Ministry of Education and Science of Ukraine
Vinnytsia National Technical University

Lecture notes
for the discipline
"Biochemistry"
Module "Biomaterials"
for applicants for higher education in the specialty
163 – Biomedical Engineering





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Lecture 1. The concept of biomaterials and their application in medicine.

The use of materials to replace and restore bone tissue began more than 2,000 years ago, and research in this area is still ongoing. The main feature of the new millennium is the growing interest in increasing the quality and duration of human life. Thus, the XX century was marked by a sharp leap in the field of biomaterials for the replacement and restoration of bone tissue, which is associated with the use of hydroxyapatite (HAP) as a bone implant. Innovative application of specially designed ceramic materials for the treatment of diseased or damaged parts of the body opens the way to increase the period of active human life. This area of modern materials science is called bioceramics. It includes materials for endoprostheses in traumatology and orthopedics, filling materials in dentistry, implants in maxillofacial surgery, medical and cosmetic products.

All of us from childhood are familiar with the characters from the fairy tale by Lyman Frank Baum "The Wonderful Wizard of Oz", in which the Scarecrow dreamed of brains, and the Iron Lumberjack - of the heart. There were other characters who would like to get their bodies back, such as Robocop and Professor Dowell. They could be helped by modern developments in the field of biomaterials (Fig. 1.1).

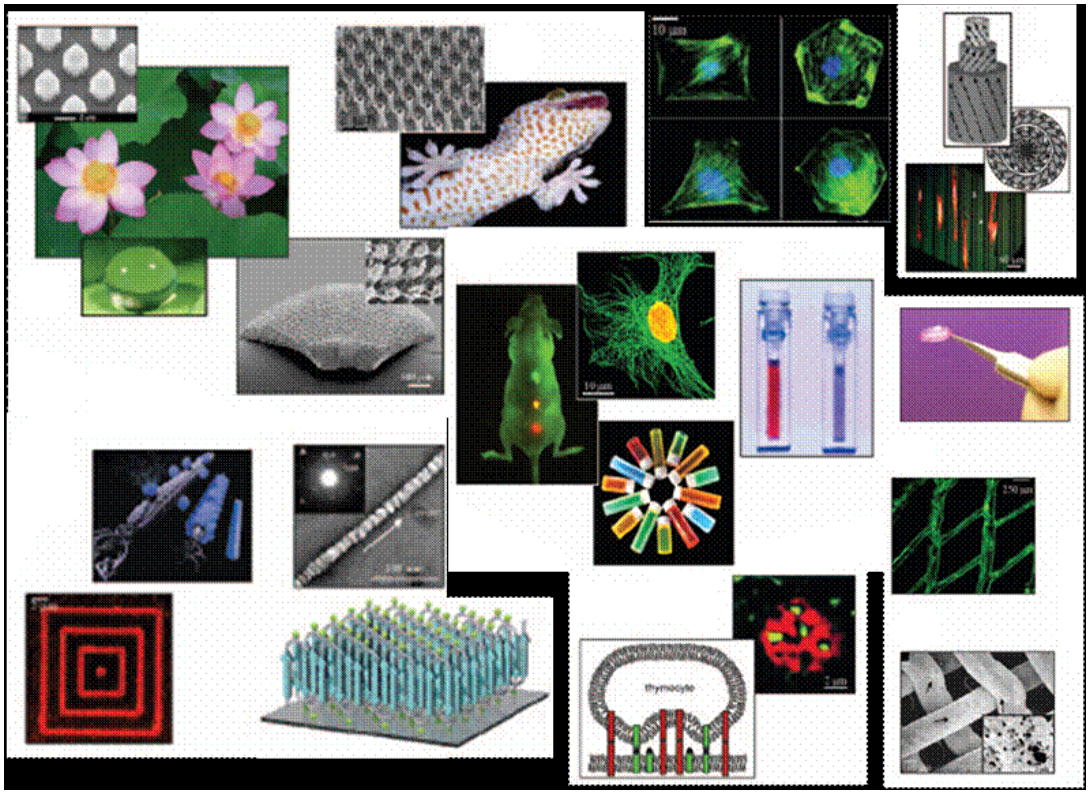


Fig. 1,1. Diversity of biomaterials

Biomaterials are materials designed to replace damaged parts of the body, their individual organs and tissues (Fig. 1.1). For example, a fracture or injury to a bone leads to the need to replace the damaged area with an artificial implant.

Since the first attempts to use calcium phosphates in medicine, the concept of using biomaterials has undergone significant changes. The so-called regenerative approach came to the fore, in which the emphasis is on replacing the biomaterial with native (own) growing bone, the material is assigned the role of (active) source of elements necessary for the construction of bone tissue. It is expected that the "ideal implant" should gradually dissolve in the body, while performing its supporting functions, and in its place should form new bone tissue. Obviously, the resorptive function (dissolution) of the biomaterial is extremely important for the successful integration (introduction) of the material into the body. The rate of bone regeneration depends on several factors, such as porosity, composition, solubility and the presence of certain chemical elements that are obtained during the development (dissolution) of ceramic material, facilitating bone regeneration by special cells, osteoblasts. In comparison with actively used in medical practice calcium hydroxyapatite Ca_{10} $(PO_4)_6$ $(OH)_2$ (HAP), a material based on nanoscale carbonate-containing hydroxyapatite Ca_{10}-xNax $(PO_4)_6$-x (CO_3) x $(OH)_2$ KDAP). It has a number of advantages: more accurately reproduces the composition of bone tissue in comparison with HAP and has increased bioresorption and osteoinduction. This means that the implant with nano-KGA (Fig. 1.2, 1.3), gradually dissolving, will be replaced by a newly formed, natural bone, which will completely replace the implant.

With the development of bioengineering technologies it will be possible to create bone tissue in a natural biological way using stem cells. For example, it will be possible to create dental germs that will germinate naturally after implantation. However, according to forecasts, in the coming decades, only biomaterials of artificial (synthetic) origin will be actually available.

The production of modern biomaterials is regulated by the international standard DIN VDI 5701-2018 Biomaterials in medicine - Classification, requirements, and applications.

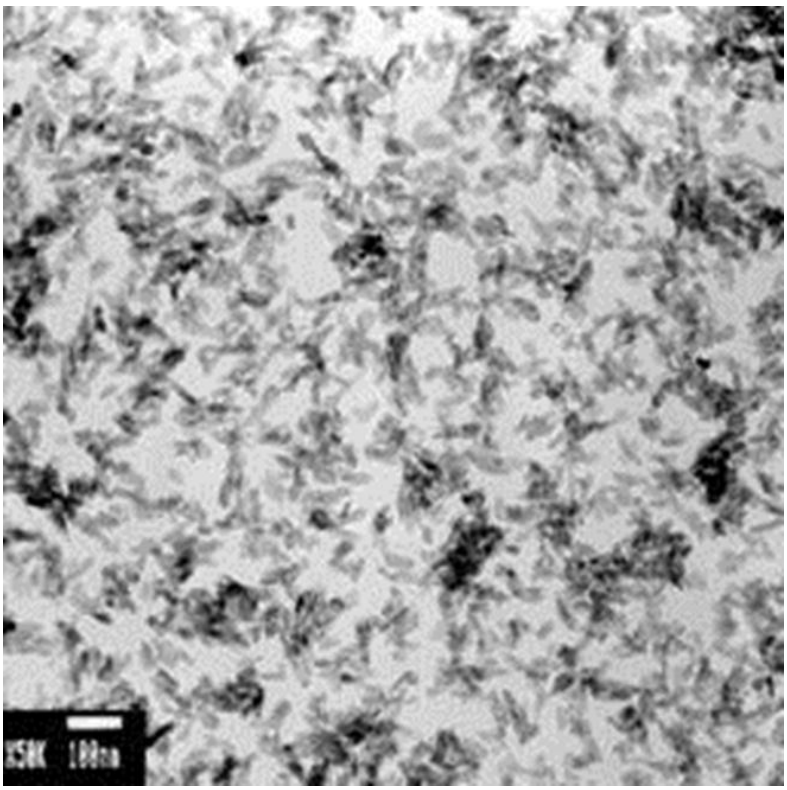


Fig. 1.2. Micrograph of nanocrystalline carbonate hydroxyapatite

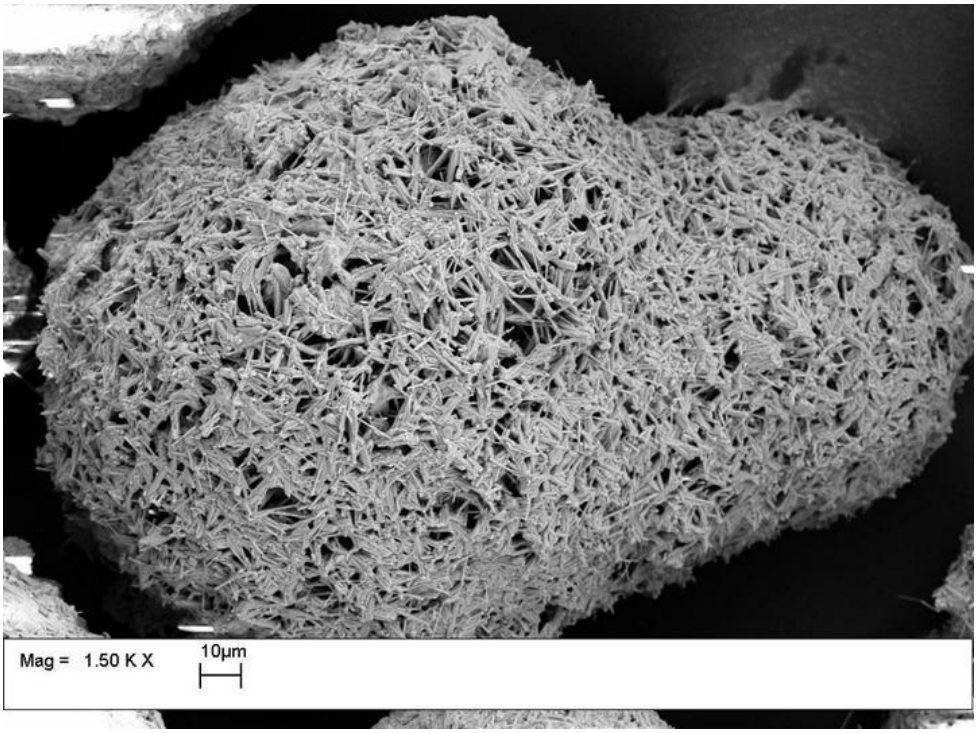


Fig. 1.3. Microphotograph of a ceramic granule of nanocrystalline carbonate hydroxyapatite ("mini implant")

Materials used in ophthalmology

In ophthalmology, polymers are most often used for the manufacture of contact lenses, artificial lenses, for the replacement of parts of the cornea, for the manufacture of eye prostheses.

An eye prosthesis is an implant that looks like the front of a person's eye. They fill the space in the orbit that is released after the removal of the eyeball.

Brief historical background.

30-40 years of the XIX century, Germany, USA - production of prostheses from silicate glasses

The first half of the twentieth century - tested aluminum, rubber, ivory, porcelain and other materials.

1944, England - developed technology for the manufacture of eye prostheses from polymethyl methacrylate.

Currently, prostheses with 26 colors of the sclera and 105 colors of the iris have been developed.

Contraindications to the use of artificial eyes made of glass - hypersensitivity to the prosthesis material.

In recent years, eye prostheses made of Teflon and silicone rubber have been developed and used. The peculiarity of these materials is that they are heat resistant. Therefore, their repeated sterilization is possible.

The advantage of plastic prostheses:

1. durability,

2. lower thermal conductivity than glass prostheses,

3. can be made of any complex shape.

An intraocular implant with a magnet was created. The disadvantage of this prosthesis is its increased mobility.

There are known cases of using silicone rubber for prosthetics.

Contact vision correction

Contact lenses worn directly on the cornea must be permeable to oxygen, resist deforms whose action eyelids during blinking and well moistened tearfully th fluid. The possibility of using a contact lens is determined by its interaction with the cornea. One of the functions of the corneal epithelium is to extract oxygen from the air and transfer it through the tear fluid to replenish the energy of metabolism. If the cornea is not provided with sufficient oxygen, then there is an accumulation of lactic

acid, the epithelium swells, the cornea thickens. The consumption of oxygen by the corneal epithelium is 3.5 μl / cm2 h . To transfer this amount of oxygen, the partial pressure in the corneal epithelium should be 15-20 mm. rt. Art. This calculation fully applies to contact lenses. When wearing them, the consumption of oxygen by the cornea should not change.

Modifications of contact lenses:

1. Hard. Made of polymethyl methacrylate. They have good physicochemical, optical properties, are physiologically inert and are easy to cut. The exchange of lacrimal fluid occurs during blinking. The tear fluid brings new portions of oxygen, so it is not lacking.

H edoliky, they are limited in the number of hours ; they require careful fitting of size and shape.

Currently, a number of other materials are used, in particular, polymer floor and - and acetobutyrate - cellulose.

P erevaha: permeability of oxygen in them 100 times higher than that of methyl methacrylate.

2. M ' as and . Made of hydrogels by the method of reaction injection molding.

P erevahy, less visible on the cornea without causing discomfort and irritation.

H edoliky, less transparency, less durability than hard lenses.

Hydrogels are soft elastic materials that are crosslinked polymers swollen in water. In arid conditions get glassy polymer from which the lens is cut, and their agricultural and dratuyut b to form to form soft elastic gel.

The material for soft contact lenses is aqueous collagen, the main component of which is Poly-HEMA.

Soft's contact lens thickness 0,03-0,05 mm, made of siloxane rubber on kisnet penetration knosti far superior lenses with other polymers.

H edoliky: poor wetting, uncomfortable for extended wear.

Blood substitutes

Blood substitutes are materials that are used for the necessary time for therapeutic purposes as substitutes or correctors of blood composition. They are used for transfusion therapy in various pathological conditions.

The drugs used are divided into six groups:

1. blood substitutes with the function of oxygen transfer

2. regulators of acid-base and water-salt balance

3. anti-shock

4. for the treatment of intoxications

5. drugs for parenteral nutrition

6. drugs of complex action.

Requirements for blood substitutes:

1. Drugs must be completely eliminated from the body.

2. Should not cause sensitization of the body.

3. Must be non-toxic.

4. Should not change the physicochemical properties.

Materials for artificial skin design

The problem of obtaining artificial skin is associated with the need to treat burns, injuries, injuries.

The material of artificial leather must meet the following requirements:

1. prevent dehydration injuries of dehydrated parts of the body,

2. promote the transmission of water vapor

3. prevent the penetration of microorganisms into the wound

4. Promote faster regeneration Brief historical background

1962 - the use of formalin sponge made of polyvinyl alcohol. The experiments were also performed with a silicone sponge and polyurethane foam. The silicone sponge does not take root well, the polyurethane foam takes root well, but a week later it completely disintegrated as a result of hydrolysis.

As implants are used:

1. gauze made of nylon and silicone

2. ultra-thin gas-permeable films of unfilled silicone rubber

3. films obtained by hardening of blood plasma

4. fibrin films

5. gauze treated with fats

The methods of treatment using poly-2-ca si metakr a patch and polyethylene glycol, and non-woven fabric of collagen.

The benefits of collagen ovoho nonwoven fabric, well considered living organism is not immune activity , with you ooze Yue tissue regeneration, good adhesion to the surface of the wound, hatrna adsorption fluid, lung scarring, no rejection and inflammation .

When using Poly-HEMA and PEG, PEG is applied to the wound surface and sprinkled with Poly-HEMA powder. The polymers cover the wound with a film.

Advantages of a film: elastic, capable to pass water vapors, simplicity of diffusion of the dissolved substances through a film, does not pass microorganisms, interferes with development of microflora.

Artificial membranes based on siloxane elastomer can function similarly to human second skins and .

Single-layer and multilayer membranes of various designs are currently being developed. For example, single-layer membranes made of siloxane rubber with multiple channels for drug administration are used. The outer layer of the membrane is made of transparent siloxane elastomer and is designed to protect the wound from infection and dehydration, and the lower layer is a porous polymeric material based on collagen. This two-layer membrane does not need to be removed and replaced with a new one. It can remain on the wound for fifty days - a period sufficient for the healing of small burns . After the wound has healed, the top layer is involuntarily removed as the skin grows, and the bottom is broken down by enzymes. Healing of large wounds is slower than the destruction of the membrane, so it must be removed and replaced. On the surface roses on the work of men between the village yloksanov im elastomer coating of collagen and epidermis placed cial skin cells.

Lecture № 2 . Biocompatibility of materials.

Biomaterial - material from living tissues, synthetic or natural, used in a medical device or in contact with biological systems. Biomaterials are designed to replace damaged parts of the body: their individual organs and tissues.

Biomaterial - material for cytological or cytogenetic studies. It can be taken from a patient with the help of a fine-needle puncture biopsy, an imprint on a glass slide from the cut surface of the organ and with the help of special tools.

Grafts - organs and tissues transplanted from the patient or his close relatives (eg, kidney, bone, skin). In this case, the problem of compatibility of the material either does not arise, or, conversely, the body is rejected, but with a successful result, it fully provides the necessary functioning.

Implants are "inanimate" materials that are not directly related to the body: polymers, ceramic blocks, coral skeletons, and so on. In the case of implants, the problem of genetic incompatibility of the material does not arise, the question arises about its fundamental toxicity or biocompatibility. Implants can be manufactured in any quantity to meet the required demand, which is their undoubted advantage, but they are not able to fully restore the functions of the replacement organ.

Depending on the reaction of the tissue to the implant, there are 4 categories of materials:

- toxic (kill surrounding tissues);

- inert (around such in the body fibrous non-adjacent tissue is formed);

- bioactive (there is an adjacent interfloor connection of material and fabric, encapsulation is minimal);

- bioresorption (material as it dissolves is replaced by tissue of the host organism, the products of dissolution must be non-toxic).

The above categories of materials, with the exception of toxic, belong to the class of biocompatible.

The concept of biocompatibility refers to the interaction between the tissues and physiological systems of the patient and the device treated with a medical device. The biocompatibility assessment is part of the overall safety assessment of the material (device).

The biocompatibility of medical devices has been investigated using analytical chemistry, in vitro tests and animals. The biocompatibility of the device depends on the following factors:

- chemical and physical structure of component materials

- the types of tissues of the patient that are exposed to the device

- exposure time for this unit

The assessment of the biocompatibility of the medical device is actually made to ensure patient safety. When programming a biocompatibility test, manufacturers must consider their objectives and compliance risks. In fact, the assessment of the biocompatibility of a medical device is a risk assessment study. All medical devices contain a degree of risk. When developing medical devices, companies try to minimize these risks and maximize the benefits they provide to patients.

The main standard for biocompatibility testing is the ISO 10993 standard. This standard is also published by the Turkish Standards Institute (TSE) in our country: TS EN ISO 10993 Biological assessment of medical devices. The first part of this standard is a test selection guide. The second part contains requirements for animal welfare. The following sections address specific testing processes and other test-related issues. The full list of the standard is as follows:

Section 1: Evaluation and experiment

Section 2: Animal welfare requirements

Section 3: Genotoxicity, carcinogenicity and reproductive toxicity test

Section 4: Selection of blood interaction experiments

Section 5: Body-free cytotoxicity assays

Section 6: Experiments on local exposure after implantation

Section 7: ethylene oxide sterilization residues

Section 8: Selection and properties of reference materials for biological experiments

Section 9: Research to identify and quantify potential degradation products.

Section 10: Experiments on skin irritation and sensitivity

Section 11: Systemic toxicity tests

Section 12: Sample preparation and reference materials

Section 13: Identification and quantification of decomposition products of polymer medical devices.

Section 14: Identification and quantification of ceramic decomposition products

Section 15: Identification and determination of degradation products of metals and their alloys

Section 16: Design of toxicokinetic studies for decomposition products and soluble products.

Section 17: Determination of permissible limits for leachates

Section 18: Chemical properties of materials

Biocompatibility test data are almost always required for devices with significant contact. To determine whether a medical device requires a biocompatibility test, the biocompatibility matrix of the ISO 10993-1 material is used.

If the manufacturer has data from previous deliveries, data from companies supplying materials or components, analytical data and clinical data, the number of tests will be slightly reduced.

The main purpose of the ISO standard is to check the suitability of the device for its purpose. In this process, biological testing is the most important step in assessing biocompatibility. The standard classifies devices according to the type and duration of body contact. It also contains a list of potential biological effects. Manufacturers are required to collect safety data for all components and materials used in the medical device.

Biocompatibility - the ability of the material to be incorporated into the patient's body, not to cause clinical side effects and to induce a cellular or tissue response necessary to achieve the optimal therapeutic effect.

Requirements for modern biomaterials are formed and change with the development of medical and diagnostic technologies. Initially, the main requirement for materials was safety, which was achieved due to their chemical and biological inertness. Materials had to be non-toxic, non-carcinogenic, non-allergenic, non-thrombogenic. This list of missing properties defined the concept of biocompatibility. Materials of this type include metal alloys based on titanium and platinum, polymers based on polyethylene and silicone.

Chemical biocompatibility requirements: non-toxicity, corrosion resistance, hypoallergenicity. Mechanical compatibility requirements: low modulus of elasticity, as close as possible to the modulus of elasticity of human bones, which does not exceed 30 GPa; resistance to cyclic loads, which shows how many cycles (movements) can withstand a structural implant to failure; significant reversible deformation, as this figure for human bones is about 4%. Requirements for physical compatibility: high X-ray contrast, which is necessary for proper installation of the structure; low magnetic susceptibility, which is caused by the increasing use of magnetic resonance imaging in diagnosis; low density. Implant materials must be much stronger than any human tissue, because in many cases they carry the same load at a much smaller size than biological tissues. On the other hand, these materials must be ductile, as they almost always have to withstand a large deformation to be able to give the products the desired / desired shape and size.

Information on the biocompatibility of metals can be obtained by analyzing the solubility of their neutral hydroxide and determining the size of the pH range in which this neutral hydroxide predominates.

The creation of semi-finished biocompatible materials is a significant step in the development of high technologies that will be able to meet both the needs of domestic medicine and become competitive globally. At present, biocompatible metal structures for domestic medicine are purchased abroad. This direction of development of medical materials science has significant prospects and is important for Ukraine in the field of minimally invasive interventions.

Lecture № 3. Bioceramics.

Bioceramics and bioglass are biocompatible ceramic materials. Bioceramics is an important subset of biomaterials. Bioceramics are used in many types of medical procedures, in particular as rigid materials for surgical implants, although some types of bioceramics are flexible.

Now ceramics are widely used in medicine as dental and bone implants. Surgical cermets are used all the time. Artificial joints are usually covered with bioceramic materials to reduce wear and prevent inflammatory reactions of tissues. Other examples of applications in medicine include elements of bioceramics in the design of pacemakers, artificial kidney apparatus and respirators. The global market for medical ceramics and ceramic components was valued at approximately $ 9.8 billion in 2010. The projected annual growth of 6-7% in the coming years, the world market value will increase to $ 15.3 billion by 2015 and reach $ 18.5 billion by 2018.

Mechanical properties.

Bioceramics are intended for use in extracorporeal circulation systems (for example in dialysis) or special bioreactors; however, they are most often used as implants. [7] Ceramics are widely used as biomaterials due to their physicochemical properties. Its main advantages are bioinertness in the human body, hardness and resistance to wear, which makes it useful for bone implants and dentures. Some types of ceramics also have good friction resistance, which makes it possible to use it as a material to replace damaged joints. Properties such as appearance and electrical insulation are also of particular interest for specific biomedical applications. Examples of bioceramic products are shown in Figures 3.1 and 3.2 .

Bioceramics is a subspecies of ceramic materials that are designed specifically for medical and dental purposes. It consists of aluminum and zirconium, bioactive glass, coatings and composites, hydroxyapatite, resorbable calcium phosphate and X-ray contrast glass particles. Bio ceramics are widely used in the restoration of joints, for biocoating of implants, and as resorbable membranes that support a certain amount of space for a limited period of time.

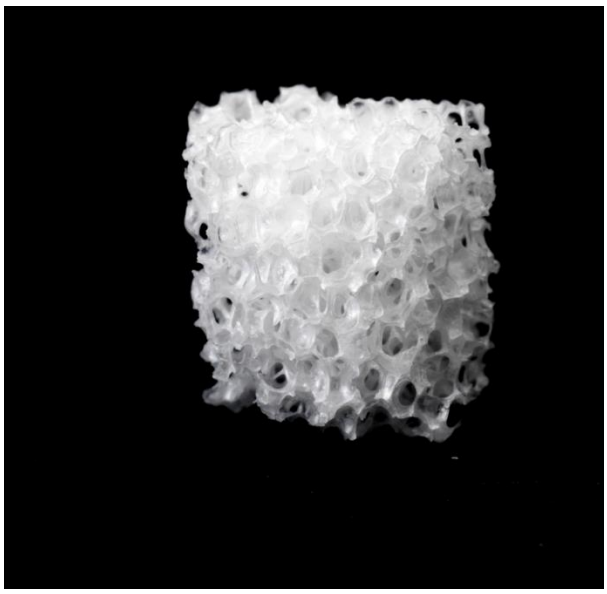


Fig. 3.1. Porous bioceramic granule



Fig. 3.2. Titanium hip arthroplasty with a ceramic head and a polyethylene acetabular bowl

Bio ceramic Ichnya materials classi th appear on the:

- would ioinertni - does not enter tion interact with biological systems;

- bioactive - resistant and tissues as and differs th ARE presence of interactions at the boundaries with the surrounding tissue;

- biorezorb tion - soluble and or rozsmoktu S supposed, in the end includes an S ARE the structure of tissues.

Currently, there are many representatives of bioceramics used in dentistry and medicine. Ceramics based on aluminum and zirconium are bioinert used in orthopedics. Bioactive glass ceramics are available in dentistry under various brand names, and porous ceramics such as calcium phosphate are often used to repair bone defects. Some representatives of bioceramics, such as those based on calcium silicate (mineral trioxide aggregate [MTA], ProRoot MTA Root Repair, Dentsply Sirona) or based on bioaggregates (DiaRoot BioAggregate, DiaDent) were also used in dentistry as materials for repairing defects in the root structure and for apical execution of endodontic space.

Properties of endodontic bioceramics

Endodontic bio ceramic and ca not sensitive to moisture and contamination of the blood, that the quality of its application is not dependent on technology implementation procedure. It is also dimensionally stable, and expands slightly during curing. In a steady state Bio Ceramics are very hard and perfectly sealed, does not dissolve for a long period of time, providing thus preventing mikrop idtikann me. During curing, the pH of the material rises to 12 as a result of the hydration reaction. In the process, calcium hydroxide is first formed, which then dissolves into calcium and hydroxyl ions. The high pH of the material during curing provides its antibacterial properties. In a stable state, the material is not only completely biocompatible, but also bioactive. Upon contact of bioceramics with the surrounding liquids, calcium hydroxide is released, which can interact with phosphates in the liquids and ensure the formation of hydroxyapatite. These properties of the material can be categorized as inductive in relation to the surrounding hard tissues. Given all this, it is obvious that Bio Ceramics is a material of choice for bridging pulp, performance space pulpotomyy after the procedure, recovery defects as a result of root perforations, filling endodontic obturation space and teeth with immature root induction process apexification.

Consider ceramic and pro and medical devices (implants, implants, systems prosthesis, their elements) based on Al_2O_3 and ZrO_2 ceramics. Products are nanostructured bioactive coating of hydroxyapatite and can be successfully used in the surgical treatment of diseases and injuries of the musculoskeletal system of man, as well as dental and maxillofacial surgery.

The structural strength of the porous structure is provided by a combination of submicron and nanosized components of ceramics . The porous structure material execu uyetsya taking into account the structure of bone tissue at the site of

implantation . Chemical and corrosion resistance ensures the absence of biochemical and allergic reactions of the body.

Pottery completely nontoxic and in terms of application. Resistance of material to various influences allows to apply repeatedly high-temperature and gas sterilization without loss of operational properties. Allows radiation sterilization.

Developed surface pore space ensures the applicability of materials in different bioactive environments. One of the highly effective decisions for clinical practice is the application for implants of specially designed technologie of "pore lining" , nanostructured with HAP.

The ceramic head and the ceramic liner in the acetabulum form a friction pair "ceramic-ceramic" for hip arthroplasty with a wear rate of 0.001-0.002 mm / year. Outstanding tryboloh and including any properties, high hardness and low roughness materials make this pair of friction excellent material for young patients. The coating of hydroxyapatite with the specified size of nanoparticles provides the formation of new bone tissue in the area of contact with the implant and long-term strong fixation of the implant in the human body.

Implants for spine (set endofiksator, and mounting plate) used in vertebrology to fix, restore substitution resistance ability pathological changes of the spine.

Simplicity and accessibility method allows wide application in trauma first practice in the treatment of patients with debris fractures of long bones in order to stimulate reparative osteogenesis, replacement of bone defects and prevention of infectious complications. The granules do not contain active ingredients, do not enter into chemical reactions and do not cause rejection reactions.

Table 3.1 - Examples of implants made of bioceramic material

PRODUCT		MATERIAL	CHARACTERISTIC
	Ceramic head and ceramic contribution	Nanostructured composite highly-densed ceramics	Crack resistance 8 MPa/m^2
	Leg	Titan covered with HAP	Biocompatibility
	Implants from = granuled ceramics	Porous nanostructured composite ceramics (Al_2O_3)	Provides free passage of biological fluids
	Endofixer	Porous nanostructured composite ceramics (Al_2O_3 + ZrO_2 + HAP)	Porosity >20 %, the structure is pore penetrated
	Vertebral plate	Nanostructured composite dense ceramics (Al_2O_3 + ZrO_2)	Bioinert, X-ray transparent
	Screws for the spine	Nanostructured composite dense ceramics (Al_2O_3 + ZrO_2)	Bioinert, X-ray transparent

Table 3.2 - Mechanical characteristics and applications of some types of bioceramics

INDICATOR	ADVANTAGE IN MEDICINE	TRADITIONAL	PSZ	NEWEST	POROUS
Compressive strength , MPa	Withstands high loads during operation	>3000	>2000	>2000	>80
Solid and Nb to B and kersu	Provides low wear at friction	1500	1800	2000	-
Porosity	Best biocompatibility for osseointegration	0	0	0	>20%
Microstructure of particles, µm	Increased strength of mplants	≤ 4	≤ 5	≤ 1,5	>5
Crack resistance	Reducing the likelihood of implant destruction	>4	>5	>9	-
Non-toxicity. Biocompatibility	Eliminates unwanted immune and metabolic reactions of the body	Non-toxic by ISO10993 Bioinert	Non-toxic by ISO10993 Bioinert	Non-toxic by ISO10993 Bioinert	Non-toxic by ISO10993 Bioinert coating
Field of application	All technologies are specialized in traumatology and orthopedics	Joint endoprostheses. Support structures of spinal implants	Joint endoprostheses. Screws for spinal implants	Endoprostheses of the hip and knee joint	Interbody fixators for implantation in the spine. Porous granular implants

Lecture № 4. Polymeric biomaterials

Polymeric biomaterials are usually understood to mean polymeric materials and articles thereof used in medicine or biotechnology. Such materials are often obtained by targeted modification of well-known polymers. In recent years, the range, scale of production and importance of biomaterials have grown significantly.

Radiation-chemical technology has now become one of the most effective ways to obtain polymeric biomaterials. Work on the use of radiation-chemical methods for the synthesis of polymeric biomaterials is carried out in the following areas: radiation modification of various polymers and products from them to obtain hemocompatibility (which work in contact with blood for a long time) of polymers, polymeric sorbents, vascular prostheses, etc. e .; immobilization of various biologically active substances (BAS) (enzymes, drugs, etc.) in polymer matrices using radiation polymerization; radiation-chemical synthesis of polymers-carriers of drugs; radiation crosslinking of polymers in order to obtain mechanically strong hydrogels (carriers BAS, dressings, eye lenses, etc.). The advantage of radiation-chemical methods of obtaining polymeric biomaterials in comparison with traditional ones is the purity of materials (no need to add additional ingredients (polymerization initiators) during synthesis), the ability to carry out processes at low temperatures and ease of process rate control by changing radiation dose rate. The advantage of radiation-chemical methods is also that biomaterials in some cases can be sterilized on the same sources of ionizing radiation that have already been used to obtain them. It should be noted that in most cases to obtain polymeric biomaterials require small doses of radiation, usually not exceeding 30 kGy, which allows the use of low power radiation sources.

The disadvantage of radiation-chemical methods is the need to use, as a rule, relatively expensive and difficult to operate sources of γ-radiation and electronic accelerators.

Obtaining hemocompatibility of polymeric material and c. Getting hemosumisn s polymer materials - a rather complicated problem. At contact of polymers with blood the biochemical reactions causing change of physiological functions of blood are initiated, blood coagulation with the subsequent thrombosis on a polymer surface is "started". Important factors that increase the hemocompatibility of polymers are their properties such as minimal ability to adhere and platelet aggregation, lack of activation of contact coagulation factors, participation in the lysis reaction, thrombus formation and selective ability to adsorb blood plasma proteins, especially albumin. According to modern ideas, the first

stage of contact of the polymer with blood is the rapid sorption of proteins from blood plasma. Nature and conformations iynyy state of the protein is determined following biochemical reactions.

Problems of protein sorption on various polymer surfaces have been considered in numerous studies. Unfortunately, currently the level of our knowledge does not allow to effectively predict the nature and properties of the polymer surface, fully satisfies the requirement of hemocompatibility.

From the text above it is clear that to obtain hemocompatibility of materials, the surface of the polymers must be modified. For this purpose:

1. Create polymers with surfaces with reduced adsorption capacity in relation to proteins and close in nature to the natural environment of the organism. These are mainly hydrogel surfaces

2. Create polymeric materials with a certain domain structure of the surface (polyurethanes).

3. Create carbon polymer materials (polyacetylenes).

4. Create polymers in which the surface by its nature simulates blood anticoagulants), which is achieved by introducing into the surface layers of polymers of sulfo- and carboxyl groups, creating a negative charge on the surface of polymers). Most often try to get a heparin-like surface, as a common method of obtaining hemocompatibility of materials by introducing heparin has a number of disadvantages due to the partial loss of heparin activity during covalent immobilization, its weak anticomplement activity and biodegradation.

5. Physiologically active substances (blood anticoagulants, enzymes, etc.) are introduced into the surface hydrogel layers, interact with blood components and stop the process of thrombosis.

When choosing a method of modifying the surface of polymers, it is necessary to take into account that the basic physical and mechanical properties of the original polymer during modification should not change significantly. One of the most effective methods of polymer modification is radiation vaccination polymerization.

Its advantages as a method of modifying polymeric materials to increase their hemocompatibility are, first, high versatility, which allows in a wide range of temperatures to modify almost any polymeric material (suture material, catheters, tubes, tablets, powders, grafts, etc. e.); secondly, the possibility of creating on the surface of polymers modified layers of different thickness. The thickness of the layer depends on the conditions of the graft polymerization - dose rate, the choice of

solvent for the monomer, etc. The modified layer is firmly bound to the substrate and is not washed away in contact with the environment of a living organism.

All this contributes to the widespread use of radiation graft polymerization to solve problems associated with increasing the hemocompatibility of various polymeric materials and products from them. The main task of such studies is to create polymers with a functionalized surface, defined by hydrophilic-hydrophobic properties and a negative charge on the surface. A significant amount of work has been done to modify various polymers using highly hydrophilic monomers, such as N-in and n and lp and roll and don, 2-hydroxyethyl methacrylate, acrylamide and its derivatives. A number of studies for the modification was pretty difficult for opolimery. Thus, for the production of vascular prostheses used mainly polyurethanes, polyesters and natural rubber.

Radiation graft polymerization in most cases was carried out by the direct method of aqueous-alcoholic solutions at low doses. In some cases, especially when grafted acrylamide, used the method of claim th ed - at prominennyam .

As a result of the performed works various modified polymeric materials with hydrogel surfaces are received. These materials are quite strong, soft and have high swelling in water. Biomacromolecules and such materials are characterized by high diffusion. Polymer hydrogels obtained by radiation-chemical methods were tested for hemocompatibility in in vitro and in vivo experiments on monkeys, sheep and dogs. In generalized form, tests for hemocompatibility of radiation-grafted polymer hydrogels showed the following: with increasing water content from 15 to 85% there is a decrease in protein sorption and increased desorption rate, the hydrogel has thrombosis, but the connection of thrombi with hydrogel surface with their connection with unmodified polymers. Significant reduction of the surface tension between the hydrogel and the aqueous solution is essential. Hydrogel coating on polymers must be prepared from very pure monomers. Thus, small admixture of methacrylic her acid in 2-hydroxyetylmetacrylate and significantly affects the quality of hydrogel th cover his hemosumisni properties.

Interesting results were obtained in the study of radiation grafted to polyethylene (PE) for opolimeriv 2 hidroksyetylmetakrylatu (hydrophilic monomer) with em and lmetakrilat (hydrophobic monomer). At low water content (~ 10%) indicated vaccinated for opolimery characterized unexpectedly low rates of adsorption of platelets, which was not due to water content and composition for Opole and mayor. At higher water contents, platelet adsorption is inversely proportional to water content. Obviously, the composition for Opole and the mayor and the state of water in it are important. The surface of radiation-grafted copolymers

is very heterogeneous (there are bumps, protrusions, etc.), the thickness of the modified layer is usually 15-45 μm. It is assumed that to increase hemocompatibility requires a certain combination on the surface of hydrophilic and hydrophobic areas.

The use of radiation crosslinking to obtain polymeric biomaterials. Currently, significantly increased interest in obtaining polymeric biomaterials by radiation crosslinking. This method is most often used to obtain hydrogels, mainly based on polyacrylamide, polyvinyl alcohol, polyethylene oxide and poly (N-vinylpyrrolidone). The advantage of radiation crosslinking is the relative simplicity of execution, the ability to widely adjust the density of the grid by selecting the irradiation conditions (dose rate, dose), the possibility of using reduced temperatures, purity of the product (no initiators) and simultaneous sterilization. Radiation-crosslinked hydrogels are used as carriers of BAS (enzymes, drugs, etc.) as implants, prostheses, ophthalmic lenses, medical membranes, dressings and biological media for the study and cultivation of microorganisms.

On the basis of radiation-crosslinked polyvinyl alcohol biomembranes for selective transport of macromolecules, and also the materials used as articular cartilages are received. The prospects of using polyvinyl alcohol hydrogels as a dressing material are shown and its advantage over gauze is noted: homogeneous adhesion throughout the wound and easy removal without damaging the skin.

Poly (N-vinylpyrrolidone) based hydrogels have high hydrophilicity and biocompatibility and can be used as a material for the treatment of burns and trophic ulcers. These materials are sold in Poland under the trademarks "HDR" and "AQUA-Gel". A therapeutic system based on poly gel (N-vinylpyrrolidone) has been developed for use in obstetric practice to accelerate childbirth and abortion. In this case, the gel is a thin rod containing prostaglandin.

The technology of obtaining hydrogels for dressings is now quite detailed, and they have undergone extensive clinical trials. Importantly, it is possible to obtain dressing gels containing drugs (eg, chloramphenicol). With large injuries, this hydrogel is significantly more effective than conventional dressings.

In medicine, silicone rubber coatings with collagen are used, followed by radiation crosslinking and sterilization. Another natural product used to make biomaterials is gelatin. The radiolysis of gelatin is studied, the conditions of formation of spatial structures at irradiation of its solutions are revealed. It is proposed to use a radiation-crosslinked composition of polyvinyl alcohol with gelatin as a dressing.

Radiation is stitching used for the manufacture of medical devices policy and loksan and in a biologically inert porous cords shpr and tsovannyh tubes, capillaries and various implants. At radiation crosslinking of a floor and dimethylsiloxane in especially pure their conditions its hemocompatibility essentially increases. Radiation yno sewn polivinilmet and lsyloksan usage ovuyetsya for the manufacture of thin membranes for medical products (eg levonorhistrel).

Radiation is stitching trans-1,4-polyisoprene used to create shrink materials for binding to major blood vessels. The materials have been extensively tested in vitro and in vivo (in dogs). Radiation modification can improve the properties of medical prostheses based on polyolefins. Using radiation crosslinking, polymeric biomaterials with high adhesion to human skin were also obtained.

In Israel, the production of synthetic dressings obtained by radiation crosslinking of hydrophilic monomers on polyurethane. The material is waterproof, transparent, adheres well to the skin and passes the drug. The material is produced under the name "Omiderm".

Methods of obtaining an artificial cornea and contact lenses with high resolution nabuha you in the water-based radiation-crosslinked polyvinyl alcohol laced hondroit and nsulfata sodium. To significantly increase the permeability of contact lenses to oxygen, it is proposed to irradiate them with accelerated heavy ions weighing 2-100 a. o .м. Hydrogel materials for soft contact lenses have been created using radiation polymerization. These materials are produced in China.

To create ophthalmic materials found use radiation-crosslinked collagen extracted from and sclera of the eye animals. This material is used to create temporary al l odrenazh along with ANT and glaucomatous operations.

Undoubtedly, in the coming years we can expect the appearance on the market of new polymeric biomaterials obtained using radiation polymerization methods.

Obtaining polymer implants.

Technical or techniques and methods used in radiation polymerization can be used for different kinds of implants, mainly for the treatment of infected skin and for making dentures. Methods for obtaining collagen implants by irradiating a mixture of monomers or polymers with collagen have been developed. Implants are well compatible with blood and do not cause inflammation. Implants are used in surgery and can be used as substrates in biotechnology. Polyesterurethane-based prostheses with a radiation-modified inner surface have been studied. The modification was carried out by radiation grafting of 2-hydroxy-methyl acrylate or acrylamide on the

inner surface of the tubes. Prostheses were studied in vivo. The histological and mechanical properties of prostheses were studied. Established their increased tromborez and stentn and Nb. A method of modifying fillers for polymers used in dental technology has been developed. Fillers based on glass or quartz fibers are modified by radiation grafting of acrylic acid from the vapor phase. The physical and mechanical properties of resins containing different amounts of modified filler have been studied in detail. The advantages of the used modified filler in comparison with the filler modified by silanes are noted. Polymer-ceramic materials for dentistry have been created using irradiation of alumina mixtures with acrylic acid. With the help of radiation graft polymerization, implants have been created for the treatment of skin on the affected areas of the human body. Silicone rubber modified by grafting hydrophilic monomers or modified vulcanized natural rubber is usually used for this purpose. Using technology created by radiation method d and bustards and L and zats uu silicone eye contact lenses. As a result of Mr. and bustards and L and zats uu Craiova second angle is reduced from 150 ° to 20 °, and the effect of g and bustards il nost and persists for a long time. Radiation-modified polymers in use ovuyutsya to initiate the growth of various cells

Immobilization of the drugs.

In the field of using radiation polymerization for immobilization of drugs, the greatest progress has been made in the immobilization of antitumor compositions in polymer matrices. As antitumor substances adriamycin, mitomyts and n-C and 5-fluorourac and l are used. In some cases, treatment with immobilized anticancer drugs is combined with hormone therapy. Immobilized antitumor substances are usually used in the form of polymer tablets or needles that are injected into the tumor. The use of immobilized antitumor drugs has the following advantages over their administration by injection or oral administration: a small concentration of drugs in the blood, the drug is distributed directly in a small area of the drug. This is a cancer cell necrosis within 0.5-1 cm 2 around the sample and diffusion of anticancer drugs terminated nekrozno th layer. This minimizes the side effects of the medication. The duration of use of immobilized antitumor drugs is several months. The rate of drug release does not change. Such drugs have been widely tested in many clinics in Japan.

For immobilization anticancer drugs usually use different copolymers and compositions polyethy and lenhlikolmetakr and Latin and in various polymers (polystyrene, polivinilformal, polyethylene, polymethylmethacrylate, polyethylene). It is emphasized that irradiation should be carried out in an oxygen-

free environment, and the dose should not exceed 10 kGy, otherwise the activity of antitumor drugs is significantly reduced

Drug release rate governing the introduction into the polymer matrix agent poroutvoryuyuchyh s or adsorbent (eg activated charcoal).

Technology use immobilized anticancer agents can be improved by varying the hydrophilic-hydrophobic properties of the polymer matrix and use biodehrad of Old polymers (polypeptides or claim olilaktyd).

Studies with immobilized monoclonal antibodies were conducted at the Pasteur Institute (Paris) as part of the International Atomic Energy Agency (IAEA) program. Immobilization of the latter is carried out by low-temperature polymerization of 2-hydroxyethyl methacrylate. Sensitivity reactions and mmob and L and zovanoho antibody to an antigen of choice depends on the monomer concentration and to create a porous medium. An important problem is to minimize non-specific reactions of the polymeric carrier with the antigen. It is necessary to increase agricultural and drofobn and Nb polymer matrix. Immobilized drugs are usually made in the form of microspheres or microcapsules. To immobilize antibodies are also microspheres obtained by polymerization akrole th district in or copolymer along with 2 hidroksyetylmetakrylat ohm or methacrylic S acid.

The advantage of radiation polymerization for immobilization of antibodies is a fairly high purity of the obtained product. These drugs can be used for immunological analysis.

A study on the immobilization of a calcium antagonist in a pre-polymer gel floor and (2-hydroxyethyl methacrylate). By radiation crosslinking and gel additive methyl methacrylate and N-vinylpyrrolidone can vary widely release rate of healing along .

Investigated immobilizatsi th hydrocortisone gel obtained th radiation S polymerization of acrylic acid. The rate of release is regulated by the radiation dose and treatment of gels with zinc acetate.

Immobilization of blood components.

However, power iyeyu the most pressing problems now are artificial substitutes that could be stored for a long time under normal conditions without requiring complicated and expensive equipment. One of the most promising areas is the immobilization of various blood components in polymer compositions using primarily radiation polymerization methods.

Since hemoglobin was also mmob and L and zovan second in the polymer matrix of poly (2-hidroksyetylmetakrylatu) using radiation n yzkotempeturno her polymerization. Particular attention was paid to the selection of optimal immobilization conditions to protect hemoglobin. Hemoglobin is suitable for studying the state and mmob and L and zovan first molecules in a polymer matrix, as it has a characteristic optical absorption. Hemoglobin in the membrane was exposed reversible second oxygenation, which has almost the same meaning as in native hemoglobin. Semi-described method of obtaining blood from karboksyhemohlobyn immobilized in .

Radiation polymerization of phospholipids was used in the works for hemoglobin immobilization. Phospholipids contain two long polymer or oktadeka Mr. dieniln and groups. Artificial red blood cells were obtained by encapsulating hemoglobin using radiation polymerization of bilayer phospholipids - liposomes. Artificial blood cells were mechanically stable, easily withstood freezing. Oxygen transport of such systems was similar to the transport of native hemoglobin. In vivo (mouse) tests were performed to indicate the biocompatibility of such cells.

Obtaining "smart" polymers and their use for immobilization of biologically active substances .

In recent years, "smart" polymers have become increasingly important for medicine and biotechnology. So-called polymers that are able to respond (compress or swell) to small changes in the environment (temperature, pH, electric field, etc.). "Smart" polymers immobilized used for the selection of drugs under certain conditions, usually at a given temperature or pH. Usually "smart" polymers are obtained by traditional methods, but recently, radiation polymerization has also been used for this purpose. Among the "smart" polymers, the largest number of publications is devoted to poly (N-isopropylacrylamide) (poly-N-IPAA). This polymer has a lower critical dissolution temperature (NCR) in water of ~ 32 ° C, ie close to the human body temperature. Above 32 ° C is the phase shift caused by second conformational transition macromolecule poly-N-IPAA with loose globules in a compact ball, accompanied by a sharp decrease in the size of the macromolecule.

The behavior of hydrogels based on poly (N-isopropylacrylamide) and the rate of diffusion of drugs immobilized in them under conditions that mimic the human body were studied . It was found that at 37 ° C and pH 1.4 (normal human conditions in the stomach) is immobilized in a slow release hydrogel and ndometats Inu and amylase, but by changing the pH to 7.4 (provided in the gut) identification of drugs significantly accelerates. Thus, it is possible to create dosage forms that allow you to deliver the drug to the affected organ without significant losses.

Another area of use of such "smart" polymers is the creation of signal-sensitive systems consisting of a biosensor, activator and reservoir for the correction of disorders of various organs in the human body. Thus , for patients with diabetes, special systems are developed from glucose biosensors, which are launched on the principle of inclusion - exclusion to allocate certain portions of insulin, and MMOB and l and called in gels, ie they work on the principle of the pancreas.

Lecture № 5. Fundamentals of fabric engineering.

The last quarter of the twentieth century was marked by the rapid development of a new branch of biology - biotechnology. Biotechnology is a science that solves biological problems with the help of technical means. Biotechnology is a set of industrial methods used to produce various substances using living organisms, biological processes or phenomena.

Such productions include ancient biotechnology of cheese-making, winemaking, brewing, baking, preparation of dairy products, souring of vegetables, ensiling.

In turn, this discipline consists of a large number of different units.

The year of birth of genetic engineering is considered to be 1972, when a group of researchers in the United States led by P. Berger received the first artificially created recombinant DNA molecule.

Execution of any genetic engineering program involves :

- the need to isolate DNA fragments that carry the desired gene;

- combining them "in vitro" with vector molecules capable of transferring this gene into recipient cells;

- creating conditions for stable inheritance and efficient expression of the transferred gene in a foreign genotypic environment;

The successful solution of these problems became possible thanks to such achievements of science.

Discovery of the phenomenon of restriction - modification of DNA and the release of specific enzymes - restrictases, necessary to obtain DNA fragments with the same final sequences;

Introduction of methods of chemical and chemical-enzymatic synthesis of genes into the practice of genetic engineering;

Detection of natural and creation of artificial vector DNA molecules capable of transferring foreign DNA fragments into the recipient cell, ensuring their inclusion in the corresponding genome and their expression;

Development of methods for combining DNA fragments of different origins with the formation of recombinant molecules;

Development of methods for cloning DNA molecules and creating a gene database (gene bank);

Development of methods of transformation and transduction for different organisms and selection of clones carrying recombinant DNA molecules.

Any DNA fragments can be cloned (propagated) by introducing a vector into a recipient cell (usually E. Coli). This is achieved by transformation, if the vector is a bacteriophage or other viruses (eg monkey virus SV40), the penetration of foreign DNA into the cell is carried out by transduction. Recipient cells and organisms with their own characteristics caused by the penetration of foreign DNA are called transformed.

Now special vectors have been constructed for the transfer (trangenosis) of foreign genes into plant and animal cells.

Existing and potential vectors for plants can be divided into several categories:

Vectors derived from bacterial vectors capable of integrating into the genome of the recipient plant are Ti plasmids and Ri plasmids.

Vectors constructed on the basis of DNA of viral and viroid pathogens of plants;

Vectors that may exist in plant cells as independent replicons (mitochondrial and chloroplast DNA);

Vectors derived from unstable components of the plant genome (so-called transposable elements);

Modern cell, tissue engineering began to take shape in an independent discipline after the work of DG Voltaire and F.R. Mayer. In 1984, they used a plastic material artificially grown from cells taken from a patient to repair a damaged cornea.

Since 1987, tissue engineering has been considered a new scientific field in medicine, based on the use of modern histotechnology.

Cell engineering - development of methods of embryonic cloning and cloning of organisms, organs, tissues, from individual cells; these are methods of working with different cells for a variety of purposes; from their cultivation to the creation of human clones. This idea has provoked many different interpretations: from immediate application in practice to the ban on any research in this area. This reaction is associated with insufficient experimental data, as serial clones of animals have not been obtained. The creation of clones is based on the simple transfer of the

somatic nucleus into an unfertilized egg, in which the nucleus itself is inactivated. In the future, such an egg is transplanted to a surrogate mother and all processes occur naturally. Since the genotype of the somatic cell nucleus is totipotent, a new organism develops that is fully responsible for its features, properties and characteristics of the one from which the somatic nucleus is taken. It is practically a copy of him, but only the younger one - for the time when the donor lived. In addition, this method allows the reproduction of animals with beneficial mutations in somatic cells, which cannot be achieved by any other methods. The method of cloning allows to preserve rare populations of animals currently listed in the Red Book.

Achievements and objectives of cell engineering.

Thanks to histotechnologies were obtained:

- cultured cells (tissues for obtaining valuable substances);

- artificial liver tissue;

- there is a reconstruction of connective tissue, especially bone;

- smooth muscle tissue, which is used to reproduce the ureters, bladder, intestinal tube;

- creation of artificial heart valves and capillary grids;

- the most important direction is the production of leather equivalents;

- cloning of organisms - a promising area of cell engineering;

- hybridization of somatic cells;

- embryonic induction - deals with the artificial change of the organism in the care of embryonic development.

Methods of tissue engineering and their essence :

- isolation of cells from the body or selection of cells from donor material;

- their transfer to artificial nutrient media;

- isolation of tissue-specific cells and their further cultivation;

- applying the resulting cell culture to the matrix followed by cultivation;

- matrices can be made of different biomaterials and should be easily destroyed in orgasm or replaced by tissues of the body.

Problems of fabric engineering :

- cells during cultivation can change the properties and turn from normal to close on characteristics to tumor;

- the cause of degeneration may be stimulators of cell proliferation;

- the process of cultivation can lead to infection of cells;

- the source of infection can be nutrient media, serum, violations of work regulations

- many problems occur inside the body after transplantation of artificial tissues.

Despite this, tissue engineering is the most promising area in biotechnology, which is developing rapidly.

Tissue engineering is an approach to the creation of tissues and organs for implantation that uses fundamental structural and functional interactions in normal and pathologically altered tissues in the creation of biological substitutes to restore or improve tissue function. Woven ynno- engineering and design are the biomedical cellular product consisting of cells (cell lines), biocompatible materials and excipients, and means any -what biomedical cellular product consisting of cell lines (cell lines) and biocompatible materials. The term "biocompatible material" in this context means any who biocompatible material protection (eg detsellyulyar and zovan and homo graft) or synthetic origin. For example, such materials include biocompatible polymers (polylactate and polygluconate), biocompatible metals and alloys (titanium, platinum, gold), biocompatible natural polymers (collagen).

Cells as part of t kan ynno- engineering second design, can be obtained from various sources and be at various stages of differentiation of undifferentiated s cells of highly specialized cells to their communities . The population of the prepared matrix by cells is an urgent problem of modern biomedicine. The surface properties of the matrix affect the colonization of cells, including the attachment of cells and their proliferation in the matrix.

There are now ways to get tkaneinzhenern s designs used cooking cell suspension and the physical application of the suspension for biocompatible material

using stepwise deposition suspension first culture to form a monolayer and roses mischennya material in solution and for a long time, enough to penetrate cells throughout about ' material, as well as the use of 3D-bio printing . Various methods of forming woven ynno- engineering s equivalents hollow internal organs such as the urethra, bladder, bile duct, trachea.

Injuries and illnesses can lead to loss of living tissue or loss of the body's ability to perform a specific function. Clinical treatment in such cases consists in replacing the lost tissue or restoring the lost function with the help of synthetic biomaterials and medical devices. To improve the characteristics of biomaterials, significant efforts have been made to elucidate the interaction of biomaterial with living tissue. The result is second- generation materials , often called bioactive. However, the best "material" for any human organ is healthy living tissue.

Living tissue engineering has become a new philosophy in the development of biomaterials. It consists of biological and technical methods of creating functional tissues that replace or improve the work of sick and pathological parts of the body. In practice, this idea is realized by growing living cells on biomaterial in the presence of bioactive molecules. Then living cells and their extracellular produced in the matrix with the substrate administered as a single cell-biomaterialnu structure. Through the use of artificial substrates living tissue engineering closely related to material m . The term "substitute for medicine" was introduced Clemens van Blittersviykom (Netherlands) to determine treatment based on the sharing of biomaterials and living tissues grown. Engineering living tissue is one of the branches of science that most developing countries. Time magazine placed living tissue engineers at the top of the table of "best jobs of the future." The peculiarity of living tissue engineering is the joint work of biologists, chemists and materials scientists. Interest in it is fueled by the policy of care for the health of the elderly, as well as the expectation of a huge impact on the methodology of clinical treatment of various diseases .

So far as the substrate biomaterials often used biodehrad of Old materials such polilaktydu. They were considered ideal because it is desirable that the material gradually disappear after implantation. To date, no attempts have been made to improve such substrates, although some decay products may inhibit cell growth and differentiation. One of the promising areas of research is the development of biologically modified biomaterials, the surface of which carries certain information for living cells that interact with this surface. The information may consist in determining where the cells should and should not land, in determining their orientation or differentiation. It is expected that such developments will provide bioengineering with a wide range of substrates. It is likely that there will biomaterials

surface which will contain intellectual biodehrad of Old layers and biologically active peptides or drugs. Such work is underway, and there are already examples of surface modification to control the planting of certain cells. Using poly (p-isopropylacrylamide), Okano and co-authors developed a biomaterial with a thermally active surface, which at temperatures above 32 ° C and drophobic, and below 32 ° C - hydrophilic. Thus, after cell growth at 37 ° C, they can be removed from the surface by lowering the temperature to 32 ° C. U S property is likely to be used to relieve skin grown from the substrate before transferring the wound.

Despite the progress in this area, the creation of truly intelligent substrates is the task of the future. Currently, the growing of certain tissues are not often able to create morphological O and biochemical at correct is the environment for planting cells, their growth and differentiation. To make use of bioengineered tissues become routine required second further development of biomaterials expertness , biology and medicine. In particular, progress is needed in technology for growing cells (including stem cells) and biocultures.

Artificial blood vessels are used to replace pathologically altered areas of the bloodstream and to create bypasses in the circulatory system. Nylon, Teflon, Orlon, and Dacron were tested as vascular substitutes. Artificial vessels made of dacron and Teflon are made of yarn with a large number of elementary threads and the structure of the material they can be woven, knitted and woven. Recently, vessels with a velor fabric structure have been produced. This structure is a modified knitted surface material received by Mr ETL S Van ing n s t approx . This structure ensures the elasticity of the vessel. Depending on the anatomical features of the transplant sites, artificial vessels can be made corrugated for areas with large bends and branched type for areas with branching.

"Semi-resorbable" prostheses and prostheses made of antimicrobial fibers are currently being developed . "Semi-absorbable" prostheses are made of polyester threads and collagen. Such prostheses have low porosity at the time of implantation. In the future, collagen is replaced by body tissues. Prostheses made of antimicrobial fibers are made on the basis of polyvinyl alcohol derivatives and their mixtures with polyester and fluorine carbon fibers.

Currently, prosthetics of large diameter arteries are quite successful. However, there are no substitutes for coronary arteries. When prosthetic venous necessary to use large diameter netromb uyuchi surface of the implant am in.

The main materials used for the manufacture of balloon segments of catheters are polyethylene and polyvinyl chloride. To improve the sliding qualities of the base

tube of the catheter use different coatings on its surface (hydrogel e , for example). Katetr cylinder and made of plastic, can develop a lot of pressure.

Coronary conductors play an important role in the installation of a balloon catheter. They have Teflon or heparin and coatings. The distal tip is prepared with a platinum coating to increase X-ray contrast.

Balloon-expandable coronary stents are made of stainless steel as well as tantalum alloys, and are divided into two main types: matrix (plate, mesh) and wire (spiral). Tantalum stents have the best visualization compared to stainless steel stents. Modern steel stents have X-ray contrast marks made of gold and platinum. To reduce the response of the vascular wall to stent implantation, they are available with diamond coating, coated with heparin, radioactive substances.

To the palate of the heart .

Titanium or stellite is used to make rigid parts of valve prostheses. Valve leaves are made of silicone rubber or fluorine-containing polyurethanes. The best material is natural latex rubber. Wings valves sheathe dakronov th Velor S cuff w .

In recent years, carbon-based materials have been considered as new materials for making heart valves.

Adhesive composites.

Most claim oshyreni biological adhesives, which are used in surgery :

1. Adhesives based on a mixture of synthetic and natural rubber.

2. Cyancrylates. Their rapid curing caused by polymerization is their main advantage.

3. Epoxies. Have high strength. Disadvantage - the low rate of formation of chemical bonds makes them unsuitable for surgery .

4. Polyurethanes. They are related to organic molecules of living tissues.

In some cases, for osteosynthesis used carpentry glue, gelatin, fibrinogen, resorcinol and resin. However, their bonding ability is not large enough.

In 1959, Kuver discovered the high gluing ability of the methyl ester of cyanoacrylic acid. Under various names it began to be made in Japan, Germany, the

USA. Cyancrylates exhibit adhesive properties against most materials at normal temperatures and in humid environments. Paste thick effect occurs rapidly and shows the transition of the adhesive polymer monomeric state to ground without changing about 'volume and heat. One of the most important properties of cyanoacrylate adhesives is their sterility. They have bactericidal and bacteriostatic action. However, it has been proven that adhesives can have an irritating effect, for example, on nerve and brain tissue.

Adhesives are used in operations on the heart, blood vessels, lungs, kidneys.

Cyancrylate and adhesives are used to fill cavities in bone tissue that form after tumor removal.

Adhesives used in ophthalmology for gluing plastic lenses to horns ing , since the suturing damaged cornea. The artificial cornea can be glued to the tissue to prevent tissue erosion and moisture seepage around the eye prosthesis.

Polyurethane Adhesive TC-3 is used in urolohich their operations in patients with the aim of removing stones from the kidney and ureter, renal anomalies and others.

Polyurethane-based adhesives are also used in peripheral nerve plastics in neurosurgery. Creation adhesive epinevraln th seam using medical adhesive polyurethane CL 3 in conjunction with biodestrukt of Old polyurethane th film substrate provides full recovery of the damaged nerve. KL-3 glue was used in seamless operations on the brain. In combination with drugs KL-3 was also used in the treatment of malignant brain tumors. The adhesive composition KL-3 was used for the treatment of intestinal and bronchial fistulas, as well as in maxillofacial and general surgery.

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