11th INTERNATIONAL CONFERENCE

BIOMATERIALS AND NANOBIOMATERIALS:

Recent Advances Safety-Toxicology and Ecology Issues

Including Russian-Hellenic Workshop and School of Young Scientists

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2020 BIONANOTOX

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INVITATION LETTER

On behalf of the organizing committee of 11th International Congress "Biomaterials and Nano-biomaterials: Recent Advances Safety - Toxicology and Ecology Issues" Including Russian Hellenic Workshop and School of Young Scientists and Symposium of Nanotoxicology, we are privileged to invite you to grace with your presence and participation the works of the Congress, which due to the COVID- 19 pandemic will be held online.

The theme of the Symposium, Biomaterials and Nanomaterials toxicology, lie at the interface of many disciplines, from biology to chemistry, toxicology, computational science chemistry, nanotechnology and biotechnology. Albeit 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, scientists from all over the world are participating.

It is anticipated that scientists from Europe, USA, the rest of the world and especially from Institutes of the Russian Academy of Science, the most prominent Universities as well as Technological Institutes and Companies and distinguished field specialists will attend the online 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.

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Aristidis Tsatsakis, PhD, DSc, ERT

Mikhail Shtilman, PhD, DSc

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Velonia Kelly	Associate Professor, Department of Materials Science and Technology, University of Crete, Greece

SCIENTIFIC PROGRAM

September 7, 2020, Monday

15.00	***Opening of The Conference***
15.00-15.10	**ABOUT SYMPOSIUM PROGRAM** **M.I. Shtilman, Head of Organizing Committee** *D. Mendeleyev University of Chemical Technology of Russia, Moscow, Russia*
15.10-20.00	***Coordinators of SESSION Prof. M.I.Shtilman, Prof. N.L. Klyachko***
15.10-15.50	**PLENARY LECTURE** **SUPER-HIGH CAPACITY POLYMERIC MICELLES FOR CANCER THERAPEUTICS AND FEW WORDS ABOUT COVID-19 THERAPIES** **A. Kabanov** *Center for Nanotechnology in Drug Delivery and Carolina Institute for Nanomedicine, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, NC 27599, USA;*
15.50-16.30	**PLENARY LECTURE** **TOXICOLOGY ISSUES RELATED TO COVID 19 OUTBRAKE: KINETICS AND DIDYNAMICS OF COVID-19 DIAGNOSIS AND POTENTIAL TREATMENT** **T.K. Nikolouzakis, D. Petrakis, A. Tsatsakis** *Department of Forensic Sciences and Toxicology, Faculty of Medicine, University of Crete, 70013 Heraklion, Greece*
16.30-16.45	**BREAK**
16.45-17.20	**COMPREHENSIVE RESEARCH OF THE PHYSICO-CHEMICAL AND SORPTION PROPERTIES OF THIN FILMS AND COMPOSITES OF PHENYL/PHENYL END-CAPPED TETRAMER OF ANILINE AS A STRUCTURAL ANALOG OF POLYANILINE** **E.Y.Yagudaeva[1], D.V. Kapustin[1], A.A. Vikhrov[1], Y.N. Malakhova[2], A.N. Korovin[2], N.N. Kononov[3], A.I. Prostyakova[1], V.P. Zubov[1]** *[1]M.M. Shemyakin & Yu.A. Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences, Moscow, Russia* *[2]National Research Center «Kurchatov Institute», Moscow, Russia* *[3]Prokhorov General Physics Institute of the Russian Academy of Sciences, Moscow, Russia*
17.20-17.55	**HOW THE DRUG LOADING METHOD AFFECTS CELLULAR UPTAKE OF PVP-BASED NANOCARRIERS** **L. Gurevich[1], L. Collin Nelemans[1], C.P. Pennisi[1], G. Christiansen[1], A.L. Luss[2], P.P. Kulikov[2], A.N. Kuskov[2], M.I. Shtilman[2]** *[1]Aalborg University, Denmark* *[2]Dmitry Mendeleev University of Chemical Technology of Russia, Russia*

September 7, 2020, Monday

17.55-18.30 **COVID-19 VACCINES: AN UPDATE AND ETHICAL CONSIDERATIONS**

D. Calina[1], A. Docea[2], A. Tsatsakis[3]

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[3]Department of Forensic Sciences and Toxicology, Faculty of Medicine, University of Crete, 71003 Heraklion, Greece

18.30-18.50 **BREAK**

18.50-19.25 **DETECTION OF PHYCOTOXIN MICROCYSTIN-LR BY FLUORESCENCE POLARIZATION IMMUNOASSAY**

S.A. Eremin[1], O.D. Hendrickson[1], K. Maximova[2], A.P. Bondarenko[2], L.I. Mukhametova[2]

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19.25-20.00 **SYNTHESIS OF OLIGOSACCHARIDES RELATED TO *Klebsiella pneumoniae* O-ANTIGENS AND THEIR USE IN ANALYSIS OF ANTIBODY REACTIVITY**

V.B. Krylov, D.A. Argunov, M.I. Petruk, A.S. Trostianetskaia, E.A. Kurbatova, N.E. Nifantiev

Laboratory of Glycoconjugate Chemistry, N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospect 47, 119991 Moscow, Russia

September 8, 2020, Tuesday

10.00-13.55 ***Coordinator of SESSION Prof. S.A. Eremin***

10.00-10.35 **SYNTHETIC AMINOSUGAR CYCLOOLIGOMERS AS SCAFFOLDS FOR DESIGN OF ARTIFICIAL ION-TRANSPORT SYSTEMS**

Y. Tsvetkov[1], O. Yudina[1], M. Gening[1], P. Talukdar[2], N. Nifantiev[1]

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[2]Department of Chemistry, Indian Institute of Science Education and Research Pune, Dr. Homi Bhabha Road, Pashan, Pune 411008, Maharashtra, India

10.35-11.10 **ENHANCED COVID-19 HEALTH PROBLEMS RELATED TO COMORBIDITIES AND CHEMICAL EXPOSURES**

D. Petrakis, A. Tsatsakis, T.K. Nikolouzakis

Department of Forensic Sciences and Toxicology, Faculty of Medicine, University of Crete, 70013 Heraklion, Greece

11.10-11.45 **CONTROLLED MAGNETIC NANOPARTICLES HYPERTHERMIA INHIBITS TUMOR PROGRESSION DEPENDING ON THE TEMPERATURE**

A. Garanina[1], V. Naumenko[2], A. Nikitin[1,3], E. Myrovali[4], M. Angelakeris[4], A. Savchenko[1], U. Wiedwald[1,5], A. Majouga[1,3,6], M. Abakumov[1,7]

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11.45-12.10 **BREAK**

September 8, 2020, Tuesday

12.10-12.45 **HIDDEN HUNGER AND METABOLIC LINKS IN COVID-19**

D. Tsoukalas[1,2], E. Sarandi[2,3], C. Daniela[1], A. Tsatsakis[3]

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[3]Laboratory of Toxicology and Forensic Sciences, Medical School, University of Crete, 71003 Heraklion, Greece

12.45-13.20 **INFLUENCE OF GLYCOSAMINOGLYCANS ON ANGIOGENESIS**

N. Ustyuzhanina, A. Grinkova, D. Vinnitskiy, P. Fomitskaya, A. Tokatly, N. Nifantiev

N.D. Zelinsky Institute of Organic Chemistry, Moscow, Russia

13.20-13.55 **BIOMEDICAL MATERIALS BASED ON NITROGEN-CONTAINING ELECTRICALLY CONDUCTIVE POLYMERS**

Y.O.Mezhuev, Yu.V. Korshak

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

13.55- 14.30 **NUTRIONAL ASPECTS RELATED TO COVID-19**

D. Margina[1], A. Ungurianu[1], D. Tsoukalas[2]

[1]Faculty of Pharmacy, University of Medicine and Pharmacy, Bucharest, Romania

[2]Health Clinics for Autoimmune and Chronic Diseases, Athens, Greece

14.30 ***Closing of The Conference***

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M.A. Ostrovsky

Emanuel Institute of Biochemical Physics, RAS, Department of Molecular Physiology, Faculty of Biology, Lomonosov Moscow State University

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B.B. Dzantiev

A.N. Bach Institute of Biochemistry, Federal Research Centre "Fundamentals of Biotechnology", Russian Acad. Sci., Moscow 119071, Russia

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

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A.M. Nechaeva[1,2], M.M. Gasimov[1,2], S.Z. Rogovina[2], S.M. Lomakin[2]

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P 05 **ENVIRONMENTAL-FRIENDLY NANOPOLYMERS FOR AGRICULTURE**

S. Rashidova

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N.R. Kildeeva, N.A. Sazhnev, V.A. Zakhsrova, A.A. Gubochkina

A.N. Kosygin Russian State University, Moscow, Russia

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S.A. Eremin[1], S.S. Babkina[2], Yu.S. Lebedin[3]

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P 08 **LIQUID POLYMER SUBSTANSES IN SURGERY**

O.A. Legonkova[1], A.V. Chupin[1], A.C.Оганнисян[1], V.V. Stafford[2], I.P.Savchenkova[2]

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Department of High-Energy Chemistry and Radioecology, D. Mendeleev University of Chemical Technology of Russia, Moscow, Miusskaya Square, 9, Russia

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A.N. Kuskov[1], L.Yu. Basyreva[2], E.V. Voinova[2], A.A. Gusev[2], E.V. Mikhalchik[2], S.A. Gusev[2], M.I. Shtilman[1], A.M. Tsatsakis[3]

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E. Zelinskaya, N. Tolmacheva, A. Kurina, N. Garashchenko

Department of environment, Irkutsk National Research Technical University, Irkutsk,664074, Russia

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I.L. Rastunova, A.Yu. Chebotov, I.A. Vorakso

D. Mendeleev University of Chemical Technology of Russia, 9 Miusskaya sq., Moscow, Russia

P 13 **FRACTIONATION OF HYDROGEN ISOTOPES BETWEEN HYDRATED AND FREE WATER MOLECULES IN AN AQUEOUS SOLUTION OF METAL SALTS**

V. Pokalchuk, E.Magomedbekov, J. Kondakova, I. Shestakov

Department of High-Energy Chemistry and Radioecology, D. Mendeleev University of Chemical Technology of Russia, Moscow, Miusskaya Square, 9, Russia

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A. Zharikov, E. Magomedbekov

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

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A.V. Gromov[1], F.S. Senatov[2], A.V. Chubrik[2], A.I. Zimina[2], K.E. Nikitin[1], P.A. Orlova[1], T.M. Grunina[1,2], M.S. Poponova[1], N.V. Strukova[1], M.S.Krivozubov[1], V.G. Lunin[1,2], A.S. Karyagina[1,3,4]

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[4]A.N. Belozersky Institute of Physical and Chemical Biology, M.V. Lomonosov Moscow State University, Moscow, Russian Federation

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[3]Institute of Agricultural Biotechnology, Moscow, Russian Federation

[4]A.N. Belozersky Institute of Physical and Chemical Biology, M.V. Lomonosov Moscow State University, Moscow, Russia

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G.I. Boyko[1], R.G. Sarmurzina[2], N.P. Lyubchenko[1], U.S. Karabalin[2], D.S. Tiesov[3], Ye.S. Panova[1]

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[2]Association «Kazenergy», Astana, Kazakhstan

[3]JSC «Kazakhstan Petrochemical Industries», Atyrau, Kazakhstan

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Ya.O. Mezhuev[1], Yu.V. Korshak[1], M.I. Shtilman[1], I.V. Plyushchii[1], A.L. Luss[1], M.V. Motyakin[2], V.A. Dyatlov[1], A.M. Tsatsakis[3]

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[3]University of Crete, Heraklion, Greece

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P. Voskanyan, A. Tovmasyan

National Bureau of Expertises of the Republic of Armenia, Yerevan, Armenia, 0004, Ave. Isakov, 24

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T. Kovshova[1,2], N. Osipova[2], A. Alekseeva[3,4], G. Pavlova[3], A. Belov[2], A. Budko[5], O. Maksimenko[2], V. Balabanyan[1], S. Gelperina[2]

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T. Kovshova[1,2], N. Osipova[2], A. Belov[2], O. Maksimenko[2], V. Balabanyan[1], S. Gelperina[2]

[1]M.V. Lomonosov Moscow State University, Moscow, Russia

[2]D.I. Mendeleev University of Chemical Technology of Russia, Moscow, Russia

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Yu. Nashchekina

Center of Cell Technologies Institute of Cytology Russian Academy of Sciences, St. Petersburg, Russia

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

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Ju. Fidorovskaya, E. Medusheva, N. Oltarzhevskaya
Limited liability company «COLETEX», Moscow, Russia

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M.I.Gladyshev[1,2], O.N.Makhutova[1,2], V.N. Morgun[2,3], N.N. Sushchik[1,2]
[1]Institute of Biophysics of Siberian Branch of Russian Academy of Sciences, Akademgorodok, 50/50, Krasnoyarsk 660036, Russia
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P 26 **HEAT-RESISTANT COMPOSITION**

N. Ormotsadze[1], M. Meskhishvili[1], D. Bibileishvili[2]
[1]Akaki Tsereteli State University
[2]Georgian Technical University

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G. Yu. Ostaeva, I.V. Morenko, E.A. Eliseeva, A.A. Litmanovich
Moscow Automobile and Road Construction State Technical University (MADI), Leningradskii pr. 64, Moscow 125319, Russia

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E.A. Trufanova, T.V. Tikhonova, A.N. Kuskov
D. Mendeleev University of Chemical Technology of Russia, Moscow, Russia

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N.E. Sedyakina[1], V.Yu. Reshetova[2], A.F. Krivoshchepov[2], I.A. Butorova[2], A.N. Kuskov[2]
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A. Svitsov, N. Kruchinina
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Yu.A. Penkina, D.V. Barabash, I.A. Butorova
Department of Technology of Chemical Pharmaceutical and Cosmetic Products, D.I. Mendeleev University of Chemical Technology of Russia, Geroev Panfilovtsev st., 20, 125480 Moscow, Russian Federation

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A. Luss, K. Kushnerev, M. Tarasova, Y. Mezhuev, M. Shtilman, V. Dyatlov
D.Mendeleyev University of Chemical Technology of Russia, Moscow, Miusskaya Sq, 9.

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O 01

SUPER-HIGH CAPACITY POLYMERIC MICELLES FOR CANCER THERAPEUTICS AND FEW WORDS ABOUT COVID-19 THERAPIES

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Poly(2-oxazoline) polymeric micelles (PM) display unprecedented high loading with respect to water-insoluble active pharmaceutical ingredients (APIs). This drug delivery platform greatly enhances the solubility and stability of drugs and drug candidates and improves their efficacy and safety in a transformative way. The technology has been validated for more than 20 extremely poorly soluble APIs. The injectable aqueous solutions are readily prepared that are stable and contain up to 50-100 g/L of extremely poorly soluble APIs, at least 10 to 100 times greater amounts than most other solubilization methods. The drug to excipient ratio in poly(2-oxazoline) PM is also 10 to 100 times better than the ratios of excipients in other approaches. One example is a Cremophor- and PEG-free paclitaxel in poly(2-oxazoline) PM. It has demonstrated potential to increase treatment efficacy of cancers by using high-dose therapy and shown superiority in treatment of tumors in animal models when compared to marketed paclitaxels. For many of the drug candidates, poly(2-oxazoline) PM platform represents the only possibility for a parenteral drug application and enables major contribution to patient care. Chemo-sensitizing agents and agents modifying tumor microenvironment in poly(2-oxazoline) PM were shown to improve chemo- and immunotherapy of cancers in both prevalent and orphan diseases in animal models. Poly(2-oxazoline) PM platform allows easy co-formulation of multiple APIs to 1) decrease burden of administering these APIs separately to a patient in combination drug therapy, and 2) improve treatment efficacy by simultaneous delivery of these APIs to biological targets. Superior antitumor activity of PM with co-loaded drugs compared to single drug micelles or their combination was demonstrated. A rational, computer-aided approach to reliable selection of hydrophobic molecules with dramatically improved solubility in poly(2-oxazoline) PM was developed to enhance the throughput and success of formulation development for new APIs. The work has been supported by the United States National Institutes of Health (1U54CA198999).

O 02

TOXICOLOGY ISSUES RELATED TO COVID 19 OUTBRAKE: KINETICS AND DIDYNAMICS OF COVID-19 DIAGNOSIS AND POTENTIAL TREATMENT

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SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) pandemic has become a great stressor for health systems worldwide. In the meanwhile global scientific community is trying to effectively understand key aspects of this infection in order to halt its progression. Such key aspects are the kinetics and dynamics of COVID-19 diagnostic protocols and potential treatments. COVID-19 diagnosis has become great challenge given the similarity of the symptoms proclaimed with other viral respiratory infections. National and local authorities have endorsed COVID-19 testing both for symptomatic and asymptomatic individuals who fulfill certain criteria and for public health or infection control purposes. Current diagnostic modalities include: (1) Nucleic acid amplification testing (NAAT), most commonly with a reverse-transcription polymerase chain reaction (RT-PCR) assay (at the moment is the preferred initial diagnostic test for COVID-19). RT-PCR is primarily used for the diagnosis of current infection as it combines high analytic sensitivity and specificity in ideal settings. However, its clinical performance depends on the type and quality of the specimen and the duration of illness at the time of testing allowing for reported false-negative rate ranges from <5 to 40%, depending on the test used (2) Antigen testing— Tests that detect SARS-CoV-2 antigen can be performed rapidly and at the point of care. Clinicians should be aware of the possibility of false-negative results given the relative low sensitivity of the test (3) Serologic detection of antibodies against SARS-CoV-2 generally take several days to weeks to develop, and the time to antibody detection varies by test. Depending on the time of symptom onset IgM may be detected in 23% by one week, in 58% by two weeks, and in 75% by three weeks while the corresponding detection rates for IgG may be 30, 66, and 88 %. As for the

treatment, there are FDA-approved drugs for the treatment of COVID-19. Definitive clinical trial data are needed to identify safe and effective treatments for COVID-19. The current practice of SARS-CoV-2 treatment is based greatly on symptomatic care with critical care support applied when heamodynamic, respiratory or renal insufficiency is needed. Antiviral therapies aiming the inhibition of viral entry (via the ACE2 receptor and TMPRSS2), viral membrane fusion and endocytosis or the activity of the SARS-CoV-2 3CLprotease and the RNA-dependent RNA polymerase. Moreover, agents that modulate the immune response such as human blood-derived products and immunomodulatory therapies are being explored as adjunctive treatments for the management of moderate to critical infection. In addition to the antiviral medications and the immune-based therapies administration of antithrombotic therapy, vitamin C, D and zinc is suggested.

O 03

COMPREHENSIVE RESEARCH OF THE PHYSICO-CHEMICAL AND SORPTION PROPERTIES OF THIN FILMS AND COMPOSITES OF PHENYL/PHENYL END-CAPPED TETRAMER OF ANILINE AS A STRUCTURAL ANALOG OF POLYANILINE

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Polyaniline (PANI) is a polyconjugated polymer that has attracted the attention of scientists for many years because of the possibility of its use in both organic electronics including medical use, thanks to its rather high conductivity, chemical stability, the ability of redox and non-oxidative doping, biocompatibility and selective affinity for different types of biopolymers. However, due to volatility of physical and chemical properties of PANI, this polymer is not suitable for direct production of devices, which limits its wide practical application. Those drawbacks could be overcome by oligomers of aniline which demonstrate reliable control and adjustment of their structure, better solubility and processability. In current research we examined physical and chemical properties of phenyl-N-capped tetraaniline (TANI) films and composite materials based on this oligomer, which is the lowest molecular weight conductive derivative of aniline with comparison to PANI. The structural and electrical properties of TANI and its composites with silicon nanoparticles as a potential component of electronic devices, such as electrochemical memristive elements, anodes of lithium batteries, capacitors were investigated. Self-organized thin film structures of TANI with well-defined morphology were created by transfer of Langmuir films created on the water-air interface. The behaviour of TANI as bioseparation material (in comparison with PANI) was studied with spectral correlation technique on the examples of sorption activity to nucleic acids and proteins.

O 04

HOW THE DRUG LOADING METHOD AFFECTS CELLULAR UPTAKE OF PVP-BASED NANOCARRIERS

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A common class of drug delivery nanocarriers is based on amphiphilic block copolymers (ABCs) composed of hydrophobic and hydrophilic blocks. When these polymers are dissolved in an aqueous solution at a concentration above their critical micelle concentration (CMC), they self-assemble into aggregates with a hydrophobic core and hydrophilic corona. Hydrophobic drugs can then be loaded into the core of such micelles and transported to their target in the body. This loading process however significantly affects the physical properties of a micelle, including its stability, shape, size and size distribution, and hence nanocarrier interaction with the body. In this presentation we report size distribution, morphology and specifics of cellular uptake of poly-N-vinyl-2-

pyrrolidone thiooctadecyl nanocarriers loaded with a hydrophobic DiI dye (as a hydrophobic drug model) prepared by ultrasonic dispersion and co-solvent evaporation methods. We observe that co-solvent evaporation technique tends to yield nanocarriers with a narrower size distribution, more regular morphology and smaller average size. However, nanocarriers prepared by ultrasonic dispersion exhibit a higher drug load and higher affinity to cellular membranes in in-vitro studies. We attribute these differences to lower thermodynamic stability of ultrasonically produced nanocarriers and discuss the experimental evidence and further implication of this phenomenon.

O 05

COVID-19 VACCINES: AN APDATE AND ETHICAL CONSIDERATIONS

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The pandemic associated with the new SARS-CoV-2 coronavirus continues to spread worldwide. The most favorable epidemic control scenario, which provides long-term protection against COVID-19 outbreaks, is the development and distribution of an effective and safe vaccine. The need to develop a new COVID-19 vaccine is pressing; however, it is likely to take a long time, possibly several years. This is due to: i) The time required to demonstrate the safety and efficacy of the proposed vaccine; and ii) the time required to manufacture and distribute millions of doses. The process of creating a new vaccine begins with a so-called 'candidate' vaccine, which a team of scientists believes has potential. A number of 'candidate vaccines' despite all promise fail during the testing process. This evaluation of the candidate vaccine is the most rapid part of the process and can take up to a few weeks. The further development and safety testing of the most promising 'candidate' vaccine takes much longer and is far more costly than the candidate vaccine evaluation process. To accelerate this development and associated safety testing, the intentional infection of healthy volunteers has been suggested. Although this procedure raises serious ethical concerns, medical authorities who support the benefits of voluntary SARS-CoV-2 infection studies describe a key advantage: Speeding up the study process of approving an effective vaccine.

O 06

DETECTION OF PHYCOTOXIN MICROCYSTIN-LR BY FLUORESCENCE POLARIZATION IMMUNOASSAY

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Phycotoxins are highly toxic metabolites of a number of algae, microalgae and cyanobacteria. As well as these organisms form initial points of aquatic food chains, phycotoxics are transferred to fishes and other harvested and farmed aquatic organisms. So the control of phycotoxins in food for human health protection is in demand. The dominating techniques for this control such as chromatography, microplate immunoenzyme assays etc. are rather long-term and labor-consuming, require expensive equipment and qualified personnel.
Fluorescence polarization immunoassay (FPIA) could be better technique to screen samples for presence and content of phycotoxins. The FPIA is a homogeneous analytical technique (without separation and washing) that is based on the competitive binding of controlled and fluorophore-labeled analyte molecules with specific antibodies and the measurement of fluorescence polarization value depending on the analyte content in the sample. The assay can be implemented with small volumes of samples (approx. 50 µL); the total time required for FPIA is few minutes. Preliminary results of microcystin-LR detection by FPIA were obtained. Using different combination of immunoreactants (labeled antigens and antibodies), specificity of the assay can be modulated. Limit of microcystin-LR detection calculated using $mP_{min} = mP_0 - 3SD$ was found to be in the range from 7.5 to 20 ng/mL for different antibodies. These results confirm a competitive potential of FPIA compared to other techniques for phycotoxins detection.
The work was supported by the Russian Science Foundation (Project 20-43-07001).

O 07

SYNTHESIS OF OLIGOSACCHARIDES RELATED TO *Klebsiella pneumoniae* O-ANTIGENS AND THEIR USE IN ANALYSIS OF ANTIBODY REACTIVITY

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Klebsiella pneumoniae is a Gram-negative pathogenic bacterium that emerges a challenge for modern medicine due to intensively rising multi-drug resistance. Specific LPS O-chains, namely galactans, represent promising targets for development of vaccines for immunoprophylaxis or immunotherapy of *K. pneumoniae*-caused diseases. Herein, we report the synthesis of oligosaccharides which represent different structural fragments of *K. pneumoniae* galactans. The galactofuranoside building block used for assembling of the galactan's chains was prepared by pyranoside-into-furanoside (PIF) rearrangement of the corresponding galactopyranoside precursor bearing an acid-labile temporary protecting group at O(3). The synthesized set of K. pneumoniae antigenic oligosaccharides in the form of their biotinylated derivatives was used to create a glycoarray which was applied for the screening of antibodies in anti-*K. pneumoniae* sera. The obtained results demonstrate the immunological identity of the syntetic antigens to the natural ones which stimulates further detailed investigations directed to vacine design.

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O 08

SYNTHETIC AMINOSUGAR CYCLOOLIGOMERS AS SCAFFOLDS FOR DESIGN OF ARTIFICIAL ION-TRANSPORT SYSTEMS

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Carbohydrate macrocycles, mainly cyclodextrins, are widely used as a platform for the synthesis of multivalent conjugates including improved drug and gene delivery systems, carbohydrate displays, artificial ion channels etc. However, the modest difference in the reactivity of hydroxyl groups in cyclodextrins often complicates their site-specific modification. Recently synthesized by us macrocyclic oligo-b-(1→6)-d-glucosamines of variable size as well as mixed glucose-glucosamine cycles with different mutual monosaccharide arrangement are devoid of this shortcoming. By using highly selective modifications at the amino groups of those macrocycles, we have synthesized a series of multivalent glycoclusters with galactose residues on the periphery that demonstrated high potency to inhibit the bacterial lectin LecA. Unlike cyclodextrins, the cavity in cyclic oligo-b-(1→6)-d-glucosamines is hydrophilic making especially attractive their application to design of artificial transmembrane ion-transport systems. Thus, these macrocycles, being equipped with long hydrophobic chains at the amino groups, were capable of forming ion channels specific to halide ions. In continuation of this investigation, we are developing novel cyclic tetrasaccharide scaffolds with axial amino groups based on 3-amino-3-deoxyallose and 4-amino-4-deoxygalactose. Contrary to oligo-b-(1→6)-d-glucosamines whose amino groups are equatorial, axial orientation of the amino groups may provide a parallel arrangement of attached ion-recognizing functionalities, thus making anion recognition more efficient. The synthesis of this novel tetrasaccharide scaffolds and potential anion-transporter therefrom will be presented.

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O 09

ENHANCED COVID-19 HEALTH PROBLEMS RELATED TO COMORBIDITIES AND CHEMICAL EXPOSURES

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The SARS-CoV-2 infection has risen great concern both to civilians and health care professionals both due to its increased transmissibility and due to the enhanced health problems created to COVID-19 patients. The impact of real-life exposures to multiple toxic stressors degrading the immune system may have made individuals not only prone to infection but also to the onset of the severe symptomatology. While there is some decline in the immune system with age, comorbidity is a more reliable predictor of impaired immunity than chronological age in older adults as exhibited by the ICU admitted patients. Hypertension, diabetes, cardiovascular diseases, chronic respiratory disease, renal insufficiency, immune compromised status, cancer and obesity, metabolic stress also contributes significantly to the dysfunctional immune response and, thus, to the increased risk associated with viral exposure. It is well established that long-term low-dose occupational or environmental exposure to chemical mixtures (e.g., endocrine-disrupting chemicals, microplastics, heavy metals, pesticides, nanoparticles, PFOA, PCBs, PAHs, PFOS, fine particulate matter, air pollution, acrylamide, aromatic halogenated disinfection byproducts, benzene, benzo(a)pyrene, is linked to immunodeficiency as does the intentional, unintentional or iatrogenic exposure to various drugs, biotoxins/biomaterials and immunomodifyiers. Taken all together, it is evident that there can be no universal solution to COVID-19 since the aetiology governing the disease is multiplex and complex. However, global health organizations have to appreciate the existence of these entities if effective and long term health plan is their plan.

O 10

CONTROLLED MAGNETIC NANOPARTICLES HYPERTHERMIA INHIBITS TUMOR PROGRESSION DEPENDING ON THE TEMPERATURE

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Controlled magnetic hyperthermia (MHT) is a promising approach for antitumor therapy. However, the optimal heating temperature for MHT – 43°C or above 50°C – is still under debate. Here, we first present a comparative temperature-dependent analysis of the cobalt ferrite nanoparticles-mediated MHT effectiveness in two murine tumors models (4T1 (metastatic breast cancer) and CT26 (non-metastatic colon carcinoma)) *in vitro* and *in vivo*. The overall MHT killing capacity *in vitro* increases with the temperature and CT26 cells are more sensitive than 4T1 when heated to 43°C. Well in line with the *in vitro* data, such heating cures non-metastatic CT26 tumors *in vivo*, while only inhibiting metastatic 4T1 tumor growth without improving the overall survival. High-temperature MHT (>47°C) results in complete 4T1 primary tumor clearance, 25–40% long-term survival rates, and, importantly, more effective prevention of metastasis comparing to surgical extraction. Moreover, we demonstrate CT26 tumor rejection and decreased 4T1 tumor growth rate after rechallenge of tumor cells to mice cured by MHT. Thus, the temperature must be defined for each tumor type to ensure antitumor effectiveness of MHT. In addition, MHT is suggested to impact immune system, that makes it a perspective approach for tumors treatment in combination with immunotherapy and should be studied further.

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O 11

NUTRIONAL ASPECTS RELATED TO COVID-19

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Inflammation constitutes one of the main biochemical lesions found at the root of several pathological processes (cardio-vascular disease, obesity, type II diabetes mellitus, neurodegeneration, etc). Diets rich in lipids and refined sugars promote metabolic impairments associated with inflammation and decrease the ability of the immune system to react to pathogen exposure.
Nutritional research shows that there are some types of diets able to mitigate inflammation (carbohydrate–restricted diets/ low glycaemic index food, ketogenic diet, high-fiber diets, Mediteaneean diet/Nordic diet, etc). The anti-inflammatory benefits of these diets are generated by specific components such as omega 3 fatty acids or polyphenols.
COVID 19 is associated with a severe inflammatory response of the body; according to clinical assessment, patients with previous low grade inflammatory pathology (obesity,. type II diabetes) are at high risk of severe pathological response to SARS-Cov2 exposure.
So, it is of extreme importance to evaluate the ability of certain dietary components to improve the immune response and to reduce the risk of severe pathology associated with COVID 19. There are some promising reports regarding the potential benefits of proteins, vitamin D and zinc, but the large scientific data is still missing and needs to be evaluated in the on-going pandemic.

O 12

INFLUENCE OF GLYCOSAMINOGLYCANS ON ANGIOGENESIS

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Angiogenesis is a process of new blood vessels formation, which takes place both in healthy and pathological states. Tumor growth is usually accompanied with the construction of capillar and vessel net necessary for the transport of oxygen and nutrients. Last decades inhibition of angiogenesis is considered as one of the approaches in cancer therapy and the development of effective drugs with anti-angiogenic effect is still demanded. In this communication we report the results of the study of several glycosaminoglycans (GAGs) as inhibitors of blood vessels formation. The studied compounds included GAGs presented in mammalia such as chondroitin sulfates, hyaluronic acid, heparinoids, as well as unusual GAGs from echinoderms fucosylated chondroitin sulfates. Related synthetic oligosaccharides differed in length of chain and pattern of sulfation were studied as well. The ability of the poly- and oligosaccharides to influence angiogenesis was assesed *in vitro* using endothelial cells and matrigel as a medium. It was shown that the biological effect depended on the type of GAG, length of chain and pattern of sulfation. The suggested mechanism of action is connected with the ability of GAGs to bind to growth factors bFGF and VEGF which are essential to angiogenesis development.
The work was supported by Russian Scientific Foundation (Grant 19-73-20240).

013

BIOMEDICAL MATERIALS BASED ON NITROGEN-CONTAINING ELECTRICALLY CONDUCTIVE POLYMERS

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The recent advances in the synthesis and application of polyaniline, polypyrrole and polydopamine in medicine and biology are reviewed. The interrelation of the structural features of nitrogen-containing polyconjugated systems with their biocompatibility and functional properties was found. New possibilities for the synthesis of stimulus-sensitive hydrogels using immobilized dopamine fragments as active groups providing cross-linking are described. New approaches have been developed for the processing of polyaniline and polypyrrole into medical materials by carrying out reactions of their synthesis on the surface or in the bulk of the reaction system in the presence of stabilizers. It has been shown that nitrogen-containing polyconjugated systems can be promising as carriers of drugs, as well as for ensuring hemocompatibility. Some aspects of the toxic effect of polyaniline and its derivatives are analyzed.

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014

HIDDEN HUNGER AND METABOLIC LINKS IN COVID-19

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Coronavirus disease 2019 (COVID-19) pandemic is rapidly evolving and attention has been given to understand the factors that facilitate infection. Clinical data have shown that type 2 diabetes, hypertension, obesity and metabolic syndrome are central risk factors for COVID-19 morbidity and disease progression. Collectively, these complications are characterized by metabolic dysfunction proposing that management of the metabolic factors could benefit COVID-19 patients or people at risk. The metabolic network and the immune system are two closely related systems. Metabolic dysfunction predisposes to a non-effective immune response failing to combat SARS-CoV2 infection which rather causes organ damage and severe pathology. In addition, virus infection has been proposed to affect metabolic factors aggravating the metabolic dysfunction and related complications of the host leading to a vicious cycle of health deterioration and poor outcome. Nutrient deficiency or hidden hunger is a key factor leading to metabolic dysfunction as a result of modern lifestyle and dietary habits. Diet has been reported to be the primary cause of non-communicable diseases related deaths worldwide due to the central role of nutrients on the immune system function. During COVID-19 outbreak, limited access to nutrient dense food and sedentary life has contributed to the deterioration of metabolic health and the immune system. Conclusively, COVID-19 pandemic clinical data highlight the importance of monitoring the metabolic health of patients and non-patients and provide personalized solutions to address the risk factors of COVID-19 and other infectious or chronic diseases.

P 01

MOLECULAR PHYSIOLOGY OF VISION: SUPRAMOLECULAR ORGANIZATION OF RODOPSIN IN THE PHOTORECEPTOR MEMBRANE

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The traditional idea of the vertebrates phototransduction mechanism is based on the free movement in the liquid (viscosity of about 2 poise) photoreceptor membrane of both rhodopsin itself and the proteins of the enzymatic amplification cascade. Absorption of only one photon (twilight vision) is sufficient for the appearance of a photoreceptor signal in a retina rod cell. In this case, the first step in the phototransduction mechanism is the activation of about 200 transducin (G-protein) molecules by one rhodopsin molecule. Rhodopsin in monomeric form is able to interact and activate not only transducin, but also other proteins of the photoreceptor cascade [1]. At the same time, in recent years a whole series of studies has appeared, carried out mainly by atomic force and cryo-electron microscopy, according to which rhodopsin in the photoreceptor membrane is in dimeric or oligomeric form, moreover, it is able to form a paracrystalline structure. Summarizing these works, four hierarchical levels of the oligomeric organization of rhodopsin in the photoreceptor membrane can be distinguished: a) a dimer, b) a series formed by about ten dimers, c) two such rows forming a strip and, finally, d) several parallel arranged bands. On the one hand, the oligomerization of rhodopsin is incompatible with the concept of free diffusion of rhodopsin in the photoreceptor membrane. On the other hand, a number of papers discuss the advantages of the paracrystalline organization of rhodopsin for the implementation of the phototransduction process. The data obtained to date, including ours [2], indicates that rhodopsin molecules can be in the photoreceptor membrane in equilibrium monomeric and dimeric forms. The ratio of these forms may depend on a number of factors. As the results of our small-angle neutron and small-angle x-ray studies show, the rhodopsin molecules in the photoreceptor membrane are diffusely arranged with an extremely high density and without any regular packing [2]. It can be assumed that rhodopsin oligomers do not participate in the phototransduction process and that rhodopsin oligomerization regulated by light is one of the physiological mechanisms of photoreceptor cell adaptation to changing lighting conditions [3]. Evidence in favor of this assumption is recent x-ray structural data, according to which rhodopsin dimerization inhibits the conformational rearrangements of the protein part of the molecule at the stage of metarodopsin II formation, namely, it suppresses these rearrangements in transmembrane alpha-helical strands that are key to rhodopsin activation [4].

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P 02

COMPLEXES OF ANTIBODIES AND APTAMERS WITH NANOPARTICLES: PROPERTIES AND ANALYTICAL APPLICATION

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The intense use of nanoparticles as carriers and markers for receptor molecules, components of various bioanalytical systems, leads to interest in the properties of complexes that are obtained under different immobilization conditions and at different receptor: nanoparticle ratios. To correctly measure the composition of the nanoparticle - antibody complexes and assess their antigen-binding capacity, we have proposed methods based on recording the fluorescence of tryptophan residues and taking into account the factors that affect the intensity of the exciting and emitted light in different media. These methods were used to study immobilization of antibodies on the surface of different types of gold nanoparticles (commonly used quasi-spherical nanoparticles obtained by citrate reduction, strictly uniformed superspherical nanoparticles obtained by two-stage synthesis, nanoparticles with a highly branched surface ("nanoflowers")), naked and polymer-coated magnetite particles, fluorescent semiconductor nanoparticles (quantum dots). Concentration dependences of the antibody-binding processes were determined for different conditions of the immobilization. Changes in the affinity of interactions with varying surface density of bound antibodies were shown; conditions of monolayer and multilayer immobilization were identified. A similar characteristic was carried out for complexes of aptamers with gold nanoparticles. Antigen-binding capacities for the rows of the obtained preparations were considered. It was shown that traditional adsorptive monolayer immobilization is accompanied by inactivation of up to 75% of antibodies. Possibilities of indirect immobilization of antibodies through their interaction with various immunoglobulin-binding reagents were characterized. The effect of the composition of receptor-nanoparticle complexes on the detection limits in analytical systems (primarily in immunochromatographic analysis) with their use was studied. The experimental dependences were compared with the predictions of the developed theoretical models of analytical processes. The differences in the requirements for the complexes used for one-site competitive and two-site non-competitive assays were shown. The established regularities were used to develop highly sensitive test systems for the detection of antibiotics, mycotoxins, cardiomarkers and inflammatory markers.
The work was supported by the Russian Science Foundation (Project 19-14-00370).

P03

BIODEGRABLE FILMS ON THE BASE OF POLYLACTIDE - POLY(3-HYDROXYBUTYRATE-CHITOSAN AND THEIR SORPTION CAPACITY

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The films from polylactide (PLA), poly(3-hydroxybutyrate), which are thermoplastic polyesters originated from the nature raw and chitosan, obtained from nature polysaccharide chitin, have been obtained from chloroform solution. These polymers present an alternative to the polymers, which are synthesized from crude oil, are of constantly growing interest. The increasing cost of oil barrel and the gradual exhaustion of oil resources make these polymers competitive relative to large-tonnage synthetic polymers.
Using the DSC method, it was established that the initial polyesters are immiscible polymers. The degrees of crystallinity and melting enthalpies of the polymers in the individual state and in blends have been calculated. It has been shown that the mechanical properties of compositions depend on the presence of poly(ethylene glycol) plasticizers of different molecular masses. The experiments on the action of mold fungi on the films have observed that poly(3-hydroxybutyrate) is a fully biodegradable polymer unlike polylactide, whereas the biodegradability of the obtained compositions is determined by their composition. and sorption activity The sorption of films of poly(3-hydroxybutyrate)-polylactide-chitosan relative to ions of Fe^{3+} and Cr^{2+} has been studied and the possibility of their use as absorbents in wastewater treatment from these metals has been demonstrated.
This work was supported by the Russian Foundation for Basic Research, grant No 18-29-05017.

P 04

NEW COMPOSITES BASED ON LOW-DENSITY POLYETHYLENE, POLYLACTIDE AND REDUCED GRAPHENE OXIDE

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Physical and chemical modification of polymers by mixing them with various fillers allows one to obtain new composite materials with improved mechanical, thermal and other characteristics. In present research the composites of low-density polyethylene (LDPE) and polylactide (PLA) with reduced graphene oxide (rOG) were obtained in solid state under conditions of shear deformation on the different types of equipment (Brabender mixer, extruder) and their mechanical and thermophysical properties were investigated.

Reduced graphene oxide was obtained by oxidation of graphite according to Hammers method. The concentration of rOG in these mixtures varied from 0.05 to 0.25 wt.%. The thermophysical properties of composites were studied by the DSC method. It was shown that the temperature of cold crystallization of PLA growths monotonously with increasing concentration of rOG in mixtures. At the same time, the value of the heat of cold crystallization of PLA reduces with increasing of filler concentration, that indicates a decrease of the segmental mobility of PLA macromolecules in the presence of rOG. It was found that an increase of the filler concentration in the mixture leads to reduce the degree of crystallinity of the PLA in the composites. At the same time, no changes in thermal transitions in the compositions of LDPE-rOG were observed, that indicates different mechanisms of interaction between rOG with PLA and LDPE. The mechanical parameters of these two compositions also changed in a various way. Thus, for LDPE-rOG composites the modulus of elasticity, strength and elongation at break were slightly reduced with adding rOG to the mixtures. At the same time, for composites PLA-rOG the increase of the filler concentration leads to an insignificant growth in the corresponding characteristics.

Thus, the properties of the obtained composite materials depend both on the nature of the polymer, the amount of introduced rOG and on the type of mixer used. By varying these parameters, composites with the desired properties can be obtained.

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P 05

ENVIRONMENTAL-FRIENDLY NANOPOLYMERS FOR AGRICULTURE

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Scientific research in the field of nanopolymers carried out for more than 10 years makes it possible to formulate the ways of synthesis, to identify the factors influencing the formation of the structure of nanopolymers, as well as the field of application of nanopolymers in agriculture. It is shown that the synthesis of environmental-friendly nanopolymers depends on a number of factors: pH of environment, duration and reaction temperature.

For the first time on the basis of chitosan isolated from silkworm pupae, a waste of silk-winding production were synthesized such environmental-friendly nanopolymers as: nanochitosan, nanoascorbate chitosan, nanopolymermetal complexes and used as nanopesticide - agropreparates with complex action of a disinfectant with a stimulating effect. It is known from the scientific literature that environmental-friendly nanopolymers based on chitosan Bombyx mori have not previously been used as a growth regulator and plant protection agent. Agropreparates are being tested for the third year already, our products are low-toxic.

P 06

BIOLOGICALLY ACTIVE FILMS AND FIBERS BASED ON CHITOSAN CROSS-LINKED BY GENIPIN

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Chitosan is a promising environment friendly polymer packaging material due to its biodegradability exceptional film forming capacity, great mechanical strength, appropriate barrier property along with intrinsic antioxidant and antimicrobial features [1, 2]. Films and fibers obtained from chitosan solutions are water-soluble. Bifunctional reagents are used to obtain insoluble chitosan-based films, fibers, and other materials with high rate of water swelling.

Crosslinking with genipin (Gp), which is a reagent of natural origin, improves swelling, water resistance and mechanical properties of the biopolymeric materials [3, 4]. It is shown that the properties, functional characteristics (swelling degree, biodegradation rate) and porous morphology of the obtained materials depend on the ratio of functional groups in the chitosan acetate– Gp system. Cross-linking of the chitosan by a bifunctional reagent in the solution fixes the mutual location of polymer chains, not allowing them to take equilibrium conformations during solvent evaporation, which leads to a deterioration in the physical and mechanical properties of the resulting films and fibers. Only at a very low content of the cross-linking reagent (0.0025 mol/mol), at which there is no gel formation in the molding solution, fixation of macromolecular chains occurs in the position where intermolecular interactions are realized to the greatest extent, which, in its turn, leads to a significant increase in the strength of chitosan materials. The results of research into the properties of chitosan films with significantly different Gp contents can be used to determine the direction of programming of cross-linked biopolymer films and fibers properties for food packaging, edible coatings or for medical use to increase strength and regulate moisture absorption. Biologically active films based on chitosan cross-linked by Gp have been used as a biocompatible therapeutic system for the controlled delivery of an anesthetic agent. The features of the mechanism of release of lidocaine from cross-linked chitosan films have been established.

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P 07

DETECTION OF ANTIBIOTICS AND MYCOTOXINS BY CHEMILUMISCENCE ENZYME-LINKED IMMUNOSORBENT ASSAY (CL-ELISA)

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The immunochemical methods based on the specific and high affinity antibodies are widely used for high-throughput screening (HTS) and monitoring of food contaminants. At first it is important for detection of poisons and toxic organic chemicals like pesticides, antibiotics, mycotoxins and others. The Enzyme-Linked Immunosorbent Assay (ELISA) is one of widely used immunoassays. The ELISA could be optimized with photometric and chemiluminescent detection. The method was optimized for full automatic analyzer. The experimental ELISA kits for antibiotics and mycotoxins were produced by "XEMA" (Russia) and were used as simple, quick, preliminary test for detection toxic compounds in food sample.

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P 08

LIQUID POLYMER SUBSTANSES IN SURGERY

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Currently, in treatment of congenital diseases of blood vessels (arteriovenous malformations, hereinafter referred to as AVM), the embolization procedure has become very popular. The embolization procedure is a method for minimally invasive treatment as intentional blockage (occlusion) of one or more blood vessels. This embolization technique is being used also for other pathologies such as vascular aneurysms, uterine fibroids, hypervascular tumors, injuries with severe bleeding, as well as with the aim of preoperative preparation of the patient for surgery to reduce blood loss. The goal of embolization at AVM is to completely fill the pathology centre, while undesirable reflux in the arteries supplying healthy tissues should be minimized and premature embolization of the draining veins should be avoided.Fragments of muscle tissue, adipose tissue or the meninges, hemostatic sponges and stainless steel pellets were among the first materials that served to clog up the vessels. Currently, a wide variety of embolic agents including microspheres of various compositions, cylinders, occluders, embolic spirals based onsynthetic polymers are available for clinical practice in vascular surgery. From our point of view the most interesting embolic agent is the liquid embolic system – Onyx. It was established that the polymer embolus should be well wetted by the blood components, and its surface energy is slightly lower than the surface energy of multipotent mesenchymal stromal cells' culture (MSCs), which are close in nature to the blood vessels' walls' cells. There is an opinion that MSCs are similar to pericytes. Pericytes are comprised into the walls of blood vessels. The predecessors of pericytes are adventitious cells, that are poorly differentiated fibroblast cells in the blood vessels. The results obtained by testing the polymer embolus in MSCs culture, allowed us to assume the presence of sufficient level of adhesion of the developed composition to the vessel walls.

P 09

THE MAIN RESEARCH DIRECTIONS IN THE FIELD OF VOLATILE RADIONUCLIDES CONTROL

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During the operation of nuclear power plants (NPPs), fission products from fuel elements enter the primary circuit of the reactor, and than are distributed through the working premises. The main gas radioactive components at nuclear power plants are xenon and krypton isotopes, as well as radioiodine. One of the most important issues that needs to be addressed when organizing the purification of NPPs technological gas streams from radioiodine and inert gas isotopes is the assessment of the minimum required sorbent volume in order to provide the required degree of purification and thereby reliably and effectively protect the atmosphere and environment. This is also important from the standpoint of energy conservation, since the energy consumption associated with the operation of gas- purification equipment directly depends on their hydraulic resistance, i.e., on the sorbent layer height. To date, at the department of High-Energy Chemistry and Radioecology has developed an unified approach to assessing the sorption materials quality applied to gas streams purification from volatile radionuclides. In this regard, an extremely important stage is the development of certified laboratory facilities, on the basis of which tests of such sorbents will be carried out. Researchers at the department are working on a multifunctional facility for studying the behavior of volatile radionuclides. It is planned that it will simulate the actual operating conditions of sorbents in the NPPs gas purification systems in a wide temperature range, providing for both standard operation and probable emergency situations. The installation is supposed to study the properties of both iodine-selective sorbents and materials capable to trapping other gaseous radionuclides – inert gases, tritium and radiocarbon. An important factor is that students and graduate students are actively involved in the work on the development of a laboratory facility, as well as in the testing and development of new types of sorbents. Young researchers gain valuable experience when working on the most advanced equipment and certified devices.

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P 10

DRUG SHIELDING BY POLYMERIC NANOSCALED CARRIERS FOR INHIBITION OF NEUTROPHIL EXTRACELLULAR TRAPS FORMATION

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Formation of neutrophil extracellular traps (NETs), also known as NETosis, was first revealed as novel immune response to bacterial infections, but then was found to occur abnormally during other different inflammatory diseases including cancer. At the same time venous thromboembolism is a frequent complication occurring in patients, suffering from neoplastic diseases. Since NETs play an important role both in the development of the tumor growth process and in inducing complications such as thrombosis, indubitably the investigation of the effect of anti-tumor drugs on the formation of neutrophil extracellular traps and on the ability of such drugs to prevent NETs contribution on carcinogenesis is of great interest.
In the present work we studied the effect of 5-fluorouracil (5FU) and its shielded by amphiphilic poly-N-vinylpyrrolidone (Amph-PVP) nanoparticles polymeric form on the activation of human neutrophils under ex vivo conditions. Free 5FU at concentrations varying from 0.01 to 10 mg/ml was found to cause a signifcant (two to three times) and rapid (after 20 min) increase in the total amount of NETs in the blood. Importantly, when 5FU-loaded Amph-PVP nanoparticles were studied under the same conditions, the appearance of NETs in the blood was completely blocked providing strong evidence of their potential as delivery system for 5FU in antitumor therapy.
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P11

INFLUENCE OF NEW CONSTRUCTION PRODUCTS ON THE AIR ENVIRONMENT

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The main global trends in the development of the building materials industry in recent years have become:
- transition to a new level of energy efficiency of production;
- reducing the negative impact on the environment;
- involvement of waste in the production of building materials.

The main requirements for building materials include, among other things, environmental safety for humans and animals.
We have carried out a study of the obtained samples of new construction products for the release of harmful substances into the air. Building composite materials are obtained on the basis of a polymer matrix and mineral filler. Fly ash from thermal power plants, mineral calcium and silicon-containing dust, as well as mica waste were used as a filler.
The compliance of the emission of harmful substances into the air of new construction products with the requirements of regulatory documents was determined.
The cumulative emission of chemicals into the indoor air, taking into account the joint use of building materials used in a capital construction facility was investigated.
The test results showed that the content of dibutylphthalate is not more than 0,005 mg/m^3 with an acceptable level of not more than 0,1; dioctylphthalate, respectively, 0,01 mg/m^3, if required no more than 0,02; methylmethacrylate less than 0,01 (if required no more than 0,01); styrene 0,002 (if required no more than 0,002); formaldehyde 0,01 (if required no more than 0,01). Tests of samples for the migration of harmful chemicals into the air were carried out under simulated conditions in a climatic chamber: material saturation 1,0 m^2; the air exchange rate is 1,0.
The research results show that the concentration of substances released into the atmospheric air from new construction products does not exceed the maximum permissible concentration. Consequently, the materials can be used in the national economy.
Based on the results of the studies and the above-mentioned hygienic characteristics, an expert opinion was received on the compliance with regulatory documents of the results of laboratory studies, tests, measurements for the entire line of new building materials.

P 12

NEW CONTACT DEVICES FOR CHEMICAL ISOTOPE EXCHANGE IN THE WATER-HYDROGEN SYSTEM

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The separation of hydrogen isotopes by the isotope exchange method between hydrogen and liquid water is traditionally carried out in vertical countercurrent columns with the hydrophobic catalyst and the hydrophilic packed bed. Due to the hydrophobic properties of the catalyst, the speed of hydrogen saturated with water vapor in them usually does not exceed 0.3 m/s, which limits the scale of production, and the need for vertical arrangement of column, requires significant heights of production facilities.

At the D. Mendeleev University of Chemical Technology of Russia was developed an alternative membrane contact device (MCD) in which the vapor-gas stream passing through the catalyst is separated from the liquid water stream by means of a membrane. The process takes place in two stages - the isotopic exchange between hydrogen and water vapor takes place in the MCD filled with the catalyst, and the isotopic exchange between liquid water and its vapor passes on the surface of the membrane.

The report presents various membrane contact devices with a Nafion-type membrane containing water clusters, but not permeable to liquid water and the results of laboratory tests of membrane contact devices in the temperature range 333–358 K at a pressure of 0.1–0.3 MPa and steam and hydrogen flow velocities of 0.15–2.0 m/s. A multi-stage laboratory bench with MCD shows the possibility of creating compact countercurrent separation units that do not require a vertical arrangement.

The study was conducted with financial support from the Ministry of Science and Higher Education of the Russian Federation as part of FSSM-2020-0004 state project.

P 13

FRACTIONATION OF HYDROGEN ISOTOPES BETWEEN HYDRATED AND FREE WATER MOLECULES IN AN AQUEOUS SOLUTION OF METAL SALTS

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Tritium is one of the most significant biologically radionuclides. It's a heavy isotope of hydrogen and it can be part of many organic compounds, including biologically important ones. Its radioactive ß-decay leads to destruction of molecular structures and intermolecular bonds under the influence of inner ß- decay, as a result of the conversion of tritium into the helium-3. The main source of tritium in the environment is the nuclear industry, in particular, nuclear reactors and Nuclear fuel reprocessing plants. Currently, dump tritium water streams are diluted and poured into the ocean. Therefore, it is necessary to conduct research in the field of methods for handling large amounts of radioactive waste containing tritium. A promising method is rectification using various extractants, i.e. the so-called "salt" rectification. For the effective use of this method, it is necessary to determine the separation coefficients in the system which the separation of heavy hydrogen isotopes will occur. The most modern and accurate theoretical method for determining the separation coefficients at the moment is the methods of quantum chemistry and static thermodynamics. In this paper, we studied the contribution of individual cations and anions of metal salts. The cations and anions of the most common elements, namely potassium, sodium, lithium, zinc and nickel cations, were chosen as objects of study. Among the anions, nitrate, acetate, chloride, and carbonate were calculated. The calculated equilibrium constants for the tritium exchange reactions between water molecules and ions are in the range from ~ 1.21 to ~ 1.46 (i.e.,> 1 in the studied temperature range). There is an increase in the separation coefficient in the series of cations K +> Na +> Li +; Zn2 +> Ni2 +, anions NO3 -> CH3COO-> Cl-> CO3 -. The enhancement of the thermodynamic isotope effect when metal salts are added to water can be used to purify tritium-contaminated aqueous media from aqueous process streams by the salt rectification method.

P 14

COMLEXATION OF METALS Ga^{3+}, Gd^{3+}, Tb^{3+}, La^{3+} NATURAL ISOTOPIC COMPOSITION WITH ORGANOTROPIC CONJUGATES TO PROSTATIC SPECIFIC MEMBRANE ANTIGEN

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One of the most common malignancies in men is prostate cancer, which is often associated with higher levels of prostate-specific antigen (PSA) in serum. Initial diagnosis and screening of prostate cancer are usually performed by determining the level of PSA in the serum. A more accurate diagnosis can be achieved by using positron emission tomography (PET) using radiopharmaceuticals (RFP). To develop new and effective anti-PSMA-specific conjugates was investigated by different radiopharmaceuticals, some of which showed great potential not only in preclinical studies but also in clinical practice [1,2]. The approach, which uses radioactively labeled molecules with a low molecular weight, aimed at the enzymatic activity of PSMA, increasing interest in clinical practice [2,3]. The typical radionuclides for PET diagnostics are the gallium-68 and gadolinium-64 for an MRI and for therapy of Tb-149, Ac-225. In this paper, the authors used the metal of natural isotopic composition, identical in their chemical properties, the corresponding beta and alpha emitters, which is much cheaper and safer. The aim of this work was to study the thermodynamic stability of the complexes of analogs of PSMA-conjugate PSMA-617 with gallium, gadolinium, terbium ions and lanthanum-analog of actinides, as component models for theranostics radiopharmaceuticals. Complexes of Ga^{3+}, Gd^{3+}, Tb^{3+} and La^{3+} have to meet certain basic conditions, namely to be thermodynamically stable at physiological pH values and/or kinetically stable during the period corresponding to the time of the medical examination [4].To further develop effective radiopharmaceuticals Ga-68, Gd-64, Tb-149, Ac-225 for PET, MRI and therapy accordingly, an important task is the determination of the equilibrium constants of the complexes of gallium(III), gadolinium (III), terbium (III) and lanthanum (III) conjugates of PSMA, for which the equilibrium constants of the studied complexes with analogs of conjugate PSMA-617 based on the chelator DOTA, was investigated by HPLC. The obtained equilibrium constants of complexation reactions with metals of natural isotopic composition based on PSMA conjugates showed a difference associated with the unequal solvation of both the initial conjugates and the resulting coordination compounds.

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P 15

COMPARISON OF VARIOUS SYNTHETIC CARRIERS AS COMPONENTS OF OSTEOPLASTIC MATERIALS FOR RECONSTRUCTIVE SURGERY WITH THE ADDITION OF BMP-2 AND ERYTHROPOIETIN

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The golden standard among materials used in bone surgery is an autologous bone that has high osteoinductive properties and safety of use. Its use is associated with a number of disadvantages associated with a limited amount of material and additional trauma to the patient. A promising solution to this problem is the development of new materials that have osteoinductive properties due to the presence of biologically active components. Choosing a safe carrier that provides a prolonged effect of bone growth stimulants is an urgent task of modern traumatology and orthopedics. The synthetic materials possessing the required properties are, in particular, non-resorbable ultrahigh-molecular weight polyethylene (UHMWPE) and polyetheretherketone (PEEK), as well as resorbable polylactide (PLA).

We used porous variants of UHMWPE, PEEK and PLA activated by hydroxylapatite (HA) introduced into their structure in combination with recombinant BMP-2, erythropoietin (EPO) or both proteins to study osteogenicity in the model of cranial critical-sized defects (CSD) regeneration in mice.

The recombinant proteins used were BMP-2 and EPO with additional protein domains providing improvement of solubility and ability to self-induced binding to the carrier. Both recombinant proteins are capable to spontaneous sorption on hydroxyapatite (HA).

The study was carried out on 100 outbred male ICR (CD-1) mice of 38-47 days old. Animals were distributed into 10 groups, 10 mice per group. UHMWPE/HA, PEEK/HA and PLA/HA disks of 1.0 (thickness) x 4.0 (diameter) mm with/without bound proteins were sterilized and implanted into 4 mm CSD of mice. In group 1 (control) CSD were empty; in groups 2, 3, 4 CSD were filled with the UHMWPE/HA, PEEK/HA and PLA/HA disks (respectively); in groups 5, 6, 7 CSD were filled with disks containing BMP-2; in groups 8, 9, 10 CSD were filled with disks containing both BMP-2 and EPO. Tomography was carried out on 0, 3 and 6 weeks post-surgery; euthanasia and histomorphometry were performed on 42 day after surgery. According to the results of tomography and histological analysis all implanted biocomposites demonstrated high biocompatibility. The addition of rhBMP-2 to different scaffolds resulted in significant osteogenic effect and formation of large mineralization areas within 3 weeks after surgery. The lowest volume of new bone tissue was demonstrated in the group with PEEK/HA possibly due to the difficulty of sprouting blood vessels inside the implant. The effect of erythropoietin addition is maximal in the case of PLA/HA possibly due to the resorbable properties of the carrier.

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NEW RESORBABLE OSTEOPLASTIC MATERIALS FOR RECONSTRUCTIVE SURGERY BASED ON POLYLACTIDE

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Polylactide (PLA) is a well-characterized bioresorbable polymer. However, for improvement of fusion with bone tissue, the possibility of joint use with protein factors possessing osteogenic properties is relevant. The task of protein factors' introducing into polymeric synthetic materials is not easy and requires special technological solutions such as introducing nanoparticles of hydroxyapatite (HA, the main mineral component of bone) into their composition.

Polylactide (molecular weight of 110 kg / mol; Ingeo 4032D by Natureworks LLC) in pellet form was used as the main material for the preparation of porous scaffold. Hydroxyapatite (HA needle particles 90 nm in size, Polistom, Moscow) was used as a component that increases the bioactivity of implants. The evaporated salt was used as a pore-forming agent. Solvent casting and salt leaching method was utilized for the preparation of polylactide/HA scaffolds. The resulted porosity was 74%vol. Scanning electron microscopy study of the microstructure of the obtained samples showed the presence of a system of open pores with a size of 300–400 μm and a thickness of the pore wall of 1–2 μm.

The recombinant proteins used were rhBMP-2 and erythropoietin proteins with additional protein domains providing improvement of solubility and ability to self-induced binding to the carrier.

The study was carried out on 50 outbred male ICR (CD-1) mice of 38-47 days old. Animals were distributed into 5 groups, 10 mice per group. PLA/HA disks of 1.0 (thickness) x 4.0 (diameter) mm with/without bound proteins were sterilized and implanted into 4 mm CSD of mice. In group 1 (control) CSD were empty; in group 2 CSD were filled with the PLA/HA disks; in group 3 CSD were filled with PLA/HA disks containing erythropoietin; in group 4 CSD were filled with PLA/HA disks containing rhBMP-2; in group 5 CSD were filled with PLA/HA disks containing both rhBMP-2 and erythropoietin. Tomography was carried out on 0, 3 and 6 weeks post-surgery; eutanasia and histomorphometry were performed on 42 day after surgery. All implanted materials demonstrated good biocompatibility and no inflammatory reactions. The largest volume of newly formed bone, as well as an increase in the density and size of blood vessels, was observed in the group using both factors.

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PURIFICATION OF CONTAMINATED WITH ETOXICANTS WASTEWATER OF OIL INDUSTRY ENTERPRISES

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The industrial wastewater of the oil industry enterprises contains heavy metal ions, contaminated with oil and oil products. Purification of contaminated water is one of the main environmental problems. The sorbtion method of wastewater treatment is the most promising.

The aim of the work is to improve the quality of wastewater treatment to the standards necessary for re-use in technological processes applying aluminum alloys activated by activating metals (AAA). Alloys of Wood, Rose and Darce were first tested as an activating additives. The interaction of AAA with water is accompanied by heat release, as well as the release of active hydrogen and solid products - aluminum hydroxides. The efficiency of

wastewater treatment with AAA was studied on two types of contaminated water: sedimentary produced water of the Karazhanbas "Severniy" oilfield (SPW) and water after the destruction of oil sludge emulsion from ponds of additional sludge (PAS) of "ANPZ" LLP into water, oil phases and solid residue.
The physicochemical analysis show that SPW has the following characteristics: pH 7,3, density of water 1,04 g/cm^3, conductivity 72,0 mS/cm, total salt content 6338 mg/l. After processing the water with an AAA, the content of ions (ppm) decreases: Ca^{2+} from 1745 to 64,5, Mg^{2+} from 833,4 to 9,48, Fe from 0,0065 to 0,0011 (spectrometer ICIP-7400). Oil content decreases from 6.8 mg/l to trace concentration, the NTU turbidity from 128 to 1-2.
PAS wastewater is less mineralized (total salt content 2100 mg/l), density of water 1,022 g/cm^3, pH 8,34, conductivity 3,19 mS/cm, oil content 404 mg/l. After treatment with an AAA (consumption 70 mg/l), the content of ions (ppm) decreases: Ca^{2+} from 44,1 to 12,1, Mg^{2+} from 15,4 to 1,75, Fe from 1,56 to 0,008, oil content from 404 mg/l to 17,5 mg/l.
The highest degree of water purification is achieved in high pH environments at 70-90°C and 10 mass% of activating additive in the alloy.
The possibility of using AAA for the destruction of oil sludge with the simultaneous treatment of sedimentary wastewater is shown. Purified water meets the requirements for the quality of injected water into the well to maintain reservoir pressure and use in the circulating water supply system for oil production.

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ABOUT THE POSSIBILITY REACTION ZONE LOCALIZATION OF AROMATIC AMINES OXIDATIVE POLYMERIZATION

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The application of polyconjugated systems on substrates of dielectrics is possible only as a result of chemical aromatic amines oxidative polymerization, that determines the main difficulties in controlling the morphology of the applied coating and its heterogeneity in thickness. In the case of using conductors and semiconductors as substrates, these difficulties are partially eliminated by the possibility of applying a layer of a polyconjugate system by electrochemical oxidative polymerization. In the electrochemical oxidative polymerization of aromatic amines, the reaction zone is known to be localized near the surface of the electrode. The localization of the reaction zone in the vicinity of the surface of the dielectric substrate is difficult, but necessary to minimize the number of coating defects. Carrying out chemical oxidative polymerization of aromatic amines in the presence of substrates, precipitation of polyconjugated systems is observed on their surface, which are formed both as a result of a reaction at the interface, and as a result of the polymer deposition formed in the volume of the reaction system. In this work, we propose a method for conducting chemical oxidative polymerization of aromatic amines, which ensures the localization of the reaction zone at the surface of the substrate. Localization of the reaction zone is achieved by applying an insoluble in the reaction medium oxidizing agent to the surface of the substrate. This approach allows us to exclude the occurrence of the reaction in the volume of the reaction system, to achieve control of morphology and minimize the number of coating defects. It was shown that in this case, the oxidative polymerization of aromatic amines proceeds at the phase boundary, and the reaction rate is limited by the diffusion of the monomer from the bulk of the solution to the surface of the substrate. The developed coating method may be of interest for the manufacture of sensors, systems with controlled release of biologically active substances and substrates for the growth of nerve tissue under electrical stimulation.
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THE USE OF INNOVATIVE MECHANISMS OF IMPROVEMENT OF QUALITY OF MATERIOLOGICAL EXPERT PRODUCTION

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One of the ways to improve the efficiency of conducting forensic expertise is considered to be the use of validation mechanisms of methodological materials, including procedures such as sampling and sample preparation. In the Physical and Technical Examinations and Chemical Expertises Department of the National Bureau of Expertises of the Republic of Armenia (hereinafter referred to as the Bureau), when conducting expert studies, it becomes necessary to determine the belonging of the object submitted for expertise to narcotic or psychotropic, highly active or toxic substances. Considering the importance and practical nature of this issue, as well as the obligation of conducting the mentioned expertise in accordance with the requirements of the international standard ISO / IEC 17025:2017, over the past three years validated methods of quantitative calculation and assessment of measurement uncertainty based on the active ingredient for drugs from the current list of the most popular drugs of high demand in Armenia have been developed in the Bureau and implemented in forensic practice.

In this case, the algorithm for calculating the assessment of the measurement uncertainty was based on quantitative determinations prepared by the fractional addition of methanol to pre-concentrated standard solutions of active components of narcotic and psychotropic substances in concentrations from 0.5 to 8 mg in 1 ml of methanol. Using the retention time obtained in the course of experimental studies, processing of the constructed calibration dependences and the calculated values of the peak areas, the values of the coefficients "k" and "s" were calculated, which were subsequently used to determine the values of the measurement uncertainty for delta-9-tetrahydrocannabinol, codeine, methamphine, diazepam, lorazepam, buprenorphine, methadone and tramadol. We should also note that validation of the developed methods was carried out in accordance with the following parameters: "Specificity", "Linearity", "Accuracy", "Repeatability" and "Intermediate precision".

Thus, at present in the Bureau quantitative calculations for the determination of the abovementioned active components in the composition of the examined narcotic objects submitted for expertise are carried out on the basis of validated methods, which provide more trustworthy and reliable results when conducting materiological and gas chromatographic analyzes.

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BIOPHARMACEUTICAL ANALYSIS OF THE DOXORUBICIN-LOADED PLGA NANOPARTICLES WITH DIFFERENT RELEASE PROFILES OF DOXORUBICIN

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Ddevelopment of the drug delivery systems based on biodegradable PLGA nanoparticles (NPs) is a promising area of pharmaceutical technology. At the same time, the influence of the physicochemical parameters of PLGA NPs for IV administration on the *in vitro* release profile and *in vivo* PK has not been thoroughly elucidated. In accordance with the FDA recommendations, the pharmacokinetic study (PK) of the drug products that contain nanomaterials requires determination of not only the total drug concentration in plasma (free and bound to the carrier), but also the concentration of these fractions separately.

The objective of the present study was to perform a pharmacokinetic study of doxorubicin-loaded PLGA NPs (Dox-PLGA NPs) modified with poloxamer 188 (P 188) with different drug release rates in comparison with the drug substance.

The PLGA-Dox NPs were obtained using a double emulsion technique. A 1% solution of polyvinyl alcohol in phosphate buffer at pH 7.4 (PLGA-Dox/7.4) or 6.4 (PLGA-Dox/6.4) was used as the external aqueous phase. The kinetics of doxorubicin release from the NPs ***in vitro*** was determined by ultracentrifugation in a 1% solution of P 188. Doxorubicin formulations were injected IV to healthy Wistar rats at a dose of 5 mg/kg. The main PK parameters were calculated for both free and total doxorubicin using the non-compartment model.
Compared to the PLGA-Dox/7.4 NPs (average size 114 nm), the PLGA-Dox/6.4 NPs (average size 142 nm) were characterized by a lower encapsulation efficiency (79% and 92%, respectively) and a higher ***in vitro*** doxorubicin release rate. Binding of doxorubicin to the NPs significantly increased the concentration of total doxorubicin in plasma during the first minutes after administration and prolonged the drug circulation time, reduced the drug stationary distribution volume and clearance (Cl_{total}) and increased the AUC. The influence of the drug release rate on the plasma concentration profiles as well as the PK parameters was observed during the first hour post injection.
The study was funded by Russian Foundation of Basic Research (no. 20-015-00276).

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OPTIMIZATION OF THE METHOD FOR EVALUATION OF DOXORUBICIN RELEASE FROM PLGA NANOPARTICLES INTO MODEL MEDIA AND BLOOD PLASMA

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Establishment of the correlations between the kinetics of the drug release ***in vitro*** and its pharmacokinetics (PK) ***in vivo*** (IVIVC) for the drug-loaded nanoparticles is a complex problem that requires employment of the adequate methods for evaluation of the ***in vitro*** drug release from the nanoparticles. In this study, kinetics of the doxorubicin release from the doxorubicin-loaded nanoparticles based on copolymers of lactic and glycolic acids (Dox-PLGA) into model media and blood plasma was studied after the nanoparticles separation using the FDA-approved techniques such as ultracentrifugation and dialysis. Moreover, the approaches to the mathematical description of the release profiles were considered.
The Dox-PLGA nanoparticles were prepared by a double emulsion technique using Resomer® 502H (Evonik, Germany). 1% solutions of polyvinyl alcohol in phosphate buffer (PBS) at pH 7.4 (Dox-PLGA/7.4) or 6.4 (Dox-PLGA/6.4) were used as the external aqueous phase. Optimization of the ultracentrifugation method was carried out by varying the following parameters: receiving medium (water, 0.9% sodium chloride, PBS, HEPES buffer, 1% poloxamer 188, 1% polysorbate 80, blood plasma), dilution (1:5; 1:25), incubation temperature (+25 °C; +37 °C) and centrifugation mode (15000×g; 48254×g). The content of free doxorubicin in the plasma after separation of the nanoparticles was determined by HPLC, in other media – by UV spectrophotometry. Mathematical description and comparison of the release profiles of doxorubicin in different media was carried out using the different mathematical models (zero and first order, Higuchi, Hickson-Crowell, and Korsmeyer-Peppas models).
The average hydrodynamic size measured by dynamic light scattering of PLGA-Dox/7.4 and PLGA-Dox/6.4 nanoparticles were 114 nm (ζ-potential -9.5 mV) and 142 nm (ζ-potential -4.8 mV), respectively. The average size determined using transmission electron microscopy was 50±16 nm. It appeared that the Dox-PLGA nanoparticles obtained at different pH had distinct doxorubicin release profiles. Among the tested methods, the method using ultracentrifugation (48254×g, +4 °C) for the nanoparticles separation was best suited when using 1% poloxamer 188 as a receiving medium.
We suggest that thus optimized method for evaluation of the ***in vitro*** release profile is suitable for the establishment of IVIVC for the Dox-PLGA nanoparticles.
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P 22

PHYSICAL AND CHEMICAL METHODS FOR COLLAGEN GEL FIXATION

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Natural polymers gels are widely used in tissue engineering and regenerative medicine. One of the promising natural polymers that form a gel under certain conditions is the extracellular matrix protein type I collagen. Collagen is the main component of human connective tissue and it is often used for scaffold formation for cell cultivation and transplantation in the area of damage. Despite the high biocompatibility of this polymer, collagen gels have low mechanical characteristics and a high degradation rate. The purpose of this study was to develop methods for physical and chemical fixation of collagen gel. The effect of UV irradiation on the stability of the collagen gel was studied as a physical effect. It is shown that the properties of the gel are affected by UV radiation, as well as the concentration of collagen and the time of exposure. At a low concentration of collagen (0.5 mg/ml), irradiation for 30-120 minutes has a positive effect, reducing the degradation of collagen. When exposed to UV radiation on a collagen gel with a concentration of 2 mg/ml for 180 minutes, the gel stability decreases.
As a chemical cross-linking agent used is glutaraldehyde. The effect of the glutaraldehyde concentration, which has the ability to cross-link type I collagen molecules, on its stability, mechanical strength, and cytotoxicity was studied. It has been shown that under physiological conditions, collagen-containing 10 and 18% of glutaraldehyde has the highest stability. The results of the rheological analysis showed that at a minimum concentration of glutaraldehyde (1%), the mechanical characteristics of collagen hydrogels significantly improve. However, the concentration of glutaraldehyde above 10 % reduces cell viability by 50%.
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ENCAPSULATION OF COUMARIN-6 IN POLYMERIC MICELLES BASED ON HYDROPHOBIZED HIALURONIC ACID

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Low molecular weight hyaluronic acid (approx. 5-20 kDa) hydrophobized with oleic acid (HA C18:1) is a non-toxic, biocompatible and biodegradable amphiphilic polymer that is used to produce self-assembled structures (polymeric micelles) [1]. One of the key parameters defining micelle stability in highly diluted solutions is critical micelle concentration (CMC). The main focus of this study has been to investigate the effect of organic solvents on the CMC of HA C18:1-based polymeric micelles obtained in the presence of coumarin-6 fluorescent dye. The CMC was measured by the spectrofluorimetric method. The sizes of the obtained self-assembled systems were determined by dynamic light scattering (DLS). HA C18:1 polymeric micelles were produced by the solid dispersion and solvent evaporation techniques. The following solvents were used: isopropyl alcohol, acetone, chloroform, and dichloromethane.
It has been found that self-assembled structures of approximately 200 nm, characterized by a wide size distribution, are formed from HA C18:1 in water solutions. Incorporation of coumarin-6 produces micelles of smaller sizes (136.7 ± 31.5, PDI 0.18). It has also been established that the CMC and coumarin-6 incorporation level into polymeric micelles are influenced by the choice of organic solvent. Choloroform, for example, enables a more effective incorporation of coumarin-6 into the micellar structures, and the CMC of the obtained micelles is high (0.10 mg/ml). Dichloromethane, on the contrary, reduces the CMC value to 0.015 mg/ml.
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P 24

BIOPOLYMER HYDROGEL COMPOSITIONS WITH A COMPLEX THERAPEUTIC EFFECT FOR THE TREATMENT OF INFANTILE WOUNDS

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Proteolytic enzymes are the optimal choice for stopping inflammation at the first stage of the wound process and accelerating wound regeneration.
The body's natural capabilities do not cope with the task of lysis of necrotic tissues and exogenous enzymes are required to enter the inflammation focus, and not native, but immobilized and dosed into the wound from a biologically active coating. Two versions of polymeric materials are offered: hydrogel composition: gels and a textile material covered with gel to fill the wound for its closure from the external environment. In this case, it is a composition based on a natural polymer-polysaccharide sodium alginate, which has a spectrum of useful properties, including the ability to swell and become a gel, hemostatic activity, biocompatibility, anti-allergenic properties and complete safety for the patient.
However, there is one negative property - a change in rheological characteristics under the influence of gamma irradiation during sterilization. In order to maintain the optimal viscosity of the composition after sterilization, another polymer, hydroxypropyl methylcellulose (HPMC), was added. HPMC is widely used in medicine due to its high hydrophilicity and viscosity, and is also used as an "artificial tear". The selected ratio of polymers allows maintaining the viscosity of the polymer composition after sterilization in the required range. The choice of a proteolytic enzyme was carried out by comparative analysis of proteolytics of animal (chymopsin) and plant origin (papain, bromelain).
It has been shown that it is advisable to use papain, which exhibits sufficient proteolytic activity. The attachment of the enzyme was carried out by physical immobilization of polymers in the gel. It is proposed to simultaneously introduce silver salts, which have a broad spectrum of antibacterial properties at low concentrations and transform into a nano-form due to reducing agents-biopolymers, since in addition to lysis, an antibacterial effect on wound substrates is necessary.
Thus, the proposed polymer composition is based on two polymers-polysaccharides, which has therapeutic properties and serves as a "depot" for drugs: the enzyme papain, which cleanses the wound and creates favorable conditions for complete healing, and silver salt, which has an antibacterial effect.

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EFFECT OF SMOKING DOES ON CONTENTS OF LONG-CYFIN POLYUNSATURATED FATTY ACIDS IN SIBERIAN WHITEFISH

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Raw and cold smoked 'whitefish' species of genus Coregonus, least cisco *(C. sardinella)*, Arctic cisco *(C. autumnalis),* muksun *(C. muksun)* and broad whitefish *(C. nasus),* caught in the Yenisei River (Siberia, Russia) were analysed. Contents (mg per g of product) of long-chain polyunsaturated fatty acids of omega-3 family (LC-PUFA), namely eicosapentaenoic acid (20:5n-3, EPA) and docosahexaenoic acid (22:6n-3, DHA), as well as whole fatty acid (FA) profiles were measured. There were no significant decrease of EPA+DHA contents in the smoked fish compared to the raw fish. Moreover, in least cisco, a significant increase of EPA+DHA contents in smoked fish occurred, probably due to a decrease of moisture contents. Consequently, the smoked fish of studied species are believed to be valuable products for human nutrition regarding EPA and DHA contents. Total FA composition of the fish were not changed significantly during smoking. Thus, the FA composition of smoked fish could be used for verification of trade information on fish origin and identity at shelves.

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HEAT-RESISTANT COMPOSITION

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Step-by-step process may be among efficient decisions associated with elaboration of the method for preparation of pressmaterials on the basis of polynaphtoilenebenzimidazoles (PNBI) practically insoluble in organic solvents in the conditions of the reactions of thermal polycondensation providing the potential possibility for increase of their processing to the products.
The essence of proposed elaboration involves performing of the synthesis of polymeric binder – PNBI by the method of thermal polycondensation of bis(o-phenylendiamines) with bis (naphtalic dianhydrides) in the composite - inhomogenous medium – in carbon filler – at presscomposite formation. For this purpose the fine-dispersed equimolar mixture of initial monomers – bis(o-phenylendiamine)(3,3-diaminobenzidine or 3,3,4,4-tetraaminodiphenylenoxide) and dianhydride of naphthalene-1,4,5,8-tetracarbon acid was coated on carbon filler. Oligomer synthesis was performed immediately on the filler surface at $T_{reac}<T_{m.p}$ of tetraamine component - 1st step; hereafter in the conditions of thermal pressing the formation of coal plastic was carried out (pressure – 15 kgf·cm^{-2}, maximum pressing tempetature comprises 673K, rate of temperature increase – 5°min^{-1}). Elaborated method of preparation of structural coal plastics on the basis of PNBI was approved and was positively estimated. Elaboration of new method for preparation of coal plastic allowed at first to produce the mentioned materials on the basis of PNBI. It should be noted that although prepared coal plastics for the present are inferior to coal plastics, based on polyimides, by absolute values of physical-mechanical characteristics, but outperform them by the level of conservation of strength properties in the conditions of high temperatures (preservation of bending strength comprises 90% at 573K).

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FORMATION OF COPPER-CONTAINING NANOPARTICLES IN AQUEOUS POLYMER SOLUTIONS

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Among the new materials, biomedical nanomaterials occupy the most important place. The range of nanomaterials used is quite wide: metals and their oxides, silicates, carbon materials, polymers and composites. Systems containing transition metal nanoparticles, in particular, copper, are of heightened interest. The catalytic, optical and bactericidal properties of copper are well known. Copper nanoparticles were obtained in aqueous solutions of poly(N-vinylpyrrolidone), poly(ethylene oxide), poly(acrylic acid), amphiphilic polymers of N-vinylpyrrolidone and pluronics. These polymers are successfully used in medicine, agriculture and the cosmetic industry. The process of formation of copper nanoparticles is considered in the framework of the pseudo-matrix synthesis theory, which is based on the idea of the cooperative nature of non-covalent interactions of macromolecules with the surface of nanoparticles. As a result of the interaction of the macromolecule and the nanoparticle, a polymer shield is formed on the nanoparticle surface. The growth of the particle stops. First, this makes it possible to effectively control the size characteristics and, secondly, the polymer macromolecules protect the nanoparticles from oxidation. When copper ions are reduced in PVP or PAA solutions, sols with particles of 3-12 nm that are resistant to aggregation and oxidation are formed. Moreover, in PAA solutions, the average particle size is slightly smaller. However, the oxidation stability is much lower than that of nanoparticles obtained in PVP solutions. Regardless of the molecular mass of the polymers, sediments rather than sols are formed in PEO solutions. At the same time, copper particles do not oxidize for a long time, i.e. they are protected by a polymer shield. Extremely stable copper sols are formed in solutions of amphiphilic polymers of N-vinylpyrrolidone containing one terminal n-alkyl group with 6-18 carbon atoms as a hydrophobic fragment. In solutions of pluronics (tri-block copolymers of PEO-PPO-PEO) sediments are formed. In this case, nanoparticles formed in solutions of amphiphilic polymers, both in the case of PVP derivatives and in solutions of pluronics, are included in micelle aggregates.
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SORPTION PROPERTIES OF NATURAL ANIONIC HYDROCOLLOIDS AND THEIR MIXTURES IN ORDER TO CREATE SELF-GELLING SYSTEMS FOR EXUDATING WOUNDS

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Marine polysaccharides are widely used in medicine and pharmaceuticals, in particular as dressings for wounds. To obtain stable structures of medical materials, various modifications of the raw material are carried out. The most common modification technology is chemical crosslinking of polymer molecules.
Researchers are interested in finding soft natural crosslinking agents, especially, when it comes to medical means that have direct contact with damaged tissues and physiological fluids.
It is known that a significant amount of charged particles, in particular H^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, and other elements that form the overall positive charge of the wound, accumulate in the exudate. Calcium ions initiate the process of gelation of sodium alginate with the formation of ionic bonds when cations interact with COO^- groups, which leads to crosslinking of macromolecules. K^+ and Ca^{2+} ions are cross-linking agents in the case of k-carrageenan, which, being in an unordered conformation, shows high sensitivity to counter-ions, which leads to the formation of stable gel structures In our research, we used a Ringer-Locke solution that simulates the composition of the exudate. It is assumed that the cations included in the exudate will contribute to the crosslinking of polysaccharide molecules and the formation of a gel, thereby retaining the exudate in its volume. The kinetics of the sorption process and the sorption capacity were determined by weight method for individual polymers and their mixtures. It was found that the greatest sorption in 24 hours in the presence of Na^+, K^+, Ca^{2+} cations was sodium alginate (35.4 g/g), but the sorption rate in the first 15 minutes was low (3.8 g/g). The highest sorption rate for 15 minutes was shown by a mixture of 1: 2 sodium alginate and k-carrageenan (19.8 g/g). The choice of the ratio of hydrocolloids is determined by the degree of exudation of the wound.

P 29

PREPARATION AND ANTIBACTERIAL PROPERTIES OF CHITOSAN BEADS LOADED WITH SILVER NANOPARTICLES

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In the present work the chitosan beads modified with colloidal silver nanoparticles for creating wound dressings with an antibacterial effect have been developed. Silver nanoparticles with particle sizes from 20 to 100 nm were synthesized by reducing AgNO3 in the presence of humic acids in an aqueous ammonia medium. The beads were obtained by introducing nanosilver into a solution of chitosan, drops of which were cured by ionotropic gelation followed by covalent cross-linking of the polymer matrix with an adipic acid. The diameters of chitosan beads ranged from 1.0 to 2.0 mm. The surface morphology of the obtained beads was studied using scanning electron microscopy (SEM). The antibacterial activity of unloaded chitosan beads and the samples modified with silver nanoparticles was tested against ***St. aureus*** and ***E. Coli*** by agar diffusion test. The results suggested that the chitosan beads modified with nanosilver demonstrated an antibacterial effect on both Gram-positive and Gram-negative bacteria. Based on the results of this study, the prepared nanosilver-loaded chitosan beads could be promising candidates for development antimicrobial wound dressings product.

P 30

NEW TECHNOLOGY FOR CLEARING WASTEWATER CONTAINS PHARMACEUTICAL SUBSTANCES

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Wastewater containing pharmaceutical substances is produced in pharmaceutical factories and hospitals. The traditional biological treatment of this wastewater is barely effective. Now, with the aim to produce local cleaning plants being so common, new technologies are searching for the solution. Our technology, which includes three stages, may be applied. 1 – the addition of a dispersed sorbent from solid organic waste from chemical and processing factories; 2 – concentration of the formed suspension on porous microfiltration membranes; 3 – complete oxidation of the membrane concentrate by means of oxygen, from the air, in water under its supercritical parameters. No reagents are used, nor is any waste formed. Once the amount of the saturated sorbent has reached a specific amount, there will be enough released heat from the exothermic oxidation reaction to compensate the energy used and even utilize excess energy, which is recycled on the spot. The article presents results of this work applied to moduled wastewater containing acetylsalicylic acid, tetracycline and sulfadimezin. The sorbents tested included rice husks, peat and graphite dust. Concentration of the suspension was completed on ceramic microfiltration membranes. Presented is a supercritical water oxidation pilot plant. Under the initial concentration, 500 mg/l, of the pharmaceutical substance, the addition of various sorbents ranges from 3 to 30 g/l, concentration of the suspension continues until the dispersed phase reaches 80 g/l and the water oxidation of the mixture is under the pressure of 25 MPa and temperature of 450 °C. Water was cleaned from 98.0 – 99.8% of organic substances. The heat and material balance calculated prove the possibility of an autothermal operating mode.

P 31

DEVELOPMENT OF THE PERSONAL CARE PRODUCTS EVALUATION METHOD BY THE DEODORANT ACTION PARAMETER

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According to legal requirements, confirmation of the claimed consumer properties of cosmetic products is mandatory, but there are no legislatively approved methods for their assessment. Therefore, the development of standardized methods for evaluating of sweat odor control agents by the deodorant action and the antiperspirant one is relevant.

GARNIER MINERAL DEODORANT aerosol deodorant-antiperspirant (L'Oreal CJSC) and REXONA motionsense aerosol antiperspirant (Unilever Rus LLC) were used for the experiments. The intrinsic antibacterial activity of the compositions used was estimated by the disc diffusion method according to the size of the growth inhibition zone of the sanitary indicator microorganisms ***Staphylococcus aureus, Pseudomonas aeruginosa*** and ***Bacillus subtilis.*** No antibacterial activity was detected against these microorganisms, growth inhibition zones around each paper disc being absent. The deodorant action was evaluated by the rinse test from the axillary cavities of volunteers 4 hours and 8 hours later after applying the composition to pure skin, followed by inoculation to agar media. All tests were performed in triplicate for each method (inoculation type). On the axillary skin not treated with deodorant the number of microorganisms (CFU) after 8 hours (from $3.01 \cdot 10^5$ to $4.11 \cdot 10^5$) is 1.5 – 2.5 times higher than after 4 hours (from $0.38 \cdot 10^5$ to $2.10 \cdot 10^5$). The use of deodorants reduces the microorganisms amount on the skin, and both compositions ensure adequate protection both after 4 hours and 8 hours. After their application the microorganisms amount on the volunteers skin was up to 20 CFU per the axillary surface. Thus, the rinse test is suitable for evaluation of deodorants and antiperspirants by the deodorant action parameter. This work was supported by D. I. Mendeleev University of Chemical Technology of Russia. Project number K-2020-007.

P 32

AMPHIPHILIC POLYMERS AS A CARRIERS OF MEDICINE SUBSTANSES

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Nanosized polymer carriers are of interest as components of medicinal systems that allow for targeted transport of biologically active substances, prolong their action, prevent side consumption, and reduce toxicity. The best studied nanosized carriers are liposomes capable of delivering biologically active substances to cells through various mechanisms, in particular, due to the fusion of liposomes with cell membranes, which is accompanied by the entry of biologically active substances into the cytoplasm, due to the adsorption of liposomes on the cell surface, and finally, due to endocytosis of various types. when the liposome enters the primary endosome of the cell. Developed in recent decades, nanosized particles of synthetic amphiphilic polymers, primarily poly-N-vinylpyrrolidone and 2-cyanoacrylic acid esters, have significant advantages compared to liposomes - resistance to various destructive factors, in particular, the action of polycations, no side biodegradation, and their high resistance to oxidation. compared to lipids, low toxicity. However, the mechanism of penetration of these particles into cells is not well studied. Thus, methods have been developed for the synthesis of surface active esters of 2-cyancrylic acid and adducts at the double bond of 2-cyanoacrylates, as well as amphiphilic poly-N-vinylpyrrolidone with a terminal thioctadecyl and alkylamine groups, as well as methods for obtaining on their basis a wide range of nanosized drug carriers in the range sizes from 20 to 200 nm. The work was supported by Ministry of Education and Science of the Russian Federation as part of the state assignment for the FSSM-2020-0004 project.

P 33

PHYSIOLOGICALLY ACTIVE BIOCOMPOSITE MATERIALS BASED ON POLYSACCHARIDE GELS

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One common cause of mobility loss and mortality of elderly is bone fractures caused by geratic osteoporosis. Reduction of bones strength causes serious difficulties in prosthetics, and existing methods of osteoporosis and its consequences treatment are less effective and are considered one of the most expensive in the world. This study was carried out within the framework of the general concept of creating physiologically active biocomposite materials and devoted to the creation of materials necessary for replacement of damaged bone tissue capable of locally releasing antibiotics into the bloodstream. A method has been developed for treating biological tissue (bovine bone) used as the basis for a physiologically active biocomposite. It contains a polymeric active bioabsorbable polysaccharide gel cross-linked with epichlorohydrin and bis-epoxides under alkaline conditions. Commonly used clinical blood substitutes hydroxyethyl starch and dextran as well as carboxymethyl cellulose was used as a polysaccharide base. A method enables to protect implant from bacterial infection for a long period of time, by locally immobilizing a broad spectrum aminglycoside antibiotic, amikacin, at polysaccharide gel located on the surface and inside the pores of the bone implant has been developed. The dynamics of antibiotic release was studied. It has been shown that in the absence of bacterial attack, the dextran-based gel does not decompose or release an antibiotic into the bloodstream. Under the influence of the dextranase enzyme released by staphylococcus, the gel decomposes with local antibiotic release, which provides local protection against bacterial attack. The effectiveness of the protection was confirmed in the *in vitro* experiments. Thus, biocomposite materials based on bovine bone and a polysaccharide gel with an immobilized antibiotic have been created. It allows to protect the implantation site from bacterial infection for a long time. The study was conducted with financial support from the Ministry of Science and Higher Education of the Russian Federation as part of FSSM-2020-0004 state project.

P 34

SYNTHESIS OF HYDROSOLS OF COPPER USING HUMIC ACIDS

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The purpose of this work was to select synthesis conditions for obtaining stable hydrosols of copper. Humic acids sodium salt as well as a stabilizer and a reducing agent at the same time were chosen to synthesis of copper hydrosols. Unfortunately we were not successful to synthesize stable copper hydrosols according to the method described above. Therefore, based on on the method described in literature, it was decided to use core-shell method to synthesize bimetallic nanoparticles. The method was developed for the preparation of Ag/Cu bimetallic nanoparticles and their stabilization with sodium humate. To producing hydrosols we used glucose as a reducing agent and humic acids as a stabilizer. A portion of copper sulfate was selected in such an amount that the molar ratio $C_6H_{12}O_6$:$CuSO_4$*$5H_2O$ was 1.75:1. This ratio was selected according to the results of the work, since at this ratio the maximum yield of copper nanoparticles was observed. Sodium humate was added at the end of the synthesis in amounts of 0-0.4 g. In the hydrosol using sodium humate as a reducing agent and a stabilizer, a precipitate was formed instantly; in a hydrosol using sodium humate only as a stabilizer, complete sedimentation of nanoparticles was observed for 1.5 hours. It was proved that the combination of silver and copper should lead to the most stable heteroclusters. It was found that hydrosols with a molar ratio Cu:Ag=5.78:1 with the addition of sodium humate from 0.1 g and more are stable for more than 30 days. The sizes of nanoparticles in the obtained hydrosols were about 70-110 nm.

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CHITOSAN-BASED NANOGELS AS AN EFFECTIVE WAY OF DRUG DELIVERY

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At present, the theme of ecology and green chemistry is more relevant than ever, which is why the direction of natural biodegradable polymers is developing so expressive. Since chitosan is the most common biopolymer in the world, materials based on it have double attractiveness. It is also worth noting such properties of chitosan as its polycationicity, which allows it to be used as a base for medicated ointments, non-toxicity and biodegradability, as well as the manifestation of antibacterial properties. There are a large number of works devoted to the study of chitosan hydrogels for various applications. Unlike classical gels, ours have a nanoscale structure. This is possible due to the chemical modification of chitosan (polymers with different molecular weights, namely 100, 250 and 400 kDa, were used as raw materials). Particle size was studied both by dynamic light scattering and by transmission electronic microscopy. The results showed that the size of the formed particles averages from 70 to 150 nm. The zeta potential of such systems is in the range of 22-25 mV. An important point in the work was the selection of a preservative agent, since various fungal cultures perfectly develop on polysaccharides. Diverse commercial products, based on benzyl alcohol, benzoic acid, levulinic acid, as well as a number of natural preservatives (based on mandrake extracts), have been tested as preservatives. The results of microbiological studies showed that the most effective in our case was a benzyl alcohol-based preservative (with an efficiency of 95%).
Due to the presence of a large number of functional groups and a developed surface, the hydrogel is able to retain various medicinal substances, both water and fat-soluble. Vitamin E (dl-alpha-tocopherol), vitamin A (retinol palmitate), and niacinamide were selected as model drugs. The resistance of vitamins to oxidation was studied during accelerated aging by chromatographic method. It has also been shown that fat-soluble vitamins A and E bind well to chitosan in therapeutic doses.

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SYNTHESIS OF COBALT HYDROSOLS AND THE STUDY OF THEIR COLLOIDO-CHEMICAL PROPERTIES

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Hydrosols of metals are currently finding wider application in various fields, including medical. Such systems can be used as antibacterial agents, drug carriers, etc. The aim of this work was the synthesis of aggregatively stable cobalt hydrosols and the study of their colloido-chemical properties. Hydrosols were prepared by chemical reduction of ions from salt solutions in the presence of a stabilizing ligand. As precursors, cobalt chloride and sulfate, sodium borohydride were used. The main problem in obtaining stable sols was the selection of stabilizing ligands. During the experiment, it was found that the most effective stabilizer is sodium humate. Also tested as stabilizers: polyvinylpyrrolidone, carboxymethyl cellulose, a copolymer of polyacrylamide with acrylic acid, Tween 80, however, the hydrosols obtained with their help did not show aggregative stability. Using sodium humate, it was possible to obtain aggregatively stable sols with a high concentration of cobalt (0.2% wt). The zeta potential of the resulting system was determined by dynamic light scattering on a Zetasizer instrument, it was -20 mV, the particle size of sols was measured using the Photocor analyzer by the same method, the average particle diameter was 40-50 nm. From the data obtained, it can be concluded that the aggregative stability of the obtained hydrosols is ensured by the combined action of the electrostatic and steric components of the proppant pressure. The resulting hydrosols are of interest as an perspective means of drug delivery.

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ULTRA-LOW-DENSITY Ca-ALGINATE BASED CRIOGENICALLYSTRUCTURED SPONGES

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Fields of application of biopolymers are expanding every year. Alginic acid and its salts that are the most common used polysaccharides obtained from red, brown and some green algae. These macromolecular non-toxic and biocompatible compounds are widely used in the pharmacy, cosmetic and food industries as thickening and gelling agents.

In this work, spongy ultra-low-density materials based on calcium alginate have been prepared and studied. Since these materials have excellent biocompatibility, low toxicity, and they also have a large number of macropores, it was proposed to use them as hemostatic agents. For this application, the sodium form is not suitable, since it will not hold the form when in contact with liquids, so a technique was developed for producing calcium-containing sponges (since it is stable in a wider pH range). The developed materials have a density of 0.01-0.03 g/cm^3, and the pore size ranges from 50 to several hundred microns, and the pores are interconnected. Such Ca-alginates cryogenically-structured sponges have high stability in a wide pH range from 3 to 9 (for more than two weeks). The dependences of bending strength, calcium content, pore size and morphology, and also swelling parameters of the resultant materials were studied as dependent on the initial polymer concentration.

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FOLATE-ASSOCIATED LIPOSOMES OBTANED BY THE POST-MODIFICATION TECHNIQUE: PREPARATION AND EVALUATION IN 2D ABD 3D IN VITRO MODELS

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The aim of the work was to obtain cationic folate-associated liposomes (FLPs) loaded with doxorubicin (DOX) for active targeted drug anticancer delivery and to investigate it using 2D and 3D *in vitro* models. The FLPs formation was carried out with two different approaches, namely by a thin film technique (TFT), as well as by the new post-modification (PMT) one. The first method is to form the thin film directly from a mixture of conventional lipids (without ligands) and ligand-associated ones. The second method (B) is to obtain liposomes from a mixture of conventional lipids and lipids with a special linker site with chemically active groups. When processing these already formed and drug-loaded liposomes with folate ligands containing the response active groups, their covalent binding with the liposome surface will occur. Thus, the PMT approach makes it possible to obtain basic universal drug-loaded liposomes and to easily modify their surface with desired ligands or other molecules. The preparation technique was showed to significantly influence the FLPs diameter. Thus, in the case of the TFT, the FLPs mean diameter was 250±17 nm, while the diameter of FLPs obtained by PMT was twice smaller, namely 135±8 nm. However the FLPs ζ-potential values were +47±9 mV for both FLPs. All obtained liposomal dispersions remained stable at least for three weeks. DOX loading was 40% (w/w). The UM-87MG, MCF-7, C6 and MSC cells were used as 2D (monolayer culture) and 3D (tumor spheroids) *in vitro* models, since these cell lines are known to differ in a folate receptors expression (FRE) levels. The cytotoxicity of FLPs was investigated using MTT-test, while accumulation efficiency assay was conducted with confocal microscopy as well as with flow cytometry. Liposomes without folate ligands (LPs) were used as a control. It was shown that in the case of cell lines with normal FRE (MSC and U-87MG) the FLPs and LPs accumulation levels as well as cytotoxicity were almost the same. However in the case of cells with high FRE (MCF-7 and C6) the FLPs accumulated in cells and cause it death mush faster than LPs. Thus, the FLPs obtained by PMT are promising anticancer agent in terms of its phisycal-chemical parameters and cytotoxicity. The work was supported by the RFBR (grants 17-54-33027 in part of liposomes characterization, 18-34-00919 in part of *in vitro* investigaton and 18-04-01087 in part of the tumor spheroids).

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STRAINTRONICS FOR NANOBIOMEDICINE: STIMULATION BIOCHEMICAL SYSTEMS VIA CONTROLLABLE MACROMOLECULAR NANODEFORMATION

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Here we review the possibilities of control over biochemical systems via selective deformation of biomolecular structures by functionalized magnetic nanoparticles (MNPs) that are set in rotating oscillations with a low-frequency (< 1 kHz) non-heating magnetic field (MF). Physical models of such nano-magneto-mechanical actuation of biomolecular structures are developed. Deformation localized at nanoscale makes it possible to control enzyme activity and drug release from MNP's polymer shells or by disordering the membranes of transport nanocontainers such as vesicles and micelles with either imbedded or conjugated MNPs. Possible mechanisms of impact on membrane structural elements, cytoskeleton, cell receptors and their influence on vital processes through mechanotransduction are thoroughly analyzed. In the latter case, there is an ability to induce both apoptosis of malignized cells and, on the contrary, stimulate direct growth and proliferation of healthy cells in favor of regenerative medicine. Main advantages of nano-magnetomecanical actuation by non-heating MF are non-invasiveness, biosafety, controllability, easy to dose, selectivity and targeting of therapeutic treatment. It gives an opportunity for developing methods and protocols of drugless therapy of many diseases.
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LOW-FREQUENCY NON-HEATING MAGNETIC FIELD PROMOTE RELAXATION RATE IN AOT REVERSE MICELLES WITH SOLUBILIZED MAGNETITE NANOPARTICLES

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Reverse micelles are self-organized nanosized structures consisting of amphiphilic molecules (surfactants) in non-polar solvents containing a water pool. The system equilibrium is usually followed by the formation of optically transparent solution; however further size and concentration changes can occur. Such processes affect properties of solubilized molecules such as proteins. In the work presented, we solubilize magnetite nanoparticles in AOT reverse micelles and study the influence of low-frequency non-heating magnetic field (LF-NH-MF) on kinetic parameters of equilibrium.

Magnetite nanoparticles (MNPs) were synthesized by thermal decomposition of Fe(Acc)3 in benzyl alcohol and characterized by TEM, Moessbauer spectroscopy, magnetic measurements and X-ray diffraction. MNPs dissolve in AOT reverse micelles. Solubilized MNPs (S-MNPs) were characterized by TEM and DLS.

The kinetics of establishing equilibrium in the micellar system was monitored spectrophotometrically by changing in p-nitrophenol absorbance at 305 and 380 nm. The change in absorbance over time is described by the sum of two exponentials. The dependence of rate constants (first-order rate constants) on w0 is linear, both with or without MNPs. Application of LF-NH-MF (50 Hz, 100 mT) increased the equilibrium establishment rate dramatically. A maximum is observed on the curve of the rate constant dependence on w0, and their values increased by an order of magnitude. The mechanism of such field effect, and the possibility of its application in biotechnology, for example, for enzyme solubilization is discussed.

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ELECTROCHEMICAL METHOD FOR TESTING THE EFFICACY OF NEW ANTICANCER CONJUGATES FOR THE TARGETED DELIVERY

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Reactive oxygen species (ROS) is associated with induction of apoptosis. The study of intracellular ROS levels may represent one possibility to research the effects of drugs in inflammatory cells. ROS are released from cells during apoptosis, play a crucial role in the development of cancer and neurodegenerative diseases. Nowadays, there is the problem of developing methods for treating cancer tumors, and quickly evaluation of the anticancer drugs efficiency is the priority. The ROS determination using nanosensors in single cells has gained increasing attention. However, traditional fluorescent dyes have a number of disadvantages. These dyes are known to be intrinsically cytotoxic and thus can significantly alter cellular metabolism.

Here, we have developed an electrochemical method for determining the ROS inside the cells. Using this method, it is possible to evaluate the effect of the developed drugs on the cells. We evaluated the effect of ASGP-R (Asialoglycoprotein receptor) - specific carrier equipped by docetaxel on cancer cell lines with (HepG2) and without (PC-3) ASGP receptors. Our data obtained by using carbon-filled quartz nanopipettes with platinum tips showed

a ROS increase using conjugates compared with native drugs. We also studied the effect of ASGP-R specific carrier equipped by betulin with (HepG2) and without (PC-3) ASGP receptors. In the future, this method may allow evaluating the effect of drugs *in vitro* and to help validate drug candidates for preclinical evaluation.

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DEVELOPMENT AND EVALUATION OF BETULIN CONJUGATES FOR ASGPR-TARGETED DRUG DELIVERY TO HEPATOCYTES

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Hepatocellular carcinoma (HCC) is third most common cause of cancer mortality, accounting for more then 90% of global cases of primary liver cancer. The asialoglycoprotein receptor (ASGPR) is a C-type (Ca^{2+}-dependent) lectin highly expressed on the surface of liver parenchymal cells. The primary physiological role of ASGPR has been considered to be the binding, internalization, and subsequent clearance from the circulation of galactose- and N-acetylgalactosamine-terminated glycoproteins. The location and the function makes the receptor an ideal target for delivery of therapeutic agents to liver cells.

Betulin and betulinic acid are natural products with a range of biological effects, one among others being potent antitumor activity due to the ability to induce apoptotic cell death in cancer cells by triggering the mitochondrial pathway of apoptosis. Taken into account the high therapeutic potential of these substances for treatment HCC, they were modified for targeted delivery in hepatocytes.

The covalent conjugates of betulin and N-acetyl-D-galactosamine were synthesized and their affinities to ASGPR has been assessed using surface plasmon resonance (SPR) spectroscopy technique. Betulin conjugates exhibited strong binding affinity with K_D values in the nanomolar range, that considerably exceed the affinities of native ASGPR ligands – GalNAc and galactose. Obtained results confirmed that the presence of the N-acetyl-D-galactosamine moiety in the structure of betulin conjugate has a synergic effect on binding to ASGPR. The *in vitro* cytotoxicity of betulin conjugates to HepG2, Huh7 and PC3 cell lines was assessed using MTT assay. The betulin itself was less tolerated by all the tested cell lines than its conjugates. That loss of activity is related to structural features, in particular to modification of C-3 and C-28 hydroxyl groups of betulin molecule. The degradation products of betulin conjugates were studied via HPLC-MS. The result suggests that betulin have to be released from its conjugates after cellular uptake. The *in vivo* distributions of fluorescently labeled GalNAc-modified and non-modified conjugates were studied using intravital microscopy technique. Pattern of distribution for ASGPR-targeted conjugates differed from those for conjugates without targeting moiety. The ability of GalNAc-modified betulin conjugates to selective penetrate into hepatocytes was demonstrated.

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SYNTHESIS AND STUDY OF THE STRUCTURE OF NEW POROUS SORBENTS BASED ON MODIFIED POLYVINYL ALCOHOL

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Disinfection of air in various rooms is an important task solved in various fields on the border of medical, hygienic, sanitary-epidemiological, materials science and technological approaches.
Particularly acute is the issue of air disinfection in enclosed spaces in which people stay for a long time. This is especially true for spacecraft such as the International Space Station, where the total air volume is limited and cannot be quickly replaced by forced external ventilation.
At present, the most common approaches to air disinfection are chemical and physical methods. Chemical methods include the use of bactericidal aerosols, photocatalytic effects on microorganisms, and ozonation. The physical methods include UV radiation, exposure to electric fields, filtration. All the methods described, with the exception of physical filtration, have a number of features that make their use impossible in confined spaces.
In this regard, we set ourselves the task of creating new composite filtering systems for air disinfection with biodegradable components based on porous polymer matrices. These systems must ensure multiple contact of the air mass with the biocidal surface formed in them, intended for disinfection.
At the first stage of our work, we developed methods for preparing porous PVA cryogels and estimated the surface morphology of the obtained samples.
As a result, it was found that the porous structure of the samples is characterized by a bimodal distribution of through pores in size. Large pores have an average size of ~ 30 μm, micropores - 3-5 μm in transverse diameter. The pore walls are formed by PVA lamellae, the thickness of which is ~ 0.5-1.0 microns. The pores located in the volume of the sample are bottle-shaped. Part of the pores from the morphological point of view are gaps located between the lamellae. In general, all the pores are interconnected and are characterized by a rather complex geometry, which indicates a stepwise mechanism of the phase decomposition of a PVA solution during cryogenic freezing.
At the next stage of the work, it is planned to study the gas permeability and vapor permeability of the obtained sorbents and evaluate the change in their properties during operation.
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SYNTHESIS AND STUDY OF DIAGRAMS OF THE PHASE STATE OF THE PVA-WATER SYSTEM IN A WIDE RANGE OF TEMPERATURES AND COMPOSITIONS

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Polyvinyl alcohol is a synthetic polymer that is widely used in industry for commercial, medical, and food applications. Crosslinked PVA can be used as high porosity hydrogels due to the network structure of crosslinked polymer chains that induces molecular diffusion. [1] Small molecules (eg peptides, proteins) can diffuse in and out of the matrix, while larger molecules (eg plasmid DNA) often enter the pores and become trapped within the mesh. This property makes it possible to use crosslinked PVA as porous hydrogel filter systems.
In this regard, we are faced with the task of obtaining composite porous filtration systems that allow multiple contact of the air mass with the biocidal surface formed in these systems intended for disinfection.
At this stage, a diagram of the phase state of the PVA - water system was constructed in a wide range of temperatures and compositions, from which it can be seen that the phase equilibrium in the PVA - water system is characterized by a complex amorphous-crystalline equilibrium
It has been established that for the formation of porous hydrophilic sorbents with a predominantly binding and stable pore system under conditions of prolonged operation in humid environments, it is necessary - (1) to carry

out the process of structure formation in the PVA region, solutions in water corresponding to the location of the water liquidus line on the phase state diagram; (2) a network of chemical bonds should be created in the dispersed phase of the sorbent, which can then be used to regulate and stabilize the hydrophilic properties of the sorbent during its operation and regeneration.

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SYNTHESIS OF NEW POROUS MATRICES BASED ON MODIFIED POLYVINYL ALCOHOL FOR AIR FILTRATION

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The use of polymeric cryogels based on PVA for the creation of composite filter systems for the disinfection of the gaseous medium in confined spaces is of great interest in connection with the information that has appeared on the low efficiency of the Potok device used at the International Space Station for air purification [1].

It is known that carrying out the process under cryostructuring conditions makes it possible to obtain PVA cryogels with directed pores, which makes it possible to use the samples as filtering systems.

To date, a number of methods are known for obtaining physically and chemically crosslinked PVA gels. However, the gels obtained by the methods described in the literature have relatively low porosity. One of the ways to overcome this problem is the original approach proposed by us earlier, which consists in crosslinking in water-frozen systems of acrylic derivatives of PVA [2]. This method makes it possible to obtain a product with a porosity of 85-86% from polymer solutions with a concentration of ~ 4%.

However, to obtain matrices with even higher porosity, a new combined approach was developed in this work. At the first stage, the PVA solution is frozen with an initiator, followed by freeze drying, as a result of which a three-dimensional porous structure is formed. In the second stage, crosslinking occurs under controlled heating.

As a result, it was possible to obtain crosslinked systems even with a polymer concentration in the solution of only 1%.

At the next stage, the equilibrium swelling of the obtained samples was assessed. It has been established that with prolonged heat exposure, a decrease in equilibrium swelling is observed. This fact can be associated both with a change in the hydrophilicity of the crosslinked polymer chains due to the oxidation of hydroxyl groups under the influence of an excess of initiator, and due to a change in the porosity of the system.

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