

Current Status of Wound Dressing Research in Biomaterials

Yang Yang

School of Material Science and Engineering, Xi'an Shiyou University, Xian 710065, China

ABSTRACT

Skin is the body's first defense against external injuries, in daily production life, skin as an organ is easily injured, forming surface trauma. Wound dressings play a pivotal role in the process of skin wound repair. In order to meet the clinical demand for wound dressings, functional wound dressings with excellent biocompatibility, excellent antimicrobial activity, absorption of wound exudate and promotion of wound tissue repair have been developed. We categorize wound dressings into traditional medical dressings and novel medical wound dressings, and review the wound dressings included in the latter in terms of types, preparation methods, and effects. In future treatments for chronic wounds, researchers will integrate and utilize the antimicrobial activity, biocompatibility, and mechanical properties of wound dressings to investigate advanced wound dressings with multiple functions.

KEYWORDS

Skin wounds; Wound healing; Biomaterials; Wound dressings.

1. INTRODUCTION

Skin is the largest organ of the human body, the main use in maintaining homeostasis and preventing microbial invasion, its healing process is more cumbersome[1]. Skin wounds are the destruction of normal skin tissues, with many external factors, such as sharp objects, excessive heat, chemicals and other external factors, as well as other pathologic factors, such as diabetic foot ulcers, hypertrophic scarring, etc. Millions of people suffer every year due to physical and chemical factors or diseases. Every year, millions of people suffer skin injuries due to physical or chemical factors or diseases, and the subsequent wound infections and severe tissue necrosis endanger human lives. In recent years, wound dressings have become an indispensable element of clinical wound care due to their low cost, ease of use and effectiveness.

According to the time and characteristics of the healing process, wounds can be categorized into acute and chronic wounds. Acute wounds are like skin wounds or surgical wounds, while chronic wounds are like pressure sores, leg ulcers, severe burns and diabetic ulcers. While acute wounds usually heal completely within 4 weeks at an expected or predictable rate without complications, chronic wounds are more difficult to control, have slower and longer healing times, have longer durations, have abnormal healing processes, and can lead to serious complications that require tissue removal. In order to solve these problems, researchers have begun a new exploration of dressings. In 1962, Winter[2] first proposed the concept of wet healing, which theorized that the rate of wound healing is significantly higher in wet environments than in dry environments (which can be two to four times higher) because wound dehydration disrupts the microenvironment required for wound healing, which in turn can impede the healing process[3]. Therefore, an ideal non-toxic, non-allergenic, non-adhesive skin wound dressing is very important in daily life to absorb excess exudate and maintain a moist environment on the wound surface. Meanwhile, moreover, it should have good properties such

as antimicrobial and biocompatibility to promote wound healing, as well as self-cleaning ability to prevent contamination[4] .

2. TRADITIONAL WOUND DRESSING

Traditional dressings, including Band-Aids, gauze, bandages and other items, can be used for open exogenous wounds as well as chronic wounds, and are only suitable for the emergency treatment of small wounds, and are hardly useful for larger wounds. Traditional dressings have obvious disadvantages, such as poor breathability and waterproof, once soaked by wound exudate or external liquid will lose its original role, mainly due to the fibers in the healing process will be adhered to the newborn granulation tissue, and in the removal of pain and tear, seriously affecting wound healing, there is a need for frequent replacement, increase the patient's cost, soaking wet easy to cause wound infection and other shortcomings, traditional Traditional wound dressings also have important advantages, such as low price, simple process, easy access, and the ability to absorb wound exudate. In addition, skin wound healing is often accompanied by various complications, including but not limited to bacterial infections, skin cancer, and skin appendage injuries, which poses a great challenge to clinical wound management. For this reason, researchers have developed various advanced wound dressings to address different wound problems.

3. NEW WOUND DRESSING

With the rapid development of material science and technology, new medical wound dressings (hydrogels, electrostatically spun fibers, films, sponges, etc.) have become a promising strategy for wound healing management. Ideal wound dressings should be non-toxic, biodegradable, biocompatible, moderately strong mechanically, easy to peel off from the wound surface, antimicrobial, pro-healing, and beneficial in reducing scar formation. To this end, researchers have utilized different types of biomaterials to design novel medical wound dressings with different functions. Currently, research is focused on improving the quality of survival of patients with traumatic injuries by enhancing the performance of wound dressings and improving the effectiveness of wound treatment and management.

3.1. Natural Polymer Wound Dressing

3.1.1. Hyaluronic acid

Hyaluronic acid is an anionic mucopolysaccharide composed of D-glucuronic acid and N-acetylaminoglucosamine alternately linked, distributed in vertebrate extracellular matrix, skin, vitreous humor of the eye, cartilage and joint fluid. The physicochemical properties of hyaluronic acid include hydrophilicity, antioxidant properties, fluidizing properties, and viscoelasticity. The biological functions of hyaluronic acid are related to its molecular weight, e.g., high molecular weight hyaluronic acid has the ability to inhibit inflammatory response, anti-angiogenesis, and inhibit scarring, while low molecular weight hyaluronic acid acts to promote angiogenesis, cause inflammatory response, and promote scarring. Due to the limited role of endogenous hyaluronic acid, the preparation of different types of wound dressings from exogenous hyaluronic acid is important for wound repair and has a wide range of applications in biomedical fields. In a recent study, Szarpak A et al[5] reported that hyaluronic acid mono-network hydrogels with high tensile and elastic properties were prepared under physiological conditions using conventional cross-linking agents (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride) and N-hydroxysulfosuccinimide. Platelet-rich plasma (PRP) contains a large number of biologically active substances, which are clinically important in the treatment of various wounds. Su Sena et al[6] extracted hyaluronic acid and keratins from animals and loaded them into coaxial electrostatically spun fibrous structures as

bioactive agents for wound treatment. Sun Juan-feng et al. [7] successfully prepared electrostatically spun nanofibers from a composite cohesive solution composed of chitosan and hyaluronic acid.

3.1.2. Chitosan

Chitosan is the product of removing part of the acetyl group of the natural polysaccharide chitin, with biodegradability, biocompatibility, non-toxicity, bacteriostatic, anticancer, lipid-lowering, immune-enhancing and other physiological functions, widely used in food additives, textiles, agriculture, environmental protection, health care, cosmetics, antimicrobial agents, medical fibers, medical dressings, artificial tissue materials, materials for the sustained release of medicines, carriers for gene transduction, biological medical fields, medical absorbable materials, medical and drug development and many other fields and other daily-use chemical industries. In addition, chitosan has been found to promote wound healing [8, 9], which provides a new option for the production of novel dressings. Klara J et al [10] added lysine-functionalized chondroitin sulfate into the polymerization network to enhance the bioactivity of collagen/chitosan-based hydrogels, and crosslinked them with the bio-crosslinking agent genipin, which prepared injectable hydrogels with promising prospects for tissue engineering applications. Yin H et al [11] crosslinked the aldehyde group of polypropylene oxidized microcrystalline cellulose with the amino group of carboxymethyl chitosan to form a hydrogel with good mechanical properties, controlled drug release, and self-healing properties by Schiff base reaction. Correia C et al [12] prepared a blend of chitosan and catechol-modified collagen with the ability to restore the structure and function of damaged soft tissues with an Adhesive, biodegradable films. Carvalho DN et al [13] produced hydrogels from collagen, chitosan, and fucoidan using newly developed environmentally friendly compression and absorption methods and encapsulated chondrocytes into them for biomedical articular cartilage therapy.

3.1.3. Alginate

Alginate is a natural polyanionic polysaccharide with the advantages of hydrophilicity, biocompatibility, biodegradability and non-toxicity, and the molecular chain is rich in β -D-mannuronic (M) and α -L-guluronic (G) fragments. Alginate hydrogel dressings are suitable for use as wound dressings because of their excellent ability to absorb fluids and good elasticity, which can absorb a large amount of biological fluids from the wound site and form a gel film between the wound and the dressing to provide a wet healing environment and promote wound healing. Alginate hydrogels can be made by ionic cross-linking of alginate with solutions of magnesium, zinc, and calcium; the physicochemical properties can be further enhanced when alginate is modified by cross-linking with other polymers.

Hu H et al [14] prepared a biocomposite hemostatic membrane with calcium/ flavopiridol double crosslinked alginate/chitosan/collagen, which has good biocompatibility and biodegradability, and can be used to inhibit bacteria for a long period of time and promote wound healing. Chronic diabetic foot ulcer is a devastating complication of diabetes mellitus, which affects the morbidity, mortality and quality of life of patients. Theocharidis G et al [15] prepared alginate bandages with micrometer pore size and loaded with M2 macrophages through lyophilization, calcium cross-linking, and secondary lyophilization steps, and showed that the dressings could be used as a delivery platform for topical treatment of diabetic wounds. Jing Y et al [16] loaded antimicrobial curcumin nanoparticles onto a composite hydrogel of filipin protein and sodium alginate as a dressing for bacterial infection wound healing. The results showed that the porous three-dimensional (three-dimensional, 3D) structure of the composite hydrogel dressing facilitated the absorption of exudate from the wound site and promoted the incorporation of cellular nutrients and metabolites, and that the hydrogel improved cell proliferation, anti-inflammation, and benefited vascular remodeling and collagen deposition at the wound site, which significantly improved closure of bacterial infected wounds.

3.2. Synthetic Polymer Wound Dressing

3.2.1. Polycaprolactone

Polycaprolactone is a synthetic biodegradable aliphatic polymer approved by the U.S. Food and Drug Administration (FDA) that can be degraded through body erosion or hydrolysis and has a low melting temperature (60°C). The combination of polycaprolactone with other functional polymers in the preparation of scaffolds overcomes its limitations and gives the composites excellent properties. For example, Xi Y et al [17] prepared electrostatically spun nanofibrous matrices with bionic elasticity, bacteriostasis, and biocompatibility by coupling polycaprolactone with poly (citrate) and ϵ -polylysine. He J et al [18] prepared a series of antimicrobial, antioxidant, and electroactive electrostatically spun nanofibrous membranes by coupling polycaprolactone and quaternized chitosan-grafted polyaniline, which were used for healing of full-length cutaneous wounds. In addition, Xuan C et al [19] developed biological dressings with a dual structure, where one layer was gelatin nanoflakes modified with dopamine and antimicrobial peptides and mixed with Ca^{2+} , which had coagulation, antimicrobial and hemostatic functions upon contact with the wound site, and the other layer was polycaprolactone nanoflakes, which could serve as a physical barrier to protect the wound.

3.2.2. Polylactic acid

PLA is a linear aliphatic polyester and an FDA-approved synthetic biodegradable polymer with good mechanical properties, good thermal stability, degradability, processability, and biocompatibility. Zhang S et al [20] prepared silver metal-organic framework-POLA based electrostatic spinning fiber membranes by an electrostatic spinning process, which could effectively inhibit the growth of multiple bacteria growth. Wang C et al [21] prepared injectable cholesterol-enhanced stereocomplexed PLA thermogels to optimize cartilage regeneration. Wang L et al [22] mixed PLA with polyaniline to prepare nanofibrous structures with electrical conductivity, which can be used for cardiac tissue engineering and cardiomyocyte-based 3D bioactuators.

3.3. Functional Biological Wound Dressing

3.3.1. Antimicrobial Biological Wound Dressing

Ideal wound dressings should not only be safe, have few toxic side effects and be easy to use, but also prevent wound infection. Traditional antibiotics can lead to bacterial resistance, and metal and its oxide nanomaterials (e.g., gold, silver, and copper) have been identified as suitable alternatives due to their strong antimicrobial spectrum, antimicrobial properties, and resistance resistance. Xu L et al [23] synthesized nano-silver from bovine serum albumin and carboxymethyl chitosan, and modified calcium alginate film, and prepared a bovine serum albumin/ carboxymethyl chitosan/ nano-silver/calcium alginate film with good mechanical properties and antimicrobial properties. Zhao ZY et al [24] prepared homogeneous and stable hesperidin-pectin-nanosilver antimicrobial nanomaterials by a simple microwave-assisted method, using hesperidin and pectin as the reducing and stabilizing agents. The results showed that the synergistic effect of hesperidin and pectin significantly enhanced the antimicrobial properties of nanosilver. Liu Y [25] doped the nanosilver into polyvinyl alcohol and carboxymethyl chitosan hydrogels crosslinked by borax, which endowed it with a strong antimicrobial effect.

4. SUMMARY

The application of dressings in medical treatment is becoming more and more widespread, and the development of a dressing that can effectively promote wound healing will be very beneficial to reduce the pain of patients and the burden of healthcare workers. In order to cope with the characteristics of different wounds, multifunctional wound dressings have received more and more

attention, and relevant researchers have conducted a lot of research on them. In this paper, we briefly summarize the research progress on several common dressings that facilitate wound healing, have good mechanical properties and help keep the site free from microbial infection. In addition, they are generally cross-linked by physical and chemical means and can be loaded with bioactive substances to accelerate wound healing. Future research will make hydrogel-based dressings smarter and more multifunctional by intersecting with multiple fields, combining the latest engineering technologies, bioprinting, stimulus-responsive and biodegradable hydrogels with growth factors and anti-inflammatory active compounds to improve therapeutic efficacy and extend life expectancy.

REFERENCES

- [1] He Y,Zhao W W,Dong Z X,et al.Int.J.Biol.Macromo.,2021,167:182.
- [2] Winter G D.J.Wound Care,1995,(8):366.
- [3] Nuutila K,Eriksson E.Adv.Wound Care,2021,10(12):685.
- [4] Li H J,Tan C,Li L.Mater.Des.,2018,159:20.
- [5] Szarpak A, Auzély-Velty R. Hyaluronic acid single-network hydrogel with high stretchable and elastic properties[J]. Carbohydr Polyme,2023,320:121212-121212.
- [6] Su S,Bedir T,Kalkanedlen C,et al. Coaxial and emulsion electrospinning of extracted hyaluronic acid and keratin based nanofibers for wound healing applications[J].European Polymer Journal,2021,142:110158.
- [7] SUNJ,PERRYSL,SCHIFFMANJ D.Electrospinning Nanofibers from Chitosan/Hyaluronic Acid Complex Coacervates[J].Biomacromolecules,2019,20(11):4191-4198.
- [8] Biranje S S,Madiwale P V,Patankar K C,et al.Carbohydr.Polym.,2020,239:116106.
- [9] Lan G Q,Li Q,Lu F,Yu K,Lu B T,Bao R,Dai F Y.Cellulose,2020,27(1):385.
- [10] Klara J, Marczak A, Łatkiewicz A, et al. Lysine-functionalized chondroitin sulfate improves the biological properties of collagen/chitosan-based injectable hydrogels[J]. Int J Biol Macromol, 2022, 202: 318-331.
- [11] Yin H, Song P, Chen X, et al. A self-healing hydrogel based on oxidized microcrystalline cellulose and carboxymethyl chitosan as wound dressing material[J]. Int J Biol Macromol, 2022, 221: 1606-1617.
- [12] Correia C, Sousa RO, Vale AC, et al. Adhesive and biodegradable membranes made of sustainable catechol - functionalized marine collagen and chitosan[J]. Colloids Surf B Biointerfaces, 2022, 213: 112409-112409.
- [13] Carvalho DN, Williams DS, Sotelo CG, et al. Marine origin biomaterials using a compressive and absorption methodology as cell-laden hydrogel envisaging cartilage tissue engineering [J]. Biomater Adv, 2022, 137: 212843-212843.
- [14] Hu H, Luo F, Zhang Q, et al. Berberine coated biocomposite hemostatic film based alginate as absorbable biomaterial for wound healing[J]. Int J Biol Macromol, 2022, 209(Pt B): 1731- 1744.
- [15] Theocharidis G, Rahmani S, Lee S, et al. Murine macrophages or their secretome delivered in alginate dressings enhance impaired wound healing in diabetic mice[J]. Biomaterials, 2022, 288: 121692-121692.
- [16] Jing Y, Ruan L, Jiang G, et al. Regenerated silk fibroin and alginate composite hydrogel dressings loaded with curcumin nanoparticles for bacterial-infected wound closure[J]. Biomater Adv, 2023, 149: 213405-213405.
- [17] Xi Y, Ge J, Guo Y, et al. Biomimetic elastomeric polypeptidebased nanofibrous matrix for overcoming multidrug - resistant bacteria and enhancing full-thickness wound healing/skin regeneration[J]. ACS Nano, 2018, 12(11): 10772-10784.
- [18] He J, Liang Y, Shi M, et al. Anti-oxidant electroactive and antibacterial nanofibrous wound dressings based on poly (ε-caprolactone)/quaternized chitosan-graft-polyaniline for fullthickness skin wound healing[J]. Chemical Engineering Journal, 2020, 385: 123464-123464.
- [19] Xuan C, Hao L, Liu X, et al. Wet-adhesive, haemostatic and antimicrobial bilayered composite nanosheets for sealing and healing soft-tissue bleeding wounds[J]. Biomaterials, 2020, 252: 120018-120018.
- [20] Zhang S, Ye J, Sum Y, et al. Electrospun fibrous mat based on silver(I) metal-organic frameworks-poly(lactic acid) for bacterial killing and antibiotic-free wound dressing[J]. Chemical Engineering Journal, 390: 124523-124532.
- [21] Wang C, Feng N, Chang F, et al. Injectable cholesterol -enhanced stereocomplex poly(lactide) thermogel loading chondrocytes for optimized cartilage regeneration[J/OL]. Adv Healthc Mater, 2019, 8(14): e1900312-e1900312.
- [22] Wang L, Wu Y, Hu T, et al. Electrospun conductive nanofibrous scaffolds for engineering cardiac tissue and 3D bioactuators[J]. Acta Biomater, 2017, 59: 68-81.

- [23] Xu L, Zhao K, Miao J, et al. High-strength and anti-bacterial BSA/carboxymethyl chitosan/ silver nanoparticles/calcium alginate composite hydrogel membrane for efficient dye/salt separation[J]. *Int J Biol Macromol*, 2022, 220: 267-279
- [24] Zhao ZY, Li PJ, Xie RS, et al. Biosynthesis of silver nanoparticle composites based on hesperidin and pectin and their synergistic antibacterial mechanism[J]. *Int J Biol Macromol*, 2022, 214: 220-229.
- [25] Liu Y, Mao J, Guo Z, et al. Polyvinyl alcohol/carboxymethyl chitosan hydrogel loaded with silver nanoparticles exhibited antibacterial and self-healing properties[J]. *Int J Biol Macromol*, 2022, 220: 211-222.