

Biopolymer-Based Hydrogel Wound Dressing

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1. INTRODUCTION

Chronic ulcer is a critical healthcare problem worldwide. A retrospective study in 2018 demonstrated that 8.2 million people experienced wounds whose treatment cost ranging from 28.1 to 96.8 billion USD [1]. In such wounds, the healing process is impaired due to several diseases and conditions such as peripheral vascular insufficiency, age, poor nutrition, diabetes, and local pressure effects which disrupt organized cellular and molecular processes required for wound healing [2]. Nonhealing wounds impose a significant cost on the patient and the medical system [3]. Their prevalence rate is reported to be 2% of the population and it was demonstrated that 6.5 million people were affected by chronic wounds in 2009 only in the United States [4].

Injuries because of a disease or accidental/intentional trauma lead to disruption of the integrity of the tissue (mucosa, skin, or any organ) activating a cascade of cellular pathways to restore the tissue integrity. In general the healing process involves hemostasis, inflammation, proliferation, and tissue remodeling. At the time of the damage, the arterial vessels are constricted to prevent exsanguination leading to hypoxia and acidosis and consequent release of nitric oxide and vasodilation. The enhanced release of histamine improves vascular permeability and infiltration of inflammatory cells into the wound environment. In the inflammatory phase, chemotaxis and the entrance of neutrophils, macrophages, and lymphocytes remove bacteria and also the damaged host tissue called debridement. Besides, they stimulate angiogenesis and release of growth factors regulating the inflammatory response. As long as the bacteria and the debris exist, the inflammatory phase persists that leads to tissue damage, delayed proliferation leading to nonhealing wound. After achieving the

hemostasis and the inflammatory balance, proliferation phase begins through angiogenesis, collagen deposition, and re-epithelialization [5]. Keratinocytes are the major cells which migrate from the wound edge to the wound to restore the epidermis.

Conventional wound dressings were made of cotton gauze which acts as a physical barrier to pathogens. However, their capacity to absorb the wound exudate is low. Besides, such dressings adhere to the damaged area and hurt the fragile neotissue [6]. Among different wound dressings, hydrogel-based dressings are of great interest. Hydrogel is a 3D cross-linked network of hydrophilic polymer chains which can absorb high amounts of water between the chains [7]. In addition to high water content, flexibility, good mechanical stability, and the availability of gaseous exchange, hydrogels can incorporate bioactive materials, regenerative cells, and drugs thus making them ideal wound dressings. This feature is due to the similarity between the hydrogels and extracellular matrix (ECM) that both are made of polymeric networks in aqueous environment [8]. Xiao et al. developed collagen-chitosan hydrogels loaded with QHREDGS peptide to protect keratinocytes against oxidative stress in wounds in diabetic mouse model to enhance re-epithelialization [2]. Hydrogels are produced from the biopolymers, the synthetic polymers, or the composites. Biopolymers are polymers made of natural sources. Natural polymers are made of animals [gelatin, chitosan, silk, collagen, and hyaluronic acid (HA)], plants (starch and cellulose), or algae (alginate). Their main advantage is biocompatibility and biodegradability [9] mimicking the ECM of the injured tissue. Liu et al. fabricated hydrogels composed of chondroitin 6-sulfate (CS) and heparin which were used to deliver basic fibroblast growth factor (bFGF) to improve healing process of full thickness