BIONANOTOX 2013

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4th International Conference

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

Including Russian-Hellenic Workshop and School of Young Scientists

5-12 MAY, 2013 Heraklion, Crete, Greece

UNIVERSITY OF CRETE

D. MENDELEYEV UNIVERSITY OF CHEMICAL TECHNOLOGY OF RUSSIA

M. LOMONOSOV MOSCOW STATE UNIVERSITY

M.SHEMYAKIN AND YU.OVCHINNIKOV INSTITUTE OF BIOORGANIC CHEMISTRY

SOCIETY OF BIOCHEMICAL & EXPERIMENTAL TOXICOLOGY OF RUSSIA

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Final Program/Abstract Book

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D. MENDELEYEV UNIVERSITY OF CHEMICAL TECHNOLOGY OF RUSSIA

HELLENIC SOCIETY OF TOXICOLOGY

SOCIETY OF BIOCHEMICAL & EXPERIMENTAL TOXICOLOGY OF RUSSIA

Welcome Letter

On behalf of the Organizing Committee of the 4th International Conference "Biomaterials and Nanobiomaterials: Recent Advances and Safety and Ecology Issuess" Including Russian-Hellenic Workshop and School of Young Scientists 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 2013.

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 form many countries will attend the symposium. Very low package fees including registration, accommodation, lunch meals and congress material have been secured for participants.

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

Co-President **Torchilin Vladimir**

Co-President **Khokhlov Alexey**

International Advisory Board

Co-President	Torchilin Vladimir	Professor, Director of Center of Pharm. Biotech & Nanomedicine, Northeastern University, Boston, USA
Co-President	Khokhlov Alexey	Academician of RAS, Vice-Rector of M. Lomonosov Moscow State University, Moscow, Russia
	Anastasiadis Spiros H.	Professor, Foundation for Research and Technology - Hellas (FO.R.T.H.), Institute of Electronic Structure and Laser (I.E.S.L.)
	Berlin Alexander	Academician of RAS, Director of N. Semenov Institute of Chemical Physics of RAS, Moscow, Russia
	Kabanov Alexander	Professor, Director of Center for Drug Delivery and Nanomedicine, University of Nebraska, Omaha, USA
	Kolesnikov Vladimir	Professor, Rector of D.Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
	Lappas Alexander	Principal Researcher, Foundation for Research and Technology, Crete
	Neufeld Ron	Professor, Queen's University, Kingston, Ontario, Canada
	Ozerin Alexander	Corresponding member of RAS, Director of N. Enikolopov Institute of Synthetic Polymeric Materials of RAS, Moscow, Russia
	Panarin Eugenie	Corresponding member of RAS, Director of Institute of Macromolecular Compounds of RAS, St. Petersburg, Russia
	Poncelet Denis	Professor, ONIRIS, UMR CNRS GEPEA 6144, Nantes, France
	Rizos Apostolos	Professor, Department of Chemistry, University of Crete, Iraklion, Greece
	Tkachuk Vsevolod	Academician of RAS and RAMS, Dean of Faculty of Fundamental Medicine, M. Lomonosov Moscow State University, Moscow, Russia
	Tsakalof Andreas	Professor, Medical Chem. Dep., 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, Prague, Czech Republic
	Zezin Alexander	Corresponding member of RAS, Head of Chair, M. Lomonosov Moscow State University, Moscow, Russia

Organizing Committee

Co-chairman of Symposium	Tsatsakis Aristidis	Professor, Director of Forensic Sciences & Toxicology Dep., University of Crete, Iraklion, Greece
Co-chairman of Symposium	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
	Markvicheva Elena	Professor, M.Shemyakin-Yu.Ovchinikov Institute of Bioorganic Chemistry, Moscow, Russia
	Shashkova Irina	PhD, Senior scientific worker, D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
	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, Senior scientific worker, 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

Sunday, May 5, 2013

Arrival - Registration

20.00 **Welcome Cocktail**

Monday, May 6, 2013

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, Heraklion, Crete, Greece

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

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10.20-11.00 ***OPENING LECTURE***
ENZYMES FOR REACTIONS WITH ORGANOPHOSPHATES: CHOLINESTERASES, ORGANOPHOSPHATE-HYDROLASES AND RELATED ENZYMES
S.D.Varfolomeev
N. Emanuel Institute of biochemical physics, Moscow, Russia

11.00-11.30 **Coffee break, Poster session**

11.30-12.30 ***MORNING SESSION***

Chairman: Prof. S. Varfolomeev

11.30-12.00 **BIOTECHNOLOGY – THE WAY TO THE FUTURE**
T. G. Volova[1,2]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk Russia [2]Siberian Federal University Institute of Fundamental Biology and Biotechnology, Krasnoyarsk, Russia

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12.00-12.30 **ENHANCED CHEMILUMINESCENCE AS A TOOL TO STUDY FREE RADICAL REACTIONS PRODUCED BY TOXIC NANOMATERIALS**
Yu. A. Vladimirov[1], E. V. Proskurnina[2], A. M. Polimova[1], A. V. Alekseev[1]
[1]Shubnicov Institute of Crystallography, Russian Academy of Science, Russia
[2]Lomonosov Moscow State University, Russia

12.30-13.00 **SYNTHESIZED NANO AND MICROFIBER MATRIX NETWORKS SUPPORT IMMUNOISOLATED PANCREATIC ISLETS FOR IMPLANTATION**
J. A. M. Steele[1], E. Carmona[2], J-P. Halle[2], A. E. Barron[3], R. J. Neufeld[1]
[1]Queen's University, Kingston, Ontario, Canada, [2]Université de Montréal, Maisonneuve Rosemont Hospital Research Centre ,[3]Stanford University, Palo Alto, CA

13.00-14.00 **Lunch**

14.00-16.30 **Break**

16.30-18.00 ***EVENING SESSION - Young Scientists Session***

Chairman: Prof. N. Klyachko

16.30-16.50 **EFFECT OF MAGNETIC FIELD ON ENZYME_MAGNETITE NANOCOMPLEXES**
K. Y. Vlasova[1], M. A. Abakumov[1], Yu. I. Golovin[1,3], N. L. Klyachko[1,2], A. V. Kabanov[1,2], M. Sokolsky[2]
[1]Department of Chemistry, Lomonosov Moscow State University, Moscow, Russia, [2]University of North Carolina at Chapel Hill, USA,[3] G.R.Derzhavin Tambov State University, Tambov, Russia

16.50-17.10 **ANTISTAPHYLOCOCCAL ENDOLYSINES AS PERSPECTIVE ANTIMICROBIALS**
L. Yu. Filatova[1], D. N. Lebedev[1], A. D. Priyma[1], D. M. Donovan[2], S. C. Becker[2], A. V. Kabanov[1], N. L. Klyachko[1]
[1]M.V. Lomonosov Moscow State University, Chemistry Department, Moscow, 119991, Leninskie Gory, 1-11, [2]ARS-USDA Beltsville Agricultural Research Center, USA

17.10-17.30 **COMPLEXES OF POLYANILINE AND POLYPYRROLE WITH WATER-SOLUBLE POLYMERS**
Ya. O. Mezhuev, Yu. V. Korshak, A. I. Piskareva, S. V. Osadchenko, I. V. Solovyova, M. A. Salop, M. I. Shtilman
D. Mendeleev University for Chemistry Technologies of Russia, Moscow, Russia

17.30-17.50 **MACROPOROUS HYDROGELS VERSUS CONVENTIONAL DRESSINGS IN THE TREATMENT OF CHRONIC WOUNDS: A RETROSPECTIVE STUDY**
D. E. Lisovyy[1], S. M. Chudnykhr[1], A. A. Artyukhov[2], M. I. Shtilman[2]
[1]Moscow State University of Medicine and Dentistry, Moscow, Russia, [2]Mendeleyev University of Chemical Technology of Russia, Moscow, Russia

18.00-19.00 **Break**

19.00-20.00 **Dinner**

Tuesday, May 7, 2013

08.00-09.30 **Breakfast**

10.00-12.30 ***MORNING SESSION***

Chairman: Prof. T. Volova

10.00-10.30 **INNOVATIVE ENZYME CONTAINING NANOFORMULATIONS FOR DIAGNOSTICS AND THERAPY**

N. L. Klyachko[1], E. A. Zaitseva[1], E. N. Efremenko[1], O. A. Kost[1], N. V. Nukolova[2,1], L. Yu. Filatova[1], S. A. Legotsky[1], Yu. I. Golovin[4,1], A. G. Majouga[1], M. A. Abakumov[3,1], A. B. Belova[1], V. P. Chekhonin[2,3], A. V. Kabanov[5,1]

[1]M. V. Lomonosov Moscow State University, Department of Chemistry, Moscow, Russia, [2]Center for Social and Forensic Psychiatry, Moscow, Russia, [3]Russian State Medical University, Moscow, Russia, [4]GR Derzhavin Tambov State University, Russia, [5]Eshelman School of Pharmacy, Univ.of North Carolina-Chapel Hill, Chapel Hill, USA

10.30-11.00 **MOLECULARLY IMPRINTED POLYMERS AS SYNTHETIC ANTIBODIES FOR TEST-METHODS**

S. A. Eremin[1], Thi Dieu Thuy Nguyen[2]

[1]Department of Chemical Enzymology, Faculty of Chemistry, M.V. Lomonosov Moscow State University, Moscow, 119991, Russia, [2]Institute of Biotechnology, Vietnam Academy of Science and Technology, Ha Noi, Viet Nam

11.00-11.30 **STRUCTURE AND MECHANICAL PROPERTIES OF THE ULTRAFINE-GRAINED BIOINERT TITANIUM AND ZIRCONIUM PRODUCED BY SEVERE PLASTIC DEFORMATION AND THEIR MEDICAL APPLICATION**

Yu. P. Sharkeev, A. Yu. Eroshenko, O. A. Belyavskaya

Institute of Strength Physics and Materials Science, SB RAS, Tomsk, Russia

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

Chairman: Prof. M. Shtilman

12.00-12.30 **PROGRESS IN DESIGNING OF BIOCOMPATIBLE MAGNETICALLY TARGETED NANOSYSTEMS FOR A SMART DELIVERY OF THERAPEUTIC PRODUCTS**

A. V. Bychkova, M. A. Rosenfeld, V. B. Leonova, A. L. Kovarskii

Federal state budgetary institution of science Emanuel Institute of Biochemical Physics of Russian Academy of Sciences, Moscow, Russia

12.30-13.00 **INTERACTION OF CARBON NANOPARTICLES WITH ANTIBODIES: ANALYTICAL AND TOXICOLOGICAL ASPECTS**

B. B. Dzantiev, O. D. Hendrickson, A. V. Zherdev

Institute of Biochemistry Russian Academy of Sciences, Leninsky prospect 33, 119071 Moscow, Russia

13.00-14.00 **Lunch**

14.00-16.30 **Break**

16.30-18.00 ***EVENING SESSION - Young Scientists Session***

Chairmen: Prof. E. Markvicheva

16.30-16.50 **SYNTHESIS AND INVESTIGATION OF SUPEROXIDE DISMUTASE NANOZYMES USING MODEL OF SPINAL CORD INJURY IN RATS.**
A. D. Aleksashkin[1], A. Yu. Morozova[2], T. B. Mustafina[2], V. P. Chekhonin[2], N. L. Klyachko[1], D. S. Devika, 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, [2]Siberian Federal University, Institute of Fundamental Biology and Biotechnology, Krasnoyarsk, Russia

16.50-17.10 **NEW MINIMALLY INVASIVE METHODS OF TREATMENT OF ACUTE CHOLECYSTITIS WITH USE OF MODIFIED PVA**
S. M. Chudnykh[1], D. E. Lisovyy[1], Yu. V. Kulezneva[1] A. A. Sidoruk[1], A. A. Artyukhov[2], M. I. Shtilman[2]
[1]Moscow State University of Medicine and Dentistry, Moscow, Russia
[2]Mendeleyev University of Chemical Technology of Russia, Moscow, Russia

17.10-17.30 **CHARACTERISATION OF BACTERIOPHAGE S-394 ENDOLYSIN AND ITS APPLICATION AGAINST GRAM-NEGATIVE BACTERIA**
S. Legotsky[1], A. Priyma[1], K. Vlasova[1], K. Miroshnikov[2], A. V. Kabanov[1], N. Klyachko[1].
[1]M.V. Lomonosov Moscow State University, Department of Chemistry, Moscow, Russia,
[2] M. Shemyakin and Yu. Ovchinnikov Institute of Bioorganic Chemistry, RAS, Moscow, Russia

17.30-17.50 **BIOLOGICAL EFFECTS OF NANO-COMPLEXES BASED ON SUPEROXIDE DISMUTASE IN THE ACUTE CONTUSION SPINAL CORD INJURY IN RATS**
A. Y. Morozova[1], A. D. Aleksashkin[2] , T. B. Mustafina[1], N. V. Nukolova[1], V. P. Chekhonin[1], N. L. Klyachko[2], A. V. Kabanov[2]
[1]The Serbsky Nationale Reserce Center for Social and Forensic Psychiatry, Moscow, Russia
[2]Department of Chemistry, M.V. Lomonosov Moscow State University, Moscow, Russia

17.50-19.00 **Break**

19.00-20.00 **Dinner**

Tuesday, May 7, 2013

Wednesday, May 8, 2013

08.00-09.30 **Breakfast**

10.00-13.00 ***MORNING SESSION***

Chairman: Prof. R. Neufeld

10.00-10.30 **INCORPORATION OF ANTIMICROBIAL PEPTIDES INTO NANOFIBRES AS A POTENTIAL ANTIMICROBIAL SURFACE COATING OF INANIMATE SURFACES**
T. H. B. Eriksen[1], E. B. Moeller[1], P. Fojan[2]
[1]Danish Building Research Institute (SBi), Aalborg University, A. C. Meyers Vænge 15, DK-2450, Copenhagen SW, Denmark, [2]Department of Physics and Nanotechnology, Aalborg University, Skjernvej 4A, DK-9220, Aalborg East, Denmark

Wednesday, May 8, 2013

10.30-11.00 **IMMUNOTROPIC AND ANTIBACTERIAL PROPERTIES OF BIOMATERIALS BASED ON CHITOSAN SALTS**
I. V. Zudina, A. B. Shipovskaya, V. I. Fomina, N. V. Petrova
Saratov State University named after N.G. Chernyshevsky, Saratov, Russia

11.00-11.30 **TRANSFECTION OF KASUMI-1 CELLS WITH A NEW TYPE OF POLYMER CARRIERS LOADED WITH MIR-155 AND ANTAGO-MIR-155**
O. V. Klimenko, M. Shtilman
D.I. Mendeleyev University of Chemical Technology, 9 Miusskaya Square, Moscow, Russia

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

Chairman: Prof. B. Dzantiev

12.00-12.20 **TARGETED LIPOSOMAL NANOCARRIERS FOR ANTICANCER DRUGS BASED ON PLATINUM SALT**
I. I. Kuznetsov[1,2], T. O. Sandalova[1], K. Y. Vlasova[1,3], A. V. Kabanov[3,4], N. V. Nukolova[1,3], V. P. Chekhonin[1]
[1]Serbsky National Research Center for Social and Forensic Psychiatry, Moscow, Russia, [2]Department of Materials Science, Lomonosov Moscow State University, Moscow, Russia, [3]Department of Chemistry, Lomonosov Moscow State University, Moscow, Russia, [4]Center for Nanotechnology in Drug Delivery and Division of Molecular Therapeutics, University of North Carolina at Chapel Hill, Chapel Hill, USA

12.20-12.50 **ENZYME-CONTAINING SYSTEMS BASED ON Fe_3O_4Au MAGNETIC NANOPARTICLES: PREPARATION AND PROPERTIES**
D. N. Lebedev[1,2], A. A. Kuznetsov [2], A. G. Majouga[2], Y. I. Golovin[2,3], A. V. Kabanov[2,4], N. L. Klyachko[2,4]
[1,2]Department of Materials Science (1) and Department of Chemistry (2) M.V. Lomonosov Moscow State University, Moscow, Russia, [3]Tambov State University, Tambov, Russia, [4]The University of North Carolina at Chapel Hill, Chapel Hill, USA

12.50-13.10 **THE FUNCTIONALIZATION OF THE SURFACE OF MAGNETITE NANOPARTICLES WITH ENZYME: THE EFFECT OF MAGNETIC FIELD**
M. V. Efremova[1], N. L. Klyachko[1], Yu. I. Golovin[2], A. A. Kuznecov[1], A. G. Majouga[1], A. V. Kabanov[3]
[1]Moscow State University, Moscow, Russian Federation, [2]Tambov State University, Tambov, Russian Federation, [3]Center for Drug Delivery and Nanomedicine, University of Nebraska

13.00-14.00 **Lunch**

14.00-16.30 **Break**

16.30-18.00 ***EVENING SESSION***

Chairmen: Prof. S. Eremin

16.30-17.00 **DESIGN OF POLYMERIC BIOMATERIALS BASED ON CHITOSAN FOR OPHTHALMOLOGY APPLICATION**
A. B. Ismailova[1], E. O. Batyrbekov[2], Z. T. Utelbaeva[3]
[1]Kazakh-British Technical University, Almaty, Kazakhstan, [2]Institute of Chemical Sciences, Almaty, Kazakhstan, [3]Kazakh National Medical University, Almaty, Kazakhstan

17.00-17.30 **ABSORPTION AND DISTRIBUTION OF LIPOSOMAL FORMULATIONS WITHIN THE RAT LIVER**
R. A. Mukhamadiyarov[1], M. A. Pautova[2], E. A. Velikanova[1]
[1]Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia,[2] Kemerovo State University, Kemerovo, Russia

17.30-18.00 **INTERACTIONS OF HIV-1 INTEGRASE AND REVERSE TRANSCRIPTASE: CHARACTERISTICS AND INHIBITION BY NANOCOMPLEXES**
O. V. Kondrashina[1], E. S. Knyazhanskaya[1], S. P. Korolev[1]
[1]Lomonosov Moscow State University, Chemistry Department, Moscow, Russia

18.00-18.30 **BIODEGRADATION OF POLYHYDROXYALCANOATES IN TROPICAL CONDITIONS**
A.N. Boyandin[1], S.V. Prudnikova[2], 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

18.30-19.00 **Break**

19.00-20.00 **Dinner**

Thursday, May 9, 2013

08.00-09.00 **Breakfast**

10.00-13.00 ***MORNING SESSION***

Chairmen: Prof. Yu. Vladimirov

10.00-10.30 **DEVICES FOR BIOMEDICINE, PRODUCED BY NATURAL BIODEGRADABLE POLYMERS**
E.I. Shishatskaya[1,2]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia

10.30-11.00 **BIODEGRADABLE HYBRID NANOGELS FOR COMBINATION THERAPY IN CANCER**
T.K. Bronich
College of Pharmacy and Center for Drug Delivery and Nanomedicine, University of Nebraska, Medical Center, Omaha, NE, USA

11.00-11.30 **GREASY RANCIDITY OF CELL DEATH**
V. Kagan
University of Pittsburg, Department of Environmental and Occupational Health, USA

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

Chairman: Prof. A. Kovarskii

12.00-12.30 **COMPARATIVE ANALYSIS OF HYDRODYNAMIC PARAMETERS OF HEART VALVE BIOPROSTHESES: "UNILINE" AND "PERICOR"**
K. Klyshnikov[1], E. Ovcharenko[1], D. Malcev[2], I. Zhuravleva[1]
[1]Siberian Branch RAMS Institution "Scientific-Research Institute for Complex Problems of Cardiovascular Disease", Kemerovo, Russia, [2]"NeoCor" Company, Kemerovo, Russia

12.30-13.00 **THE ANALYSIS OF EPOXY-TREATED STENTED HEART VALVE BIOPROSTHESES DYSFUNTIONS IN MITRAL POSITION**
V. Borisov, A. Burago, Yu. Odarenko, N. Rutkovskaya
Federal State Budgetary Institution Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

13.30-14.00 **Lunch**

14.00-17.00 **Break**

17.00-18.00 ***EVENING SESSION***

Chairman: Prof. E. Shishatskaya

17.00-17.30 **ANALYSIS OF NEW HIGH-MOLECULAR BIODEGRADABLE NONIONIC SURFACTANTS**
G. I. Boiko[1], Y. Orazbekuly[1], N. P. Lubchenko[2], T. P. Maimakov[2], Y. M. Shaihutdinov[1]
[1]Kazakh National Technical University named after K.I. Satpaev, 22 Satpaev str., Almaty, Kazakhstan, 050013, [2]Highest educational college "UNAT", 22a Satpaev str., Almaty, Kazakhstan

17.30-18.00 **BIODEGRADATION OF POLYHYDROXYALCANOATES IN TROPICAL CONDITIONS**
A. N. Boyandin[1], S. V. Prudnikova[2], 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

18.00-19.00 **Break**

19.00-20.00 **Dinner**

Friday, May 10, 2013

08.00-09.00 **Breakfast**

10.00-12.30 ***MORNING SESSION***

Chairmen: Prof. Yu. Sharkeev

10.00-10.30 **NANOMECHANICAL APPROACH TO THE CONTROL OF BIOCHEMICAL REACTION**
Yu. I. Golovin[1,2], N. L. Klyachko[2,3], D. Yu. Golovin[1], M. V. Efremova[2], D. N. Lebedev[2], M. M.Veselov[2], A. A. Samodurov[1], M. Sokolsky-Papkov[3], A. V. Kabanov[3,2]
[1]Nanocenter, Derzhavin Tambov State University, Tambov, Russia, [2]Lomonosov Moscow State University, Moscow, Russia, [3]University of North Carolina, Chapel Hill, NC, USA

10.30-11.00 **INNOVATIVE ANTIMICROBIAL NONWOVEN - MODERN SURGICAL DRESSINGS IN THERAPY OF POSTOPERATIVE WOUNDS IN ORTHOGNATIC SURGERY**
S. K. Lopandina, Z. J. Kozinda, T. A. Podgaevskaya, O. O. Erofeev, T. V. Moreva
Central Research Studies Institute of Clothing Industry, Moscow, Russia

11.00-11.30 **3-D IN VITRO SYSTEMS BASED ON POLYELECTROLYTE MICROCAPSULES AND RGD-PEPTIDES FOR ANTITUMOR DRUG SCREENING**

R. Akasov[1], M. Drozdova[1], D. Zaytseva-Zotova[1], S. Burov[2], A. Marc[3], I. Chevalot[3], E. Markvicheva[1]

[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia, [2]Institute of Macromolecular Compounds, St-Petersburg, Russia, [3]Laboratoire Réactions et Génie des Procédés, UPR CNRS 3349, ENSAIA-INPL, 2, Avenue de la Forêt de Haye, BP 172, Vandoeuvre-lès-Nancy, 54505, France

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11.30-12.00 **NANOFIBERS AND THEIR POTENTIAL AS A RELEASE MEDIUM OF PHARMACEUTICAL DRUGS**

D. Vynias

Laboratory of Toxicology, Medical School, University of Crete, Heraklion, Greece

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12.00-12.30 **DIAGNOSTIC DNA MICROARRAYS FOR DETERMINATION OF PATHOGENS ANDANTIBIOTIC RESISTANCE**

A. M. **Egorov**

Enzymology division, Department of Chemistry, M. V. Lomonosov Moscow State University, Russia, Moscow, 119992, Leninskie Gory d. 1/11

12.30-13.00 **Coffee break, Poster session**

CLOSING CEREMONY

13.00-14.00 **Farewell Address – Closing Remarks**

14.00-15.00 **Lunch**

19.00-22.00 **Farewell Dinner**

Saturday, May 11, 2013

08.00-09.00 **Breakfast**

10.00-13.00 **Excursion**

13.00-14.00 **Lunch**

19.00-22.00 **Dinner**

Sunday, May 12, 2013

08.00-09.00 **Breakfast**

Departure of Participants

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General Information

Conference Venue

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Abstract Book

BIOTECHNOLOGY – THE WAY TO THE FUTURE

T. G. Volova[1,2]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk Russia,[2]Siberian Federal University Institute of Fundamental Biology and Biotechnology, Krasnoyarsk, Russia

Nowadays in a world growing rates of consumption of food and energy resources, population increase, and human-induced impacts have reached the limit beyond which uncoordinated economic activity can lead to irreversible changes in the biosphere. The only way to achieve harmonic coexistence between the growing population of our planet and the biosphere is to pursue coordinated development of science and technology. Development of novel technologies for complete treatment of natural resources and production of environmentally friendly energy sources and materials, that can be involved in the biospheric cycling, are the objectives of conception of the "Agenda of the Twenty-first Century". Biotechnology, as well as nanotechnology, is among the currently most popular words and areas of study in the world. It has been discovered that properties of individual molecules are quite different from those of their large aggregates and that microorganisms are actually chemical reactors. If we have a great number of these reactors and successfully control them, we'll be able to synthesize the substances we wish to produce. Hydrogen bacteria proper, bacteria oxidizing hydrogen, or "detonating gas" bacteria, may synthesize wide spectrum of molecules, including single cell protein, SCP, and reserved macromolecules - polyhydroxyalkanoates, PHAs. Practical interest in hydrogen bacteria is caused with their potential use as a regenerative component in closed biotechnological life support systems. More recently, hydrogen bacteria, which grow much faster than other chemoautotrophic organisms, attracted the attention of researchers as a potential source of feed, or even food, protein, SCP. The late 1980s and the early 1990s saw an upsurge of interest in hydrogen bacteria as very promising producers of polyhydroxyalkanoates – polymers, similar to polypropylene but degradable in the natural environment and biocompatible. Our group established three Pilot Production Facilities (PPF) exploiting hydrogen bacteria, with different volumes of cultivating vessels, having data of determination of mineral and biochemical composition of biomass, evaluation of parametric growth dependencies of bacterial cells and their nutritional requirements, and designing of laboratory equipment for continuous bacterial cultures. Two targets are in the focus of investigation – PHAs and SCP. The facilities produced sufficient amounts of biomass for experiments with agricultural animals, aimed at assessing its biological value, so as up to 50 kg of PHAs per year, for tests of biological safety and producing of biomedical devices.

ENHANCED CHEMILUMINESCENCE AS A TOOL TO STUDY FREE RADICAL REACTIONS PRODUCED BY TOXIC NANOMATERIALS

Yu. A. Vladimirov[1], E. V. Proskurnina[2], A. M. Polimova[1], A. V. Alekseev[1]
[1]Shubnicov Institute of Crystallography, Russian Academy of Science, Russia, [2]Lomonosov Moscow State University, Russia

The reactions of free radicals are usually very exergonic, i.e. produce a large portions of energy; that is why many of them are associated with light emission, known as *chemiluminescence* (CL). One example is the disproportionation reaction of two peroxyl radicals $ROO^{\bullet}$ resulted in appearance of excited ketone molecule with subsequent light emission. In biochemical systems this sort of reaction between peroxyl radicals ($LOO^{\bullet}$) of polyunsaturated fatty acid chains (PUFA) brings about *ultra-weak* chemiluminescence produced by living cells and increasing in pathological situations. The intrinsic CL of biological objects is really very weak and not very specific, but can be enhanced by many orders of magnitude by adding specific luminescent substances, known as *CL enhancers*. Among them three compounds are most popular: (1) luminol, a non specific chemiluminescent probe for "reactive oxygen species" (a mixture of superoxide, hydroxyl and lipid radicals with hydrogen peroxide and eventually hypochlorite produced mainly by phagocytes), (2) lucigenin, a rather selective CL probe for superoxide anion radical ($O_2^{\bullet\square}$), and (3) C-525, a quinolisine coumarine derivative, specific sensitizer of the chemiluminescence associated with the disproportionation reaction of two lipoperoxyl radicals ($LOO^{\bullet}$).
The general response of live cells and tissues on the unfavorable environment, including toxic nanoparticles, is the increased production of free radicals: superoxide, hydroxyl, and lipid radicals responsible for chain lipid peroxidation. The literature data and our own experience are considered in the presentation. The general conclusion as that the enhanced chemiluminescence is a sensitive and specific method of investigation of free-radical mechanisms of damaging effects of nano materials on the living objects.

SYNTHESIZED NANO AND MICROFIBER MATRIX NETWORKS SUPPORT IMMUNOISOLATED PANCREATIC ISLETS FOR IMPLANTATION

J. A. M. Steele[1], E. Carmona[2], J-P. Halle[2], A.E. Barron[3], R. J. Neufeld[1]
[1]Queen's University, Kingston, Ontario, Canada, [2]Université de Montréal, Maisonneuve Rosemont Hospital Research Centre, [3]Stanford University, Palo Alto, CA

A novel method was developed to produce and incorporate a network of discrete, genipin-crosslinked gelatin nano or microfibers around a pancreatic islet within a barium alginate microcapsule. This technique allows for the encapsulation of a porous extracellular protein-like matrix without the limitations of cellular aggregate seeding geometries that preclude their use in microparticles without diffusional limitations. Nanofibers were electrospun, and microfibers were produced from a newly developed vortex-drawn extrusion system with an alginate support matrix. Optimization of the extrusion methodology culminated in a hydrated fiber diameter of 22.3 ± 0.4 µm, a 98% reduction in cross sectional area, while making the process more reliable and less labour intensive. The optimized microfibers were encapsulated at 40 vol% within 294 ± 4 µm 1.6% barium alginate microparticles by an electrostatic-mediated dropwise extrusion system. Pancreatic islets extracted from Sprague Dawley rats were encapsulated within the microparticles, and analyzed over a 21-day study. Acridine orange and propidium iodide fluorescent viability staining and light microscopy indicated a significant

increase in viability for the fiber-laden particles at days 7, 14, and 21, relative to fiber-free controls. The fiber-laden microcapsule system reduced the incidence of disrupted islet morphologies from 31% to 8% at day 21, and showed evidence of islet-fiber adhesion after only 1 hour of co-incubation and 24 hours of encapsulation. The novel microencapsulation method developed in this investigation could be developed into a modular scaffold system for tissue engineering beyond the field of islet research.

EFFECT OF MAGNETIC FIELD ON ENZYME_MAGNETITE NANOCOMPLEXES

K. Y. Vlasova[1], M. A. Abakumov[1] , Yu. I. Golovin[1,3], N. L. Klyachko[1,2], A. V. Kabanov[1,2] , M. Sokolsky[2]
[1]Department of Chemistry, Lomonosov Moscow State University, Moscow, Russia, [2]University of North Carolina at Chapel Hill, USA, [3]G.R.Derzhavin Tambov State University, Tambov, Russia

Introduction. Magnetic nanoparticles (MNPs) possess unique physicochemical and surface properties. They find application in various areas such as drug delivery, hyperthermia, magnetic resonance imaging (MRI), tissue engineering and repair, biochemical separations. "Theranostics" is a new area of medicine, which combines drug delivery (theraphy) and imaging of diseases (diagnostics). One of the bases for creating theranostic systems is MNPs. Many works are devoted to investigation of systems based on immobilized on the MNPs surface enzymes. Superoxide dismutase 1 (SOD1) is an important antioxidant defense enzyme working in cells exposed to reactive oxygen species (ROS). Nowadays, the mainstream of work with this enzyme is to prepare antioxidant theranostic formulations for treatment of ROS-associated diseases (heart attack, stroke), and magnetic nanoparticles are the most appropriate platform for this aim.
The goal of our work is to get colloidal stable system of MNPs, covered with SOD1 on its surfaces (MNP-SOD1) and to study the effect of magnetic field application on the enzyme activity. *Materials and methods.* SOD1 immobilized by covalent binding of SOD1 molecules to MNP, coated with BSA (MNP-BSA) and by electrostatic sorbtion of SOD1 molecules on MNP, coated by polylysin-PEG block-copolymer (MNP-PLL-PEG). For covalent binding EDC and NHS solutions in DI water and SOD1 solution (0,1M HEPES, pH 7.4) were added to the MNP-BSA solution (PBS buffer). For non-covalent binding, SOD1 was immobilized on MNP-PLL-PEG by adding the solution of SOD1 in HEPES (pH=7.4) to MNP-PLL-PEG solution. The unbound enzyme in both systems was removed by centrifugation through 100kDa filters. The size and surface charge of the nanoparticles was determined using DLS. The concentration of iron was determined by the reaction with sodium salt of 3 - (2-pyridyl) -5,6-diphenyl-1,2,4-triazine-4 ', 4"-disulphonic acid. Enzyme activity before and after magnetic field application was measured using pyrogallol autoxidation inhibition. The field intensity and time of incubation were varied. *Results* Sizes and ζ-potentials of particles of MNP-BSA-SOD1 and MNP-PLL-PEG-SOD1were 300±4 and 112±3 nm, -4,2 ±0,3 and +27,0±0,6 mV, respectively. MNP-BSA-SOD1 didn't show changes in enzyme activity after MF application. MNP-PLL-PEG-SOD1 showed increase of enzyme activity after MF acting.
Conclusion. We obtained stable formulation that pretends to be antioxidant theranostic drug. In future studies, the effect of SOD1-magnetite complexes on cell viability at hypoxic conditions will be studied.
The study was supported by Russian Ministry of Science and Education (grant No11.G34.31.0004).

ANTISTAPHYLOCOCCAL ENDOLYSINES AS PERSPECTIVE ANTIMICROBIALS

L. Yu. Filatova[1], D. N. Lebedev[1], A. D. Priyma[1], D. M. Donovan[2], S. C. Becker[2], A. V. Kabanov[1], N. L. Klyachko[1]
[1]M.V. Lomonosov Moscow State University, Chemistry Department, Moscow, 119991, Leninskie Gory, 1-11, [2]ARS-USDA Beltsville Agricultural Research Center, USA

Staphylococcus aureus causes many dangerous diseases in living organisms. The majority of *Staphylococcus aureus* strains resistant to antibiotics, so there is a question of finding alternative ways to treat staphylococcal infections. Lytic enzymes of bacteriophages (phage lysines, lysozymes) may be adequate alternative to antibiotics. Since the seventies of the last century, interest of scientists aims at investigation of structure, mechanisms of action, enzymological properties and pharmacokinetics of bacteriophage lytic enzymes (phage endolysines, lysines), which may be regarded as a fundamentally new type of antibacterials.
The work was supported by project of Russian Federation Ministry of Education 11.G34.31.0004.

COMPLEXES OF POLYANILINE AND POLYPYRROLE WITH WATER-SOLUBLE POLYMERS

Ya. O. Mezhuev, Yu. V. Korshak, A. I. Piskareva, S.V. Osadchenko, I. V. Solovyova, M. A. Salop, M. I. Shtilman
D. Mendeleev University for Chemistry Technologies of Russia, Moscow, Russia

Polyaniline and polypyrrole has the set of special properties including electroconductivity, low toxicity and potential biocompatibility polyaniline that defined prospects of their using in biomedical areas. However producing of practically acceptable materials on their base is is not straightforward because of their infusibility and insolubility in doped form. Therefore it is worth to note the possibility of producing the on the base of aqueous dispersions stabilized by water-soluble polymers. It was shown that oxidative polymerization of aniline and polypyrrole in aqueous solution of poly-(N-vinylpyrrolidone), polyethyleneglycol and polyvinyl alcohol induced by ammonium persulfate leads to nanoscale particles creation with diameters varies from 100 to 1500 nm. It was determined that particles size of dispersion phase regardless of using the polymer nature decreases with the raise of its molecular weight and concentration in the reaction system. By means of infrared spectroscopy it was established that particles of the disperse phase formed of polyaniline or polypyrrole chains interacting by hydrogen bonding with using polymer. Hence creating nanodisperse represent polymer-polymer complexes. Investigations of the kinetics of oxidative polymerization of aniline and pyrrole in aqueous solution PVP, PVA and PEG showed considerable influence of their molecular weights and concentrations on the process rate. Generation of water compatible hydrophilic polymer-polymer complexes lets expect the expantion of spheres of using polyaniline and polypyrrole in medicine and biology. In particular synthetize highly productive composite nano filtration membranes with high selectivity to substances with molecular weight more than 900 Da, that can be used for separating of numbers of biologically active substance and pharmaceuticals from salts and other low-molecular organic compounds.

MACROPOROUS HYDROGELS VERSUS CONVENTIONAL DRESSINGS IN THE TREATMENT OF CHRONIC WOUNDS: A RETROSPECTIVE STUDY

D. E. Lisovyy[1], S. M. Chudnykhr[1], A. A. Artyukhov[2], M. I. Shtilman[2]
[1]Moscow State University of Medicine and Dentistry, Moscow, Russia, [2]Mendeleyev University of Chemical Technology of Russia, Moscow, Russia

Abstract. Successful wound care involves optimizing patient local and systemic conditions in conjunction with an ideal wound healing environment. This paper reports a newly fabricated macroporous hydrogels of polyvinyl alcohol by cross-linking of polyvinyl alcohol acrylic derivatives wound dressing. Such hydrogels are impermeable to bacteria, and create the most physiological interface between the wound surface and the environment. Macroporous hydrogels dressings have other advantages over conventional dressings in terms of ease of application, non-immunogenic, non-pyrogenic, hypo-allergenic, and pain-free. This study aims to compare the efficacy of macroporous hydrogels in treating chronic wounds with that of conventional dressing materials.
Materials and Methods: The records of 120 patients with chronic wounds of varied etiologies and with mean age 50.2 years were collected and analyzed. The patients had been treated either with macroporous hydrogels or other conventional dressing materials including silver sulfadiazine, nadifloxacin, povidone iodine, or honey (traditional dressing material). Patients with co-morbidities that could grossly affect the wound healing like uncontrolled diabetes mellitus, chronic liver or renal disease, or major nutritional deprivation were not included. For the purpose of comparison the patients were divided into two groups; 'Hydrogel group' and 'Conventional group', each having 60 patients. For assessment the wound characteristics (size, edge, floor, slough, granulation tissue, and wound swab or pus culture sensitivity results) were recorded. With start of treatment, appearance of granulation tissue, completeness of healing, need for skin grafting, and patients' satisfaction was noted for each patient in both groups.
Results: With two weeks of treatment, 90% of the 'collagen group' wounds and only 42% of the 'conventional group' wounds were sterile (P=0.03). Healthy granulation tissue appeared earlier over hydrogel-dressed wounds than over conventionally treated wounds (P=0.03). After six weeks, 56 (93%) of 'hydrogel group' wounds and 28 (47%) of 'conventional group' wounds were healed (P=0.21). Twelve patients in the 'conventional group' needed partial split-skin grafting (P=0.04). Hydrogel-treated patients enjoyed early and more subjective mobility.
Conclusion: There is significant better results in terms of completeness of healing of chronic wounds between hydrogel dressing and conventional dressing were found. Hydrogel dressing, however, may avoid the need of skin grafting, and provides additional advantage of patients' compliance and comfort.
Keywords: Chronic wounds, hydrogel dressing, Macroporous hydrogels, polyvinyl alcohol.

INNOVATIVE ENZYME CONTAINING NANOFORMULATIONS FOR DIAGNOSTICS AND THERAPY

N. L. Klyachko[1], E. A. Zaitseva[1], E. N. Efremenko[1], O. A. Kost[1], N. V. Nukolova[2,1], L. Yu. Filatova[1], S. A. Legotsky[1], Yu. I. Golovin[4,1], A. G. Majouga[1], M. A. Abakumov[3,1], A. B. Belova[1], V. P. Chekhonin[2,3], A. V. Kabanov[5,1]
[1]M. V. Lomonosov Moscow State University, Department of Chemistry, Moscow, Russia, [2]Center for Social and Forensic Psychiatry, Moscow, Russia, [3]Russian State Medical University, Moscow, Russia, [4]GR Derzhavin Tambov State University, Russia, [5]Eshelman School of Pharmacy, University of North Carolina-Chapel Hill, Chapel Hill, USA

In 2010, the Laboratory of Chemical Design of Bionanomaterials was established at the MV Lomonosov Moscow State University. The main activities of the laboratory were directed to fundamentals and applications of new classes of bionanosystems based on proteins, enzymes, polymer coatings, magnetic nanoparticles for treatment and diagnostics of a number of diseases such as brain CNS diseases, inflammatory, cardiovascular and cancer at al.
Special attention was attached to the development of the approach based on the technology of NanoZYMES™ for therapeutic proteins immobilization and functions (USP WO No2008/141155 A1). Using this approach, novel types of nanozymes have been obtained. So, organophosphate hydrolase containing nanozymes possessing the ability to decompose organophosphorus neurotoxins were synthesized as well as antioxidative nanozymes based on superoxide dismutase for eye inflammation and spinal cord injury treatment. Nanozymes containing stabilized bacteriolytic enzymes PlyC and LysK are promising for the treatment as antibacterials.
Hybrid nanomaterials containing enzymes and superparamagnetic nanoparticles promising for theranostics were created. Magnetic iron oxide nanoparticles stabilized by BSA and conjugated with monoclonal antibodies to vascular endothelial growth factor have been synthesized. The potential for diagnosing brain tumors via the vector MRI-contrast agent based on superparamagnetic nanoparticles in diagnostics of brain tumors was shown.
The procedure of preparative synthesis of nanoparticles with a magnetic core and a gold shell, modified by organic ligands and enzymes, was designed. The magnetic materials obtained, have been studied in conditions of a low-frequency magnetic field using a device specially constructed for the purpose. Effects of low frequency magnetic fields on the conformation and the catalytic activity of enzymes attached to the surface of magnetic nanoparticles, which is the first example of a mechanical-magnetic effect in nanobiocatalysis, have been discovered. These studies offer the possibility of superparamagnetic materials as a relay for remote monitoring of chemical reactions, which can be used in the construction of a number of functional units, including the controlled release of drugs.
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MOLECULARLY IMPRINTED POLYMERS AS SYNTHETIC ANTIBODIES FOR TEST-METHODS

S. A. Eremin[1], Thi Dieu Thuy Nguyen[2]
[1]*Department of Chemical Enzymology, Faculty of Chemistry, M.V. Lomonosov Moscow State University, Moscow, 119991, Russia,*
[2]*Institute of Biotechnology, Vietnam Academy of Science and Technology, Ha Noi, Viet Nam*

In this time many efforts have attempted to design and synthesize the antibody-like recognition element for replacing antibodies. As recognition elements could be used many biological compounds, including: bacteria, receptors, proteins, enzymes, peptides, oligonucleotides (aptamers), and etc. Molecular imprinting polymers is one of the promising compound to be applied for analytical purposes and have nick-name – "synthetic antibodies". The molecularly imprinted polymers (MIPs) exhibit high selectivity, physiochemical stability and applicability in any chemical media, and have been applied in separation processes and chemical sensors.
MIPs could be synthesized by co-polymerization of functional and cross-linking monomers in the presence of a molecular analyte. After removal of the analytes and chemicals from solid-polymer by washing, the MIP with binding sites are obtained that allow binding of the analyte with some affinity and specificity. MIP membrane could be directly synthesized on the well surface of polysterene microtitration plate in aqueous environment as used for direct competitive biomimetic enzyme-linked immunosorbent assay (BELISA). The examples for analytical applications of MIPs will be presented and discussed.
Acknowledgement.
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References:
Karsten Haupt. Molecularly imprinted polymers in analytical chemistry. Analyst, 126(4), 747-756 (2001).
Shiho Tokonami, Hiroshi Shiigi, Tsutomu Nagaoka. Review: Micro- and nanosized molecularly imprinted polymers for high-throughput analytical applications. Anal. Chim. Acta, 641(1-2), 7-13 (2009).
Yannick Fuchs, Olivier Soppera, Karsten Haupt. Photopolymerization and photostructuring of molecularly imprinted polymers for sensor applications - A review. Anal. Chim. Acta, 717, 7-20 (2012).
Xuan-Anh Ton, Victor Acha, Karsten Haupt, Bernadette Tse Sum Bui. Direct fluorimetric sensing of UV-excited analytes in biological and environmental samples using molecularly imprinted polymer nanoparticles and fluorescence polarization. Biosens. Bioelectron., 36(1), 22-28 (2012).
Qing, Sun; Longhua, Xu; Yue, Ma; Xuguang, Qiao; Zhixiang, Xu. Study on a biomimetic enzyme-linked immunosorbent assay method for fast determination of trace acrylamide in French fries and cracker samples. J. Sci. Food Agric. (in-press 2013).

STRUCTURE AND MECHANICAL PROPERTIES OF THE ULTRAFINE-GRAINED BIOINERT TITANIUM AND ZIRCONIUM PRODUCED BY SEVERE PLASTIC DEFORMATION AND THEIR MEDICAL APPLICATION

Yu. P. Sharkeev, A. Yu. Eroshenko, O. A. Belyavskaya
Institute of Strength Physics and Materials Science, SB RAS, Tomsk, Russia

One of the ways to increase mechanical properties of metals is formation of ultrafine-grained or nanostructured state in the bulk of metals by severe plastic deformation (SPD). At present a set of the SPD methods has been developed. There are many experimental data illustrating a great improvement of mechanical characteristics (ultimate strength, yield strength, fatigue strength, wear resistance, microhardness and so on) of metals after SPD. Today, the combined methods of SPD, for example, the abc-pressing in a press-mold in conjunction with multiple rolling, are used to produce the billets of the bioinert titanium and zirconium in nanostructured / ultrafine-grained state for medical applications.
The abc-pressing in a press-mold represents the three cycles of uniaxial pressing of coarse-grained billet in a press-mold with a successive decrease of temperature in the range between 500°C and 400°C. Each cycle at a preset temperature includes triple-step pressing with the change in deformation axis by turning the billet around the longitudinal axis by 90°. The multiple rolling is performed in the grooved or flat rollers. Finally pre-recrystalline annealing is carried out. The SPD method allows us to produce the bioinert metal rods in nanostructured / ultrafine-grained state with a homogenous structure in the bulk and with the average size of the elements of the grain-subgrain structure (grains, subgrains, fragments) of 100 nm and less.
Mechanical properties (yield point, ultimate stress, hardness and microhardness, cyclic life and fatigue strength) of the nanostructured titanium and zirconium, produced by the SPD combined method, coincide to those of the medical medium-strength titanium alloys, i.e. Ti-6Al-4V. The nanostructured titanium and zirconium remain the stable microstructure and properties in the temperature interval from a room temperature up to 350°C.
It was found that the zirconium and titanium substrates in nanostructured / ultrafine-grained state have very good biocompatibility. The modern constructions of intraosseal screw dental implants with instruments and implements from the VT1-0 nanostructured / ultrafine-grained titanium have been developed. The clinical tests of nanostructured titanium dental implants have been completed. They have confirmed that the implant constructions correspond to the modern state of implantology and their usage does not trigger any complications at the surgical and orthopedic stages of the treatment.

PROGRESS IN DESIGNING OF BIOCOMPATIBLE MAGNETICALLY TARGETED NANOSYSTEMS FOR A SMART DELIVERY OF THERAPEUTIC PRODUCTS

A. V. Bychkova, M. A. Rosenfeld, V. B. Leonova, A. L. Kovarski
Federal state budgetary institution of science Emanuel Institute of Biochemical Physics of Russian Academy of Sciences, Moscow, Russia

Magnetically targeted nanosystems are considered in the present time as promising objects for a smart delivery of drugs to targeting cells [1]. These systems represent magnetic nuclea (magnetite e.g.) coated with biocompatible diamagnetics which can physisorb or chemisorb biologically active substances. In our work the problem of creation of such nanosystems has been solved with

the application of a principally novel one-step free radical linking method of obtaining of stable polyfunctional protein coatings [2]. The method is based on the ability of proteins to form interchain covalent bonds under the action of free radicals which are generated locally on nanoparticles surfaces. By the set of physically chemical and biochemical methods it has been proved that the free radical linking of proteins allows obtaining stable single layer protein coatings in thickness of several nm. The coatings are formed on the surface of individual magnetic nanoparticles with free radical processes taking place strictly in the adsorption layer. On the example of thrombin and immunoglobulin G it was demonstrated that the free radical linking of proteins on the surface of nanoparticles almost completely keeps native properties of the protein molecules. The free radical linking method reveals new possibilities of design of single layer multiprotein polyfunctional coatings on all the surfaces containing metals of variable valence (for example, Fe, Cu, Cr). The method may be used to reach various biomedical goals including a smart delivery of drugs and biologically active substances.

[1]. A.V. Bychkova, O.N. Sorokina, M.A. Rosenfeld, A.L. Kovarski. Multifunctional biocompatible coatings on magnetic nanoparticles. Russian Chemical Reviews. Vol. 81, No 11. P. 1026-1050 (2012).
[2]. A.V. Bychkova, M.A. Rosenfeld, V.B. Leonova, O.N. Sorokina, S.M. Lomakin, A.L. Kovarski. Free-Radical Cross-Linking of Serum Albumin Molecules on the Surface of Magnetite Nanoparticles in Aqueous Dispersion. Colloid Journal. Vol. 75, No. 1. P. 7–13 (2013).

INTERACTION OF CARBON NANOPARTICLES WITH ANTIBODIES : ANALYTICAL AND TOXICOLOGICAL ASPECTS

B. B. Dzantiev, O. D. Hendrickson, A. V. Zherdev
Institute of Biochemistry Russian Academy of Sciences, Leninsky prospect 33, 119071 Moscow, Russia

The increasing application of engineered carbon nanoparticles, mostly fullerenes and carbon nanotubes, in different fields of industry and medicine causes a necessity to develop new approaches for their control in living organisms and the environment. In comparison to HPLC which nowadays serves as a main technique for the detection of carbon nanoparticles (CNP), immunochemical assay can be considered as a promising alternative due to rapidity, high sensitivity and possibility to analyze a row of probes simultaneously.
The aim of this study is production of poly- and monoclonal anti-fullerene C_{60} antibodies, characterization of their affinity and specificity, development of enzyme-linked immunosorbent assay (ELISA) for the detection of free fullerenes C_{60} and C_{70} and multi-walled carbon nanotubes in solutions and in organs and tissues of animals administered with fullerenes.
Carbon nanoparticles appear to be unconventional immunogens having unique structure without typical inducers of immune response. This may be an impediment to the production of CNP–specific antibodies. In addition, solubilization of highly hydrophobic CNP in aqueous media or in polar solvents compatible with immune interactions are of great challenge.
Polyclonal antisera and monoclonal anti-fullerene antibodies were produced by immunization of rabbits and mice correspondingly by the conjugates of fullerene C_{60} carboxylic derivative with thyroglobulin and soybean trypsin inhibitor synthesized by carbodiimide activation technique. The specificity of the antibody–fullerene binding was confirmed. The affinity of the produced antibodies to fullerene was characterized by the registration of surface plasmon resonance changes in Biacore system. The equilibrium association constants of the interaction between antibodies and a number of fullerene derivatives measured by this technique are in the range of $1.6 \cdot 10^6 – 6.6 \cdot 10^7$ M^{-1}.
The developed indirect competitive ELISA allows to detect not only water-soluble fullerene forms (such as protein-conjugated fullerene, fullerene aminocaproic acid and fullerenol), but also pristine fullerenes C_{60} and C_{70} and multi-walled carbon nanotubes in solutions. The detection limit of the developed ELISA varies from 0.04 to 5.5 ng/ml depending on CNP type; the duration of the assay is 2 h.
Fullerene C_{60} was detected by the developed ELISA in organs of rats intraperitoneally and intragastrically administered with C_{60}. To reduce the influence of biomatrix on the assay results a technique was developed for the pretreatment of biological samples by toluene extraction of C_{60} and dissolution of the fullerene-containing extract in the above mentioned water-organic media.
After single intraperitoneal administration (250 mg/kg) fullerene C_{60} was detected in liver, spleen, kidneys, lungs and brain of rats. The fullerene was found in liver, brain, and intestine of rats at days 7, 18 and 30 of chronic intragastrical administration with different doses (0.5-50 mg/kg). The obtained results correlate to HPLC data. Thus, the immunoassay procedure allows the detection of fullerene C_{60} in animals` organs and tissues.
The obtained results open opportunities for applying the produced antibodies and the developed assay to toxicological studies, environmental monitoring and technological control of the CNP production.
The work was supported by the FP7 EC project MARINA and the Russian Federal Target Program "Scientific and Scientific-Pedagogical Personnel of Innovative Russia for 2009–2013" (contract 8284).

SYNTHESIS AND INVESTIGATION OF SUPEROXIDE DISMUTASE NANOZYMES USING MODEL OF SPINAL CORD INJURY IN RATS

A. D. Aleksashkin[1], A. Yu. Morozova[2], T. B. Mustafina[2], V. P. Chekhonin[2], N. L. Klyachko[1], D. S. Devika, 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

Usually injury accompanied by a process of inflammation. During inflammation the balance between the production of radicals and their neutralization is broken. In this case, introduction of an additional amount of antioxidants may be effective, in particular, the antioxidant enzymes (catalase and superoxide dismutase (SOD)). However, in practice the use of natural enzymes is ineffective because of their instability. The purpose of our work was to develop the SOD nanoparticles and analyze their biological

effects on model of spinal cord injury (SCI).
Synthesis was carried out by simple mixing of SOD solutions and block copolymer (polylysine-polyethylene glycol) followed by covalent cross-linking. The samples were characterized by dynamic light scattering (Zetasizer Nano ZS), electrophoresis under denaturing conditions, MTT assay. Specific activity was determined using pyrogallol assay. *In vivo* experiments were performed on Wistar rats using SCI model. SOD nanoparticles (from 500 to 20 000 units of activity per kg of body weight) were intravenously injected in 30 min after injury. The total volume of spinal cord injury (inflammation and traumatic cysts) was evaluated by magnetic resonance imaging. We developed the stable active SOD nanoparticles (diameter 40 ± 5 nm). MRI data suggested that 20 days after the treatment by SOD nanoparticles the volume of a spinal cord injury decreased 2-fold compared with the native enzyme and 3-fold compared with the control. Also the dose-administration relationship was established. Thus, we found the bell-shaped form with maximum around 5000 units per kg of body weight.
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NEW MINIMALLY INVASIVE METHODS OF TREATMENT OF ACUTE CHOLECYSTITIS WITH USE OF MODIFIED PVA

S. M. Chudnykh[1], D. E. Lisovyy[1], Yu. V. Kulezneva[1] A. A. Sidoruk[1], A. A. Artyukhov[2], M. I. Shtilman[2]
[1]Moscow State University of Medicine and Dentistry, Moscow, Russia, [2]Mendeleyev University of Chemical Technology of Russia, Moscow, Russia

The relative quantity of destructive forms of acute cholecystitis in patients above 60 years of age amounts, according to the literature data, to 40.5-92.8%. Total postoperative lethality varies in different institutions within 2-12%, has no reducing trend and reaches in case of operations at the peak of attack to 14-15% and in the elderly – to 20% sharply increasing with age. In case of emergency operations in patients above 80 years of age suffering from severe co-morbidity the postoperative lethality exceeds 40-50%, which makes those operations extremely risky. At the same time elective and delayed operations performed against the background of remitted acute inflammatory phenomena, after thorough examination and preparation of patients, give considerably better results. The postoperative lethality in such cases does not exceed 0.5-1%.
On the basis of experience practice of treatment of patients of elderly and old age there was planed a therapeutic approach for acute cholecystitis using minimally invasive methods under ultrasonic control. It is indicated that it is optimal to perform sanation decompression punctures of gallbladder under ultrasonic control. In case of their ineffectiveness application of external cholecystostomas is performed under ultrasonic control. In 10 cases implantation of synthetic material, on base of crosslinkable acrylated polyvinyl alcohol, into the gallbladder cavity has been carried out for obliteration thereof.
The given method is less traumatic, it enables to perform procedures under local anesthesia without application of narcosis, it has no impact on quality of patients' life allowing to avoid continuous standing of cholecystostoma and any complications associated with it, prevents relapses of acute cholecystitis and necessity of surgical intervention. Complications developed when performing percutaneous transhepatic interventions controlled by ultrasound investigation, as a rule, are not fatal and can be eliminated by way of minimally invasive procedures. Our first experiment has shown that application of the method of obliteration of the gallbladder by way of administration of crosslinkable in vivo polymeric macromers on base of acrylated PVA through percutaneous cholecystostoma can be a method of choosing surgical treatment in multimodality therapy of patients with acute cholecystitis at elderly and old age with severe co-morbidity. This approach needs further development and study of long-term results. This approach needs further development and study of long-term results.

CHARACTERISATION OF BACTERIOPHAGE S-394 ENDOLYSIN AND ITS APPLICATION AGAINST GRAM-NEGATIVE BACTERIA

S. Legotsky[1], A. Priyma[1], K. Vlasova[1], K. Miroshnikov[2], A. V. Kabanov[1], N. Klyachko[1].
[1]M. V. Lomonosov Moscow State University, Department of Chemistry, Moscow, Russia, [2]M. Shemyakin and Yu. Ovchinnikov Institute of Bioorganic Chemistry, RAS, Moscow, Russia

Bacteriophage endolysins are enzymes which hydrolyze the peptidoglycan of bacterial cell wall at the end of replication cycle of lytic phages. Endolysins possess high activity against antibiotic-resistant microflora therefore these enzymes are considered as alternative effective antibacterials. But endolysin therapy is restricted by insensitivity of Gram-negative bacteria for lytic action "from without" since peptidoglycan is covered by outer membrane (OM). To solve this problem, several approaches can be suggested. In particular, OM can be permeabilized by numerous chemical agents.
This research deals with the characterization of endolysin Lys394 encoded in genome of bacteriophage S-394 specific to Enterobacteriaceae and testing the combination of Lys394 with several OM permeabilizing agents.
Recombinant endolysin Lys394 was synthesized in *E. coli* C41(DE3) and purified to homogeneous state by Ni^{2+} affinity chromatography. Molecular weight of enzyme determined by SDS-PAGE is 18 kDa, isoelectric point is close to 7.0, gel filtration indicates monomeric form of Lys394 in solution. The dependence of bacteriolytic activity of chloroform treated cells on concentration of enzyme yields the typical saturation curve. Lys394 retains maximum activity in pH range between 7.5 and 9 at low ionic strength.
It was shown that Lys394 lyses living plankton cells of *E. coli* in presence of cationic OM permeabilizers: 10-20 μg/mL of polyarginine (5-15 kDa), 30-50 μg/mL of Lys_{30}-PEG_{114} copolymer or 10-20 μg/mL of antibacterial peptide PGLa. The permeabilization activity of these compounds was proofed by detecting of periplasmic beta-lactamase leakage.
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BIOLOGICAL EFFECTS OF NANO-COMPLEXES BASED ON SUPEROXIDE DISMUTASE IN THE ACUTE CONTUSION SPINAL CORD INJURY IN RATS.

A.Y. Morozova[1], A. D. Aleksashkin[2], T. B. Mustafina[1], N. V. Nukolova[1], V. P. Chekhonin[1], N. L. Klyachko [2], A. V. Kabanov [2]
[1]The Serbsky Nationale Reserce Center for Social and Forensic Psychiatry, Moscow, Russia
[2]Department of Chemistry, M.V. Lomonosov Moscow State University, Moscow, Russia

Introduction: Numerous central nervous system (CNS) disorders accompanied with activation of microglial cells, which is linked to overproduction of the reactive oxygen species and subsequent neuronal damage. The use of the antioxidant enzymes (such as superoxide dismutase, SOD) is considered for therapy of pathological processes in CNS. The goal of this study was to investigate the influence of SOD formulations in the acute contusion spinal cord injury in rats.
Methods: Nanozymes based on block-ionomer complexes of SOD and poly-L-lysine-PEG was synthesized using cross-linker DTSSP (1). We used a standard model of acute contusion spinal cord injury in rats using IH Spinal Cord Impactor 0400 («Precision Systems and Instrumentation», USA). Animals were divided on 3 groups (n = 8) and injected with nanozyme and native SOD at 20,000 U/kg or the same volume of saline (control) in 30 min after formation of trauma. MRI control of post-traumatic injury size was performed on day 3 and week 6 after surgery. The recovery of sensorimotor function of rats with spinal cord injury was monitored by standard BBB-test during two months. After that, the immunohistochemical analysis was performed with application monoclonal antibodies to MBP and 2B6.
Results: Stable nanozymes with average size about 30 nm were synthesized and characterized. Comparison of pharmacokinetic parameters of formulations showed that nanozyme had prolonged circulation in blood in comparison with free SOD. SOD-formulations promoted the recovery of animals after spinal cord trauma. MRI analysis showed, that the size of the spinal cord injury was significantly smaller in the groups that were administered experimental drugs, compared with control group on day 3.
Conclusion: According to our data one can conclude that formulations based on SOD had a biological anti-inflammatory effect, which was fixed by MRI analysis on day 3.

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INCORPORATION OF ANTIMICROBIAL PEPTIDES INTO NANOFIBRES AS A POTENTIAL ANTIMICROBIAL SURFACE COATING OF INANIMATE SURFACES

T. H. B. Eriksen[1], E. B. Moeller[1], P. Fojan[2]
[1]Danish Building Research Institute (SBi), Aalborg University, A. C. Meyers Vænge 15, DK-2450, Copenhagen SW, Denmark
[2]Department of Physics and Nanotechnology, Aalborg University, Skjernvej 4A, DK-9220, Aalborg East, Denmark

During the last couple of years there has been an increased awareness of the importance of hygiene in order to reduce the danger level of infections. As pathogens can persist on inanimate surfaces for weeks and even months, inanimate surfaces can act as reservoirs for pathogens if left untreated. Effective reduction of the total amount of pathogens present on the respective surfaces can be difficult to achieve by traditional cleaning. We believe that a combination of traditional cleaning and bioactive surface coatings of inanimate surfaces could be an effective way to reduce the danger level of infections. Antimicrobial peptides (AMPs) are prime candidates for being incorporated into such bioactive surface coatings due to their characteristic mode of action both as antimicrobial- and immunological agents.
The focus of the presented work is to explore the possibility of reducing the risk of infections by utilising bioactive nanofibres as an antimicrobial surface coating of inanimate surfaces. To test this hypothesis, polyethylene oxide (PEO) and poly(ε-caprolactone) (PCL) nanofibres loaded with fluorescently labelled AMPs were produced by electrospinning. By labelling the AMPs, it was possible to investigate both the spatial distribution of the AMPs within the fibres and their release characteristics. Furthermore, the activity of the loading agents both before and after being incorporated into nanofibres was investigated.
Our investigations have shown that it is possible to incorporate antimicrobial agents including antimicrobial peptides into nanofibres. Based on the polymer and solvent used in the process, it seems that it is possible to both obtain different degrees of loading efficiencies along with different degrees of uniformity in the distribution of the loading agents within the fibres. Furthermore, we found that there seems to be a difference in both the release rate and the release profile of the different loaded fibres depending on the type of loading agent being released. Many of the results obtained in this work are not limited to surface coatings of inanimate surfaces but could be used for a broad range of applications within the fields of nanobiotechnology and drug delivery.

IMMUNOTROPIC AND ANTIBACTERIAL PROPERTIES OF BIOMATERIALS BASED ON CHITOSAN SALTS

I. V. Zudina, A. B. Shipovskaya, V. I. Fomina, N. V. Petrova
Saratov State University named after N.G. Chernyshevsky, Saratov, Russia

Often, attempts to eliminate the infectious agents do not represent a definitive therapy in a lot of diseases and the exploiting more sophisticated treatments are required. The pharmaceutical inhibition or control of all pathways associated with inflammation and tissue destruction may prove to be an effective treatment strategy. Our researches were focused on the use of chitosan acid salts as active antimicrobial and immunomodulatory biomaterials which could be easily formed as gels, films, membranes and nanofiber scaffolds.
Chitosan preparations of several viscosity-averge molecular weights and degrees of deacetylation were used (39, 200 kDa and 79,

82%, respectively). Chitosan salts were obtained by mixing chitosan with acetic acid, ascorbic acid, or glycolic acid and were produced as films, nanofiber scaffolds, and gels. Bacterial killing assays were performed using *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aerugenosa* and *Bacillus cereus* cultures. Numerous animal studies (mouse, rat and rabbit models) on using chitosan salts to treat of wounds of various origins were carried out. The levels of pro- and anti-inflammatory cytokines in culture media and in the different biological liquids were estimated by Enzyme-linked immunosorbent assay (ELISA).
Our in vitro studies revealed that the chitosan acid salts were effective in inhibiting the growth of most of the tested bacteria, except for *Bacillus cereus*. In vivo animal tests demonstrated that the chitosan salt films, nanofiber scaffolds, and gels eliminated the microbial cells in wounds and burns due to both the antimicrobial properties of chitosan and its ability to enhance the functions of neutrophils, macrophages and fibroblasts.
The application of the chitosan acetate nanofiber wound dressing on wounds of various origins caused an acute decrease in levels of some proinflammatory cytokines in serum, promoted a shortened phase of exudation, and stimulated tissue regeneration. The effect of the gum treatment with the gel-like form of the chitosan ascorbate on the levels of cytokines in the periodontal pockets liquid was studied. Chitosan ascorbate has been found to exhibit a pronounced anti-inflammatory activity, probably through regulation of the IL-1β and TNF-α cytokine levels in the inflammatory focus.
These results suggest that chitosan salts will continue to be important biomaterials in the management of wounds, burns, and many infectious diseases.

TRANSFECTION OF KASUMI-1 CELLS WITH A NEW TYPE OF POLYMER CARRIERS LOADED WITH MIR-155 AND ANTAGO-MIR-155

O. V. Klimenko, M. Shtilman
D. I. Mendeleyev University of Chemical Technology, 9 Miusskaya Square, Moscow, Russia

Previous studies have demonstrated functional roles for miRNAs in various aspects of normal and malignant haematopoiesis, including lineage commitment, differentiation, apoptosis, and maturation. In vivo delivery of naked DNA, oligonucleotides and miRNAs is complicated by their low stability, rapid degradation and inefficient delivery into target cells. In our experiments, we used a new type of polymer carriers to monitor the effects of miR-155 and antago-miR-155 on the morphology and genetics of Kasumi-1 cells. The carriers were used aggregates of amphiphilic Poly-N-vinylpyrrolidone having Mn=3500, containing one hydrophobic n-octadecyl end group. Total RNA was extracted from cell culture using the RNAeasy Mjni kit (Qiagen, USA) according to the manufacturer's protocol. In our experiments we used a two-step reverse transcriptase-PCR procedure with some modifications of the PCR amplification step. Leishman-Romanowsky staining of the Kasumi-1 cells we made in accordance with Blood safety and clinical technology guidelines on standard operating procedures for hematology. We obtained platelet-like cells from leukemic cells, and detected the expression of platelet marker genes after transfection with antago-miR-155. Our findings suggest that administration of miR mimics or antago-miRs as therapeutic agents is a desirable goal for future treatment of hematologic malignancies and that polymer-based carriers for the delivery of miR mimics or antago-miRs may provide a solution to the challenges of standard miR delivery approaches.

TARGETED LIPOSOMAL NANOCARRIERS FOR ANTICANCER DRUGS BASED ON PLATINUM SALT

I. I. Kuznetsov[1,2], T. O. Sandalova[1], K. Y. Vlasova[1,3], A. V. Kabanov[3,4], N. V. Nukolova[1,3], V. P. Chekhonin[1]
[1]Serbsky National Research Center for Social and Forensic Psychiatry, Moscow, Russia, [2]Department of Materials Science, Lomonosov Moscow State University, Moscow, Russia, [3]Department of Chemistry, Lomonosov Moscow State University, Moscow, Russia, [4]Center for Nanotechnology in Drug Delivery and Division of Molecular Therapeutics, University of North Carolina at Chapel Hill, Chapel Hill, USA

Platinum derivatives are widely used for treatment of cancer, but they characterized by high systemic toxicity and rapid elimination from the body. To increase the maximum tolerated dose of such drugs and improve pharmacokinetic characteristics, drugs can be encapsulated into nanocontainer systems. The goal of this work was to develop and analyze stable targeted liposomal nanocontainers which are efficiently loaded with cisplatin (CDDP) and cis-diamindinitratplatin (II) (CDDP3).
The synthesis of drug-loaded liposomes conjugated with monoclonal antibodies (mAbs) involved three steps: 1) formation of lipid film, 2) loading of drugs by emulsification of lipids in an aqueous solution of platinum salt ([CDDP] = 3 mg/ml, [CDDP3] = 15 mg/ml) and 3) conjugation with mAbs via PEG-linker. Unbound mAbs and free drug were eliminated by gel filtration chromatography. Physicochemical characteristics of the loaded liposomes were studied by dynamic light scattering and X-ray fluorescence analysis. Activity of conjugated mAbs was determined by ELISA assay. The cytotoxic effects of obtained formulations were studied on glioma C6 cells, using MTS-test.
As a result of this study the stable negatively charged targeted-liposomes with diameter about 150 nm were prepared. Loading efficiency was 2.3±0.3 % and 11.5±2.3 % for CDDP and CDDP3, respectively. ELISA assay indicated the activity of mAbs after conjugation. Cytotoxicity of CDDP and CDDP3 decreased after their loading into liposomes, due to the slow drug release. Dil-labeled mAbs-conjugated liposomes showed enhanced internalization in comparison with untargeted liposomes in glioma C6 cells, which led to their increased cytotoxicity.
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ENZYME-CONTAINING SYSTEMS BASED ON Fe_3O_4@MAGNETIC NANOPARTICLES: PREPARATION AND PROPERTIES

D. N. Lebedev [1,2], A. A. Kuznetsov [2], A. G. Majouga [2], Y. I. Golovin [2,3], A. V. Kabanov [2,4], N. L. Klyachko [2,4]
[1, 2]Department of Materials Science (1) and Department of Chemistry (2) M.V. Lomonosov Moscow State University, Moscow, Russia, [3]Tambov State University, Tambov, Russia, [4]The University of North Carolina at Chapel Hill, Chapel Hill, USA

In the modern literature magnetic nanoparticles are actively suggested for use in different biomedical applications: improving of MRI contrast, targeted drug delivery, hyperthermia. This work describes study of a novel effect: influence of a low frequency non-heating magnetic field on catalytic properties of alpha-chymotrypsin immobilized on Fe_3O_4@Au core-shell magnetic nanoparticles.
In this work Fe_3O_4 magnetic nanoparticles were synthesized by coprecipitation from solution of iron chlorides in ammonia aqua solution. These nanoparticles were subsequently coated with gold shell and finally stabilized by mixture of ligands: lipoic acid and polyethylene glycol in different ratios.
Obtained nanoparticles were characterized by TEM, AAS, optical spectroscopy, NTA, magnetic measurements. Nanoparticles were ferromagnetic and thus external changing magnetic field should lead to oscillations (turns) of nanoparticles. Concentrations of particles were $5*10^9$ – 10^{11} part/ml, size of magnetic core – 10 ± 2 nm.
Immobilization of alpha-chymotrypsin on surface of nanoparticles was made with use of carboxyl groups of lipoic acid and surface amine groups of enzyme. Enzyme activity was determined spectrophotometrically at 380 nm by increase of BTNA hydrolysis product concentration.
In order to reveal effect of low-frequency magnetic field (50Hz, 110kA/m) on -chymotrypsin – nanoparticles system, enzyme activity was measured after exposure of cuvette with immobilized chymotrypsin to magnetic field. Influence of magnetic field was estimated as ratio of enzyme activity in exposed cuvette to control cuvette. As a result, each subsequent exposure in magnetic field leads to decrease of enzymatic activity down to 10%-50% of initial activity after 4 exposures. Changing of catalytic activity arise from action of deforming forces, which change active enzyme conformation. These forces arise as a result of turns of magnetic nanoparticles in changing magnetic field.
Thus it was shown that non-heating low-frequency magnetic field decrease activity of enzyme, immobilized on magnetic nanoparticles. Obtained results indicate the ability of a control of biochemical reactions in suspensions of magnetic nanoparticles by applying of external changing magnetic field.
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THE FUNCTIONALIZATION OF THE SURFACE OF MAGNETITE NANOPARTICLES WITH ENZYME: THE EFFECT OF MAGNETIC FIELD

M. V. Efremova[1], N. L. Klyachko[1], Yu. I. Golovin[2], A. A. Kuznecov[1], A. G. Majouga[1], A. V. Kabanov[3]
[1]Moscow State University, Moscow, Russian Federation, [2]Tambov State University, Tambov, Russian Federation, [3]Center for Drug Delivery and Nanomedicine, University of Nebraska

At the present time, some attempts of the application of superparamagnetic Fe_3O_4 nanoparticles as agents-intermediaries of localized control of biochemical reactions are known, in which radio frequency magnetic field can play a role of trigger which activates or interrupts/slows down an enzymatic reaction. The goal of this work was to investigate effects of magnetic field on catalytic properties of the magnetite-immobilized chymotrypsin.
Nanoparticles of iron oxide Fe_3O_4 were coated with gold or functionalized with oleic acid, then different organic molecules (L-cysteine, lipoic, 3- mercaptopropionic acids, dodecanoic and PEG acid with HS-groups or copolymers PAA-PEG/PMA-PEG) were bound to these complexes, then the enzyme was attached.
To study the effect of magnetic field on catalytic properties, the reaction of hydrolysis of N-benzoyl-L-tyrosine-para-nitroanilide catalysed by chymotrypsin was used. In all samples (except containing dodecanoic and PEG acids) which were exposed to magnetic field the enzyme inactivation after each exposition was observed, even if the substrate was added after the expositions. That indicates the direct influence on immobilized chymotrypsin. The absence of any effect for the samples with dodecanoic and PEG acid with HS-groups can be explained by big length and flexibility of these molecules and weaker binding between nanoparticle and the enzyme molecule in this case.
Also the enzyme activity versus field intensity at the frequency of 50 Hz was studied. It can be mentioned that all series of activity-field intensity curves have maximum (corresponding to inactivation at the level of 30 ± 5%). The presence of maxima in these plots indicates the existence of competitive processes which appear as a result of magnetic field different intensity and influence the kinetics oppositely. The most probable reason for the observed effect is the change of active centers topology on the enzyme surface as a result of its deformation under applied forces.
Thereby, the effect of magnetic field on catalytic properties of chymotrypsin immobilized on magnetite nanoparticles, notably the slowdown of catalysed reaction, was found. From practical point of view it can give an instrument for drug delivery and remote dosage of their activity.

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DESIGN OF POLYMERIC BIOMATERIALS BASED ON CHITOSAN FOR OPHTHALMOLOGY APPLICATION

A. B. Ismailova[1], E. O. Batyrbekov[2], Z. T. Utelbaeva[3]
[1]Kazakh-British Technical University, Almaty, Kazakhstan, [2]Institute of Chemical Sciences, Almaty, Kazakhstan, [3]Kazakh National Medical University, Almaty, Kazakhstan

Polymer-based biomaterials are becoming increasingly important in ophthalmology due to considerable advantages of improving drug availability and decreasing side effects compared to conventional therapeutic methods. In the present study the design and properties of polymeric biomaterials based on chitosan for ophthalmology application in the treatment age-related macular degeneration have been described. The chitosan gels and films containing different doses of emoxipine or mexidole were developed. The release of drug from chitosan biomaterials was studied in vitro experiments. The effect of polymers concentration and the drug loading (1.0, 5.0 and 10%) on the release profile of mexidole were investigated. The amount of drug release was much higher initially (approximately 25%), followed by a constant slow release profile. All the release data show the typical pattern for a matrix controlled mechanism. The cumulative amount of released drug was linearly related to the square root of the time and the release rate decreased this time. It was established that process of release occurs on the mechanism of diffusion and erosion with reduction of rate. Polymeric biomaterials were used for treatment of age-related macular degeneration at 24 patients. The experimental and clinical tests show that implantation of films to suprahoroidal area did not cause the pathological changes in the membrane of eyes and help to activate the formation of vascular anastomoses in 1 month. The positive effect is prolonged up to 6 month in 63 %. The results obtained in the present work have shown the perspectives of use polymeric biomaterials based on chitosan as a matrix for prostaglandins delivery for application in ophthalmology for the treatment age-related macular degeneration.

ABSORPTION AND DISTRIBUTION OF LIPOSOMAL FORMULATIONS WITHIN THE RAT LIVER

R. A. Mukhamadiyarov[1], M. A. Pautova[2], E. A. Velikanova[1]
[1]Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia, [2]Kemerovo State University, Kemerovo, Russia

Aim. In our study we used fluorescent dye PKH-26 to evaluate the absorption and distribution of liposomal formulations within the rat liver.
Materials and methods. Liposomal formulations were obtained from egg lecithin and cholesterol in a molar ratio of 7:5. The dye was introduced into the lipid membrane of liposomes at the stage of the preparation of the lipid film. We used 3 different types of liposomal formulations, namely, (1) multilamellar vesicles (800-1500 nm) obtained from hydration of the lipid film and 5 consecutive freeze-thaw cycles, (2) liposomes with a diameter of 90-120 nm, obtained from multilamellar vesicles by 10-fold extrusion through polycarbonate filters with a pore size of 100 nm, and (3) liposomes with a diameter of 60-75 nm obtained from the second type of liposomes by extrusion 20-fold extrusion through polycarbonate filters with a pore diameter of 50 nm. Liposomal formulations were introduced into the tail vein of rats. Evaluation of the accumulation of liposomes in the cells was performed on cryosections after 1, 2, and 24 hours using the fluorescent microscope. The quantity of liposomes was assessed by the magnitude of luminescent signal in the chloroform-methanol extract obtained from tissue homogenate.
Results. Labeled liposomal formulations were used to evaluate the absorption of vesicles by the liver and in addition, to visualize the distribution of the dye in different liver cells. We found that absorption depended on the size of particles introduced to the liposome. The dynamics of the fluorescent label was same for all the liposomal formulations. The maximum of the fluorescent dye concentration was observed at 1 hour after administration of formulations. The highest concentration of the dye was observed for multilamellar vesicles (80%). Lower concentration was observed for 50 and 100 nm liposomes. The concentration of the fluorescent label decreased at the 2 hour of administration. The highest decrease in dye concentration was observed for multilamellar vesicles (50% lower). At the same time, 100 nm liposomes demonstrated the lowest rate of decrease. 50 nm liposomes had intermediate values of decrease. All groups demonstrated an increase in the concentration of the dye in the liver after 24 hours after administration.
The analysis of images revealed that introduction of labeled dye resulted in a bright glow of tissues in the red spectrum corresponding to emission from the dye PKH-26. These findings indicate active absorption of liposome formulations by liver tissue. The fluorescence of the dye was sufficient to detect the histological structure of the organ. The dependence between the absorption of lipid vesicles and the diameter of the particles was revealed.

INTERACTIONS OF HIV-1 INTEGRASE AND REVERSE TRANSCRIPTASE: CHARACTERISTICS AND INHIBITION BY NANOCOMPLEXES

O. V. Kondrashina[1], E. S. Knyazhanskaya[1], S. P. Korolev[1]
[1]Lomonosov Moscow State University, Chemistry Department, Moscow, Russia

Oligonucleotide-peptide nanocomplexes were shown to inhibit early stages of HIV-1 replication cycle: reverse transcription and integration. These steps are catalyzed by viral enzymes reverse transcriptase (RT) and integrase (IN), respectively. On the assumption of the retroviral replication mechanism, RT and IN should interact. *In vitro* experiments show a mutual binding between IN and RT and domains responsible for binding were identified in both proteins. Inhibition of this interaction can cause a decrease of virus infectivity. The binding between IN and RT was inhibited by oligonucleotide-peptide nanocomplexes. To study the mechanism of inhibition we tried to explore the details of IN and RT interaction and to define the IN structural elements necessary for RT binding.
We prepared several IN mutants containing substitutions in the C-terminal domain (CTD), which is both necessary and sufficient for binding RT. IN mutants K258A, W243E and V250E are shown to inhibit reverse transcription within HIV-1 infected cells. We also prepared integrases containing mutations R228A, D229A, R231A, D232A, K236A in the CTD, but not in the region 242-258, which is shown to be important for IN-RT interactions. Finally, IN C130S contained a mutation in the catalytic domain. All mutants were tested for their catalytic activity. It was established that the W243E substitution almost completely inhibits IN activity. IN catalytic activity was also significantly decreased by mutations R228A and K258A; mutations D229A, D232A, and K236A reduced the catalytic activity of the enzyme in half, and the mutation D231A increased it. The direct physical interaction between IN mu-

tants and RT was studied in GST pull-down assay using purified proteins. The effect of all mutants obtained on the RNase, DNA- and RNA-dependent DNA polymerase activities of RT was also studied. No significant effect on the efficiency of DNA/RNA substrate hydrolysis was detected for any of the IN samples. In the case of DNA- and RNA-dependent DNA synthesis a slight inhibitory effect of all samples except IN mutants R228A, W243E, V250E, and K258A was revealed.

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BIODEGRADATION OF POLYHYDROXYALKANOATES IN TROPICAL CONDITIONS

A. N. Boyandin[1], S. V. Prudnikova[2], 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

As the volume of production increases and the fields of PHA application are extended, it becomes relevant to study the mechanisms of their destruction under various natural conditions. Biodegradation of film and pellet specimens from polyhydroxyalkanoates (PHAs) of two types – poly-3-hydroxybutyrate (PHB) and poly-3-hydroxybutyrate-co-3-hydroxyvalerate (PHBV) – was analysed in different environments in Vietnam: tropical sea waters of the South China Sea (Nha Trang), fresh waters of stagnant reservoir in Dam Bai Environmental Station and Kai River (Nha Trang), and soils in the environs of Hanoi and Nha Trang.
PHA films (30 mm diameter disks) were prepared by casting chloroform solution technique. Compact pellets (10 mm diameter) were prepared by cold compaction of powdered polymer. PHA specimens (3 of each type) were weighed and placed in close-meshed gauze jackets, and then buried in water or soil. At definite time intervals, specimens were taken out from one of jackets, cleaned, dried, and weighed. Biodegradation of PHAs was evaluated by decrease in the mass of the specimens and changes in the molecular weight of polymers. For isolation of PHA degrading microorganisms, samples from the surface of polymer specimens were inoculated onto the mineral medium with 0.25% powdered poly-β-hydroxybutyrate as sole carbon source. Growth of true PHA degraders was accompanied by the formation of clear zones around colonies of microorganisms. Bacteria and fungi isolated were identified by their cultural and morphological properties, biochemical tests and 16S rRNA gene sequence analysis. PHA film specimens were degraded at a faster rate than polymer pellets. In seawater and Kai River water, the mass loss of the specimens of both polymer types (PHB and PHBV) was almost equal. In tropical soils and in stagnant reservoir (Dam Bai), PHB degraded quicker than PHBV. This discrepancy can be accounted for by differences in soil microbial communities and, hence, substrate specificity of secreted extracellular PHA depolymerases. Molecular mass of PHA specimens decreased during biodegradation. In the tropical sea conditions, PHA degrading microorganisms were represented by bacteria of Enterobacter, Bacillus and Gracilibacillus genera. Burkholderia, Alcaligenes, Bacillus, Mycobacterium and Streptomyces genera were identified in soils. Micromycetes of Gongronella, Paecilomyces, Penicillium and Trichoderma genera exhibited PHA degrading activity in soils. In tropical fresh water conditions, PHA degrading bacteria of Bacillus, Micrococcus, Streptomyces genera were identified.

DEVICES FOR BIOMEDICINE, PRODUCED BY NATURAL BIODEGRADABLE POLYMERS

E. I. Shishatskaya[1,2]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia, [2]Siberian Federal University, Institute of Fundamental Biology and Biotechnology, Krasnoyarsk, Russia

Tissue restoration after traumas, surgical operations and other damaging situations is very actual medical problem and needs new materials. Polymers of various origins are under the focus of researchers in cross-emerging disciplines.
We are synthesizing highly purified PHAs-samples, Bioplastotan™, synthesized by bacteria Ralstonia eutropha B5786 under specific grow conditions for the developing and production of devices for reconstructive medicine, as a scaffolds for tissue engineering and other implantable constructions. Basing on high biocompatibility and having techniques of varying polymer properties and rates of biodegradability of implants, we can made practically whole human body components of one natural material. Biocompatibility of polyhydroxyalkanoates of various compositions with trademark Bioplastotan™ was proved in the numerous in vitro and in vivo works. Wide range of physical properties, causing by various copolymer compound make possible different processing techniques for the developing and production of various biomedical devices. Gel-spun technology and melt extrusion were used to produce solid monofilaments which were proved to be suitable as a bioresorbable surgical suture material. Electrospinning is in use for the production of nonwoven tissue and 3D devices. Various ways of molding and scanning are approved for the imitation of extracellular matrix of hard tissues so as fixing implantable devices. Experiments are performed in vitro, ex vivo, in vivo. The first stage of clinical trials was performed for some devices – bile stents, surgical meshes, nonwoven. Fabrics, which were assigned for the tissue reconstruction as a artificial ECM-scaffolds, shown as biocompatible towards cultures of cells of different origins. This type of natural microbial polyesters is very perspective for the restoration of soft tissues - skin, mucosa, ducts, ligaments, so as hard one, as bone and cartilage.

COMPARATIVE ANALYSIS OF HYDRODYNAMIC PARAMETERS OF HEART VALVE BIOPROSTHESES: "UNILINE" AND "PERICOR"

K. Klyshnikov[1], E. Ovcharenko[1], D. Malcev[2], I. Zhuravleva[1]
[1]Siberian Branch RAMS Institution "Scientific-Research Institute for Complex Problems of Cardiovascular Disease", Kemerovo, Russia, [2]"NeoCor" Company, Kemerovo, Russia

Aim: To make a comparative assessment of hydrodynamic parameters of Russian xenoaortical bioprostheses "PeriCor" and xenopericardial bioprostheses "UniLine".
Research methods: there have been studied 16 bioprostheses "PeriCor" and 14 bioprostheses "UniLine", designed for clinical use;

rim diameter 28 mm. The research was done in Vivitro pulse duplicator (Vivitro Labs Inc., Canada) which allowed to simulate the physiological mode of a mitral valve.
Results: Peak gradient median for "UniLine" group equals 5,3 mm Hg, with 6,1 mm Hg for "PeriCor" group. Average gradient median for "UniLine" group equals 3,0 mm Hg, with 2,8 mm Hg for "PeriCor" group. Effective orifice area for "UniLine" group equals 2,3 cm^2, with 2,6 cm^2 for "PeriCor" group. The performance index was 37.4% and 42.2% respectively. Leakage volume was 2,7 ml per cycle in "PeriCor" group and 3,4 ml in "UniLine" group.
Conclusion: The research have not elicited any statistically significant difference between the mentioned types of bioprostheses in terms of hydrodynamic parameters. Hydrodynamic parameters of the both groups of bioprostheses are consistent with literature data on world equivalents. There have been fixed incomplete opening and leaflets overstrain of bioprosthesis "UniLine", which causes inefficient constructive stenosis. This fact suggests the possibility of leaflet apparatus and support frame revision in order to improve the hydrodynamic performance.

THE ANALYSIS OF EPOXY-TREATED STENTED HEART VALVE BIOPROSTHESES DYSFUNTIONS IN MITRAL POSITION

V. Borisov, A. Burago, Yu. Odarenko, N. Rutkovskaya
Federal State Budgetary Institution Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

Kemerovo Cardiac Center has a leading position in development and production the epoxy-treated biological implants for cardiovascular surgery. Also it has a unique clinical trial of these bioprostheses.
From 1991 till 2009, December the 368 epoxy-treated heart valve bioprostheses were implanted in mitral position. Mean age of patients was 52,6±8,7 (13-73 yrs) years.
Aim: Analysis the dysfunction reasons of the "KemCor" and "PeriCor" heart valve bioprostheses removed on the re-operations in mitral position.
Material and methods: At the present time the 88 bioprostheses were removed due to dysfunction. All the bioprostheses were underwent macroscopic description and the histological tests. The microscopic slides were prepared using hematoxylin-eosin, Van Geison and Koss methods. The structure of calcium deposits in biomaterial, bacterial contamination was studied using scanning electron microscopy (SEM) on Hitachi S3400N microscope and the Bruker Quantax EDX-spectrometer.
Results: The 66 samples of "KemCor" and the 22 PeriCor" heart valve bioprostheses were studied. It is the 23.9% from the total amount of the implanted ones. In 34 cases (38.6%) the infective endocarditis was the reason of dysfunction. Histologically tests showed the colonies of bacteria, local leucocytes deposits, and some calcified bacteria. SEM method also determined the calcified cocci in the some samples.
The primary tissue failure with calcification was observed in the 40 cases (45.5%), without calcification - 10 cases (11.4%). The calcium deposits are located in the spongy layer of the bioprostheses leaflets predominantly. SEM and X-ray spectrum analysis determined that the calcium crystals are the hydroxyapatite presented in the amorphous and crystal forms.
Thrombosis and the non-valve related dysfunctions were observed in 4 cases (2 and 2).
*Conclusions:*The main reason of the epoxy-treated heart valve bioprostheses dysfunction in mitral position was primary tissue failure with calcification (10.9% from the total amount of implanted bioprostheses). The risk of tissue degeneration without calcification is 2.7%.

ANALYSIS OF NEW HIGH-MOLECULAR BIODEGRADABLE NONIONIC SURFACTANTS

G. I. Boiko[1] , Y. Orazbekuly[1], N. P. Lubchenko[2], T. P. Maimakov[2], Y. M. Shaihutdinov[1].
[1]Kazakh National Technical University named after K.I. Satpaev, 22 Satpaev str., Almaty, Kazakhstan, 050013, [2]Highest educational college "UNAT", 22a Satpaev str., Almaty, Kazakhstan

The method of chemical modification of copolymers of maleic anhydride with surfactants was developed. By catalytic esterification the new high-molecular nonionic surfactant «SMATWEEN» was obtained.
Based on data of kinetic studies designed optimal synthesis conditions. It has been suggested that the optimal synthesis conditions of novel reagent is 130°C for 80 minutes. The rate constant and activation energy were calculated. It was concluded that the catalytic esterification of Polyoxyethylene sorbitane Trioleate with copolymer of styrene and maleic anhydride in the presence of pyridine is of the 2nd order and proceeds by bimolecular mechanism.
To gain insight into the chemical composition of Polyoxyethylene sorbitan Trioleate,-Monooxycarbonylbutenic acid, copolymer was analyzed using NMR spectrometry. 1H nuclear magnetic resonance (NMR), ^{13}C NMR, COSY and HSQC spectra were obtained in deuterated dimethylsulfoxide with Bruker Avance-3-400 device.
In the ^{1}H NMR spectrum of the synthesized reagent the peak at δ =4.17 ppm may be assigned to -CH_2-C(O)-O-C- in the formation ester group and δ = 2.58 ppm is attributed to two methylene protons in -(-OOC)HC-CH(COO-)-.
In the ^{13}C NMR spectrum of the product band at δ = 61 ppm is attributed to -C-O-C- and band at δ = 163.5 ppm to C=O in formation ester group. The band at δ = 205 ppm is attributed to the C=O bonds in the -COOH group. The peak at δ = 41.5 ppm is attributed to the –HC-CH– bonds in -(-OOC)HC-CH(COO-)-. Due to the formation of the complex has been a shift of band of the carboxyl group to 205 ppm.
In the 2D COSY spectrum the order of the methyl and methylene groups in the structure of reagent was found. The COSY spectra assisted in confirming the assignment of CH2 groups of -CH2-C(O)-O-C- in the formation ester group (4.17 ppm) that correlate with the neighboring CH_2 group in -CH_2-O-CH2- in polyoxyethylene moiety (3.5-3.6 ppm). In the HSQC spectra bands at δ=2.58 ppm and δ=5.3 ppm shows a cross peak at δ=41.5 and δ=130 ppm, related to the methylene groups of –HC-CH– and –HC=CH– bonds in the formation ester group and oleic moiety respectively. The band at δ=4.17 ppm gives a cross peak to the band at δ=41.55 ppm, which belongs to -CH_2-C(O)-O-C- bond in the formation ester group.
Molecular mass characteristics of the modified polymers were determined by gel permeation chromatography using a device «Shi-

madzu Prominence GPC System». Fourier transform infrared (FTIR) spectra were registered on a Shimadzu FTIR-8400.
The possibility of use the reagent as emulsifiers, solubilizers, dispersants, wetting agents, defoaming agents, excipients, and demulsifying agent to create or destroy water-oil emulsions was shown.

NANOMECHANICAL APPROACH TO THE CONTROL OF BIOCHEMICAL REACTION

Yu. I. Golovin*[1,2], N. L. Klyachko[2,3], D. Yu. Golovin[1], M. V. Efremova[2], D. N. Lebedev[2], M. M.Veselov[2], A. A. Samodurov[1], M. Sokolsky-Papkov[3], A. V. Kabanov[3,2]
[1]Nanocenter, Derzhavin Tambov State University, Tambov, Russia, [2]Lomonosov Moscow State University, Moscow, Russia, [3]University of North Carolina, Chapel Hill, NC, USA

In this study, we have proposed and tested a new area in the use of single domain magnetic nanoparticles (MNPs) as messengers for nanomechanical control of topology and catalytic properties of bioactive macromolecules (e.g., enzymes). The deforming force is applied to macromolecules as a result of turning MNPs under exposure to an external low frequency magnetic field (LF MF). Depending on whether the macromolecule is linked to one or two/several MNPs (which is determined by the concentration of MNPs in the suspension), two different mechanisms of action of magnetic field on macromolecules—hydrodynamic and contact can be realized. The first is similar to the hydrodynamic stretching of a macromolecule in a liquid. The force applied to the macromolecule in this case is proportional to LF MF frequency *f*, suspension viscosity n, and hydrodynamics radius *Rhd* of MNPs. The second situation is similar to macromolecule deformation with magnetic tweezers. In this case, maximum deforming force is inversely proportional to *Rhd* and does not depend on n and *f* .
To test this concept, we performed experiments to identify a possible effect of LF MF (H = 0 – 220 kA/m, f = 50 Hz) on the reaction $E + S$ (where *E* is the enzyme (chymotrypsin) and *S* is the substrate (*N*-benzoyl-*L*-tyrosine *p*-nitroanilide (BTNA)) in a magnetic suspension (Fe3O4 nanoparticles with a mean radius of 8–12 nm according to electron microscopy data, kindly provided by J. Riffle, Virginia Tech.). The enzyme macromolecules were linked to the MNPs through an intermediate linker molecule (polymethacrylic acid–polyethylene glycol (PEG-PMA) block ionomer 10–20 nm long). According to dynamic light scattering data, the hydrodynamic radius of nanoparticles with a coat of different block ionomers ranged from 20 to 28 nm. Then, the substrate was added to the magnetic suspension and the sample was placed in an LF MF.
The kinetics of the reaction was monitored using a Beckman spectrophotometer with a thermostated sample compartment, which recorded accumulation of the product of BTNA hydrolysis catalyzed by chymotrypsin. In samples exposed to LF MF, the reaction was decelerated after each exposure in the field. The greatest deceleration of the reaction was observed after the first exposure to the magnetic field. The effect increased with field intensity at H values up to ≈100 kA/m and began to decrease under exposure to a strong magnetic field.
Heating the suspension in a magnetic field of such a low frequency (f = 50 Hz) can be neglected (both the overall heating of the sample and the local heating of MNPs during the exposure to the magnetic field, according to our estimates, did not exceed 10^{-4}K).
The most likely cause of the observed effect is the change in the topology of the active site of the enzyme molecule as a result of its irreversible (or at least long-stored) deformation by the applied forces.
Thus, we propose a new approach to the control of biochemical reactions and discovered the effect of a weak LF MF on the kinetics of the enzymatic reaction in the magnetic nanosuspension. Magnetomechanical spectroscopy of relaxation processes in the system can provide information about the elementary acts and intermediate states in the system, as well as elucidate the atomic/molecular mechanisms of catalysis and functioning of active sites in the enzyme macromolecule. From the practical point of view, this may provide novel approach to control targeted delivery of drugs, their remote release, etc.

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INNOVATIVE ANTIMICROBIAL NONWOVEN - MODERN SURGICAL DRESSINGS IN THERAPY OF POSTOPERATIVE WOUNDS IN ORTHOGNATIC SURGERY

S. K. Lopandina, Z. J. Kozinda, T. A. Podgaevskaya, O. O. Erofeev, T. V. Moreva
Central Research Studies Institute of Clothing Industry", Moscow, Russia

The goal of the study was the development of production technology and study of innovative antimicrobial nonwoven for the treatment of postoperative wounds in orthognatic surgery.
Scientists of OJSC "Central Research Studies Institute of Clothing Industry" developed antimicrobial multilayer nonwovens consisting of viscose, polyester and polypropylene fibers and made by way of needle-punched.
For antimicrobial treatment the nonwoven web, adjoining to the wound surface, were used broad-spectrum drugs:
- compounds of a variety of furan;
- surface-active materials with antiseptic properties;
- sulfanilamides.

The tests *in vitro* have showed that the treated materials have a high antimicrobial activity toward the most gram-positive and gram-negative aerobic and anaerobic microorganisms.
It is developed a method to determinate the sorption capacity of nonwoven web, which allows to determine the capillary properties in horizontal way what simulates the absorption process of exudate from the wound surface. It is realized a comparison of the kinetic parameters of the absorption process of the different nonwoven webs with agent, similar to the pH and the relative density of the exudate, by using this method.
This allowed the selection of the raw materials, structure and technical process parameters to manufacture nonwoven web, which ensure maximum sorption capacity. This nonwoven web made of polypropylene and polyester fiber was used as the inner layer of a multilayer nonwoven.

The outer layers of a multilayer nonwoven made of hydrophilic viscose fibers have less porous structure than the inner layer because of the high density of punching. This creates optimal conditions for antimicrobial treatment of the bottom layer, adjoining to the wound surface, of nonwoven material and reduces exudate penetration of the top layer.
Thus was formed multilayer nonwoven each structural component of which has a specific function on-treatment of post-operative wounds.
Conclusions:
- antimicrobial multilayer nonwovens with sorption capacity are developed;
- it is established that biologically active agents selected for treating the nonwovens, ensure antimicrobial activity correspond to the medical-technological requirements;
- it is showed that as a result of the chosen combination of raw materials, their chemical nature and production process parameters is obtained a multilayer nonwovens with high sorption capacity and antimicrobial activity.

3-D IN VITRO SYSTEMS BASED ON POLYELECTROLYTE MICROCAPSULES AND RGD-PEPTIDES FOR ANTITUMOR DRUG SCREENING

R. Akasov[1], M. Drozdova[1], D. Zaytseva-Zotova[1], S. Burov[2], A. Marc[3], I. Chevalot[3], E. Markvicheva[1]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia, [2]Institute of Macromolecular Compounds, St-Petersburg, Russia, [3]Laboratoire Réactions et Génie des Procédés, UPR CNRS 3349, ENSAIA-INPL, 2, Avenue de la Forêt de Haye, BP 172, Vandoeuvre-lès-Nancy, 54505, France

Presently, biocompatible materials are widely employed in tissue engineering and biotechnology. For example, biomaterials are used for preparation of biocompatible polyelectrolyte microcapsules with entrapped mammalian cells. Microencapsulation is a promising technique for diabetes treatment, somatic gene therapy, anticancer drug screening using microencapsulated multicellular tumor spheroids (MTS). As well known, the most common in vitro cell model is monolayer culture. However, cells in monolayer can not properly mimic behaviour of small size solid tumors in vivo. To generate MTS, two new approaches were proposed. First, MTS were formed by long-term cultivation of cells in polyelectrolyte alginate-oligochitosan microcapsules for 2-3 weeks, as previously described [Zaytseva-Zotova et al. (2011) J Biomed Mater Res B Appl Biomater. 97(2):255-62]. Secondly, MTS were obtained by cell aggregation induced with RGD-peptides which contain arginine-glycine-aspartic acid sequence in their structure. We have demonstrated that two peptides (e.g. cyclo-RGDfK and cyclo-RGDfK-Mod) can cause cell aggregation with further MTS formation within a range of peptide concentrations of 10-100 μM.
The aim of this study was to evaluate cytotoxicity of doxorubicin (DOX) and its derivatives in monolayer culture (2D) and in MTS (3D). The spheroids generated by long-term cell cultivation in polyelectrolyte microcapsules were used to evaluate five new DOX derivatives : two DOX preparations modified with palmitic acid (N-Palm-DOX, and Palm-N2H-DOX), DOX/5-fluorouracil, DOX-triphenylphosphine (DOX-TPP) and DOX-aminoguanidine. The spheroids generated by cell aggregation induced with RGD-peptides were treated only with DOX. Murine melanoma cells (M3) and two human breast adenocarcinoma cell lines (MCF-7 and DOX-resistant MCF-7/DXR cells) were used in this study. Cell morphology was monitored using optical and confocal microscopy. Cell viability was calculated by MTT assay in 24, 48 and 72 hours after incubation with DOX samples.
Evaluation of DOX derivatives on the spheroids derived from MCF-7 cells showed that in the case of MTS higher doses were needed to achieve the same effect like in the 2D model. This difference decreases with increasing incubation time of the cells with the drug. Both techniques mentioned above have been successfully used for MTS generation. It was obvious that the MTS due to three-dimensional structure represent a more appropriate model in vitro, than the 2D model based on monolayer cultures.

NANOFIBERS AND THEIR POTENTIAL AS A RELEASE MEDIUM OF PHARMACEUTICAL DRUGS

D. Vynias
Laboratory of Toxicology, Medical School, University of Crete, Heraklion, Greece

Electrospinning is a facile technique for fabricating fibers with average diameters in the range of micrometers to nanometers. The fibers produced by this interesting process have a high surface area to mass ratio, a small pore size with high porosity. In addition, functionalized nanofibers can be prepared with enhanced properties compared to conventional fibers. These electrospun fibers are good candidates for a wide range of applications including novel drug delivery systems. In this study, the potential use of nanofibers as drug release carriers is discussed and the parameters involved in their production are analyzed. The release characteristics of hydrophobic/hydrophilic drugs incorporated into electrospun membranes are examined.
Keywords: nanofibers, electrospinning, drug delivery, membranes, nanotechnology

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DIAGNOSTIC DNA MICROARRAYS FOR DETERMINATION OF PATHOGENS AND ANTIBIOTIC RESISTANCE

A. M. Egorov
Enzymology division, Department of Chemistry,M.V. Lomonosov Moscow State University, Russia, Moscow, 119992, Leninskie Gory d. 1/11

The aim of present study was to develop DNA microarray for the identification of single nucleotide polymorphisms (SNPs) of extended spectrum beta-lactamases and to apply it for characterization of clinical enterobacterial isolates.
The method of DNA microarray consisted of several steps involving DNA extraction from clinical samples, amplification and labeling of target DNA with different labels by PCR and subsequent hybridization of PCR product with oligonucleotide probes immobilized on epoxy-glass slides. After hybridization biotin in duplexes was developed with conjugate streptavidin-horseradish peroxidase (HRP) followed by the detection of HRP with chromogenic substrates. We developed two types of DNA microarrays with fluorescent and colorimetric detection for rapid identification of mutations in CTX-M β-lactamase genes. The sensitivity of SNP detection with colorimetric microarray was comparable with that of fluorescent microarray, the discrimination power for selected SNPs was higher for the colorimetric microarray. The concordance of CTX-M subtype identification with DNA microarray and DNA sequencing was 100%. DNA microarray technique offers the identification of a pathogen and its antibiotic resistance at the molecular level and is proposed as useful tool for epidemiological investigation of ESBL-producing organisms.
The work was supported by Russian Federal Programme "National Technological Resources"

Posters

P01

BIODEGRADABLE MICROCAPSULES/NANOPARTICLES WITH ENTRAPPED PLASMID DNA FOR DEVELOPMENT OF NEW DNA VACCINES

O. Selina[1], A. Goryachaya[2], P. Kulikov[2], V. Balysheva[3], N. Vlasova[3], I. Imatdinov[3], M. Shtilman[2], E. Markvicheva[1]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences, Moscow, Russia. [2]D.Mendeleyev University of Chemical Technology of Russia, Moscow, Russia. [3]National Research Institute for Veterinary Virology and Microbiology, Russian Academy of Agricultural Sciences, Pokrov, Russia

Polymer gene delivery systems are of great interest in gene therapy because of their safety compared to that of viral vectors. In the present study two simple universal methods for preparation of biodegradable micro- and nanocarriers with entrapped plasmid DNA were proposed and optimized. Biocompatible polyelectrolyte multilayer microcapsules (mean size 3-8 μm) were fabricated by layer-by-layer adsorption of various polyelectrolytes (such as alginate, poly-L-lysine, κ-carrageenan, modified dextrans) on calcium carbonate templates. Nanoparticles were prepared from amphiphilic derivatives of N-vinylpyrrolidone (MM 3500) modified with amino acid fragments of b-alanine ($PVPON_{Ala}$) or glycine ($PVPON_{Gly}$). It is shown that amphiphilic polymer $PVPON_{Ala}$ and $PVPON_{Gly}$ were able to form nanoparticles with an average size of 100-300 nm in aqueous solutions. They spontaneously condensed DNA by electrostatic interaction between positively charged groups of amino acid fragments and phosphate groups of DNA and formed complexes. To conduct *in vivo* tests, several sets of microcapsules and nanoparticles loaded with recombinant plasmids containing Gn/Gc glycoproteins genes and oligonucleotide CpG-motif (an adjuvant) were prepared. The techniques for immobilization of genetic materials in both types of the carriers (microcapsules and nanoparticles) which allowed to entrap 70–90 % of plasmid DNA and 70–80 % of CpG-motif were developed. An injection of these microcapsules/nanoparticles into mice was found to induce an immune response which was revealed by determination of antibodies titers in mouse sera. The enhanced response was observed for the mice immunized with carriers loaded with CpG-motif compared to these immunized with microcapsules/ nanocarriers which did not contain the adjuvant.

P02

APPLICATION OF POLYMERIC MICROSPHERES IN TECHNOLOGICAL PROCESSES OF OPERATION AND STORAGE OF LIGHT-SENSITIVE LAYERS

I. A. Gritskova[1], M. A. Sakvarelidze[2], S. M. Levachev[3], A. S. Mikhailov[2], A. E. Kharlov[2]
[1]Moscow State Academy of Fine Chemical Technology n.a. M.V. Lomonosov, Moscow, Russia, [2]Moscow Cinema Video Institute, Moscow, Russia. [3]Moscow State University n.a M.V. Lomonosov, Moscow, Russia

Investigated colloid-chemical properties of polymeric microspheres with different structure of the surface layer in order to find the conditions for their use as solid stabilizers emulsion systems, anti-static and anti-friction coating of photosensitive layers.
By Langmuir methodology studied the structure of the polymer microspheres "core-shell", defined colloid-chemical properties of 2D films formed from solid particles, and showed that the surface-active properties of the polymer particles can be changed in a wide range, the nature of the functional groups in the interphase layer of polymer particles determines their emulsifying ability.
Found regularities of changes colloid-chemical properties of 2D films formed from polystyrene microspheres when administered into the system of electrolyte (solutions of ammonium sulfate, zinc, and manganese (II)). Defined the connection between the colloid-chemical parameters of 2D films and emulsifying ability of polystyrene microspheres at different concentrations of the electrolyte in aqueous phase.
Received isotherms of two-dimensional pressure of 2D films formed from polymeric microspheres containing silicone surfactant on the surface and its mixture with gelatin.
Studied the rheological parameters of interfacial adsorption layers consisting of gelatin and polydimethylsiloxane at the interface water/xylene. Found that the flow curves have yield strengths specific to viscoelastic bodies.
Technological tests performed. Shown the possibility to use polymeric microspheres as anti-static components of protective layers and anti-friction coating of photographic materials.

P03

ENERGY EFFICIENCY ENHANCEMENT AND ENVIRONMENTAL FRIENDLINESS OF POLYMERIC SULFUR PRODUCTION PROCESS THROUGH HYDROACOUSTIC CAVITATION TECHNOLOGY

R. Ya. Deberdeev, K. A. Tereshchenko, E. B. Shirokikh, E. S. Akhmetchin, T. R. Deberdeev, N. V. Ulitin
Kazan National Research Technological University, Kazan, Russian Federation

Environmental protection is one of the major challenges of the Mankind nowadays. This challenge can be paraphrased as development of waste-free or low-waste industrial plants. For instance, one of problems of petrochemical processing industry is utilization of the by-product sulfur which can be further used in individual branches of the chemical industry. Nevertheless, apart from amorphous sulfur, there is an increasing demand in polysulfur. The interest in polysulphur in rubber production plants and in the tire industry is associated with higher quality of finished products, and their higher operational performance as compared to the use of conventional amorphous sulfur. Polymeric sulfur is obtained by shock chilling of sulfur vapors, being at 500°C, up to minus196°C which is energy inefficient and ecologically unfriendly. Therefore, the purpose of this research is to develop a lesser power and utility consuming method. It is to develop the least power and utility consuming method of polymeric sulfur

production, the product quality continued or improved hereby.
A polymeric sulfur obtaining method based on simultaneous impact of temperature up to 160-180°C, pressure up to 20 MPas, intensive shear deformations with hydroacoustic oscillatory influences over 1 kHz is offered. Formation of acoustic radiation in liquid with sound pressure amplitude causes appearance of bubbles in the liquid stream the collapse hereof builds short-term pressure impulses.

Table 1. Comparative Analysis of Polymeric Sulfur Experimental Samples and Cristeks OT-33 Polymeric Sulfur Grade

Parameters	Cristeks OT-33 Polymeric Sulfur Grade	Sample 1	Sample 2
Total Sulphur, mass %	66	78	70
Sulphur Insoluble, mass %	63	72	64
Oil, mass %	33	20	30
Ash, mass %	0,05	0,02	0,01
Acidity in terms of Sulphuric Acid, %	0,05	0,08	0,04
Thermal stability at 115°C	73	77	70

It is experimentally confirmed that when intensifying the sulphur melt treatment process at temperatures up to 160-180°C, a high-molecular product is obtained due to cavitational impact on the reaction medium,. Application of cavitational impacts on the molten sulfur reduction of the reaction process initial temperature. And it means that the developed technology is energy saving. The obtained polysulfur samples have passed all the required tests and showed the results of same level irrespective of the used sulfur type.

P04

BIODEGRADABLE ELECTRET COMPOSITE MATERIAL BASED ON POLYETHYLENE

R. Ya. Deberdeev, M. F. Calikhanov, A. A. Guzhova
Kazan National Research Technological University, Kazan, Russian Federation

Prospective way to impart biodegradability to polymers is addition of fillers, which can be a source of food for bacteria and fungi and simultaneously promote degradation of polymer chains to oligomeric fragments easily assimilated by the microorganisms. At the same time electric fields negatively affect vital processes of various microorganisms. In this case, polymer electrets, as materials producing a constant electric field possibly cannot undergo biodegradation even when modified with various fillers. Thus, the objective of the study was the development of electret biodegradable polymer material that is resistant to microorganisms during storage and operating time and biodegrade after use and landfilling.
Low Density Polyethylene (LDPE) and Starch were used as a polymer matrix and biodegradable filler respectively. Polymer compositions were mixed on laboratorial microrolls with controlled electrical heating. Samples were prepared as 0.4 mm films and plates on hydraulic press. Samples were heated in heat chamber and then cooled in the field of negative corona discharge.
The electret surface potential difference U_{EPD} of the charged samples was measured by the vibrating electrode method with compensator. Surface potential V_s, electric field strength E, and effective surface density of the electric charges σ_{ef} were measured by the method of periodic shielding of the receiving electrode located at 2 cm distance from the electret surface.
It has been shown that increase of electret effect for LDPE compositions occurs at 6 – 9 vol. % starch content due to Maxwell-Wagner polarization (on polyethylene-starch interphase) that significantly contributes to formation and transformation of electret state in heterogeneous systems. Following mechanism of filled polyethylene electret characteristic increase is rather feasible. Starch molecules as dipole traps for injected charges attract and hold them in virtue of Coulomb attraction i.e. starch molecules act as supplier of traps for injected charge carriers. PE possessing low electrical conductivity and constituting continuous phase, prevents depolarization and determines high stability of composition electret properties.
Biodegradation process was estimated by appearance and weight loss of the samples in Saburo soil-simulative medium. Charge of polymer compositions prevents their assimilation by the microorganisms during storage, usage and first days of disposal, but rapidly relaxes at humid conditions. Biodegradation of electrets after charge relaxation in the soil occurs at a higher rate compared to uncharged samples due to destruction of polymer macromolecules when charged in corona discharge.

P05

MODELING OF KINETIC PROCESSES AND HEAT EXCHANGE AT ISOBUTYLENE AND ISOPRENE COPOLYMERIZATION IN THE PRESENCE OF ALUMINIUM TRICHLORIDE

R. R. Nabiev, N. V. Ulitin, K. A. Tereshenko, R.Ya. Deberdeev
Kazan National Research Technological University, Kazan, Russian Federation

Butyl rubber is the product of copolymerization of isobutylene and a small amount of isoprene in the presence of aluminum trichloride in methyl chloride at low temperature. Process of synthesis goes on the cationic mechanism and is very fast. All reactors which are applied to industrial receiving butyl rubber are the same volume reactors of mixing. Shortcomings at these reactors much, however, the main minus is need of frequent flushing of the polymerization reactor owing to ratholing of polymer to

walls. This phenomenon is reflected in environmental friendliness of production: despite multistage treatment of wash medium, negative influence on environment it is great.
Proceeding from it, actual there is an increase in operating time of reactors before flushing by means of studying of influence of heat exchange and hydrodynamics processes. Research consisted in modular modeling of process of receiving butyl rubber. The kinetic module which is switching on kinetic model in the form of the differential balance equations on each component of studied system was initially developed. The model was given to MMD moments with use of the apparatus of generating functions. Kinetic constants of separate reactions were received from the literature, missing constants were defined by the solution of the inverse task. Theoretically and experimentally certain molecular mass characteristics of butyl rubber received at various temperatures and conversion of monomer adequacy of model of 92% showed comparison.
At the following investigation phase the heat-exchange module in the form of the differential equation of thermal balance was developed. Proceeding from it, at non-isothermal problem statement the equations of material and thermal balance taking into account dependence of reaction rate on temperature and heat-transfer process in common were solved. Adequacy of the generalized model of kinetics and heat exchange (90%) was checked by comparison of theoretically certain and experimental values of temperature and molecular mass characteristics of butyl rubber at various temperatures and at various conversion.
Thus, the complex model of copolymerization of isobutylene with isoprene in the presence of aluminum trichloride in the media of methyl chloride is developed. It is possible to believe that this model will act as a basis of an automated control system for technological process of receiving butyl rubber.

P06

INNOVATIVE METHOD OF POLYMERS' MOLECULAR-MASS PROPERTIES CALCULATION. CONCEPTION OF LINKS' BLOCKS AND ITS REALIZATION BY THE EXAMPLE OF EPOXY RESINS' HARFENING PROCESS MODELING

N. V. Ulitin, R. Ya. Deberdeev, D. A. Shyan., K. A. Tereshenko, T. R. Deberdeev
Kazan National Research Technological University, Kazan, Russian Federation

It's seldom to find in one material such successful combination properties such as in epoxy resins. Diversity of epoxy-amine matrices requires the fundamental approach of their properties estimation. One of the most important research areas is creation of hardening processes' kinetics mathematical models for theoretical determination of gelation time, from which depends acceptable time of composite materials (CM) molding, that is the task of this research.
To the base of developed model was assumed conception of links' blocks.
Calculation of this model is realized in three stages:
1. Calculation of concentration of unreacting epoxy groups and various functionality nodes concentrations:

$$\frac{dA(42)}{dt} = -(4k_1 + 2k_2)BA(42)$$
$$\frac{dA(41)}{dt} = 2k_2BA(42) - (4k_1 + k_2)A(41)B$$
$$\frac{dA(40)}{dt} = k_2BA(41) - 4k_1A(40)B$$
$$\frac{dA(23)}{dt} = 4k_1BA(42) - (2k_1 + 3k_2)A(23)B$$
$$\frac{dA(22)}{dt} = 4k_1BA(41) + 3k_2A(23)B - 2(k_1 + k_2)A(22)B$$
$$\frac{dA(21)}{dt} = 2k_2BA(22) + 4k_1A(40)B - 2(k_1 + k_2)A(21)B$$
$$\frac{dA(20)}{dt} = k_2BA(21) - 2k_1A(20)B$$
$$\frac{dA(04)}{dt} = 2k_1BA(23) - 4k_2A(04)B$$
$$\frac{dA(03)}{dt} = 4k_2BA(04) + 2k_1A(22)B - 3k_2A(02)B$$
$$\frac{dA(02)}{dt} = 3k_2BA(03) + 2k_1A(21)B - 2k_2A(02)B$$
$$\frac{dA(01)}{dt} = 2k_2BA(02) + 2k_1A(20)B - k_2A(01)B$$
$$\frac{dA(00)}{dt} - k_2A(01)B$$

where A(m,n) – part of three-ethylen-tetra-amine, which have m of primary and n of secondary reactive capable hydrogen's atoms.
B – part of non-reacted epoxy groups. Calculated as:

$$B = B_0 - 0 \cdot A(42) - 0.5A(41) - A(40) - 0.5A(23) - A(22) - 1.5A(21) - 2A(20) - A(04) - 1.5A(03) - 2A(02) - 2.5A(01) - 3A(00),$$

k_1 and k_2 – effective constants of reaction of epoxy groups with primary and secondary amine's hydrogen respectively.
Initial conditions B_0 = 0,75; A(m,n) = 0 except for the A(4,2) = 0,25.
2. Mixture molecular-mass distribution's calculation on the base of data about concentrations of various functionality grids' nodes A(m,n).
Concentration of macromolecules or their fragments of a certain type can be calculated statistically by the theory of branching processes when concentration of smaller chain's fragments is known.
3. Calculation of viscosity of mixture with known molecular-mass distribution.
Compositions viscosity was calculated on the basis of logarithmic rule of mixture:

$$Lg\eta = \sum_i \phi_i Lg\eta_i,$$
$$\eta_i \sim M_i,$$

where n – the whole mixture's viscosity, n_i – viscosity of mixture components, certainly of molecules, including i of epoxydiane links, M_i – molecular masses of components, φ_i – mass part of components.

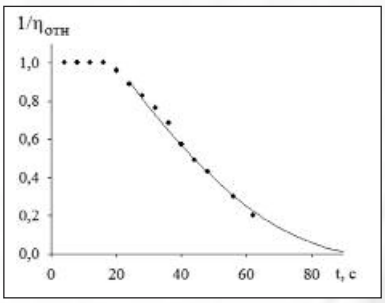

Fig.1. Comparison of experimental and calculation curves of resin ED-20 hardening at temperature 20°C (n_{ot} – ratio of viscosity at the moment to initial, points – experiment, line – calculation)

Was made parametric identification of model (fig.1), in the network of which were determined temperature dependences of hardening constants of mixtures of resins with ED-16, ED-20, DER330 brand by three-ethylen-tetra-amine. Model showed its adequacy.
Developed of hardening of epoxides ED-16, ED-20, DER330 by three-ethylen-tetra-amine allows to adequately estimate rheological conduct and gelation time of these compositions. Minimization of time and processing temperature of CM reduces power inputs, reducing harmful emissions.

P07

THE SOLUTION OF THE DIRECT KINETIC AND THE INVERSE KINETIC PROBLEM WHEN MODELING KINETICS OF ISOBUTYLENE COPOLYMERIZATION WITH THE ISOPRENE ON ALUMINIUM TRICHLORIDE IN THE media OF METHYL CHLORIDE

N. V. Ulitin, K. A. Tereshenko, R. R. Nabiev, R. Ya. Deberdeev
Kazan National Research Technological University, Kazan, Russian Federation

Butyl rubber is the basic raw material for receiving automobile tyres, rubber fabrics of different purpose. Butyl rubber as raw materials source consumes products of re-cycling petroleum, without demanding thus, unlike natural rubber, plant raw materials that reduces ecological damage to environment.
In different fields of application of butyl rubber various demands are made to it both on properties. However now in fact there are no adequate mathematical models on the basis of which implementation of regulation of the complex of its properties is possible. Therefore the purpose of this work was creation of the mathematical model describing kinetics of synthesis of butyl rubber and allowing to carry out estimate of its molecular mass characteristics.
Model operation of the kinetics of the copolymerization of isobutylene with isoprene was carried out in conditions in which butyl rubber receive industrially, namely cationic copolymerization of monomers on aluminum trichloride in the media of methyl chloride. Thanks to the analysis of literary data it was succeeded to establish the complete set of the reactions which are flowing past in system and reaction rate constants. The received mechanism was formalized mathematically in the form of differential equation system of chemical kinetics. Further this system was transformed to system of differential equations concerning the moments of molecular mass distribution of copolymer.
The experimental dependences of conversion, weight-average and number-average molecular weight, polydispersity for processes were defined. From values of the first group experimental data the solution of the inverse kinetic task in two stages (the first stage – definition of reaction constants of cationic polymerization of the isobutylene, the second stage – definition of the remained reaction constants of the copolymerization of isobutylene with an isoprene) were defined missing kinetic constants. On a value of the second group of the experimental data adequacy of model was proved.
Numerical experiments on influence of initial concentration of monomers, the catalyst, temperature showed possibility of a variation in a wide limit of molecular mass characteristics of polyisobutylene and its copolymer with an isoprene. It creates the favorable preconditions to increase in a share of production of synthetic rubbers.

P08

INFLUENCE OF HYDRODYNAMIC CONDITIONS AND REACTOR'S GEOMETRY ON THE MOLECULAR MASS PROPERTIES OF COPOLYMER OF ISOBUTYLENE WITH ISOPRENE

K. A. Tereshenko, R. Ya. Deberdeev, R. R. Nabiev, N. V. Ulitin
Kazan National Research Technological University, Kazan, Russian Federation

Polymers and copolymers of isobutylene play important role in polymeric chemistry field. Obviously, that production's technology of this material must be as much as possible cheap, simple and safe. The complicacy in this case is that fact, that cation polymerization of isobutylene and copolymerization of isobutylene with isoprene are fast chemical processes. Constants of ratio of initiation and chain's growth of isobutylene are not below 10^5-10^6 l/(mole•s), that is the flow of these reactions is limited by diffusion. From the other side, high ratio and exothermicity of process create difficulties with heat removal. Both these problems can be solved by intensification of hydrodynamic conditions in the reactor. Therefore, the aim of this work was the development and experimental testing of the mathematical model of interacting processes of chemical transformation, hydrodynamics and heat transfer, occurring in compact tubular reactor, which is the optimal replacement of the reactors of confusion.
Initially was created module of solution of the direct kinetic problem of isobutylene polymerization and copolymerization of isobutylene with isoprene in isothermal formulation of the problem. Then were developed modules of defining temperatures' concentrations fields and flow ratios, which were based on the fundamental principle of continuity, the laws of conservation of momentum and energy. Solution of the task of concentrations fields' constructions and ratios in the network of this module was carried out by numerical solution of differential equations of the model on the grid with the boundary conditions imposed by the

geometry of the machine. The adequacy of the developed model was confirmed by the comparison of the experimental molecular mass properties of butyl-rubber and polyisobutylene, received in the media of methylchloride with the use as catalyst aluminium chloride with the same analytic values.
According to the obtained model were carried out numerical experiments, in which for the apparatus of diffuser-confuser type were varied such geometrical parameters as the number of sections, the length of the section, the ratio of the section's diameter to its length, angle of confuser opening. The presence of three hydrodynamic modes (flare, intermediate regimes and regime of quasi-ideal wipe) was revealed. The obtained result may become the basis of new constructive solutions for the creation of small-sized tubular apparatuses.

P09

FORMALIZATION OF DEFORMATION birefringence OF CROSS-LINKED POLYMERS WITH APPLICATION OF THEORIES OF HEREDITY AND STATISTICAL FRACTALS

I. I. Nasyrov, N. V. Ulitin, R. Ya. Deberdeev, R. R. Nabiev
Kazan National Research Technological University, Kazan, Russian Federation

Experts need to make expensive and power expensive researches for definition of mechanical, electromagnetic and polarizing and optical characteristics of polymers, besides negatively influencing environment. The actual task arising at application of cross-linked epoxyamine polymers as matrixes for radiotransparent fibreglasses is decreasing of deformation birefringence. Therefore the work purpose is creation of the mathematical model allowing a priori to estimate deformation birefringence of cross-linked polymers. The model is developed on the basis of the hereditary theory. It was postulated that rated on unit distribution of times of a large-scale relaxation for shift pliability and an electromagnetic susceptibility same and was set by Rabotnov's distribution. The contribution of local relaxation transitions to equilibrium shift pliability and equilibrium electromagnetic susceptibility was considered by the weight coefficients. The model parameters (glass transition temperature, coefficients of thermal expansion, constant of high-elastic state, equilibrium elastic coefficient of electromagnetic susceptibility, weight coefficients) make clear physical sense and therefore can be found both analytically, and empirically. Experimental objects are polymers on the basis of bisphenol A diglycidyl ether cured by mixes hexylamine and hexamethylenediamine, with various cross-link density. To calculate model parameters, it is necessary to know fractal dimension of architecture of cross-linked polymer, number-average polymerization degree of internodal chain and average quantity of elastic effective cross-links. For definition of the first characteristic, with use of the Bullet Physics Library computer modeling of architecture of experimental objects is carried out. For definition of two other characteristics, the architecture was modeled with use of the theory of graphs. As result fractal and incremental approach was developed for the theoretical estimate of parameters of model. The relaxation spectrum parameters are found from creep and photocreep curves removed in transitional zone for series of temperatures, within the solution of the inversre task. Dependence of average times of the large-scale relaxation on temperature above and lower than glass transition temperature completely submits to the equation offered within model. Adequacy of model was shown on the example of reproduction of change of deformation birefringence of experimental objects in heating and cooling modes. Thus, the developed model can be applied to prior estimate of deformation birefringence of cross-linked epoxyamine polymers in known conditions of operation of fibreglass.

P10

STYRENE RADICAL POLYMERISATION PROCESS BY REVERSIBLE CHAIN TRANSFER IN THE PRESENCE OF TRITHIOCARBONATES: SIMULATION OF INTERRELATED PROCESSES OF HEAT EXCHANGE AND CHEMICAL TRANSFORMATION

E. S. Akhmetchin, N. V. Ulitin, A. V. Oparkin, T. R. Deberdeev, R. Ya. Deberdeev
Kazan National Research Technological University, Kazan, Russian Federation

Commercially produced polystyrene does not always meet specified requirements as to molecular weight and coefficient of polydispersity. This problem can be solved due to the polystyrene use for synthesis of living free radical polymerization in accordance to reversible chain transfer in the presence of sulfur-containing agents – thiocarbamates, thiobenzoates, etc. (RAFT – reversible addition-fragmentation chain transfer). However, simulation of the RAFT-polymerization of styrene in terms of system-related review of the interdependent processes of heat exchange and chemical transfomation has not been carried out. Therefore, the purpose of this research is a mathematical simulation in view of heat exchange of RAFT-polymerization of styrene in a reactor-mixer with dibenzyltrithiocarbonate (DBTC).
The mathematical model of kinetics of the RAFT-polymerization in the form of the balance differential equations on each component has been developed within the frame of the kinetic approach, and the kinetic circuit included all currently known stages: material initiation (the initiator – 2,2'-azobis(isobutyronitrile)), thermal initiation, chain growth, inherent chain transfer, reversible chain transfer, stopping of chain. The kinetic constants of separate stages of the reversible chain transfer have been achieved by us on the basis of theoretical (Fucuda model) and observational (DAK-1-1 microcalorimeter) studying of kinetics. The kinetic model was adjusted to statistics MMD by the method of generating functions. It is shown, that the kinetic model presents molecular-mass performances of the polysterene produced at various temperatures and at various conversion rates of monomer, with adequacy of 90%. Temperature effect, concentrations of the initiator, DBTC and monomer effect on molecular-mass performances of polysterene has been studied on the isothermal model.
Heat transfer in the reactor-mixer has been simulated close to ideal mixture. Sufficiency of the general model of kinetics and the heat exchange has been shown by comparison of the calculated and observational values of temperature in a laboratory glass reactor and molecular-mass performances of polysterene produced at various jacket temperatures of the reactor and at various

conversion rates of monomer. Adequacy of the model is 89 %.
Thus, the developed general model can be used for an optimum technological implementation of the RAFT styrene polymerization process in the reactor-mixer.

P11

POLYBUTYLACRYLATE SYNTHESIZED BY RAFT-POLYMERIZATION IS A PROMISING MATERIAL FOR OPTICAL WAVEGUARDS

D. Sh. Kalinina, N. V. Ulitin, E. V. Samarin, R. Ya. Deberdeev, T. R. Deberdeev
Kazan National Research Technological University, Kazan, Russian Federation

The Internet is an everyday reality of modern life. However, development of global computer networks is still going on. Polymeric optical fiber takes the place of glass optical fiber. A real time problem is loss of signal at large distances. To solve this problem, it is necessary to bring down inductivity of an optical fiber polymeric matrix. Therefore, a challenge of the research was to produce a new polymeric material for effective waveguides which will allow not only to considerably dilate the Internet coverage, but also to increase the speed of data transmission. The selected by us radical RAFT-polymerization under control (in English "reversible addition-fragmentation chain transfer") allows to produce a narrow molecular weight distribution polymer (coefficient of polydispersity < 1.5) and low electronic inductivity. The RAFT-polymerization of butyl acrylate in the presence of dibenzyltrithiocarbonate (DBTC) produces a linear-branched polymer that improves stability and durability of the material. Polybutylacrylate is selected as matrix for polymeric waveguides in demand.
The kinetic model of polymerization has been made in the form of the balance differential equations on each builder, and then adjusted to statistics MMD by the method of generating functions. The kinetic circuit included all currently known stages. The kinetic constants of the elemental responses of reversible chain transfer have been obtained due to theoretical (Fucuda model) and observational (DAK-1-1 microcalorimeter) kinetics study. The kinetic model reproduces molecular-mass performances polybutylacrylate at various temperatures and various conversion rates of monomer with an adequacy of 85%. Temperature effect, concentrations of the initiator (2,2'-azobis(isobutyronitrile), DBTC and butyl acrylate effect on molecular-mass performances of polymer has been studied on the kinetic model. Simulation of inductivity has been carried out by use of a combination of the semi-empirical and incremental approaches. Adequacy of formality (84%) is confirmed by comparison of calculated and observational values MMP and inductivity (25°C).
The result of this research is a synthesis control theory, polybutylacrylate structure and polarization control theory, synthesized by living free radical polymerization process in presence of sulphocarbonates in accordance with reversible chain transfer. Polybutylacrylate produced by RAFT-polymerization is a promising material for optical fiber matrixes the advantages hereof would be aesthetic quality, environmental friendliness, longevity and safety of fiber optic cables.

P12

COMPOSITE PVA-CHITOSAN ELECTROSPUN NANOFIBERS AS DRESSING FOR WOUND HEALING

M. G. Drozdova[1], A. N. Sonina[2], G. A. Vikhoreva[2], E. A. Markvicheva[1]
[1]M. Shemyakin and Yu. Ovchinnikov Institute of Bioorganic Chemistry, RAS, Moscow, Russia. [2]A. N. Kosygin Moscow State Textile University, Moscow, Russia

Currently, nanofiber-based wound dressings are widely employed for regenerative medicine. Nanofibrous wound dressings have several advantages over other conventional dressings. They have rather high sorption capacity and allow to remove wound exudates. Nanofibers prevent the wound from microbial penetration due to nanoscale size of fibers and interfiber spaces but at the same time well provide gas exchange.
Polyvinyl alcohol (PVA) is widely used to fabricate nanofibers by electrospinning for non-biomedical applications. On the other hand, due to its biocompatibility and high swelling properties this polymer is already successfully used in biomedicine as well (drug delivery, polymer films for wound healing etc). Chitosan was proposed in this study in order to enhance antimicrobial and adhesion properties of the nanofiber dressing.
The aim of the study was to produce composite PVA-chitosan nanofibers and to evaluate *in vitro* cytotoxicity of the obtained dressings. For this purpose, a mixture of chitosan and PVA (10:90, 25:75, 30:70 and 50:50 w/w) in 30% acetic acid was electrospun into nanofibers with average diameter of 200 nm. To stabilize the obtained water-soluble nanofibers, they were heated at 80-120
C for 1-4 hours. This heat-treatment promoted strengthening intermolecular interactions with followed compacting of the nanofiber structure. As a result of these interactions and even possible cross-linking, nanofibers lost their water solubility. Besides, heat-treatment reduced an acetic acid content in nanofiber mats compared to non temperature-treated samples.
As well known, cytotoxicity of biomaterials used for regenerative medicine is one of the key characteristics. Since nanofibers were prepared by electrospinning from the polymer mixture containing acetic acid, it was needed to test cell viability. The cytotoxicity of the nanofibers was studied by MTT assay in extraction and direct contact tests. Mouse fibroblast cell line (L929) was used in this study. The growth and proliferation of the cells was monitored using an optical microscope. For extraction test, nanofibers were previously incubated in cell cultivation medium for 24 hs, and then the cells were cultivated with these extracts before cell viability was measured. The contact-test allowed to estimate cell monolayer-nanofibers interaction within 24 hs. Cell growth on nanofibers was also studied for 1 week cultivation.
The results showed that composite PVA-chitosan nanofiber mats did not inhibit cell viability. Also it was shown that electrospun nanofibers were able to maintain cell growth and proliferation. Thus, these nanofibers can be proposed as wound dressings for regenerative medicine.

P13

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

D. B. Goncharov[2], A. G. Sukovatyi[1], E. D. Nikolaeva[1], E. I. Shishatskaya[2], T. G. Volova[1]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Akademgorodok 50, Krasnoyarsk, Russia 660036
[2]Siberian Federal University, 79 Svobodnyi Avenue, Krasnoyarsk, Russia 660041

In our work we used polymers synthesized in the Institute of Biophysics SB RAS. *Ralstonia eutropha* B5786 and B8562 and *Cupriavidus eutrophus* B10646, hydrogen-oxidizing bacterial strains, were used as PHA producers. The strains were grown under different conditions of carbon nutrition, which had been developed previously, and this enabled production of PHAs with different chemical compositions. Four types of PHAs were studied: a homopolymer of 3-hydroxybutyric acid [P(3HB)]; copolymers of 3-hydroxybutyric acid and 4-hydroxybutyric acid [P(3HB-*co*-4HB)]; copolymers of 3-hydroxybutyric acid and 3-hydroxyvaleric acid [P(3HB-*co*-3HV)]; and copolymers of 3-hydroxybutyric acid and 3-hydroxyhexanoic acid [P(3HB-*co*-3HHx)]. P(3HB-*co*-3HV) was extracted from bacterial biomass with chloroform and precipitated in hexane. The main process parameters that influence fiber diameter and properties (polymer concentration, solution feeding rate, working distance, and applied voltage) have been investigated and their effects evaluated. As polymer concentration in the solution increases from 1 to 8 wt%, fiber diameter increases from 0.45 to 3.14 μm and mechanical properties of the fibers are changed; elongation to break increases more than twofold (from 4.5 to 10.6%), with tensile strength decreasing from 23.16 to 6.65 MPa and Young's modulus from 1.16 to 0.3 GPa. Mechanical strength of aligned fibers prepared from different PHAs is higher than that of randomly oriented ones; no significant effect of fiber orientation on surface properties has been found. The study revealed electrospinning parameters for the production of high-quality fibers and determined which parameters should be varied to tailor the properties of the products. None of the nanofibrous mats electrospun from PHAs had any adverse effects on attachment, growth, and viability of NIH 3T3 mouse fibroblast cells, and all of them were found to be suitable for tissue engineering applications.

P14

OSTEOPLASTIC PROPERTIES OF RESORBABLE POLY-3-HYDROXYBUTYRATE IN MODELS OF SEGMENTAL OSTEOTOMY AND CHRONIC OSTEOMYELITIS

A. A. Shumilova[1], E. I. Shishatskaya[2]
[1]Siberian Federal University, Krasnoyarsk, Russia, [2]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia

A series of 3D implants and filling materials prepared from powdered biodegradable polymers, polyhydroxyalkanoates (PHAs), have been designed for the purposes of reparative osteogenesis (остеогенез–сам по себе восстановление). The 3D implants are made of resorbable polymer of hydroxybutyric acid (poly-3-hydroxybutyrate, P3HB) and a composite of this polymer with hydroxyapatite (HA) (P3HB/HA). The properties of the implants were studied in vivo in a model of segmental osteotomy and compared with commercial material Bio-OSS®. All implants containing poly-3-hydroxybutyrate as the main component facilitate reconstructive osteogenesis. P3HB and P3HB/HA show pronounced osteoplastic properties; their in vivo degradation is slow and corresponds to the growth of new bone tissue, facilitating normal reparative osteogenesis. Also, powdered P3HB and PHB/tienam can be used as filling materials for osteoplasty of bone cavities infected by Staphylococcus aureus. Filling of infected bone defects of long bones, which have been subjected to surgical debridement, with hydrophobic P3HB and P3HB/tienam results in quicker subsidence of infection, regeneration of bone defects, and recovery of the support ability of the affected limb than in the control group of animals (with defects filled with bone allograft). Biodegradable 3D implants and PHB-based filling materials show pronounced osteoplastic properties and degrade in vivo at a slow rate, enabling normal reparative osteogenesis.

P15

PRODUCTION OF LOW MOLECULAR WEIGHT HEPARIN

K. R. Mochalova[1], G. V. Avramenko[2], L. E. Frumin[1], G. A. Kostakova[1], K. G. Khlyabich[1]
[1]Federal Institute of Blood Substance and Pharmaceuticals, Lavrov lane 6, 109044, Moscow, Russia. [2]D. Mendeleyev University of Chemical Technology of Russia, Miusskaya sq.9,125047, Moscow, Russia

The present domestic invention relates to a process for preparing of pharmaceutical substance of low molecular weight heparin (LMWH) on original technology, biosimilar enoxaparin sodium, an anticoagulant, which is widely used in the treatment of thromboembolism, cardiovascular diseases. LMWH with the average molecular weight of between 2000 and 8000 Da by the stage of forming an intermediate heparin benzethonium salt, from this latter a water soluble heparin ester and subjecting ester controlled depolymerization with bases to form said low molecular weight heparin, finally product by reducing the impurities preparative liquid chromatography. The substance has a mean molecular weight 4200 Da. More than 75% polysaccharides chains have a molecular weight from 3800 to 5000 Da. Product contains a 1,6-anhydro ring structure at the reducing ends in the range 20±5%. Terminal 1,6-anhydro-aminosugars was determined by H^1 NMR. The degree of sulfation is not less than 1.8 per disaccharide unit. LMWH has a molar ratio for sulfate/carboxyl groups more than 2 using conductometric titration. LMWH has a specific anticoagulant activity of the anti-factor Xa in the range 90-125 IU/mg and activity of the anti-factor IIa 20-35 IU/mg. The ratio of anti-factor Xa activity to anti-factor IIa activity is between 3.3 to 5.3. Anticoagulant activity substance was determined using amidolytic method with a chromogenic substrate. Biosimilar enoxaparin passed the stage of pre-clinical trials. Substance meets the require-

ments of European, US pharmacopoeias. The original technology provides producing a pharmaceutical substance enoxaparin developed by Federal Institute of Blood Substance and Pharmaceuticals.

P16

POLY(ETHYLENEOXIDE) AS PSEUDO-TEMPLATE REGULATOR FOR PRODUSING NANOSCALE COPPER PARTICLES IN DILUTE AQUEOUS SOLUTIONS

V. V. Grushina, G. Yu. Ostaeva
Moscow Automobile and Road State Technical University (MADI), Moscow, Russia

The size of metal nanoparticles in sols stabilized with polymers as well as the stability of the sols to aggregation and oxidation of metal particles play key role in the application of the sols in various fields including biomedicine.
In this work, we studied the influence of different factors such as molar mass of poly(ethyleneoxide), dispersion medium, etc., on the characteristics of Cu(0) dispersions formed in course of the reduction of Cu^{2+} ions in water solutions of the polymer.
In the solutions of high molecular poly(ethyleneoxide) (MM~200 000), stable Cu(0) sols were formed. The diameter of metal nanoparticles in the sols can be varied from a few to about 20 nm dependently on conditions. The decrease in initial pH and the increase in polymer concentration helped to reduce the particle size, but did not improve the aggregation stability of sols obtained. The stability of the sols to aggregation and oxidation of metal nanoparticles can be significantly improved with the addition of poly(vinyl pyrrolidone).
In the case of poly(ethylene glycol))with MM 40000) (which can be regarded as low molecular poly(ethylene oxide)) the reduction of Cu^{2+} ions results in formation of dark precipitate, but the sols can be prepared in salt solutions (0.4 M of either sodium sulfate or sodium chloride). The sols thus formed are not stable. However, very stable copper sols can be prepared by the reduction of copper ions in mixed poly(ethylene glycol) - poly(vinyl pyrrolidone) solutions.

P17

PRECURSORS AND SOLS OF METAL NANOPARTICLES IN A POLYMER SOLUTION OF POLY(ACRYLIC ACID) AND POLY(ETHYLENE GLYCOL) MONOLAURATE

G. Yu. Ostaeva, E. A. Eliseeva, I. M. Papisov
Moscow Automobile and Road State Technical University (MADI), Moscow, Russia

A common method of preparation of metal colloidal dispersions with nanosized metal particles and narrow size distribution of these particles is the reduction of metal ions in a polymer solution.
According to the current ideas, the formation of nanoparticle-macromolecule complex is accompanied by appearance of protective screen on a particle surface and cessation of the particle growth.
The efficiency of the screening depends on the nature of both the polymer and the metal, and other conditions (such as m.w. of the polymer, dispersion medium, temperature etc.).
Interpolymer complexes formed with poly(ethylene glycol) monolaurate (PEGML) and high molecular poly(acrylic acid) (PAA) were investigated in this work. The reduction of Cu^{+2} ions by hydrazine borane was carried out in water solutions of polymers.
There were found the conditions of preparation of homogeneous aqueous solutions of copper precursor sols - ternary complexes including cupper ions, PAA and PEGML. Preliminarily polyacrylate copper was obtained (pH of at least 4.5; PAA/Cu^{+2}>5 unit-mol/mol) and then, the solution PEGML was added.
The regions of the existence of ternary complexes were defined and the study the effect of the composition of the complexes on the size of its particles was studied by potentiometric titration, measuring the viscosity, UV spectroscopy, and dynamic light scattering.
The disagreement between the dependencies of particle size both of PAA-PEGML and ternary complexes PAA-Cu^{+2}-PEGML and viscosity of their solutions was found.
A special study was conducted in order to select the conditions under which the method of the DLS could measure the size of the polymer-metal particles produced in the reduction process of Cu^{+2} ions in solution of PEGML or the ternary complex PAA-Cu^{+2}-PEGML. It is possible to show, that in sols obtained in solutions PEGML, free of surfactant micelles in the sol are absent and, even at relatively high concentrations of surfactants observed two fractions of particles with size on the order of 70 - 100 and 10 - 15 nm. It is indicate that the aggregation micelles around the copper nanoparticles takes place.
In the solutions of PAA and PEGML mixtures very stable copper sols with the diameter of copper nanoparticles 3-6 nm were obtained. The data of DLS and transmission electron microscopy are in good correlation.

P18

REMOVAL OF EMULSIFIED OIL FROM THE WASTE WATER USING COALESCENCE FILTRATION AND MEMBRANE SEPARATION

L. E. Kopylova, A. A. Svittsov
D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia

According to UNESCO oil is among the ten most dangerous pollutants for the environment and at the same time oil is among the most common man-made water pollutants. Most of the known filters achieve a residual concentration of oil in the water about 10 mg/l. This paper considers the possibility to create a device for removing emulsified oil with a residual oil content of about 0.05

mg/l. To do this, the device will combine coalescing filtration and membrane separation.
The polymeric fibrous material was used in research. The emulsion flows through the material in coalescing filter. Drops of the dispersed phase are fixed on the material. Structure of the material is corrugated, with large free volume and the average affinity for the dispersed phase. Such intermediate wettability should be sufficient to adhere microdroplets to the fibers, but not enough to hold the large droplets, which operate the lift. The material structure is optimal for the separation of fine emulsions. Cumulative output of the dispersed phase is carried out by separation and surfacing of large drops on flexi hose material, which prevents it from blocking and provides a constant regeneration. The material worked well in the experiments, it cleared the emulsion with a concentration of 50 mg / l to the residual concentration of 1 mg/l.
Micro - and ultrafiltration are widespread for a deep cleaning water from oil. Tubular ceramic microfiltration membrane was used in this study.
The project developed a unique device that allows to carry out coalescing filtration and membrane separation in a single unit. Once in the unit, the cleaning liquid first passes through the coalescing material, with most of the emulsified oil coalesces into the chamber and the accumulation of oil. The filtrate was fed to membrane separation, organized in the same unit. The membranes are located in the immediate vicinity of the coalescing material. Permeate completely purified from oil. The concentrate was also cleared of emulsified oil, which is due to the increased local concentration can coalesce on the material.
Thus, this combination of processes allows to achieve maximum purity from the oil in a single pass through the unit. The unit accumulates almost dehydrated oil, it can be removed from the unit and reused.

P19

CYTOTOXICITY OF CALCIUM-PHOSPHATE POROUS BIOMATERIALS

P. D. Sarkisov[1], N. Yu. Mikhailenko[1], E. E. Stroganova[1], N. V. Buchilin[1], N. S. Sergeeva[2], I. K. Sviridova[2], V. A. Kirsanova[2], S. A. Ahmedova[2]
[1]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia. [2]P.Gertsen Science-research oncological institute of Moscow, Moscow, Russia

Materials for medical uses shall correspond to a number of physical, chemical, technological, medical and biological requirements. Certain physical and chemical properties ensure safety of the materials composition being introduced to a living tissues, certain technological properties provide a possibility of production set products therefrom, and certain medical and biological properties provide compatibility of the materials with living media.
Calciumphoshpate bioglassceramics having various types of porous structure was developed and sintered starting from mixture of thin glass powders (composition mol.% P_2O_5 – 45; CaO – 50; Al_2O_3 – 5; with small additions of B_2O_3; ZrO_2; TiO_2) and burn down additives. Sintered materials are characterized with the open porosity of 65 - 85% and the with the following: the first type structure is characterized with the channel porosity (diameter of channels of 120 - 550 microns) and the second demonstrates coarse-cellular porosity (diameter of cells of 200 - 1800 microns, patent RU 2462272). Furthermore, all materials had interchannel and intercell porosity capable of impregnating with physiological liquids.
Medicalbiological *in vitro* tests were conducted in order to estimate acute cytotoxicity and matrix properties of a surface of a granulated samples of the porous materials. Before research, all samples were sterilized by c-irradiation. *In vitro* tests were carried out on human immobilized fibroblast (FH) (FGUN "Institute of Molecular Biology of V. N. Engelgardt"). Viability of FH was estimated in MTT-test, 1 day - to determine of the acute cytotoxicity, 3, 7, 10 and 14 days – to evaluate matrix properties.
Most of the test results demonstrates that calcium phosphate bioglassceramics is not toxic in respect to FH. Viable cells pool in 24 hours remains on the level 91,7%. The ceramics also demonstrate moderate matrix properties of a surface: viable cells pool for the 3rd, 7th, 10th and 14th days of cultivation didn't exceed 100%.
The obtained results allow to conclude that the biomaterial supports an attachment and proliferation of human immobilized fibroblast at the level of control (on polystyrene) and thus can be recommended for *in vivo* research of biocompatibility and osteoreplacing.

P20

DETECTION OF ABUSED DRUGS IN SWEAT AND SKIN WASHOUTS BY IMMUNOCHROMATOGRAPHY

V. S. Morozova, N. S. Gorbacheva, A. I. Levashova, M. A. Myagkova
Institute of Physiologically Active Compounds of Russian Academy of Science, Chernogolovka, Russia

One of the most acute problems in today's society is drugs of abuse (DOA) administration and addiction. It is very important to improve methods for DOA detection and to diagnose drug addiction timely. The most convenient and inexpensive screening method for drug analysis is immunochromatography assay (ICA). Disadvantage of widely used urine ICA tests is inability to identify the current drug intoxication state.
Objectives: To develop express screening "on site" method of drug intoxication determination. Use of sweat and skin washouts as a biological sample can solve the problem of identifying individuals who are intoxicated at the time of testing. In addition, the sample collection is non-invasive, doesn't violate the right to privacy, as opposed to urine tests. Moreover, sweat testing exclude sample adulteration or substitution that is very common in urine analysis. Collecting of skin washouts from hands and around mouth can increase detection sensitivity (compared with the same purpose blood and saliva tests) due to the presence of DOA traces on the skin after drug use.
Methods: Earlier we developed urine ICA tests for six DOA groups: opiates, amphetamines, cannabinoids, ecstasy, benzodiazepines

and methadone. In the present study a procedure and reagent kits were developed for sampling, concentrating and ICA analysis of traces of the above mentioned drugs in sweat and skin washouts. The sample preparation includes skin swabbing with the use of alcohol, the alcohol evaporation by means of simple drying and dissolution of the residue in phosphate buffer. No other reagents or laboratory equipment is used; all the necessary materials are contained in the reagents kit.
Results: The developed preparation procedure allows using earlier developed urine ICA tests for skin washouts and sweat analysis. The limits of detection of drugs in the concentrated extracts were 300 ng/mL (opioids), 50 ng/ml (cannabinoids), 300 ng/ml (amphetamine), 300 ng/ml (ecstasy), 200 ng/ml (benzodiazepines), 300 ng/ml (methadone).
Conclusions: Developed test kits are intended for the express screening for drug intoxication in the "field" conditions and have a wide range of applications: for drivers testing on roads, workers testing before shift and after some accidents, especially in risky and hazardous jobs (transport, big industries, etc.). The analysis procedure can be performed "on site" and does not require skilled personnel.

P21

CORRECTION OF DISORDERS DEVELOPING DURING CHRONIC LIVER FAILURE THROUGH VARIOUS LIPOSOMAL FORMULATIONS

R. A. Mukhamadiyarov, V. V. Borisov, Yu. A.Kudryavtseva, I. Yu. Zhuravleva
Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

The aim of the study is to evaluate the impact of the "empty" lecithin-cholesterol liposomes and liposomes loaded with antioxidants and macroergic compounds on hepatocytes in rats with chronic liver failure.
Materials and methods. We stimulated chronic liver failure in Wistar rats by partial ligation of the hepatic veins, and it developed in 2 months. Three types of liposomal compositions were used for intravenous administration, namely, (1) the "empty" liposomes, (2) liposomes containing creatine phosphate and ATP, and (3) liposomes containing a-tocopherol, superoxide dismutase and reduced glutathione. Administration consisted of 15 consecutive injections with an interval of 48 hours. Control mice were administered by saline solution at the same mode. Changes within the liver were assessed by determining the activity markers of cytolysis in the blood, level of oxidative stress in homogenates of liver cells, and histological changes in liver structure.
Resutls. We found that all liposomal formulations had a pronounced hepatoprotective effect, manifested in reduced activity in the blood of hepatic cytoplasmic enzymes, decreased activity of lipid peroxidation in liver and partial restoration of the histological structure of the liver. The maximum effect was observed for liposomes containing antioxidants.
To summarize, we suggest that observed effect is due to membrane stabilizing properties of liposomes.

P22

ELASTIC CHITOSAN BIOCOATINGS FOR REGENERATIVE THERAPY

A. B. Shipovskaya, V. I. Fomina, D. A. Rudenko
Saratov State University named after N.G. Chernyshevsky, Saratov, Russia

In the last decade, film chitosan materials have been intensely penetrating into many spheres of human life. Their biocompatibility with living tissues, the proximity to the dermal components by physiological activity, and other valuable properties determine the outlook of the use of films made of this aminopolysaccharide as wound dressings, matrices for cell cultivation, etc. Condensed chitosan film forms not only preserve the complex of valuable properties of the initial polymer but also can acquire new qualities and functional abilities as a result of directed modification. However, rather low elasticity indices are the main demerit constraining introduction of chitosan films into medical practice.
Here a modification way of chitosan films obtained with the use of traditional solvents (acetic and amber acids) directed to an increased elasticity of the film material is discussed. The essence of this way consists in keeping of chitosan films, in their salt and basic forms, in the vapor of water or water–acid media (hydrochloric or amber acid solutions) or keeping of basic chitosan films in a liquid (water, physiological solution).
The stress–strain curves of the initial films made of chitosan acetate or succinate have ranges of elastic and plastic (or forced high-elastic) deformations. Their treatment in a basis almost does not change the nature of deformation of these film samples.
Sorption of water vapor or the vapor over a 0.5 N HCl solution by chitosan acetate and succinate films and water sorption by the same films converted into their basic form have been found to increase the value of relative elongation at break from 5–15% (initial samples) up to 40–100%. The durability of the modified films remains sufficient for their use as biocoatings. The deformation curve shape of the modified films gives evidence of development of strongly pronounced plastic deformation in them. The highest value of relative elongation is observed for the modified film structure (polysalt or polybasis) obtained from high-molecular chitosan samples.
The modified chitosan films possess a high ability to absorb wound exudate, antibacterial, immunomodulating and recycling effects. The set of useful properties of the modified films allows considering them as promising biocoatings for treatment of lesions of epidermal covers.

P23

BIODEGRADABLE POLYHYDROXYALKANOATE MEMBRANES FOR ADHESION PREVENTION IN CARDIOVASCULAR SURGERY

M. V. Nasonova, T. V. Glushkova, L. V. Antonova, V. V. Borisov, Y. A. Kudryavtseva
Federal State Budgetary Institution Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

Adhesions are a serious postoperative complication in cardiac surgery, which increases the risk of reoperations. Anti-adhesive membranes are a necessary component, which should be used to prevent the development of adhesive process. To create anti-adhesive membranes polyhydroxyalkanoate polymers were evaluated.
Objective. Comparative study the bio- and hemocompatible properties of membranes prepared using the polyhydroxybutirate and polyhydroxybutirate-hydroxyvalerate polymers with different molecular weight.
Methods. The polyhydroxybutirate (PGB) with 309 kDa and 541 kDa and polyhydroxybutirate-hydroxyvalerate (PGBV) polymers with 2307 kDa molecular weight were used. The chloroform used as a solvent. The membranes were prepared on the glass surface. The stress/strain properties and hemocompatibility were studied. The rate of membranes biodegradation was studied using the subcutaneous implantation in the Wistar rats.
Results. The elasticity of the PGBV membranes (501%) was significantly higher than the PGB ones (4%), but the strength value was same. The membranes did not make the negative influence on blood cells – erythrocytes and thrombocytes. When rat mesenchymal stem cells were cultivated on the surface, the cells survival was 66-73%, which showed high biocompatibility of the polymers under study. The rate of PGB membranes biodegradation was similar in both molecular weight samples. During the first two months after implantation the membranes structure is stable and membranes located into the fibrous capsule. The first features of destruction were observed after 3 months of implantation, the membranes gradually destroying into the capsule without inflammation. The PGBV membranes were demonstrated the higher rate of biodegradation then PGB ones. After 2 months of implantation the membranes structure were soft, the features of destruction were more significant in their edges. The foamy structure of the membranes residual was observed after 4 months of implantation. The PGB and PGBV membranes are perspective material for the adhesion prevention, the adhesions are not observed up to 28 days of implantation.
Conclusion. Co-polymer polyhydroxybutirate-hydroxyvalerate is perspective polymer for preparing the anti-adhesive membranes for cardiovascular surgery. Its have the optimal biodegradation rate, satisfactory stress/strain and hemocompatible properties and effectively prevent the adhesion process.

P24

EPOXY CONSERVATION AT MANUFACTURING VALVED CONDUIT FROM BOVINE JUGULAR VEIN

T. V. Glushkova, M. V. Nasonova, T. N. Akentyeva, Y. A. Kudryavtseva
Federal State Budgetary Institution Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

The Contegra pulmonary valved conduit (Medtronic Inc., USA) is widely used in clinical practice to restore blood flow from the right ventricle into the pulmonary artery. This conduit was made from the glutaraldehyde-treated (GA) bovine jugular vein. As a treatment agent, glycol diglycidyl ether (DGE) has a number of advantages over glutaraldehyde, including higher resistance to calcification.
Objective. Study of the DGA-treated bovine jugular vein as a candidate for the extracardiac valved conduit.
Methods. Valved segments of bovine jugular vein treated with GA and DGE. Physical-mechanical properties of the vein wall were examined in longitudinal and transversal directions using a uniaxial tension machine (Zwick/Roell). Human pulmonary artery collected at autopsy was set as control. The examined DGE-treated veins were further treated with aminophosphonate in order to prevent calcification. The calcium-binding activity of veins was assessed in the standard model of accelerated calcification by subcutaneous implantation of the veins to male Wistar rats after 60, 120 and 180 days. Quantitative assessment of calcium accumulation was carried out using atomic-absorption spectrophotometer (1g of dry tissue). To assess calcium accumulation in implants, these were compared with the metabolic calcium content in the controls samples.
Results. The strength of the autopsy material in longitudinal and transversal directions made up 0,53±0,06 and 1,14±0,09 MPa, relative elongation - 81,44±6,56% and 77,54±3,26%, respectively. GA- and DGE-conserved veins were stronger than the autopsy material (by 35% and 63%, respectively). Relative extension of the veins averaged 60% in comparison with the autopsied material regardless of the type of conservation. After 180 days of implantation GA-treated veins, calcium level increased by a factor of 200 (122±5,07mg/g). Accumulation of calcium in the DGE-treated veins was less intensive - after 180 days of implantation these had 3.6 times less calcium as compared with the GA-conserved ones ($p<0.05$). However, the amount of calcium in the DGE-conserved veins was higher in comparison with the controls samples ($p<0.05$). The DGE-conserved veins treated with aminophosphonate had the lowest amount of calcium (0,61±0,09 mg/g).
Conclusions. DGE-treatment imparts satisfactory physical and mechanical properties to bovine jugular veins. DGE-treated veins show lower calcium-binding activity as compared to those treated with GA. Aminophosphonate significantly reduces calcium-binding activity of DGE-treated veins.

P25

BIORESORPTION CHARACTERISTICS OF PLAIN AND CELL-LOADED POLYHYDROXYALKANOATE AND POLYCAPROLACTONE FILM SCAFFOLDS IN CHRONIC LONG-TERM EXPERIMENT

L. V. Antonova, A. Y. Burago, V. G. Matveeva, Y. A. Kudryavtseva, M. V. Nasonova, Y. G. Toropova, E. A. Velikanova, A. S. Golovkin

Federal State Budgetary Institution Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

Abstract. The study was aimed at examining the biodegradation speed of polyhydroxyalkanoate and polycaprolactone copolymer compositions, potentially suitable for small vascular graft production, with and without multipotent mesenchymal stromal cells derived from the bone marrow (MMSC BM).

Materials and methods. The study compared film scaffold (FS) No1 made from 5% polyhydroxybutirate-valerate (PHBV) and 10% polycaprolactone (PCL) and film scaffold (FS) No2 made from 7,5% PHBV and 10% PCL. MMSCs BM were derived from Wistar rat femoral bones. Cell phenotype was determined using flow cytometry with monoclonal CD 90, 45, 106 and 11b antibodies, cell viability was tested by staining with 0.1% trypan blue solution and vascular endothelial growth factor (VEGF) expression was measured by immunofluorescent staining of histological sections. Histological signs were assessed monthly up to 12 months with hematoxylin and eosin stain.

Main results. Light microscopy was used to assess the bioresorption characteristics of film scaffolds made out of PHBV and PCL after subcutaneous implantation to rats. Inflammatory infiltration of the surrounding tissues in the implantation site was found to be moderate or focal lymphohysteocytic infiltration and to stay not more than 1 month. The surface fragmentation of 7,5% PHBV and 10% PCL scaffolds occurred after 8 months; multichamber thin-wall capsules were formed with no signs of perifocal inflammation. 5% PHBV and 10% PCL scaffolds did not have any obvious signs of destruction after 12 months. The presence of MMSC BM delayed the start of copolymer scaffold bioresorption for 1 month and reduced the duration of inflammatory response in the surrounding tissues. At the same time, maximal VEGF expression in the tissues surrounding MMSC BM samples was registered during the first month, which indirectly demonstrated that MMSC BM were still viable on the scaffolds after the implantation.

Conclusion. Thus, the optimal co-polymer composition for a vascular graft scaffold is 5% PHBV and 10% PCL. The presence of MMSC BM does not reduce the biodegradation time of copolymer scaffolds.

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COMPARATIVE STUDY OF LIPOSOMAL AND FREE EMOXIPINE ON FREE-RADICAL STATUS OF THE ISOLATED RAT HEARTS AFTER NORMOTERMIC ISCHEMIA AND FURTHER REPERFUSION

Y. G. Toropova, R. A. Mukhamadiyarov, A. S. Golovkin

Federal State Budgetary Institution Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

Abstract. In experiments on the isolate perfusate heart of a rat was learnt an influence of free and liposomal emoxipine on forming on a free-radical status of the myocardium, damaging during ischemia and reperfusion.

Materials and methods. Concentration emoxipine in liposomes made 0,25 mg/ml and 0,1 mg/ml. Concentration emoxipine in a free form made 0,25 mg/ml. In experiments on the isolate perfusate heart of a rat the intensity of free radical processes (the level MDA) were assessed.

Main results. Against introduction of 0,1 mg/ml and 0,25 mg/ml liposomal emoxipine the MDA level made 18,0 (17,0-19,0) μmol / l*g and 14,7 (13,7-15,1) μmol / l*g respectively, while at introduction free emoxipine – 15,3 (15,1-16,1) μmol / l*g ($p<0,05$).

Conclusion. The obtained results show that 0,1 mg/ml liposomal emoxipine has the greatest effect on the process of a peroxide oxidation of lipids in ischemiced myocardium in period of the reperfusion. Probably, including emoxipine in structure of liposomes promoted bioavailability augmentation. In this connection, emoxipin showed pro-oxidant effects.

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DEVELOPMENT OF ALGINATE MICROPARTICLES AS ANTITUBERCULAR DRUGS CARRIERS

E. O. Batyrbekov[1], A. B. Ismailova[2]

[1]Institute of Chemical Sciences, Almaty, Kazakhstan, [2]Kazakh-British Technical University, Almaty, Kazakhstan

The goal of the present work is development of new drug delivery systems based on alginate microparticles for the treatment of tuberculosis by pulmonary administration to the lungs. Calcium alginate microparticles, modified by a surface layer of chitosan, have been studied for controlled release of antitubercular drugs ethionamide or rifampicin. The drug release behaviour and antibacterial effect of the drug loaded alginate beads were discussed. Modified microparticles were obtained by syringed dropwise of drug-containing solution of sodium alginate into a solution of chitosan in calcium chloride. The obtained alginate microparticles consisting of immobilized drug were covered by a surface layer of chitosan. The influence chitosan concentration on thickness of surface layer of alginate microparticles was studied. With increase in the concentration of a polymer from 0.5 up to 1.5 % the thickness of the modified layer increases from 5 up to 60 mkm. Microparticles containing antitubercular drugs were evaluated for *in vitro* and *in vivo* release profiles. The release behaviour of drugs from alginate microparticles was examined by means of immersing the polymeric samples in a modelling biological medium at 37°C. The total amount of drugs was released in 1-3 days

in dependence of loading of drugs and thickness of surface layer. The antitubercular action were studied in experiments on animals. Three groups of guinea pigs, consisting of 20-25 animals, were infected with a 6-week culture of a laboratory strain of *Mycobacterium tuberculosis*. Treatment was started 2 weeks after infection. The animals in the first group were untreated. Animals of second experimental groups were treated by injection once a week with alginate containing a 5-day dose of ethionamide. Animals of third groups were treated by daily oral administration of a day's dose of the same drugs. The weights of the guinea pigs and the dimensions of ulcers at the site of infection were periodically determined during the experiment. All untreated animals died 1.5-2 months after infection. The animals of the other groups were killed with ether 2·5 months after the beginning of the treatment. Guinea pigs were dissected and damage to lungs, livers, spleens and lymphatic ganglions was determined. Data of medical-biological and clinical tests show the advantages of polymeric drug delivery systems based on alginate microparticles for tuberculosis treatment in comparison with low-molecular drugs.

P28

BIOLOGICALLY ACTIVE POLYMERS FOR AGRICULTURE

B. A. Zhubanov[1], M. B. Umerzakova[1], G. Meirova[2], B. A. Ismailov[3]
[1]Institute of Chemical Sciences, Almaty, Kazakhstan, [2]Kazakh National Pedagogical University, Almaty, Kazakhstan, [3]Centre of Stock-breeding and Veterinary, Almaty, Kazakhstan

In the territory of Kazakhstan about 70 % of lands are subject to desertification. In this regard in recent years hard works on fight against it are carried out. We developed synthesis of the bioactive polymer containing two complementary each other derivatives of pyperidol: the fospinol-basis, more influencing growth of green material, and the akpinol-basis, strengthening a formation of root. The industrially copolymer of styrene and maleic anhydride (stiromale) are used as polymer carrier. The possibility of the immobilization of two piperidols derivatives on polymeric matrix are showed by carried-out researches. Thus, it is possible to regulate BAS ratio as a part of bioactive polymer by changing reaction conditions.
New polymeric regulators of growth and development of plants on a basis of γ-and β-isomers 1,2,5-trimetyl-4-atsetinylpiperidol-4 and dihydrochloride of 1,4-bis (-1,2,5-trimethylpiperidol-4-) butadiin-1,3 (AE), immobilized on copolymers of maleic anhydride with acrylic acid and styrene are also had. It is revealed that almost quantitative immobilization AE on STMA unlike the piperidole-basis is carried out in absence of tertiary amines.
The received connections were tested with good results for energy of germination and sprout of seeds zhitnyac in experiment in field conditions in Mangistau area of Kazakhstan. Thus a difference between sprout of seeds zhitnyac, processed by the polymeric growth regulator, and control in field conditions more than in case of laboratory trials that can be caused by climatic conditions of a semidesertic zone of Mangistau area.
Economic longevity of the seeds which are storing in Genetic bank, is measured by duration of the period during which they keep sprout at least individual seeds that can be used for their reproduction. The influences of the synthesized biopolymers on sprout of seeds of lucerne grade of "Yaroslavn" at 9-year period of storage are studied. It is revealed that at optimum concentration of the polymeric akpinola-basis of 0,001 % the sprout of seeds increased raised to 70 %, and energy of germination to 61 %. Seeds with such sprout can be used for crops.

P29

MODIFICATION OF BIOPOLYELECTROLYTE CAPSULE SHELLS BY IN SITU-SYNTHESIS OF MAGNETIC NANOPARTICLES

S. S. Rumyantseva, I. V. Marchenko, S. N. Sulyanov, S. S. Starchikov, I. S. Lyubutin, T. V. Bukreeva
A. V. Shubnikov Institute of Crystallography of RAS, Moscow, Russia

Drug delivery based on magnetic carriers (magnetic delivery) makes it possible to affect a limited, strictly determined area of an organism; decreases the amount of injected functional compound and reduces the concentration of medicinal preparation for the minimization of side effects.
Method of *in situ*-synthesis of magnetite nanoparticles on the shell of biopolyelectrolyte capsules has been developed. The nanoparticles were synthesized by chemical condensation of magnetite (Elmore's method) in the capsules suspension. The process was carried out at 37°C because for the encapsulation of biologically active compounds it is undesirable to use higher temperatures - heating may result in the loss of functional activity of the substance. Conditions under which the capsule shell contains quite monodisperse magnetite nanoparticles with an average size of 8 nm were chosen. Encapsulation of model compounds into magnetic nanocomposite shells was performed.
A comprehensive study of the structure of nanocomposite capsules and magnetite nanoparticles formed on biopolymer shells was performed. X-ray diffraction using synchrotron radiation source revealed that in the obtained nanoparticles dominating phase is Fe_3O_4 – magnetite (cubic inverse-spinel-type structure, space group Fd3m, calculated unit cell parameter a = 8.3486 Å). Mössbauer spectra of the nanoparticles were obtained in the temperature range from 90 to 297 K. The low-temperature spectra indicate the relaxation behavior of the magnetic moments of iron and demonstrate the characteristics of superparamagnetism. At room temperature the relaxation character of the spectrum is clearly shown, but the magnetic phase has not yet fully turned into the paramagnetic phase. The area of the magnetic component is about 80% of the area of the spectrum therefore the blocking temperature of the magnetic moments of iron is above 297 K.
The study was supported by the Ministry of Education and Science of Russian Federation, project 14.B37.21.0457, and the Russian Foundation for Basic Research, project 11-03-01169a.

P30

INVESTIGATION OF CALCIUM CARBONATE MICROCONTAINERS WITH LOPERAMIDE FOR CREATION OF NEW INTRANASAL DELIVERY SYSTEM

D. B. Trushina[1,2], B. V. Nabatov[1], T. N. Borodina[1], V. V. Artemov[1], T. V. Bukreeva[1]
[1]A. V. Shubnikov Institute of Crystallography of RAS, Moscow, Russia, [2]M. V. Lomonosov Moscow State University, Moscow, Russia

One of the common methods to provide a systemic action of the medicine is an oral administration, but this way has low efficiency on account of over 95% of the present medication cannot pass the blood-brain barrier. Nasal administration is an alternative way to the brain drug delivery. We assumed that the calcium carbonate microparticles owing to its porous structure and good adhesive feature can be successfully used as drug carriers to intranasal delivery.
Spherical mesoporous calcium carbonate microparticles were prepared by mixing $CaCl_2$ and Na_2CO_3 aqueous solution. The particles embedding and release of the central anesthetic loperamide have been investigated. Loperamide absorption process was studied from ethanol and the aqueous/ethanol solutions. It was found that an addition of water to the ethanol solution activates the absorption process. The loperamide-loaded particles were modified with a hyaluronic acid or poly-L-lysine by exposure to their solutions.
The amount of encapsulated loperamide was determined by spectrophometry at 259 nm. The data show enhance of the encapsulation efficacy when using more concentrated solution of the drug. The most effective absorption of loperamide was observed at the ethanol/water ratio of 1/3 with all used loperamide concentrations (the process saturated). The study of loperamide release was performed in ethanol. The initial burst release was shown for the uncoated particles, where almost 80% of loperamide was found in a supernatant. The initial burst effect was slightly decreased in the case of the microcontainers followed by a slow release (60% at the same time). The further release kinetics was not significantly different in the absence or presence of the polymer coating. It is clear that the one polymer layer is not enough to prolong notably the release of the encapsulated component. On the other hand, the obtained extension together with the mucoadhesive properties of the microcontainers is well enough to increase the residence time of the drug in the nasal cavity, prolonging and improving its absorption.
The study was supported by the Ministry of Education and Science of Russian Federation, project 14.B37.21.0457, and the Russian Academy of Sciences, Program for Basic Research no.22.

P31

ATCUN PEPTIDES FOR SITE-SPECICIFIC DNA MODIFICATION AND THE STUDY OF DNA-PROTEIN INTERACTIONS

E. S. Knyazhanskaya[1], O. V. Kondrashina[1], S. P. Korolev[1]
[1]Lomonosov Moscow State University, Chemistry department, Moscow, Russia

The current approaches for directed DNA modification are based on the use of retroviral integrases, transposases and zinc-finger nucleases (ZFN) of which the later is so far the most promising one. ZFN uses a hybrid protein composed of FokI nuclease DNA binding domain and a synthetic zinc finger protein that specifically binds a 9-12 bp DNA sequence. The FokI dimerisation is required for successful DNA cleavage. ZFN systems have been used for targeted DNA modification in a variety of human, animal and plant models. A considerable drawback of the ZFN approach is a relatively high cytotoxicity originating from nonspecific DNA binding that in turn probably results from a rather small size of the specific DNA sequence.
We propose a novel system for directed DNA modification based on a synthetic six-domain zinc-finger protein (tRL18) designed by our group in a way that it binds an 18bp region in the human genome located within Leu tRNA gene. The zinc-finger domain carries an ATCUN peptide on its N terminus. ATCUN peptides are tripeptides with a canonical NH_2-GGH structure that strongly binds zinc and copper ions. When treated with reducing agents Cu(II) in complex with ATCUN transfers to Cu(I) that generates hydroxyl radicals. The ATCUN(Cu(II))-zinc finger hybrid protein is expected to bind to its specific DNA sequence while the reduction of Cu(II) would lead to DNA oxidative cleavage.
We constructed the plasmid coding for two variants of the ATCUN-tRL18 hybrid: the GGH and the GSH variant. Both were purified in bacteria and tested for their ability to specifically bind and cleave an oligo duplex carrying the specific 18 bp sequence.
The ATCUN peptide can also be used for the study of DNA-protein interactions. The specificity of DNA-protein interactions is determined on one hand, by the nucleotide sequence of the DNA-ligand and, on the other hand, by the amino acid sequence and spatial structure of the DNA-binding protein. Modified analogs of DNA-ligand are one of the tools for studying the changes in the structure of DNA-protein complexes. We designed DNA analogues conjugated to ATCUN-peptides and aim to use the oxidative cleavage profile of the protein bound to such a ligand analog to study the DBA-protein interaction within the complex.
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P32

PHYSICOCHEMICAL PROPERTIES OF POLYHYDROXYALKANOATES WITH DIFFERENT CHEMICAL STRUCTURE

T. G. Volova[1,2], N. O. Zhila[1,2], E. I. Shishatskaya[1,2], A. G. Sukovatyi[1], D. A. Syrvacheva[2], O. N. Vinogradova[2]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk, Russia, [2]Siberian Federal University, Institute of Fundamental Biology and Biotechnology, Krasnoyarsk, Russia

Polyhydroxyalkanoates of different composition: a homopolymer of 3-hydroxybutyric acid (poly(3-hydroxybutyrate) and copolymers of 3-hydroxybutyrate with 4-hydroxybutyrate, 3-hydroxyvalerate or 3-hydroxyhexanoate with various contents of monomers

have been synthesized. Physical and chemical properties of the polyhydroxyalkanoates have been studied using IR spectroscopy, X-ray structure analysis, differential scanning calorimetry, gel-permeation chromatography and electron microscopy. No relationship has been found between molecular weight and polydispersity of polyhydroxyalkanoates and their composition. The type and content of monomers in polyhydroxyalkanoates influence their melting and decomposition temperatures and crystallinity. Incorporation of 4-hydroxybutyrate, 3-hydroxyvalerate or 3-hydroxyhexanoate into the chain of poly(3-hydroxybutyrate) decreases the melting and decomposition temperatures relative to poly(3-hydroxybutyrate) (175 ± 5°C and 275 ± 5°C, respectively). The larger the content of the second monomer in the chain of poly(3-hydroxybutyrate), the more significant the changes are. It is important to note that as melting and decomposition temperatures of copolymers decrease, the difference between them, amounting to 90-100°C, is not reduced. The crystallinity of copolymers is generally lower than that of poly(3-hydroxybutyrate) (75 ± 5%). The strongest influence on the ratio between the crystalline and amorphous phases of copolymers is exerted by 4-hydroxybutyrate; the influence of 3-hydroxyhexanoate is less pronounced, and 3-hydroxyvalerate has the least influence on this parameter. Copolymers of 3-hydroxybutyrate with 4-hydroxybutyrate have the lowest crystallinity (below 20%). Having determined how the melting and decomposition temperatures and crystallinity of polyhydroxyalkanoates are related to their composition, one can prepare copolymers with different properties, from hard thermoplastics to elastomers. The composition of polyhydroxyalkanoates influences the structure and surface properties of membranes prepared from polyhydroxyalkanoates (contact angle for water in air, surface free energy, interphase surface energy and adhesive force).

P33

NANOPARTICLE TOXICITY: CORRELATION TO EXTRACELLULAR MATRIX REMODELLING

D. Nikitovic[1], A. Tsatsakis[2], G. Tzanakakis[1]
[1]Dept. Histology-Anatomy-Embryology, Medical School, University of Crete, Heraklion, Greece, [2]Dept. of Toxicology, Medical School, University of Crete, Heraklion, Greece

Nanoparticles (NPs) have been shown to cause adverse effects *in vitro* and *in vivo.* The toxicity behaviour of NPs is distinguished from bulk materials because of the different toxicological profiles. NPs penetrate cells without the use of specific receptors possibly by a passive uptake or adhesive interaction. Depending on their localization inside the cell NPs can damage organelles, DNA and ultimately cause cell death. These responses occur after the activation of different cellular pathways. Studies have implicated three groups of MAP kinase cascades ERK (extracellular signal-regulated kinases), p38 mitogen-activated protein kinase and JNK (c-Jun N-terminal kinases), as well as redox-sensitive transcription factors such as NFkappaB and Nrf-2 in the action of NPs. It has furthermore been established that NPs create reactive oxygen species (ROS) and thereby modulate intracellular calcium concentrations, activate transcription factors and induce cytokine production. Extracellular matrices (ECM) represent a complex network of proteins, including collagens, elastin, laminins, and glycosaminoglycans (GAGs), constituting the cell microenvironment. ECM provides the bulk, shape and strength of tissues *in vivo*. Moreover, ECM provides much more than just mechanical and structural support, as it is critically important for cell growth, survival, differentiation and key to various disease processes including inflammation and cancer. The above render significant the investigation of NP exposure and modulation of ECM organization, metabolism and signaling. Recently, first efforts have been made in this direction. Thus, human keratinocytes exposed to TiO2 NPs showed altered expression of genes involved in matrix metalloproteinase activity (MMP-9 and MMP-10) and cell adhesion (fibronectin, integrin ITGB-6 and mucin) suggesting that these nanoparticles regulate cell-matrix adhesion of keratinocytes through ECM remodeling. In addition, expression of ECM proteins, collagen and fibronectin was diminished in human dermal fibroblast cells exposed to gold NPs. Cells cultured on the fibronectin/NP surfaces adopted an irregular shape and an aberrant organization of actin cytoskeleton. These first reports indicate that NPs are indeed involved in ECM remodeling directly correlated to modulations of key cellular functions.

P34

SOME ASPECTS OF COMPLEX POLYANILINE WITH POLYETHYLENEGLYCOL SYNTHESIS IN MEDICINE AND BIOLOGY

I. V. Solovyova, A. I. Piskareva, Ya. O. Mezhuev, M. I. Shtilman, Yu. V. Korshak
D. Mendeleev University for Chemistry Technologies of Russia, Moscow, Russia

Due to its considerable chemical stability, electroconductivity, low toxicity and potential biocompatibility polyaniline is a perspective material for using in medicine and biology. However polyaniline low solubility in the most organic solvent limits possibilities of it farther appliance. Formation of stable aqueous dispersion of polyaniline and polyethyleneglycol complexes during oxidative polymerization of aniline in aqueous solutions of polyethyleneglycol of different molecular weights and concentrations is represented in this research. It was shown that polyethyleneglycol molecular weight and concentration in aqueous solutions have a significant effect on the rate of aniline oxidative polymerization and the size of forming nanoparticles polymer-polymer complexes. Hydrophilic water compatible polyaniline and polyethyleneglycol complexes makes possible to apply coatings and pour films from aqueous solutions. Considering sufficient chemical stability of polyethyleneglycol polyaniline and polyethyleneglycol complexes can find application in bioanalytical and bioseparation system construction.

P35

SYNTHESIS AND POSSIBLE USING OF POLYANILINE AND POLYVINYL ALCOHOL COMPLEXES IN MEDICINE AND BIOLOGY

M. A. Salop, I. V. Solovyova, S. V. Osadchenko, Ya. O. Mezhuev, Yu. V. Korshak, M. I. Shtilman
D. Mendeleev University for Chemistry Technologies of Russia, Moscow, Russia

In spite of considerable perspectives of polyaniline appliance in sensor system producing which includes ones usable for determining of number of biologically active substance and metabolites its using is limited by difficulties of its processing into practically suitable materials. Formation of stable aqueous dispersion of polyaniline and polyvinyl alcohol complexes during oxidative polymerization of aniline in aqueous solutions of polyvinyl alcohol of different molecular weights and concentrations is represented in this research. The rate increase of oxidative polymerization of aniline with the raise of polyvinyl alcohol molecular weight in aqueous solution was determined. Considerable reduction of polyaniline and polyvinyl alcohol complexes particles size with the increase of polyvinyl alcohol molecular weight and concentration in reaction system was shown.
Forming of water compatible patterns of polyaniline during oxidative polymerization of aniline in aqueous solutions of polyvinyl alcohol makes possible their using in biosensors constructing.

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THE COMPLEX OF POLYANILINE – POLY-(N-VINYLPYRROLIDONE) IN DEVELOPMENT OF NANOFILTRATION MEMBRANES

S. V. Osadchenko, Yu. V. Korshak, Ya. O. Mezhuev, M. A. Salop, M. I. Shtilman, I. V. Solovyova
D. Mendeleev University for Chemistry Technologies of Russia, Moscow, Russia

Polyaniline due to its high chemical inertness, conductivity, and biocompatibility has a unique set of properties. Currently, the possibility of polyaniline to create biosensors, substrates for genetic engineering, and the ability to form complexes with DNA. However, the low solubility of polyaniline limits its further application. This paper shows the formation of stable aqueous dispersions of polyaniline - poly-(N-vinylpyrrolidone), which allows to put them on different surfaces. Modification of the ultrafiltration membrane was obtained by applying a selective layer based on system polyaniline - poly-(N-vinylpyrrolidone), which allowed to synthesize membranes of nanofiltration range. The high performance of composite nanofiltration membranes with a selective layer based on system polyaniline - poly-(N-vinylpyrrolidone) was shown for substances with a molecular weight of more than 900 Da, that can count on the use of membrane separation techniques in the number of biologically active substances close molecular weight.

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SYNTHESIS OF POLYPYRROLE-POLY-(N-VINYLPYRROLIDONE) COMPLEXES AND PROSPECTS OF THEIR USING IN BIOMEDICAL AREAS

A. I. Piskareva, I. V. Solovyova, Yu. V. Korshak, Ya. O. Mezhuev, M. I. Shtilman
D. Mendeleev University for Chemistry Technologies of Russia, Moscow, Russia

A unic set of polypyrrole properties provides the possibility of its using in different biomedical areas. High chemical stability, hemocompatibility and low toxicity of polypyrrole make possible its using for obtaining products which can function in contact with blood. However polypyrrole producing by oxidative polymerization is a cross-linked and infusible polymer that makes obtaining from it materials for medical and biological purposes more difficult. The possibility of hydrophilic water compatible polypyrrole-poly-(N-vinylpyrrolidone) complexes synthesis is shown in this research. Polypyrrole-poly-(N- vinylpyrrolidone) complexes can be applied from aqueous dispersions to the different surfaces so producing of materials applicable in hemosorbtion and bioanalytic systems construction.
It was determine that kinetics of oxidative polymerization of polypyrrole in aqueous solution of poly-(N-vinylpyrrolidone) induced by ammonium persulfate obeys the equation
$-d[Pyr]/dt=k_1[Pyr]([Ox]_0-([Pyr]_0-[Pyr]))+ k_2([Pyr]_0-[Pyr])[Pyr]$
[Pyr]-pyrrole concentration; [Ox]- ammonium persulfate concentration.
Rate constants of single electron transfer from pyrrole molecule to peroxydisulfates ion (k_1) are 0.024; 0.026; 0.028 l/(mol s) at temperatures 25, 30 and 35^{0}C respectively. Single electron transfer activation energy is 12 kJ /mol.
Rate constants of complexing (k_2) are 0.913, 1.17 and 1.371 l/(mol s) at temperatures 25, 30 and 35^{0}C respectively.
Pyrrole autocatalyzed oxidation activation energy is - 81 kJ /mol and is a fictitious value.
It was represented that size of polypyrrole-poly-(N- vinylpyrrolidone) complex particles depends on poly-(N- vinylpyrrolidone) molecular weight and pyrrole concentration in the initial solution and varies from 100 to 1000 nm.

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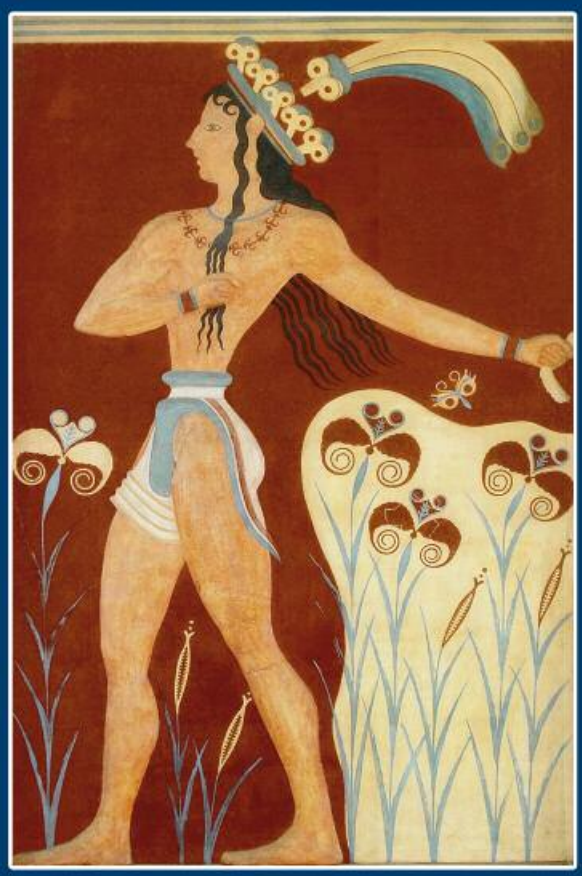

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