BIONANOTOX 2015

www.bionanotox.org

6th International Conference

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

Including Russian-Hellenic Workshop and School of Young Scientists

3-10 MAY, 2015 Heraklion, Crete, Greece

HELLENIC SOCIETY OF TOXICOLOGY

M.SHEMYAKIN AND YU.OVCHINNIKOV INSTITUTE OF BIOORGANIC CHEMISTRY

UNIVERSITY OF CRETE

EUROTOX

BIONANOTOX CONGRESSES

www.bionanotox.org

AMPHION

M. LOMONOSOV MOSCOW STATE UNIVERSITY

D. MENDELEYEV UNIVERSITY OF CHEMICAL TECHNOLOGY OF RUSSIA

ToxPlus

Final Program/Abstract Book

Contents

Page

Welcome letter 1

Committees 2

Scientific program 4

List of posters 12

General Information 15

Abstract book 16

List of Chairs, Speakers, Authors 45

Invitation Letter

On behalf of the organizing committee of 6th International Congress "Biomaterials and Nanobiomaterials: Recent Advances Safety - Toxicology and Ecology Issues" Including Russian-Hellenic Workshop and School of Young Scientists and Symposium of Nanotoxicology, we are privileged to invite you to grace with your presence and participation the works of the Congress, which is to be held in Heraklion, in the beautiful island of Crete, in May 2015.

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. Reduced registration rates will be provided, in order to enable more young scientists to attend the Symposium.

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

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

Co-Chairmen of the Organizing Committee

Aristidis Tsatsakis, PhD, DSc, ERT

Mikhail Shtilman, PhD, DSc

Committees

International Advisory Board

Honorary Chairman	Torchilin Vladimir	Professor, Director of Center of Pharm. Biotech & Nanomedicine, Northeastern University, Boston, USA
Honorary Chairman	Khokhlov Alexey	Academician of RAS, Vice-Rector of M. Lomonosov Moscow State University, Moscow, Russia
	Rakitskii Valerii	Academician of RAS, Head of F.Erisman Federal Center of Hygiene, Moscow, Russia
	Anastasiadis Spiros H.	Professor Director, 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
	Dimostenis Sarigiannis	Professor, Aristole University of Thesaloniki, Greece
	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
	Kouretas Demetrios	Professor, Vice Rector, University of Thessaly, Larissa, Greece
	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
	Syed F. Ali	Ph.D., Fellow ATS, National Center for Toxicological Research/USFDA, USA
	Tkachuk Vsevolod	Academician of RAS and RAMS, Dean of Faculty of Fundamental Medicine, M. Lomonosov Moscow State University, Moscow, Russia
	Ulbrich Karel	Professor, Head of Dept. of Biomedicinal Polymers, Institute of Macromolecular Chemistry, Prague, Czech Republic
	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
	Zezin Alexander	Corresponding member of RAS, Head of Chair, M. Lomonosov Moscow State University, Moscow, Russia

Organizing Committee

Co-President of the Congress	Tsatsakis Aristidis	Professor, Director of Forensic Sciences & Toxicology Dep., University of Crete, Iraklion, Greece
	Shtilman Mikhail	Professor, Head of Center "Biomaterials", D.Mendeleyev University of Chemical Technology of Russia, Moscow, 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
	Rizos Apostolos	Professor, Department of Chemistry, University of Crete, Iraklion, Greece
	Shishatskaya Ekaterina	Professor, Head of Chair Medical Biology, Siberian Federal University, Krasnoyarsk, Russia
	Stivaktakis Polychronis	PhD, Research Scientist, University of Crete, Iraklion, Greece
	Tsakalof Andreas	Professor, Medical Chem. Dep., University of Thessaly, Larissa, Greece
	Tzatzarakis Manolis	PhD, Assistant Professor, University of Crete, Iraklion, Greece
	Vamvakaki Maria	Associate Professor, Department of Materials Science and Technology, University of Crete
	Velonia Kelly	Associate Professor, Department of Materials Science and Technology, University of Crete
	Vynias Dionysios	PhD, Research Scientist, University of Crete, Iraklion, Greece

Sunday, May 3, 2015

Arrival - Registration

20.00 Welcome Cocktail

Monday, May 4, 2015

08.00-09.30 Breakfast

10.00 OPENING CEREMONY

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

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

10.20-11.00 ***OPENING LECTURES***
MULTIFUNCTIONAL AND STIMULI-SENSITIVE NANOSIZED DRUG DELIVERY SYSTEMS
V.P.Torchilin Co-President of Symposium
Northeastern University, Boston, USA

11.00-11.30 Coffee break, Poster session

11.30-12.30 ***MORNING SESSION***

Chairs: Prof. V.P.Torchilin, Prof. A.A.Berlin

11.30-12.00 STIMULATION OF REGENERATIVE AND REPARATIVE PROCESSES USING STEM CELL DERIVED EXTRACELLULAR VESICLES
V.A.Tkachuk, T.V.Lopatina, N.I.Kalinina
Faculty of Medicine, Lomonosov Moscow State University, 31-5, Lomonosovsky av., Moscow 119192 Russia

12.00-12.30 NANOPARTICLES, VESICLES, NANOFIBERS, MICROSPHERES, MACROSPHERES, CYLINDERS, FILMS, FOAMS, EMULSIONS... IT CAN ALL MAKE YOUR HEAD SPIN UNDER THE CRETAN SUN
R.J.Neufeld
Department of Chemical Engineering
Queen's University, Kingston, Ontario, Canada

12.30-13.00 **CONSTRUCTION OF SYNTHETIC POLYMERIC BIOMATERIALS**
M.I.Shtilman
Russian University of Chemical Technology Mendeleev, Russia, Moscow

13.00-14.00 Lunch

14.00-16.30 Break

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

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

16.30-16.50 **MAGNETIC NANOPARTICLES CROSS-LINKED BY CHYMOTRYPSIN. NANOMECHANICAL CONTROL OF ENZYME ACTIVITY VIA LOW-FREQUENCY MAGNETIC FIELD**
M.M. Veselov[1], M.V. Efremova[1], P.G. Rudakovskaya[1,2], A. Machulkin[1], S.L. Gribanovsky[4], I.V. Uporov[1], A.V. Kabanov[3,1], A.G. Majouga[1,2], Yu.I. Golovin[4,1], N.L. Klyachko[1-3]
[1]Lomonosov Moscow State University, Chemical Enzymology Department, School of Chemistry, Moscow, Russia; [2]National University of Science and Technology MISiS, Moscow, Russia; [3]Eshelman School of Pharmacy, University of North Carolina-Chapel Hill, Chapel Hill, USA; [4]Derzhavin Tambov State University, Tambov, Russia

16.50-17.10 **INTERACTION OF LIPOSOMES AND MAGNETIC NANOPARTICLES**
I.M. Deygen[1], E.O. Kutsenok[1], M.V. Efremova[1,2], P.G. Rudakovskaya[1,2], A.G. Majouga[1,2], Yu.I. Golovin[1,3], E.V. Kudryashova[1], A.V. Kabanov[1,4], N.L.Klyachko[1,2,4]
[1] M.V. Lomonosov Moscow State University, Faculty of Chemistry, Moscow, Russia
[2] National University of Science and Technology "MISIS" (MISIS), Moscow, Russia
[3] G.R. Derzhavin Tambov State University, Tambov, Russia
[4] University of North Carolina, Chapel Hill, NC, USA

17.10-17.30 **SAFETY WAYS OF POLYPROPELENE PRODUCTION WASTE`S UTILIZATION**
Sh.Askarova[1], G. Boyko[1], N.Lyubchenko[1], R.Sarmurzina[2],
[1]Kazakh National Technical University named after K.I.Satpayev, Almaty, Kazakhstan
[2]National joint-stock company "KazMunayGaz", Astana, Kazakhstan

17.30-17.50 **ACTIVATED ALUMINUM ALLOYS FOR WATER PURIFICATION**
B.S. Moldabekov[2], R.G. Sarmurzina[1], G.I. Boyko[2], N.P. Lubchenco[2], K.M. Kassymgaliyev[3], Ye.A. Issabayev[2]
[1] JSC «NC Kazmunaigas»
[2]Kazakh national technical university after K.I.Satpayev
[3] JSC «Embamunaigas»

17.50-18.10 **OSTEOGENIC POTENTIAL OF POLYMERIC POROUS SCAFFOLDS BASED ON POLYHYDROXYALKANOATES FOR REGENERATION OF BONE DEFECT OF RATS CRANUM**
A. Shumilova[1,2], 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

18.10-19.00 Break

19.00-20.00 Dinner

Tuesday, May 5, 2015

08.00-10.00 Breakfast

09.30-13.00 ***MORNING SESSION***

Chairs: Prof. M.A.Ostrovskii, Prof. S.Z.Rogovina

09.30-10.00 LIFE OF MOLECULES UNDER THE EXTREME COMDITIONS. STABILITY OF PROTEINS, NUCLEIC ACIDS, LIPIDS IN EXTHERMOFILES
S.D.Varfolomeev
Institute of Biochemical Physics of the Russian Academy of Sciences and Department of Chemical Enzymology of Moscow State University.

10.00-10.30 NANOPARTICLES AS TOOLS FOR HIGH-SENSITIVE IMMUNOASSAYS
B.B. Dzantiev
A.N. Bach Institute of Biochemistry, Federal Research Centre «Fundamentals of Biotechnology» of the Russian Academy of Sciences, Moscow, Russia

10.30-11.00 FUNDAMENTAL BASIS OF PRODUCTION AND APPLICATION OF BIODEGRADABLE POLYHYDROXYALKANOATESs
T.G. Volova[1,2], E.I. Shishatskaya[1,2], N.O. Zhila[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

11.00-11.30 Coffee break, Poster session

Chairs: Prof. T.G. Volova, Prof. K.B..Dzantiev

11.30-12.00 NANOPARTICLE-BOUND DOXORUBICIN FOR CHEMOTHERAPY OF BRAIN TUMOURS: PHARMACOLOGICAL AND TOXICOLOGICAL ASPECTS
S. Gelperina[1], A. Khalansky[2], V. Fedoseeva[2], E. Pereverzeva[3], I. Treschalin[3], V. Razzhivina[4], V. Balabanyan[4]
[1] Nanosystem Ltd., Moscow, Russia
[2] Institute of Human Morphology, Moscow, Russia
[3] Gauze Institute of New Antibiotics, Moscow, Russia
[4] Drug Technologies Ltd.

12.00-12.30 HARMFUL BISRETINOID SIDE PRODUCTS OF RHODOPSIN PHOTOLYSIS: PHYSIOLOGICAL AND PHARMACOLOGICAL WAYS OF EYE RETINA AND RETINAL PIGMENT EPITHELIUM PROTECTION
M. A. Ostrovsky
Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, Moscow, Russia

12.30-13.00 DNA APTAMERS AS AFFINITY PROBES IN KINETIC CAPILLARY ELECTROPHORESIS
Sv.M. Krylova and S.N. Krylov
Department of Chemistry and Centre for Research on Biomolecular Interactions, York University, Toronto, Ontario, Canada M3J 1P3

13.00-14.00 Lunch

14.00-16.30 Break

16.30-18.00 ***EVENING SESSION***

Chairs: Prof.A.M.Egorov, Prof. E.A.Markvicheva

16.30-17.00 **FUNDAMENTAL APPROACHES TO DEVELOPMENT OF TRANSDERMAL THERAPEUTIC SYSTEMS**
A.A. Shcherbina, A.E. Chalykh, R.R. Khasbiullin, A.D. Aliev A.N.
Frumkin Institute of Physical Chemistry and Electrochemistry of Russian Academy of Sciences, Moscow, Russia

17.00-17.30 **INVESTIGATION OF BINARY AND TERNARY BIODEGRADABLE COMPOSITIONS BASED ON POLYETHYLENE AND DIFFERENT POLYSACCHARIDES**
S.Z. Rogovina, K.V. Aleksanyan, A.A. Berlin
Semenov Institute of Chemical Physics, Russian Academy of Sciences, Moscow, Russia

17.30-18.00 **KINETIC SEPARATION: A CONCEPTUAL PLATFORM FOR DEVELOPMENT OF HOMOGENEOUS KINETIC AFFINITY METHODS**
S.N. Krylov
Department of Chemistry and Centre for Research on Biomolecular Interactions, York University, Toronto, Ontario, Canada M3J 1P3

18.00-19.00 **Break**

19.00-20.00 **Dinner**

Wednesday, May 6, 2015

08.00-09.30 **Breakfast**

10.00-13.00 ***MORNING SESSION***

Chairs: Prof. B.B.Dzantiev, Prof. R.Neufeld

10.00-10.30 **LINKING LONG TERM LOW DOSE EXPOSUE TO CHEMICALS TO HEALTH EFFECTS AND DESEASES: THE CURRENT STATUS AND FUTURE NEEDS**
Aristidis M. Tsatsakis
Department of Toxicology and Forensic Sciences, Medical School, University of Crete, Greece

10.30-11.00 **IMMUNOASSAY OF CHEMICAL CONTAMINANTS AS SCREENING METHOD FOR FOOD SAFETY**
S.A.Eremin
Department of Chemical Enzymology, Faculty of Chemistry, M.V.Lomonosov Moscow State University, Moscow, Russia and A.N. Bach Institute of Biochemistry, Federal Research Centre «Fundamentals of Biotechnology», Russian Academy of Sciences, Moscow, Russia

11.00-11.30 **KINETIC SIZE-EXCLUSION CHROMATOGRAPHY WITH MASS SPECTROMETRY DETECTION (KSEC-MS): AN APPROACH FOR SOLUTION BASED LABEL FREE KINETIC ANALYSIS OF PROTEIN-DRUG INTERACTION**
Sv.M.Krylova, S.N.Krylov
Department of Chemistry and Centre for Research on Biomolecular Interactions, York University, Toronto, Ontario, Canada M3J 1P3

11.30-12.00 Coffee break, Poster session

Chairs: Prof. V.G.Lunin, Prof. Prof. K.S.Golohvast

12.00-12.30 INTERACTIONS BETWEEN NATURAL MINERAL NANO- AND MICROPARTICLES WITH BACTERIA
K.S. Golokhvast, V.V. Chaika, S.Yu. Borisov
Far Eastern Federal University, Vladivostok, Russian Federation

12.30-13.00 MICROBIAL RESISTANCE TO ANTIBIOTICS AND ECOLOGY PROBLEMS
A.Egorov, V.G.Grigorenko, M.Yu.Rubtsova
Department of Chemistry, M.V. Lomonosov Moscow State University, GSP-1, Leninskie Gory, Moscow 119991, Russia

13.00-14.00 Lunch

14.00-16.30 Break

16.30-18.00 ***EVENING SESSION*** **- Round table workshop:**
Grants for Science and Technology in Nanotechnology and Materials in European Environment Introduction

Chairmen: Prof S.A.Eremin, Prof. A.Rizos

16.30-17.00 CRITICAL OVERVIEW OF THE MAGNIFICANT INCREASE INN VOLUME AND SPEED OF THE BIOMEDICAL SCIENTIFIC DATA AND ITS RELEVANCE TO HUMAN PROSPERITY
D.Spandidos
Department of Toxicology and Forensic Sciences, Medical School, University of Crete, Greece

17.00-17.30 GRANTS FOR SCIENCE AND TECHNOLOGY IN NANOTECHNOLOGY
D.Vynias
Toxplus SA

17.30-19.00 Break

19.00-20.00 Dinner

Wednesday, May 6, 2015

Thursday, May 7, 2015

08.00-09.00 Breakfast

10.00-13.00 ***MORNING SESSION***

Chairs: Prof. S.A.Eremin, Prof. M.I.Shtilman

10.00-10.30 NEW GENERATION OSTEOPLASTIC MATERIALS
A.V. Gromov, M.S. Bartov, D.M. Savina, K.E. Nikitin, M.S. Subbotina, T.M. Grunina, L.A. Soboleva, Z.M. Galushkina, A.S. Semikhin, A.S. Karyagina, V.G. Lunin
Gamaleya Research Center for Epidemiology and Microbiology, Moscow, Russian Federation

Thursday, May 7, 2015

10.30-11.00 **ANTIBACTERIAL ENZYMES - AN ALTERNATIVE TO ANTIBIOTICS. DELIVERY MATTERS**

N.L. Klyachko[1,6], L.Yu. Filatova[1], K.A. Miroshnikov[3], S.A. Legotsky[1], A.D. Priyma[1], T.S. Belyy[1], A. Usvaliev[1], P.G. Rudakovskaya[1], S.L. Gribanovsky[5], E.A. Zaitseva[1], A.B. Belova[1], A.G. Majouga[1,4], Yu.I. Golovin[1,5], A.V. Kabanov[1,6]

[1] M.V. Lomonosov Moscow State University, Faculty of Chemistry, Moscow, Russia
[3] M.M. Shemyakin & Yu.A. Ovchinnikov Institute of Bioorganic Chemistry, Moscow, Russia
[4] National University of Science and Technology "MISIS" (MISIS), Moscow, Russia
[5] G.R. Derzhavin Tambov State University, Tambov, Russia
[6] University of North Carolina, Chapel Hill, NC, USA

11.00-11.30 **BENEFIT-RISK RATIO OF FOOD FISH INTAKE AS THE SOURCE OF ESSENTIAL FATTY ACIDS VS. TOXIC HEAVY METALS: A CASE STUDY OF SIBERIAN GRAYLING FROM THE YENISEI RIVER**

M.I. Gladyshev[1,2]

[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Akademgorodok, Krasnoyarsk, Russia
[2]Siberian Federal University, Svobodny av. 79, Krasnoyarsk, Russia

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

Chair: Prof. M.I. Gladyshev

12.00-12.30 **HYALURONAN – IN VITRO MARKER OF KERATINOCYTE CONTACT ALLERGEN SENSITIZATION**

D.Nikitovic[1], R.M.Kavasi[1], K.Kechagias[1], I.Mantas[1], A.Tsatsakis[2], E.Corsini[3], G.N. Tzanakakis[1]

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

---

12.30-13.00 **INFLUENCE OF MULTIWALLED CARBON NANOTUBES ON COGNITIVE INDICATORS OF RATS**

K.S. Golokhvast[1], N.V. Sayapina[2], T.A. Batalova[2], V.V. Chaika[1], V.L. Kuznetsov[3], V.P. Kolosov[4], Y.M. Perelman[4],

[1] Far Eastern Federal University, Vladivostok, Russian Federation
[2] Amur State Medical Academy, Blagoveshchensk, Russian Federation
[3] Boreskov Institute of Catalysis SB RAS, Novosibirsk, Russian Federation
[4] Far Eastern Scientific Centre of Physiology and Pathology of Breathe, Blagoveshchensk, Russian Federation

13.00-14.00 **Lunch**

14.00-19.00 **Break**

19.00-20.00 **Dinner**

Friday, May 8, 2015

08.00-09.00 Breakfast

10.00-11.30 ***MORNING SESSION***

Chairmen: Prof. S.Krylov, E.A.Markvicheva

10.00-10.20 HIGHLY POROUS POLYMERIC MATERIALS FOR MEDICINE AND BIOTECHNOLOGY
N.R.Kildeeva[1], V.I. Lozinsky[2]
[1]Moscow State University of Design and Technology, Moscow
[2]A.N. Nesmeyanov Institute of Organoelement Compounds, RAS, Moscow

10.20-10.40 THE TOXIC EFFECT OF METRIBUZIN
V.Rakitskii, K.Lokhin
The Federal Budgetary Establishment of Science «Federal Scientific Center of Hygiene named after F.F.Erisman» of the Federal Service for Supervision in Protection of the Rights of Consumer and Man Well-being, Mytishi, Russia

10.40-11.00 BIOSAFETY ASSESSMENT OF POLYMER MATERIALS
O.A.Legonkova[1], M.S.Belova[1], I.P.Savchenkova[2].
[1]A.V. Vishnevsky Institute of Surgery, Moscow, Russia, 117997, Moscow, Bolshaya Serpukhovskaya Street, 27
[2]Y.R. Kovalenko All-Russian Research Institute of Experimental Veterinary, Moscow, Russia 109428, Moscow, Ryazanskiy Prospekt, 24-1

11.00-11.30 BIOCOMPATIBLE POLYSACCARIDE MICROCONTAINERS FOR DRUG DELIVERY : PREPARATION AND ACCUMULATON IN MULTICELLULAR TUMOR SPHEROIDS
A. Sumina[1], R. Akasov[1,2], T. Borodina[2], T. Bukreeva[2], E. Markvicheva[1]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia,
[2]Shubnikov Institute of Crystallography RAS, Moscow, Russia

11.30-11.45 Coffee break, Poster session

Chair: E.Vakonaki

11.45-12.00 SYNTHESIS OF POLYMERS WITH HIGH 3HHX CONTENT BY THE WILD-TYPE STRAIN *CUPRIAVIDUS EUTROPHUS* B10646 AND STUDY OF THEIR PROPERTIES
D.A. Syrvacheva[1,2], N.O. Zhila[1,2]
[1]Siberian Federal University, Institute of Fundamental Biology and Biotechnology, Krasnoyarsk, Russia
[2]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk Russia

CLOSING CEREMONY
Farewell Address – Closing Remarks

13.00-14.00 Lunch

19.00-22.00 Farewell Dinner

Saturday, May 9, 2015

08.00-09.00 Breakfast

10.00-13.00 Excursion

13.00-14.00 Lunch

19.00-22.00 Dinner

Sunday, May 10, 2015

08.00-09.00 Breakfast

Departure of Participants

List of Posters

P01
PROPERIES OF RARE-EARTH DOPED NANOPARTICLES AS BIOMARKERS
E. Wolska[1], J. Kaszewski[1,2], Ł. Wachnicki[1], B. Witkowski[1], P. Kiełbik[2,3], M. M. Godlewski[2,3] M. Godlewski[1,4]
[1]Institute of Physics, Polish Academy of Sciences, Al. Lotników 32/46, 02-668 Warsaw, Poland
[2]Department of Physiological Sciences, Faculty of Veterinary Medicine, Warsaw University of Life Sciences – SGGW, Nowoursynowska 159, 02-776 Warsaw, Poland
[3]Veterinary Research Centre, Warsaw University of Life Sciences – SGGW, Warsaw, Poland
[4]Dept. of Mathematics and Natural Sciences College of Science,
Cardinal S. Wyszyński University, Dewajtis 5, 01-815 Warsaw, Poland

P02
SILVER AND TITANIUM DIOXIDE INDUCED DNA DAMAGE AND REPAIR IN THREE HUMAN CELL LINES
L. Kapka-Skrzypczak[1,2], M. Czajka[1], K. Sawicki[1], T. Iwanenko[3], S. Sommer[3], M. Wojewódzka[3], M. Kruszewski M[1,2,3]
[1]Department of Molecular Biology and Translational Research, Institute of Rural Health, Lublin, Poland
[2]Department of Medical Biology and Translational Research, Faculty of Medicine, University of Information Technology and Management, Rzeszów, Poland
[3]Institute of Nuclear Chemistry and Technology, Centre for Radiobiology and Biological Dosimetry, Warsaw, Poland

P03
CELLULAR DISTRIBUTION AND TOXICITY OF SILVER AND TITANIUM DIOXIDE NANOPARTICLE IN A549 and HEPG2 CELLS
M. Kruszewski[1,2,3], S. Męczyńska-Wielgosz[2], M. Czajka[1], K. Sawicki[1], L. Kapka-Skrzypczak[1,3]
[1]Department of Molecular Biology and Translational Research, Institute of Rural Health, Lublin, Poland
[2]Institute of Nuclear Chemistry and Technology, Centre for Radiobiology and Biological Dosimetry, Warsaw, Poland
[3]Department of Medical Biology and Translational Research, Faculty of Medicine, University of Information Technology and Management, Rzeszów, Poland

P04
QUANTITATIVE ASSESSMENT OF ADHESIVE CONTACT BETWEEN CARBON FIBER AND EPOXY BINDING
V.A. Nelub
Scientific and educational center "Russian Composites", Bauman Moscow State Technical University, Moscow, 105005, Russia

P05
NOVEL SELF-ASSAMBLING AMPHIPHILIC POLYMERS FOR DRUG DELIVERING SYSTEMS
P. P. Kulikov[1], A. N. Kuskov[1], A. Tsatsakis[2], M. I. Shtilman[1]
[1]Mendeleyev University of Chemical Technology of Russia, Miusskaya sq. 9, Moscow, 125047, Russia
[2]Laboratory of Toxicology, Medical School, University of Crete, Heraklion, Voutes, 71003, Crete, Greece

P06
WATER-SOLUBLE COPOLYMERS OF ACRYLIC ACID AND ALLYL AMIDES OF CARBOXYL PLANT GROWTH REGULATORS
A. L. Luss[1], A. A. Dobrynin[1], A. M. Tsatsakis[2], M. I. Shtilman[1]
[1]D. Mendeleev University of Chemical Technology of Russia, Moscow, Russia
[2]University of Crete, Iraklion, Greece

P07
THE SYNTHESIS AND CROSS-LINKING OF AMPHIPHILIC POLYACRYLIC ACID FOR PRODUCING OF BONE CEMENT
S. E. Pokhil, Ya. O. Mezhuev, P. P. Kulikov, M. I. Shtilman, Yu. V. Korshak
Mendeleev University for Chemistry Technologies of Russia

P08
THE SYNTHESIS OF AN AQUEOEUS DISPERSION OF POLYPYRROLE STABILIZED BY POLYVINYL ALCOHOL AND PRODUCING OF HEMOCOMPATIBLE FILMS BASED ON IT
Ya. O. Mezhuev, A. I. Piskareva, A. A. Artyukhow, M. M. Goldin, S. E. Pokhil, M. I. Shtilman, Yu. V. Korshak, S. V. Osadchenko
Mendeleev University for Chemistry Technologies of Russia

P09

APPLICATION OF BIOMATERIALS AS ANTICANCER DRUG CARRIERS

A. B. Ismailova[1,2], E. O. Batyrbekov[1], D. Loca[3], A. O. Baiyrkhanova[4]
[1]Institute of Chemical Sciences, Kazakh-British Technical University, Almaty, Kazakhstan
[2]Kazakh Leading Academy of Architecture and Civil Engineering, Almaty, Kazakhstan
[3]Cimdins Riga Centre for Biomaterial Innovation and Development, Riga, Latvia
[4]Semey State Medicine University, Semey, Kazakhstan

P10

GLASS-BASED BIOCOMPOSITES IN THE EXPERIMENT "IN VITRO" AND "IN VIVO"

E. E. Stroganova[1], N. Yu. Mikhailenko[1], A. B. Elfimov[1], V. N. Sigaev[1], A. A. Artyukhow[1], M. I. Stilman[1], N. S. Sergeeva[2], I. K. Sviridova[2]
[1]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
[2]P. Hertsen Research Oncology Institute, Moscow, Russia

P11

DEVELOPMENT AND RESEARCH OF COMPOSITE MATERIAL FOR FORMATION A CELLULAR SCAFFOLD FOR THE ACCELERATED GROWTH OF CELLS

R. A. Morozov[1], A. V. Romashkin[1], A. V. Nikitina[1]
[1]Zelenograd Nanotechnology Center, Moscow, Russia

P12

DETERMINATION OF TRACE IMPURITIES OF METALS IN BIOLOGICAL OBJECTS BY MEANS OF ATOMIC ABSORPTION SPECTROSCOPY

G. I. Kandelaki, J. O. Mezhuev, Yu. V. Korshak
D. I. Mendeleev University for Chemical Technology of Russia, Russia, Moscow, 125047, Miusskaya Sq. 9

P13

MULTIFUNCTIONAL DRUG DELIVERY SYSTEM BASED ON POLYSACCHARIDES' CONTAINERS AND INORGANIC NANOPARTICLES

M. S. Miljohin[1], T. N. Borodina[2], D. A. Elfimov[3], Y. V. Grigoriev[2], T. V. Bukreeva[1,2]
[1]National Research Centre "Kurchatov Institute", Moscow, Russia
[2]Shubnikov Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia
[3]Lomonosov Moscow State University, Moscow, Russia

P14

POLYMER BIODEGRADABLE MATRICES WITH ENHANCED SURFACE PROPERTIES FOR TISSUE ENGINEERING

E. Markvicheva[1], M. Drozdova[1], T. Demina[2], M. Zlobina[3], A. Artyukhov[3], M. Shtilman[3], T. Akopova[2], Ch. Grandfils[4]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chem., Rus. Acad. Sci., Miklukho-Maklaya Str 16/10, 117997, Moscow, Russia
[2] Enikolopov Institute of Synthetic Polymer Materials, Rus Acad. Sci., Profsoyuznaya Str., 70, 117393 Moscow, Russia
[3]Mendeleev University of Chemical Technology of Russia, Miusskaya Sq., 9 125047 Moscow, Russia
[4]Interfacultary Research Centre on Biomaterials (CEIB), University of Liège, Chemistry Institute, B6C, B-4000 Liège (Sart-Tilman), Belgium

P15

HYDROGELS BASED ON HYALURONIC ACID AND CHITOSAN POLYELECTROLYTE COMPLEX FOR BONE TISSUE REGENERATION

T. S. Demina[1], S. A. Uspenskii[1,2], M. G. Drozdova[3], O. A. Dregval[4], A. I. Gaidar[5] N. R. Kildeeva[6], A. N. Zelenetskii[1], M. A. Selianin[2], E. A. Markvicheva[3]
[1]Enikolopov Institute of Synthetic Polymer Materials RAS, Moscow, Russia
[2]IRC "Martinex", Moscow, Russia
[3]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia
[4]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
[5]Research Institute of Advanced Materials and Technology, Moscow, Russia
[6]Moscow State University of Design and Technology, Moscow, Russia

P16

POLYMER MACROPOROUS SCAFFOLDS MODIFIED FOR PROMOTING STEM CELL ATTACHMENT AND DIFFERENTIATION

M. Drozdova[1], A. Artyukhov[2], S. Burov[3], M. Shtilman[2], E. Markvicheva[1]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia
[2]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
[3]Institute of Macromolecular Compounds RAS, Saint-Petersburg, Russia

P17
SUBMICRON CALCIUM CARBONATE PARTICLES: STRUCTURE AND LOADING WITH A PHOTODYNAMIC DYE
D. B. Trushina[1,2], I. V. Marchenko[2,3], T. N. Borodina[2], M. A. Vantsyan[3], S. N. Sulyanov[2], B. V. Nabatov[2], T. V. Bukreeva[2,3]
[1]Lomonosov Moscow State University, Moscow, Russia
[2]Shubnikov Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia
[3]National Research Centre "Kurchatov Institute", Moscow, Russia

P18
CALCIUMPHOSPHATE GLASSES AND GLASS-MATERIALS WITH HIGH IRON CONTENT
A. B. Elfimov[1], E. E. Stroganova[1], K. V. Poholok[2]
[1]D. I. Mendeleev University of Chemical Technology of Russia, Moscow, Russia
[2]M. V. Lomonosov Moscow State University, Moscow, Russia

P19
PREPOLYMERIZATION COMPLEX MODELING FOR MOLECULAR IMPRINTING PARAMETERS' ASSESSMENT
Y. V. Dolgaya, V. V. Barkaline
Belarusian National Technical University

P20
DEVELOPMENT OF NATURAL POLYSACCHARIDES FOR CONTROLLED RELEASE OF CLONIDINE
E. O. Batyrbekov, A. B. Ismailova
Institute of Chemical Sciences, Almaty, Kazakhstan

P21
NOVEL HYDROPHILIC POLYMERIC MATERIALS BASED ON WASTE OF POLYOLEFIN PRODUCTION
G. I. Boiko[1], N. P. Lubchenko[1], R. G. Sarmurzina[3], G. S. Aitkaliyeva[1], T. P. Maimakov[2], YU. V. Korshak[4]
[1]Kazakh National Technical University after K. I. Satpayev, Almaty, Kazakhstan
[2]Unat University, Almaty, Kazakhstan
[3]JSC NC "KazMunaiGas", Astana, Kazakhstan
[4]D. Mendeleev University of Chemical Technology of Russia, Moscow, Russia

P22
THE CATALYTIC ACTIVITY REGULATION OF ENZYME – INHIBITOR PAIR IMMOBILIZED ON MAGNETITE-GOLD NANOPARTICLES VIA ULTRA LOW MAGNETIC FIELD APPLICATION
A. V. Barulin[1], M. V. Efremova[1, 4], P. G. Rudakovskaya[1], O. N. Metelkina[1], A. V. Kabanov[1,2], Y. I. Golovin[1,3], A. G. Majouga[1,4], N. L. Klyachko[1,2]
[1]Laboratory for Chemical Design of Bionanomaterials, Chemical Enzymology Department, M.V. Lomonosov Moscow State University, Moscow, Russian Federation
[2]Eshelman School of Pharmacy, University of North Carolina at Chapel Hill (UNC), North Carolina, USA
[3]R.G. Derzhavin Tambov State University, Tambov, Russian Federation
[4]National University of Science and Technology MISiS, Moscow, Russian Federation

P23
IMPACT OF HEMORHEOLOGICAL PROPERTIES IN BLOOD TRANSPORTATION EFFICACY
I. Tikhomirova, A. Muravyov, E. Petrochenko, Y. Malysheva
Yaroslavl State Pedagogical University, Dept. Medicine & Biology, Yaroslavl, Russia

P24
NEW VISCOSUPPLEMENT FOR THE TREATMENT OF OSTEOARTHRITIS
A. V. Gromov, V. P. Gudov, N. N. Durmanov, M. S. Bartov, D. M. Savina, K. S. Savin, K. E. Nikitin, E. V. Razumkina, M. S. Subbotina, T. M. Grunina, L. A. Soboleva, A. S. Semikhin, O. A. Gra, A. S. Karyagina, V. G. Lunin
Gamaleya Research Center for Epidemiology and Microbiology, Moscow, Russian Federation

P25
Q-FISH ANALYSIS OF METAPHASE SPREADS FOR CLINICAL PURPOSE
P. Fragkiadaki[1], E. Vakonaki[1], E. Kouvidi[2], D. Vynias[1], D. Tsoukalas[1], A. M. Tsatsakis[1]
[1]Laboratory of Toxicology, Division of Morphology, Medical School, University of Crete, Voutes, Heraklion 71003, Crete, Greece
[2]Department of Haematology, University of Crete School of Medicine, *Voutes, Heraklion 71003, Crete, Greece*

General Information

Conference Venue

Agapi Beach
PO Box 2007 710 02 N.Stadion,
Heraklion, Crete, Greece

Tel: +30 2810 250502
Fax: +30 2810 258731
Website: http://www.agapibeach.gr/

Within close proximity to the Ancient Minoan Palace of Knossos and the town of Heraklion, Agapi Beach is the ideal all-inclusive family resort.

The Heraklion hotel's prime location allows guest to relax on the beautiful beach or explore the wonders of the Minoan civilization. With three pools, a long sandy beach and endless gardens, the Heraklion resort is the perfect place for families. Every day there are many activities and sports for parents and children. Showcasing a celebrated cuisine from the Hellenic and Cretan traditions, along with many international dishes, guests can enjoy the dining experience they want at the Main Restaurant, the Beach Front Taverna Akrogiali or at the Gourmet Italian Restaurant. Our vibrant lounge decorated with paintings and fine art and lobby bar are also focal points of the evening activity before or after dinner.

All 320 guestrooms are furnished in a contemporary style with light summer colours. Guestrooms and bungalows are located in the 5 floor main building, the award winning annex or throughout the gardens and will match your expectations for a true summer vacation place.

Symposium language

English and Russian

Symposium Secretariat

Triaena TOURS & CONGRESS S.A. EN ISO 9001:2000

Triaena Tours & Congress S.A.
16, Kifissias Ave., 115 26, Ampelokipoi, Athens, Greece
Tel : + 30 210 7499318/ 300, Fax: + 30 210 7705752
Email: information@bionanotox.org
Website: www.triaenacongress.gr, www.bionanotox.org

Abstract Book

COMBINATION siRNA/drug NANOPREPARATION FOR MULTIDRUG RESISTANT CANCERS

V. P. Torchilin
Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, Boston, MA 02115, USA

Tumor therapy, especially in the case of multidrug resistant cancers, could be significantly enhanced by using siRNA down-regulating the production of proteins, which are involved in cancer cell resistance, such as Pgp or survivin. Even better response could be achieved is such siRNA could be delivered to tumors together with chemotherapeutic agent. This task is complicated by low stability of siRNA in biological surrounding. Thus, the delivery system should simultaneously protect siRNA from degradation. We have developed several types of lipid-core polymeric micelles based on PEG-phospholipid or PEI-phospholipid conjugates, which are biologically inert, demonstrate prolonged circulation in the blood and can firmly bind non-modified or reversibly-modified siRNA. Additionally, these nanopreparations can be loaded into their lipidic core with poorly water soluble chemotherapeutic agents, such as paclitaxel or camptothecin. In experiments with cancer cell monolayers, cancer cell 3D spheroids, and in animals with implanted tumors, it was shown that such co-loaded preparations can significantly down-regulate target proteins in cancer cells, enhance drug activity, and reverse multidrug resistance.
In order to specifically unload such nanopreparations inside tumors, we made them sensitive to local tumor-specific stimuli, such as lowered pH, hypoxia, or overexpressed certain enzymes, such as matrix metalloproteases. Using pH-, hypoxia-, or MMP2-sensitive bonds between different components of nanopreparations co-loaded with siRNA and drugs, we were able to make the systems specifically delivering biologically active agents in tumors, which resulted in significantly improved therapeutic response.

STIMULATION OF REGENERATIVE AND REPARATIVE PROCESSES USING STEM CELL DERIVED EXTRACELLULAR VESICLES

V. A.Tkachuk, T. V. Lopatina, N. I. Kalinina
Faculty of Medicine, Lomonosov Moscow State University, 31-5, Lomonosovsky av., Moscow 119192 Russia

Current paradigm of human tissue regeneration implies stem cells abilities to replenish the number of cells damaged or lost due to disease or trauma. Therefore adult stem cells, including mesenchymal stem cells, isolated from bone marrow or adipose tissue (ADSCs), were suggested as therapeutics for the treatment of various human disorders, in particular when traditional methods fail. However results of ADSCs transplantation have soon challenged the initial idea that stem cells work only via structural cell replacement. Thus, transplantation of human ADSCs to immunodeficient NUDE mice stimulated the growth of recipient-derived (mouse) blood vessels without any evidences for incorporation of transplanted cells into growing vasculature. This indicated that ADSCs exert their beneficial effects on regeneration rather by establishing intercellular information exchange with recipient cells. Recent studies suggest that extracellular vesicles (EVs) might play a central role in the communication of transplanted stem cells with recipient tissue. These membrane entities with a size range 50 – 200 nm can transfer bioactive lipids, membrane receptors and enzymes between a stem cell and its target counterpart in the recipient tissue. Furthermore, stem cell-derived EVs can also deliver mRNAs and microRNAs to the target cell and this can result in changes of its phenotype or functionality. We demonstrated that EVs mediate the ability of ADSCs to stimulate the growth of blood vessels. Mechanisms of this EVs action included the transfer of metalloproteinases, growth factors and receptors to endothelial cells. Furthermore, ADSC utilized the transfer of angiogenic and antiangiogenic microRNAs to control the endothelial cell behavior. High efficiency of stem cell-derived EVs for the stimulation of tissue regeneration suggested them as novel therapeutics, which might replace approaches based on the cell transplantation.
This work was funded by Russian Ministry of Science and Education project No 14.610.21.0001.

LIFE OF MOLECULES UNDER THE EXTREME COMDITIONS. STABILITY OF PROTEINS, NUCLEIC ACIDS, LIPIDS IN EXTHERMOFILES

S. D. Varfolomeev
Institute of Biochemical Physics of the Russian Academe of Sciences and Department of Chemical Enzymology of Moscow State University.

The nature of thermal stability of biomacromolecules at extreme thermal conditions in unusual forms of life is discussed. The lecture is based on many years research of thermopiles and hyper thermopiles of hot springs of volcanic areas of Kamchatka. In details the following aspects are discussed:

- Physical chemistry of thermo inactivation and thermo stabilization of proteins, stability of enzymes of hyper thermopiles.

- Structural basis of protein stability of thermopiles. Bioinformatics and essential role of ion-ion interaction and salt bridges in hyper stable proteins.
- Thermal stability engineering. Methods of protein stabilization.
- Plasmids and viruses of thermopiles.
- Nature of stability of DNA.
- Nature of stability of lipids and membranes.
- Thermal cycles as driving forces of prebiological synthesis and selection of biopolymers.

The conclusions are made about the limits of existence of life under extreme conditions.

MULTIFUNCTIONAL AND STIMULI-SENSITIVE NANOSIZED DRUG DELIVERY SYSTEMS

Vladimir Torchilin
Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, Boston, MA 02115, USA

Various pharmaceutical nanocarriers, including liposomes and polymeric micelles, are frequently used for the delivery of a broad variety of both soluble and poorly soluble pharmaceuticals. Using nanoparticulate pharmaceutical carriers to enhance the *in vivo*efficiency of many drugs is now well established. Now, within the frame of this concept, it is important to develop multifunctional stimuli-responsive nanocarriers, i.e. nanocarriers that, depending on the particular requirements, can circulate long; target the site of the disease via both non-specific and/or specific mechanisms, such as enhanced permeability and retention effect (EPR) and ligand-mediated recognition; respond local stimuli characteristic of the pathological site by, for example, releasing an entrapped drug or deleting a protective coating under the slightly acidified conditions inside tumors facilitating thus the contact between drug-loaded nanocarriers and cancer cells; and even provide an enhanced intracellular delivery of an entrapped drug. Additionally, these carriers can be supplied with contrast moieties to follow their real-time biodistribution and target accumulation. Among new developments to be considered in the area of multifunctional pharmaceutical nanocarriers are: drug- or DNA-loaded delivery systems additionally decorated with cell-penetrating peptides for the enhanced intracellular delivery; "smart" multifunctional drug delivery systems, which can reveal/expose temporarily hidden functions under the action of certain local stimuli characteristic for the pathological zone; new means for controlled delivery and release of siRNA; and nanocarrier-based new targeted contrast agents for diagnostic imaging.

MAGNETICALLY ANISOTROPIC BIODEGRADABLE COMPOSITES BASED ON POLY(3-HYDROXYBUTYRATE) AND CHITOSAN FOR CONTROLLED DRUG RELEASE

A. L. Iordanskii[1], A. V. Bychkova[2], O. N. Sorokina[2], A. L. Kovarski[2], R. Yu. Kosenko[1], V. S. Markin[1], K. Z. Gumargalieva[1], S. Z. Rogovina[1], A. A. Berlin[1]
[1]*Semenov Institute of Chemical Physics, Russian Academy of Sciences, Kosygin St. 4, Moscow, Russia*
[2]*Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, Kosygin St. 4, Moscow, Russia*

To increase the therapeutic efficiency of drugs, a procedure for their encapsulation into amphiphilic compositions based on poly(3-hydroxybutyrate) and chitosan was developed. For the control of drug release rate we introduced magnetite (Fe_3O_4) particles, since the type of their distribution in the matrix can be controlled by outer magnetic field. These composites represent a new class of biodegradable materials: magnetic biodegradable nanocomposites (MBNC) with drug transport rate controlled by magnetic field.

The MBNC with the general composition yXT+0.2PHB + 0.05drug + xFe_3O_4 (y=0.63-0.75; x=0–0.12) were studied by ferromagnetic resonance (FMR) spectroscopy and scanning electron microscopy (SEM).

The MBNC films were produced by the casting a water–organic solution onto a glass substrate placed between the poles of a permanent magnet (field strength ≈ 2kG). The poles were located parallel and perpendicular to the plane of the films. The average diameter of the magnetic nanoparticles (MNPs) used was ≈35nm. The rate of drug (dipyridamole) release into water was recorded on a Beckman DU62 spectrophotometer.

Under the action of magnetic field MNPs are arranged in linear aggregates according to FMR data. These aggregates situated along the field direction were ≈500–800 nm in length and ≈80–100 nm in width (SEM). So we had samples with different orientation of the linear aggregates of MNPs or without any aggregates (in case of the film preparation without a magnetic field). The formation of oriented particle associates markedly affects the rate of drug release from MBNC films. The drug release rate is higher for magnetically anisotropic samples than for isotropic samples.

Thus, it was demonstrated that the rate of drug release from MBNC depends on the spatial arrangement of magnetic nanoparticles. The formation of ordered MNP structures (linear aggregates) by means of external magnetic fields can be used to vary the kinetic profiles of drug release.

The work was supported by the Division of Chemistry and Materials Science of the RAS (basic research program OKhNM-1 "Design of Macromolecular Structures of New Generations") and by the Russian Foundation for Basic Research (project 11–03–00405a).

NANOPARTICLES, VESICLES, NANOFIBERS, MICROSPHERES, MACROSPHERES, CYLINDERS, FILMS, FOAMS, EMULSIONS... IT CAN ALL MAKE YOUR HEAD SPIN UNDER THE CRETAN SUN

Ronald J. Neufeld
Department of Chemical Engineering, Queen's University, Kingston, Ontario, Canada

Abstract
This year -2015- represents the 5th year that I will have the opportunity to present a talk at BIONANOTOX, assuming that my abstract is accepted for inclusion in the program.
Looking back over my abstracts from previous years, I noticed two things. One is that the abstracts seemed to get shorter year by year. If the trend continues, this abstract will be nearly complete. The second thing that I observed is that all of the abstracts relate in some way to the delivery of insulin from nano/micro/macro this and that, as illustrated in Table 1.

Table 1: Theme of talks presented by RJN at BIONANOTOX
2010: Biomaterial choices in design of nanoparticulate carriers for insulin
2011: Fate and toxicity of nanoparticulate carriers delivering insulin
2012: I wasn't at Bionanotox 2012, but I was thinking of you from cold Canada
2013: Nano and microfiber networks supporting pancreatic islets for implantation
2014: Microparticulate carriers embedded in wound dressing releasing insulin
2015: How do we make sense out of it all?

My goal in 2015 is to take us back to the future. What are we trying to do, how are we trying to do it, where will it all go, when will it all end? The focus will revolve around carriers for actives such as insulin, but will break new ground by describing cylinders and implants and vesicles and emulsions and films.
If successful, you will feel that we may have learned something new. If unsuccessful, you can tell me about it at the pub by the beach. Either way, we come out as winners, both you and I.

CONSTRUCTION OF SYNTHETIC POLYMERIC BIOMATERIALS

M. I. Shtilman, A. A. Artyuhov, A. V. Goryachaya, O. V. Klimenko, P. P. Kulikov, A. N. Kuskov, Ya. O. Mezhuev, A. A. Morgacheva, S. V. Osadchenko
Russian University of Chemical Technology Mendeleev, Russia, Moscow

In the example of water-soluble polymer hydrogels and amphiphilic polymers demonstrate the influence of various factors (such as input reactants, the reaction conditions, conditions of formation of the polymer structure) on the properties of the resulting biomaterial - their bio- and hemocompatibility, biodegradability, possible immobilization of different ligands, and the physico-chemical other properties are determined by the conditions of operation.
The possibility of producing polymer gels based on cross-linked polyvinyl alcohol with different properties - isotropic highly swellable gels, hydrogels porous hydrogels highly branched polymer hydrogels densified polymeric structure allowing to obtain a variety of medical products used for topical application and implantation.
Methods of synthesis of amphiphilic semitelehelevyh N-vinylpyrrolidone polymers with different molecular weight, hydrophobic block structure containing various polar functional groups in the block, which allows their use as carriers for various biologically active substances.

INVESTIGATION OF BINARY AND TERNARY BIODEGRADABLE COMPOSITIONS BASED ON POLYETHYLENE AND DIFFERENT POLYSACCHARIDES

S. Z. Rogovina, K. V. Aleksanyan, A. A. Berlin
Semenov Institute of Chemical Physics, Russian Academy of Sciences, Moscow, Russia

Constantly increasing interest to biodegradable polymers led to appearance of a large variety of different compositions on their base. One of the most efficient and economically profitable methods of creation of the polymer materials, which are characteristic of biodegradability under the environmental conditions, is their production via mixing of synthetic and natural polymers. Such polymer compositions allowing one to use properties of each component are successfully applied in numerous areas especially for production of packing materials, films for food products and also articles for short-term usage.
Among various polymers of natural origin using in production of biodegradable composite materials the polysaccharides, which are almost inexhaustible raw materials, are widely used.
The compositions of natural polysaccharides and their derivatives: cellulose, starch, chitin, chitosan and ethyl cellulose with low-density polyethylene (LDPE) are produced by ecologically pure method in absence of solvents in solid phase under conditions of shear deformations in the rotor disperser at 130-150°C. This method allows one to ob-

tain highly dispersed polymer powders even in the case when one of the components of the system grinded is an infusible polymer (polysaccharide). The mechanical properties, structure and capacity to biodegradation with using of different physico-chemical methods of analysis (X-ray diffraction analysis, DSC, SEM) are studied. For increasing of biodegradation of these compositions the two ways are used:
The addition in the system of poly(ethylene oxide) of different molecular weight. The choice of PEO is connected with its hydrophilic property that promotes the increase of the final material biodegradation and due to its plastification improves the mechanical properties of the final compositions.
The obtaining of ternary compositions based on two polysaccharides with LDPE.
It is established that the addition of poly(ethylene oxide) as well as polysaccharides as a third component promotes a significant increase in the biodegradability of compositions and, consequently, results in the expansion of the possible areas of application of the related materials.

This work was supported by the Russian Science Foundations, project no. 14-13-00803.

SAFETY WAYS OF POLYPROPELENE PRODUCTION WASTE`S UTILIZATION

G. Boyko[1], N. Lyubchenko[1], R. Sarmurzina[2], Sh. Askarova[1]
[1]Kazakh National Technical University named after K.I.Satpayev, Almaty, Kazakhstan
[2]National joint-stock company "KazMunayGaz", Astana, Kazakhstan

The paper presents a safe method for using atactic polypropylene which is the waste of isotactic polypropylene production. By radiation-chemical modification of atactic polypropylene was created new reagents APP:MA/200, APP:MA/400, APP:MA/800 and APP:MA/1200.
The structure of new reagents was proved by using IR-spectroscopy.
The intrinsic viscosity of the samples was determined by Ubbelohde viscometer in benzene. On the basis of intrinsic viscosity according to the Mark-Houwink formula was calculated the average viscosity-molecular weight. There was revealed that molecular weight of samples increasing from 7900 to 22400 subject to irradiation doze. Most likely, increasing of irradiation degree has a positive effect on the ability of monomer to immobilization onto atactic polypropylene.
We determined the grafting degree of monomer by using potentiometric titration method. It was found that grafting degree of monomer growth with irradiation dose and so sample`s molecular weight increasing. Samples with irradiation degree 800kGray and 1200kGray characterized with a maximal immobilization degree in 94 mole %
There was involved X-ray analysis for determining the effect of lateral graft copolymer's functional groups on the structure and phase composition of samples. Graft copolymers characterizing with a slight changes in a unit crystal cell parameters. However, we may observe an amorphization of samples increase to 53% with growing irradiation.
Changes in samples thermal characteristics were observed by differential scanning calorimetry (DSC). Revealed that reactants melting temperature growth with increasing molecular weight of samples, as well as monomer`s immobilization degree. The highest melting temperature shows reagent APP:MA/1200, it is 270^{0}C. Probably, with the amount of side functional groups increase sample's melting temperature.
Modified polymer samples were tested as asphalt-resin-paraffin deposit's inhibitors and as oil additives. The results show that reagents can be used in oil transportation.

BENEFIT-RISK RATIO OF FOOD FISH INTAKE AS THE SOURCE OF ESSENTIAL FATTY ACIDS VS. TOXIC HEAVY METALS: A CASE STUDY OF SIBERIAN GRAYLING FROM THE YENISEI RIVER

M. I. Gladyshev[1,2]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Akademgorodok, Krasnoyarsk, Russia
[2]Siberian Federal University, Svobodny av. 79, Krasnoyarsk, Russia

Consuming of fish is known to provide many benefits for human health due to high contents in the products of essential polyunsaturated fatty acids of ω3 family (EFA), namely eicosapentaenoic acid (EPA, 20:5ω3) and docosahexaenoic acid (DHA, 22:6ω3). A regular consumption of EFA (EPA+DHA) prevents cardiovascular diseases and neural disorders. However, fish products are often contaminated by toxic organic compounds and heavy metals. Thus, recently a number of researches started a quantitative estimation of risks versus benefits of fish intake for human health. A formula was derived for quantification of benefit-risk ratio (hazard quotient) for intake of product, contained essential polyunsaturated fatty acids vs. heavy metals. The quotient was used in three years case study of contents of essential fatty acids and heavy metals in Siberian grayling (*Thymallus arcticus* Pallas), the main food fish from middle section of the Yenisei River. As found, in general the fish intake was potentially very beneficial for human health, except few occasions, when the risk overweighed the benefit because of high contents of chromium in the fish muscle tissue. The data demonstrated a necessity of a regular monitoring of the hazard quotients for food fish in wild conditions, based at least on monthly sampling frequency.

FUNDAMENTAL BASIS OF PRODUCTION AND APPLICATION OF BIODEGRADABLE POLYHYDROXYALKANOATESs

T. G. Volova[1,2] E. I. Shishatskaya[1,2], N. O. Zhila[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

Microbial polyhydroxyalkanoates (PHAs) have long been studied due to their potential for replacement of petroleum-based plastic. The study addresses the effect of different conditions of carbon nutrition on synthesis of polyhydroxyalkanoates by the bacterium *Ralstonia eutropha*. First and foremost, PHAs are carbon storage compounds for many organisms. There are still many aspects of the physiology of PHA accumulation and degradation that are still not understood.

Measurements of key P3HB-related enzyme activities throughout cell growth reveals correlations of acetoacetyl-CoA reductase and synthase enzyme activity maxima with P3HB biosynthesis. The investigation addressed kinetic parameters of growth and accumulation of polyhydroxyalkanoates and gas exchange parameters of the culture of the CO-resistant strain of the hydrogen bacteria *Ralstonia eutropha* B 5786 cultivated on synthesis gas – a product of gasification of brown coals.

The results were compared with those obtained by growing the bacteria on electrolytic hydrogen and it was concluded that synthesis gas can be successfully used to produce PHAs. In experiments with wild-type strain it has been first found that under mixotrophic growth conditions – CO_2 + co-substrate (alcanoic acids) – bacteria can synthesize multi-component PHAs, consisting of short- and medium-chain-length monomers with carbon chains containing 4 to 8 atoms. It has been shown that PHA composition is determined by the type of the co-substrate. Fatty acids with odd number of carbons induce bacteria to synthesize multi-component PHAs with 3-hydroxybutyrate, 3-hydroxyvalerate, and 3-hydroxyhexanoate as major monomers and 3-hydroxyheptanoate and 3-hydroxyoctanoate as minor, occasionally occurring, ones. Fatty acids with even number of carbons induce synthesis of not only their respective monomers (3-hydroxyhexanoate and 3-hydroxyoctanoate) but also 3-hydroxyvalerate, making possible synthesis of four-component PHAs, containing 3-hydroxybutyrate and 3-hydroxyhexanoate as major components. A family of short- and medium-chain-length four- and five-component PHAs has been synthesized and their physicochemical and biomedical-properties examined.

NANOPARTICLES AS TOOLS FOR HIGH-SENSITIVE IMMUNOASSAYS

B. B. Dzantiev
A. N. Bach Institute of Biochemistry, Federal Research Centre «Fundamentals of Biotechnology» of the Russian Academy of Sciences, Moscow, Russia

Modern medical diagnostics, ecological monitoring, and safety control need in simultaneous assays of wide rows of analytes in extremely low concentrations. In this connection the solutions combining fast not-labour (including out-of-lab) testing and low detection limits are of high demands for immunoassays. The report presents the results of our development of new sensitive immunoanalytical systems and characterization of the current level of the investigations in this field.

Different nanodispersed particles provide various novel possibilities as markers for the detection of immune complexes. The application of fluorescent semiconductor nanoparticles, quantum dots, as an alternative label for rapid immunochemical tests is a subject of specific interest. Their detection in lower concentrations as compared with the commonly used colloidal gold has been confirmed for membrane assays, and the given effect has been transformed into a lower limit of the analyte detection. The quantum dots demonstrate high stability of the fluorescence, which provides reliable documentation and quantification of the assay results. Other nanodispersed carriers, magnetic iron oxide nanoparticles, are characterized as tools for pseudo-homogeneous immunoassays combining diffusion-independent interactions in the volume of the reaction mixture with the following rapid concentration and separation of the formed immune complexes and their simple heterogeneous detection.

The applications of nanoparticles in different approaches to amplify analytical signals in the course of immunoassays are characterized, including cascade aggregation of nanoparticles via ligand-receptor interactions. The potential of multiparametric optimization of nanoparticles size, content and composition of labelled immunoreactants is discussed as way to reach maximal sensitivity of immunoassays. It was shown that such variation may change the threshold level between positive and negative results of immunochromatographic tests in 10-50 times (depending on target antigen and antibody affinity) without loss of the assay accuracy. Video digital registration of the bound label coloration was characterized as an additional tool to quantify sub-threshold concentrations of target analytes. Experimental evaluation of the effectiveness of the proposed approaches has been carried out on the examples of immunochemical test-systems for the control of low- and high molecular weight compounds (mycotoxins, cardiac markers, etc.).

This work was supported by the Russian Science Foundation (Grant 14-14-01131).

HARMFUL BISRETINOID SIDE PRODUCTS OF RHODOPSIN PHOTOLYSIS: PHYSIOLOGICAL AND PHARMACOLOGICAL WAYS OF EYE RETINA AND RETINAL PIGMENT EPITHELIUM PROTECTION

M. A. Ostrovsky
Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, Moscow, Russia.

The final step of rhodopsin photolysis is free all-*trans*-retinal release. Deficiency of all-*trans*-retinal removing system leads eventually to the bisretinoid pigment formation. Most of them are lipofuscin granules (LG) fluorophores.
Study of fluorescence spectra and LG fluorophores composition of RPE isolated from 42 human cadaver eyes (donors of different ages /from 17 to 78 years/) shown that the spectral characteristics of fundus autofluorescence may be different under certain pathological conditions from the norm.
LG are able to light-induced generation of reactive oxygen species (ROS). LG are more active in the ROS generation than its main fluorophore A2E itself. Exposure the A2E-containing liposome to light leads to release of A2E-oxidized forms that can damage other intracellular organelles and initiate apoptosis.
Melanosomes are able to protect the RPE cells from phototoxic A2E and its oxidized forms. In addition to melanosomes a protective role can play oxy-carotenoids although they are localized in the retina rather than in the RPE.
Recently we synthesized new antioxidant called «Oxybiol» that is promising substance to protect RPE cells from LG phototoxicity.

OSTEOGENIC POTENTIAL OF POLYMERIC POROUS SCAFFOLDS BASED ON POLYHYDROXYALKANOATES FOR REGENERATION OF BONE DEFECT OF RATS CRANUM

A. Shumilova[1,2], 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

Recently a constant growth the number of patients with defects of the cranium, which is observed. It is associated with an increase the number of head injuries and surgical activity at tumors growth and pathology of vascular of the brain. The search for new and improvement famous osteoplastic materials becomes paramount of cranioplasty. Polyhydroxyalkanoates (PHAs) are great interest for reconstructive surgery of bone tissue because of their slow bioresorption in vivo and mechanical strength.
The aim of this work is to study of steogenic potential of polymeric porous scaffolds from PHA on the model of bone defect of rats cranium.
The two types of experimental samples polymer scaffolds of different geometry on the basis of poly-3-hydroxybutyrate are obtained and studied. The first type of products were 3D porous implants obtained leaching technique. The second type of polymeric products are- molded plates with CO2-laser were treated (LaserProExplorer II) in the mode vector and raster engraving at power v = 4%, the rate P = 100%, the resolution (dpi = 1000). The ability of polymeric carriers from PHA to support adhesion, proliferation and directed differentiation of cells was research in culture MMSC isolated from bone marrow and adipose tissue of Wistar rats. The differentiation of MMSC into osteoblasts is confirmed with gene expression of osteocalcin (BGP) using PCR "real time", staining of the cells antibodies to osteopontin and activity of intracellular alkaline phosphatase. On the model of bone defect of rats cranium 3D porous implants from P3HB in combination with osteoblasts, differentiated from MMSC of adipose tissue, were studied.
Dynamics is filling of defect of the newly formed bone tissue in two projections, frontal and axial, was defined. According to hematological indices and activity of alkaline and acid phosphatases unreported a deviation from the norm in the experimental group was unreported.
After 120 days while filling of the defect experimental polymer implant with osteoblasts it was completely closed and did not exceed 100% of the original (0.5 mm). The size of defect in the negative control group and the comparison group was remained at 1.0-1.2 mm.

NEW GENERATION OSTEOPLASTIC MATERIALS

A. V. Gromov, M. S. Bartov, D. M. Savina, K. E. Nikitin, M. S. Subbotina, T. M. Grunina, L. A. Soboleva, Z. M. Galushkina, A. S. Semikhin, A. S. Karyagina, V. G. Lunin
Gamaleya Research Center for Epidemiology and Microbiology, Moscow, Russian Federation

Bone morphogenic proteins (BMPs) are local factors essential for bone growth and regeneration. As a component of different biomaterials BMPs possesses high potential for clinical use in reconstructive surgery of bone defects. According to the results of expanded clinical trials, osteoinductivity of composite materials containing recombinant human BMPs (rhBMPs) corresponds to that of an autologous bone graft and even exceeds it. The main role of a delivery system for BMPs is to retain these growth factors at the site of injury for a prolonged time frame, providing an initial support to which cells attach and form regenerated tissue. The carrier should provoke optimal in-

flammatory responses, be biodegradable to allow the formation of an interface with the surrounding biological tissue, present adequate porosity to allow the infiltration of cells and formation of blood vessels at the new bone and maintain BMPs bioactivity whilst releasing the protein in a time- and space-controlled way to promote the formation of new bone at the treatment site. Demineralized bone matrix (DBM) possesses all these essential characteristics, and is widely used as an osteoplastic material itself.
The new generation osteoplastic material "Gamalant" based on DBM with immobilized rhBMP-2 was developed. Biological activity of produced rhBMP-2 was demonstrated by alkaline phosphatase assay in C2C12 and C3H10T1/2 cells. The original technology of DBM production involves biochemical control of a number of parameters, including lipid, calcium, phosphorus, native BMP-2 and BMP-7 content, humidity, pH, and sterility. A wide range of "Gamalant" products was created, including bone chips of various grain size, composite materials and membranes. Regenerative potential of "Gamalant" products was evaluated in experiments on rats in models of ectopic osteogenesis, intrabone grafting and cranial defects. Biochemical and histological analysis of the implanted biocomposites demonstrated their high biocompatibility and osteoinductivity.
Clinical trials of the developed Gamalant materials performed in leading clinical centers of the Russian Federation evidenced their great performance in patients: they did not cause complications, and regeneration proceeded faster than after the analogous procedures with other materials. The developed medical products were registered and certificates of suitability were received.

ACTIVATED ALUMINUM ALLOYS FOR WATER PURIFICATION

R. G. Sarmurzina[1], G. I. Boyko[2], N. P. Lubchenco[2], K. M. Kassymgaliyev[3], B. S. Moldabekov[2], Ye. A. Issabayev[2]
[1]JSC «NC Kazmunaigas»
[2]Kazakh national technical university after K.I.Satpayev
[3]JSC «Embamunaigas»

The aim of this work is improving purification efficiency of drinking water and formation water from toxic compounds of natural and anthropogenic origin. Improvement of its quality was done by compositions based on activated aluminum alloys.
Reagents have fast reaction with water. During the exothermic reaction reagents produce hydrogen, and depending on conditions, several species of aluminum hydroxides: bayerite(α-$Al(OH)_3$), gibbsite(γ-$Al(OH)_3$), diaspore(α-AlOOH), boehmite(γ-AlOOH). They have a large active surface and they are effective adsorbents.
Water purification was carried out in water stations. After treatment river water with reagent Rau-97 in doses from 50 to 250 x 10^{-6} kg/dm^3 it meets the requirements of GOST drinking water: turbidity is reduced from 15.0 to 0.07·10^{-6} kg/dm^3 (MPC 1.5·10^{-6} kg/dm3), color from 35 to 6 Grad (MPC 20 deg), the remainder Al -0,12-0,4·10^{-6} kg/dm^3 (MPC 0.5·10^{-6} kg/dm^3). Coagulants have also a bactericidal effect. Sowing after water treatment with agent in dose 100·10^{-6} kg/dm^3 through the 3600s shown a content of bacterial 250 in 10^{-6}dm^3; through the 10800s-310 bacterial in 10^{-6} dm^3.
The reagents were tested for treatment Eastern Makat (Kazakhstan) field water. The mineral salts are 172.3 g/l, pH 4.73. Analysis of water before and after treatment was performed on a spectrometer ICP-OES 8000.Water before treatment has next parameters: redox potential(Eh) was 427.9 mV, indicating the presence of free oxygen and cation (Fe, V, Sr, Cu, Pb) in the form of its higher valence conductivity - 345 mS/cm directly depends from the concentration of salts in the solution. After treatment with reagents Rau water has next changes: there are decrease in Eh of water, salts and conductivity in the direction of lower values. With reagent Rau-92,5 Eh decreased from 427.9 to 123 mV , 7mV, conductivity from 345 to 222 mS/cm, total mineralization from 172.3 to 111.2 g/l and pH of 4.91 to 4,73. Fe total content decreased from 203 mg/l to 0.53 and 1.33 mg/l after treatment with reagents Rau-92,5 and Rau-85, respectively, Mg^{+2} ions from 1920 mg/l to 620 and 893 mg/l, Ca^{2+} from 4600 to 3821 and 3683 mg/l. These data confirm the high adsorption ability of coagulants to ions Fe total, average to ions Mg^{+2} and low ability to Ca^{+2} and Na^{+}.

THE TOXIC EFFECT OF METRIBUZIN

Valerii Rakitskii, Konstantin Lokhin
The Federal Budgetary Establishment of Science «Federal Scientific Center of Hygiene named after F.F.Erisman» of the Federal Service for Supervision in Protection of the Rights of Consumer and Man Well-being

Metribuzin is selective synthetic herbicide of triazinone group that inhibits of photosynthesis (photosystem II). The products using this active substance is applied for pre- and post-emergence treatment against a broad range of annual grass and dicotyledonous weeds.
The comparative toxicological study was carried out to clarify toxic action of metribuzin in nano- and macroforms. NOEL, biological action and toxicokinetic parameters were evaluated in chronic and subchronic experiments on the white male rats.
The results revealed that $NOEL_{ch}$ of both pesticide forms based on haematological, biochemical, physiological and

morphological parameters were the same. Moreover, the tendency of more expressed influence of nanoform compared with macroform on parameters studied was noticed at high and middle doses.
The study of toxicokinetic parameters in kidneys, liver, testicles, brain, urine and feces have shown greater permeability histo-hematological barriers of nanoform metribuzin. The maximum accumulation of nanoform was observed in parenchymal organs.

INFLUENCE OF MULTIWALLED CARBON NANOTUBES ON COGNITIVE INDICATORS OF RATS

K. S. Golokhvast[1], N. V. Sayapina[2], T. A. Batalova[2], V. V. Chaika[1], V. L. Kuznetsov[3], V. P. Kolosov[4], Y. M. Perelman[4],
[1]Far Eastern Federal University, Vladivostok, Russian Federation
[2]Amur State Medical Academy, Blagoveshchensk, Russian Federation
[3]Boreskov Institute of Catalysis SB RAS, Novosibirsk, Russian Federation
[4]Far Eastern Scientific Centre of Physiology and Pathology of Breathe, Blagoveshchensk, Russian Federation

Modern nanomaterials are increasingly going into our lives, and living organisms including humans constantly contact with environment and continuously feel the influence of its factors. Usually the criterion negative or positive reactions of the organism to environmental factors is considered the shift of physiological or other indicators selected by researcher for evaluation. Behaviour as a complex act consisting of a set of elements, is regarded as one of the most important ways of adaption. For example, the behaviour of exploratory rats is expressed by certain acts and postures that may be analyzed.
Against this background the area of influence of water-insoluble substances - nanomaterials - on the higher nervous activity of animals remains practically unexplored.
The paper presents the results of the first study of influence of nanomaterials on search activity and emotional status of laboratory rats via the test named "opened field".
During 3 days and 10 days rats got with fodder multiwall carbon nanotubes (MWCNT) with a diameter of 8-10 nm at a dosage of 500 mg / kg.
The integrated indicator of the level of anxiety is shown to have started to grow already on 3rd day and on 10th day have increased in 2 times in the group of rats treated by MWCNTs. Also MWCNTs are demonstrated to reduce the integral indicator of search activity on the 3rd day - nearly in 2 times - and 10th day - nearly in 4 times.

NANOPARTICLE-BOUND DOXORUBICIN FOR CHEMOTHERAPY OF BRAIN TUMOURS: PHARMACOLOGICAL AND TOXICOLOGICAL ASPECTS

S. Gelperina[1], A. Khalansky[2], V. Fedoseeva[2], E. Pereverzeva[3], I. Treschalin[3], V. Razzhivina[4], V. Balabanyan[4]
[1]Nanosystem Ltd., Moscow, Russia
[2]Institute of Human Morphology, Moscow, Russia
[3]Gauze Institute of New Antibiotics, Moscow, Russia
[4]Drug Technologies Ltd.

Among the most promising approaches to the non-invasive brain delivery is the drug binding to nanoparticles. In particular, poly(lactide-co-glycolide) (PLGA) nanoparticles coated with poloxamer 188 delivered to the brain an antitumour antibiotic doxorubicin that cannot independently penetrate across the BBB and, therefore, is not used for the chemotherapy of brain tumours. In contrast to the conventional formulation, the nanoparticle-bound doxorubicin (Dox-PLGA) considerably inhibited growth of the intracranially implanted glioblastoma in rats due to the effective intratumoral penetration and accumulation of the nanoparticles.
The PLGA nanoparticles are comprised of a relatively safe biodegradable and biocompatible polymer. However, since the nanoparticles not only enable a drug transport across the BBB but additionally alter its overall body distribution, thorough toxicological investigations of the nanoparticle-bound doxorubicin have been performed.
It was demonstrated that binding of doxorubicin to the nanoparticles did not enhance its acute toxicity. The studies of the chronic toxicity performed in rats and rabbits indicated that the surfactant-coated nanoparticle formulation of doxorubicin has a favourable toxicological profile. The most important finding is the reduction of cardiotoxicity, evidenced by both functional and histological assessment. The lower toxicity of the nanoparticle formulation is most probably explained by the altered biodistribution of the drug mediated by the nanoparticles.

FUNDAMENTAL APPROACHES TO DEVELOPMENT OF TRANSDERMAL THERAPEUTIC SYSTEMS

A. A. Shcherbina, A. E. Chalykh, R. R. Khasbiullin, A. D. Aliev
A. N. Frumkin Institute of Physical Chemistry and Electrochemistry of Russian Academy of Sciences, Moscow, Russia

Transdermal therapeutic systems (TDS) are now widely used as an alternative way of drug delivery into human body. These systems have different design: drug-in-adhesive, island structure, reservoir structure and etc., which defined by several parameters, such as the limit of drug solubility in polymeric matrix, the therapeutic dose, transport characteristics of drug in polymeric matrix and wearing time of TDS.
Using optical interferometry, refractometry and DSC, we investigated miscibility in wide temperature range of commercial drugs and acrylic copolymer that is approved by FDA for transdermal systems. Phase state diagrams for binary systems "drug – adhesive" were plotted, and concentration-temperature parameters were determined for the formation of homogeneous drug-in-adhesive TDSs.
Human and cadaver skin structure was investigated by transmitting and scanning electron microscopy, and by contact angle technique. The 180° peel-test was used to estimate adhesive performance of acrylic adhesive in contact with human skin during 3 and 7 days wearing. The kinetics of formation of "TDS – human skin" adhesive contact was investigated for placebo and model patches. It was suggested the schema of long-term wearing, which takes into account life-cycle of human skin cells and rheological behavior of adhesive.

HYALURONAN – IN VITRO MARKER OF KERATINICYTE CONTACT ALLERGEN SENSITIZATION

D. Nikitovic[1], R. M. Kavasi[1], K. Kechagias[1], G. Mantas[1], A. Tsatsakis[2], E. Corsini[3], G. N. Tzanakakis[1]
[1]Laboratory of Anatomy-Histology-Embryology, School of Medicine, University of Crete, Heraklion, Greece;
[2]Department of Forensic Sciences and Toxicology, University of Crete, Heraklion, Greece;
[3]Laboratory of Toxicology, DiSFeB, Università degli Studi di Milano, Italy

Low molecular weight hyaluronan (LMWHA), an endogenous molecule and a member of the so-called damage associated molecular patterns (DAMPs), has been suggested to elicit immune-stimulatory effects. The objective of this study was to examine utilization of changes in HA deposition as possible markers of keratinocyte sensitisation. Human keratinocyte NCTC2544 cells were stimulated with the contact sensitizers 2,4-dinitrochlorobenzene (DNCB) and PPD, whereupon their IL-18 production as measure of stimulation was measured by ELISA. Changes in HA metabolism were determined by Real-time PCR and immunofluorescence. Both contact allergens were able, upon sensitisation, to enhance hyaluronidase (HYAL)1 and 2 expression inducing HA degradation as demonstrated by utilization of biotinylated HA-binding protein and immunoflourescence. Changes in HA deposition are correlated to keratinocyte sensitisation and could pose a basis of an in vitro assay.

KINETIC SEPARATION: A CONCEPTUAL PLATFORM FOR DEVELOPMENT OF HOMOGENEOUS KINETIC AFFINITY METHODS

Sergey N. Krylov
Department of Chemistry and Centre for Research on Biomolecular Interactions, York University, Toronto, Ontario, Canada M3J 1P3

Non-covalent binding of biological molecules controls cellular regulation, it is also pivotal to action of modern drugs and molecular diagnostics of diseases. Therefore, understanding molecular mechanisms of biological processes as well as the development of drugs and design of diagnostic systems require affinity methods suitable for three types of applications: (i) kinetic studies of affinity interactions, (ii) selection of affinity ligands from combinatorial libraries, and (ii) the use of affinity ligands as diagnostic probes in molecular diagnostics of diseases. Our answer to this challenge is Kinetic Separation - a conceptual platform for the development of homogeneous kinetic affinity methods suitable for all three applications. One-dimensional (column) separation of any nature, e.g. gel-filtration, electrophoresis, thermophoresis, sedimentation, that can segregate affinity complexes from the unbound interactants can be used as the basis for kinetic separation. A variety of different detection methods can be employed in kinetic separation including fluorescence and mass-spectrometry (MS); the latter can uniquely facilitate label-free kinetic analysis of biomolecular interactions. In this lecture, we will explain the physical principles underlying kinetic separation and discuss its practical implementation in a mode of Kinetic Capillary Electrophoresis with Laser-Induced Fluorescence detection (KCE-LIF). The example for discussion will be the use of KCE-LIF for selection, kinetic characterization, and analytical use of DNA aptamers. Major limitations of kinetic separation will be outlines to identify the boundaries of its applicability.

KINETIC SIZE-EXCLUSION CHROMATOGRAPHY WITH MASS SPECTROMETRY DETECTION (KSEC-MS): AN APPROACH FOR SOLUTION-BASED LABEL-FREE KINETIC ANALYSIS OF PROTEIN-DRUG INTERACTIONS

S. N. Krylov, Sv. M. Krylova
Department of Chemistry and Centre for Research on Biomolecular Interactions, York University, Toronto, Ontario, Canada M3J 1P3

Studying the kinetics of reversible binding between a protein and a small-molecule drug is a major challenge. The available approaches require that either the small molecule or the protein be modified by labeling or immobilization on a surface. Not only can such modifications be difficult to do but they can also drastically affect the kinetic parameters of the interaction. To solve this problem, we developed kinetic size-exclusion chromatography with mass-spectrometry detection (KSEC-MS), a solution-based label-free approach. KSEC-MS utilizes the ability of size-exclusion chromatography (SEC) to separate any small molecule from any protein-small-molecule complex without immobilization and the ability of mass-spectrometry (MS) to detect small a molecule without a label. The rate constants of complex formation and dissociation are deconvoluted from the temporal pattern of small molecule elution measured with MS at the exit from the SEC column. In this lecture, the concept of KSEC-MS will be explained and examples of its use for studying kinetics for protein-drug interactions will be presented.

DNA APTAMERS AS AFFINITY PROBES IN KINETIC CAPILLARY ELECTROPHORESIS

Sv. M. Krylova, S. N. Krylov
Department of Chemistry and Centre for Research on Biomolecular Interactions, York University, Toronto, Ontario, Canada M3J 1P3.

Development of DNA aptamers for *E.coli* and human 2OG/Fe(II)-dependent oxygenases was motivated by a high demand for both regulators of the enzymatic activity and reliable affinity probes, allowing measurements of the expression level of enzymes in complex biological matrices. The Non-Equilibrium Capillary Electrophoresis of Equilibrium Mixtures methodology offerin rapid selection of strong DNA binders *via* systematic evolution of ligands by exponential enrichment from large libraries of random-sequence ssDNA was used to select a panel of DNA aptamers for both *E.coli* and human oxygenases with a range of K_d values between 5 and 500 nM. Here, we describe a simple procedure that facilitates simultaneous determination of both the equilibrium constant K_d for binding an aptamers with a protein (oxigenase?) and an unknown protein concentration. The experimental dependence of the fraction of unbound on its concentration is fitted with a function describing their theoretical dependence. Both K_d and the concentration are used as fitting parameters and their sought values are determined as the ones that generate the best fit. The method showed consistent values of K_d and protein concentrations with variation coefficient about 10% across the concentration of protein. experiments performed at the different concentration of protein. experiments Hence, DNA aptamers were proven to be effective general tool for a quantitative detection of oxygenases in an affinity analysis using aptamers over a wide range of protein concentrations from 1 to 1000 nM. We hope that this work will stimulate future selection and study of aptamers as affinity probes to human 2OG/Fe(II)-dependent oxygenases *in vivo*.The CE-based technology can support high-throughput measurements of protein concentrations in order to monitor the expression levels of the target gene and potential diagnostics of various diseases.

BIOCOMPATIBLE POLYSACCARIDE MICROCONTAINERS FOR DRUG DELIVERY : PREPARATION AND ACCUMULATON IN MULTICELLULAR TUMOR SPHEROIDS

A. Sumina[1], R. Akasov[1,2], T. Borodina[2], T. Bukreeva[2], E. Markvicheva[1]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia,
[2]Shubnikov Institute of Crystallography RAS, Moscow, Russia

Three-dimensional (3D) multicellular tumor spheroids (MTS) are promising for testing various anticancer drug delivery systems. The MTS are preferable over commonly used 2D models based on monolayer cultures, since they can better mimic small size solid tumors in vivo.
The aim of the study was to fabricate microcontainers (MC) based on chitosan and xanthan gum and to study distribution and accumulation of these vehicles in MTS.
A series of microcontainers with a mean size ranging from 0.5 to 5 μm were fabricated by ultrasonication technique, as described earlier (Borodina et al. 2014). In this study, two MC samples with the sizes of 510±80 (MC-0.5) and 2050±200 (MC-2) nm were evaluated. MTS with a mean size of 100-120 μm were formed by addition of RGD-peptide to M3 mouse melanoma cells (a monolayer culture) and then incubation at CO2-incibator for 72 h. The cells were cultivated in DMEM supplemented with 10 % fetal bovine serum. The final peptide concentration in the medium was 20 μM/ml. The mechanism of MC penetration and accumulation inside the cells in function of MC size

was studied by confocal microscopy and flow cytometry. To study MC uptake by tumor spheroids, confocal microscopy was also used. MC were incubated with spheroids for 1 and 4 hours. Both MC-0.5 and MC-2 samples were found to penetrate inside the spheroids in a time-dependent manner. Thus, after 1 h incubation the MCs were found to be localized in the spheroid outer layer, while in 4 h they were already observed in the spheroid center. The highest accumulation of the MC-0.5 was confirmed by fluorometry. For this experiment, previously internalized MC were extracted from the spheroids with DMSO and fluorescence levels were measured. It was found that in the case of 4 h incubation, accumulations of the MC-0.5 and MC-2 were similar. However, after 8 and 24 h incubation, the uptake of the MC-0.5 was double higher compared to that for the MC-2 sample. This observation confirmed an idea that smaller particles could be more promising for drug delivery.
Thus, the obtained MC will be loaded with anticancer lipophilic drugs and used as drug delivery systems, while multicellular tumor spheroids obtained by RGD-induced formation technique could be used a good tool to study accumulation of these vehicles inside small size solid tumors.
References
Borodina T.N., Grigoriev D.O., Carillo M.A., Hartmann J., Moehwald H., Shchukin D.G., ACS Appl Mater Interfaces. 2014, 14; 6(9):6570-8.

ANTIBACTERIAL ENZYMES - AN ALTERNATIVE TO ANTIBIOTICS. Delivery matters.

N. L. Klyachko[1,6], L. Yu. Filatova[1], K. A. Miroshnikov[3], S. A. Legotsky[1], A. D. Priyma[1], T. S. Belyy[1], A. Usvaliev[1], P. G. Rudakovskaya[1], S. L. Gribanovsky[5], E. A. Zaitseva[1], A. B. Belova[1], A. G. Majouga[1,4], Yu. I. Golovin[1,5], A. V. Kabanov[1,6]
[1]M.V. Lomonosov Moscow State University, Faculty of Chemistry, Moscow, Russia
[3]M.M. Shemyakin & Yu.A. Ovchinnikov Institute of Bioorganic Chemistry, Moscow, Russia
[4]National University of Science and Technology "MISIS" (MISIS), Moscow, Russia
[5]G.R. Derzhavin Tambov State University, Tambov, Russia
[6]University of North Carolina, Chapel Hill, NC, USA

Substantial number of pathogenic microorganisms resistant to small molecule of antibiotics causing the need for new substances with antimicrobial activity, lacking the drawbacks of traditional antibiotics. The use of bacteriophage enzymes that destroy bacterial cell wall is of particular interest. Enzymes LysK of bacteriophage K, specific towards staphylococci, and S 394/1, specific for Salmonella and E. coli, their properties, especially the lysis of pathogens, stability and the possibility of stabilization using polyelectrolytes are discussed. Possibilities of creating stable and effective enzyme preparations treating bacterial infections are discussed. Peculiarities of the structure of the cell wall of Gram-negative bacteria dictate, in particular, the need for additional helpers "disordering" outer cell membrane. One of the approaches developed describes the introduction of additional antimicrobial peptides, helping the antibacterial enzyme. Another approach is the use of magnetic nanoparticles in the form of "sticks", adsorbed on the cell wall of pathogens, "disordering" under the effect of low-frequency magnetic fields the outer membrane of pathogens and allowing the antibacterial enzyme more efficiently destroy the peptidoglycan of bacterial cell wall.
The work was supported by grants RSF 14-13-00731 and K1-2014-022 (in part of magnetic properties measurements)

MICROBIAL RESISTANCE TO ANTIBIOTICS AND ECOLOGY PROBLEMS

A. M. Egorov, V. G. Grigorenko, M. Yu. Rubtsova
Department of Chemistry, M.V. Lomonosov Moscow State University, GSP-1, Leninskie Gory, Moscow 119991, Russia

Microbial resistance to antibiotics is a serious and growing threat to public health. In recent years, the problem has become even more alarming due to the dissemination of panresistant microorganisms and the rapid development of resistance even to new antibiotics. There are several mechanisms of antibiotic resistance. The most prevalent bacterial resistance mechanism is the production of enzymes beta-lactamases. These enzymes are evolving at high rate, amenable to mutations and have noticeable structural variability. Dissemination of antibiotic resistance not only concerns people's health, but also represents a serious problem for the environment, as many are not even aware. Widespread and often uncontrolled use of antibiotics in medicine and agriculture, uncontrolled migration, as well as environmental pollution accompanied by the spread of antibiotic-resistant pathogens on a global scale.

IMMUNOASSAY OF CHEMICAL CONTAMINANTS AS SCREENING METHOD FOR FOOD SAFETY

S. A. Eremin
Department of Chemical Enzymology, Faculty of Chemistry, M.V.Lomonosov Moscow State University, Moscow, Russia and A.N. Bach Institute of Biochemistry, Federal Research Centre «Fundamentals of Biotechnology», Russian Academy of Sciences, Moscow, Russia (saeremin@gmail.com)

Screening of chemical contaminants such as pesticides, mycotoxins, veterinary drugs, hormones, detergents, color-dyes and others toxic organic compounds are a serious and growing problem for food quality control. It is clear, that the food control must be in quantitative and global scale for multi analytes with high-throughput screening (HTS). The current methods for detection of toxic organic compounds are chromatography techniques with different detection. But these techniques have several limitations for HTS. Moreover, these methods for the determination of toxins in food samples needs special sample pretreatment, which time consuming and labor intensive. The immunochemical methods based on the specific and high affinity antibodies are more applicable for HTS and monitoring of many toxicants in food samples. At this time the enzyme-linked immunosorbent assay (ELISA) and lateral flow immunoassay (immunochromatographic strip-test) are more commonly used now for detection of organic compounds. The current trend of immunoassay is developing multi-analyte immunoassay for more than one analyte can be detected per test. Fluorescence Polarization Immunoassay (FPIA) could be the optimal method for screening and quantitative monitoring of organic compounds in food samples. The FPIA is homogeneous method based on the competitive binding and the measurement of fluorescence polarization value for reaction mixture of sample (typically 10-50 µl) and immunoreagents: fluorescent-labeled antigen (tracer) and specific antibodies. The total time required for an assay is few seconds or minutes. The limit of detection is 10-100 ng/mL and could be reached lower than typical Maximum Residue Limit. The recent results for development of ELISA and FPIA for detection of sudan, amaranth, ofloxacin, ciprofloxacin, orbifloxacin, benzoate, deoxynivalenol, aflatoxin B1, dichlorophenoxyacetic acid (2,4-D) and carbofuran (Food Control, 47, 472-477 (2015)) will be discussed.

Acknowledgements:
The research was supported by Grant of Russian Foundation for Basic Research (14-03-00753-a) and the Russian State Targeted Program «Research and Development in Priority Areas of Development of the Russian Scientific and Technological Complex for 2014–2020» (contract 14.613.21.0028), and the Fundamental Studies Program of the Presidium of the Russian Acad. Sci. No 10.

References:

Jin-Yi Yang, Yan Zhang, Hong Wang, Zhen-Lin Xu, Sergei A. Eremin, Yu-Dong Shen, Qing Wu, Hong-Tao Lei & Yuan-Ming Sun. Development of fluorescence polarization immunoassay for carbofuran in food and environmental water samples. Food Agric. Immunol. 26(3), 340-355 (2015).

Zhihuan Xu, Lei Zheng, Yongmei Yin, Jing Wang, Peng Wang, Linlin Ren, Sergei A. Eremin, Xiaodan He, Meng Meng, Rimo Xi. A sensitive competitive enzyme immunoassay for detection of erythrosine in foodstuffs. Food Control, 47, 472-477 (2015).

Hongtao Mu, Baoling Wang, Zhenlin Xu, Yuanming Sun, Xinan Huang, Yudong Shen, Sergei A. Eremin, Anatoly V. Zherdev, Boris B. Dzantiev, Hongtao Lei. Stereospecific recognition and quantitative structure-activity relationship between antibodies and enantiomers: ofloxacin as model hapten. Analyst, 140(3), 1037 - 1045 (2015).

Bo Zhang, Daolin Du, Meng Meng, Sergei A. Eremin, Victor B. Rybakov, Junhong Zhao, Yongmei Yin, Rimo Xi. Determination of Amaranth in Beverage by Indirect Competitive Enzyme-linked Immunosorbent Assay (ELISA) Based on Anti-amaranth Monoclonal Antibody. Food Anal. Meth., 7, 1498–1505 (2014).

Y. Guo, M. Sanders, A. Galvita, A. Heyerick, D. Deforce, M. Bracke, S. Eremin, S. De Saeger. Heterologous screening of hybridomas for the development of broad-specific monoclonal antibodies against deoxynivalenol and its analogues. World Mycotoxin Journal, 7(3), 257-265 (2014).

I. A. Shanin, N. T. D. Thuy, S. A. Eremin. Determination of Levofloxacin (the Levorotatory Stereoisomer of Ofloxacin) in Milk by an Indirect Enzyme_Linked Immunosorbent Assay. Moscow University Chemistry Bulletin, 69(3), 136-141 (2014).

Bo Zhang, Daolin Du, Meng Meng, Sergei A. Eremin, Victor B. Rybakov, Xiaodan He, Yongmei Yin & Rimo Xi. A Magnetic Particle-Based Competitive Enzyme Immunoassay for Rapid Determination of Ciprofloxacin: A Potential Method for the General Detection of Fluoroquinolones. Anal. Lett. 47(7), 1134-1146 (2014).

Tiejun Mi, Xiao Liang, Long Ding, Suxia Zhang, Sergei A. Eremin, Ross C. Beier, Jianzhong Shen and Zhanhui Wang. Development and optimization of a fluorescence polarization immunoassay for orbifloxacin in milk. Anal. Methods, 6(11), 3849-3857 (2014).

SHENG Ya Jie, EREMIN Sergei, MI Tie Jun, ZHANG Su Xia, SHEN Jian Zhong, and WANG Zhan Hui. The Development of A Fluorescence Polarization Immunoassay for Aflatoxin Detection. Biomed Environ Sci, 27(2), 126-129 (2014).

Nadezhda A. Byzova, Nataliya I. Smirnova, Anatoly V. Zherdev, Sergei A. Eremin, Ilya A. Shanin, Hong-Tao Lei, Yuanming Sun, Boris B. Dzantiev. Rapid immunochromatographic assay for ofloxacin in animal original foodstuffs using native antisera labeled by colloidal gold. Talanta, 119, 125-132 (2014).

Linlin Ren, Meng Meng, Peng Wang, Zhihuan Xu, Sergei A. Eremin, Junhong Zhao, Yongmei Yin, Rimo Xi. Determination of sodium benzoate in food products by fluorescence polarization immunoassay. Talanta, 121, 136-143 (2014).

HIGHLY POROUS POLYMERIC MATERIALS FOR MEDICINE AND BIOTECHNOLOGY

N. R. Kildeeva[1], V. I. Lozinsky[2]
[1]Moscow State University of Design and Technology, Moscow, e-mail: kildeeva@mail.ru
[2]A. N. Nesmeyanov Institute of Organoelement Compounds, RAS, Moscow

A highly porous materials based on biodegradable and biocompatible polymers in recent years has become particularly urgent owing to the development of modern reconstructive biomedical technologies: when restoring the structural integrity of the skin and soft tissues damaged by burns or other influences.
For this purpose use biodegradable porous polymer matrix. Porous materials act as a skeleton for the surface for adhesion and cell growth, which should gradually replace evolving from these cells living tissues. In addition, the system of interconnected pores is required for mass transfer when using the material as a sorbent in detoxification of the body or of drug controlled release system.
There are a number of techniques to increase the specific surface of a polymer material, but not all of them are suitable for biopolymer materials.
The report discusses the three main methods of obtaining porous polymeric materials: a method of phase separation, electrospinning and the preparation of composite cryogels method. Phase separation method is considered on the example of the mixture of biodegradable polyesters: polyhydroxybutyrate and polycaprolactone. Mixed solutions of polyesters in chloroform received composite film with different pore size and composition, as well as the repetition of nanofibers with antimicrobial and proteolytic activity. Highly porous biosorbent for selection of radionuclides produced by cryogelation of chitosan in the presence of cross-linking reagents.

BIOSAFETY ASSESSMENT OF POLYMER MATERIALS

O. A. Legonkova [1], M. S. Belova [1], I. P. Savchenkova [2].
[1]A. V. Vishnevsky Institute of Surgery, Moscow, Russia, 117997, Moscow, Bolshaya Serpukhovskaya Street, 27 e-mail: ospolimed@mail.ru
[2]Y. R. Kovalenko All-Russian Research Institute of Experimental Veterinary, Moscow, Russia 109428, Moscow, Ryazanskiy Prospekt, 24-1

Creation and implementation of new medical polymer products influence on the progress of modern surgery significantly. But the question of biosafety is very actual issue for today. Questions about the ethical using of animals in contemporary medical and biological tests are increasingly attracting professionals and the public.
Within this work on evaluating the properties of biomedical hydrogels and experimental samples of microgels of different series, both native and degraded in sterilization processes at various ways and modes, mouse embryonic fibroblasts (STO) and multipotent mesenchymal stem cells (MMSC), extracted from bone marrow of cattle were used .
The obtained data indicate the ability of regenerative cells manifestation MMSC in the presence of experimental samples, as in the simulation burn and cut at modeling. In case of STO cell cultures regenerative ability is lower than in case of MMSC cells, but in case of simulation vitality burn exceeds the values obtained by simulation cut.
The study found out that the vitaliy of the cell cultures combined specimens hydrogels and microgels exceed the reference values. This can contribute to regenerative processes in the healing of wounds. Also degraded samples of the hydrogels and microgels based on recombinant spidroin non-toxic and biosafety.

SYNTHESIS OF POLYMERS WITH HIGH 3HHX CONTENT BY THE WILD-TYPE STRAIN CUPRIAVIDUS EUTROPHUS B10646 AND STUDY OF THEIR PROPERTIES

D. A. Syrvacheva[1,2], N. O. Zhila[1,2]
[1]Siberian Federal University, Institute of Fundamental Biology and Biotechnology, Krasnoyarsk, Russia
[2]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Krasnoyarsk Russia

Polyhydroxyalkanoates (PHAs), which are accumulated by numerous bacteria as carbon and energy storage materials under nutrient limitation and carbon excess, are aliphatic polyesters with thermoplasticity, optical activity, and biodegradability. Properties of PHAs are determined by the PHA structure. Copolymers of 3-hydroxybutyrate (3HB) and 3-hydroxyhexanoate (3HHx) or 3-hydroxyhexanoate (3HHx) and 3-hydroxyvalerate (3HV) have been found to exhibit particularly useful material properties relative to other PHAs. However, synthesis of PHAs of a definite structure is a technological challenge; therefore, PHAs of a definite structure can only be produced based on the fundamental knowledge of their synthesis. Thus, this study addressed synthesis of copolymers of 3HB and 3HHx or 3HHx and 3HV by the bacterium *Cupriavidus eutrophus* B10646 and properties of the copolymers.
Bacterial cells were cultured under special conditions of carbonic nutrition (with such sources of carbon as fructose, salts of organic acids with length of carbon chain C_5-C_6). To obtain P(3HB-co-3HHx) and P(3HB-co-3HV-co-3HHx), different concentrations of sodium valerate, sodium hexanoate and sodium acrylate (inhibitor of β-oxidation of fatty acids) in the medium were used. Maximal content of 3HHx in P(3HB-co-3HHx) was 70 mol.% and maximal con-

tent of 3HV and 3HHx in P(3HB-co-3HV-co-3HHx) was 41 mol.% and 55 mol.% correspondingly.
The polymers were examined to determine their molecular mass, crystallinity, temperature characteristics and surface texture of the polymeric films, physical and mechanical (Young's modulus, stress at break, elongation at break) properties. Degradation of films of P(3HB-co-3HHx) copolymers was studied in laboratory conditions.
Thus, we obtained high yields of P(3HB-co-3HHx) and P(3HB-co-3HV-co-3HHx) copolymers containing high percentages of 3HV and 3HHx monomers. Differences in the physical properties of these copolymers make them potentially usable in diverse areas.

MAGNETIC NANOPARTICLES CROSS-LINKED BY CHYMOTRYPSIN. NANOMECHANICAL CONTROL OF ENZYME ACTIVITY VIA LOW-FREQUENCY MAGNETIC FIELD

M. M. Veselov[1], M. V. Efremova[1], P. G. Rudakovskaya[1,2], A. Machulkin[1], S. L. Gribanovsky[4], I. V. Uporov[1], A. V. Kabanov[3,1], A. G. Majouga[1,2], Yu. I. Golovin[4,1], N. L. Klyachko[1-3]
[1]Lomonosov Moscow State University, Chemical Enzymology Department, School of Chemistry, Moscow, Russia; [2]National University of Science and Technology MISiS, Moscow, Russia; [3]Eshelman School of Pharmacy, University of North Carolina-Chapel Hill, Chapel Hill, USA; [4]Derzhavin Tambov State University, Tambov, Russia

Magnetic nanoparticles can be used for nanomechanical control of biochemical properties of macromolecules via low-frequency non-heating magnetic field. In this concept, magnetic nanoparticles can convert energy of alternating magnetic field to changing conformation of immobilized macromolecules. If a macromolecule is fixed between two magnetic nanoparticles, it may undergo deformation such as stretching, compression and/or torsion. The deformation occurs due to Brownian relaxation of single domain magnetic nanoparticles. This means that the particle in a magnetic nanosuspension exposed towards external magnetic field will be turning together with its magnetic moment vector.
It was shown previously that, in such way, super-low-frequency magnetic field (50Hz) reduces on 25% the rate of the reaction catalyzed by the enzyme (α-chymotrypsin), immobilized on copolymer-MNP aggregates [1]. The aim of this paper was to explore the effects provided by relaxation of magnetic nanoparticles on enzyme, immobilized on its surface. To do this, we studied the effect of radial force (80 pN during 10 nsec) applied to the chymotrypsin molecule by dynamic molecular modeling. This showed that in result of stretching catalytic center remains unchanged, while the binding site undergoes significant changes. Thus, such exposure should lead to changes only Michaelis constant. To confirm this, we have determined the α-chymotrypsin kinetic parameters change, immobilized on magnetic nanoparticles surface, under the influence of external magnetic field. As a result, we have established that the K_M is increase by 2,5 times, while V_M is not changed.
The work was supported by grants RSF 14-13-00731 and K1-2014-022
Reference:
1. N.L. Klyachko, M. Sokolsky-Papkov, et al. Angew. Chem. Int. Ed. 2012, 51, 12016 –12019

INTERACTIONS BETWEEN NATURAL MINERAL NANO- AND MICROPARTICLES WITH BACTERIA

K. S. Golokhvast, V. V. Chaika, S. Yu. Borisov
Far Eastern Federal University, Vladivostok, Russian Federation

Bacteria are the most ancient inhabitants of the planet Earth. They interact with different granulometric types of mineral particles from nanolevel to macrolevel in a more intimate manner and for a longer time than any other organisms.
This study is devoted of aspects of the interaction bacteria with particles of natural minerals (zeolititic tuff from some deposits in the Far East and Siberia, Russia) using size fractions 0.05-1, 1-10 and 10-50 μm.
We took cultures of opportunistic pathogenic bacteria E. coli (25922) and St. aureus (209-P) to determine the microbiological activity of different-sized tuff particles (Vanchinskoye, Shivertuyskoye, Kulikovskoye, Lyutogskoye, and Lyulinskoye deposit fields). We used standard methods and culture media: meat-peptone agar (MPA) and Endo agar. After preparing the solution (1 billion cells) according to the turbidity standard, zeolites were incubated together with bacteria for 1 hour. Different-sized tuff particles were added to the bacteria at concentrations of 10, 20 and 50 mg/ml. Then, using standard methods, we inoculated the suspension onto MPA and Endo agar and placed it in a thermostatic oven for 24 hours at a temperature of 37°C. The calculation of colony forming units (CFUs) was visual. The used zeolite particles were sterile (treatment in an autoclave oven at 180°C for 3 hours).
It is shown that particles 0.05-1 and 10-50 μm in size have virtually no effect on microorganisms. Whereas microparticles (1-10 μm) from different deposits have a significant effect depending on the type of a rock-forming mineral: clinoptilolite has a bacteriostatic effect, and mordenite – bacteriostimulating effect.
According to the data obtained, it must be concluded that the relationships between different-sized mineral particles and bacteria are often ambiguous and require further in-depth research.
Search for the mechanism of relationships between microorganisms and particles of mineral dust deserves focused attention, if only because every grain of atmospheric mist inhaled by us carries on its surface tens and hundreds of

bacteria and viruses.
This study is supported by the Scientific Foundation of the Far Eastern Federal University (13-06-0318-m_a) and the Grant from the Ministry of Education and Science of the Russian Federation (RFMEFI59414X0006).

LINKING LONG TERM LOW DOSE EXPOSUE TO CHEMICALS TO HEALTH EFFECTS AND DESEASES: THE CURRENT STATUS AND FUTURE NEEDS

Aristidis M. Tsatsakis
Department of Toxicology and Forensic Sciences, Medical School, University of Crete, Greece

Linking of long term low dose chemical exposure to health effects and diseases has been reported in experimental studies and in epidemiology research so far. One major problem for the inadequacy of validated linking of chemical exposure to health problems refers to the biomarkers used for the studies. This issue is complicated due to the complexity of the overall human exposure and the multiple effects excreted by one chemical in terms of the mechanisms of toxicity. There are considerable uncertainties concerning health risks as a consequence of long term and low dose chemical exposure. An important factor in these apparent discrepancies is the difficulty in reliable identification of exposed and control groups. Furthermore, the characteristics of exposure, in particular concerning duration and involvement of variable environmental factors and mixtures make any epidemiological approach very difficult. Biomonitoring of chemical pollutants in low level long-term exposure show the problems related to identify suitable biomarkers. Real life is a variability and diversity of exposures the overall effect of which is pending on the certain case. The complex issue of linking exposures to diseases/health effects can be summarized under the term "web of interactions". Several issues contribute to this due to the large number of diseases and/or disorders involved, the expanding number of exposures to specific substances or categories of pollutants and the effect of various types of confounders on both exposure and disease manifestation. Using database-derived terminology, the type of problems and interactions can be described as a many-to-many relationship. In most of the cases, the direct pollutant-disease interaction has not been studied due to the enormous number of possible pairs. There is a long list of issues that can lead to controversies as hidden effects from other pollutants, unknown or not studied confounders, problems with chemical analysis, misclassification of exposure or disease, variability in response. The exposure scenarios and the inherent toxicity issue of the chemical must be considered as a web of interactions revealed, well identified and quantified and not revealed. Exposure effects in reality are not always monomodal or monotonic events even in very low, low and/or high exposures.

THE TOXIC EFFECT OF METRIBUZIN

V.Rakitskii, K.Lokhin
The Federal Budgetary Establishment of Science «Federal Scientific Center of Hygiene named after F.F.Erisman» of the Federal Service for Supervision in Protection of the Rights of Consumer and Man Well-being, Mytishi, Russia

Metribuzin is selective synthetic herbicide of triazinone group that inhibits of photosynthesis (photosystem II). The products using this active substance is applied for pre- and post-emergence treatment against a broad range of annual grass and dicotyledonous weeds.
The comparative toxicological study was carried out to clarify toxic action of metribuzin in nano- and macroforms. NOEL, biological action and toxicokinetic parameters were evaluated in chronic and subchronic experiments on the white male rats.
The results revealed that NOELch of both pesticide forms based on haematological, biochemical, physiological and morphological parameters were the same. Moreover, the tendency of more expressed influence of nanoform compared with macroform on parameters studied was noticed at high and middle doses.
The study of toxicokinetic parameters in kidneys, liver, testicles, brain, urine and feces have shown greater permeability histo-hematological barriers of nanoform metribuzin. The maximum accumulation of nanoform was observed in parenchymal organs.

Posters

P01

PROPERIES OF RARE-EARTH DOPED NANOPARTICLES AS BIOMARKERS

E. Wolska[1], J. Kaszewski[1,2], Ł. Wachnicki[1], B. Witkowski[1], P. Kiełbik[2,3], M. M. Godlewski[2,3], M. Godlewski[1,4]
[1]Institute of Physics, Polish Academy of Sciences, Al. Lotników 32/46, 02-668 Warsaw, Poland
[2]Department of Physiological Sciences, Faculty of Veterinary Medicine, Warsaw University of Life Sciences – SGGW, Nowoursynowska 159, 02-776 Warsaw, Poland
[3]Veterinary Research Centre, Warsaw University of Life Sciences – SGGW, Warsaw, Poland
[4]Dept. of Mathematics and Natural Sciences College of Science, Cardinal S. Wyszyński University, Dewajtis 5, 01-815 Warsaw, Poland

Oxide nanoparticles (NPs) doped with rare-earth ions are tested for applications as nanomarkers in biology and medicine, e.g. for early cancer diagnostics. In this work we describe properties of such markers obtained by a microwave hydrothermal technology. Nanomarkers based on oxide materials (ZnO) are grown and tested for medical and biological applications.
Modern interest is focused on properties of rare-earth (RE) doped nanoparticles. The rare earths, with their characteristic energy structure and defined spectral emission regions in visible and infrared ranges, are often applied as the luminescence activators.
A hydrothermal method with microwave heating is faster, economical and allows for a pure products than a classical hydrothermal method, which is due to the rapid heating time to the temperatures at which crystallization processes occur and a related fast crystallization. A crystalline material is obtained with narrow particle size distributions, controlled particle size and morphology.
From physico-chemical point of view, we focus on their light emission (i.e., photoluminescence (PL) and PL excitation (PLE)). Using the PLE investigations we searched for excitation processes in a visible light spectral region. This allowed us to avoid UV excitation, which itself is highly photo-toxic for living cells and organisms. From a biological point we describe the use of the new generation of RE-doped oxides as nanomarkers. We test their biocompatibility, biodistribution and search for possible routes of elimination of NPs from a living organism.

The research was partially supported by the National Science Centre project 20/0139/N/ST3/04189

P02

SILVER AND TITANIUM DIOXIDE INDUCED DNA DAMAGE AND REPAIR IN THREE HUMAN CELL LINES

L. Kapka-Skrzypczak[1,2], M. Czajka[1], K. Sawicki[1], T. Iwanenko[3], S. Sommer[3], M. Wojewódzka[3], M. Kruszewski M[1,2,3]
[1]Department of Molecular Biology and Translational Research, Institute of Rural Health, Lublin, Poland
[2]Department of Medical Biology and Translational Research, Faculty of Medicine, University of Information Technology and
Management, Rzeszów, Poland
[3]Institute of Nuclear Chemistry and Technology, Centre for Radiobiology and Biological Dosimetry, Warsaw, Poland

Three human cell lines, HepG2, HT29 and A549, were treated for 2 or 24 h with bare 20 nm or 200 nm silver nanoparticles (AgNPs, Plasmachem GmbH) and TiO_2NP 21 nm (Aeroxide® TiO_2 P25) from Evonik (Degussa) was examined in relation to formation and repair of DNA breakage estimated by the comet assay and oxidative base damage recognized by formamido-pyrimidine glycosylase (FPG) and estimated with the FPG+comet assay, frequencies of histone γH2AX foci and micronuclei (MN). 20 nm AgNPs induced marked damage in all cell lines tested, whereas 200 nm AgNPs and TiO_2 NP induced remarkably lower amount of DNA damage. Each cell line studied had a different pattern of DNA breakage and base damage versus NPs concentration and time of treatment. The DNA damage observed in A549 cells after 2 or 24 h treatment was similar, whereas in HT29 longer treatment induced more DNA damage. In opposite, longer treatment with AgNPs of HepG2 AgNPs resulted in decrease of DNA damage. Interestingly, in contrast to AgNPs, TiO_2 NP induced more damage in A549 cells than in HepG2 or HT29 cells. There were no increases in the frequencies of histone γH2AX foci and MN as compared to those in the untreated cells. Obtained results indicate that the main cause of AgNPs toxicity is induction of oxidative DNA damage than the double strand breaks, and that toxicity of nanomaterials is dependent on cellular context.

This work was supported by the National Science Centre, decision number DEC-2013/09/B/NZ7/03934.

P03

CELLULAR DISTRIBUTION AND TOXICITY OF SILVER AND TITANIUM DIOXIDE NANOPARTICLE IN A549 AND HEPG2 CELLS

M. Kruszewski[1,2,3], S. Męczyńska-Wielgosz[2], M. Czajka[1], K. Sawicki[1], L. Kapka-Skrzypczak[1,3]

[1]Department of Molecular Biology and Translational Research, Institute of Rural Health, Lublin, Poland
[2]Institute of Nuclear Chemistry and Technology, Centre for Radiobiology and Biological Dosimetry, Warsaw, Poland
[3]Department of Medical Biology and Translational Research, Faculty of Medicine, University of Information Technology and Management, Rzeszów, Poland

The aim of this work was to investigate the uptake and cellular toxicity of silver (AgNPs) and titanium dioxide (TiO_2NPs) nanoparticles in A549 (human lung adenocarcinoma) and HepG2 (human hepatocellular liver carcinoma) cells in vitro. AgNP of a nominal size of 20 nm and 200 nm were purchased from Plasmachem GmbH and TiO_2NP 21 nm (Aeroxide® TiO_2 P25) from Evonik (Degussa). Stock solutions of nanoparticles (2 mg/mL) were prepared in sterile distilled water (800 µL), sonicated and mixed with 100 µL of 15% BSA and 100 µL 10xPBS. The sizes of the nanoparticles in solutions were investigated by DLS and were 130.6±23.13 nm for AgNP and 126.3±25.12 nm for TiO_2NP. A549 and HepG2 *cells* were incubated in 50 µg/mL nanoparticle solution for 24 and 48 and 72 h. Ultrathin sections of the cells were analyzed in a transmission electron microscope to reveal the biodistribution of nanoparticles. Nanoparticles were found to distribute throughout the cytoplasm, inside lysosomes and nuclei depending on the time of treatment. We observed large endosomes with nanoparticles in the cytoplasm and in the vicinity of the plasma and nuclear membranes. This suggested that nanoparticles were entering the cells through endocytosis. AgNPs also were deposited inside mitochondria and were observed in the nucleus and nucleolus, whereas TiO_2NPs were seen mostly in endosomes. The acute toxicity of nanoparticles was determined by MTT assay after 24, 48 and 72 h of treatment with doses 10, 50 and 100 µg/mL. We conclude that 20 nm Ag-NPs caused cytotoxic effect especially in the HepG2 cells but this effect is not accompanied by the massive apoptosis or necrosis.

This work was supported by the National Science Centre, decision number DEC-2013/09/B/NZ7/03934.

P04

QUANTITATIVE ASSESSMENT OF ADHESIVE CONTACT BETWEEN CARBON FIBER AND EPOXY BINDING

V. A. Nelub
Scientific and educational center "Russian Composites", Bauman Moscow State Technical University, Moscow, 105005, Russia, e-mail:mail@emtc.ru

We evaluated properties of carbon fiber before and after gaseous oxidation with Raman spectroscopy and electron paramagnetic resonance. The paper shows that oxidation increases the fraction of amorphous phase on the surface of carbon fiber and quantity of paramagnetic centers. The increase in these parameters is accompanied by strength enhancement of carbon fiber at interlaminar shear. We propose two attributes as a measure of interaction between the fiber and a matrix: a fraction of amorphous phase on the surface of fiber and a difference between the content of paramagnetic centers in the fiber and the CFRP.
We chose Russian carbon fibers of brands LU and ELUR as research objects in an initial state and after an oxidation. We investigated foreign carbon fiber of brand AS-4 of company Hexel for comparison, also before and after an oxidation. We chose a Russian binding of brand ENFB based on epoxy-novolak resin and hardening agent which presents BF3 complex with benzylamine as a binding. Carbons based on the binding were hardening at a temperature of 160° C for 4 hours. The fiber content in the CFRPs was 63± 5 %. Using the EPR method we demonstrated that thermo-oxidation contributes to saturation of surface of carbon fibers with oxygenated functional groups that can be considered as charge-transfer complexes that can form donor-acceptor chemical bonds with polymers.
Acknowledgement
The research was supported by grant agreement No 14.577.21.0130 of 28 October 2014. Ministry of Education and Science of the Russian Federation.Unique identifier for Applied Scientific Research RFMEFI57714X0130.
References:
Bazhenov SL, Berlin A. A., Kulkov A. A., Oshmyan V. Polymer composite materials. Dolgoprudnyi: Dolgoprudnyi. Publishing House "Intellect", 2010. - 352 p.

P05

NOVEL SELF-ASSAMBLING AMPHIPHILIC POLYMERS FOR DRUG DELIVERING SYSTEMS

P. P. Kulikov[1], A. N. Kuskov[1], A. Tsatsakis[2], M. I. Shtilman[1]
[1]Mendeleyev University of Chemical Technology of Russia, Miusskaya sq. 9, Moscow, 125047, Russia
[2]Laboratory of Toxicology, Medical School, University of Crete, Heraklion, Voutes, 71003, Crete, Greece.

It is known that amphiphilic polymers are capable to form self-assembled nanostructures due to the presence in their chain of hydrophobic and hydrophilic moieties. By changing the chemical structure of the synthesized polymer and nature and distribution of functional groups the molecular assembly process that provides a variety of structures with unique properties can be efficiently controlled.
The aim of this work is to develop methods for producing the novel low-toxic amphiphilic polymers based of N-vinyl-2-pyrrolidone.
On the first stage of the research a few samples of amphiphilic polymers were synthesized by radical polymerization method in the presence of a chain transfer agent (alkyl-thiols). For these polymers the critical micelle concentrations (CMC) and the average molecular weight were determined. The structure of synthesized polymers was confirmed by using NMR (^{13}C, H^1) and IR-spectroscopy. The results of determination of CMC and the average molecular weight are shown in Table 1.
Table 1. Selected amphiphilic polymers of N-vinyl-2-pyrrolidone and results of CMC evaluation

Polymer's conventional designation	The hydrophobic part of the polymer	Average molecular weight, kDa	Value of CMC*10^2, mmol/l
PVP-HM-3,5	Hexyl	3,5	200
PVP-DM-3,5	Decyl	3,5	100
PVP-ODM-1	Octadecyl	1	4,4
PVP-ODM-3,5	Octadecyl	3,5	6,9
PVP-ODM-6	Octadecyl	6	7,3
PVP-ODM-10	Octadecyl	10	10
PVP-ODM-20	Octadecyl	20	130

This studies allowed to obtained data that characterize novel amphiphilic polymers based on N-vinyl-2-pyrrolidone as a perspective drug delivery agent.

P06

WATER-SOLUBLE COPOLYMERS OF ACRYLIC ACID AND ALLYL AMIDES OF CARBOXYL PLANT GROWTH REGULATORS

A. L. Luss[1], A. A. Dobrynin[1], A. M. Tsatsakis[2], M. I. Shtilman[1]
[1]D. Mendeleev University of Chemical Technology of Russia, Moscow, Russia
[2]University of Crete, Iraklion, Greece.

Polymer derivatives of plant growth regulators capture attention due to a number of their unique properties. Decreased toxicity, low phytotoxicity, prolonged release of the active substance and wider stimulating concentrations comparing to low molecular weight analogs are among them. Also immobilized in the system but not released regulator has no activity and is protected from lateral expenditure.
Features of the synthesis methods and properties of phytoactive polymers are reviewed in a number of articles. Nevertheless the search for optima and most preferable methods of synthesis of phytoactive polymers still continues.
An important feature of phytoactive polymers is ability to obtain water-soluble derivatives of water-insoluble plant growth regulators.
The degree of solubility in water depends on the presence of a polar fragments and ionogenic groups in macromolecular system.
In present work 2,4-dichlorphenoxyacetic acid (2,4-D) was used as the main test substance. 2,4-D is the most known and widely used agent that protects cultivated crops from weeds. But in polymeric form 2,4-D also shows growth-regulatory activity.
In this study a novel method of synthesis of polymeric derivatives of this well-known auxin group plant growth regulator that improve callus formation and growth (2,4-D), was introduced consisting of copolymerization of allylamide of 2,4-D and acrylic acid.

It was shown that the obtained water-soluble polymer form have a high growth-regulatory activity and lower toxicity in comparison with its low molecular weight counterparts.
The influence of impact copolymerization time, total concentration of monomers, temperature of the process, the amount of initiator and the monomers in mixture and other parameters on copolymerization process and product yield and properties was determined.
Obtained results allow determine optimal conditions for maximum yield of the product, high content of active groups, and a low viscosity of prepared copolymers.

P07

THE SYNTHESIS AND CROSS-LINKING OF AMPHIPHILIC POLYACRYLIC ACID FOR PRODUCING OF BONE CEMENT

S. E. Pokhil, Ya. O. Mezhuev, P. P. Kulikov, M. I. Shtilman, Yu. V. Korshak
Mendeleev University for Chemistry Technologies of Russia

An amphiphilic polyacrylic acid was produced by the reaction of radical polymerization of acrylic acid in a solution of dioxane that initiated by AIBN in the presence of various long-chain mercaptans. The kinetics of the process was studied, the reaction order with respect to the concentration of initiator and monomer was established, and the activation energy of the reaction was determined. The structure of the synthesized polymer products was characterized by infrared and NMR-spectroscopy. The dependence of the critical micelle concentration of resulted amphiphilic polyacrylic acid from the length of the alkyl in an aqueous medium was indicated. Adsorption isotherms of various amphiphilic polyacrylic acids were constructed for the interface water-air, the values of surface activity were identified.
The solubilization of a number of moderately polar and non-polar substances was investigated by obtained amphiphilic polyacrylic acids. The strong correlation between the polarity of solubilizate, surface activity of amphiphilic polyacrylic acid and the value of the solubilization was determined. The dimensions of the native micelles and swollen micelles were defined.
It had been shown that the synthesis of the zinc and calcium salts of amphiphilic polyacrylic acids in the solid phase allows forming compositions with high mechanical properties that enables its use in dentistry. The prospects of application of such materials are designated for the producing of bone cements.
The study was financially supported by the Ministry of Education and Science of the Russian Federation within the framework of fulfillment of the base part of the state task.

P08

THE SYNTHESIS OF AN AQUEOEUS DISPERSION OF POLYPYRROLE STABILIZED BY POLYVINYL ALCOHOL AND PRODUCING OF HEMOCOMPATIBLE FILMS BASED ON IT

Ya. O. Mezhuev, A. I. Piskareva, A. A. Artyukhow, M. M. Goldin, S. E. Pokhil, M. I. Shtilman, Yu. V. Korshak, S. V. Osadchenko
Mendeleev University for Chemistry Technologies of Russia

It has been established that increasing of molecular weight and concentration leads to decreasing of particle size of the dispersion phase in the reaction of oxidative polymerization of pyrrole in an aqueous solution. It has been shown that a shape of the particles of the dispersion phase is close to spherical, besides the effect of stabilization is provided by the formation of hydrogen bonds O–H - - - N–H between the chains of polypyrrole and polyvinyl alcohol. It has been established that increasing of molecular weight leads to increasing of the size of stabilizing particles of hydrated shells. It has been shown that the films obtained by drying-out of aqueous dispersions of polypyrrole stabilized by polyvinyl alcohol have really high robustness.
To verify the hemocompatibility of produced polypyrrol films obtained from aqueous dispersions stabilized by polyvinyl alcohol an analysis of free hemoglobin was conducted as well as a morphological analysis and hematological analysis followed by its interaction with an erythrocyte concentrate. It has been shown that the samples containing excess or deficiency of polypyrrole don't register any hemocompatibility. During its contact with an erythrocyte concentrate there is observed a decrease in total hemoglobin level, destruction of red blood cells with normal structure (the so-called discocytes) and a sharp increase of concentration of defective erythrocytes such as erythrocytes with a ragged edge, echinocytes and especially destroyed red blood cells (the so-called "shadows" of erythrocytes). Most hemocompatibility was detected for the sample containing 10% by weight of polypyrrol and therefore its properties are superior to commercial material produced be "Sever" using as implant. The observed extreme dependence of hemocompatibility of films of polyvinyl alcohol from containing of polypyrrole is corresponded to the literature

confirming that there is a great need to design a surface with optimal hydrophilic properties to ensure its hemocompatibility.
The study was financially supported by the Ministry of Education and Science of the Russian Federation within the framework of fulfillment of the base part of the state task.

P09

APPLICATION OF BIOMATERIALS AS ANTICANCER DRUG CARRIERS

A. B. Ismailova[1,2], E. O. Batyrbekov[1], D. Loca[3], A. O. Baiyrkhanova[4]
[1]Institute of Chemical Sciences, Kazakh-British Technical University, Almaty, Kazakhstan
[2]Kazakh Leading Academy of Architecture and Civil Engineering, Almaty, Kazakhstan
[3]Cimdins Riga Centre for Biomaterial Innovation and Development, Riga, Latvia
[4]Semey State Medicine University, Semey, Kazakhstan

Biodegradable biopolymer chitosan film with 5-FU (5-fluorouracil) for its delivery to cancer cells was developed. The novel polymeric film was prepared by cross-linking method. The 5-FU drug was incorporated into the carrier using cross-linking reaction. 2% chitosan polymer was dissolved in 1% v/v hydrochloric acid solution. The drug loading efficiency, film size and chemical compositions of the film loaded drug were confirmed by UV/VIS spectrophotometer and Fourier transform infrared spectroscopy. In vitro release kinetics of drug from the polymeric films was investigated to determine the drug release properties. The drug release was determined using UV/VIS spectroscopy at 266 nm in quartz cuvettes with thick of 10 mm at 37 °C in Ringer-Locke solution. It was established that the release consisted of three main stages: water sorption by a film and its swelling, the drug diffusion in a film at the phase interface "polymer system-environment" and the drug diffusion in the solvent volume. To determine the influence of drug loading on its release kinetics, polymer films were loaded with 125 mg/g and 250 mg/g of 5-FU. Increasing doses of the drug does not affect on the release of FU. Obtained results showed that the drug was diffused practically completely into Ringer-Locke solution within 15-20 h.
Partial operation "Vitrectomy"- intravitreal injection of chitosan film loaded 5-FU was carried in Centralized Research Laboratory of KazNMU. Analgesic and antispasmodic effect is achieved by intramuscular injection of 0.1-0.4 ml of Xylavet, 3- multiple instillation of inokain. Polymeric implant introduction into the vitreous cavity was carried out as follows. Sclerectomy was hold applying blepharostat and undermining of conjunctiva from the limbus in 5 mm. A partial vitrectomy was carried out and chitosan film with 5-FU was implanted intravitreal in both eyes in a set dosage. Enucleation of both rabbits' eyes was on the 7 th, 14 th, 28 th days. In vivo study was showed in the concentration range of 100 – 1000 mg/ml are nontoxic to an array of cell lines.
Further uses of the film loaded 5-FU may provide an efficiency deliverable for ophthalmic administration. The determined consistent patterns allow to predict drug release and to create polymeric biomaterials with necessary rate of delivery drug in organism.

P10

GLASS-BASED BIOCOMPOSITES IN THE EXPERIMENT "IN VITRO" AND "IN VIVO"

E. E. Stroganova[1], N. Yu. Mikhailenko[1], A. B. Elfimov[1], V. N. Sigaev[1], A. A. Artyukhow[1], M. I. Stilman[1], N. S. Sergeeva[2], I. K. Sviridova[2]
[1]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
[2]P. Hertsen Research Oncology Institute, Moscow, Russia

Creating of a new generation materials for treatment of injuries and diseases of soft and bone tissues using the biocompatible bioresorbable and osteoinductive materials are based on the results of standardized tests in the complex environments "in vitro" and "in vivo"
In the first series of tests "in vitro" in distilled water and SBF biocomposites were used which are based on the fine powders of biocompatible calciumphosphate glasses and GM-PVA hydrogels with a filler content of from 20 to 80 wt. % . Test conditions: the ratio of the material : water solution 1: 100, at the temperature of 37°C, exposure 1, 7, 13, 24, 48, 72, 144 hr.
It was found that in water in presence of matrix a slightly alkaline solution is formed and in presence of filler - slightly acidic solution. Tests in the SBF demonstrate that in the presence of a material containing 60% filler, the indicator of medium is stabilized at 7.2 after two days of exposure.
The aim of second series of *in vitro* tests in the MRIO by P.A. Hertsen was to identify surface properties of the matrix and to evaluate acute cytotoxicity of materials. It was shown, that the calciumphosphate glass filler (CP) and the composite material (CP: PVA-GM) are not cytotoxic and have moderate matrix properties.

Studies 'in vivo" on animals have demonstrated the biocompatibility - the absence of acute inflammatory and toxic reactions when implanted hydrogel GM PVA in soft and bone tissues of mice and rats within 3 weeks.
When defect tibia of Wistar rats were substituted by hydrogel GM-PVA, no reduction of defect volume at the implantation site occurred, however the material demonstrated a low biodegradation rate the first three weeks after surgery.
"In vivo" implants of GM-PVA and CP:GM-PVA were placed into defect of the tibia rats Wistar. As a result of "in vivo" tests within 3 weeks, the absence of inflammation in the area of implantation, the consolidation of the composites with the surrounding cancellous bone and the presence of the bone stromal hematopoiesis were detected.
The results of a comparative evaluation of medical and biological characteristics of the developed polymer-inorganic materials based on CP and GM-PVA indicate the volubility of further research aimed to create on their base a line of implants for replacement defects of soft and bone tissues.

P11

DEVELOPMENT AND RESEARCH OF COMPOSITE MATERIAL FOR FORMATION A CELLULAR SCAFFOLD FOR THE ACCELERATED GROWTH OF CELLS

R. A. Morozov[1], A. V. Romashkin[1], A. V. Nikitina[1]
[1]*Zelenograd Nanotechnology Center, Moscow, Russia*

Regenerative medicine – one of the most dynamically developing directions of modern medicine. It is based on recuperation of structural integrity of integuments and acceleration of growth of again formed cells of tissue.
There is a need for development of new types of the polymeric biodegradable matrixes possessing a special complex of properties: mechanical durability, adhesion to fabrics, sorption of a large amount of liquid, a biodegradation, bioactivity. Options of the cellular scaffold (CS) known now don't combine all set of necessary properties, as defined the area of work. Besides, analogs incorporate acid that can cause allergic reactions.
Protein collagen and polysaccharide chitosan are the most appropriate for manufacturing of cellular scaffold due to its bioactive properties. For providing all complex of necessary properties the multilayered acid-free design of cellular scaffold representing a combination of the nanostructured layers consisting of collagen and a chitosan with addition of albumine as the connecting component was offered. Mechanism of interaction between materials it was determined by resources of the atomic force microscopy (AFM). The top and low collagen layers provide adhesion and possess styptic properties. For an assessment of efficiency of cellular scaffold the researches proving were conducted that scaffold possesses ability to increase proliferation of the regenerated cells. Experiments were made at first on cells of a liver, and then samples passed preclinical tests – on mice.
The technique of AFM of research cellular scaffolds was as a result developed and the prototypes possessing the high speed of absorption of wound exudate, biocompatibility and a biodegradation in combination with the sufficient mechanical durability and the accelerated recovery of the damaged tissue are created.

P12

DETERMINATION OF TRACE IMPURITIES OF METALS IN BIOLOGICAL OBJECTS BY MEANS OF ATOMIC ABSORPTION SPECTROSCOPY

G. I. Kandelaki, J. O. Mezhuev, Yu.V. Korshak
D. I. Mendeleev University for Chemical Technology of Russia, Russia, Moscow, 125047, Miusskaya Sq. 9

Increasing standards to material quality especially for medical and biological purposes requires strict control over the purity of these materials. Special attention in recent years is paid to the definition of the content of heavy metal impurities in aqueous media, as well as in biomaterials, which are in direct contact with living tissues of the body.
It should be noted that the content of heavy metals in water and biological materials is often in the range of ppm concentrations, which requires the use of highly sensitive methods for their determination and modern equipment.
One of the reliable and well-established methods for analyzing metal impurities in samples of biological tissues and aquatic environments is atomic absorption analysis.
The data of a number of analyzes determining the content of various metals in tissue samples and various biological objects presented in this paper are put in order and evaluation of the accuracy of definitions and sources of possible error is carried out.

P13

MULTIFUNCTIONAL DRUG DELIVERY SYSTEM BASED ON POLYSACCHARIDES' CONTAINERS AND INORGANIC NANOPARTICLES

M. S. Miljohin[1], T. N. Borodina[2], D. A. Elfimov[3], Y. V. Grigoriev[2], T. V. Bukreeva[1, 2]
[1]National Research Centre "Kurchatov Institute", Moscow, Russia
[2]Shubnikov Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia
[3]Lomonosov Moscow State University, Moscow, Russia

Development of hydrophobic drugs' delivery carriers is an important task of nanoengineering due to inability to these substances transport independently by bloodstream. Polysaccharide containers obtained by using low frequency ultrasound have been proposed as such systems [1]. Modification of the containers by inorganic nanoparticles can be used to add additional functionalities to the proposed systems. In this work, containers' shells formed by xanthan gum and chitosan were modified by gold nanoparticles to improve surface enhanced Raman spectrum (SERS) properties. The gold nanoparticles were prepared by two different methods. The first one is reduction of nanoparticles from chloroauric acid by ascorbic acid on containers shells. The second comprises particles adsorption from a sol on the containers' surface. SERS properties of the obtained systems were confirmed by preliminary experiments.

In addition, magnetic nanoparticles were embedded into containers' shells to enable delivery of encapsulated substances to be driven by external magnetic field. Magnetite particles were synthesized by chemical condensation of di- and trivalent iron followed by stabilization of the particle surface by citrate ions. The nanoparticles were adsorbed on the containers' surface by layer-by-layer technique. The high sensitivity of the containers to constant magnetic field has been successfully demonstrated.

The described approaches allow creating the containers consisting both the gold and magnetic nanoparticles. We demonstrated the formation of polysaccharide containers, which may comprise diagnostic elements and act as the multifunctional delivery systems of hydrophobic drugs.

This work was performed using the equipment of the Shared Research Centre IC RAS and was supported by the Russian Ministry of Education and Science *(project RFMEFI62114X0005).*

1. T.N. Borodina et al // ACS Appl. Mater. Interfaces. 2014. V. 6(9). P. 6570-8.

P14

POLYMER BIODEGRADABLE MATRICES WITH ENHANCED SURFACE PROPERTIES FOR TISSUE ENGINEERING

E. Markvicheva[1], M. Drozdova[1], T. Demina[2], M. Zlobina[3], A. Artyukhov[3], M. Shtilman[3], T. Akopova[2], Ch. Grandfils[4]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chem., Rus. Acad. Sci., Miklukho-Maklaya Str 16/10, 117997, Moscow, Russia
[2] Enikolopov Institute of Synthetic Polymer Materials, Rus Acad. Sci., Profsoyuznaya Str., 70, 117393 Moscow, Russia
[3]Mendeleev University of Chemical Technology of Russia, Miusskaya Sq., 9 125047 Moscow, Russia
[4]Interfacultary Research Centre on Biomaterials (CEIB), University of Liège, Chemistry Institute, B6C, B-4000 Liège (Sart-Tilman), Belgium.

Nano- and microfibers, microcarriers (microbeads 150-250 μm), macroporous hydrogel-based matrices are the most promising scaffolds in tissue engineering, since they can provide 3D cell growth. More over, they can be loaded with various drugs, growth factors and other bioactive molecules.

The aim of the study was to get a set of novel biodegradable matrices (fibers, macroporous hydrogels and microcarriers) with enhanced surface characteristics promoting cell adhesion and growth. All scaffolds were fabricated from biocompatible synthetic and natural materials, such as natural polysaccharide chitosan, biodegradable synthetic polylactides, namely PLLA, poly(D,L-lactide (PDLLA), and polyvinyl alcohol (PVA). Mouse fibroblast L929 and human stem cells (MSC) were used as model cells. To enhance cell adhesion, spreading and proliferation, surface of previously obtained PLLA and PDLLA microbeads was modified by adsorption of polycations, such as chitosan, poly(2-dimethylamino ethylmethacrylate (PDMAEMA). More over, amphiphilic chitosan-g-poly(D,L-lactide) copolymers have been fabricated by single-step solid-state reactive blending (SSRB). These copolymers were used to stabilize microbeads obtained by oil/water emulsion technique and to enhance their surface. Introduction of the copolymers in water phase allowed to replace a non-degradable PVA emulsifier, while their addtion to the oil phase resulted in bringing amino-saccharide positively charged segments to the microbead surface. This strategy allows to obtain «a self-stabilizing» system in one step, without any emulsifier in the aqueous phase. Total microbead yield as well as size distribution and surface morphology were optimized as a function of the copolymer composition.

Macroporous PVA-based hydrogels with modified surface (AA, DMAEMA, HEMA) were successfully used for cultivation of mouse fibroblasts L929 and human stem cells in vitro. Cell adhesion, spreading and distribution inside

the hydrogel matrices was studied by confocal laser microscopy.
Composite PVA-chitosan fibers with mean diameter ranging from 200 nm to 1.4 μm were fabricated by electrospinning, and treated in autoclave (120 C, 30 min), in order to make them water insoluble and to sterilize at the same time. Then so-called extract- and contact tests with L929 cells were carried out to test nanofiber cytotoxicity. Optical, confocal laser microscopy and SEM were used to observe cell growth. Cell viability was determined by MTT-test on day 2. 4, and 7 of cultivation. Cell attachment, spreading, growth and proliferating were found to greatly depend upon polymer composition. The scaffolds will be loaded with bioactive peptides/proteins and their effect on cell growth will be studied in the nearest future.
The research was supported by RFBR (grants 14-04-31986 and 14-04-01861).

P15

HYDROGELS BASED ON HYALURONIC ACID AND CHITOSAN POLYELECTROLYTE COMPLEX FOR BONE TISSUE REGENERATION

T. S Demina[1], S. A. Uspenskii[1,2], M. G. Drozdova[3], O. A. Dregval[4], A. I. Gaidar[5] N. R. Kildeeva[6], A. N. Zelenetskii[1], M. A. Selianin[2], E.A. Markvicheva[3]
[1]Enikolopov Institute of Synthetic Polymer Materials RAS, Moscow, Russia
[2]IRC "Martinex", Moscow, Russia
[3]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia
[4]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
[5]Research Institute of Advanced Materials and Technology, Moscow, Russia
[6]Moscow State University of Design and Technology, Moscow, Russia

Development of polymeric scaffolds that could serve as temporary supporting structures for 3D cell growth leading to tissue repair is one of the most important issues of tissue engineering strategy. Among a variety of polymers proposed for tissue engineering, natural ones are promising due to a diverse set of functions in their native setting. Hyaluronic acid is a naturally occurring biodegradable polysaccharide with a variety of applications in medicine, including tissue engineering, dermatological fillers, wound healing, etc. Another polymer used in our study is chitosan, which received a great attention for medical and pharmaceutical applications due to its biocompatibility and degradability by certain human enzymes. Moreover, it is the only natural cationic polymer at physiological pH. Due to hyaluronic acid and chitosan are oppositely charged polyelectrolytes, they could form polyelectrolyte complexes that are insoluble in aqueous solutions.
The research aims to fabricate macroporous chitosan/hyaluronic acid hydrogels, including ones additionally modified by hydroxyapatite nanoparticles (1, 5 and 10% mass) to promote bone tissue regeneration. The study of the fabricated scaffolds morphology in dried and swollen states using SEM and CLSM showed interconnected porous network with a pore mean size in a range of 30-150 μm. According to elemental analysis data, the polymer composition of the hydrogels consisted of ~50 wt-% of chitosan for all samples. Equilibrium swelling degree and mass loss of hydrogels was evaluated and showed to be a function of hydroxyapatite nanoparticles content and used medium.
A cytotoxicity of the obtained hydrogels was studied in extract test using human osteoblastic cell line (HOS) as a model. In order to study cell proliferation HOS cells and mesenchymal stromal cells (MSC) derived from human adipose tissue were cultured directly on the hydrogels. Relative cell viability was measured by MTT assay after 7 days of cultivation. The hydrogels were shown to support cell growth and proliferation and the maximum of cell growth was obtained in hydrogels with hydroxyapatite content of 10% mass.

This research was supported by a grant from the Russian Foundation for Basic Research (No15-04-07669).

P16

POLYMER MACROPOROUS SCAFFOLDS MODIFIED FOR PROMOTING STEM CELL ATTACHMENT AND DIFFERENTIATION

M. Drozdova[1], A. Artyukhov[2], S. Burov[3], M. Shtilman[2], E. Markvicheva[1]
[1]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow, Russia
[2]D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia
[3]Institute of Macromolecular Compounds RAS, Saint-Petersburg, Russia

Mesenchymal stromal cells (MSC) is a promising source of cells for tissue engineering due to their ability to differentiate to a number of cell phenotypes. In order to direct a cell differentiation into selected cell phenotype, differ-

ent molecular keys could be used. For instance, surface modification with RGD-peptide, which is known to promote cell adhesion, and thereby contributes to osteogenic differentiation of MSC, could be proposed.
The aim of the study was to prepare macroporous hydrogel-based matrices modified with RGD-peptide and to evaluate cell growth and differentiation within these scaffolds using in vitro model.
In this study, poly(vinyl alcohol) (PVA) was modified with epoxide groups, in order to provide covalent attachment of the peptide to the hydrogel surface. The efficiency of the peptide conjugation and peptide distribution was evaluated using fluorescamine staining. Bioactivity of the RGD-peptide modified matrix oncell attachment, proliferation and morphology was studied. In order to study cell proliferation in the modified PVA hydrogel-based scaffolds, fibroblasts L929 and MSC from human adipose tissue were cultured directly within the hydrogels. Cell viability was estimated by MTT-assay. Cell morphology and distribution within the hydrogels was studied by confocal microscopy. To visualize living cells, vital Calcein-AM dye (staining in green) was used. Cell nuclei and hydrogel structure were stained with DAPI dye in blue. Bioactivity of the peptide modified scaffold was assessed by measuring alkaline phosphatase activity, which is an early marker of the osteogenic differentiation.
It was shown that the modification of the macroporous PVA hydrogels allowed to enhance cell adhesion, growth and proliferation as well as to promote osteogenic differentiation of MCS.
Thus, the modification of the macroporous PVA-based matrices with RGD-peptide is a promising strategy for tissue repair.
This research is financially supported by the *Russian Foundation of Basic Research* (Grant No 14-04-31986-mol_a).

P17

SUBMICRON CALCIUM CARBONATE PARTICLES: STRUCTURE AND LOADING WITH A PHOTODYNAMIC DYE

D. B. Trushina[1,2], I. V. Marchenko[2,3], T. N. Borodina[2], M. A. Vantsyan[3], S. N. Sulyanov[2], B. V. Nabatov[2], T. V. Bukreeva[2,3]
[1]Lomonosov Moscow State University, Moscow, Russia
[2]Shubnikov Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia
[3]National Research Centre "Kurchatov Institute", Moscow, Russia

Calcium carbonate has gained a lot of attention as a material for biomedical applications owing to excellent biocompatibility, physical stability and mild decomposition conditions. Among the polymorph modifications of calcium carbonate, vaterite particles are favourable due to their porous structure, ability to absorb and release a variety of bioactive compounds. The common $CaCO_3$ synthesis method of mixing aqueous solutions of calcium chloride and sodium carbonate allows spherical vaterite particles with the size ranging from 5 μm to 15 μm, while drug delivery applications require carriers small enough to penetrate the blood capillaries and cells. So the size of calcium carbonate particles has to be reduced and the main goal of the research is to develop a synthesis method that allows submicron porous vaterite particles in a size-controlled manner.
To obtain submicron colloidal particles by precipitation from supersaturated solution ethylene glycol and glycerol co-solvents were used in our protocol. Size and surface morphology of the precipitated particles were analysed using a scanning electron microscope. The phase composition of the $CaCO_3$ was investigated by X-ray powder diffraction. The strong influence of mixing time on the size and structure of colloid calcium carbonate particles was observed. Stable vaterite particles with average diameter 500 nm were synthesized in the presence of ethylene glycol or glycerol in a reaction mixture and agitation for more than 30 min. It was shown that these spherical particles are formed by attachment of vaterite nanocrystallites with well-defined anisotropic shape, which can be described by biaxial ellipsoid. Owing to such structure submicron vaterite spheres possess a high degree of porosity and therefore good absorption ability that makes them suitable for encapsulation purposes. Surface area of the particles with average size of 500 nm determined by the method of gas adsorption/desorption amounted to 16.1 m^2/g, and the pore size – 30-80 nm. These parameters are close to ones for particles synthesized without additives.
Calcium carbonate particles with average size 4 μm precipitated in pure water and 850 nm precipitated in water/glycerol medium were loaded with photoditasine by adsorption from aqueous solutions. This dye used in photodynamic therapy requires more efficient formulation. By confocal laser scanning fluorescence microscopy and spectrophotometry it was found that photoditasine forms a shell on the particle surface. Electron absorbance spectra of photoditasine loaded particles demonstrate the dye existence in the form of monomer, dimer and J-aggregate mixture. The amount of photoditasine incorporated in the calcium carbonate particles was determined by spectrophotometry and amounted to 6.1 mass percent for large particles and 8.3 mass percent for small ones.
This work was performed using the equipment of the Shared Research Centre IC RAS and was supported by the Russian Ministry of Education and Science (project RFMEFI62114X0005) and the Russian Foundation for Basic Research (project 14-03-31889).

P18

CALCIUMPHOSPHATE GLASSES AND GLASS-MATERIALS WITH HIGH IRON CONTENT

A. B. Elfimov[1], E. E. Stroganova[1], K. V. Poholok[2]
[1]*D. I. Mendeleev University of Chemical Technology of Russia, Moscow, Russia.*
[2]*M. V. Lomonosov Moscow State University, Moscow, Russia.*

The aim of this investigation was to study the conditions of stabilization of Fe^{3+} in calciumphosphate glasses, because crystalline compounds of Fe^{3+} have paramagnetic properties required for magnetic therapy.
During the work the glasses in the CaO-P_2O_5-Fe_2O_3-B_2O_3-Al_2O_3 system with variable molar ratio of CaO/P_2O_5 (from 0.58 to 0.9) and the content of Fe_2O_3 (from 15 to 25 mol.% beyond one hundred) were synthesized.
Investigation of the crystallization properties of glasses was carried out by the methods of mass crystallization (MC, from 700°C to 900°C) and differential thermal analysis (DTA, from 0°C to 1000°C). The oxidation state of iron in the glasses was determined by Mössbauer spectroscopy (NGR), and phase composition of the crystallized material - by X-ray phase analysis (XRPA).
During the investigation of glasses by NGR the extremes associated with the presence of Fe^{2+} and Fe^{3+} were found at spectra. Thus, weight ratio of Fe^{2+}/Fe^{3+} is on average 20/80% (± 2%) for ultraphosphate glasses compositions ($CaO/P_2O_5 \leq 0,7$) and for metaphosphate - ($CaO/P_2O_5 > 0,7$) the proportion of Fe^{2+} increases to 40/60%.
Visual evaluation of results of heat treatment indicates that glass is crystallized from surface, but not in the bulk. It was found that the thickness of the crystal layer and the crystal size increase with the increasing of content of iron and calcium oxides in the glass composition.
The thermograms of ultraphosphate glasses contain the exothermic peaks associated with the process of crystallization only with the introduction into structure of 25 mol.% of iron oxide, whereas for metaphosphate glasses presence of exothermic effects of varying intensity recorded with a minimum (of 15 mol.%) content of Fe_2O_3.
The phase composition of the crystallized material (according to XRPA) is represented mainly with b-calcium pyrophosphate. At the transition of structure of original glasses from ultra- to metaphosphates, the proportion of calcium and iron (+2 and +3) orthophosphate is increasing in glass-ceramic materials.
Further researches will be focused on the optimization of crystallization conditions for obtaining the highest number of paramagnetic phases containing Fe^{3+}, and research of magnetic properties of crystallized materials.

P19

PREPOLYMERIZATION COMPLEX MODELING FOR MOLECULAR IMPRINTING PARAMETERS' ASSESSMENT

Y. V. Dolgaya, V. V. Barkaline
Belarusian National Technical University

Molecularly imprinting is a promising way for creating polymer materials which can be used as artificial receptors and anticipated as synthetic imitation of natural antibodies. Preparation stage of molecularly imprinted polymer design begins with the selection of monomers having been bound with template molecule, solvent for preparation of prepolymerization complex, optimal functional monomer and monomer/template ratio of the complex.
Calculation methods can be used to estimate broad range of imprinting parameters in different conditions and understand the better way to improve the polymer characteristics. The difficulty is that some properties such as hydrogen bonding could be modeled by quantum methods only but this approach demands a lot of computational resource. QM/MM method allows one to use molecular mechanics and quantum mechanics methods for different parts of modeled system. At present study the QM/MM approach is realized in NWChem 6.0 package to estimate parameters for tri-O-acetyladenosine imprinting into polymer matrix. This system is considered as a synthetic reproduction of adenosine triphosphate binding site. The optimized geometrical structure and the energy of prepolymerization complexes of tri-O-acetyl adenosine template with three different monomers — methacrylic acid, 3-vinyl benzoic acid and acrylamide in vacuum were calculated using QM/MM approach in vacuum to estimate the method suitability [1]. These calculations demonstrate that methacrylic acid forms the most stable complex with template, the next is 3-vinyl benzoic acid complex and the third - acrylamide one. The bond energies of the complexes are shown to increase monotonically as more monomers are linked to the template. The same conclusions are made from purely quantum self-consistent field calculations of pre-polymerization complex energy and structure. Hybrid calculation is shown to be effective and can substantially optimize the development of the molecularly imprinting technology.
Then modeling in water and benzene solvents were performed for methacrylic acid and acrylamide prepolymerization complexes. Comparison of calculated bond lengths between monomers and template molecule for systems with minimum energy shows that using of benzene as solvent leads to inessential bond elongation or even bond

contraction in the case of methacrylic acid functional monomer while using water leads to essential bond elongation and even bond break in all cases. Due to QM/MM approach the calculation time for solution do not differ essentially from that for vacuum calculation.

[1] Barkaline V, Douhaya Ya, Tsakalof A (2013) – J Mol Modeling 19:359-369.

P20

DEVELOPMENT OF NATURAL POLYSACCHARIDES FOR CONTROLLED RELEASE OF CLONIDINE

E. O. Batyrbekov, A. B. Ismailova
Institute of Chemical Sciences, Almaty, Kazakhstan

Natural polysaccharides successfully have been used in pharmaceutical technology to develop a new drug delivery systems. Natural polysaccharides have great potential for applications as drug carriers due its biodegradability, biocompatibility, non-toxicity and versatile chemical and physical properties. The aim of the present work is the evaluation of natural polysaccharides as carriers for controlled release of clonidine. Polymers used in the investigation were dextran, sodium salts of carboxymethylcellulose, alginic or pectic acid. The interaction of clonidine with biodegradable polymers was studied from the viewpoint of thermodynamic behavior. The free drug concentration was determined from residual drug concentration; the binding constants were calculated from Klotz equation. The small drug interaction was observed for nonionogenic polymer such as dextran. In this cause of ionogenic polymer like sodium salt of carboxymethylcellulose or pectic acid the enthalpy and free energy had negative values and the entropy was positive.

For these processes the electrostatic binding plays the significant role. In all cases the thermodynamic parameters and their temperature dependence show the existence of hydrophobic interaction between drugs and polysaccharides. The release of drug into model biological medium at 37°C was studied. The correlation between release rates and binding parameters was determined. It has been shown that dosed release proceeds during 5-7 days and depends on nature of polymers, their concentration, pH of solution and ratio of components.Films of polysaccharides containing various doze of drug have been prepared by solution casting method from 5-10% solutions. Influence of various factors on process of drug release from films in conditions «*in vitro*» was investigated.

Coefficients of diffusion of released drugs have been calculated and is shown that with increase in thickness of the films in 3 times this parameter decreases approximately in 2 times. The profile of kinetic curves testifies that process of release occurs according to the first order kinetic and controlled by diffusion of the therapeutic agent in polymeric matrix. In according with Higushi equation, describing kinetic of drug diffusion from monolithic systems with the dissolved therapeutic agent, dependence of amount of diffused drugs from films versus root of square time had linear character. Calcium-alginate gel beads containing clonidine were synthesized. Release of drug from the alginate gel beads of various mannuronic/guluronic ratios in physiological solution was examined. It was found that discontinuous time of the Fickian diffusion of the drug was followed by a burst release of the remaining drugs.

The lag time preceded the burst release depended on mannuronic/guluronic ratio. It was revealed that the burst release of drug was initiated by a swift disintegration of calcium-alginate due to exchange on sodium ions.The buccal polymeric films containing clonidine were created on the basis of pectin and cellulose derivatives. Controlled drug release from films was limited by rate of swelling and following dissolution of polymeric matrix. Films were used to treat arterial hypertension and prevent hypertensive crisis. Data of medical-biological and clinical tests show the advantages of natural polysaccharides application as clonidine carriers in comparison with low-molecular drug.

P21

NOVEL HYDROPHILIC POLYMERIC MATERIALS BASED ON WASTE OF POLYOLEFIN PRODUCTION

G. I. Boiko[1], N. P.Lubchenko[1], R. G. Sarmurzina[3], G. S. Aitkaliyeva[1], T. P. Maimakov[2], YU. V. Korshak[4]
[1]Kazakh National Technical University after K.I.Satpayev, Almaty, Kazakhstan
[2]Unat University, Almaty, Kazakhstan
[3]JSC NC "KazMunaiGas", Astana, Kazakhstan
[4]D.Mendeleev University of Chemical Technology of Russia, Moscow, Russia

In this paper immobilization of hydrophilic monomer (vinyl ether glycol) on the waste of isotactic polypropylene production for recycling of production wastes of isotactic polypropylene and on this base creation of polymeric materials with valuable properties was done. The method of radiation graft polymerization was used. The radiation doses were 200 and 1200 kGy.

Comparative analysis of the IR spectra of the original atactic polypropylene and grafted forms indicate that in the

modified APP, obtained by exposure 200kGy, appears a new absorption band at 1100- 1215 cm^{-1}, which is characteristic of the ether C-O-C group, and observed the appearance of a sufficiently high intensity peak in the 3400 cm^{-1}, responsible for the vibrations of OH groups of the grafting monomer. Revealed, that with increasing of radiation dose increases the intensity of the absorption ether C-O-C band, which shows the degree of grafting.
On ^1H NMR spectrum of the graft copolymer APP-VEEG/200 was noted the appearance of a new signal with a chemical shift of 2.6 ppm with integral 0.59, corresponding to the signal of the proton of the OH group. There are new signals which are characteristic of the group = CH_2 protons at δ 4.04 ppm and proton of groups -OCH = δ 3.7 -3.8 ppm. With increasing of irradiation dose up to 1200 kGy in copolymers significantly increases the intensity of the shifts corresponding to vinyl ether of ethylene glycol: increases the integral of the chemical shift of 2.6 ppm proton of the -OH group to 1, as well as changes significantly the intensity of the chemical shifts δ 3.7- 3.8, 4.04 ppm to 5.
X-ray analysis revealed that the degree of crystallinity of APP is 37 %, for modified forms the content of the crystalline phase depends on the radiation dose: at low dose crystallinity reaches 26% and at a high dose - 22%.
The developed new copolymers can be used in broad industrial fields. It is a topical solution not only from the standpoint of environmental protection, but also from an economical standpoint.

P22

HE CATALYTIC ACTIVITY REGULATION OF ENZYME – INHIBITOR PAIR IMMOBILIZED ON MAGNETITE-GOLD NANOPARTICLES VIA ULTRA LOW MAGNETIC FIELD APPLICATION

A. V. Barulin[1], M. V. Efremova[1,4], P. G. Rudakovskaya[1], O. N. Metelkina[1], A. V. Kabanov[1,2], Y. I. Golovin[1,3], A. G. Majouga[1,4], N. L. Klyachko[1,2]
[1]Laboratory for Chemical Design of Bionanomaterials, Chemical Enzymology Department, M.V. Lomonosov Moscow State University, Moscow, Russian Federation
[2]Eshelman School of Pharmacy, University of North Carolina at Chapel Hill (UNC), North Carolina, USA
[3]R.G. Derzhavin Tambov State University, Tambov, Russian Federation
[4]National University of Science and Technology MISiS, Moscow, Russian Federation

Magnetite nanoparticles Fe_3O_4 (MNP) are widely applied in biomedical research, namely for improvement the contrast range of MRI, immunoassay, etc. In the scientific publications, the magnetic nanoparticles are proposed to use for treatment of cancer by targeted drug delivery. MNP could carry the specific drug to a tumor along the bloodstream and release it by magnetic field (MF). Moreover, the magnetic nanoparticles can influence on the chemical reactions in the body, for example, on enzymatic reactions. A combination of those ideas is being considered in the current report as pretty attractive and relevant things for humanity. The active site of enzyme immobilized on the nanoparticles can be deformed by their rotation under magnetic field exposure without heating. This rotation may be initiated by exposure to low frequent (LF) alternating magnetic field (50-100 Hz). The reorientation**T** of magnetic moments of Fe_3O_4 in nanoparticles (d>6 nm) exposed into MF leads to the rotation of magnetic particles on Brown mechanism. Once the enzyme is deformed, it will leave nominal catalytic activity. But Fe_3O_4 are toxic and could rapidly aggregate without stabilizers. That is why an important issue of the work performed with MNPs is the development of methods of covering the magnetic core. For example, MNPs coated with gold shell possess low toxicity in the body, show less ability to aggregate and can easily be functionalized with different organic ligands via SH-groups.
This paper presents a synthesis of magnetic (Fe_3O_4) and magnetic gold particles (Fe_3O_4@Au) with the core-shell structure, confirmed by micrographs EPMA (electron probe microanalyzer). For the surface functionalization of nanoparticles lipoic and dimercaptosuccinic acids were used as organic ligands. The results of nanosystem studying represent some approaches to description of nanoconjugates (NP-enzyme-) and the effect of LFMF on catalytic activity of immobilized enzymes via such linkers.

Acknowledgement:
The work was supported by grants RSF 14-13-00731 and K1-2014-022 (in part of EPMA method)

P23

IMPACT OF HEMORHEOLOGICAL PROPERTIES IN BLOOD TRANSPORTATION EFFICACY

I. Tikhomirova, A. Muravyov, E. Petrochenko, Y. Malysheva
Yaroslavl State Pedagogical University, Dept. Medicine & Biology, Yaroslavl, Russia

Hemorheological properties are the main determinants of blood transportation efficacy at the level of microcirculation, so the oxygen delivery to tissue as well as the carrying of drugs is substantially depend on blood viscosity. The factors that determine the rheological behavior of blood, a two-phase fluid, include the relative volume of each phase (blood cells and plasma), plasma viscosity and microrheological properties of red blood cells (aggregability and deformability). The reversible aggregation of red blood cells affects the low shear blood viscosity and microvascular flow dynamics, and can be markedly enhanced in several clinical states. Erythrocyte deformability becomes important when vascular caliber is comparable with red blood cell diameter.
Worsened in pathology blood rheological properties may impede not only oxygen delivery, but also deteriorate the drug transportation. The erythrocyte, a cell responsible for carrying and delivering oxygen in the body, has often been regarded as simply a vehicle for the circulation of hemoglobin. However, it has become evident that this cell also participates in the regulation of vascular caliber in the microcirculation and interacts with biologically active substances circulating in blood. Our results indicated that the hemorheological consequences of the drug therapy are mainly due to the alterations of the blood cellular properties their aggregation and deformability.
Work was supported by RSCF grant 14-15-00787

P24

NEW VISCOSUPPLEMENT FOR THE TREATMENT OF OSTEOARTHRITIS

A. V. Gromov, V. P. Gudov, N. N. Durmanov, M. S. Bartov, D. M. Savina, K. S. Savin, K. E. Nikitin, E. V. Razumkina, M. S. Subbotina,
T. M. Grunina, L. A. Soboleva, A. S. Semikhin, O. A. Gra, A. S. Karyagina, V. G. Lunin
Gamaleya Research Center for Epidemiology and Microbiology, Moscow, Russian Federation

Osteoarthritis (OA) is a major pathology in modern western societies, particularly affecting the elderly, who account for an increasing share of today's population. The disease is generally divided into primary OA, related to age and genetic factors, and secondary OA, related to different kinds of joint injuries, such as trauma, surgery and infections. OA occurs in 2% of the population under the age of 45 years, 30% aged 45-64 years and 63-85% over 65 years. The intra-articular management of OA (viscosupplementation) is currently based on the injection of hyaluronic acid, the viscoelastic mucopolysaccharide component of synovial fluid, has recently seen increased popularity in the nonoperative treatment of OA. The main function of this treatment is to lubricate and amortize the articular surfaces. However, viscosupplementation is insufficient to suppress the activity of inflammatory processes. Furthermore, the high rate of biodegradation or elimination of hyaluronic acid leads to the necessity of repeated injections accompanied by additional injury. Therefore, there is a significant need to develop a new viscosupplement for the treatment of OA, which provide chondroinductive effect by stimulating cartilage regeneration.
The new viscosupplement "Gamalant-Chondro" for treatment of OA is developed. It is based on cross-linked hyaluronan nanoparticles dissolved in hyaluronan with a smaller percentage of crosslinking, and is supplemented by recombinant protein component providing chondroinductive function.
The rheological properties, the size and amount of hyaluronan nanoparticles, and the biological activity of chondroinductive component, recombinant growth factor, of developed viscosupplement "Gamalant-Chondro" were investigated. Appropriate crosslinking sites and the absence of impurities were confirmed by NMR.
Viscosupplementary properties of "Gamalant-Chondro" were evaluated in experiments on rats in models of the knee injury (anterior cruciate ligament injury) compared to a commercially available viscosupplements. Histological and X-ray tomographic analysis demonstated high chondroprotective properties, biocompatibility, hypoallergenity and non-toxicity of the developed viscosupplement "Gamalant-Chondro".

P25

Q-FISH ANALYSIS OF METAPHASE SPREADS FOR CLINICAL PURPOSE

P. Fragkiadaki[1], E. Vakonaki[1], E. Kouvidi[2], D. Vynias[1], D. Tsoukalas[1], A. M. Tsatsakis[1]
[1]Laboratory of Toxicology, Division of Morphology, Medical School, University of Crete, Voutes, Heraklion 71003, Crete, Greece
[2]Department of Haematology, University of Crete School of Medicine, *Voutes, Heraklion 71003, Crete, Greece*

Background:Telomeres are specialized nucleoprotein structures located at the extremities of linear chromosomes providing the cell with a certain lifespan while at the same time they supply this part of the DNA with certain extraordinary qualities. Telomeres associate with shelterin proteins and form a complex protecting the chromosomal deoxyribonucleic acid (DNA) from recognition by the DNA damage repair system. When telomeres reach a critical length the cell will not further undergo cell divisions and become senescent or otherwise dysfunctional. Telomere shortening has not only been linked to aging but also to several age associated diseases, including tumorigenesis, coronary artery disease, and heart failure.
Methods: We studied the role of telomere biology in relation to cancer, aging and aging associated diseases. In order to study telomere repeats at individual chromosomes, we developed quantitative fluorescence in situ hybridization procedures (Q-FISH) using labeled (C3TA2)3 peptide nucleic acid (PNA) probe, the DNA dye DAPI and digital imaging microscopy. Separated images of FITC and DAPI fluorescence are acquired and processed with a dedicated computer program (TFL-TELO). With the program, the intergrated fluorescence intensity value for each telomere, which is proportional to the number of hybridized probes, is calculated.
Conclusion: Telomeres shortening have been found to be involved in cancer, in liver dysfunction, in cardiovascular, Alzheimer and many metabolic and inflammatory diseases. In this study we tried to construct a database in order to associate the reduction of telomeres length with the diseases that can cause, in order to help the doctor for a superior handling of the patient.
Keywords: Telomeres, shortening, diseases, cancer

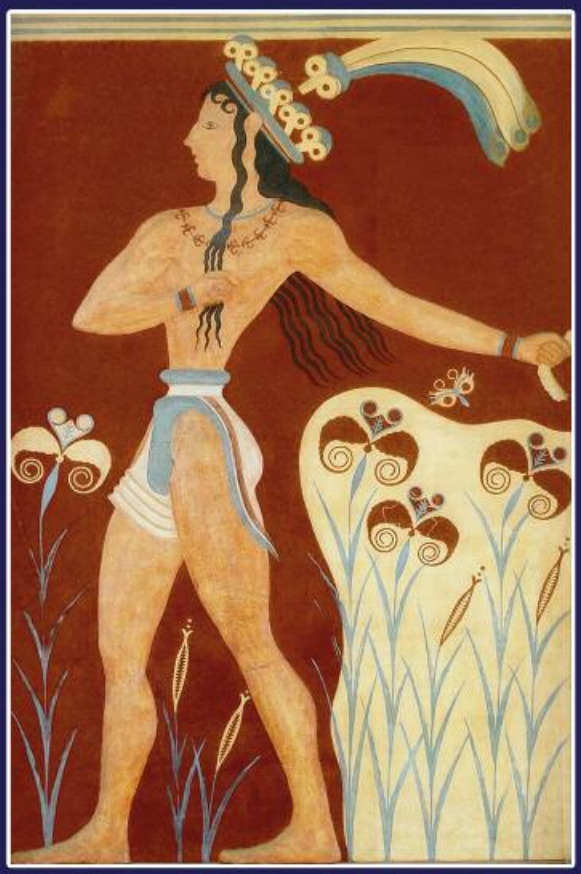
List of Chairs, Speakers, Authors

Aitkaliyeva G. S.
Akasov R.
Akopova T.
Aleksanyan K. V.
Aliev A. D.
Artyukhov A.A.
Artyukhow A. A.
Askarova Sh.
Baiyrkhanova A. O.
Balabanyan V.
Barkaline V. V.
Bartov M. S.
Barulin A. V.
Batalova T. A.
Batyrbekov E. O.
Belova A. B.
Belova M.S.
Belyy T. S.
Berlin A.A.
Boiko G. I.
Borisov S. Yu.
Borodina T. N.
Boyko G. I.
Bukreeva T. V.
Burov S.
Bychkova A.V.
Chaika V. V.
Chalykh A. E.
Corsini E.
Czajka M.
Demina T. S.
Deygen I. M.
Dobrynin A.
Dolgaya Y. V.
Douhaya Y.
Dregval O. A.
Drozdova M. G.
Durmanov N. N.
Dzantiev B. B.
Efremova M. V.
Egorov A.M.
Elfimov A. B.
Elfimov D. A.
Eremin S. A.
Fedoseeva V.
Filatova L. Yu.
Fragkiadaki P.
Gaidar A. I.
Galashkina Z. M.
Gelperina S.
Gladyshev M.I.
Godlewski M.
Godlewski M.M.
Goldin M. M.
Golokhvast K. S.
Golovin Yu. I.
Goryachaya A. V.
Gra O. A.
Grandfils Ch.
Gribanovsky S. L.
Grigorenko V. G.
Grigoriev Y. V.
Gromov A. V.
Grunina T. M.
Gudov V. P.
Gumargalieva K.Z.
Iatrou E.
Iordanskii A. L.
Ismailova A. B.
Issabayev Ye. A.
Iwanenko T.
Kabanov A. V.

Kalinina N.I.
Kandelaki G. I.
Kapka Skrzypczak L.
Karyagina A. S.
Kassymgaliyev K. M.
Kaszewski J.
Kavasi R. M.
Kechagias K.
Khalansky A.
Khasbiullin R. R.
Kielbik P.
Kildeeva N. R.
Klimenko O.V.
Klyachko N. L.
Kolosov V. P.
Korshak Yu. V.
Kosenko R. Yu.
Kouvidi E.
Kovarski A. L.
Kruszewski M.
Krylov S. N.
Krylova S. M.
Kudryashova E. V.
Kulikov P.P.
Kuskov A.N.
Kutsenok E. O.
Kuznetsov V. L.
Legonkova O. A.
Legotsky S. A.
Loca D.
Lokhin K.
Lopatina T.V.
Lozinsky V. I.
Lubchenco N. P.
Lunin V. G.
Luss A. L.
Lyubchenko N.
Machulkin A.
Maimakov T. P.
Majouga A. G.
Malysheva Y.
Mantas G.
Marchenko I. V.
Markin V.S.
Markvicheva E.
Meczynska- Wielgosz S.
Metelkina O. N.
Mezhuev J. O.
Mezhuev Ya. O.
Mikhailenko N. Yu.
Miljohin M. S.
Miroshnikov K. A.
Moldabekov B. S.
Morgacheva A. A.
Morozov R. A.
Muravyov A.
Nabatov B. V.
Nelyub V. A.
Neufeld R.J.
Nikitin K. E.
Nikitina A.V.
Nikitovic D.
Osadchenko S. V.
Ostrovsky M. A.
Perelman Y. M.
Pereverzeva E.
Petrochenko E.
Piskareva A. I.
Poholok K. V.
Pokhil S. E.

Priyma A.D.
Rakitskii V.
Razumkina E. V.
Razzhivina V.
Rogovina S.Z.
Romashkin A.V.
Rubtsova M. Yu.
Rudakovskaya P. G.
Sarmurzina R. G.
Savchenkova I. P.
Savin K. S.
Savina D. M.
Sawicki K.
Sayapina N. V.
Selianin M. A.
Semikhin A. S.
Sergeeva N. S.
Shcherbina A. A.
Shishatskaya E. I.
Shtilman M.I.
Shumilova A.
Sigaev V. N.
Soboleva L. A.
Sommer S.
Sorokina O. N.
Spandidos D.
Stilman M.
Stroganova E. E.
Subbotina M. S.
Sulyanov S. N.
Sumina A.
Sviridova I. K.
Syrvacheva D. A.
Tikhomirova I.
Tkachuk V. A.
Torchilin V.P.
Treschalin I.
Trushina D. B.
Tsakalof A.
Tsatsakis A. M.
Tsoukalas D.
Tzanakakis G. N.
Tzatzarakis M.
Uporov I. V.
Uspenskii S. A.
Usvaliev A.
Vakonaki E.
Vantsyan M. A.
Varfolomeev S.D.
Vasilaki F.
Veselov M.M.
Volova T. G.
Vynias D.
Wachnicki L.
Witkowski B.
Wojewodzka M.
Wolska E.
Zaitseva E. A.
Zelenetskii A. N.
Zhila N. O.
Zlobina M.

Notes



BIONANOTOX CONGRESSES

www.bionanotox.org

BIONANOTOX CONGRESSES

www.bionanotox.org

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

EUROTOX

HELLENIC SOCIETY OF TOXICOLOGY

TOXPLUS

AMPHION