ABSTRACT

to the dissertation for the degree of Doctor of Philosophy (PhD) in the educational program

"6D074000 – Nanomaterials and nanotechnology".

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on the topic "Synthesis and application of modified nanocellulose in biomedicine"

General characteristics of the work. The dissertation work is devoted to the development of modified nanocellulose materials for biomedical use with medicinal properties and their laboratory study of effectiveness.

Relevance of the research topic. In recent years, interest in biocompatible and biodegradable materials has increased significantly as they offer promising solutions for various medical applications, including tissue regeneration, drug delivery and implants. Nanocellulose, due to its unique properties, occupies a leading position in this area. Nanocellulose is a material consisting of nano-sized cellulose fibers that can be obtained from various biological sources. It has high strength and rigidity, chemical inertness, biodegradability and biocompatibility.

Nanocellulose synthesis processes face a number of important technical and economic challenges that must be taken into account during development and scale-up. One of the main problems is the high cost of producing nanocellulose, especially when using traditional mechanical grinding methods.

An interesting method for the production of nanocellulose is the use of bacteria of the genus Gluconacetobacter, especially species such as Gluconacetobacter xylinus, known for their ability to synthesize bacterial nanocellulose from sugar solutions. These bacteria can produce pure, high molecular weight cellulose with unique properties such as high tensile strength, flexibility and the ability to form gel-like structures.

Research is aimed at optimizing the composition of nutrient media to increase the yield and quality of cellulose produced. Genetically modifying bacteria can improve their productivity and adapt them to use different substrates, including agricultural or food processing waste such as nitrogen-containing waste. Developing more efficient processes could reduce the cost of producing bacterial cellulose, making it more accessible for widespread use.

Changing the structure and composition of modified nanocellulose makes it possible to optimize its mechanical, thermal and chemical properties. The development of modified nanocellulose based on bacterial nanocellulose (BNC), combining other polysaccharides and inorganic substances, opens interesting possibilities for controlling the physicochemical properties of these composites. This allows the development of materials with specific functional characteristics tailored to specific applications in biomedicine, biotechnology and other technological fields.

The aim of the work Obtaining modified nanocellulose by changing the nitrogen content in the standard Hestrin-Schramm nutrient medium and studying its physicochemical properties.

Work objectives. To achieve the goal of the dissertation work, the following tasks are set:

1. Obtaining bacterial nanocellulose by changing the nitrogen content in a standard Hestrin-Schramm nutrient medium using a synthetic method, as well as determining the morphological structure and characteristics of the resulting nanocellulose using physicochemical research methods.

2. Obtaining a modified biocomposite by adding aloe vera extract to the nutrient medium and studying its mechanical and physicochemical properties.

3. Preparation of a biocomposite with antibacterial properties by introducing a silver particle into a modified nanocellulose matrix using the hydrothermal reduction method and studying its physicochemical properties.

4. Determination of antibacterial activity and adsorption-desorption properties of a modified biocomposite based on nanocellulose.

Basic provisions for defense:

1. Bacterial nanocellulose, synthesized at a concentration of glucose 20 g/l and rice bran 5 g/l at a temperature of 30°C, has the following physicochemical properties: water absorption - 20 ml/g, average diameter of nanofibrils - 95.5 nm, diameter pores – 24.5 nm, surface area – 11.4 m^2/g, tensile strength – 45.41 MPa, elongation rate – 2.71%, Young's modulus – 163.5 MPa. The high surface area of nanocellulose allows for the efficient delivery of polysaccharides, allowing it to be used in biomedicine for wound healing and drug delivery.

2. The modified biocomposite obtained by adding 30% aloe vera extract has the following improved properties: water absorption increases by 0.5 ml/g, tensile strength increases by 32 MPa, elongation increases by 4.66%, Young's modulus increases by 16.8 MPa, the surface area increases by 3.5 m2/g, the average diameter of the nanofibers decreases by 23.5 nm, and the pore diameter decreases by 10 nm. These properties make it suitable for use in wound dressings and drug delivery systems due to its improved elasticity, strength and adsorption properties.

3. The introduction of silver particles into the modified nanocellulose matrix using the method of hydrothermal reduction at a temperature of 60°C led to the production of a biocomposite with a high level of antibacterial activity against the Bacillus strain: the diameter of the growth inhibition zone of the test strains was 12±1 mm. This allows this material to be used as an effective means for preventing infections and protecting medical devices.

4. The modified biocomposite based on nanocellulose showed the following adsorption-desorption properties: adsorption time for organic oils - 120 minutes, desorption time for aloe vera extract - 75 minutes, essential oil - 90 minutes, organic oil - 300 minutes, buffer solution with pH 6 These properties make it an effective tool for repairing damaged tissue, skin regeneration and drug delivery.

The object of the study is acetic acid bacteria, bacterial nanocellulose products, as well as experimental samples of a modified biocomposite containing aloe vera extract, silver particles and antibacterial properties.

The subject of the study Synthesis of modified nanocellulose.

Research methods

The following research methods were used in the work: IR spectrum "Specrum 65 FT—IR spectrometer" (Simex, Russia), X—ray diffractometric analysis on a Dron—4 diffractometer ("Petrel", Resen), ultraviolet (UV) spectroscopy Varian Cary 500, (USA), tensile strength VEM10ST.300 Tinius Olsen (UK), scanning electron microscopy Quanta 3D 200i Dualsystem FEI (USA), Brunauer—Emmett—Teller method (BET) 3H—2000ps (Beijing, China), determination of the contact angle on flat surfaces DSA—25e "Kruss", (Germany) and statistical methods for processing experimental data.

Scientific novelty of the work

In this work, the following results with scientific novelty were obtained:

1. For the first time, bacterial nanocellulose was synthesized at a temperature of 30°C and a synthesis time of 7-9 days using the Gluconacetobacter xylinus strain and rice bran as an alternative source of nitrogen. The crystal size was 11 nm.

2. For the first time, aloe vera extract was added to obtain a new modified biocomposite, resulting in improved elasticity, flexibility of the material, ability to stretch and bend, and also increased its chemical resistance.

3. The introduction of silver nanoparticles with a diameter of ~90 nm into the biocomposite matrix by hydrothermal reduction at a silver ion concentration of 0.0001 M significantly improved the antimicrobial activity, mechanical strength, biological activity and thermal stability of the material.

Theoretical significance.

The theoretical significance of the thesis is to fill the gap in the use of nanomaterials for the development of new dressings with improved therapeutic and preventive properties. This includes expanding our knowledge of how nanomaterials affect biological skin cells, increasing the efficiency of their use and the use of natural ingredients to create innovative and safe remedies for the treatment of burns and skin diseases.made of BNC and natural polymers, they have high biocompatibility and are able to decompose without contamination.

Practical significance

From a practical point of view, the importance of the work lies in the creation of modified coatings based on bacterial nanocellulose from natural raw materials that have the ability to stimulate regenerative processes, promote the restoration of the basement membrane and accelerate epithelialization and scarring of wounds, as well as burns treated with such coatings heal faster and leave fewer scars. The results obtained in the work can be used for lecturing and conducting practical classes on industrial biotechnology and the specialty OP "8D074000-Nanotechnology and nanomaterials" in higher educational institutions.

The personal contribution of the doctoral student. In the course of independent research, the doctoral student performed a search and analysis of literary data. Conducted experimental research in accordance with the set goal and objectives. He conducted a theoretical and practical analysis of the obtained research results, summarized them in the form of a dissertation work.

Publications.

Publications

Based on the materials of the dissertation work, 11 scientific papers were published, including 2 articles in journals included in the Scopus database (Digest Journal of Nanomaterials and Biostructures and Int.J. Nanosci. Nanotechnol.), 4 publications in journals recommended by the Control Committee in sphere of education and science of the Republic of Kazakhstan, including “Science News of Kazakhstan” and “Industry of Kazakhstan”. Materials have also been published at international scientific and practical conferences and symposiums, such as the XI International Symposium “Combustion and Plasma Chemistry” (Almaty, November 20-22, 2019), Student Electronic Scientific Journal (2021), “New Polymer Composite Materials. Mikitaev Readings" (July 3-6, 2022), International scientific and practical conference "Resource-saving technologies in the mineral-industrial mega-complex in conditions of sustainable economic development" (Almaty, March 14-15, 2024). One project for a utility model was received in the Republic of Kazakhstan for 2023-2025, project “IRN AP19679937 “Synthesis and properties of hybrid gels based on cellulose nanofibers with tetracycline/CuO nanoparticles and alginate” (2023-2025, Ministry of Education and Science of the Republic of Kazakhstan)” (executor).

Research results

1. At a glucose concentration of 20 g/L and rice bran of 5 g/L at a temperature of 30°C and a synthesis time of 7-9 days, bacterial nanocellulose with an average nanofiber diameter of 95.5 nm was synthesized. X-ray spectroscopy showed a crystallization degree of 87% and an α-cellulose content of 93.9%, indicating a triclinic structure of Iα. IR spectroscopy revealed the presence of absorption bands of amino acid groups, indicating the presence of a nitrogen source in the rice bran nutrient medium. The presence of amino acid groups increases the biological activity of the material and its ability to interact with biomolecules.

2. A modified biocomposite based on nanocellulose was obtained with the addition of 30% aloe vera extract at a temperature of 30°C and a synthesis time of 7-9 days. SEM results showed that the diameters of the fibers in the structure of the modified biocomposite are 20-145 nm. IR spectroscopy revealed absorption bands of acetyl groups at 1750-1500 cm^{-1}, which confirms the presence of acemannan from aloe vera. Acemannan acts as a natural plasticizer, improving the elasticity and strength of the biocomposite. The presence of acemannan improves the interaction of the material with living tissues, which is important for biomedical applications.

3. Silver ions in concentrations of 0.01 M, 0.001 M and 0.0001 M were introduced into the biocomposite matrix using the method of hydrothermal reduction at a temperature of 60°C. To obtain silver nanoparticles with a diameter of ~80 nm, a

solution with a silver ion concentration of 0. 0001 M. IR spectroscopy showed a significant decrease in the intensity of absorption bands at 3304.06 cm^{-1} - 3295.18 cm^{-1}, 1745.02 - 1740.98 cm^{-1} and 1647.27 - 1642.98 cm^{-1}, which indicates the replacement of hydrogen atoms with silver ions. Using the disk diffusion method, it was found that the diameter of the growth inhibition zone of the test strains of Bacillus subtilis is 12±1 mm, which indicates a decrease in the number of bacteria Staphylococcus aureus, Bacillus subtilis, Escherichia coli and Candida albicans.

4. A modified biocomposite based on bacterial nanocellulose with antibacterial properties showed a sorption time for organic oils of 120 minutes, a desorption time for aloe vera extract of 75 minutes, essential oil of 90 minutes, organic oil of 300 minutes, at a buffer solution pH of 6. This makes it an effective remedy. for the restoration of damaged tissues, skin regeneration and drug delivery based on adsorption-desorption processes.

Structure and scope of the dissertation

The dissertation is completed on 120 pages (without appendices) and contains 49 figures and 16 tables. The work consists of an introduction, literature review, experimental methodology, results and discussion, conclusion and a list of used sources of 196 titles.