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Interaction of New Nanosized Macro-molecular Systems with Biopolymers and Living Objects

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Abstract

Methods of synthesis of amphiphilic derivatives of a number of water-soluble polymers, in particular, poly-N-vinylpyrrolidone, have been worked out. In experiments on cells and experimental animals, the harmlessness of the polymers obtained was shown. The synthesized amphiphilic polymers are capable of spontaneous aggregation in aqueous solutions with the formation of nanoscale micelle-like aggregates and are suitable for modifying liposomal membranes. The influence of the structure of amphiphilic polymers on the tendency to aggregation has been established. Such systems can be used as carriers of poorly soluble and water-insoluble medicinal substances. It was shown, what aggregates of amphiphilic polymers of N-vinylpyrrolidone proved to be suitable for use as carriers and modifiers of various proteins and peptides (blood factor IX, angiostatin, Bowman-Birk soybean proteinase inhibitor (BBI)). In these cases, immobilization with the use of polymeric aggregates increases the resistance of proteins to denaturing effects, and thereof their total biological activity. Methods have been developed for the introduction into the synthesized amphiphilic polymers of various functional groups. For example, introduction of additional side aminoacid groups in the polymeric part of amphiphilic systems allows the use of aggregates as carriers of nucleic acids and their subsequent application for transfection in genetic engineering. Using fluorescent labels and probes, it was shown that the immobilized substance introduced into larger size aggregates penetrates into the living cell due to endocytosis, localizing in the cytoplasm inside the endosome. On the other hand, when immobilized active agent is introduced in smaller-sized aggregates, it evenly spreads both in the cytoplasm of the cell and in its nucleus. When studying the transport of aggregates of amphiphilic polymers of Nvinylpyrrolidone in the body (rats), it was established that a fluorescent probe immobilized in aggregates of amphiphilic polymers, when injected into the tail of experimental animals, quickly reaches the vessels of the eye.

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Biography

Mikhail I.Shtilman is the head of Biomaterials department and professor at the Mendeleyev University of Chemical Technology of Russia. He completed his Ph.D. Diploma in 1964 and D.Sc. Degree in chemistry in 1985. His main research interests lie in the synthetic design of polymeric biomaterials with specific properties – biocompatibility, compatibility with blood, biodegradability, bioactivity – for medicine, agriculture, biotechnology, genetic engineering. He developed a new two-semester course of lectures for masters and graduated students "Application of Biomaterials. He is research supervisor of 45 Ph.D. theses and 4 D.Sc. Author of more 850 articles, patents, theses, and 7 monographs. He was awarded The Leibnitz Medal, The Leonard Euler Medal, "Orden of Ehre" by European Academy of Natural Sciences.

The Effect of Assembly and Loading Methods on the Size Distribution and Uptake of Poly-N-vinyl-2-Pyrrolidone Thiooctadecyl Polymeric Nanocarrier

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Abstract

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 thiooctadecylnanocarriers 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.

Biography

Leonid Gurevich got his Ph.D.in Physics at the Institute of Solid State Physics (Chernogolovka, Russia) in 1994. During his postdoc stay at Delft University of Technology he became excited about nanotechnology and a possibility of charge transport through a single molecule. Currently, he is an Associate Professor at Aalborg University. His research interests include self-assembly phenomena in biophysics, nanotechnology in general and biosensors.

Biomaterials Based on Polyconjugated Systems

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Abstract

Various areas of polyconjugated systems application in medicine and biology are described. The relationship between the patterns of formation of chains containing a system of conjugated bonds with their properties, including biocompatibility, has been established. Questions of the kinetics and mechanism of oxidative polymerization, as well as theoretical approaches to calculating the molecular masses of polyaniline derivatives are considered. It is shown that the oxidative polymerization of aromatic amines is accompanied by frontal initiation, which is a consequence of the autocatalysis effect. The regularities of the interfacial polymerization of aniline and pyrrole at the solid/liquid interface are described, and the rate limitation of this reaction by monomer diffusion is proved. The possibilities of using composite materials and nanomaterials based on polyaniline and polypyrrole in imparting hemocompatibility to surfaces, as well as for delivery of biologically active substances, are shown. The prospects for increasing the response of nitrogen-containing electrically conductive polymers to various stimuli are discussed.

In connection with the growing interest in the pathologies of the metabolism of dopamine derivatives, the kinetic regularities of its oxidation by ammonium peroxodisulfate have been established and the first general order of this reaction has been shown. An approach to immobilization of dopamine on a copolymer of N-vinylpyrrolidone and allyl glycidyl ether has been developed, which makes it possible to form hydrogels in the presence of oxidants and transition metal ions. The resulting hydrogels were pH sensitive and degradable in aqueous media. In connection with the reversibility of the oxidative cross-linking of dopamine immobilization products in the presence of sodium periodate, assumptions have been made about the mechanism of dopamine oxidative polymerization.The work was supported by Mendeleev University of Chemical Technology of Russia. Project Number K-2020-001.

Biography

Mezhuev Yaroslav Olegovich was born in 1985 year, in 2008 year was graduated from D. Mendeleev University of Chemical Technology of Russia, where he continued his research activity. PhD from 2011 year, DSc from 2013 year, professor from 2016 year, specialist in the field of kinetics and mechanisms of macromolecules synthesis reactions as well as obtaining polymer composite materials for medical and biological purposes.

Polyvinyl alcohol polymer hydrogels for biomedical application

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Abstract

The necessity and relevance of development of new biocompatible materials stems from the existing high demand for such biomaterials from medicine, cosmetology, pharmaceuticals and biotechnology. The creation of new biomaterials for medical purposes and medical devices based on them, intended for contacting with organs and tissues of a living organism, is an extremely complicated task. The development of new medical materials for use in reconstructive and regenerative medicine is a particularly complex problem. Among the most prospective biomaterials for these purposes are hydrogels based on natural and synthetic polymers. However, the use of hydrogel materials is very limited because of a number of unresolved problems that lie both in the field of technology and materials science, and in the field of economics. Particularly, a significant limitation of the use of a number of very prospective hydrogel polymer systems is their low storage stability and low resistance to the main sterilizing factors, which does not allow for achieving their any widespread implementation in everyday clinical practice.

In an effort to overcome this obstacle and eliminate a number of other practically significant drawbacks, we have developed a method for obtaining polyvinyl alcohol hydrogels based on the crosslinking of its unsaturated derivatives in frozen water systems.

This approach made it possible to obtain polymer hydrogels that are stable even under thermal (steam) sterilization conditions, which are characterized by high biocompatibility, low toxicity, and biodegradability with the formation of non-toxic compounds within 4-6 months. The biodegradation rate depended on the site of implantation and the nature of the porous structure of the introduced. Tests carried out using experimental animals showed that a significant advantage of the developed hydrogel systems is an extremely mild inflammatory reaction, which makes it possible to regenerate not by the scar formation type, but with the formation of tissues and anatomical structures indinginous for the implantation site. A number of systems based on the obtained materials were proposed for use in ophthalmology, thoracic, abdominal and purulent surgery, some of which successfully passed the stage of clinical trials proving their high efficiency.

This work was supported by Russian Foundation to Basic Research 18-29-18039.

Biography

Artyukhov Alexander Anatolyevich - Professor of the Department of Biomaterials, Mendeleev University for Chemistry Technology of Russia. Research interests - synthesis and application of new polymeric materials, primarily hydrogels based on synthetic and natural polymers, in the fields of medicine and biotechnology. Author of over 140 scientific publications and patents.

Nanoscale Drug Carriers Obtained by Polymerization of Surfactant 2-Cyanoacrylate Monomers

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Abstract

2-cyanoacrylic acid esters are widely used to obtain polycyanoacrylate nanocapsules that are used as drug carriers. Its popularity is explained by ability to polymerize in an aqueous medium by the anionic mechanism without radical initiators giving biodegradable polymers. The study presents methods for preparation of nanocapsules with a partially crosslinked shell formed by surface active 2-cyanoacrylate monomers that are esters and adducts of 2-cyanoacrylic acid containing aliphatic and aromatic fatty moieties. This approach makes it possible to obtain nanoscaled carriers with sizes in the range from 20 to 200 nm. The introduction of two fatty substituents into the structure of the monomer allows to control the surfactant properties and obtain monomolecular Langmuir layers of high stability. The synthesis of 2-cyanoacrylate capsules is carried out in aqueous media and avoids the use of organic solvents, capsules are easily resuspended after lyophilization and do not exchange contents with each other and the environment. Capsules are suitable for clinical use. It's capable of biodegradation and excretion from the body, as well as the absence of toxicity of cyanoacrylates have been approved for medical application as components of surgical adhesive compositions. Thus, a method has been developed for the synthesis of surface active esters of 2-cyanoacrylic acid and adducts at the double bond of 2-cyanoacrylates, as well as methods for obtaining a wide range of hollow nanoparticle for drug delivery.

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

Biography

Luss Anna Leonidovna was born in 1991 year, in 2014 year was graduated from D. Mendeleev University of Chemical Technology of Russia. PhD from 2019 year, assistant professor from 2020 year, specialist in the field of composite biomaterials and nanoscale drug delivery systems.

Biodegradable Composite Materials for Reconstructive Surgery Containing Controlled Drug Release Systems

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Abstract

Recent studies demonstrated that biological inertness alone is not enough for the successful use of polymers for tissue substitution in restorative surgery. For example, in the case of reconstructive osteoplasty in the first period after the operation, the release of wound healing active is required, however for a longer period local release of morphogenetic proteins is necessary. The work studies approaches to the creation of biodegradable materials capable of releasing several active substances into the bloodstream, each with its own, independent release kinetics. The approach was studied using biodegradable foamy protein-polycyancarylate composite material applied for bone tissue substitution. It comprises porous poly-2-cyanoacrylate scaffold containing, collagen, bone morphogenetic protein (BMP) and insulin as wound healing stimulator. This combination of biologically active substances allows for local growth and differentiation of bone tissue osteoblasts, ensuring gradual substitution of the biodegradable implant with its own bone tissue. To ensure the independent release of drugs into the bloodstream, a combination of chemical methods of covalent binding of drugs to the scaffold material and physical encapsulation in polyethylene cyanoacrylate capsules with a permeable porous wall have been used. The rate of biodegradation was controlled by the addition of fluorinated hydrophobic cyanoacrylates. The efficacy was confirmed by in vitro experiments using tooth tissue cell cultures, as well as in vivo experiments on the model of bone union of the critical anastomosis of the rat tibia.

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

Biography

Dyatlov Valerie Alexandrovich was born in 1956 year, graduated from Moscow Mendeleev Chemical Technological Institute (D.Mendeleev University of Chemical Technology of Russia) in 1978. PhD from 1991 year, DrSc from 2016 year. Professor from 2016 year. Expert in the area of polysaccharides, drug delivery systems, cyanoacrylates and polymer composite materials for medical application.

Создание тест-систем для определения количества нейтрофильных внеклеточных ловушек.

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Abstract

Известно, что кровь человека и животных содержит нейтрофильные лейкоциты, которые играют важную роль в поддержании врожденного иммунитета. При воспалении они первыми приходят в очаг, где захватывают и устраняют микроорганизмы. Одним из способов ликвидации микроорганизмов является образование активированными нейтрофилами сетеподобных структур - нейтрофильных внеклеточных ловушек (НВЛ).

В системном кровотоке НВЛ могут механически нарушать кровообращение в тканях и органах и способствовать развитию и осложнению протекания различных патологических состояний.

Наиболее приемлемым и легкодоступным подходом в обнаружения НВЛ и подсчета их количества является метод,в основе которого использованы полимерные микросферы в качестве сорбента.Полистирол-метакриловые микросферы с диаметром 0,25 мкм были использованы для созданияполимерного сорбента, способ получения которого состоял в

следующем.На поверхность микросфер, содержащую карбоксильные группы, через стадию аминирования ковалентно иммобилизовали кислый аминополисахарид - гепарин. Гепарин, благодаря своему строению, а именно содержанию отрицательно заряженных сульфогрупп, должен электростатически взаимодействовать с положительно заряженными белками-гистонами в составе ловушек. В таком случае диагностикум, полимерная микросфера-гепарин, будет сорбироваться на поверхность ловушек, оседать за счет повышенной массы и систему диагностикум-НВЛ можно отделить и измерить количество ловушек.

Для определения количества и состава НВЛ методом конфокальной микроскопии былииспользованы полимерные микросферы диаметром 140 мкм с аминогруппами на поверхности. Для специфического связывания НВЛ из цельной крови был выбран гепарин, который способен связываться с гистонами, входящими в состав НВЛ. Полимерные микросферы, содержащие иммобилизованный гепарин, после добавления цельной крови, окрашивали этидий бромидом после добавления цельной крови. Анализ профиля интенсивности флуоресценции показал, что на поверхности этих микросфер закрепляются гистон содержащие нити ДНК. Таким образом, было показано, что полистирольные микросферы диаметром 140 мкм, содержащие ковалентно иммобилизованный гепарин, могут быть использованы в качестве сорбентов для выделения и анализа гистон-содержащих ДНК-структур. Показано наличие зависимости между количеством НВЛ, содержащихся в цельной крови, и интенсивностью флуоресценции.

Biography

Сиваев Андрей Александрович в 2019 году окончил ФГБОУ ВО «МИРЭА -РТУ» по программе подготовки научно-педагогических кадров в аспирантуре по направлению подготовки «Химические науки». Защитил диссертацию на соискание учёной степени кандидата химических наук на тему «Функциональные полистирольные и полиглицидилметакрилатные микросферы, получение, модификация и свойства для создания диагностических тест-систем» на кафедре химии и технологии высокомолекулярных соединений имени С.С. Медведева Института тонких химических технологий имени М.В. Ломоносова ФГБОУ ВО «МИРЭА -РТУ»

New Initiating System for the Polymerization of Formaldehyde Based on Ionic Liquid and Elemental Sulfur

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Abstract

High-molecular compounds synthesized by the mechanism of anionic polymerization are widely used for medical purposes. For example, polyformaldehyde is used to create bone implants.

It is known that ionic liquids can act as a green alternative to traditional organic solvents, including the ones used in the process of polymerization of electron-deficient monomers, such as methyl methacrylate.

This paper reports on the preparation of a new initiating system based on dimethylphosphate-containing ionic liquids and elemental sulfur for the synthesis of polyoxymethylene that meets the principles of green chemistry.

The initiating system was obtained as follows:

50 ml of benzene was poured into a round-bottom flask 1.5 g of S_8 powder was dispersed on a magnetic stirrer, and then tri-n-butylmethylphosphonium dimethylphosphate or 1,3-dimethylimidazolium dimethylphosphate was added in an equimolar amount relative to sulfur. After mixing the reagents, the sulfur was dissolved and the brown color of the reaction system deepened. A denser dark red reaction product was accumulating at the bottom. The reaction product was isolated by separating the lower layer on the dividing funnel.

The reaction of elemental sulfur with dimethylphosphate-containing ionic liquids proceeds by the mechanism of nucleophilic attack by the oxygen atom of the dimethylphosphate anion on the S_8 cycle. The product of sulfur oligomerization was found

to be active in initiating the anionic polymerization of a number of electron-deficient monomers, including formaldehyde. The isolated formaldehyde oligomerization product was characterized by IR, ^{1}H NMR, ^{13}C NMR, HSQC and HMBC spectroscopy.

The work was supported by Dmitry Mendeleev University of Chemical Technology of Russia. Project number 2020-040.

Biography

Natalia Pavlovna Tarasova was born in 1948, in 1972 graduated from Moscow Institute of Chemical Technology named after D. I. Mendeleev (now D. Mendeleev University of Chemical Technology). In 1982 she graduated from Moscow Institute of Electronic Machinery Building (MS in computational mathematics). She holds PhD in Radiation Chemistry (1976), DSci in inorganic chemistry (1994), both from Mendeleev University where she continues her research in green chemistry for sustainable development. She is the corresponding member of the Russian Academy of Sciences (1997), division of chemistry and material sciences.

Aspects Of Aerogels Biomedical Appications

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Abstract

Due to numerous unique properties of aerogels they can be applied in a various industries - from space industry to medicine. Mechanical strength, low density, large surface area and open pore structure allow aerogels to be considered as materials for artificial valve flaps of prosthetic heart. Aerogels can serve as matrix carriers of drugs, cells and metal compounds, providing controlled delivery and prolonged release of their components.Traditional method of aerogelsobtaining is lyophilic (cryogenic) drying. This method allows to avoid capillary forces influence on gel structure. However, this method has a significant limitation –gels must be water-based before drying.Another method – supercritical drying technology has restrictions related to the stage of initial organic solvent replacing before supercritical drying. As a result,physical and chemical properties of gels and aerogelscan be possibly changed.Alginate-based aerogels are of interest to pharmaceutical industry and medicine because of their proven reparative, hemostatic and anti-inflammatory properties.However, clinical applicationof aerogels is still limited.

Aerogels can be obtained from insoluble gels bymixing of sodium alginate aqueous solutions with solutions containing calcium ions (for example, calcium chloride). In addition, it is possible to replace traditional crosslinking agents based on calcium salts with water-soluble lanthanide salts, for instance, cerium salts, which have regenerative properties, tissue-preserving, and anti-inflammatory effects in local treatmentof burn wounds.

Despite of aerogels undeniable potential in terms of biomedical applications, they must be effective and safety. However, when obtaining these materials using supercritical drying technology, special attention should be paid to initial components selection, their combination with various solvents, and removing these solvents from pores ofobtained gel.

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