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Chitosan/polyethylene glycol fumarate blend film: Physical and antibacterial properties

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ABSTRACT

The objective of this work was to prepare chitosan/polyethylene glycol fumarate (chitosan/PEGF) blend films as wound dressings and to evaluate the influence of composition ratio on the blending properties of the films. Blending chitosan with PEGF obviated the brittleness of neat chitosan film. Film topography performed by atomic force microscopy illustrated that blending could increase and control the surface roughness of the neat film. Their water vapor transmission rates were close to the range of 904–1447 g^{-2} day^{-1} found to be proper candidates for dressing the wounds with moderate exudates. Controlled water solubility, swelling, wettability and surface tension of the blend films were also evaluated. The blend films showed a powerful antibacterial activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Kill% > 99.76 ± 0.16%). Physical properties as well as antibacterial activity assessments showed that among different compositions, the film comprising 80 wt% chitosan and 20 wt% PEGF is a suitable candidate for biomedical applications as a wound dressing material.

1. Introduction

Recently, there is an increasing interest in the development of wound dressing based on biopolymers as they are biocompatible, biodegradable, and renewable (Boateng, Matthews, Stevens, & Eccleston, 2008). An ideal wound dressing should maintain a moist milieu, absorb excess exudates, allow gaseous exchange, be easy to apply and remove without causing new trauma as well as being antimicrobial, nontoxic and biocompatible (Elsner, Shefy-Peleg, & Zilberman, 2010). Considering exudates discharge and injury location, each type of wound requires specific dressing; hence, the physicochemical and mechanical properties of the dressing should be adjusted (Elsner et al., 2010). Different wound dressings are available commercially in the market, but some of them cannot effectively prevent subsequent microbial outbreak (Seyednejad, Imani, Jamieson, & Seifalian, 2007). Some wound dressings with antibacterial activity make benefit from Ag ion release (Krishna Rao, Ramasubba Reddy, Lee, & Kim, 2012), causing argyria as well as toxicity from the salt or complexes of Ag (Demling & DeSanti, 2001), and the other are based on the releasing of antibacterial agents. There have been noted some side effects for the latter such as microbial resistance due to chronic application of antibacterials and consequent health problems (Atiyeh, Costagliola, Hayek, & Dibo, 2007).

Chitosan, isolated from chitin, is the linear and partly acetylated (1–4)-2-amino-2-deoxy-β-D-glucan (Muzzarelli, 1977, 2012), a well known functional aid for the ordered regeneration of human tissues (Hirano & El-Gewely, 1996; Muzzarelli, Greco, Busilacchi, Sollazzo, & Gigante, 2012). Chitosan is biodegradable, biocompatible, non-antigenic, nontoxic, biofunctional and antimicrobial (Kim, 2011). Chitosan has recently received great attention for different biomedical applications due to its beneficial intrinsic properties. Using intrinsic antibacterial activity of chitosan for wound dressing applications seems promising (Wang, Zhu, Xue, & Wu, 2012) however, chitosan suffers from a relatively poor mechanical characteristic, mainly involving less flexibility resulted in their brittleness at room temperature. There are many reports on blending of chitosan with natural polymers such as konjac glucomannan (Ye, Kennedy, Li, & Xie, 2006), zein (Torres-Giner, Ocio, & Lagaron, 2009), curdlan (Sun et al., 2011) and with synthetic polymers such as poly(ethylene oxide) (Zivanovic, Li, Davidson, & Kit, 2007), poly(vinyl alcohol) (Yang, Su, Leu, & Yang, 2004), poly(vinyl pyrrolidone) (Zeng, Fang, & Xu, 2004), poly(lactic acid) (Suyatma, Copinet, Tighzert, & Coma, 2004) to improve chitosan properties. Several blends, based on chitosan, have also been reported for biomedical applications such as bone (Malafaya & Reis, 2009), cartilage (Alves

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da Silva et al., 2010), skin (Azad, Sermsintham, Chandrkrachang, & Stevens, 2004) and nerve (Haipeng et al., 2000) tissue engineering as well as drug delivery (Wang, Dong, Du, & Kennedy, 2007).

Usually, polymer blends, rather than single ones, are designed to achieve performances of their constituting ingredients synergistically (Boateng et al., 2008). Blending of two or more polymers has gradually become an important approach to develop new biomaterials exhibiting combinations of properties that could not be achieved by applying each individual polymer (Chen, Wang, Mao, Liao, & Hsieh, 2008). Blends made of both synthetic and natural polymers can provide the wide range of physicochemical properties and processing techniques of synthetic polymers as well as the biocompatibility and biological interactions of natural polymers (Sarasam & Madihally, 2005). To this end, chitosan has been selectively blended with poly(ε-caprolactone) (García Cruz et al., 2008), a biodegradable aliphatic polyester, to obtain desirable mechanical properties.

Fumarate-functionalized unsaturated aliphatic polyesters with tunable mechanical properties have been synthesized as biodegradable materials including polypropylene fumarate (Suggs, Payne, Yaszemski, Alemany, & Mikos, 1997), poly ethylene glycol fumarate (PEGF) (Hashemi Doulabi, Mirzadeh, et al., 2008; Hashemi Doulabi, Sharifi, Imani, & Mirzadeh, 2008), poly(ε-caprolactone) fumarate (Sharifi et al., 2008), polyhexamethylene carbonate fumarate (Sharifi et al., 2011). They have been used as bone cements and substitutes (Holland, Bodde, et al., 2005), cartilage scaffolds (Holland, Tabata, & Mikos, 2005) and drug delivery carriers (Sharifi et al., 2009) but not for wound dressing to the best of our knowledge. PEGF is a biocompatible, cytocompatible, biodegradable member of unsaturated polyesters (Hashemi Doulabi, Mirzadeh, et al., 2008; Shin, Temenoff, & Mikos, 2003) but its weak film forming properties limits its application as a wound dressing material.

For obviating the previously mentioned problems with using neat chitosan and PEGF for wound dressing applications and improving PEGF biological properties, blending of PEGF with chitosan was examined here. It may be an approach to develop new biomaterials exhibiting a combination of properties that could not be obtained by individual ones, *i.e.*, also improved film formation, mechanical properties, tunable water vapor transmission rate, wettability, and ductility of the films.

The objective of the present work was to assess the blend characteristics and evaluate them as wound dressing materials comprising of chitosan and PEGF. This article is dealing with the antibacterial activities of the prepared films to be suitable as a wound dressing. To the best of our knowledge, there is no report in the literature to discuss about chitosan and PEGF blending and the blend properties as a potential biocomposite for wound dressing applications.

2. Experimental

2.1. Materials

Low viscosity chitosan (20–200 mPa s, DDA = 80%, Fluka, Germany) was purified as reported elsewhere (Hashemi Doulabi, Mirzadeh, & Imani, in press). PEG diols (M_w = 3 kDa), calcium hydride, fumaryl chloride, and propylene oxide were all purchased from Aldrich (Milwaukee, MN, USA). Sodium hydroxide, methylene chloride, and acetic acid were obtained from Merck Chemicals (Dusseldorf, Germany). Fumaryl chloride was purified by distillation at 161 °C under ambient pressure. Anhydrous methylene chloride was obtained by distillation under reflux condition for 1 h in the presence of calcium hydride. All of the other chemicals and reagents were of analytical grade and used as received without further purification.

2.2. Methods

2.2.1. Film preparation

PEGF macromer (M_n and $M_w \cong 10$ kDa and 12.2 kDa, respectively, as determined by GPC) was synthesized by esterification of fumaryl chloride with PEG diol in the presence of propylene oxide as a catalyst and proton scavenger, as described in detail elsewhere (Hashemi Doulabi, Mirzadeh, et al., 2008). Chitosan/PEGF blends were prepared by solution casting of polymer solutions in different chitosan/PEGF ratios (0/100, 20/80, 40/60, 60/40, 80/20, 100/0) both dissolved in 1% (v/v) acetic acid. The total concentration of the polymer blends was set on 1 g dL^{-1} for all of the samples composition. After filtration through a syringe filter (Jet Biofil®, 0.45 μm, China), 10 mL of the solution was cast into polystyrene petri dishes ($D \approx 5$ cm). The mixture was left to get completely dried at room temperature then dried *in vacuo* for 48 h. Samples were stored in a refrigerated desiccator until used.

2.2.2. Scanning electron microscopy

Blend films were examined using a T-Scan (Vega II, Czech Republic) scanning electron microscope (SEM). All specimens were coated with a conductive layer of sputtered gold. The micrographs were taken at an accelerating voltage of 15 kV in secondary electron mode to ensure a suitable image resolution.

2.2.3. Swelling behaviors

The fluid absorbing efficiency of a wound dressing is a key design criterion for providing and maintaining a moist environment over the wound bed. It was determined with a gravimetric method. The samples (n = 3) were cut into 1 cm × 1 cm rectangles then dried *in vacuo* (T = 35 °C, P = 0.2 bar) for 24 h and weighted (W_0). Afterward, the samples were immersed in an excess amount of PBS (0.1 M, pH = 7.4) at 25 °C for 24 h. They weighted 10 times at 1 h intervals after removing the water from the surface with blotting paper (W_t). The water uptake (W_u%) was calculated using the Eq. (1):

$$W_u \ (\%) = \frac{(W_t - W_0)}{W_0} \times 100 \quad (1)$$

Water uptake of the blend films at equilibrium condition (EW_u) was obtained using Eq. (1) where the value of the W_t was substituted by the sample weight after 24 h.

2.2.4. Water solubility

The dried films were immersed in methanol, as a non-solvent, for 24 h to remove any residual acetic acid. Then, the samples were taken out and dried *in vacuo* (T = 35 °C, P = 0.2 bar) overnight and weighed (W_1). Afterward, the films (n = 3) were immersed in distilled water for 24 h, dried *in vacuo* overnight, then weighed again (W_2). Water solubility (W_s) was calculated using Eq. (2).

$$W_s \ (\%) = \frac{(W_1 - W_2)}{W_1} \times 100 \quad (2)$$

2.2.5. Water vapor transmission rate

Water vapor transmission rate (*WVTR*) of the sample films was determined according to ASTM E96/E96M-10 (ASTM, 2010) procedure with minor modifications. A glass bottle containing anhydrous silica gel desiccant was covered by the films under test (15 mm diameter in exchange area) and sealed using paraffin wax. The assembly was weighed 8 times at 1 h intervals and kept in a humidity chamber maintaining 75 ± 3% of relative humidity (T = 25 ± 1 °C) using standard saturated solution of sodium chloride. Weight variations of the bottles were plotted *versus* time. *WVTR* was determined