

Advance of the Biocompatible Hydrogels in Medical Applications

Xinyan Wang^{1,a,#}, Ruizhen Li^{1,b,#}, Yihang Zhang^{1,c,#}, Zihe Zhang^{1,d,#}

¹Beijing 21st Century International School, Beijing, China

^a15589905826@163.com, ^blsusu0613@163.com, ^c3390151081@qq.com, ^d2368809392@qq.com

[#]Co-first author

Abstract: Hydrogels are widely used because of their strong water absorption, adhesion and biocompatibility. This article briefly analyzes the application of hydrogel dressing, type I collagen hydrogel and hydrogel in oral and bone tissues, and puts forward the existing problems, the future development trend and the prospect of its development.

Keywords: Hydrogel, Medical Field, Current Situation, Application Prospect

1. Introduction

Hydrogels have a three-dimensional spatial network structure system, which is soft and can maintain certain shapes. Also, hydrogels have strong water absorption, swelling and adhesion, so it is a good function of a new polymer material. In medical field, different from traditional medical materials, hydrogels are permeable to water, which can prevent bacteria from entering, and it have strong environmental sensitivity, modifiable and biocompatibility, so that they can obtain good mechanical properties after special preparation [1]. Therefore, hydrogels are widely used in the field of biomedicine, such as medical dressing, gingival tissue regeneration, bone repair, and so on, and they are one of the most potential medical materials in the future.

2. Typical Collagen Hydrogels

2.1. Type I Collagen Hydrogel

Type I collagen was first used in tissue engineered cartilage because of its wide distribution and easy extraction. Wakitani et al. [2] tried to repair full-thickness cartilage defects of rabbit femoral trochlea by mixing type I collagen gel with rabbit chondrocytes. The biomechanical parameters of the defect site were similar to normal after 12 weeks and were identical after 48 weeks. Kuroda et al. [3] reported the clinical application of collagen gel. Autologous bone marrow mesenchymal stem cells combined with collagen gel were implanted into the medial femoral condyle of the patient to cover the autologous periosteum. A year later, he was back to his pre-injury level. Recently, Gavenis et al. [4] designed a cell-free type I collagen plug that can promote the migration of surrounding chondrocytes to the material. It was confirmed by gross observation and immunohistochemistry that migrating chondrocytes could grow on the material and secrete type II collagen. This finding suggests the feasibility of using simple materials to induce chondrocyte migration around the defect to repair cartilage.

2.2. Type II Collagen Hydrogel

Although the source of type II collagen is not as extensive as that of type I collagen, and it is not easy to extract, it is the structural protein of the extracellular matrix of chondrocytes, which can maintain the phenotype of chondrocytes, promote chondrocyte differentiation, and provide the basis for chondrocyte adhesion. These advantages make it a research hotspot of collagen hydrogels in recent years. Bosnakovski et al. [5] compared the chondrogenic differentiation of bovine BMSCs in alginate gel, type I collagen gel and type II collagen gel, and the results showed that in type II collagen gel, BMSCs differentiated most significantly in the direction of cartilage. Funayama et al. [6] implanted the Type II collagen gel-chondrocyte complex into the missing trochlear cartilage of rabbit knee joint and observed it at 8, 12 and 24 weeks. By gross observation and histological staining, well-formed hyaluronogenesis

was observed beginning at week 8. At 12 to 24 weeks after transplantation, the regenerated cartilage was rich in type II collagen, and the histological score of repairing the defect was significantly different from that of the control group. However, studies have shown that the occurrence of rheumatoid arthritis is related to the autoimmune reaction of type II collagen [7-9] and immunizing some animals with type II collagen can induce experimental arthritis [10-13]. Therefore, the safety of type II collagen as a carrier for cartilage tissue engineering needs to be further studied.

3. Biomedical Applications

3.1. Absorbent Hydrogel Dressing

As a medical dressing, hydrogel can cover the wound and realize rapid healing. Gelatin as a dressing, has lots of advantages: relative soft; Good elasticity; relieving pain; Breathable and permeable; Bacteriostasis to reduce wound surface infection; Ensuring a suitable moist environment [14] for wound healing and other advantages. Drugs can also be embedded in hydrogels to improve wound healing. Hydrogel dressing includes chitosan-based hydrogel dressing, gelatin-based hydrogel dressing, hyaluronic acid-based hydrogel dressing, etc.

Adsorption hydrogel dressing has physical and chemical adsorption. It has superior performance in terms of drug loading capacity through the physical adsorption or chemical bonding of some drug, which play a therapeutic role in human body when the release of drug factors. Qi et al. use citric acid and acetic anhydride to chemically modify zein, and the obtained zein electrospinning fiber film has dual responsiveness of selective protein adsorption and slow-release performance [15]. Compared with the unmodified protein, hydrogel membrane has better protein adsorption, selectivity and slow-release properties. Positively charged proteins, such as cytochrome C, have both rapid biodegradation behavior and qualified cytotoxicity. Yu et al. prepared graphene/carboxymethyl cotton fiber hydrogel, which has adsorption properties for Sinomenine, which has pharmacological effects such as local anesthesia, anti-inflammatory, analgesic, antiarrhythmic, antihypertensive and immunosuppressive. The hydrogel dressing can absorb a large amount of wound exudate in the nursing of bleeding and discharge wound. Its gel structure provides a moist environment for wound healing and can release drugs to play an anti-inflammatory and analgesic role. Effectively accelerate wound healing [16]. These hydrogels loaded with biomolecules by adsorption can desorption under appropriate conditions, so they are widely used in drug release research systems, expanding the application of hydrogel dressings in drug loading.

3.2. Oral Cavity

In oral diseases, there are different degrees of defects in soft and hard tissues, and it is necessary to implant implants in the defect site for repair in order to obtain the ideal tissue shape and repair effect [17]. The hydrogel's affinity for muscle and nerve cells makes it possible for mouth protection. Zhu et al. [18] proposed that the use of light-cured hydrogel adhesives can quickly repair the oral mucosa. However, the light-induced radical polymerization mechanism used to construct dental materials cannot be simply grafted onto hydrogel adhesives for mucosal repair. On the one hand, free radicals have certain biological toxicity and will cause further damage to the mucous membrane. On the other hand, free radical polymerization has the problem of oxygen inhibition, which reduces the crosslinking efficiency of material. This problem is especially prominent in the preparation of thin-layer hydrogels, and even completely hinders the formation of hydrogels. In the previous work, the team proposed and developed a class of non-radical-based photocoupling reactions, which trigger the coupling reaction of aldehyde groups and amino groups by light to form a hydrogel crosslinking network and anchor the adhesive layer on the tissue surface. Hydrogel technology not only overcomes the inherent defects of free radical systems, but also has excellent tissue adhesion properties. However, the slow kinetics of the reaction of aldehyde groups with amino groups limits its application in moist and dynamic oral environments.

Studies have shown that composite materials prepared by loading sodium fluoride on chitosan (CS) nanoparticles can be used for tooth decay and dental caries treatment [19]. Galler et al. [20] found that the gel scaffold material prepared by CS could be used for pulp regeneration and promote the formation of oral connective tissue and new teeth. However, the single-component CS hydrogel is brittle and easy to degrade, so it is considered to introduce new groups in the structure to improve performance. Chenite et al. [21] mixed β -glycerophosphate (GP) with acidic CS solution to obtain a CS/GP thermosensitive hydrogel with neutral pH value. A preliminary experimental study for periodontal tissue regeneration found that the drug-loaded gel can not only degrade, but also inhibit bacteria, providing a new material

option for the surgical treatment of periodontal disease. Liu et al. [22] used the silicone oil as the medium to prepare polyhydroxy ethyl methyl acrylate (PHEMA) hydrogel with ideal particle size by drop-in synthesis method, which greatly reduces the sensitivity to the body and can be used as a soft lining Oral layer material.

3.3. Bone Tissue Engineering

Hydrogels are widely used as bone tissue scaffolds. Its characteristics make cells easy to adhere, and it can carry two kinds of cells at the same time, as a carrier for cell growth. Repair, regeneration, and replacement of bone tissue require implants that can rapidly absorb the load, friction, and mechanical response of joints and other structures. Most studies have shown that conventional materials do not fully achieve the flexibility and high elasticity required for implants [23]. The "Double Network Gel" (DN Gel) theory was proposed by Gong, who combined "hard and brittle" and "soft and tough" polymers to keep the two independent network structures, resulting in DN hydrogels, is comparable to biological cartilage [24].

He et al. [25] prepared a tri-inlay hydrogel with the polyoxyethylene and polyoxypropylene as raw materials, mixed ceramic bone powder with the gel, and applied it to the artificial skull defect experiment in rats. Under the combined action of recombinant human bone morphoprotein-2 and growth factor- β , bone tissue was formed at the skull defect, and bone connection was formed with the broken end of the wound boundary. Gel can transmit information to cells, serve as a carrier for cell growth and function, increase particle spacing and degrade [26], promote blood vessel formation, and accelerate new bone formation. Cong et al. [27] prepared chitosan-gelatin hydrogel loaded with erythropoietin (EPO) and proved that the gel can promote the formation of new bone after maxillary sinus lifting in rabbits. Hoemann et al. [28] used CS/GP thermosensitive hydrogel to simulate the composite chondrocytes of chondrocyte extracellular matrix. In culture experiments, it was found that chondrocytes grew well and still functioned as chondrocytes. Subsequently, combined with autologous blood for systematic in vivo and in vitro experiments, cartilage regeneration in animal models of cartilage defects was successfully obtained [29].

Some natural materials combined with amino acid gels as bone tissue materials can promote the growth of fine cells. Karp et al. [30] prepared PLGA/ fibrin hydrogel by mixing fibrin with PLGA successfully replaced the missing tissue in the living biological model and achieved bone regeneration. In addition, in bone tissue engineering, modified alginate and the gel prepared by mixing RGD can improve the adhesion of osteoblasts and promote bone regeneration [31]. Chang et al. [32] grafted polyglutamic acid (γ -PGA) onto polyglycolactone doped with chondroitin sulfate to obtain a composite material, which not only had good cell recognition and adhesion properties of polyamino acids, but also had good mechanical and mechanical properties of polycaprolactone. It also has good hydrophilicity and degradability.

3.4. Medical Cosmetology

Polyacrylamide hydrogel (HPAMG) was used in female breast surgery and rhinoplasty, but it developed inflammation about 6.1 years after injection [33] and was banned in 2006. At present, silicone is the most commonly used filler in breast plastic surgery, but it has the disadvantage of causing tissue inflammation [34]. Therefore, it is necessary to develop effective alternative materials.

The hydrogel patch prepared by Ren et al. [35] has good stability and no irritation to the skin. Chinese herbs can also be added. Sui et al. [36] conducted injection experiments on 70 patients with facial plastic surgery using Lengning Kang products. The main component of Lengning Kang products was PVA.

The nano hydroxyapatite/carboxymethyl chitosan (N-HA /CMCTS) hydrogel studied by Cai et al. [37] has the advantages of injectable, promoting collagen secretion, small wound surface, quick recovery and quick cosmetic effect. After injection, the concave defect site can be filled in the early stage to promote the growth of local tissue, and gradually degraded in the late stage to be replaced by new tissue. Madhumathi et al. [38] mixed CS condensates with HA to obtain a hydrogel film with certain mechanical strength. The membrane was applied to MG-63 osteosarcoma cells and proved to have good biocompatibility and mechanical properties. Zhang et al. [39] prepared injectable physical thermosensitive hydrogels of triblock copolymer (PCLA-PEG-PCLA). Compared with traditional injectable chemical crosslinking hydrogels, they do not require chemical reactions in vivo and have higher biocompatibility and safety.

4. Outlook and Prospect

Although hydrogels have the advantages of good biocompatibility and cell adhesion, natural hydrogels have poor mechanical properties due to the uneven network structure. This deficiency can be improved by cross-linking, crystallization, and other means through fabrication of double network structure of polymers. Therefore, on the one hand, it is necessary to continue to explore the broader properties and applications of biocompatible hydrogels. On the other hand, it is necessary to further study the theory and improve the existing medical hydrogels. Combination of the theoretical research with the product performance can reduce the limitations and blindness of research to a certain extent.

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