomes in this compartment.
The study presents a methodological approach for detecting intracellular localization of the liposomes in nuclei and mitochondria using vital dyes for labeling liposomes and intracellular organelles. Vital staining allows determining initial liposome localization as well as subsequent intracellular migration of liposomal material. The fluorescent probes were used to label lipophilic (PKH- 28 , Sigma-Aldrich) and hydrophilic (FITC-dextran, Sigma-Aldrich) portions of liposomes. Lipophiliccompounds within the membranes and hydrophilic ones within aqueous cores suggest that such liposomal formulation allows determining the localization and migration of the structural components of liposomes separately. Hoechst 33342 (Sigma-Aldrich) was used for fluorescent staining of nuclei, MitoTracker Deep Red (Molecular Probes) - for mitochondria. These fluorescent probes have different peaks of excitation and emission providing opportunity to visualize multiple labels in one sample. The presented approach for localization has proven its effectiveness and may be used in experiments aiming to create liposomal formulations specifically oriented at certain intracellular organelles.

P15

ENCAPSULATION OF THE ANTICANCER DRUG DOXORUBICIN CARBOXYL DERIVATIVES HYPERBRABCHED POLYESTERS

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Studied the encapsulation of the anticancer drug doxorubicin carboxyl derivatives hyperbranched polyesters third generation (Boltorn H30). The particle size of the joint units doxorubicin-hyperbranched polyesterpolycarboxylic acid range from 30 to 200 nm. Size of the aggregates is stable after loading and does not change with time.

P16

POLYNUCLEAR Cu(II) COMPLEXES WITH NANOLIGANDS ON THE BASIC OF THE HYPERBRANCHED POLYESTERPOLYAMINES

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Coordinationally active polydentate nanoplatforms on the basis of amino-modified hyperbranched polyesters containing 7 terminal amino fragments are synthesized. Synthetic procedure is developed and polynuclear Cu(II) complexes with polyesteropolyamines are prepared. Their composition and stability of the complex forms in DMSO-water solutions are evaluated. It is found that all the compounds obtained exhibit biological activity with respect to the induced asparagine proteinase *of Candida albicans*.

P17

PREPARATION AND CHARACTERIZATION OF CHITOSAN-POLYVINYL ALCOHOL BLENDS FOR THE CONTROLLED RELEASE OF FLUOROURACIL

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Chitosan has a great potential for applications in ophthalmology due its biodegradability, biocompatibility, non-toxicity and versatile chemical and physical properties. In the present study the preparation and characterization of chitosan-polyvinyl alcohol blends for the controlled release of anticancer drug fluorouracil have been developed. Samples of films, containing various doze of drug, Films of chitosan-polyvinyl alcohol blends in different compositions containing various doze of drug have been prepared by solution casting method from 5-10% solutions. Influence of various factors on process of drug release from films in conditions «*in vitro*» was investigated. It was shown that pharmacology active substance practically completely diffused in Ringer-Lock solution within 4-6 hours, not undergoing any changes. With increase in thickness of film process of drug diffusion is slowed down. The 50 % of drugs from system by thickness 0,3 mm was released for 2,5-2,8 h, but the same quantity of drugs by thickness of film 0,6 mm was diffused for 4,3-4,5 h. Coefficients of diffusion of released drugs have been calculated and is shown that with increase in thickness of the films in 3 times this parameter decreases approximately in 2 times. The profile of kinetic curves testifies that process of release occurs according to the first order kinetic and controlled by diffusion of the therapeutic agent in polymeric matrix. In according with Higushi equation, describing kinetic of drug diffusion from monolithic systems with the dissolved therapeutic agent, dependence of amount of diffused drugs from films versus root of square time had linear character. Values of the diffusion coefficients has appeared within the limits of 2,5-3,0×10-7 sm^2/s for four concentration that testified to absence of significant influence of drug loading for rate release from films.
Polymeric chitosan-polyvinyl alcohol films were testified for inhibit proliferative vitreous retinopathy at fifteen chinchilla rabbits. The experimental and clinical tests show that implantation of films to suprahoroidal area did not cause the pathological changes on intraocular structure and intraocular pressure and help to activate the formation of vascular anastomose. The results obtained in the present work have shown the perspectives of use polymeric films based on chitosan-polyvinyl alcohol blends as a matrix for fluorouracil delivery for application in ophthalmology in vitreoretinal surgery.

P18

SYNTHESIS OF NANO-FILTRATIONAL MEMBRANES BY THE METOD OF MODIFICATION OF ULTRA-FILTRATIONAL POLYSULFONE MEMBRANES BY COMPLEXES OF POLYANILINE

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Today, significant success has been achieved in the synthesis of reverse-osmotic and ultra-filtrational membranes with sufficient performance and high selectivity simultaneously. However, commercial reverse-osmotic membranes are effective in filtering salts (with molecular weight up to 300 Da), while the vast majority of ultra-filtrational membranes is effective in filtering of substances with molecular weight of more than 3000 Da. However, selective filtering of substances with molecular weight in the range of 300 – 3000 Da (nano-filtration) from inorganic salts with acceptable performance is rather problematic. The most membranes actually used in this range has a very low performance and often except of filtrated substances holds significant amounts of salts. In this paper we propose a fundamentally new approach to the formation of the selective layer of nano-filtrational membranes that are effective in filtering of substances with molecular weight of more than 850 Da from salts at filtering of relevant water solutions. Synthesis of nano-filtrational membranes was carried out by surfacing of ultra-filtrational membrane PS-100, which is used as substrate, by the layer, containing polyaniline and poly (N-vinylpyrrolidone) which provides with high performance and high selectivity simultaneously for the substances with molecular weight of more than 850-900 Da.

P19

ANTIMICROBIAL BIODEGRADABLE FIBROUS IMPLANT

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Nowadays biodegradable threads made from co-polymers of glycolic and lactic acids with the added triclosan and chlorhexidine diacetate that have antimicrobial effect are being widely used abroad for the development of new surgical sutures, mesh endoprostheses for herniaplastics and urogynecology, as well as for cardiovascular implants.
Taking into account that these combinations are toxic, within the scope of this investigation we used antiseptic miramistin (miramistamido-propildimethylbenzol ammonium chloride, monohydrate) from cationic detergent group. Due to the fact that it is soluble in a number of organic solvent, that dissolve also polyglactin 370 (copolymer of glycolic and lactid acids, mass ratio 30:70), special method of coating of PGA absorbable thread was chosen. Such a coating is composed from solvent of polymer containing miramistin.
Investigation of polyglactine 370 solution viscosity revealed that miramistin implementation influences much on their relative viscosity, that increases much with the growth of polymer concentration. More than 5% growth in polymer concentration in solvent leads to logical increase in its content on the threads and results in significant increase of threads' stiffness. However, threads' strength and thickness remain almost the same.
Growth of miramistin concentration in solvent does not affect on the count of polymer being inserted, does not influence on physical and chemical properties of threads. That is why it is it is preferable to use impregnating solution with polyglactin 370 concentration falling within the limits of 2-5% that contains 5-8% miramistin by comparison to polymer mass.
After PGA drying process (temperature 60°C) the miramistin content made 0.6-0.8%, St. Aureus ATCC 29213 lysed zone mass 9 mm.
The study of miramistin destruction of threads in different pathogen zones gave the possibility to predict the duration of antibacterial effect depending on their concentration of miramistin. Explicit upward trend in antibacterial effect and action time with the increase in polymer coating content, miramistin concentration and threads' stiffness was discovered.
Antibacterial coating practically does not affect on the strength of PGA threads being implanted for 14 days (maximum time-limit for uncontaminated wound healing) as well as the period of absorption.

P20

STABILIZED POLYANILINE DISPERSION IN AQUEOUS POLYVINYL ALCOHOL SOLUTION

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Polyaniline-based materials are known to have a number of valuable properties such as electrical conductivity, response to changes of acidity, absorption spectrum and electrical conductivity in the presence of oxidants and reductants. Noted properties determined polyaniline ampermetric sensors, biosensors and artificial muscles production prospects. Polyaniline complexes with number of proteins and amino acids production possibility was reported and can promote their appliance in the field of gene and protein engineering.
However polyaniline is one of the refractory polymers. In this research aqueous polyaniline dispersions stabilized by polyvinyl alcohol with different molecular weights and hydrolysis degrees synthetic method was suggested. Productions of polyaniline com-

plexes hydrogen bonds stabilized possibility films was demonstrated. The obtained materials compatibility with the number of biological fluids was established.
The oxidative polymerization of aniline in polyvinyl alcohol aqueous solution kinetics was investigated, unit steps rate and energy constants were calculated. Aniline oxidative polymerization rate degree change with the reaction temperature and polyvinyl alcohol increase in water solution was shown.

P21

NANOSCALE TRANSPORT SYSTEM FOR DRUG DELIVERY BASED ON AMPHIPHILIC POLYMERS.

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The aim of this work is to develop methods for producing the new nanoscale polymeric form of the model drugs based on amphiphilic polymers of N-vinyl-2-pyrrolidone.
As a model drug in this paper proposed to use non-steroidal anti-inflammatory drug indomethacin, and broad-spectrum antibiotic - rifabutin.
The main characteristics of the nanoscale form of drugs are their content in the form, the average size of the particles and the stability of the colloidal system in time. For amphiphilic polymers of N-vinylpyrrolidone it is also important to know the molecular weight of the polymer and the ratio of the hydrophobic and hydrophilic moiety in the polymer molecule.
At the first phase of the research a few samples of amphiphilic polymers were selected (data not shown) and were determined value of the critical micelle concentration (CMC) for all samples.
The extent of incorporation of rifabutin and indomethacin into micelles was determined for these polymers. The results are shown in a Table 1 and 2.

Table 1.
The results of measuring the degree of incorporation of the rifabutin into the micelles.

Polymer's conventional designation	The degree of incorporation of the rifabutin χ, %	Ratio polymer/rifabutin, g/g
PVP-ODM-1	28	1: 0,1
PVP-ODM-3,5	36	1: 0,1
PVP-ODM-6	80	1: 0,1
PVP-ODM-10	97	1: 0,1

Table 2.
The results of measuring the degree of incorporation of the indomethacin into the micelles.

Polymer's conventional designation	The degree of incorporation of the rifabutin χ, %	Ratio polymer/rifabutin, g/g
PVP-ODM-1	46	1: 0,8
PVP-ODM-3,5	80	1: 0,8
PVP-ODM-6	86	1: 0,8
PVP-ODM-10	75	1: 0,8

From these data it can be concluded that in the case of the rifabutin the polymer PVP-ODM-10 has an optimal hydrophilic-hydrophobic balance, providing the highest degree of inclusion of rifabutin (close to 100%) at a relatively low CMC values.
If as a model drug was used more hydrophobic indomethacin the greatest inclusion of the active substance has been achieved using amphiphilic polymer PVP-ODM-6 having a greater hydrophobicity compared with PVP-ODM-10.
These studies allowed obtaining data that characterize nanoscale form of the model drugs based on amphiphilic polymers of N-vinylpyrrolidone, and identifying the most suitable polymers for the immobilization of biologically active substances.

P22

BIOCOMPATIBLE CONTAINERS FOR TARGETED DELIVERY OF LIPOPHILIC ANTITUMORAL DRUGS

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In recent years, considerable efforts have been focused on the development of nano- and microcarriers for encapsulation of antitumor drugs. Biocompatible containers are of a great interest for biomedical applications due to novel properties and functionalities they impart to an encapsulated material. These properties are an enhanced drug solubility, targeted delivery and prolonged release.
The goal of the current study was development of biocompatible containers based on chitosan and xanthan gum for encapsulation and delivery of lipophilic antitumor drugs. We have chosen thymoquinone which is a main active component of the black seed oil as a model antitumor substance.
The containers were fabricated by applying a low frequency ultrasound to polysaccharides solutions (0.25 w%, pH 2) layered with thymoquinone previously dissolved in soybean oil. The obtained containers loaded with thymoquinone (100 mg/ml) were separated by centrifugation and washed several times with water. The containers containing a fluorescence hydrophobic dye Nile-Red were prepared following the same procedure but the dye was previously dissolved in soybean oil together with thymoquinone.
The obtained containers have a core-shell structure confirmed by cryo-SEM observations. The size of the containers could be varied from 350 nm to 7500 nm by changing an oil/water ratio. The surface of the containers could be easily modified with different polymers and/or nanoparticles on demand.
We studied a behavior of the containers (500 nm and 2 μm, 100 mg/ml of thymoquinone) towards M3 mouse melanoma cells. Results of flow cytometry analysis demonstrated the containers internalization by cells after 5 min of their incubation. It was found that encapsulated thymoquinone inhibited a growth of M3 cells (IC_{50} 150 μg/ml) while blank containers (without thymoquinone) had no cytotoxic effect on the cell growth. The confocal observations showed accumulation of the containers within a cellular phospholipid bilayer but not within endosomes, that could occur due to a lipid-based nature of the microcontainers and their negative charge. The mechanisms that mediate direct delivery to the cell membrane are the contact mediated pathways of intermembrane lipid exchange or mixing and lipid particle fusion. The further delivery of the lipophilic drug could be realized directly to the cell membrane with subsequent trafficking via lipid raft-dependent pathways [1].
K. C. Partlow, G. M. Lanza, S. A. Wickline, *Biomaterials* **29**, 3367 (2008).

P23

APPLICATION OF SEGMENTED POLYURETHANE AS PLASTIC MATERIAL IN THE ESOPHAGUS SURGERY

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Segmented polyurethanes are an important class of polymers that have found many applications as biomaterials due to their excellent physical properties and relatively good biocompatibility. The purpose of this work is the development of artificial esophageal prosthesis based on segmented on segmented polyurethanes for treatment of damage and cancer of esophagus. Polymeric implants based on segmented poly-urethanes with different content of hard and soft segments were prepared by a two-step polymerization using a number of polyethylene and propylene glycols and 2,4-tolylene-diisocyanate. The molar ratio of polyol and diisocyanate was 1,0:2,5. The reaction proceeded at 100-120°C for 2 h in the argon flow. For preparation of polyurethane tubes, prepolymer was placed in special forms made form of the glass or metal cylinders, preliminary processed by paraffin. Implantable artificial esophagus consists of bilayer polyurethane tube, cuff at upper part of tube and original antireflex device in lower part of tube, which avoids the leakage of gastric juices into esophagus. The external layer of tube is porous and contains different antitumour drug doxyribicine, the inner layer of tube is monolithic. The influence of esophageal tissue on biodestruction parameters of polyurethane and the drug release characteristics were studied under condition in vitro and in vivo. The minimal histotoxic action of polymeric implants on esophageal tissue of animal organism was shown. All the release data show the typical pattern for a matrix controlled mechanism. The total amount of drugs is released in 25-30 days and depends of polyurethane structure and contents of high segments in polymer. Polyurethane tubes were successfully used for treatment of cancer of esophagus in clinics when standard technique of surgical bypass of the nonfunctioning esophagus can not be used. In comparison with traditional ways of treatment the intubation of polyurethane implants has following advantages: the polymeric tube provides long medical effect directly on a wall of the defected esophagus; the soft elastic consistence of polymeric tubes excludes an opportunity of formation nekroses from squeezing; the microporous structure of prosthesis promotes a rapid growth of tissue; constructional features of tube provide to most patients a normal eating.

P24

NATURAL ANTIBODIES AGAINST ENDOGENOUS BIOREGULATORS AND PAIN INTENSITY AT LOW BACK PAIN

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Molecular mechanisms of pain are extensively studied. Pain mediators of peptide and monoamine nature are discovered. It was shown that immune molecules also take part in the pain processing. It is little known about role of natural antibodies (n-Abs) in chronic pain. The aim of our study was to determine whether the relation between the pain intensity and nAbs against pain neuromediators exists.

The examination of 180 patients with low back pain syndrome and 36 healthy individuals was carried out during 21 days. Pain intensity was measured by differential analog scale. We found that pain intensity decreased as follows: spontaneous pain > pain during activity > night pain > pain at rest. Spontaneous pain was the most intensive. It was significantly ($p < 0.01$) decreased to 21th day of treatment in both men's and women's group up to 62%.

Many endogenous bioregulators are involved in the pain processing. In our study we have shown that levels of n-Abs against several endogenous bioregulators – peptides, including opioids (beta-endorphin END and orphanin OFQ), and angiotensin (ANG), and also biogenous amines (dopamine DA, serotonin 5-HT, histamine HIS) are significantly increased in patients with chronic LBP in compare with healthy individual ($p < 0.0001$).

Also we have revealed some features in n-Abs levels depending on gender. In women group the high levels (M of healthy controls +3σ and higher) of anti-END n-Abs (53% of women) and anti-OFQ n-Abs (56%) were detected. The same parameters were statistically lower for anti-DA Abs (30%, $p = 0{,}00017$), for anti-5-HT (22%, $p < 0.0001$) anti-ANG n-Abs (19%, $p < 0.0001$). In men group the comparison of the frequency of detection of high n-Abs levels has shown that anti-END n-Abs occur more frequently (41% of men) that anti-Ser n-Abs (20%, $p = 0.007$) and anti-ANG n-Abs (10%, $p < 0.0001$). High levels of anti-OFQ n-Abs were detected at 26% men. The high anti-HIS e-Abs levels were detected in both groups (49% of women and 50% of men).

The assessment of the relationship between pain intensity and n-Abs levels using a nonparametric rank Spearman correlation analysis has shown positive correlations ($r = 0{,}31$-$0{,}37$) in the men group, and negative correlations (-0.32 ..-0,41) in the women group.

Thus the specific n-Abs profile indicates the degree of imbalance on the immune level and might be considered as a marker for chronic LBP. Future researches of dynamic of n-Abs levels will allow make prognosis about the LBP chronicization.

P25

DIFFERENTIATION OF ANTAGO-miR-155 TRANCFECTED KASUMI-1 CELLS INTO THE PLATELET-LIKE CELLS IN CONNECTED WITH INCREASED OF FOXP3 GENE AND TGFBR GENE AND PROTEIN EXPRESSION

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Abstract. Transformation of leukemic Kasumi-1 cells into platelet-like cells after transfection with antago-miR-155 was recently obtained. In this study we detected relation between dynamic of transformation of Kasumi-1 cells into platelet-like and changes of expression levels of immunoregulatory transcription factor FOXP3, TGFBR, and RUNX1 in dynamics of transfection.

Introduction. In our previous study we transfected Kasumi-1 cells with miR-155 and antago-miR-155. As the result we obtained platelet-like cells, which expressed platelet's marker GP5 gene. In recent articles authors indicated the role of FOXP3 in the megakaryocytopoiesis. In series of experiment we investigated FOXP3 gene expression levels after transfection of Kasumi-1 with miR-155 and antago-miR-155 in dynamics. FOXP3 is a transcription regulator for Tregs. FOXP3 interacts with a range of partner proteins including transcription factors such as Forkhead box protein P1 (FOXP1), NFAT, NF-kB, runt-related transcription factor 1/acute myeloid leukemia 1 (RUNX-1/AML1), AP-1, and post-translational modification enzymes such as histone deacetylase HDAC1, HDAC7, and HDAC9. FOXP3 may form differential dynamic multi-protein/DNA complexes to regulate gene transcription. FOXP3 was qualified as cancer suppressor for Her2/neu gene. Up-regulation of FOXP3 inhibits cell proliferation, migration and invasion in epithelial ovarian cancer. It was also observed that FOXP3 expression was detected in epithelial cancer cells. It was observed earlier that platelet formation is depends on FOXP3-regulated TGFBR-connected PDGF.

Results and Discussion. In series of experiments we investigated expression of FOXP3 and TGFBR gene and protein in Kasumi-1 cells in 24 hours, 2 days, and 10 days after transfection with miR-155 and antago-miR-155. We obtained minimum two-fold increase of FOXP3 and TGFBR genes expression levels in the 10 day after transfection with antago-miR-155 that correlated morphological transformation of leukemic cells and changed expression of RUNX1 gene. The FOXP3 protein expression was increased in the 10 day after transfection with antago-miR-155. We didn't detect any changes in expression of TGFBR protein. In our previous work we obtained changes of expression of RUNX1/RUNX1T1 gene expression in the 10 day after transfection with antago-miR-155.

Lack of FOXP3 leads to a fatal autoimmune disease known as IPEX (immunedysregulation, polyendocrinopathy, enteropathy, X-linked), which is characterized by immunodysregulation and thrombocytopenia[5]. Scurfy mice showed platelet abnormalities, and megakaryocyte progenitor number and colony size were greatly reduced. Foxp3 deficient megakaryocytic cells failed to proliferate. Foxp3 is a seminal regulator of the megakaryocyte lineage and vital for optimal platelet production[6]. MiR-155 connected with megakaryopoiesis.

FOXP3 is both a transcriptional activator and repressor in T cells and has been shown to interact with RUNX1. FOXP3 may be acting similarly in megakaryocytes by preventing of enhancing the transcription of RUNX1 regulated genes. We can conclude, that interplay between FOXP3, TGFBR, and RUNX1/RUNX1T1 may be one of the mechanisms, which regulates transformation of leukemic Kasumi-1 cells into platelets-like and red blood-like cells after transfection with antago-miR-155.

P26

DIRECT IDENTIFICATION OF CALCIFYING NANOPARTICLES (NANOBACTERIA) IN HUMAN ATHEROSCLEROTIC PLAQUES FROM MAJOR ARTERIES BY SCANNING ELECTRON MICROSCOPY

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Objectives: Calcifying nanoparticles (CNPs, nanobacteria, nanobacteria-like particles) were discovered as cell culture contaminant over 25 years ago; however, their nature is still obscure. They are 80-300 nm in diameter, usually have coccoid, coccobacillar, or bacillary form, and consist of a central cavity surrounded by the hydroxyapatite shell. Nowadays, CNPs are suspected to be the culprits of a number of calcification-related diseases including nephrolithiasis, cholelithiasis, and atherosclerosis. Electron microscopy methods are the gold standard for the visualization of CNPs; however, researchers usually visualize the colonies of CNPs after the culturing.

Methods: Here we perform our results of the scanning electron microscopy (SEM) of uncultured CNPs. Four human atherosclerotic plaques from major arteries were placed in a mortar with 7 ml of cold phosphate buffered saline (PBS), homogenized by a pestle, and then centrifuged at 2,500 x *g* for 10 min at 4°C to pellet debris. The supernatant was further passed through the cellulose acetate filter (0.2 μm pore size) and centrifuged at 60,000 x *g* for 1 hour at 4°C. A pellet was then resuspended in 200 μl of ddH2O, transferred to a microscope slide coated with poly-L-lysine at room temperature for 1 hour, fixed for 1 hour in 2.5% glutaraldehyde, postfixed for 1 hour with 1% osmium tetroxide solution, and finally dehydrated in a graded series of cold ethanol. Then, the slide was transferred to the critical point drying apparatus and coated with Au using a sputter coater. All samples were investigated using SEM Hitachi S3400N under high vacuum conditions.

Results: In two specimens, we observed multiple coccoid nanoparticles which were 200-300 nm in diameter and consisted of a solid nucleus surrounded by a less dense shell. Larger coccoid nanoparticles (500-700 nm) could be detected in the third specimen. No clear nanoparticles (less then 1 μm) were found in the fourth specimen. These nanoparticles were similar by their morphological features to CNPs revealed in atherosclerotic plaques and calcified valves by other research groups.

Conclusions: In human atherosclerotic plaques from major arteries, CNPs can be found using SEM even without culturing.

P27

MEDICINAL ANTICOMMISSURE MEMBRANES

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Sufficient practical and research experience has been accumulated to date pertinent to the clinical use of various medicines, physical and biological methods in order to prevent post-operative commissure formation. However, none of the available methods staves off the process securely, especially at massive surgery. So the solution of the problem is a real challenge to the world's surgical science. The membranes offered by us as a perioperative anticommissural means were manufactured using a Nanon 01A electrospinning device (MECC Inc., Japan). We used copolymers of polyhydroxibutirate/oxivalerate (PHBV) of 900 kDa molecular weight synthesized at Skryabin Institute of Microbial Biochemistry and Physiology (RAS). Dypiridamol was the medical agent. In the first membrane group the agent was equally spread throughout the volume (one-phase fiber). In the second sample group, Dypiridamol was doped in the inner fiber phase with a coaxial nozzle during electrospinning (two-phase fiber).

We investigated 100 Wistar-line male rats to see the membranes' preventive effect on postoperative commissure formation. To simulate the commissure formation process following midline laparotomy, inner abdominal- wall surface was excised in the iliac area. The formed defect was then covered with a membrane patch of 1,5x 1,5 cm. The membrane edges were fixed with PDS 6/0 absorbable suture. On the 7th, 14th, 30th and 60th day of the experiment the animals were brought out. The visual commissure formation was estimated: the entire spreading, each commissure type individually and organ deformation. The membrane tissue samples were preserved with 10% formalin solution. Paraffin sections were made and stained with hematoxylin-eosin and Van Gieson. Doping fiber composition with Dypiridamol effects the inflammation reaction and reparation in the implantation area: inflammation reduced, its phases accelerated and less manifest as compared to those in the membrane produced without doping the agent. Fiber inner phase doping with Dypiridamol prevents commissure formation in 60% cases. Implantation in experimental animals showed that doping membranes with Dypiridamol accelerates biodegradation – the period it takes is twice as short as that for one-phase samples. The results suggest further study of the commissure-formation mechanisms and thorough search for the means to delimit wound surfaces.

P28

ELECTROSTATIC COMPLEX OF MAGNETIC NANOPARTICLES WITH DOXORUBICIN FOR CANCER IMAGING AND ANTI-CANCER DRUG DELIVERY

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Cancer-related deaths are projected to increase in the future, with the World Health Organization estimating about 13,1 million deaths by the year 2030. As a result, early diagnostic and effective therapy of cancer diseases are necessary. For these goals magnetic nanoparticles (MNP) may be used.
We present iron oxide magnetic nanoparticles, which can provide cancer cell imaging by MRI and anticancer drug delivery (doxorubicin). Thus, it will be possible to evaluate effectiveness of drug delivery to the target in real time, and monitoring of disease development in response to therapy. The shell of MNP consists of bovine serum albumin (BSA) and polyethyleneglycol (PEG), therefore the electrostatic complex of MNP with doxorubicin (Dox) is possible.
After coating of MNP with BSA, the purification of MNP-BSA was occurred. In the next step these nanoparticles was conjugated with PEG. The values of T2-relaxation time and relaxivity were determined by magnetic resonance tomograph. Dox loading on MNP-BSA-PEG was carried out with analysis of electrostatic complex by method of dynamic light scattering. Release of Dox was observed in different pH-values.
We extracted two heads of MNP. Fractions have different hydrodynamic diameters (35±4 and 77±8nm) and BSA-content in the MNP shell (38,3% and 54,9%). The relaxivity of big MNP is larger than of small ones, but the bigger MNP forms aggregates. Therefore, following experiments were performed with small MNP. It was established, when doxorubicin content in the complex reaches 20% (by weight), the increase of complex size and colloidal instability was observed. Under physiological conditions (pH=7,4) the part of released drug does not exceed 25% of initial Dox-content in complex. When pH-values decrease, the release of Dox was more intensive – 55 and 80% for pH=6,5 and 5,5 respectively. In the case of HEK293 cell line cytotoxic activity of MNP-Dox was similar with free drug activity. In the case of C6 cells, we found, that Dox-loaded MNP had higher cytotoxic activity rather than Dox without MNP.
Thus, electrostatic complex Dox-MNP was obtained. This complex is perspective as MRI contrast agent and anti-cancer drug.
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P29

SYNTHESIS AND CHARACTERIZATION OF NANOSTRUCTURED FERROCENE-BASED THIN FILMS

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ABSTRACT. The pharmacological activity of ferrocene-based compounds is quite important and recently they have important medical applications. Many authors have demonstrated that some ferrocenyl derivatives are highly actives against several diseases particularly because their anticancer activity.
In this work, we present the synthesis and characterization of four amphiphilic organometalic compounds based in ferrocene units. The four compounds; two of them are ferrocenyl amides with general formula $FcC{=}MNH(CH_2)_{15}CH_3$, where M = S or Se, and other two; ferrocenyl aminocarbene with general formula $FcC{=}M(CO)_5NH(CH_2)_{15}CH_3$, where M = Cr or W are described as ultrathin ferrocenyl derivatives of Langmuir-Blodgett (LB) films.
The LB technique was used for the building of ordered nanostructures in molecular assemblies of ferrocenyl derivatives. These compounds formed Langmuir monolayers at the air-water interface, which were characterized by isotherms surface pressure versus molecular area (*π-A*), and compression/expansion cycles, Brewster angle microscopic images were also obtained. The LB molecular monolayers were transferred onto glass substrates. These nanostructures films, were characterized by atomic force microscopy (AFM) and X-ray diffraction (DRX) techniques
Keywords: Langmuir-Blodgett films, organometallic complexes, thin films
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ESTIMATION OF THE ROLE OF EFFECTIVE MICRO-ORGANISMS OF THE PREPARATION "BAIKAL EM1"

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During evolution on the ground exclusively important mechanism of cooperation – symbiosis between plants, animals, insects, the lowest invertebrate and micro-organisms which now is broken was generated.
Crisis in biosphere – most a vital issue in modern history of mankind. Occurrence of new kinds of a tuberculosis, a hepatits, virus infections, cancer diseases, the cow furiousness this in unreasonable application of antibiotics and chemicalization of an agriculture.
For last century in the best Ukrainian and Russian chernozems (black earth) the maintenance humus has decreased with 16 to 6 and less percent. In biosphere the EM-technology (EM-effective micro-organisms), in many countries of the world can solve a problem of restoration of useful micro-flora.
In a basis of the Russian EM-technology the microbiological preparation «Baikal EM 1» lays. It is a unique complex of the various micro-organisms existing in the nature and containing, including in lactic products, cheese, wine. In its structure there are groups lactic acid, nitrogen fixation, photosynthetic bacteria and yeast. Lactic acid bacteria (these are beneficial organisms widely found in fermented foods, and in the gastro-intestinal tract of healthy humans and animals): *Lactobacillus plantarum*, *Lactobacillus casei*, *Lactobacillus fermentum*, *Lactobacillus salivarius*, *Lactobacillus delbrueckii*. Phototrophic purple non-sulfur bacteria-PNSB (these are widely found in ponds, soil, on plant leaves, ice and snow): *Rhodopseudomonas palustris*, *Rhodobacter sphaeroides*, *Rhodobacter capsulatus.* Yeast: *Saccharomyces cerevisiae* (these are beneficial organisms widely found in fermented foods and the gastro-intestinal tract of healthy humans and animals).
This preparation possesses a wide range of action, that favourable distinguishes it from other microbiological preparations containing, as a rule, one-two species of useful micro-organisms.
Manufacture «Baikal EM 1» in Russia is began with 1998 year. It is a liquid with the pleasant silage smell, packaged in plastic bottles in capacity of 0,5 and 1,0 litre. A period of storage -1 year. «Baikal EM1» to improve micro-flora of soil, increases productivity of agricultural crops, raises their quality and safety. Micro-organisms of a preparation transform elements of a nutrition of plants in assimilability the form, enriches soil and composts with vitamins, amino acids and biologically active substances. The soil becomes friable and well structured. Soaking of seeds and spraying of plants during vegetation do their powerful, resistance against diseases, pests and unfavourable weather conditions.
Wide application is a preparation has found in animal industries. It enriches forages with irreplaceable amino acids (lizin, valin, metionin, leitsin, izoleitsin, tirozin, phenilalanin, gistidin, treonin).
To increase comprehensibility of forages, the micro-flora of intestines of birds and animals is normalized, gastro-enteric diseases recover, additional weights increase, solve an problems of elimination of harmful smells. «Baikal EM1» is certificated and brought in the State catalogue as micro-biological fertilizer.
Coming from foregoing, the aim of the present research was a study of antagonistic influence of preparation «Baikal EM 1» on pathogenic micro-organisms for the acceleration of their neutralization in soil. In this connection were conducted by us research on the study of antagonistic activity of this preparation on the base of bacteriological laboratory of Center of hygiene and epidemiology in the Tula area (Russia).
The method of determination of antagonistic activity is based on the exposure of suppression of height of sensible bacteria of test-culture *Salmonella enteritidis* by microbiological preparation «Baikal EM 1» during cultivation in the conditions of 37° with during 48 hours on a liquid nourishing environment and subsequent determination of amount of colonies of indicatory bacteria at sowing of mixture on a dense environment. Sowing is produced with such calculation, that the isolated colonies accessible to the quantitative account grew on a cup. On the number of growing colonies of indicatory micro-organisms determine minimum. Preparation is most active in a concentration 1: 10, because he practically fully repressed the height of indicatory bacteria in breeding to $5x10^5$ cages. In variants 1: 100 and 1: 500 repressing ability of preparation of «Baikal EM 1» also is well expressed, however weaker at higher maintenance of viable cages of test-culture. Thus microbiological preparation «Baikal EM 1» in concentrations 1: 10, 1: 100, 1: 500 showed an antagonistic effect in relation to control test-breed *Salmonella enteritidis* in a different degree.

CONCLUSION

1. Microbiological preparation «Baikal EM 1» possesses the expressed antagonistic activity in relation to microorganisms that can contaminate soil;
2. The applied methodology can be used for determination of Minimal Supression Concentration (MSK) with the purpose of creation of equilibrium between useful and pathogenic microorganisms in soil;
3. The got results allow to tell us about perspective of the use of preparation «Baikal EM 1» in biology control after the state of soil and illnesses.

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ESTIMATION OF INFLUENCE OF THE POLYSTIMULINE A-6 ON ACTIVITIES OF RESPIRATORY ENZYMES AND ABSCISIC ACID, AND PROTEIN SYNTHESIS IN ORGANS OF WHEAT UNDER CHLORIDE SALINIZATION CONDITION

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Problems of salt tolerance are comprehensively discussed in the literature, but the mechanism of influence of various salts on the physiological and biochemical processes of vital functioning is not enough descrypted. For understanding of these mechanisms it is necessary to define some basic physiological and biochemical "points" of general metabolism in isolated cell organelles, which on the one hand are more sensitive to salinity of the environment, on the other hand have crucial importance in the functioning of the organism.

As is known the primary mechanism of the toxic influence of salts is weakening of conjugation of the oxidation and phosphorylation processes by blocking of conjugation sites which leads to energy starvation, and consequently to inhibition processes of synthesis and deficiency of plastic materials. Recently in connection with the development of synthetic analogs of phytohormones interest to the problems of resistance of plants to the environmental stress factors increased significantly. Phytoactive polymers or polystimulins possess properties of auxins - A-6 (PS-A6) and cytokinins - C (PS-C) having high biological activity and a prolonged influence. These compounds are synthesized in Moscow Chemical-Technology Institute named after D.I.Mendeleev by Prof. M.Shtilman.

The aim of present work was to study respiratory activities of the enzymes of catalase and peroxidase, activity of abscisic acid (ABA) and the content of total nitrogen and protein nitrogen in the different wheat organs under the influence of poltstimuline-A6 (PS –A6) in chloride salinity conditions.

The objects of researches were the stalks and roots of wheat (*Triticum aestivum* L.) cultivated in pots during 40 days. Peroxidase activity was determined calorimetrically by A.K.Boyarkin method based on measuring of rate of the catalyzed by peroxidase reaction of oxidation of benzidine to diphenolquinoldiamin with forming a blue colored product of condensation of last molecule with benzidine; catalase activity – by gasometrical method; activity ABA – by V.I.Kefeli method. The total nitrogen and protein nitrogen content was determined by the standard method. Before planting the seeds were soaked in an aqueous solution of polystimuline-A6 based on calculation of 30 mg preparation on per liter of distilled water. The experiment was performed in the following order: initially respiratory activities of the enzymes, activity of abscisic acid, total nitrogen and protein nitrogen in the stems and roots of the seedlings grown in the control (without PS-A6 and NaCl) were determined; then experimental procedures were repeated using NaCl with concentration of salt 0.1-1.0 mM. The next series of experiments were performed using polystimuline A-6 together with NaCl.

As is well known in extreme salinity conditions in plant cells accumulates hydrogen peroxide in an amounts several times exceeding its physiological norm, increases the concentration of hormone inhibitors (ABA) and increases the content of protein nitrogen by expression of various genes. The main function of terminal oxidases is removal of excess peroxide in the cells as a by product of metabolism.

With increasing salt concentration there is observed an inhibition of the studied enzymes up to 70%. Apparently, salt react with the metal localized at the center of the molecule, disrupting Me-OH bonds, substitute OH groups by Me-Cl chelate compound, thereby causing the inactivation of the enzyme. From the series of performed analyzes is revealed that the use polystimulin reduces the negative influence of salt stress by 10-15%. It has been established that pre- treatment of seeds of the experimental plants with the same preparation promotes protein synthesis and consequently enhancement their nutritional value. Where in at processing with polystimuline significant accumulation of raw leaf biomass and dry stalk biomass is observed.

In the experimental plants content of total and protein nitrogen 5-6 times higher than that of the control group. However the content of non-protein nitrogen under polystimuline influence varies slightly. Perhaps, it is possible due to the mechanism action of growth substances on the protein synthesis and enzymes activities in leaf cells where forming new enzymatic systems capable of synthesizing proteins and carbohydrates. It can be assumed that the data obtained somewhat may justify the application prospects of the preparation as an anti-stress adaptogenic substance for stimulation of growth, development and improve tolerance of wheat plants to salinity.

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POROUS POLYMERIC HYDROGELS

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Polymeric hydrogels owing to their unique properties (high biocompatibility, swelling ability in water solutions, ability to biodegradation, elasticity, etc.) are widely applied in medicine and allied sciences in the capacity of implants, substrates in cellular engineering, materials for filling of postoperative cavities, etc. The problem of creation new hydrogel materials with the improved properties still faces to the scientists, working in the field of creation of polymeric biomaterials.

As objects of research for creation materials with the set speeds of biodegradation we have chosen derivatives of starch, polyvinyl alcohol and their mixtures. Under various conditions we had been synthesized some series of isotropic and anisotropic polymeric hydrogels. The process of gelation has been investigated in order to define the optimum conditions of reception of target products. Also it was studied modification kinetics of derivatives of starch and polyvinyl alcohol.

The carried out biological tests have shown absence of toxicity and high biocompatibility of developed hydrogel materials. It has been shown that at contact to organism living tissues the synthesized hydrogels practically did not cause inflammatory reaction, and completely degraded, being replaced with organism tissues. Speed of biodegradation was defined by character, degree of development of porous structure, quantitative composition of polymeric hydrogels and made from to 1 about 4 months.

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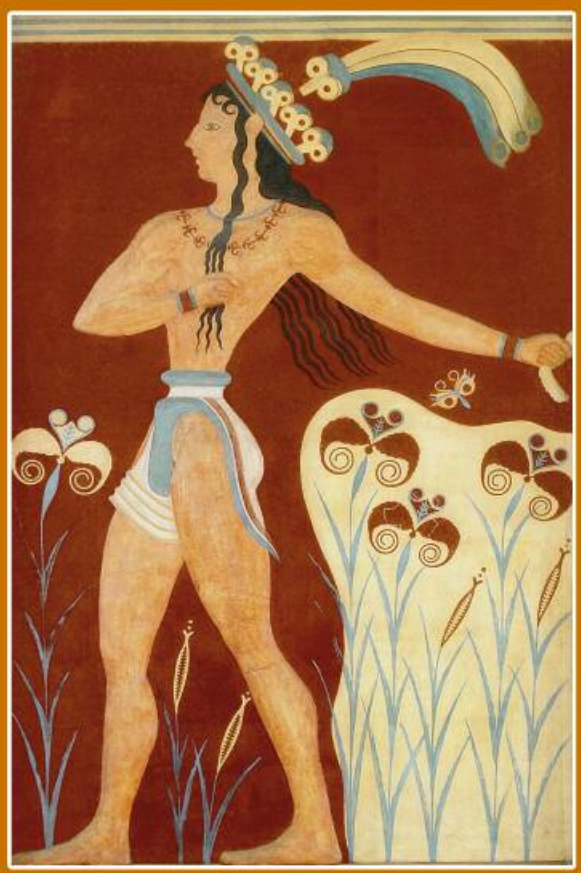

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