POLYMERS IN MEDICINE

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Presented by the Institute of Chemistry of the Tskhum-Abkhazian Academy of Sciences

Abstract. Polymers have truly revolutionized modern medicine. Healthcare and everyday life are unimaginable without their wide-ranging use. Often it becomes necessary to completely replace a damaged organ or tissue. This is possible via transplantation or implantation. Transplantation brings up a number of problems: include scientific, moral-ethical, legal issues. Existing tissue and organ banks can only satisfy about 10% of general demand and in transplant cases the most important problem is compatibility of cells. The use of polymeric materials solves all of the above problems. Polymers and polymer-based materials are extensively applied in reconstructive surgery, traumatology, orthopedics, dentistry, ophthalmology, for prosthetics of damaged organs, and so on. Special preference is given to synthetic polymeric materials because their production process allows targeted modification of the properties. Unlike donor organs, polymers have very low immunogenicity, which reduces the risk of incompatibility and the possibility of rejection by the immune system. Every implant must meet certain requirements: they must be biologically inert, maintain the necessary physical and mechanical properties for long periods of time, and possess extremely high purity (impurities must not exceed $10^{-5} - 10^{-6}$%). Polymers are also used in "targeted drug delivery systems," protecting medications from inactivation and ensuring their gradual release. Current research aims to increase the longevity, functional universality, and miniaturization of artificial organs.

Keywords: *Biodegradable and non-biodegradable medical polymers, transplantation, implantation.*

Modern medicine, as well as our daily life, is unthinkable without the use of a wide range of polymers. Polymers have made a real revolution in medicine. In recent decades, research into the synthesis and use of polymers has been particularly intensified.

Polymers for medical and biological purposes include polymers that are in contact with the biological environment of the organism.

In modern medicine, polymers are widely used in reconstructive surgery, traumatology, orthopedics, urology, dentistry, ophthalmology. Polymer materials are used as medicines, sanitary and hygienic items, packaging materials, parts of machines and devices, and are used to create artificial human organs and prosthetics of damaged organs. Both natural and synthetic and artificial polymers are used for these purposes.

Today, synthetic polymer materials are predominantly used in medicine, as their production process allows for the purposeful modification of the consumer properties of medical products.

It is well known that a living organism adapts to external factors, in particular, its ability to self-repair in the event of various wounds or traumas. For example, when the skin is damaged, the blood clotting system is activated, the blood clots, and the blood vessels close, which protects the organism from bleeding and death.

However, sometimes, depending on the causes of the trauma and the depth of the injury, in the case of severe damage, the body does not have the ability to heal and restore any organ, so external intervention, either surgically or by some other means, becomes necessary. In particularly difficult cases, it may be necessary to completely replace the damaged tissue or organ.

The question arises, how can a tissue or organ be replaced? It is possible to use the corresponding organ from a living or dying donor, or a special prosthesis that can at least partially restore the biological function of the removed organ. Today, it is possible to model almost all human organs and create a corresponding prosthesis, except for the brain and stomach.

Since the 20s and 30s of the 20th century, studies have been conducted and, accordingly, operations to replace damaged organs through transplantation. In the 30s, a kidney from a man who died of a head injury was transplanted to a girl. The patient died 48 hours later. Of great importance was the operation performed in Cape Town on December 3, 1967, when the heart of a girl who tragically died in a car accident was transplanted to a man. The patient died 18 days later. The cause of death was not the heart, but a decrease in immunity. The patient died of lung failure. Today, numerous transplant operations have been performed in the world, which have made it possible to extend the life of patients by ten or more years. For example, a resident of Marseille walked for hours after a heart transplant operation, cycled 30 kilometers twice a week, swam, and lived more than 15 years after the operation.

In a number of clinics, more complex operations were performed simultaneously, including the heart and another organ, e.g. the liver, or both lungs. In 1986, the English surgeon D. Wallwork was the first in the world to perform a triple transplant. A 35-year-old woman was successfully transplanted with the heart, lungs, and liver of a 14-year-old girl who had died in a car accident.

Despite the amazing successes in transplantation, there are a number of reasons that hinder the wider use of transplantation. These are scientific, moral-ethical and legal problems that hinder the use of the organ transplantation method. Many aspects of donation are insufficiently studied, the exact time of death of a person, etc. In addition, existing tissue and organ banks can only meet 10% of the total demand. Therefore, in America, organ transplantation from other types of donors began, in particular, they resorted to the use of animal tissues and organs. In January 1984, a monkey heart was transplanted into a baby on the 15th day after birth. Three weeks later, the patient died of kidney failure.

One of the most important problems of transplantation is the compatibility of organs and cells. In case of incompatibility, the body rejects the transplanted organ. Virtually all cells in the body are covered with a set of proteins called tissue compatibility antigens. The antigens of the same organ in different people are different. During transplantation, the body's defense system is activated, the entire immune system comes into play. Immunity is the body's protective reaction to any non-genetic. These can be microbes, a transplanted organ or tissue, as well as its own altered cells (tumor cells). Immunogenic control over the preservation of a person's individuality throughout life is carried out by lymphocytes, which circulate throughout the body in the blood and fluid tissue. Sensing foreign cells and molecules, they destroy them, or special proteins are produced that remove foreign antigens.

In order for the transplant to be successful, they act in two directions: 1. The antigens of the donor and the patient must be compatible with each other, or, 2. They reduce the activity of the immune system. Usually, both methods are used: the transplanted organ is processed and its immunogenicity is reduced, or the patient is given an immunosuppressant, which leads to a radical decrease in immunity and, in many cases, a fatal outcome. Therefore, they try to use medications that selectively regulate the immune response.

The vast majority of the listed problems disappear when using structures made of synthetic materials. In addition, polymers are characterized by very low immunogenicity. In addition, in the case of polymers, there are no moral-ethical and legal problems. Today, tons of polymeric materials are already used to replace human organs. Initially, existing polymers were used. In addition, the main requirement that was imposed on them was inertness and the ability to maintain the appropriate physical and mechanical properties for a long time. The scale of the use of polymeric materials has put a new problem on the agenda, namely, the problem of biocompatibility of polymers.

Today there is no need to talk about the importance of polymers. We know that living organisms consist of polymers: polysaccharides and proteins. In addition, every day at every step we encounter synthetic polymer materials, which are produced in millions of tons. Therefore, the question naturally arises - is it necessary to synthesize new polymers? Why can't we limit ourselves to using existing natural and synthetic polymers with different chemical, physicochemical and mechanical properties? At the initial stage of the use of polymer materials in medicine, the main advantages of polymers were considered to be biological inertness and a complex of physic–mechanical characteristics. Only later, after the not very successful implantation of polymer products into a living organism, it became clear that medicine is a specific field that requires either improving the synthesis conditions and processing of existing polymers, or creating fundamentally new types of materials.

It should be noted that all polymeric materials are perceived by the body as a foreign body. The first reaction that the implanted body causes is irritation, which is manifested in the inflammatory process.

The final result of endoprosthesis depends on the external shape of the endoprosthesis. The effect of materials of different shapes - triangular, pentagonal and smooth - on the surrounding tissue was studied. It turned out that the triangular material caused the most tissue damage, the smooth one caused the least. In addition, it is important where the implant is inserted into the body. An essential requirement is the placement of the implant between the layers of tissue.

In the manufacture of polymer prostheses, the purity of the polymer material is of great importance. As is known, there is no absolutely pure substance. In this regard, polymers that may contain monomer residues, initiators, dyes, stabilizers, etc. are particularly problematic. The presence of impurities in medical polymers should not exceed 10^{-5}, 10^{-6} %, which is consistent with the purity of materials used in electronics. It is not enough to obtain a pure polymer, it must be processed into a product and sterilized. It is necessary to process the polymer material, give it a shape, which occurs at high temperatures. At high temperatures, the polymer may undergo destruction, which in itself leads to contamination of the polymer. The polymer material must necessarily withstand sterilization conditions and must not undergo changes, since sterilization liquids are often adsorbed on the polymer surface. In most cases, ethylene oxide is used for sterilization. In some cases, ethylene oxide interacts with the polymer.

The role of polymers in creating artificial organs of the human body is especially important. It is worth noting that, except for the brain and stomach, which, according to the current scientific level, are not subject to replacement, all organs are being studied and modeled to create an appropriate analogue-substitute. While the functionality of natural organs is in the case when, due to trauma or other reasons, natural organs can no longer perform their intended functions, it becomes necessary to replace them with artificial ones. Since the 80s of the twentieth century, a boom in the use of artificial organs has begun. In 1990, the use of artificial organs in Japan was expressed in the following figures: artificial bones and joints - 3,000 people, blood vessels - 24,000; heart-lungs - 100,000; valves - 6,000; pacemakers - 20,000; kidneys - 38,000; hearts - 10,000 people.

Today, there is a wide range of polymeric materials that are successfully used in various fields of medicine. Demand and supply for artificial organs often do not coincide. Artificial hearts, lungs, kidneys and some other organs are used only temporarily, so the same set can be used several times, the number of used can reach several hundred. It is clear that the number of such sets will be small compared to the number of patients.

Scientific research work to create artificial organs is carried out in three directions:

1) Increasing the viability of the artificial organ;
2) Maximum universalization of functions;
3) Miniaturization of size. Creation of portable and self-healing artificial organs.

Artificial kidneys are widely used in patients with not only acute, but also chronic renal failure. Intensive research is being conducted in the field of artificial hearts and lungs. The goal of research is to extend the life of artificial organs.

When conducting experiments on a living heart, it is quite common for it to be unclear whether a medication circulating in the body is affecting the circulatory system or the heart. Whereas experiments conducted on animals with artificial hearts provide a clear answer to this question.

The effectiveness of scientific research work in the direction of creating, improving and using artificial organs, as we have mentioned, depends on the achievements of both medicine and natural sciences and technology. The list of substances that are necessary for creating artificial organs should include the following materials:

1. Biological, compatible with a living organism - Such materials include substances that, having penetrated the body, do not cause any reaction during their long-term presence in the body. Silicone, Teflon, polycarbonates, polyethylene, hydrogels and other synthetic polymer materials are widely used in this direction, as well as some metals, e.g. special grade stainless steel and titanium. A material that would be absolutely inert to a living organism does not exist today. That is, no matter what the nature of the substance and in what quantity we use it in a living organism, sooner or later, locally or throughout the body, it will inevitably cause a biological reaction.
2. Which have antithrombogenic properties (these are materials that are suitable for prolonged contact with blood and are used to make vascular prostheses, heart valves, artificial pericardium and diaphragms). Numerous fundamental studies have been conducted in the world to create antithrombogenic materials. In the case when an artificial organ is used once or several times, the problem is easily solved by adding heparin or another antithrombogenic agent. In addition, a substance has been obtained, the duration of use of which reaches several months. Thus, the prospect of creating a material with antithrombogenic properties is real.
3. Adsorbents - materials used in the construction of artificial organ devices (lungs, heart, kidneys). Currently, activated carbon, zirconium, ion-exchange resins, etc. are used as adsorbents for this purpose.
4. Artificial dialysis-diffusion aphasic materials (dialysis membranes are also made on their basis, which allow for the selective removal of urea, creatinine, and other metabolic products from the body).
5. Oxygen-carrying substances (this is a class of fluorocarbon-type substances that can dissolve in high concentrations of oxygen, as well as high-molecular compounds chemically bound to the heme of erythrocytes).
6. Fibrous materials (microporous materials with high metabolic activity, used in the construction of artificial organs, e.g. vinyl acetate fiber (artificial kidney), silicone capillaries of artificial lungs.
7. Materials for microencapsulation (which are necessary for the production of microcapsules with a diameter of the order of microns and are intended for drug delivery systems and oxygen carriers. Organosilicon polymer compounds, serum albumin, etc. are successfully used as materials for microcapsules.

The use of polymers in drug delivery systems. One of the most important problems in drug treatment is the selective (targeted) delivery of drugs to the body, since most traditional drugs act on the target and provide the desired effect, but at the same time act on other systems of the body and cause undesirable complications. Theoretically, selective drug delivery can be achieved in two ways: by different sensitivity of organs to the drug, or by different -targeted delivery of the drug. That is, drugs can be used that are distributed throughout the body, but actively affect only the target (i.e. do not / or less affect other organs), or those that are potentially capable of affecting many organs, but are arranged in such a way that they reach only the target. Traditionally, the first type of drugs is predominantly used in therapy. A good example of them are antibacterial agents that act on bacterial cells and are less harmful to human and animal cells. Obviously, the effectiveness of drug therapy will increase significantly if the drugs have a targeted delivery mechanism. The dream of giving drugs such "magic bullet" properties dates back to the time of P. Ehrlich, although this idea has only begun to be realized in recent years (P. Ehrlich is a German bacteriologist and chemotherapist, who was awarded the Nobel Prize in Physiology or Medicine in 1908. His works are devoted to the study of immunity problems, the development of methods for treating infectious diseases. P. Ehrlich is considered the founder of chemotherapy). It is no exaggeration to say that the creation of targeted drugs is tantamount to a revolution in therapy. One of the effective ways of targeted drug delivery is the use of various types of carriers. Both natural and synthetic polymers and more complex structures can be used as drug carriers, the function of which is often not limited to drug transport. They protect drugs and other biologically active substances (e.g. enzymes) from inactivation, and also perform the function of a reservoir from which the drug is gradually released.

In recent years, much work has been devoted to the use of synthetic polymers to construct drug delivery systems, which can be explained by the diversity of properties of these polymers and, in many cases, their biocompatibility.

The antibiotic doxorubicin is polymerized using pH-sensitive micelles based on an amphiphilic, self-assembling diblock copolymer. The copolymer is obtained by anionic polymerization (ring-opening) of allyl glycidyl ether in the presence of polyethylene oxide monomethyl ether as a macroinitiator.

Hydrogels, which are characterized by high water content and biocompatibility, have a wide range of applications in medical practice. They are used as surgical implants, controlled drug delivery systems, and more.

The brain has a natural protective system that protects it from the penetration of harmful substances. But at the same time, this barrier also limits the penetration of a number of therapeutic agents (especially water-soluble) for the treatment of cerebral diseases. Biodegradable polyanhydrides - polybis -p-carboxyphenoxypropane / sebacic acid, which are characterized by high hydrophobicity and the ability to non-enzymatic (chemical) biodegradation, were obtained. Chemotherapeutic agents were introduced into the polyanhydride (directly at the site of tumor resection) for local and prolonged delivery to brain cells. Polyanhydrides are promising for local delivery of water-soluble drugs to brain tissue, which ensures a high concentration of the drug at the target site.

Polymers that form micelles and are promising for drug delivery have been obtained through polymer-analogous transformations of cellulose.

Polymers of various structures containing hydrophobic groups are known in the scientific literature, which find great use both in catalytic processes and for the construction of targeted drug delivery and controlled release systems.

8. Elastic-ductile wear-resistant materials (materials intended for the creation of artificial bone, blood vessels, heart valves. These materials must exhibit complex physical and mechanical properties and must maintain these properties during long-term operation under mechanical load.
9. Biological adhesives for joining living tissue (bioadhesives are used to join skin, tissue, intestinal fragments, blood vessels, bile ducts, etc.). In addition, various types of bioadhesives are created to join artificial organs, e.g. blood vessels, urethra, bile ducts to a living body, as well as to glue an artificial valve to a natural heart. Adhesives must meet the requirements: they must not emit heat, harmful substances, must not react with living substance, must not undergo degradation in the body and must have a fast (instant) effect.
10. Polymer composite materials, including those for multiple use (such materials can be created by combining similar types of polymers, synthetic materials and metals, biopolymers with synthetic polymers, or metals. All possible combinations and combinations are used. The resulting compositions must have properties that would make it possible to create materials for the appropriate purpose from them.

The current level of implant surgery is unthinkable without the use of polymers and materials based on them. An implant is a medical device made of synthetic or artificial material, which is surgically inserted into the human body to perform certain functions for a long time and which has contact with blood and lymph.

All implants, depending on their field of application, will be subject to certain requirements, however, there are requirements that are common to all types of implants.

The introduction of an implant into the body is a complex surgical operation, accompanied by tissue rupture, which causes local and general changes in the body.

These processes are actually a protective reaction of the body to a foreign body, this is a tendency to restore and heal the damaged structure. The body's reaction is the same not only to the implant, but also to natural causes - the formation of hematomas as a result of trauma, bone fragments, etc.

In general, the body's reaction is expressed in the form of a number of processes:

1) Inflammatory processes.
2) Biodegradation of the implant.
3) Adaptation of the organism to the implant, through the formation of a capsule around it.
4) In some cases, the body expels the implant. A foreign body - an implant - can cause necrosis of the surrounding tissue, which is accompanied by pathological complications. In this case, it is necessary to surgically remove the implant.
5) Crystallization of inorganic salts (calcium-containing salts) - the so-called calcification - can occur on the surface and in the mass of the implant, which leads to a deterioration in the properties of the implant - especially its elasticity.
6) Insufficient purity of the implant material can lead to the release of carcinogenic and allergenic substances from it.
7) The behavior of an implant in the body is influenced by its dynamic interaction with the surrounding tissue.

Depending on the purpose, the implant can be replaced by living tissue or function in the body for a long time.

Materials that have the ability to decompose in the body by various mechanisms (biodegradable materials) are used to produce a large group of implants, among which the following are important:

1. Sutures.
2. Abutments and sheet materials for covering wounds.
3. Details for connecting bone fractures.
4. Foam-forming materials for filling cavities after surgery.
5. Filler compositions for filling bone defects.

Adhesive compositions used to bond bones and soft tissues must also have high biodegradability.

Replacing an implant with living tissue involves two parallel processes, the rates of which, namely, the rates of biodegradation and tissue regeneration, must match each other.

It should be noted that there are two periods of the "fate" of a polymer material. During the first period, the implant material performs its function, while being replaced by living tissue. During the second period (passive period), the already formed new tissue begins to perform its functions, and the implant continues to only decompose. The duration of the processes is determined by both the type of material and the place of implantation. Both natural and synthetic carbo- and heterochain polymers are widely used to create implants.

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წარმოადგინა ცხუმ-აფხაზეთის მეცნიერებათა აკადემიის ქიმიის ინსტიტუტმა

აბსტრაქტი. პოლიმერებმა ნამდვილი რევოლუცია მოახდინა თანამედროვე მედიცინაში. ჯანდაცვა და ყოველდღიური ცხოვრება წარმოუდგენელია მათი ფართო სპექტრის გამოყენების გარეშე. ხშირად, რთულ შემთხვევებში, აუცილებელი ხდება დაზიანებული ორგანოს, ან ქსოვილის სრული შეცვლა. ეს შესაძლებელია, განხორციელდეს ტრანსპლანტაციის, ან იმპლანტაციის საშუალებით. ტრანსპლანტაციის დროს ჩნდება მთელი რიგი პრობლემები. ეს არის: სამეცნიერო, მორალურ-ეთიკური და იურიდიული, ასევე ქსოვილებისა და ორგანოების დეფიციტი, რადგანაც ქსოვილებისა და ორგანოების არსებულ ბანკებს შეუძლია მხოლოდ საერთო მოთხოვნების 10%-ის დაკმაყოფილება, ასევე გადანერგვის შერმთხვევაში ყველაზე მნიშვნელოვანი პრობლემაა უჯრედების თავსებადობა. პოლიმერული მასალების გამოყენება ხსნის ყველა ჩამოთვლილ პრობლემას. მედიცინაში ფართოდ გამოიყენება როგორც კარბოჯაჭვური, ასევე ჰეტეროჯაჭვური აღნაგობის ბუნებრივი, ხელოვნური და სინთეზური პოლიმერები. პოლიმერები და მათ საფუძველზე მიღებული მასალები გამოიყენება აღდგენით

ქირურგიაში, ტრავმატოლოგიაში, ორთოპედიაში, სტომატოლოგიაში, ოფთალმოლოგიაში, ადამიანის ხელოვნური ორგანოების შესაქმნელად, დაზიანებული ორგანოების პროთეზირებისათვის და ა.შ. დონორის ორგანოებისგან განსხვავებით, პოლიმერებს ახასიათებთ ძალიან დაბალი იმუნოგენურობა, რაც ამცირებს შეუთავსებლობის რისკს და იმუნური სისტემის მიერ მათი მოცილების საფრთხეს. ყველა იმპლანტანტს, მათი გამოყენების სფეროდან გამომდინარე, წაეყენება გარკვეული მოთხოვნები, თუმცა არსებობს მოთხოვნები, რომლებიც საერთოა ყველა იმპლანტანტისთვის. პოლიმერების გამოყენება მკაცრ მოთხოვნებს აწესებს მასალებზე: ისინი უნდა იყოს ბიოლოგიურად ინერტული, შეინარჩუნონ შესაბამისი ფიზიკური და მექანიკური თვისებები ხანგრძლივი დროის განმავლობაში და ჰქონდეთ უკიდურესად მაღალი სისუფთავე. პოლიმერები გამოიყენება ასევე სამკურნალო საშუალებების „მიზნობრივი მიწოდების სისტემებისთვის", სადაც ისინი მოქმედებენ როგორც გადამტანები, იცავენ წამლებს ინაქტივაციისგან, უზრუნველყოფენ ეტაპობრივ გამოთავისუფლებას და ა.შ. მიმდინარე კვლევები მიზნად ისახავს ხელოვნური ორგანოების სიცოცხლისუნარიანობის გაზრდას, ფუნქციების უნივერსალიზაციასა და მინიატურიზაციას.

საკვანძო სიტყვები: *ბიოდეგრადირებადი და არაბიოდეგრადირებადი სამედიცინო პოლიმერები, ტრანსპლანტაცია, იმპლანტაცია.*