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Therapeutic biomaterials – application in neurology and cardiology

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ABSTRACT

Biomaterials are of interest in most medical fields. It's hard to imagine life without them. And due to the ever-increasing demand, scientists are developing new materials. Diseases of the nervous and cardiovascular systems are still a big problem, which are associated with a limited ability to regenerate brain or heart tissues. Therefore, this review discusses the advancement in biomaterial engineering for the treatment of neurological and cardiovascular diseases. Neurodegenerative diseases affect a large percentage of older people. Therefore, the review presents treatment options for Alzheimer's (AD), and Parkinson's diseases (PD). Another serious problem is cardiac ischemia. To regenerate heart tissue, scientists have proposed the use of extracellular vesicles, injectable hydrogels, and biomaterial-based cardiac patches. In addition to tissue engineering, implants are also developing in the field of cardiology. More and more modern materials are being created, e.g., for valve prostheses or vascular stents.

INTRODUCTION

The demand for biomaterials is constantly growing. Biomaterials are used in virtually every field of medicine. Biomaterials science can help create more effective vaccinations, medication delivery systems, and treatments, that can be used to treat or prevent various diseases.

Regardless of their purpose, they must meet several of the most important features. The requirements for the acceptability of biomaterials include technical functionality relating to implant-specific mechanical properties, sufficiently high stability in terms of physiological circumstances, and good biocompatibility. Maintaining biofunctionality over a long period of time is the aim of using biomaterials for implants (Sternberg, 2009). For instance, biomaterials that are administered to the brain must meet several general requirements. The material should correspond to the mechanical properties of the place where it is implanted. Softer materials tend to be less stable and stiffer materials can cause gliosis. It is also important to control the rate of degradation because rapid degradation can impair functionality, but non-degradable materials are associated with chronic inflammation and neuronal loss. The material should not be cytotoxic, immunogenic, or cause excessive secondary damage to nearby cells by causing oedema. A wide range of biomaterials has been used in the brain, e.g. in the form of hydrogels, particles, and electrospun fibers. Hydrogels and particles can be injected into the brain parenchyma, resulting in less trauma, than other forms of surgical implantation, but less structural control, than preformed biomaterials (Lally, 2022). For comparison natural biomaterial has many advantages, i.e. biocompatibility, biodegradability – natural degradation mostly can occur in the body, low toxicity, lower costs, versatility, and integration with cells. But it also provides some disadvantages like low mechanical strength, possible immune reaction, and a risk of contamination. Protein biomaterials (collagen, gelatin, fibrin, albumin, silk fibroin) and polysaccharide biomaterials (hyaluronic acid, alginate, chitosan, heparin, cellulose) are used to repair the brain (Ucar, 2021).

Because cardiomyocytes have a limited capacity to proliferate, cardiovascular disease is a common cause of mortality and morbidity. Cell-based therapies and bioactive molecules are currently used in heart regeneration treatments (Vasu, 2021). Due to the rapid development of materials science and technology, biomaterials have been found to provide biophysical and biochemical cues to regulate the intrinsic regeneration of cardiomyocytes and an external microenvironment conducive to heart repair has recently been identified (Fan, 2023). Cell-based therapies are based on the transfer of a cell suspension to damaged muscle tissue for repairing or replacing it. The supplied cells must be able to differentiate into mature and functional cardiac tissue – it is essential for true cardiac regeneration. Contrary to the development of tissue from directly injected cells, endogenous heart regeneration is made possible by bioactive substances, that harness paracrine actions. For this purpose, growth factors can be used, because they are signaling molecules involved in several biological processes like aging and survival. The delivery of growth factors must be local and scheduled. Endogenous heart regeneration is also possible by using bioactive substances, that harness paracrine actions. Three main methods are leading in cardiac regeneration therapies: extracellular vesicles, injectable hydrogels, and biomaterial-based cardiac patches. When designing material for heart regeneration, particular attention

should be paid to biocompatibility and immunogenicity, and it is important to consider angiogenesis and vascularity to support the contained cells (Vasu, 2021).

This review aims to provide a summary of recent research and challenges on biomaterials for use in neurology and cardiology.

THERAPEUTIC BIOMATERIALS IN NEUROLOGY

Multiple types of disorders, such as neurodegenerative disorders (ND), stroke, and traumatic injury, may damage the central nervous system. Therefore, it is a very difficult problem for doctors to repair their damaged parts. Neurodegenerative disorders refer to progressive damage to neurons leading to functional loss of the nervous system and include, for example, Alzheimer's disease, Huntington's disease (HD), and Parkinson's disease (Akhtar, 2023). For this purpose, scientists have proposed several materials for medicinal purposes.

ALZHEIMER'S DISEASE (AD)

Alzheimer's disease is a multifactorial, irreversible, progressive neurodegenerative disorder. The slow degeneration of brain synapses and nerve cells is an indicator of this disease. The brain's cognitive, memory, and behavioral abilities significantly deteriorate as a result of such persistent and irreversible nerve cell injury (Agrawal, 2021; Hampel, 202; Azargoonjahromi, 2023). AD is a disorder, that becomes worse with age. It contributes to around 60–70% (Agrawal, 2021) of dementia cases worldwide, making it the most prevalent kind of cause of dementia (Agrawal, 2021). Noticeably, the two primary neuropathological markers of Alzheimer's disease are hyperphosphorylated tau and -amyloid, two proteins that accumulate and solidify to form intracellular and extracellular neurofibrillary tangles and plaques, respectively (Azargoonjahromi, 2023). The behavioral symptoms associated with AD include memory loss, cognitive decline, difficulties with learning and thinking, mood changes, problems doing routine activities, etc. A prospective diagnostic and therapeutic tool is urgently needed due to the rising number of cases of AD. Only five molecules, i.e. galantamine, donepezil, tacrine, rivastigmine, and memantine, have been approved by the USFDA for treating this disease, and even those only have symptomatic or disease-modifying effects (Agrawal, 2021).

Functional biomaterials can display desirable properties in response to any external stimulus, including changes in temperature, light, pH, a magnetic field, an electric stimulus, etc. The release of the drug to the target site or pathological circumstances, such as amyloid aggregates, tumor tissues, the site of inflammation, etc., is made possible by pH-responsive functional biomaterials. A drug delivery system, that responds to changes in pH reduces systemic exposure to AD drugs and increases drug concentration in the damaged area of the brain. It is related to the acid environment within the amyloid plaque, damaged nerve cells, or inflamed neurons, which regulates the release of the drug from this carrier or drug at the target site, causing physical or chemical changes (Agrawal, 2021). Numerous natural polymers, including chitosan, cellulose, albumin, and gelatin, exhibit behavior, that is responsive to changes in pH and temperature (Agrawal, 2021; Chatterjee, 2019). Inflamed tissues, Aβ32 aggregates, or other damaged tissues of the brain increase local temperature and scientists use this ability to create thermoresponsive biomaterials (Agrawal, 2021).

Intranasal insulin research shows, that improving insulin signaling in the brain improves memory and learning in adults with Alzheimer's disease (Gao, 2019; Dubey 2020), Gao M. et al. examined the potential of glyceryl monocaprylate–modified (GMC) chitosan on the intranasal absorption of insulin in the AD rat model. The results showed GMC-chitosan and insulin interaction at 5.8 and 6.7 pH causes insulin to be encapsulated in a polymer matrix while no/little interaction at 4.7 pH. They proved, that the tested material was a promising absorption enhancer to improve the intranasal absorption of insulin (Gao, 2019).

Zhou H. et al. designed a nanocomposite with high stability and biocompatibility by using flower-shaped hollow nano-ruthenium as a carrier. The nanocomposite contained nerve growth factor (NGF) and phase change sealing material. The blood-brain barrier was successfully penetrated by the nanocomposite due to its excellent photothermal effect under near-infrared irradiation. It can react to phase shifts in the lesion area by releasing NGF, which effectively inhibits hyperphosphorylation of tau, reduce tau aggregation, decreased oxidative stress, restores nerve damage, and maintained neuronal shape. The results showed improvement in learning and memory in the AD mice model. It indicates, that multifunctional nanocomposites may be a promising medication in the treatment of AD (Zhou, 2020).

The hydrogels, biodegradable scaffolds, carbon nanotubes, and polymeric carriers can target the medicine to the brain (Agrawal, 2021). For example, collagen can be used in wound healing, bone and cartilage repair, ophthalmology, dental applications, and peripheral nerve repair (Ucar, 2021). Foidl B.M. et al. use collagen scaffolds crosslinked with polyethyleneglycole and loaded with nerve growth factor to target the delivery of NGF to organotypic brain slices of the basal nucleus of Meyner. Collagen scaffolds enriched with small amounts of protein or drug can be easily applied directly to organotypic sections of the brain, which allows for slow, but targeted release of the protective molecule (Foidl, 2018).

PARKINSON'S DISEASE (PD)

Parkinson's disease is a neurodegenerative disease, the treatment of which is mainly centered around the supplementation of dopamine. A wide range of biomaterials ranging from biomolecules, polymers, inorganic metal, and metal oxide nanoparticles have been employed to assist in the delivery of these therapeutic agents into the brain (Krishnan, 2021). The application of biomaterials to treat Parkinson's disease is still limited, despite the constant development of materials and technology. The electroconductive hydrogel can be used as a soft material for tissue repair and regeneration of electroactive tissues, primarily nervous tissue (Xu, 2022). Xu J. et al. designed and synthesized conductive hydrogels with self-healing and anti-inflammatory properties from dialdehyde polyurethane (~36 nm) nano-crosslinker, gold nanoparticles (~15 nm), and O-carboxymethyl chitosan under physiological conditions. These hydrogels showed a stable crosslinking network, acceptable conductivity, good biodegradability, and promotion of proliferation of neural stem cells (NSCs). The results indicated an anti-inflammatory effect and the hydrogel rescued function on inflammatory NSCs. Studies have shown that injecting conductive hydrogel into the brain restores the motor function of rats with Parkinson's disease. In contrast, histological analysis showed, that injection of conductive hydrogel increased the density of tyrosine hydroxylase-positive neurons and fibers as well as reduced inflammatory responses. The proposed hydrogel may serve as a promising carrier without additional cells or drugs for the treatment of Parkinson's disease (Xu, 2022). As in PD, a nanostructured scaffold could increase the viability of the replaced cells, providing a more favorable microenvironment and promoting neurogenesis in non-neurogenetic regions. On the other hand, the nanostructured scaffold can be associated with active drugs (e.g. chemotrophic proteins) (Carradori, 2017).

GLIOBLASTOMA

Biomaterials can also be used in the treatment of glioblastoma. Natural material-based scaffolds consist of extracellular matrix-derived biomolecules, such as hyaluronic acid, collagen, fibrinogen, basement membrane extracts, and even decellularized patient tissue. The disadvantages of these materials include their origin from mammalian organisms, therefore they can contain pathogens, and also vary in soluble factors and protein concentrations. Thus, non-mammalian polymers such as alginate and chitosan can be used as they are also biocompatible with glioblastoma multiforme (GBM) cells but are not immunogenic (Stanković, 2021). Abadi B. et al. created a novel form of selenium nanoparticles functionalized with chitosan and sialic acid. They assessed the antitumor effects of obtained material on the human glioblastoma cell lines (T98 and A172). They proved that the sialic acid enhanced the stability and biological activity of biomaterial. Additionally, the nanoparticles showed better inhibitory effects on cell lines T98 (Abadi, 2023). Furthermore, Bruinsmann F.A. et al. prepared chitosan-coated simvastatin-loaded lipid-core nanocapsules (LNCSVT-chit) suitable for nose-to-brain delivery. The capsules should induce an anti-cancer effect against glioblastoma. LNCSVT-chit significantly enhanced the amount of medicine in rat brain tissue after intranasal administration. Additionally, it reduced tumor growth and malignancy in glioma-bearing rats and did not cause any toxicity (Bruinsmann, 2022). Uribe-Robles M. et al. created TiO_2 hollow nanospheres as nanocarriers for targeted drug delivery. Nanospheres were functionalized with folic acid (HT-FA) for the targeted delivery of temozolomide. HT-FA successfully delivered and internalized temozolomide to glioblastoma cancer cells with high cytotoxicity. In addition, the nanocarrier was characterized by a high loading capacity, they retain and protect the active substance for at least 48 hours. Thus, the material is a promising platform for the targeted delivery of chemotherapeutic drugs for the treatment of GBM cancer (Uribe-Robles, 2023). The materials are not only designed to deliver drugs but can also be used to increase the radiosensitivity of cancer cells. The radiosensitivity of cancer cells was also studied by Mousavi M. et al. They synthesized the SPIO@AuNP-Cisplatin-Alginate (SACA) nanocomplex, which is composed of an SPIO core, a gold shell and an alginate coating. The results indicated, that the combination of SACA and 6 MV X-rays (at the doses of 2 and 4 Gy) drastically decreased the viability of U87MG cells. Additionally, this kind of cell line treated with SACA in combination with radiation increased apoptosis, which showed that the nanocomplex effectively increases the radiosensitivity of cancer cells (Mousavi, 2023).

THERAPEUTIC BIOMATERIALS IN CARDIOLOGY

TISSUE ENGINEERING IN MYOCARDIAL REGENERATION

The major causes of death worldwide are cardiovascular diseases (CVD), which include myocardial infarction (MI) and heart failure. Cardiovascular disease is the most common non-communicable disease in the world, accounting for one-third of all fatalities with an annual death of nearly 18.6 million (Fan, 2023; Roth, 2017). MI is mainly caused by occlusion of the coronary artery, as a result of atherosclerotic and thrombotic processes, and consequent reduction of the blood flow to the heart muscle. This can lead to the death of cardiomyocytes, difficulty in the synchronous contraction of the heart, and finally life-threatening heart failure or sudden death (Pascual-Gil, 2005; Chang, 2021). Current therapies most often include surgical procedures, such as coronary bypass, balloon angioplasty, and stents. Surgical interventions are usually complemented with pharmacological treatment. However, conventional interventions can only relieve the symptoms of myocardial infarction, but cannot repair the infarcted tissue, therefore, patients after a myocardial infarction may face severe functional limitations for the rest of their lives, leading to secondary complications, that impair their quality of life (Pascual-Gil, 2015).

The greatest challenge in cardiac tissue engineering is to develop new methods for heart tissue repair and regeneration. Exploring the biological and chemical aspects of the cardiac microenvironment has been the focus of recent investigations in cardiovascular tissue engineering. Biomaterials must show high biocompatibility and biodegradability. In addition, they should reduce the local resistance of the microenvironment, promote long-term integration of transplanted cells with native tissues and serve as a carrier for the controlled release of bioactive compounds (Fan, 2023). Despite the production of various biosynthetic materials, scientists still face limitations in the form of immunological complications caused by the biodegradation of scaffolds and insufficient cell migration. Therefore, it is essential to produce natural biomaterials to aid in myocardial regeneration (Lee, 2015).

Different kinds of stem cells such as fetal cardiomyocytes, embryonic stem cells, skeletal myoblasts, crude bone marrow stem cells, hematopoietic stem cells, fibroblasts, smooth muscle cells, and induced pluripotent stem cells, have been investigated to promote myocardial repair and have shown varying degrees of success in cardiomyocyte transplantation. Several biomaterials have also been created and examined throughout the years. Injectable biomaterials, i.e. alginate, fibrin, and chitosan improve infarcted heart regeneration (Lee, 2015; Rane, 2011). Liu Z. et al. explored an injectable chitosan hydrogel for stem cell delivery into the ischemic heart. Chitosan has been commonly used as scaffolds in tissue engineering. The results of their research suggest, that chitosan hydrogel application in the ischemic myocardium could enhance the MI microenvironment. The improved MI microenvironment promoted engraftment, transplanted stem cell survival, and endogenous stem cell homing. It should be noted, that chitosan hydrogel plays relatively limited roles in controlling the MI microenvironment, mostly through reactive oxygen species (ROS) scavenging. The therapeutic effectiveness can be improved by modifying chitosan with groups like a proangiogenic peptide, a pro-adhesion peptide, and an anti-apoptotic peptide (Liu, 2012). Whereas, Wang H. et al. studied the effects of co-injection of basic fibroblast growth factor with chitosan hydrogel, which has temperature-responsive properties. The material was injected intramyocardially into the left ventricular wall of rat infarction models. The results indicate, that co-injection of basic fibroblast growth factor with temperature-responsive chitosan hydrogels enhanced the effects of basic fibroblast growth factor on arteriogenesis, ventricular remodeling, and cardiac function (Wang, 2010).

Biocompatible conductive heart patches could be a promising method of restoring cardiac function. This material supports myocardial tissue after infarction and provides sufficient electrical conductivity to transmit the heart's electrical impulses [30]. Shabankareh A.N.T. et al. fabricated electroconductive nanofibrous structures based on polyurethane/reduced graphene oxide (PU/RGO). The results of the research showed, that PU/RGO scaffolds have enhanced Young's modulus, and the ultimate tensile strength besides biocompatibility was confirmed by determining the metabolic activities of exposed endothelial and myoblast cells. PU/RGO scaffolds, even at a high amount of RGO not only did not show cell toxicity but also enhance cell proliferation. Therefore, the material could be a potential electrically conductive cardiac patch to support myocardial regeneration (Shabankareh, 2023). However, Jain A. et al. described the fabrication of nCe-decorated polycaprolactone (PCL) and PCL-gelatin blend (PCLG) nanofibers. They used an electrospinning technique for that application. The results showed, that primary cardiomyocytes cultured on nCe-decorated PCLG nanofibers showed a reduction in ROS levels when subjected to H_2O_2-induced oxidative stress. Additionally, nCe-decorated PCLG nanofibers can suppress agonist-induced cardiac hypertrophy (Jain, 2021).

BIOMATERIALS FOR HEART VALVES

Another problem in the field of cardiology is the increasing demand for replacement of heart valves. Mechanical heart valves (MHV) and biological heart valves (BHV) are the two forms of prosthetic heart valves (PHV), that were initially used in clinical settings to mimic the original features and functions of natural heart valves (Priya, 2020).

Metals like titanium or stainless steel are used to fabricate mechanical heart valves (Lam, 2012). They are generally made in a tilting-disk configuration, with one or two rigid leaflets, that rotate on hinges. The leaflets, also known as occluders, are constructed either entirely from pyrolytic carbon or graphite coated with pyrolytic carbon. These kinds of valves are generally very durable, as pyrolytic carbon is strong and quite resistant to abrasion and fatigue (Priya, 2020). Blood tends to adhere to the metal in mechanical valves, resulting in blood clots. Therefore, patients must take anticoagulant medications for the rest of their lives (Lam, 2012).

Unlike mechanical valves, natural tissue valves do not need to be treated with anticoagulants. Bovine or porcine tissues are the most often used animal sources for biological valves. Bovine valves normally last 15 to 20 years, while porcine valves typically last 8 to 15 years. On the contrary, mechanical valves made of titanium or carbon are stronger and last longer, than biological valves (usually up to 25 years). However, the body's environment is very aggressive to the material. The most common causes of bioprosthetic valve failure are calcification and tearing (Lam, 2012). Two other significant factors are fatigue and wear stress. In most cases, the body's immunological response to generated wear debris leads to biomaterial fatigue. On the other hand, transvalvular pressure (after valve closure) is considered the most stressful for mechanical valves, wear can be caused by impact and friction (Taghizadeh, 2020).

The lifespan of a replacement valve is significantly influenced by the patient's age. Due to activity and metabolism, replacement valves deplete more quickly in children and younger patients, than in elderly people. Mechanical valves are commonly implanted in patients who are 65 to 70 years old or younger; patients older than that receive bioprosthetic valves. Patients in this age group may choose any type of valve, although there is evidence, that bioprosthetic valves are a superior option since they are more likely to last the rest of the patient's life without the need to take anticoagulant drugs (Lam, 2012; Chikwe 2010).

The biopolymer materials used in the design of heart valves include silicone, polytetrafluoroethylene, polyurethane, polyvinyl alcohol or polydimethylsiloxane-polyhexamethyleneoxide-polyurethane (PDMS-PHMO-PU) (Priya, 2020). In comparison to natural biomaterials, synthetic materials are more beneficial since the synthesis process allows for precise control of their properties, including the degree of porosity, pore size, 3D structure, mechanical strength, and rate of degradation. Whereas, issues related to their biocompatibility and subsequent inflammation, thromboembolism, or thrombosis can cause limitations in their application. In addition, special attention should be paid to the toxicity of synthetic materials and biodegradable materials (Lam, 2012).

Lancellotti P. et al. produced a drug-releasing multilayer coating adherent to mechanical valves. Their coating consisted of ticagrelor- and minocycline-releasing cross-linked nanogels covalently linked to polyethylene glycol. They assessed the hydrodynamic performance, durability, and hemocompatibility of coated valves. As opposed to noncoated valves, valve thrombosis was effectively reduced, when coated valves were implanted in nonanticoagulated pigs for a month (Lancellotti, 2023). Dehghani F. et al. also worked on improving hemocompatibility. They modified nanocomposites based on polyurethane – carbon nanotubes with heparin for application in heart valves. Then the nanocomposite was subjected to sulfuric acid and nitric acid oxidization. Their results indicated, that the obtained biomaterial reduced platelet adhesion and accumulation on the surface (Dehghani, 2022). However, Zheng C. et al. proposed a glutaraldehyde-free crosslinking method. The porcine pericardium was treated with 2-isocyanatoethyl methacrylate to introduce methacrylate groups and subsequently copolymerized with crosslinker, poly(ethylene glycol) dimethacrylate (PEGDA), to prepare a PEGDA polymer crosslinked porcine pericardium. The results showed, that the cytocompatibility and stability of obtained material were significantly improved. In addition, anti-thrombotic and anti-calc properties have been confirmed (Zheng, 2022).

Nanodiamonds are used in dental care, bio-imaging, and the creation of matrix composites for drug administration because of their great biocompatibility and outstanding mechanical properties (Chernysheva, 2023). Chernysheva M.G. et al. prepared nanodiamond-chitosan on the surface of the collagen tissue

crosslinked by glutaraldehyde. They compared the biostability and mechanical properties of the coatings with positively and negatively charged nanodiamonds. The results showed, that layer-by-layer applied nanodiamond and chitosan films improved the mechanical properties of the bovine pericardium. This was noticeable for both positively and negatively charged nanodiamonds (Chernysheva, 2023). Whereas, Tang X.S. et al. fabricated molybdenum doped diamond-like carbon (Mo-DLC) coatings, which were deposited by closed field unbalanced magnetron sputtering. The findings demonstrated, that a Mo-DLC coating with a low molybdenum concentration was a protective coating with good wear resistance at an ambient temperature of 500°C, reduced residual stress, and increased cohesive strength. The results indicated that there was significantly less thrombus on the Mo-DLC nanocomposite coatings, than there was on the pyrolytic carbon films (Tang, 2014).

BIOMATERIALS FOR STENTS

The repeated narrowing of the dilated segment of a coronary artery is known as restenosis. An artery's diameter narrowing by at least 50% on a subsequent coronary angiography is known as angiographic restenosis. A stent is inserted into the coronary artery in about 80% of all percutaneous coronary procedures. Each year, about 4.0 million of these procedures are carried done globally (Sareło, 2023; Pleva, 2018). Despite a significant reduction in the incidence of this phenomenon in patients, in-stent restenosis (ISR) resulting from neointimal hyperplasia is still a real threat and affects the success of the procedure (Pleva, 2018).

Materials used in prosthetic heart valves and vascular stents must minimize thrombosis, which is responsible for the local inflammatory response. It is important to reduce the adhesion of platelets and macrophages to the scaffold material and to minimize the risk of thrombosis due to the direct contact of the material with the patient's blood (Peng, 2022). Despite having excellent mechanical properties, the metals used to fabricate stents nevertheless have certain disadvantages, including restenosis, thrombosis associated with stents, and occlusion. The primary side effects of stents, such as thrombosis and allergic reactions, are caused by the release of metal ions and should be avoided (Malisz, 2023). Drug-eluting stents (DES) are the most popular type of stents used for this purpose. Antiproliferative drugs (such as sirolimus, paclitaxel, and everolimus) are released locally by DES, preventing excessive neointimal hyperplasia following stent placement and decreasing the incidence of ISR (Pleva, 2018). Scientists are still developing biomaterials and using different substances to create the most compatible stent.

Sareło P. et al. proposed a polydopamine-based-coating functionalized with an anti-inflammatory interleukin. Polydopamine has found application in the design of drug delivery systems due to its highly desirable properties such as the ability to be loaded with drugs to their controlled release and excellent photothermal conversion efficiency. The results of *in vitro* studies showed the promotion of endothelialization in the initial stage after implantation. Although, they confirmed the immunological activity of the coating by assessing the changes in THP-1 differentiation, which indicated that the binding procedure does not impair the biological properties of the interleukin. It can be said that the proposed anti-inflammatory coating can reduce the probability of restenosis to a minimum (Sareło, 2023). Whereas, Saadatlou G.A. et al. prepared a tetra-functional coating, which contains poly(2-ethyl-2-oxazoline)-co-polyethyleneimine (PEOX-co-PEI) stabilized silver nanoparticles and heparin. The coatings were deposited on NiTi alloy and 316 L stainless steel substrates via a layer-by-layer technique. The results indicated, that the material shows anticorrosive, antibacterial, biocompatible, and anticoagulant properties (Saadatlou, 2023). However, Hua J. et al. proposed a silk fibroin/chitosan-based (SF/CS/Cu) biopolymer coating incorporating copper ions. The results indicate, that the coating allowed for the migration and proliferation of endothelial cells on the cardiovascular stent surface. In addition, the NO-generating ability of SF/CS/Cu coatings may be used in the treatment of cardiovascular diseases (Hua, 2023). The other idea was presented by Wang B. et al., who created the bioactive hydrogel coating, which was based on chitosan, catechol groups, and copper ions. The findings of the experiments showed, that it is possible to accurately regulate the creation of the chitosan hydrogel coating using electrochemical deposition and functionalize it with catechol groups to further enhance its biological properties. Additionally, it has been possible to obtain accelerated NO-generation activity and *in vitro* cell biocompatibility. This suggests that biomimetic hydrogel coating may be a potential material for vascular engineering (e.g., coronary stent) and other biomedical devices (Wang, 2021).

The stent's surface can be covered with biocompatible and protective materials such as diamond-like carbon films. Many research indicates that DLC demonstrates high biocompatibility, haemocomability, strong adhesion to the substrate and reduction of platelet adhesion, in addition, this type of coating does not cause any inflammatory response or is toxic to cells (Malisz, 2023; Okpalugo, 2004). Castllino M. demonstrated that DLC coatings, deposited by physical vapour deposition, promote endothelization of coronary stent devices. DLC film coating enhanced haemocomability and biocompatibility and promotes excellent early vascular healing of the stent, besides, extremely thin strut thickness reduces the amount of late neointima and also the risk of late restenosis (Castellino, 2013). Additionally, doping with F enhances the anti-thrombogenic properties of DLC (Malisz, 2023; Saito, 2005).

CONCLUSION

Biomaterials are a group of natural and synthetic substances used to create scaffolds, designed to support the differentiation and proliferation of stem cells and, as a result, regenerate damaged tissue, but also support, and replace a given tissue or organ or targeted treatment of tissues/organs. Materials, that are implanted in the human body meet very specific requirements, i.e. they must not be toxic or immunogenic, they must be biocompatible, and have appropriate mechanical properties, support cell proliferation, or degrade without causing inflammatory reactions. There are many expectations. Demand is growing. Despite significant progress in the field of biomaterials for use in neurology and cardiology, scientists still have many goals to achieve. Improving existing technologies, drug delivery systems or interactions of the material with the body is essential.

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