Proceedings of the 2023 International Conference on Machine Learning and Automation
DOI: 10.54254/2755-2721/32/20230194

Biodegradable materials in tissue engineering and regenerative medicine

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Abstract. Regenerative medicine signifies that medicine will step into a new era of reconstruction, manufacturing, and replacement of tissues and organs. At the same time,the mankind face many challenges which the development of medicine brings. Along with the progress and development of medical science and technology and the concepts of tissue engineering and regenerative medicine, it has a significant role in advancing the development of human medical technology and future tissue and organ regeneration and repair. This paper will introduce the concept of biodegradable materials and categorize biodegradable bio-materials into synthetic biodegradable bio-materials such as polylactic acid derivatives, copolymers of polyhydroxyacetic acid (PHA) and polylactic acid (PLA), and naturally occurring biodegradable bio-materials such as collagen, chitosan, as well as including their applications and research in tissue engineering. Finally, we make a beautiful outlook on the role of regenerative medicine in the future of human life for human health management and repair.

Keywords: tissue engineering, biodegradable materials, synthetic degradable materials, naturally occurring biodegradable material.

1. Introduction

In the survival needs are gradually satisfied on the basis of people's demand for medical level is also gradually rising, due to some major diseases will cause irreversible damage to human organs and their functions, so the regeneration of organs and tissues for the research has become a new hot spot in today's society. At the same time for some repair damage need to be ingested drugs and their carrier materials have also become a new challenge, as the drug into the body for human tissue repair or other to achieve other functions, such as the realization of the function of the fixed-point time-release drugs, the requirements of the drug in the inhalation of the human body at the same time can not be absorbed, and need to be a certain length of time to produce the effect. In order to realize this function, it is necessary for biodegradable materials to play its characteristics, because it is a biological material, so the biocompatibility should be as high as possible and the human body's rejection reaction should be reduced to none, in addition to ensure that there is a certain degree of mechanical strength and solubility, so that the carrier material can be realized to encapsulate the drug, so that the drug can’t be absorbed by the human body for its period of time to get protection from the encapsulated material is too short, and in a certain time, that is, the encapsulated material is degraded, so that the human body is unable to absorb the drug. A certain time that is, after the degradation of the carrier material, the drug can be absorbed by

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the human body, and as a biodegradable material, so the carrier material does not need to take great pains to take it out, but only needs to be allowed to be slowly decomposed and absorbed in the human body. Besides, Regenerative medicine and tissue engineering still has a lot of problems to overcome, and the research on the application of biodegradable materials in regenerative medicine and tissue engineering has only just begun, and there is still a lot of space to explore and discover. As a summary article, this paper explains the types, characteristics and applications of biodegradable materials. The biodegradable materials are divided into two categories: artificial degradable materials and natural degradable materials, and then branch out from these two categories into subdivided categories, and elaborate the characteristics and applications of each of them, for example, artificial degradable materials are divided into polylactic acid derivatives and copolymers of poly (hydroxyacetic acid) and polylactic acid, and natural degradable materials are divided into collagen and chitosan.

Biodegradable polymers can undergo chain-breaking reactions through three degradation mechanisms: photochemical degradation, thermochemical degradation, and biochemical degradation, resulting in a decrease in mechanical properties and an increase in solubility, and the degraded oligomers are further broken down into small monomeric molecules that enter the body fluid cycle. Biodegradable polymers can help simplify medical procedures as non-permanent implant materials in living organisms.

Tissue engineering as a new concept of regenerative medicine was introduced by American scientists Langer and Vacanti and is defined as the research and development of life science technologies that can repair, improve, or replace human tissues or functions [1].

2. Synthetic biodegradable polymer materials

2.1. Poly (lactic acid)-based derivatives

Polylactic acid derivatives in recent years in the biological scaffold material research room biomedical tissue engineering a hot spot, biological scaffold material as a key topic of tissue engineering research, in addition to providing a good survival microenvironment for the cells and to the cell attachment, growth, adhesion, and other positive interactions, and can be appropriate to induce the ability of differentiation. Polylactic acid (PLA), as a biodegradable material that can be used as a bioscaffold material, has its own unusual characteristics [2-3].

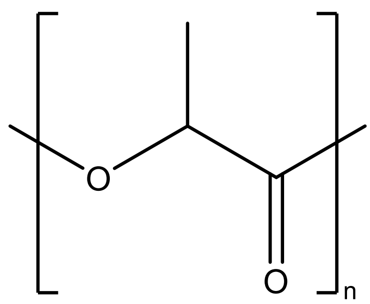

Figure 1. Molecular structure formula of polylactic acid derivatives(origin).

The molecular formula of the polylactic acid derivative is shown in the figure 1 above. Polylactic acid derivatives have been widely applied as scaffolds in tissue engineering for many years and cellular building blocks, and these biodegradable polymers are distributed and absorbed in vivo as the tissue is reconstructed. Polylactic acid has good biocompatibility and biodegradability [4] with human tissues and does not cause rejection in the body, and the hydrolysis products of Polylactic acid can participate in the metabolic process of sugars in the body without causing any residual or biological side effects, so Polylactic acid is now widely used in the production of medical materials such as sustained release drug carriers and implants for biological tissue repair.

Lactic acid has two functional groups, hydroxyl and carboxyl, and can therefore undergo a self-condensation reaction under certain conditions to produce polylactic acid, which has a life span of 4-6 months in physiological salt water. By adjusting the ratio of different polylactic acids polymerized from different chiral configurations of lactic acid, there will have an adjustment for the strength and degradation time of the material. Since hydroxyapatite is the basic component of human bones, which promotes bone growth by close bonding with collagen or cells, but presents brittle characteristics when it receives tension, which means its mechanical properties are poor, so compounding hydroxyapatite with poly (levulinic acid) to form a new biodegradable composite can improve its mechanical strength. It has been shown that introducing polymeric phase molecules into poly (levulinic acid), the mechanical strength of the material rose by five times. The combination of Polylactic acid and other materials into a composite material can make the material mechanically supportive as well as a drug carrier. Also there is a close relationship between the mechanical strength and hydrolysis rate of Polylactic acid and molecular weight distribution of the polymer and the polymer's average molecular weight; when the molecular weight increases, the mechanical strength also increases and the hydrolysis time becomes longer. When the molecular weight of Polylactic acid is lower than 2500, the mechanical strength is poor and the hydrolysis rate is too fast, while when the molecular weight is more than 1 million, the degradation reaction will not occur for a long time, so the molecular weight of Polylactic acid is a important method to regulate the degradation rate and performance. Polylactic acid is not toxic, has a certain life span in the human body, and the degraded product can be absorbed and metabolized by the human body, so it can be used as a tissue defect reinforcement material. Non-woven and mesh fabrics made from PLA fibers can be used to repair surgically removed chest walls, for example, and can be used for tendon reconstruction after de-stretching and strengthening. Polylactic acid can also be used as a bonding and fixation material for surgical procedures. Since the bending strength and bending modulus of stretched Polylactic acid are comparable to those of the original bone, it can be implanted in the body to protect the broken bone and can be absorbed by the body after healing to prevent secondary damage.

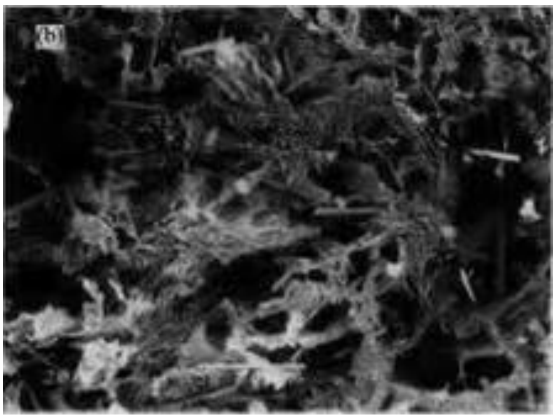

Figure 2. Scanning electron microscope micrographs of PLLA and $CaCO_3$/calcium polyphosphate/ poly-(L-Lactic acid) composite tissue engineered scaffolds [5].

The above figure 2 shows the SEM diagram of Zhu et al. showed for the construction of ball-milled calcium carbonate/polycalcium phosphate fiber/polylactic acid tissue engineering composite scaffold material, and it is observed from the figure that the scaffold composite material has a three-dimensional mesh structure within the cross-section, microporous structure, random distribution of fibers, and relatively uniform distribution of microporosity, and these structures can provide suitable nutrient transport conditions, space conditions, and excretion exchange conditions for the growth and reproduction of tissue cells, which are conducive to the specific physiological functions of bone and cartilage tissues [5].

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2.2. Polylactic acid and polyhydroxyacetic acid copolymer

Biodegradable synthetic polymers have highly controllable degradation properties as well as excellent mechanical and physical properties are suitable for making tissue engineering scaffolds. Pan et al. prepared electrospun dextran/polylactic acid-hydroxyacetic acid copolymer composite scaffolds and applied them to mice for in vivo degradation experiments. After three days, the scaffolds degraded to half of their original size, and after three weeks, three-quarters of the scaffolds were absorbed and the surrounding tissues were completely repaired. [6] Polylactic acid and polyhydroxyacetic acid can bind to cells and biomolecules to enhance biological properties, and biodegradable polymers cannot structurally replicate the mineral composition of bone. However, the biodegradability of copolymers and the ability to incorporate release signaling molecules allow copolymers to be a support for bone formation, and the biological properties of low bioactive poly(lactic acid) poly(hydroxyacetic acid) copolymers can be improved by incorporating bioactive substances to improve bone regeneration and repair.Liu et al. constructed poly(lactic acid) poly(hydroxyacetic acid) scaffolds containing simvastatin (SIM) and stromal cell-derived factors and found that SIM at 0.2 μmg/L increased the alkaline phosphatase activity of mouse bone marrow MSDs.The chemotactic ability of SDF-1α is also enhanced, and the test results showed that poly(lactic acid) polyhydroxyacetic acid with these modifications significantly promoted bone regeneration [7].

3. Natural biodegradable polymers

3.1. Collagen

Collagen is found in many tissues of humans and animals and is one of the main components of bone tissue. Collagen exists in the body in the form of collagen fibers and induces mineral deposition, which provides protection and support to cells and is closely related to cell growth. The fibrin monomers in collagen fibrils can be polymerized by thrombin into a fibrin coagulase with a homogeneous reticular cross-linked structure. Collagen and fibrin thrombin have poor mechanical properties, but fibrin thrombin can promote cell adhesion and multiplication by releasing tumor necrosis factor and platelet-derived growth factor, and fibrin thrombin has good biocompatibility and biodegradability. Zhao et al. achieved cell growth propagation and adhesion with improved mechanical properties by composing fibrin gel and chitosan into a scaffold with a three-dimensional reticular cross-linked structure [8].

3.2. Chitosan

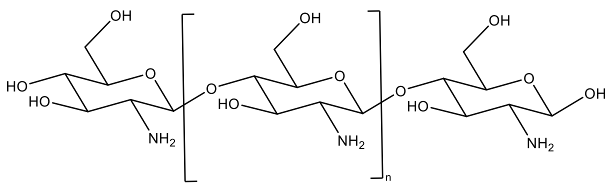

Figure 3. Chitosan molecular structure formula(original).

The molecular formula of chitosan is shown in the figure 3 above. Amaral et al. cultured murine bone marrow stromal cells in vitro knowing chitosan membranes and showed that 4% of chitosan membranes showed substantial cell adhesion, cell proliferation as well as osteogenic differentiation. Chitosan is produced by deacetylation of chitin, a natural polysaccharide found mostly in the shells of insects, etc., as well as in the cell walls of fungi. Chitosan has good biocompatibility and degradability [9]. If chitosan is made into a three-dimensional porous scaffold and implanted into the body, it can be hydrolyzed into oligosaccharides under the action of lysozyme, and then further broken down into small monomeric molecules to be metabolized and absorbed by the body. To realize the application of chitosan in tissue engineering, its mechanical properties pally an important role in this aspect. Xu et al. make a composite material of calcium carbonate and chitosan to realize the application of chitosan in bone tissue engineering to help to get the mechanical properties improved [10].

4. Conclusion

This paper firstly introduces the concepts of biodegradable materials and regenerative medicine in tissue engineering, and clarifies the prospects of biodegradable materials in biomedical applications. Then it explains and introduces different biodegradable materials and the different functional effects of different materials in tissue engineering. Firstly, we introduce the synthetic biodegradable materials, focusing on the polylactic acid derivatives and copolymers of polyhydroxyacetic acid and polylactic acid, polylactic acid derivatives because of their special physical and chemical properties, such as greater mechanical strength, higher biocompatibility, degradation of substances can be absorbed and metabolized by the human body and so on, become a slow-release drug carriers, tendon reconstruction, bone regeneration and so on, a good medical material. Then the copolymers of polyhydroxyacetic acid and polylactic acid are introduced. The biodegradable biomaterials are synthesized and polymerized to take advantage of the advantages of the monomer materials and realize the improvement of the composites biocompatibility and mechanical strength by the combination of them, and to better achieve the functions of biological tissues' repair and regeneration. Subsequently, natural biodegradable biomaterials were introduced, taking collagen and chitosan as an example, collagen can be used to achieve cell growth and reproduction by forming fibrin clotting enzymes under the action of enzymes, and polymerization with chitosan can improve the mechanical properties to achieve cell growth and reproduction, whereas chitosan improves the mechanical properties to achieve the utilization of chitosan in the bone tissues to achieve the regeneration of the bone tissues in the case of polymerization with calcium carbonate.

In the era of rapid development of medical technology, people can still see many people with physical organ defects or disabilities have many inconveniences in their lives and long-time disabilities have irreversible damage to their psychology, and the breakdown of body organs and functions will lead to the health of human beings is not optimistic. In order to restore the health of those who are physically handicapped by accidental injuries and need to take prolonged-release medication to maintain their lives, not only respect and care, but also solve the problem from the root. Researchers has make many efforts to tackle the problem at its roots to help the development and research of biodegradable materials in tissue engineering and regenerative medicine, and people are looking forward to it! We all look forward to a future where everyone is physically and mentally complete.

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