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Collagen-grafted temperature-responsive nonwoven fabric for wound dressing

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ABSTRACT

Polypropylene (PP) nonwoven fabric (NWF) was modified by direct current pulsed plasma followed by grafting with acrylic acid (AAc) to improve its surface hydrophilicity and to introduce carboxylic acid group on the surface for further conjugation with bioactive collagen biomolecule. To endow temperature-responsive property, PP-*g*-collagen NWF was further modified with poly(*N*-isopropylacrylamide) (PNIPAAm). Experimental results demonstrated that the amount of AAc and collagen grafted were 43.4 nmole/cm^2, and 35.9 μg/cm^2, respectively. The amount of PNIPAAm immobilized was 213 μg/cm^2. The physical properties, surface chemical composition, and microstructure of the NWFs were characterized. From animal study, modified NWFs were found to promote wound healing with bigraft PP-*g*-collagen-*g*-PNIPAAm NWF showing the best performance.

1. Introduction

Wound healing is a complicated sequence of cellular and biochemical events proceed through a series of different phases [1,2]. For the choice of proper biomaterials in wound dressing, the role of collagen at each phase of wound healing is well understood and appreciated [3]. Many collagen products for wound healing have been developed in the past few years, and silicon film combined with a collagen layer is usually used for these products [4,5]. However, silicone layer limits the ventilation of body fluid and the collagen sponge material is very expensive. In this study, porous polypropylene (PP) nonwoven fabric (NWF) was adopted to replace the silicon film. NWF can serve as an excellent dressing material with its high porosity and larger surface area, which provide an open structure for drainage of exudates and reduces the risk of second infection [6]. Therefore, wound dressing by grafting bioactive collagen to PP NWF is expected to show good potential to be applied as wound dressing.

A method for preparation of easily stripped off temporary wound dressing has been developed by grafting of poly(*N*-isopropylacrylamide) (NIPAAm) onto NWF [7–9]. PNIPAAm exhibits a lower critical solution temperature (LCST) and remarkable hydration–dehydration changes in response to relatively small changes in temperature [10]. Below the LCST which is around 32 °C, PNIPAAm chains hydrate to form an expanded structure; above the LCST, PNIPAAm chains dehydrate to form a shrinkage structure. By grafting PNIPAAm onto the surface of the base material of a wound dressing, the polymer becomes hydrophobic by expelling water with body temperature above the LCST. The PNIPAAm connection layer adheres well with the tissue in this case when the wound is in the moist condition. During the change of wound dressing where separation of the dressing material from the tissue is required, a low temperature treatment below the LCST of PNIPAAm to the dressing material will make the polymer swell and become hydrophilic by absorbing water. In such case, the NWF dressing could be readily stripped off from the wound site without damaging the newly regenerated tissues.

To achieve the purpose of obtaining a collagen-grafted PP NWF with temperature-responsive easily stripped off characteristic, a PP NWF was modified by DC pulsed oxygen plasma-induced grafting polymerization of acrylic acid (AAc). Chemical grafting of collagen and PNIPAAm was followed to form the bigraft PP-*g*-collagen-*g*-PNIPAAm NWF.

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2. Experiment

2.1. Preparation of PP-g-collagen

PP NWF (density 75 g/cm^3 and thickness 370 μm) was first modified by the DC-pulsed plasma system developed previously in our laboratory [11]. After 75 s treatment, the NWF (1 cm × 1 cm) was immersed in 20% (w/w) AAc aqueous solution and shaking at 60 °C for 4 h. The amount of AAc grated to the NWF was determined by Toluidine Blue [12]. After coating AAc on the surface, the NWFs were reacted with 10 mg/ml 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) in 0.1 M MES buffer (pH 6) for 4 h to activate the carboxylic groups, followed by reacting with Type I collagen solution (1.5 mg/ml) in 0.5 M acetic acid by shaking at 4 °C for 24 h. The collagen-grafted NWF was washed with 50 ml phosphate buffered saline (PBS) for five times and dried overnight in a vacuum oven at room temperature. Collagen content was determined by *p*-dimethylaminobenzaldehyde after hydrolysis to hydroxyproline [13].

2.2. Preparation of PP-g-collagen-g-PNIPAAm

PP-*g*-collagen-*g*-PNIPAAm was synthesized by conjugating the carboxylic acid end group of PNIPAM-COOH [14] to the amine group of collagen. Five milligram of PNIPAM-COOH was reacted with 2 mg EDC in 10 ml MES buffer (pH 6). The bigraft NWF was thoroughly washed with PBS and dried overnight in a vacuum oven at room temperature. The amount of PNIPAAm grafted to NWF was calculated from the weight difference before and after the grafting reaction.

2.3. Analysis of NWFs

X-ray Photoelectron Spectroscopy (XPS) was performed with a PHI 1600 ESCA Spectrometer (Physical Electrons) equipped with a spherical capacitor analyzer and a multi-channel detector. Elemental compositions at surface using C_{1s} O_{1s} and N_{1s} core level spectra were measured and calculated from XPS peak area with correction algorithms for atomic sensitivity [15]. The NWF was sputter coated with gold and analyzed by Scanning Electron Microscopy (SEM, JOEL JSM 5410).

2.4. Animal study

Wound healing test was carried out with animal models using SD rats [16]. A full thickness wound with a surface area of 2 cm × 2 cm was cut from the back of the SD rat. The wound was covered with an equal size of NWF and gauze (control). The area of the wound was measured at 3, 7, 10, 14, and 17 d by applying cold treatment at 4 °C, which is below the LCST of PNIPAAm, to the wound site before removing the wound dressing. The percentage of wound healing is defined as $(B/A) \times 100\%$, where A is the initial wound area and B is the wound area after a fixed time interval.

3. Results and discussion

The influence of polymerization time and AAc concentration on the amount of AAc grafted has been studied. The efficiency of AAc grafting increased with monomer concentration and grafting time. However, above 15% AAc concentration, self-polymerization of AAc occurred and decreased the grafting efficiency. The maximum amount of –COOH that could be introduced to NWF in this case was 43.4 ± 1.18 nmol/cm^2 (3.15 ± 0.08 μg/cm^2). This value is high enough for introducing a continuous bioactive collagen layer on the fiber surface [17]. Collagen was immobilized to the AAc-modified NWF by using the activation reagent EDC. The amount of collagen grafted to the NWF was estimated to be 35.9 ± 2.54 μg/cm^2. For grafting PNIPAAm to collagen-containing PP NWF, a similar approach was used with the activation reagent EDC and the amount of PNIPAAm grafted to the NWF was 213 ± 11.5 μg/cm^2.

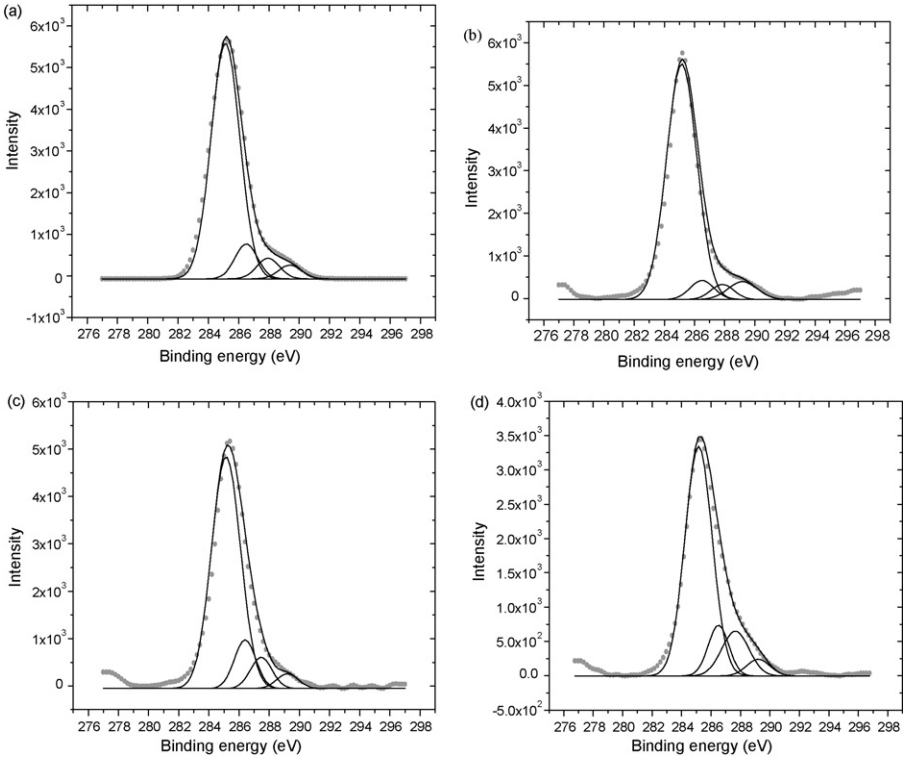

Fig. 1. High-resolution XPS C_{1s} spectra of the (a) plasma modified NWF, (b) AAc coated NWF, (c) PP-*g*-collagen NWF, and (d) PP-*g*-collagen-*g*-PNIPAAm NWF.