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Preparation and characterization of aminated hyaluronic acid/oxidized hydroxyethyl cellulose hydrogel

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ABSTRACT

Hydrogel wound dressing is a new type of biomaterial with great absorbent capacity, which has been extensively researched and its application in the field of biomedicine is common. In this study, we prepared a novel composite hydrogel made of hyaluronic acid (HA) and hydroxyethyl cellulose (HEC), both of them are natural polysaccharides. Then, the structure and properties of this composite hydrogel were characterized and tested. The results gained from these studies show that this composite materials have a series of excellent performance such as appropriate gelation time, good swelling ability, suitable water evaporation rate, well hemocompatibility and biological compatibility. In particular, the super absorbent capacity (the maximum swelling rate is 2888%), which is conducive to maintain a moist wound healing environment. Taking account of these properties, this hydrogel can be used clinically as a wound dressing.

1. Introduction

Skin is one of the main organs of the human body, which can avoid the loss of moisture and electrolytes and prevent the invasion of microorganism (Chen et al., 2015; Chopra et al., 2016; dos Santos-Silva, Trajano, Schanuel, & Monte-Alto-Costa, 2017). Skin damage caused by trauma, burns and other external causes, if not handled, will cause a series of problems to the body, and even death (Singer & Clark, 1999). Therefore, upon wounding, the use of medical dressings for timely and effective protection is very necessary (Zg linear acidic mucopolysaccharide with disaccharide repeating unithou et al., 2013). Clinically, fibers, gauze, hydrogel, medical films and alginate dressings etc., are commonly used to treat wounds as medical dressings (Fan, Yang, Yang, Peng, & Hu, 2016; Li, Williams, & Wu, 2017; Xu et al., 2015). Among these dressings, hydrogel dressings can create a moist wound healing environment, allow gas exchange, absorb extra secretions and can be removed easily without damaging the wound (Fan, Yang et al., 2016; Iswariya, Bhanukeerthi, Velswamy, Uma, & Perumal, 2016; Mozalewska et al., 2017; Zhou et al., 2013). In addition, hydrogel are structurally similar to the native extracellular matrices (ECM), and they are three-dimensional network structures which can be beneficial for cell adhesion, proliferation and transportation of cytokines, nutrients and metabolic waste (Parlato & Murphy, 2014; Rufaihah & Seliktar, 2016). Therefore, hydrogel are well suited as wound dressing materials. In recent years, the hydrogel system based on polysaccharide, including alginate, chitosan, carrageenan, dextran, cellulose, hyaluronan acid and so on, has drawn more and more attention for its excellent properties like biodegradable, renewable and easily available (Kong, Kim, & Park, 2016; Shulepov, Kozhikhova, Panfilova, Ivantsova, & Mironov, 2016).

HA is a naturally occurring linear acidic mucopolysaccharide with disaccharide repeating units of D-glucuronic acid and *N*-acetyl-D-glucosamine linked via alternating β (1/3) and β (1/4) glycosidic bonds (Khabarov, Boykov, & Selyanin, 2014; Kim et al., 2017). HA is a multifunctional matrix that displays a variety of important physiological functions such as regulating cell adsorption, growth and differentiation, lubricating joints, promoting angiogenesis and promoting wound healing, etc. (Collins & Birkinshaw, 2013; Kudryavtseva et al., 2017). In particular, HA with super water retention, is currently found in nature, the best moisture substances, known as the ideal natural moisturizing factor (Chen, Ashfaq, Zhang, Zhang, & Guo, 2018). HA is widely found in higher animal and human extracellular matrix, connective tissue, nerve tissue and epithelial tissue. Because HA is a ubiquitous polysaccharide, it avoids controversial safety issues (Becker et al., 2009; Pinto-Fraga, López-de la Rosa, Arauzo, Rodríguez, & González-García, 2017). Therefore, HA is free from the risk of toxicity or immunogenicity, and various HA products have been commercialized after FDA approval in the forms of intraarticular injection, ophthalmic solution, dermal filler and so on (Martin, Massafra, Bizzi, & Migliore,

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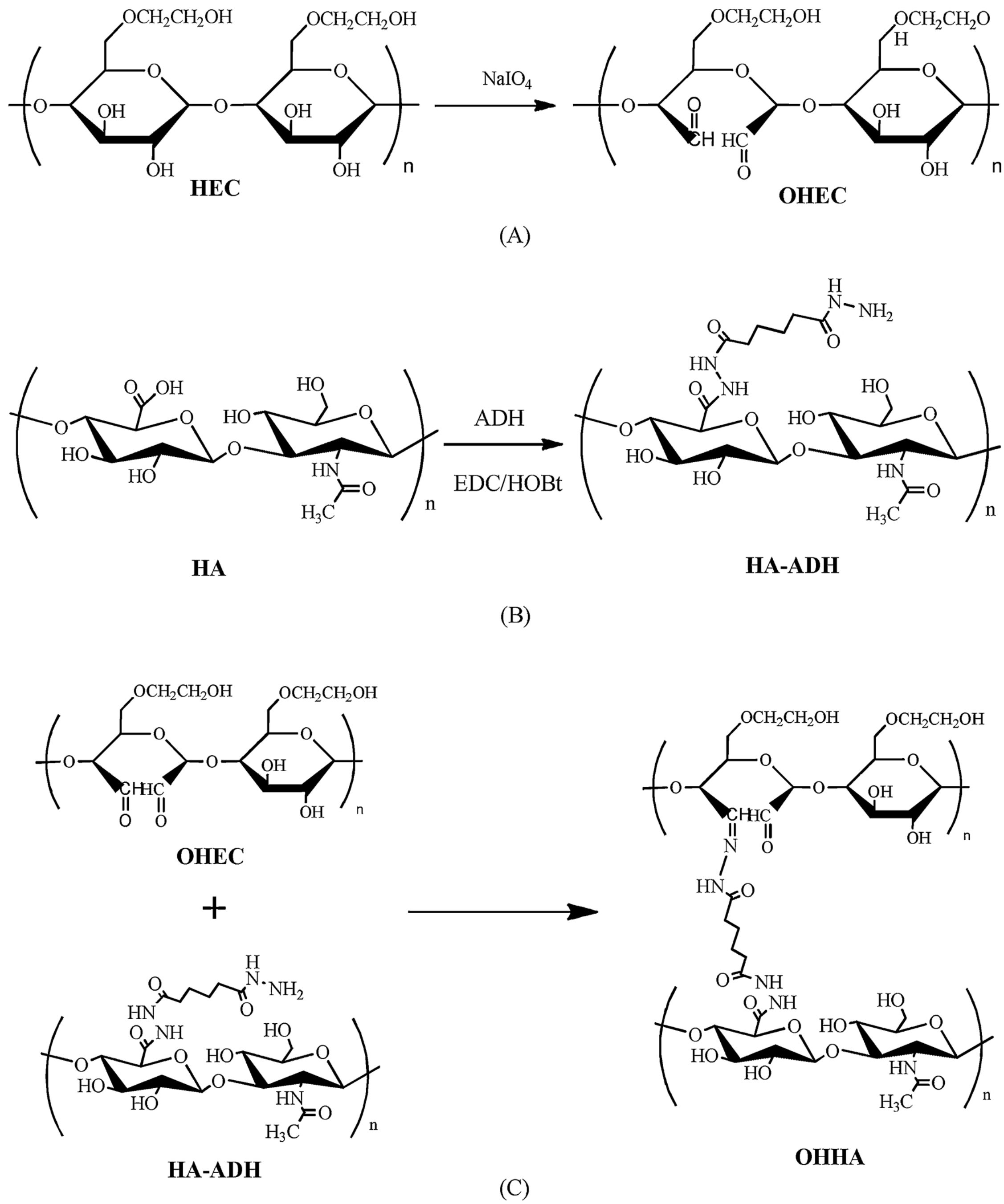

Scheme 1. (A) the synthesis of HA-ADH; (B) the synthesis of OHEC; (C) the synthesis of OHHA hydrogel.

2016; Monheit & Coleman, 2006; Pagnano & Westrich, 2005). However, HA has poor stability and fast degradation rate, which limits its application in some occasions. Therefore, it is necessary to modify HA or combine with other materials to improve the defect in order to meet different application requirements. Takahashi et al. modified the HA with azido and cyclooctyne groups, respectively, to form a hydrogel that degraded slowly, and the degradation time in PBS was more than 14 days (Takahashi et al., 2013).

Cellulose, the most abundant polysaccharide in the world, has attracted the attention of researchers because of its renewability, biocompatibility and biodegradability (Altomare, Cochis, Carletta, Rimondini, & Farè, 2016; Pandey, Takagi, Nakagaito, Saini, & Ahn, 2012). Cellulose is a linear polysaccharide with repeating units of D-glucopyranosyl linked via β (1/4) glycosidic bonds, and there are a large number of hydrogen bonds between glucose rings (Vadodaria & English, 2016; Xu, Chen, Rosswurm, Yao, & Janaswamy, 2016). Therefore, cellulose not only is difficult to dissolve in water, organic or inorganic solvents, but also it cannot melt, which greatly limits the application (Sun, Wang, & Yan, 2017). So, in order to expand the application, increasing the water-solubility of cellulose will be a precondition. HEC is one of the most important commercially available cellulose derivatives, which is a kind of non-ionic cellulose ether with good water solubility, rheological property, thermodynamic and hydrodynamic parameters (Fekete, Borsa, Takács, & Wojnárovits, 2017; Li, Meunier, & Partain, 2014). HEC had been extensively used as a thickener, stabilizer or coating at several application fields (Abbas et al., 2017; Zulkifli, Fsj, Zeyohannes, Msba, & Yusuff, 2017). At the same time, there are also a lot of studies on HEC about hydrogel synthesis (Seki, Altinisik, Demircioğlu, & Tetik, 2014). However, there are few reports about HEC used as a cross-linking to synthesize