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Modern Wound Dressing Using Polymers/Biopolymers

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Abstract

Wound dressing has remained challenging for some life-threatening wounds such as burning. Researchers have been engaged in looking for better solutions. This review paper depicted the ideal wound dressing based on the mechanism of human skins, compared traditional wound dressing methods to modern methods, and reviewed the use of polymers and biopolymers as advanced materials for wound dressing.

Keywords: Hydrogel; Wound dressing; Polymer; Biopolymer; Materials

Introduction of Skin and Would Healing Mechanism

Skin is the human body's largest organ. It is made up of three main layers – the epidermis, the dermis, and the hypodermis (subcutaneous layer) (Figure 1). The basal layer of epidermis is attached to a basement membrane, which overlies the dermis with lots of collagen fibers. Skin contains Extracellular Matrix (ECM) comprising both fibrillar collagen and basement membrane [1]. Functionally, skin effectively prevents passage of many foreign substances into the body by serving as a physical barrier as well as metabolizing large molecules. Moreover, skin regulates the body temperature and gives support to blood vessels and nerves [2]. Acting as the outermost layer and the first layer of protection to human body, skin is of essential importance to human health [3].

However, people get injured in skin very easily, which may lead to severe bleeding and sometimes fatal. The skin injury is wound. Wounds are described as defects in the skin due to mechanical/thermo damages and other accidents. Wounds are classified based on the number of skin layers damaged, the area of skin disrupted, cause of skin damage, and the nature of wound repair process. The repair process usually contains four steps: inflammation, migratory, new tissue formation, and tissue remodeling (Figure 2), which are closely related to restoring the structure and function of skin ECM. The inflammation phase is the most critical stage, protecting wounds from invading bacteria and assisting the tissue repair process [4]. The damage and restoration of skin ECM is involved with wound healing process. Most wound dressings target and facilitate the inflammation stage, and mimic the structure and functions of skin ECM [5].

Traditional Wound Dressings

Traditionally, people treat wounds through the usage of bandage or gauzes for small and light wounds. However, bandages or gauzes cannot fully cover hairy wound sites, thus giving bacteria an opportunity to enter the wound site, as well as allowing fluids and blood to leak out of the wound site. In addition, bandages and gauzes often require adhesives that are hard to clean from human skin. Moreover, bandages and gauzes are not big enough for large/deep wound sites with severe bleeding. Surgery and sutures are used to address large and deep wounds, but there are many problems and limitations such as expensive price, time-consuming and painful process, and the possibility of complications after surgery. To address these problems, modern medical technology employs colloids, hydrogels, fibers, and other biomedical adhesive materials as wound dressings.

Desired Properties for Wound Dressing Materials

Requirements for an ideal wound dressing are based on the properties of ECM of skin. The ECM consists of proteins and polysaccharides, provides mechanical and biochemical support to surrounding cells, and directs cell migration, adhesion and growth rate during tissue regeneration. Thus, ideal wound dressings should be able to mimic the skin ECMs structurally and functionally.

As a result, healing enhancement, pain control, and enhancement of skin structure reestablishment become the primary focus of advanced wound dressings [6]. Specifically, the ideal wound dressings are expected to prevent wound site dryness, be able to absorb wound fluids and exudates, prevent infections induced by microbes, stimulate the growth rate, enable oxygen passage, and be elastic, non-toxic, non-antigenic, biocompatible and biodegradable [7-10].

Modern Wound Dressing Methods

Modern methods focus on the use of synthetic polymers and biopolymers, in the form of hydrogels [11], thin films [12], and Nano fibrous scaffolds [13].

Hydrogels resemble skin ECM, thus have the potential to direct cell activities. Moreover, hydrogels provide a moist healing environment for wound sites, which simultaneously aids in healing and helps to cool down the surface of skin, thereby reduce the degree of pain and improve patient acceptability.

Researcher have been putting lots of effort adding drug contents in hydrogels to promote wound healing [14]. Gaharwar et al. [15] disclosed an injectable nanosilicates reinforced hydrogel from a polysaccharide, k-carrageenan, and produced would dressings with sustained drug release properties. Wang et al. [16] evaluated the biocompatibility and drug release behavior of a hydrogel consisting of chitosan, heparin and poly (γ-glutamic acid). It showed this hydrogel effectively promoted the repair of chronic trauma in diabetes. As a

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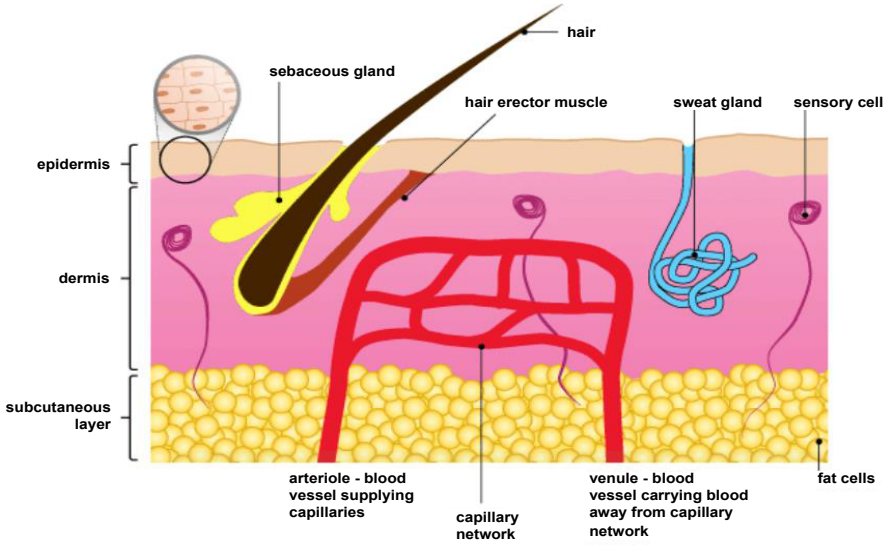

Figure 1: A simple diagram of skin structure [3].

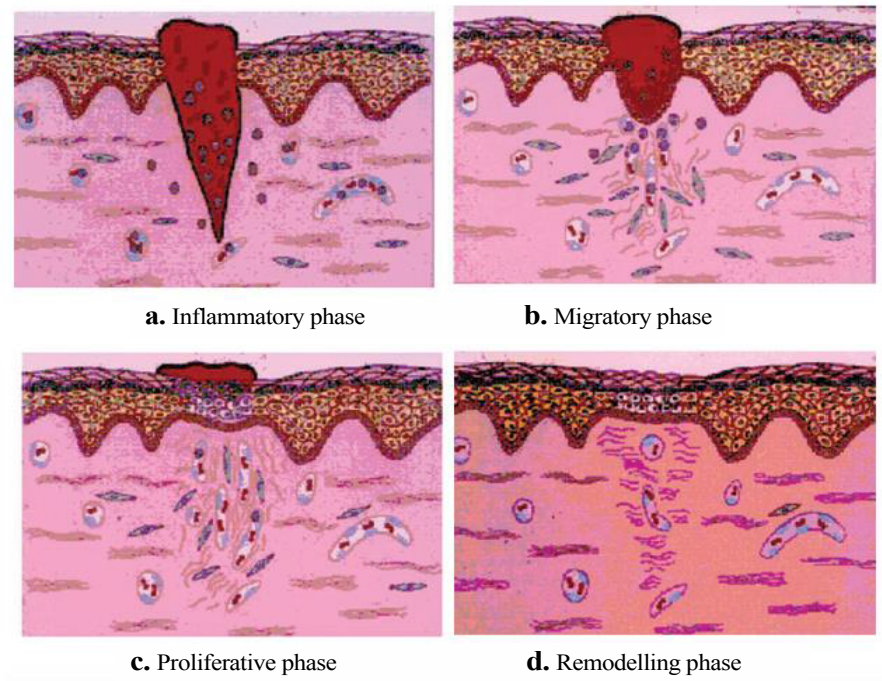

Figure 2: Wound healing process: (a) infiltration of neutrophils into the wound area (b) invasion of wound area by epithelial cells (c) epithelium completely covers the wound (d) many of the capillaries and fibroblasts, formed at early stages have all disappeared [5].

good drug carrier, hydrogels as wound dressing material showed great potential promoting the healing effectiveness.

However, hydrogels are known to have low mechanical strength [17]. Lots of work has been done to improve the mechanical strength of hydrogels. Khorasani et al. [18] reported a novel nano hybrid interpenetrating network hydrogel composed of laponite, polyvinyl alcohol, and alginate, and demonstrated adjustable mechanical strength with superior potential for wound healing application. Different of nanoparticles have been used to improve the strength of the hydrogel, while some of the nanoparticles, such as silver [19], have antimicrobial properties in nature. However, the lack of porosity, oxygen permeability, and mechanical strength of hydrogels still limit their application as ideal wound dressings.

Three-dimensional (3D) electrospun nanofibrous scaffolds better mimic the skin ECMs due to their fiber alignment, large surface area, high porosity, and small pore size. Moreover, they have strong mechanical properties [20] which can better support cell activities. 3D electrospun nanofibrous scaffolds have also shown excellent oxygen passage, prevention of microbes' invasion and water loss, and ability to absorb wound fluids. However, most studies on this application use a flat nanofibrous mesh, despite tissues are three-dimensional [21]. It is critical to employ a faster and realistic electrospun technique for 3D

scaffolds for wound dressings. On the other hand, many nanofibrous scaffolds only mimic the structure of ECM, without providing a moist environment for wound sites.

Modern Wound Dressing Materials

Synthetic polymers such as polyvinyldene floride (PVDF) and polypropylene (PP) have been widely used for wound dressing materials. Poly (ε-caprolactone) (PCL), polyethylene glycol (PEG), polyethylene oxide (PEO), polyurethane (PU), poly (vinyl alcohol) (PVA), poly (lactic acid) (PLA), and poly (lactic-co-glycolic acid) (PLGA) are frequently used synthetic materials that have been approved by Food and Drug Administration (FDA) for biomedical applications, due to their good biocompatibility, biodegradability and non-toxic properties. For example, PLGA is commercially available, inexpensive, biocompatible, biodegradable, and showed sustained drug release properties [22], making it the ideal candidate for drug delivery and other biomedical applications. Moreover, Porporato [23] discovered that lactate played an important role in promoting angiogenesis and wound healing process, and concluded that PLGA to be the most suitable polymer to provide lactate for enhanced wound management. PEG displays excellent biocompatibility, biodegradability, hydrophilicity and wettability. It is inexpensive and readily available, and therefore widely used for biomedical applications. More recently, Kim [24] has shown that PEG provides anti-fouling properties, preventing the adsorption of protein and other biomolecules on to nanofiber surface, which enhances drug release properties and aids in maintenance of nanofiber surface properties during use. Hydrogels and nanofibrous scaffolds based on these synthetic polymers have been fabricated for biomedical applications with good mechanical properties.

However, the application of these synthetic polymers alone as wound dressings are limited by their adhesive properties and their ability to accelerate wound healing process.

Therefore, it is critical to produce a new and improved wound dressing by synthesizing, modifying, and systematically designing wound dressing materials with good mechanical properties while accelerating the healing process at molecular, cellular and systematic levels. It is also desirable for wound dressings to have good drug release properties to further promote the wound healing process.

Polysaccharides in combination with these polymers provide a solution to the need for a new and improved wound dressing. This strategy combines the preferred chemical and biological properties of polysaccharides and synthetic polymers, producing wound dressings with superior performance both mechanically and biologically. The most studied polysaccharides for wound dressing applications include chitosan (CS) [6], gelatin [25], keratin [26], sodium alginate (NaAlg), agarose [6], and hyaluronic acid [27].

Among all these polysaccharides, Chitosan - Chitosan, produced by alkaline deacetylation of chitin, is the second most abundant natural polysaccharide and is composed of N-glucosamine and N-acetylglucosamine units [28]. Chitosan is inexpensive, readily available, and can be obtained from invertebrates' skeleton as well as the cell wall of fungi. It is a biocompatible, biodegradable biopolymer with antibacterial and wound healing properties, as well as low toxicity. Due to these properties, chitosan has been widely studied to produce wound dressings combined with polymers such as CS/polyethylene glycol (PEG) [29], CS/poly (vinyl alcohol) (PVA) [30], CS/poly (lactic-co-glycolic acid) (PLGA) [31] and CS/polylactide (PLA) [28].

However, because chitosan-based composite materials lack desirable adhesiveness, this along with their water-insoluble properties limits their potential for biomedical applications. Li [28] fabricated CS/PLA/PEG nanofibers for wound dressing using a solution blowing technique, and discovered quick absorption behavior, high water absorption rate, good air permeability, and good antibacterial activities against *E. coli*. Meng [31] employed electrospinning to produce PLGA/CS nanofibrous scaffold, and examined the drug release behavior of fenbufen (FBF) incorporated in the nanofibrous scaffold. The results showed that both the diameter of electrospun nanofibers and the drug release rate of FBF increased with increasing CS content. The researchers attributed the increased drug release rate to the enhancement of hydrophilicity of increased chitosan. Ryu [32] designed an injectable and thermoresponsive CS/Pluronic composite hydrogel, where catechol-conjugated chitosan was cross-linked with a Pluronic F-127 triblock copolymer to produce temperature-sensitive and adhesive sol-gel transition hydrogels. Catechol-conjugated chitosan greatly improved the adhesiveness of chitosan and thereby overcame this limitation of chitosan-based wound dressings. This modification imparted the CS/Pluronic hydrogel with stronger adhesive properties. The results showed dramatically enhanced adhesiveness to soft tissues and superior hemostatic properties. Moreover, the viscous solution state CS/Pluronic hydrogel solidified at body temperature and physiological pH, which makes these hydrogels a good candidate for injectable materials.

Future Needs for Would Dressings

Despite the various methods and materials for wound dressings, to date, no wound dressing fully satisfies the requirements of an ideal substitute for skin ECM. Most wound dressings are limited by fast degradation, weak adhesiveness and absorption, lack of drug release properties, poor oxygen permeability, as well as not being able to prevent protein adhesion onto the wound dressing surface. It is urgent to design and fabricate wound dressings which can address these problems simultaneously, thereby leading to improved wound management, creating an easy solution for wounds, and decreasing death rate induced by severe wounds and bleeding.

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