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Progress of Antibacterial Hydrogels

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Abstract
Hydrogel medical dressing refers to a kind of gel material with three-dimensional network structure but not dissolved in water prepared by natural or synthetic polymers alone or combined. It can maintain the moist environment of the wound to accelerate healing, and has good biocompatibility, optical transparency, porosity, high swelling rate and other characteristics, but there are defects in antibacterial performance. Therefore, at this stage, the antibacterial modification of hydrogel medical dressings to improve their antibacterial ability has become the main research direction. The research status of domestic and foreign scholars in antibacterial hydrogels in recent years was reported. The application of inorganic, organic, natural and composite antibacterial agents in antibacterial modification of hydrogels was reviewed. The future research direction and focus of antibacterial hydrogels were prospected.

Keywords: *Antibacterial; Hydrogel; Compound antibacterial; New medical dressing*

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I. INTRODUCTION

The skin is the largest tissue wrapped around the muscle on the surface of the body, and it is also the largest organ to protect the human body from damage and microbial invasion[1]. If this barrier is destroyed, it will not be able to maintain the normal circulation of body fluids, electrolytes and nutrients. It will also affect body temperature regulation, sensory testing, immune surveillance, etc. If improper treatment is likely to cause bacterial infection and hinder wound healing, it will even cause disease and endanger life and health[2]. In order to speed up the healing, barrier bacteria, reduce scars, the current clinical use of medical dressings external treatment of trauma[3].

Compared with traditional medical dressings, hydrogel medical dressings, as a new type of medical dressing, can provide a local wetting environment closest to the physiological state of the wound, promote epithelial cell regeneration, reduce the risk of secondary injury of the wound, and have significant advantages in biocompatibility, water vapor permeability and autologous debridement. However, because the hydrogel has high water content and excellent water absorption, the humid environment it maintains will not only promote the growth of normal cell tissues, but also facilitate the growth and reproduction of various microorganisms. Therefore, it is difficult to avoid bacterial infection in practical medical applications. In this regard, it is of great practical significance to study the preparation of antibacterial hydrogel materials for preventing self-induced infections and treating bacterial infections in damaged skin[4].

Antibacterial hydrogel is a kind of hydrogel that can effectively inhibit the growth or reproduction of bacteria and even kill bacteria[5]. Because of its dual functions of antibacterial and hydrogel, it has extremely wide application value in medical antibacterial dressings and other biomedical fields[6]. The introduction of antibacterial agents into hydrogel systems by physical encapsulation or chemical crosslinking is a common method for preparing antibacterial hydrogels. Depending on the composition of the antibacterial agent cited, the antibacterial hydrogels can be divided into four categories as shown in Table 1. In this paper, the synthesis and application of these four types of antibacterial hydrogels are introduced respectively. At the same time, it is pointed out that the antibacterial hydrogels containing composite antibacterial agents with broad antibacterial spectrum and high efficiency will become the research focus with the most development space in the future.

Table 1: Classification and advantages and disadvantages of antimicrobial hydrogels.

hydrogel types	advantages	disadvantages
1. Antibacterial hydrogels containing inorganic antibacterial agents	no pollution, good heat resistance, slow release long-acting	high cost, poor compatibility, antibacterial delayed effect, most photocatalytic antibacterial does not have the ability to choose sterilization
2. Antibacterial hydrogels containing organic antibacterial agents	strong sterilization, good instant effect	poor heat and drug resistance, short shelf life, slight environmental contamination and lack of safety
3. Antibacterial hydrogels containing natural antibacterial agents	non-toxic and non-irritating, excellent biocompatibility and safety, green environmental protection	poor heat resistance, very short validity period, unstable to chemicals
4. Antibacterial hydrogels containing composite antibacterial agents	integrates the performance of a variety of single antimicrobial agents for high-efficiency, long-lasting, broad-spectrum antimicrobials with good biosafety and color stability	fewer related studies

II. Antibacterial hydrogels containing inorganic antibacterial agents

Inorganic antibacterial agents to load silver and other metal ion load type as the main development trend.

Most metal ions have certain antibacterial effects. Among them, silver-based antibacterial agents have the best antibacterial properties, and have low cell toxicity and good stability. Therefore, they occupy a dominant position in metal ion-loaded antibacterial agents. With the growth of bacterial resistance, it has also attracted more and more attention from the biomedical community.

Shahriari et al.[7] infiltrated sodium alginate (Alg-Na) into bacterial nanocellulose (BNC) matrix by vacuum suction method, and then immersed in a separate solution of manganese, cobalt, copper, zinc, silver and cerium to synthesize six pH-responsive dual-network antibacterial hydrogels. It was found that the cationic concentration of 0.05 mol L^{-1} was suitable for the preparation of wound dressings with strong antibacterial activity, but should be further optimized to a lower concentration. They were not toxic to fibroblasts, and the cation release rate was as high as 90%. The antibacterial activity after exposure to bacteria for 24 h was in the order of BNC/Alg-Co>BNC/Alg-Ag>BNC/Alg-Zn>BNC/Alg-Cu. BNC/Alg-Mn>BNC/Alg-Ce, in which BNC/Alg-Co and BNC/Alg-Ag showed obvious bacterial growth inhibition on Gram bacteria. Because the colored Co ions may affect the optical transparency of the hydrogel, the silver-loaded BNC/Alg-Ag is slightly better.

Ferrag et al.[8] also encapsulated AgNPs in hydrogel matrix into spheres, triangles and rods to study whether hydrogels exhibited shape-dependent physicochemical and antibacterial properties. The results showed that the hydrogels doped with spherical and triangular AgNPs showed strong antibacterial activity, while the hydrogels with rod-like AgNPs had relatively low antibacterial activity. This adds a controllable factor to the application of AgNPs in antibacterial hydrogels, which may be a new research way in the future.

III. Antibacterial hydrogels containing organic antibacterial agents

Organic antimicrobial agents are mainly quaternary ammonium salts, synthetic antimicrobial peptides, organic metal compounds, imidazoles, biguanides and other main components of antimicrobial agents, a wide variety, through the role of pathogenic microorganisms biochemical reaction enzymes, cell wall and cell membrane to achieve sterilization effect.

Liu et al.[9] used a one-step method to chemically couple quaternary ammonium salts (QAS) decorated with oxadiazole groups and diethoxy groups to poly (ε-caprolactone) -poly (ethylene glycol) -poly (ε-caprolactone) (PCEC) copolymer to obtain antibacterial PCEC-QAS nanoparticles. Freeze-dried PCEC-QAS NPs spontaneously self-assembled in water and formed hydrogels after heating-cooling treatment. The PCEC-QAS nanoparticles enabled the hydrogel to exhibit a wide range of antibacterial properties against MRSA, E.coli and vancomycin-resistant S.aureus, with wound closure rates of 75%, 90% and 100% on days 4, 8 and 12, respectively.

O-carboxymethyl chitosan (CMCS) is a modified CS derivative with stronger antibacterial activity. Yu et al.[10] prepared three pH-sensitive imine dynamic hydrogels H500, H800 and H1900 by reacting diamino Jeffamine with benzene-1, 3, 5-tricarbaldehyde with molar mass of 500, 800 and 1900 respectively to form water-soluble dynamer, which was then cross-linked with CMCS via diimine bond. The antibacterial properties of the dynamic hydrogel were determined by the antibacterial experiment. At 20 ℃, H1900a and H1900b inactivated 97.11% and 99.99% of the bacteria after contact with 108 CFU mL^{-1} E.coli suspension for 3 h, respectively.

Inspired by the research of amphiphilic lipopeptides[11], Adak et al.[12] designed a short hexapeptide rich in β-sheets, with hydrophobic long chains and hydrophilic trilysine units at the N and C ends of the hexapeptide, respectively. The antibacterial lipopeptide forms a PA-NV hydrogel that is stable to enzymatic degradation. Using propidium iodide to check the permeability of bacterial plasma membrane, it was found that 2 wt% PA-NV hydrogel had sufficient ability to penetrate the plasma membrane of S.aureus and E.coli. The surface of the hydrogel was non-hemolytic to human red blood cells and had no cytotoxicity to mammalian cells.

McMahon et al.[13] encapsulated silver-based antibacterial agent silver sulfadiazine (SSD) into a hydrogel system synthesized by copolymer PEGDA-PEGMEMA and thiol-modified hyaluronic acid. Because SSD has the antibacterial effect of sulfadiazine and the inhibitory effect of silver, the antibacterial hydrogel has antibacterial durability against S.aureus, P.Aeruginosa and E.coli. In addition, in vitro toxicological evaluation showed that this low concentration (1.0% w/v) encapsulated SSD hydrogel can be used as a carrier system for human adipose-derived mesenchymal stem cells and inhibit the growth of the above pathogens. However, when the concentration of SSD in the hydrogel is higher than 1.0% w/v, SSD may be toxic to cells. Therefore, it is necessary to further optimize the long-term response/release of SSD encapsulated antibacterial hydrogels.

Wang et al.[14] prepared non-releasing poly (ionic liquid) antibacterial hydrogels PMAVs by one-pot method using polyethylene glycol dimethacrylate, N, N' -methylenebisacrylamide (MBA), methyl methacrylate (MMA), acrylamide (AM) as raw materials and 1-vinyl-3-butylimidazolium (VBIMBr) as antibacterial agent. It is worth noting that when the mass ratio of MMA : AM : VBIMBr is 5 : 14 : 3, the antibacterial rate of PMAVs against S.aureus, E.coli and Candida albicans is almost 100% after 24 h of exposure. Local use of the dressing on the injured skin of rats can effectively avoid early infection and promote wound healing.

Tian et al.[15] synthesized polytetrahydropyridine imine (PTHP) by one-pot method, and modified it with ethylenediamine to obtain aminated polytetrahydropyrimidine (PTHP-NH_2), and then reacted with the Schiff base between the polyaldehyde polymer P(DMA-VA) to form a PTHP-gel with a 3D network within 30 s. PTHP-gel can effectively kill bacteria and prevent skin infections. Even after 60 h of culture, it still has antibacterial properties. It makes up for the shortcomings of antibiotics and has great potential in the treatment of subcutaneous infections.

IV. Antibacterial hydrogels containing natural antibacterial agents

Natural antibacterial agents are derived from natural organisms and are very rich in resources, mainly including polysaccharides, peptides and other substances. It is not only the earliest antibacterial agent used by people, but also one of the main development directions of antibacterial materials in the future.

Tavakolian et al.[16] grafted ε-PL onto carboxyl-modified cellulose hydrogels by bioconjugate reaction. Hydrogels with ε-PL concentrations of 125 and 200 ppm can effectively inhibit bacteria. After gel-PLL treatment for 3 h, 99.5% of P.aeruginosa and 98.5% of S.aureus were killed.

As a natural broad-spectrum antibacterial agent, CS can effectively destroy the cell wall of bacteria through positively charged active chemical groups, and has good film-forming and adsorption properties. Kim et al.[16] synthesized epigallocatechin gallate (EGCG) chitosan-based hydrogels by one-pot method. It was confirmed that the antibacterial properties of CS and EGCG made EGCG-CS hydrogels have antibacterial activity, and it increased with the increase of EGCG concentration. Amir Shamloo et al.[17] found that honey-free chitosan-based hydrogels have shown antibacterial activity against S.aureus and P.Aeruginosa.After integrating honey into the CS-gelatin-PVA hydrogel matrix, the honey concentration affects the antibacterial properties of the hydrogel. The hydrogel sample containing 20% v/v honey has an inhibition zone diameter of 8±0.8 and 14±1 mm for the two bacteria, respectively.

Yan et al.[18] developed an antibacterial hydrogel with adhesive ability. The DMAPS part provides antifouling properties, and the introduction of CS enhances the antibacterial properties of the hydrogel. According to the plate colony counting method, the number of S.aureus and E.coli colonies on the hydrogel after 24 h of contact with the bacterial suspension was only 7.54% and 8.12% of the PAM hydrogel, respectively.

V. Antibacterial hydrogels containing composite antibacterial agents

Composite antibacterial agent is to make up for the lack of antibacterial properties of a single antibacterial agent, combined with one or more other antibacterial agents. Due to the synergistic antibacterial effect, it has a wider antibacterial range and stronger antibacterial ability.

An intelligent antibacterial hydrogel that can be released on demand at the site of bacterial infection was synthesized by Dai[19]. In the experiment, AgNPs were synthesized by using the acidic microenvironment produced by bacterial proliferation and the fifth generation polyamide-amine dendrimer G5 PAMAM as a template. The cationic polymer/nano-silver composite antibacterial hydrogel Dex-G5-Ag was obtained by forming a Schiff base bond between the amino group on the surface of G5 PAMAM and the aldehyde group on the surface of oxidized dextran. The in vitro antibacterial properties of Dex-G5-Ag were tested by plate counting method and bacterial LIVE/DEAD staining method. When the molar ratio of Ag^+ to G5 in G5-Ag solution with a concentration of 20 mg mL-1 was 30:1, the antibacterial rate against Gram-positive bacteria was almost 99.9%, and it could effectively resist skin infection caused by S.aureus. At this time, Dex-G5-Ag also had good thixotropy and biocompatibility, and was expected to become a medical device coating or anti-traumatic infection material.

Wang et al.[20] prepared a supramolecular hydrogel under alkaline conditions. When a wound with a diameter of about 1 cm on the back of a mouse was infected with a pathogenic Pseudomonas aeruginosa colony of 5×10^7 cfu, the Ag@CS-CD/DS group had the lowest cfus (only 0.2×10^7 cfu) after 6 days of treatment. The synergistic effect of Ag^+, CS and diclofenac sodium makes Ag@CS-CD/DS have excellent antibacterial properties and wound healing ability, while avoiding the potential cytotoxicity caused by high silver content. Abd El-Hady et al.[21] evaluated the synergistic effect of curcumin and AgNPs on the antibacterial properties of CS hydrogels. Studies have shown that curcumin binds to Ag^+ to form a complex and further reduces Ag^+ to a nano [Ag(curcumin)] that disrupts the charge balance of the bacterial cell wall. Due to the effective synergistic antibacterial effect of the composite composition, the hydrogel has a higher bactericidal activity against Gram bacteria than pure CS hydrogels.

Du et al.[22] designed and developed a multifunctional hydrogel patch composed of polyethylene glycol diacrylate/quaternized chitosan/tannic acid (PEGDA/QCS/TA) based on mussel heuristic chemistry. The mechanical properties of PEGDA/QCS/TA hydrogel patch are tough and biodegradable in vivo. It also contains 20 wt% PEGDA. Due to the excellent antibacterial properties of QCS and TA, the killing rate of the patch after adding QCS and TA to S.aureus is more than 23 times that of the zero-added patch, which is expected to achieve seamless wound closure.

VI. CONCLUSION

It was observed that the rerun column bottom stream temperature has greater effect on the linear alkylbenzene yield than the temperature variation of the top stream. At higher temperature of both streams , lower percentage yield of average wt.% of linear alkylbenzene was obtained with that of the top stream being the lowest at 87.5% as against 93.3% for the bottom stream. The highest linear alkylbenzene yield of 99.4%was recorded at bottom stream temperature of 280 ℃and pressure of 115 Kpa.

In the context of today's focus on health, the emergence of drug-resistant bacteria and the global population aging crisis, the demand for antibacterial products has increased dramatically. The development of high-performance and new antibacterial hydrogels will have a very broad development prospects. From the current research results, whether by loading inorganic antibacterial agents, organic antibacterial agents or natural antibacterial agents for antibacterial or even bactericidal hydrogels, it is inevitable to face some problems. The ideal antibacterial hydrogel should have broad-spectrum antibacterial properties and can meet the requirements of clinical treatment. Antibacterial efficiency, that is, less dosage and quick effect, can reduce the economic burden of patients and infection pain; antibacterial durability, can reduce the number of dressing to reduce the risk of secondary infection; low toxicity, non-toxicity, antibacterial components can not produce acute toxicity or long-term cumulative toxicity to the human body; biocompatibility, no foreign body reaction with body fluids and tissues.

The antibacterial hydrogel containing composite antibacterial agent exhibits far superior antibacterial properties to the antibacterial hydrogel containing a single antibacterial agent, and can meet people 's demand for new medical dressings in the above aspects. With the development of biomedicine, people will continue to complete the design and development of intelligent antibacterial hydrogels for acidic environment or bacterial enzyme response in the future, carry out the human safety design of composite antibacterial hydrogels, the preparation technology of composite antibacterial hydrogels acting on various bacteria, and the research work of functional antibacterial hydrogels that take into account the properties of polymer materials. In addition, in order to achieve bacteriostasis in a specific environment or meet the personalized customization of patients, more digital control should be used to strengthen the research of biological 3D printing and even 4D printing technology in hydrogel forming. Antibacterial hydrogels are developing in the direction of broad spectrum, high efficiency, persistence, intelligence, low toxicity, environmental protection and low cost. It is believed that with the deepening and refinement of research, the development and utilization of antibacterial hydrogels containing composite antibacterial agents in combination with emerging technologies will become the development trend of medical antibacterial materials in the future.

REFERENCES

[1] Ming Z, Han L, Bao M, et al. Living Bacterial Hydrogels for Accelerated Infected Wound Healing[J]. Advanced Science, 2021, 8(24): 2102545.
[2] Brown E D, Wright G D. Antibacterial Drug Discovery in the Resistance Era[J]. Nature, 2016, 529(7586): 336-343.
[3] Liu Y, Chen X, Zhang C, et al. Breathable, Moisturizing Biomimetic Wound Dressing with Broad-Spectrum Antimicrobial Properties[J]. Advanced Healthcare Materials, 2025, 14(9): 2404601.

[4] Xu T, Tian Y, Zhang R, et al. Hydrogel Vectors Based on Peptide and Peptide-like Substances: For Treating Bacterial Infections and Promoting Wound Healing[J]. Applied Materials Today, 2021, 25: 101224.
[5] Li S, Dong S, Xu W, et al. Antibacterial Hydrogels[J]. Advanced Science, 2018, 5(5): 1700527.
[6] Yin M, Wan S, Ren X, et al. Development of Inherently Antibacterial, Biodegradable, and Biologically Active Chitosan/Pseudo-Protein Hybrid Hydrogels as Biofunctional Wound Dressings[J]. ACS Applied Materials & Interfaces, 2021, 13(12): 14688-14699.
[7] Shahriari-Khalaji M, Hong S, Hu G, et al. Bacterial Nanocellulose-Enhanced Alginate Double-Network Hydrogels Cross-Linked with Six Metal Cations for Antibacterial Wound Dressing[J]. Polymers, 2020, 12(11): 2683.
[8] Ferrag C, Li S, Jeon K, et al. Polyacrylamide Hydrogels Doped with Different Shapes of Silver Nanoparticles: Antibacterial and Mechanical Properties[J]. Colloids and Surfaces B: Biointerfaces, 2021, 197: 111397.
[9] Liu W, Ou-Yang W, Zhang C, et al. Correction to "Synthetic Polymeric Antibacterial Hydrogel for Methicillin-Resistant Staphylococcus Aureus -Infected Wound Healing: Nanoantimicrobial Self-Assembly, Drug- and Cytokine-Free Strategy"[J]. ACS Nano, 2022, 16(7): 11483-11483.
[10] Yu R, Cornette De Saint-Cyr L, Soussan L, et al. Anti-Bacterial Dynamic Hydrogels Prepared from O-Carboxymethyl Chitosan by Dual Imine Bond Crosslinking for Biomedical Applications[J]. International Journal of Biological Macromolecules, 2021, 167: 1146-1155.
[11] Cai P, Leow W R, Wang X, et al. Programmable Nano–Bio Interfaces for Functional Biointegrated Devices[J]. Advanced Materials, 2017, 29(26): 1605529.
[12] Adak A, Ghosh S, Gupta V, et al. Biocompatible Lipopeptide-Based Antibacterial Hydrogel[J]. Biomacromolecules, 2019, 20(5): 1889-1898.
[13] McMahon S, Kennedy R, Duffy P, et al. Poly(Ethylene Glycol)-Based Hyperbranched Polymer from RAFT and Its Application as a Silver-Sulfadiazine-Loaded Antibacterial Hydrogel in Wound Care[J]. ACS Applied Materials & Interfaces, 2016, 8(40): 26648-26656.
[14] Wang K, Wang J, Li L, et al. Novel Nonreleasing Antibacterial Hydrogel Dressing by a One-Pot Method[J]. ACS Biomaterials Science & Engineering, 2020, 6(2): 1259-1268.
[15] Tian Y, Pang L, Zhang R, et al. Poly-Tetrahydropyrimidine Antibacterial Hydrogel with Injectability and Self-Healing Ability for Curing the Purulent Subcutaneous Infection[J]. ACS Applied Materials & Interfaces, 2020, 12(45): 50236-50247.
[16] Tavakolian M, Munguia-Lopez J G, Valiei A, et al. Highly Absorbent Antibacterial and Biofilm-Disrupting Hydrogels from Cellulose for Wound Dressing Applications[J]. ACS Applied Materials & Interfaces, 2020, 12(36): 39991-40001.
[17] Shamloo A, Aghababaie Z, Afjoul H, et al. Fabrication and Evaluation of Chitosan/Gelatin/PVA Hydrogel Incorporating Honey for Wound Healing Applications: An In Vitro, In Vivo Study[J]. International Journal of Pharmaceutics, 2021, 592: 120068.
[18] Yan J, Ji Y, Huang M, et al. Nucleobase-Inspired Self-Adhesive and Inherently Antibacterial Hydrogel for Wound Dressing[J]. ACS Materials Letters, 2020, 2(11): 1375-1380.
[19] Dai T, Wang C, Wang Y, et al. A Nanocomposite Hydrogel with Potent and Broad-Spectrum Antibacterial Activity[J]. ACS Applied Materials & Interfaces, 2018, 10(17): 15163-15173.
[20] Wang J, Feng L, Yu Q, et al. Polysaccharide-Based Supramolecular Hydrogel for Efficiently Treating Bacterial Infection and Enhancing Wound Healing[J]. Biomacromolecules, 2021, 22(2): 534-539.
[21] El-Hady M M A, Saeed S E S. Antibacterial Properties and pH Sensitive Swelling of Insitu Formed Silver-Curcumin Nanocomposite Based Chitosan Hydrogel.[J]. Polymers, 2020, 12(11): 2451.
[22] Du X, Wu L, Yan H, et al. Multifunctional Hydrogel Patch with Toughness, Tissue Adhesiveness, and Antibacterial Activity for Sutureless Wound Closure[J]. ACS Biomaterials Science & Engineering, 2019, 5(5): 2610-2620.