

Application of Silk Fibroin in the Field of Oral Clinical Medicine

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Abstract

Silk fibroin (SF) is a non-toxic and non-irritating natural polymer material extracted from silk. Silk fibroin has great application potential in biomedicine because of its unique elasticity, flexibility, biocompatibility, and biodegradability. The fusion of silk fibroin and oral clinical medicine has gradually become hot. , This paper reviews the research and application of silk fibroin and its composite materials in different fields of oral clinical medicine.

Keywords

Silk Fibroin; Tissue Engineering; Periodontal Tissue Regeneration; Oral and Maxillofacial Surgery; Oral Mucosa.

1. Introduction

Silk fibroin is a natural structural protein with no physiological activity. Silk fibroin is mainly glycine, alanine, and serine in highly repetitive polypeptide chains. Parallel β -sheet, this basic conformation gives silk fibroin more stability. Silk fibroin has extremely strong biocompatibility. It does not cause an immune response in the body, can control biodegradability, and quickly produce chemical covalently modified adhesion sites or load bioactivation factors on its surface. At the same time, silk fibroin has robust processability. That can be made into composite preparations or membranes, gels, and scaffold materials, so it has been widely studied in mucosal repair, periodontal tissue regeneration, and jaw osteogenesis. And application.

2. Research and Application of Silk Fibroin in the Osteogenesis Direction of Oral and Maxillofacial Surgery

In oral and facial surgery, bone injury and bone defects are widespread. Silk fibroin has strong mechanical properties and biocompatibility but insufficient mechanical strength. In bone tissue engineering, silk fibroin can be used alone or with other materials to prepare different forms, such as biofilms, hydrogels, scaffold materials, etc., to induce osteogenesis. Liu [1] used the extracted sheep bone marrow mesenchymal stem cells as seed cells to make cell membranes on the mandibular defect model of Xinjiang Altay Big-tailed sheep, combined with 3D printing of antler powder/silk fibroin/polyvinyl alcohol scaffolds. At the end of the first month of this experiment, the cell membrane sheet compounded with antler powder/silk fibroin/polyvinyl alcohol group had more scaffold absorption in the bone defect area, a small number of osteoblasts could be seen, no evident calcification and a large amount of fibrous tissue had grown in In the scaffold; at the end of the second month of this experiment, the cell membrane composite antler powder/silk fibroin/polyvinyl alcohol group had less scaffold material absorption, osteoblasts were active in osteogenesis with different densities of new bone formation, and a large amount of fibrous tissue grew in In the scaffold, the osteogenic effect was more evident than that of the control group; at the end of the third month of the experiment, the scaffold material in the cell membrane composite antler powder/silk fibroin/polyvinyl alcohol group absorbed more scaffold material. The bone defect area was covered with new bone, and the tissue was regular. Capillaries are abundant, which indicates that the tissue-engineered bone

of cell membrane composite antler powder/silk fibroin/polyvinyl alcohol exhibits good osteogenic performance in vivo. The results of real-time quantitative PCR showed that osteocalcin, which reflects the activity of osteoblasts, and types I collagen, which reflects the early differentiation of osteoblasts, were greater than those of the control group. The effect of polyvinyl alcohol on bone is remarkable. Quan[2] prepared silk fibroin (SF)/chitosan (CS)/hydroxyapatite (nHA) into biofilms, with SF/CS/nHA as the experimental group and SF/CS film as the control group, Taking the glass slide as the blank group, the cell adhesion rate and proliferation rate was calculated by the MG-63 cell experiment, and that ALP activity secreted by MG-63 cells was analyzed to study its osteogenic properties. The cell adhesion rate at 4, 7 hours and the ALP activity at 7, 14, and 21 days were higher than those of the control group, proving that SF/CS/nHA biofilm could induce adhesion and proliferation of osteoblasts and had a pro-osteogenic effect. Zhang[3] studied the minimally invasive lifting of the maxillary sinus in oral implant surgery and injected the slow-release hydrogel of VEGF and BMP-2 silk fibroin prepared by ultrasonic method between the mucosa and bone wall of the maxillary sinus in rabbits. The results showed that at 12 weeks after the operation, the new bone tissue could be seen in the experimental group's maxillary sinus floor of the rabbits. The height of the sinus floor was significantly higher than that before surgery.

3. Experiments and Studies of Silk Fibroin in Mucosal Repair

In the treatment of mucosal defect repair in oral clinical medicine, the main scheme of this treatment is different forms of a skin flap or skin grafting. In the course of treatment, skin graft and skin flap transplantation not only need to open up a second operation area but also due to the existence of large and small glands and unique structures in the oral mucosa; in some cases, skin graft or skin flap transplantation cannot fully restore the function of the oral mucosa. The goal of tissue engineering and in situ tissue regeneration is to construct tissues and organs with similar structure and function to the living body. Tissue engineering oral mucosa is to implant the scaffold material inoculated with the seed cells of the target tissue into the defect site so that the seed cells can proliferate and differentiate into the target tissue to restore the original shape and function. It is gradually decomposed and excreted [4]. In constructing and treating tissue-engineered oral mucosa, the scaffold material is the medium and umbrella of seed cells, which can assist and promote the expansion, differentiation, and surface adhesion of seed cells. Therefore, biocompatibility is good. It is essential. Q Yang[5] constructed a rat buccal mucosal defect model and repaired the defect mucosa through a porous silk fibroin scaffold material with a multi-layered cross-linked silk fibroin membrane. The effect and scar contracture were better than those of the control group, the histological structure was clear, the local inflammatory reaction was mild, and no obvious systemic immune response was caused in the immunohistochemistry and peripheral blood T lymphocyte examination, which proved that the silk fibroin material is a kind of repair material—ideal biomaterial for mucosal defects. Wang [6] and others implanted porous silk fibroin scaffolds on the rat buccal mucosal defect model and found that the diameter of the wound surface was significantly smaller than that of the control group and blank group 15 days after the operation. The results of hematoxylin-eosin staining 30 days after the process show that the silk fibroin fibers are partially absorbed and degraded. The number of epithelial cell spikes and fibroblasts is significantly higher than that of the control group. The number of inflammatory cells is less than that of the control group, confirming that porous silk fibroin can accelerate the epithelialization of buccal mucosa defects, which is beneficial to wound healing.

4. Experiments and Studies of Silk Fibroin in Periodontal Tissue Regeneration

Periodontal disease is one of the leading causes of the destruction and loss of periodontal structure in adults, and periodontal disease is also one of the most common oral diseases. The main manifestations of periodontal disease are the formation of periodontal pockets and the resorption of alveolar bone. Severe periodontal disease may lead to dental pulp joint disease and tooth loosening or loss. Guided tissue regeneration (GTR), proposed by Nyman et al. in 1982 [7], is a surgical procedure applied to periodontal tissue reconstruction, using a closure membrane to prevent rapidly growing connective

tissue from occupying the defect. Du Yang[8] et al. applied the histological engineering method to culture human periodontal ligament fibroblast PDLF on the prepared silk fibroin collagen scaffold. Porous network structure, the cells thrive and are in good condition. There is no statistical difference between the ALP and MTT detection and the control group, proving that the silk fibroin collagen scaffold has strong biocompatibility and no cytotoxicity and can promote growth, adhesion, and stability PDF. Proliferation is in line with the needs of periodontal tissue engineering. Catarina[9] et al. prepared silk fibroin with glycerol (GLY) or polyvinyl alcohol (PVA) solution at a weight ratio of up to 30% through a low-temperature thermal annealing stabilization process to obtain high flexibility and stability. Membrane, the morphology, physical integrity, chemical structure, mechanical properties, thermal properties, and degradability of the biofilm were observed, and the biofilm was co-cultured with human periodontal ligament fibroblasts. The study found that the silk fibroin mixed biofilm, Compared with single silk fibroin biofilm, has higher flexibility, hydrophilicity, and protein degradability. In vitro cell, experiments show that silk fibroin/glycerol biofilm enhances human periodontal ligament fibroblasts' proliferation, adhesion, and activity. The good morphological characteristics of cells were maintained, providing a theoretical basis for applying and improving the regeneration of silk fibroin/glycerol (GLY) biofilms. Ricardo et al. [10] designed and prepared silk fibroin (SF)/polyoxyethylene (PEO) composite membranes and cultured human periodontal ligament fibroblasts at the separation site with composite membranes with different PEO contents. The results showed that The composite biofilm promoted the growth of human periodontal ligament fibroblasts, and the cell proliferation was significantly increased. It was concluded that the cell adhesion of human periodontal ligament fibroblasts in the ultrasonic pretreatment and low-dose PEO biofilm group is the most proliferative and metabolic activity.

Silk fibroin has high biological safety, non-toxicity, excellent mechanical properties, and strong plasticity. Silk fibroin can be used in combination with different physical materials. It has been used in clinical products of various specifications. The research and application will continue to expand.

References

- [1] Liu Xiaoyuan, Li Lei, Zhang Kai, Li Jun, Han Xiangzhen, He Huiyu. In vivo osteogenesis of bone marrow mesenchymal stem cell membrane composite 3D printing red antler powder/silk fibroin/polyvinyl alcohol scaffold[J]. China Organization Engineering Research, 2021, 25(34): 5420-5426.
- [2] Quan Junjie, Luo Gang, Li Zhirong, Liang Ermei. Silk fibroin/chitosan/hydroxyapatite film has good biocompatibility and osteopromoting properties [J]. Journal of Molecular Imaging, 2020, 43 (03):543- 547.
- [3] Wenjie Zhang, Xiuli Wang, Shaoyi Wang, Jun Zhao, Lianyi Xu, Chao Zhu, Deliang Zeng, Jake Chen, Zhiyuan Zhang, David L Kaplan, Xinquan Jiang; The use of injectable sonication-induced silk hydrogel for VEGF(165) and BMP-2 delivery for the elevation of the maxillary sinus floor. Biomaterials 2011 Dec;32(35):9415-24 doi:10.1016/j.biomaterials.2011.08.047.
- [4] Tang Jing. Experimental study on the repair of buccal mucosa defect with three different nanostructured silk fibroin scaffolds and bovine acellular matrix [D]. Soochow University, 2014.
- [5] Z Ge, Q Yang, X Xiang, K-Z Liu; Assessment of silk fibroin for the repair of buccal mucosa in a rat model. International Journal of oral and maxillofacial surgery 2012 May;41(5):673-80 DOI: 10.1016/j.ijom.2011.11.016.
- [6] Wang Zhongchao, Fan Liyuan, Cai Wei, Jiang Junqiang. Repair of buccal mucosa defect with silk fibroin scaffold [J]. Chinese Tissue Engineering Research, 2016, 20(12): 1738-1744.
- [7] S Nyman, J Lindhe, T Karring, H Rylander; New attachment following surgical treatment of human periodontal disease. Journal of clinical periodontology 1982 Jul;9(4):290-6 doi:10.1111/j.1600-051x.1982.tb02095.x.
- [8] Du Yang, Gao Xiuqiu, Jin Ding. Study on the compatibility between silk fibroin and collagen scaffolds and human periodontal ligament fibroblasts[J]. Chinese Journal of Practical Stomatology, 2009,2(09): 534-536.
- [9] Catarina Geão, Ana R Costa-Pinto, Cassilda Cunha-Reis, Viviana P Ribeiro, Sílvia Vieira, Joaquim M Oliveira, Rui L Reis, Ana L Oliveira; Thermal annealed silk fibroin membranes for periodontal guided

tissue regeneration. Journal of materials science. Materials in medicine 2019 Feb 12;30(2):27 doi:10.1007/s10856-019-6225-y.

- [10] Ricardo Serôdio, Sônia L Schickert, Ana R Costa-Pinto, Juliana R Dias, Pedro L Granja, Fang Yang, Ana L Oliveira; Ultrasound sonication before electrospinning tailors silk fibroin/PEO membranes for periodontal regeneration. Materials science & engineering. C, Materials for biological applications 2019 May;98:969-981 doi:10.1016/j.msec.2019.01.055.