

wounds in diabetic mice [10]. They proved that the clinical potential of proteoglycans as the hydrogel and the growth factor in accelerating the healing process.

In this chapter, various biopolymeric hydrogels used in wound dressings are categorized, and recent studies describing the characteristics and their exceptional features are discussed. Additionally the ideal properties of wound dressings to accelerate the healing process and to diminish the scar formation are explained. Moreover, their clinical application and FDA-approved products are briefly described.

## 2. WOUND DRESSING AND ITS IDEAL PROPERTIES

In the past, strips soaked in oil or grease, honey, oil, and wine were used as treatment agent for wound healing. Besides, wool boiled in water or wine was applied as wound bandage. Wound dressing is placed directly on the wound and then fixed in place using bandage. During the 19th century, the antiseptic technique was discovered to manage the infection [11]. Wound dressing appeared in 20th century [12], and they were developed into more sophisticated tools in the late 20th century. Wound dressings were fabricated with increasing re-epithelialization, angiogenesis, and collagen synthesis properties by providing acidic pH and hypoxia to reduce the chance of wound infection [13]. During the mid-1990s, synthetic wound dressings with the features of providing moisture and absorbing wound exudates were considered [14].

As an ideal wound dressing, it should have properties such as preserving moist environment, improving epidermal migration, allowing gas exchange between environment and wounded tissue, increasing angiogenesis and connective tissue synthesis, defending against bacterial infection, improving leucocytes migration, having long shelf life, being free of toxic contaminants, and protecting wound from further trauma [15, 16]

## 3. WOUND DRESSING BASED ON BIOPOLYMERS

Polyphenols, peptides, polyesters, polysaccharides, and other natural polymers with repeating units/monomers originate from the living organisms such as fungi (chitin), animal (chitosan, HA, and collagen), bacteria [bacterial cellulose (BC) and exopolysaccharides], plant (natural rubber, starch, and cellulose), and algae (alginate). These polymers with biodegradability, renewability, biocompatibility, and lower antigenicity properties are preferred over the synthetic materials [17–20]. In addition, they play a key role in wound-healing process

with antiinflammatory, targeted actions to specific cells, antibacterial, and proliferative features. Biopolymers have been blended with other polymers to promote biomimetic and mechanical strength features for the development as skin substituent [21].

Considering the inherent physicochemical and biological properties of ECM, proteins, and polysaccharides possess high level of biomimicry. In the construction of hydrogel, collagen, gelatin, and HA can be considered as ECM support, while RGD and LDV sequences in silk fibroin and keratin are used as cell-recognition domains and biomolecule-binding sites. In addition, chitosan and alginate have antibacterial and antiinflammatory properties [22].

### 3.1. Dextran

Dextran is a type of polysaccharide composed of anhydroglucose rings [23]. Dextran with alpha-1,6 linked D-glucopyranose residues, possesses biodegradability, biocompatibility, nontoxicity, and hydrophilicity properties [24–26]. D-Glucopyranose residues can be easily oxidized by NaIO<sub>4</sub> to generate aldehyde groups providing then functional group to be conjugated with amine side groups of gelatin, chitosan, and other polymers to form various hydrogels as antibacterial materials, smart sustained drug delivery vehicles, and hemostatic agents. In addition, dextran-based hydrogel is used as a wound dressing due to its ability to stimulate wound-healing process [27–29].

Excessive inflammation accompanied by the immediate damage of blood flow at the injury site of burn inducing pain which are the major differences between incisional and burn wounds. Owing to the ineffectiveness of using single therapeutic agent in promoting burn wound healing, a combination therapy is usually used for the treatment. In a study, vascular endothelial growth factor (VEGF) was applied as an angiogenesis agent which is working by accumulation of inflammatory cells in the damage site and thus stimulating the proliferation and migration of the endothelial cell [30]. Although naked DNA of VEGF is unstable and displayed low transfection efficiency, gene therapy approach using polyethylenimine (PEI) combined with pDNA encoding VEGF provided versatile gene transfection ability. Moreover, resveratrol with immunomodulatory, antioxidant, and chemopreventive properties is a natural polyphenolic compound found in grape skin which could be implemented as a wound-healing accelerator [31]. Resveratrol can upregulate the expression of VEGF in human skin cells [32]. However, it has poor water solubility. To overcome this problem, a hydrogel scaffold consisted of dextran (Dex), HA, and  $\beta$ -cyclodextrin ( $\beta$ -CD) was produced