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Biodegradable Materials in Medical Applications: Research Progress

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Abstract: Recently, the application of biodegradable materials in the medical field has been growing rapidly, covering bone scaffolds, vascular bridging, drug delivery carriers, implants, surgical instruments, and biochemical signal detection sensors. Compared with traditional materials, biodegradable materials are more environmentally friendly and have good biocompatibility, durability, and non-toxicity. However, the development of biodegradable materials in medicine still faces many challenges. The degradation time of the material is too long or too short, which will affect the therapeutic effect. At the same time, the degradation of the material is affected by external influences such as temperature, pH value, and pressure, and it is not easy to manipulate. The complex degradation behavior in the body is also hard to predict, and the degradation of some materials may produce toxic substances or induce inflammatory reactions. Therefore, this article summarizes the types of medical biodegradable materials and systematically introduces the current application status of biodegradable materials in medical implants, tissue engineering, drug delivery, disease treatment, and biochemical electronic sensors. The application of biodegradable polymers in disposable medical treatment is also discussed. Specific medical application cases are studied to better explain the uses and benefits of these materials. Finally, the existing problems and future developments are discussed to provide a comprehensive reference for future research.

Keywords: Biodegradable medical polymers tissue engineering.

1. Introduction

Biodegradable materials have attracted considerable attention for the last two decades in the medical area. For a representative example, biodegradable polymers gained popularity as the replacement of plastics. Researchers have conducted polylactide, polyglycolide, polycaprolactone, and polyurethane to employ them in medical applications. Their degradation undergoes multiple steps that involve both chemical and microbial mechanisms. They have potential in drug carriers, epithelial regeneration, antibacterial packaging, surgical tools respiratory equipment, and so on. In addition, biodegradable implantable sensors are developed to test significant biomarkers with high accuracy and flexibility. Biodegradable materials also can be used in piezoelectric devices to detect important biomarkers [1].

In another aspect, patients usually need a second surgery to remove the temporary implanted devices. Biodegradable implantation materials can avoid secondary surgery and long-term complications by degrading inside the body after fulfilling their service life. In orthopedics,

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rehabilitation equipment including fracture stabilization, bone grafts, fusions, and cruciate ligament reconstruction can be implanted into the body and go through a harmless degradation as time goes on, doesn't require a second surgery to take it out, causing little waste and impairment. Additionally, have a variety of applications in tissue pool engineering and regenerative medical areas, being a substitute for impaired tissues, interacting with living tissue, providing support, and responding to external incentive factors such as light, magnetic field, and ultrasound. Some metal materials also exhibit well biodegradability and biocompatibility, which suit them for medical implants and biochemical sensors [2].

This review will comprehensively summarize biodegradable materials in medical applications based on the specific areas they are used, such as polymers, and medical implants. And go deep into the characteristics and degradation mechanisms of these materials, and present the synthesis methods and device fabrication techniques them. Besides, finding the novel medical application status biodegradable materials and discuss the problems and prospects of these materials in medical applications.

2. Biodegradable materials classification

Typically, there exist three kinds of biodegradable materials that indicate natural biomaterials, synthetic biodegradable materials and biodegradable metals. Both of them have various applications in medical areas.

2.1. Natural biomaterials

Natural biomaterials are those that natively exist in nature, composite organisms, and degrade in the body spontaneously. They are generally classified into proteins that include collagen, gelatin, fibrin, silk, and polysaccharides including Hyaluronic acid (HA), chitin or chitosan, starch, and alginate.

2.2. Synthetic biodegradable materials

This class of materials can further be divided into biosynthetic materials and artificially synthesized materials. Polyhydroxyalkanoates (PHA) is a representative natural synthetic biodegradable material that is synthesized by microorganisms to be the inherent carbon and energy-storage when facing apotrophic environments, among which the most commonly used are polyhydroxybutyrate (PHB), polyhydroxyvalernate (PHV) and their copolymer PHBV. According to synthetic biodegradable polymers' monomers' diverse chemical compounds, they are classified as saturated aliphatic polyesters including poly glycolic acid (PGA), poly lactic acid (PLA), and their copolymers PLGA, polycaprolactone (PCL), polyhydrides, polyvinyl alcohol (PVA), polyurethane (PUR), polybutylene succinate (PBS) [3].

2.3. Biodegradable metals

Another large part of biodegradable materials is biodegradable metals and their alloys. Up to now the most extensively used are Magnesium, Zinc, and Iron. These metals, particularly magnesium, the deepest studied one, have great corrosion resistance and biocompatibility, let them applied in bone and arthrosis repair as implants or brackets, are comparable to traditional medical metal implants such as steel. They as well as their degradation products are harmless and nontoxic, such as metal ions even necessary microelements for human bodies [4].

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3. Biodegradable materials application in tissue engineering

3.1. Orthopedic scaffold

Studies confirmed that PHBV electrospun scaffolds can promote the regeneration of bone tissue due to their scaffold structure, which imitates the natural ECM. Besides, the addition of HA supports the process of mineralization, further promoting the adhesion and proliferation of osteoblasts. Incorporating poly-lysine (PLL) in scaffolding systems or electrospinning PHBV polymers with PLL increases proliferation and ALP activity, supporting bone protein expression and mineralization [5].

PGA can initiate the nucleation of apatite and further promote the bone-like apatite layer to formate, because of the carboxyl groups it possesses. Combined with other components associated with bone tissue growth, such as bone morphogenetic proteins and β-tricalcium phosphate, PGA can reinforce new bone growth and address issues of poor apatite formation. PGA hydrogels can be used as injectable bone fillers.

The glutamate signal within cartilage is believed to modulate human chondrocyte behavior and enhance matrix production. Reports indicate that PGA-blended scaffolds support chondrocyte differentiation and increase ECM production in the early stage.

3.2. Cardiovascular

PLA possesses a great biocompatibility that meets the needs of arterial grafting. Electrospun PLA/chitosan copolymers have demonstrated the ability to foster the growth of cardiomyocytes. Experimental cardiac patches made of PGLA have the capability of electrophysical anisotropic function for local tissue and even can be relieved under abominable conditions like myocardial infarction [6].

3.3. Dental

PLA triumphantly integrates dental implants with native oral tissues and enhances the mechanical properties of dental resin. PLGA can serve endodontic therapies.

3.4. Wound healing

To separate damaged tissue from adhering to adjacent normal tissues, physical tissue barriers need to be stable until recovery and given enough biocompatibility to restrain serious immune responses. Studies indicated that PGA nano-fiber sheets exhibit as well as improvement in wound healing with no shrinkage, because of their great hydrophilicity. Another study also showed that PGA can significantly improve the stability of a tissue barrier formulation, which contains HA mixture and Pluronic. PGA has great cell adhesion, especially ultra-high molecular weight PGA appears better in wound healing, accompanied by a specific increase in regeneration of vascular cells and transformation of growth factor-β, and β-catenin. Additionally, researchers found that it not only promotes wound healing but also inhibits hypertrophic scars during anaphase.

4. Biodegradable materials in drug delivery and disease therapy

4.1. Cancer therapy

Polymeric nanoparticles encapsulated chemotherapeutic drugs can not only retain the therapeutic agents to enhance the antitumor efficiency and decrease the effective dose and side effects but also can overcome acquired resistance to single chemotherapeutic drugs.

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For example, etoposide is widely used in malignancy treatment by inhibiting the topoisomerase-II, activating the oxidation-reduction, and damaging the DNA, but is restricted by its short, up to 3.6h biological half-life. To prolong the time exposed to tumor cells, etoposide-loaded nanoparticles have been created, providing a continuous release of this drug for about 48h sequentially affecting cancers.

4.2. Disease

Recent studies demonstrate the ability of PGA to induce iPS cell differentiation, and repair and regenerate nerves. Injured corneas can be well treated by keratinocyte growth factors which can be delivered by thiolated PGA, which means modifying PGA with cysteine. Silicone nano-needles can permeate into the cornea in a minimally invasive way by integrating with tear-soluble contact lenses. Through months' degradation, it can achieve long-term sustained delivery of ocular drugs in painless [7,8].

Biodegradable polymeric nanocarriers loaded with insulin have nano-porous membranes that have grafted glucose oxidase, the rise of blood glucose level will modify the nano-porous and ulteriorly lead to biodegradation, resulting in the release of insulin. Also, the glucose/glucose oxidase reaction will lower the pH and swell the polymer system, enhancing the delivery of insulin.

According to research, injecting diclofenac-PGA NPs can cause intervertebral disc(IVD) to produce natively as well as reduce inflammatory reactions, supporting the success of deteriorated IVD therapy. PGA/gelatin hydrogel has good durability, which makes it significant in leakage sealing and pressure saturating of lacerated discs. PGA/collagen hydrogel can be used as injectable scaffolds for delivering antioxidant drugs into kidneys, a studied delivery is the mouse MSCs [9].

4.3. Skin wound healing

PLA can load bioactive drugs which promote healing. For example, combining bioactive ginsenoside-Rg3 with biomolecules, such as basic fibroblast growth factor in an electrospun PGLA scaffold, developed a favorable drug-therapy environment because the incorporation of biosignal compounds and PLA scaffold improved cell adhesion and proliferation. PLA also has advantages in tendon repairing, combining hydrophilic mitomycin-C (MMC) into PLA fibers which load HA creating an MMC function protecting the drug delivery system, thus stimulating the healing of the intrinsic tendon. This approach controlled the release of MMC, thus stimulating intrinsic tendon healing [10].

5. Biodegradable clinical devices

PLA is now used to produce one-used medical devices such as surgical gowns, masks, and surgical sutures to be environmentally friendly. In natural environments, PLA is mainly degraded in soil by soil microorganisms such as actinomycetes, bacteria, and fungi, but the rate is relatively slow. Research shows that the addition of enzymes, nutrients, fiber-based reinforcements, starch, and bacteria activities can accelerate the degradation. PLA also can degrade in seawater, mainly undergoes hydrolysis and the velocity is much slower. In industrial processes, PLA can go through thermal degradation when subjected to high temperatures. The thermal cracking produces propylene glycol esters, cyclic oligomers, and linear oligomers, at temperature ranges between 320 and 420 [11].

Sutures made of PLA, PGA, and polyglycolide as well as their copolymers are now popularly used in surgery not only because of their excellent biocompatibility and biodegradability that avoid irritation nor inflammation but also owe to their tensile strength that promotes closing the wound. These sutures do not need to be taken out as they gradually degrade inside the body, further facilitating the healing of wounds [12].

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6. Biodegradable biochemical signals sensor

Silk fibroin is a suitable material for medical implantable electrode devices due to its excellent mechanical flexibility. Silk plasticization and metallic thin-film are also been used to produce skin-comfortable electrodes that have a strong stretchability for wearable medical devices or implants. Cellulose paper can be used in the manufacture of wearable biosensors and electrochemical sensors, such as sweat and bio-fluid analysis, which have the advantage of inexpensive, large collection volume and improvement of contact with skin [13].

To fabricate a kind of temperature sensor that is skin imitated, PLA in a three-arm structure can be used to build both the substrate or dielectric, with high thermos stabilization and flexibility. It is shown in previous research that the requirements of long-term real-time glucose level tests with electrochemical strip tests as well as the necessary need for film strength can be achieved by adding gelatin to a PLA-polymer matrix. In healthcare diagnosis and displaying human activities, PVA-based hydrogels are applied to develop wearable sensors that transiently degrade inside the body. For example, degradable epidermal sensors can be fabricated by PVA hydrogels that in borate modifications with eutectic indium and gallium Liquid Metal Particles (LMPs). It dissolved just in 3 days at room temperature in a pH 5 solution of HCl [14].

Considering Kinds of synthetic polymers such as PVA, PLA, and PDMS are widely employed as biodegradable medical devices' dielectric layers thanks to their polar or charged terminal groups such as acid or alcohol groups. Biodegradable elastomeric polymers such as poly (glycerol sebacate) (PGS) are available to create capacitive degradable sensors due to their great reversible voltage endurance capabilities. For instance, membrane composited of PLGA-PCL can be applied in dielectric elastomeric layers to manufacture pressure sensors which can completely biodegrade with the most advanced electrospinning techniques [15].

7. Conclusion

In conclusion, biodegradable materials now have a wide range of applications in medical areas, including bone scaffolds, vascular bridges, drug delivery particles, implants, surgical tools, biochemical signal detection sensors, and so on. Compared with traditional materials in these areas, biodegradable materials are more environmentally friendly, capable, durable, and non-toxic. Drugs packaged in biodegradable nano-particles can target the pathological, extend the action time, increase the drug stability, and enhance the medicine bioavailability. Along with the hydrolysis or enzymatic decomposition of the polymers, it gradually releases the drug, causing drug concentration in a suitable scope to improve the therapeutic effect and reduce the toxicity and side effects. Biodegradable medical implants play an important role in tissue regeneration and implantable medical electronic equipment allows doctors to supervise the physiological data of patients, after the biodegradable implant operation period it will degrade in the body to avoid a second-surgery removal or long-term implantation.

However, there are still many problems and challenges in developing medical biodegradable materials. Some material's degradation time is long or too short, both of which will affect the results of therapy. The therapeutic effect is affected by the current station of the material such as temperature, pH, and pressure, these factors change all the time with the degradation of the materials and are hard to control. It is difficult to predict the complex degradation movement inside the body, some materials may create toxic substances. Some materials may cause inflammatory reactions. Considering these challenges, there is a long way for the future research of biodegradable materials to go.

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