Materials Science and Engineering C 69 (2016) 609–615

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Development of hydrocolloid Bi-layer dressing with bio-adhesive and non-adhesive properties

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ARTICLE INFO

Article history:
Received 9 March 2016
Received in revised form 5 June 2016
Accepted 12 July 2016
Available online xxxx

Keywords:
Gelatin
Chitosan
Biopolymer blend
Bi-layer film
Wound dressing material

ABSTRACT

Bio-active bi-layer thin film having both bio-adhesive and non-adhesive end composed of polyvinyl alcohol (PVA) and gelatin/chitosan/polyethylene glycol (PEG) blend was developed for biomedical applications especially as an alternative of advanced tissue scaffold. The developed composite film was subjected to mechanical, thermal and physico-chemical characterization such as tensile strength (TS) and elongation at break (Eb), differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), fluid drainage capacity and biocompatibility. Suitable packaging was also selected and stability study and aging test of the composite film were performed after packing. The incorporation of chitosan and PEG into gelatin showed improved mechanical properties of both TS and Eb, which suggested the occurrence of interaction among gelatin, chitosan and PEG molecules in the composite film. The presence of crosslinking as an interaction of above three polymers was also confirmed by FTIR study. Results from the DSC study suggested increased thermal stability after crosslinking. On the other hand, water uptake studies suggested excellent fluid drainage capability and hydro-stability of the composite film. The proposed dressing also showed excellent biocompatibility. Based on the studies related to the performance with confirmed identity, we concluded that our developed bi-layer film is very potential as an ideal wound dressing material.

1. Introduction

There has always been a scarcity of tissue availability for the purpose of tissue or organ repair. Moreover, various challenges like immune rejection, tissue mortality and morbidity, biocompatibility, proper dosage of cells, optimal timing for it etc. have been associated to methods like tissue grafting [1]. Owing to these limitations, there has been a paradigm shift in the medical field from traditional tissue transplantation to an emerging interdisciplinary engineering approach which is called Tissue Engineering. It mainly revolves around the development of artificial biological implants which can replace, regenerate or ameliorate damaged tissues and organs.

Our skin is the largest organ in our body and helps protect our body from germs (bacteria, fungi, and viruses) that live on our skin. Anything that breaks the skin is a wound, leads to the risk of germs entering into the body system and causing an infection. The importance of effective wound care cannot be underestimated. Wound care should always address the needs of the patient, promote normal healing and prevent complications. Caring for wounds after surgery, injury or disease is an important part of the recovery process. Not only proper wound care prevents infection and other complications, it also helps the wound heal faster with less scarring. Wounds especially in complex burned patients and those that are poorly managed can lead to the development of a chronic wound. This subsequently results in a significant social and financial burden to the community. So, continual attention to the wound's dressing and bandages is critical for preventing infection and for monitoring against other complications. In general, the following properties are necessary for wound dressing: (a) the dressing material must be capable of absorbing the exuded liquid from the wounded area; (b) it should permit water evaporation at a certain rate and allow no microbial transport and (c) the material should not stick to its surrounding tissue, as removal after healing could result in damage to the new skin [2].

Biomaterials such as gelatin, pectin, starch, cellulose, alginate, chitin, chitosan, collagen, polyamino acids, dextran etc. have been extensively studied as wound dressing material to enhance the healing process. Main reason to select these materials are their structures which are analogs of protein and growth factor structures in the human body and thus have a great potential to stimulate the appropriate physiological responses required for cellular regeneration and tissue reconstructing in wounds [3]. Gelatin is a protein based natural polymer derived by acid and alkaline processing of collagen [4]. It shows good film forming

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http://dx.doi.org/10.1016/j.msec.2016.07.029
0928-4931/

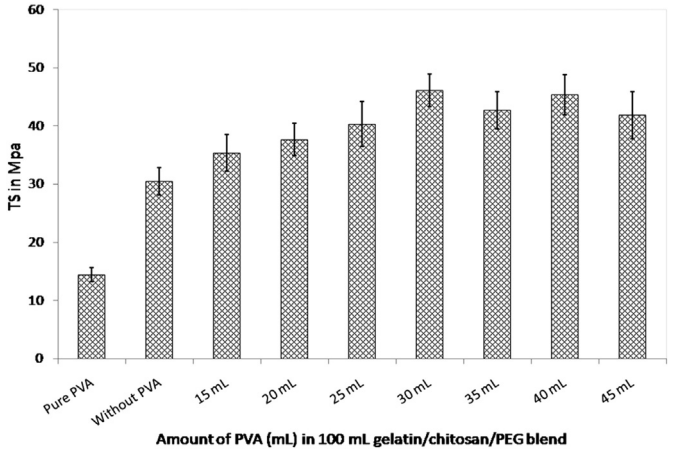

Fig. 1. Variation of tensile strength of the bi-layer composite film with respect to PVA content.

property, swelling behavior, biocompatibility and biodegradability. Hence gelatin is an intriguing candidate for drug carriers for tissue engineering and is widely being used as tissue engineering scaffold [5,6]. Besides, its water absorption capacity makes it a potential biomaterial, which can be successfully used for drug delivery purposes [7].

One of the drawbacks of gelatin for tissue engineering applications is its solubility in aqueous media; therefore, gelatin-containing structures for long-term biomedical applications need to be crosslinked [8]. The main limitation in the use of chemical crosslinkers (mostly reactive) for gelatin blends arises from the presence of some unreacted crosslinkers inside the blended matrix and develop the risk of formation of toxic products during in vivo biodegradation. So, blending with other bio-acceptable polymers like chitosan and polyvinyl alcohol can be introduced to solve the problem. Radiation induced crosslinking is also a potential candidate [9].

On the other hand, chitosan, the deacetylated derivative of chitin, has been extensively used in pharmaceutical formulations, drug delivery systems, protein recognition and separation, tissue engineering, transplant and cell regeneration, due to its excellent properties, biocompatibility and biodegradability [10]. Although lots of researches have been conducted to fabricate chitosan-based scaffolds for regenerative medicine, but its solubility in slight acidic condition sometimes limits its clinical translatability [11]. A number of researches have been conducted to solubilize it in neutral rather than acidic conditions by various chemical modifications [12,13]. Parvez et al. reported the potentiality of gelatin/chitosan blend for advanced dressing material. Blending gelatin with chitosan is also considered as a smart way to diminish the acidic effect of chitosan solution [14].

Polyvinyl Alcohol (PVA) was first synthesized by Hermann and Haehnel in 1924 by partially hydrolysing polyvinyl acetate [15]. It is a low cost synthetic polymer which shows very good film forming ability. It can be physically or chemically crosslinked to form hydrogels. Besides, it is hydrophilic in nature and has chemical stability [16]. PVA has pendant hydroxyl groups, which act as binding sites for biological molecules. PVA is elastic in nature [15] and so it can induce flexibility in a composite film. PVA has mainly been used in order to increase the mechanical property and stability of the polymeric membrane as well as to make the composite membrane non adhesive to additional support i.e. gauge dressing for proper wound care and ease of redressing.

In this research we have developed a biocompatible bilayer membrane that controls water vapor loss and provides a flexible adherent covering for the wound. The developed gelatin-chitosan biodegradable matrix provides a scaffold for cellular invasion and capillary growth while the PVA outer coating provides extra strength and flexibility as well as makes the redressing more comfortable for its non-adhesive property.

2. Materials and method

2.1. Materials

Gelatin from bovine bone having bloom strength of 240 was purchased from Merck Germany. Chitosan from prawn shell having >85% degree of deacetylation was purchased from Sigma-Aldrich, USA. All other reagents that were used were reagent grade.

2.2. Methods

2.2.1. Preparation of bi-layer film

Gelatin (10% w/v) was first dissolved in warm distilled water and crosslinked by 20% (w/v) polyethylene glycol (PEG) as suggested by Zaman et al. [17]. Chitosan (2% w/v) was dissolved in 2% (v/v) acetic acid and mixed with the crosslinked gelatin solution at 70:30 (v/v) ratio which was optimized by Parvez et al. [14]. The resulting polymer blend was casted on a preformed PVA layers and was kept for air drying at 40 °C and 40% relative humidity. Samples were dislodged carefully after drying and subjected to various characterizations.

2.2.2. Optimization of PVA layer

PVA layer was also formed by solution casting. PVA layers of different concentrations were prepared and were optimized based on the mechanical properties of resulting bi-layer composite film.

2.2.3. Characterization

2.2.3.1. Mechanical property analysis. Tensile strength (TS) and percent elongation at break (Eb) of the films were measured with Universal Testing Machine, Model: HOUNSFIELD H50 KS (UK). The load capacity was 500 N, with efficiency within ±1%. The crosshead speed was 10 mm/min. Gauze length was 40 mm. The mechanical test of the films was performed at 45% relative humidity and at room temperature to enable identical moisture content. Sample films were cut maintaining 100 mm length and 10 mm width to make ready for measurement and as well as average thickness of each sample was calculated taking measurement at least in three position.

$$\text{Tensile strength (TS)} = \frac{\text{Load}}{\text{Thickness(mm)} \times \text{With(mm)}}\ \text{MPa}$$

$$\text{Elongation at break (Eb)} = \frac{\text{Displacement at break}}{\text{Gauze length}} \times 100\%$$

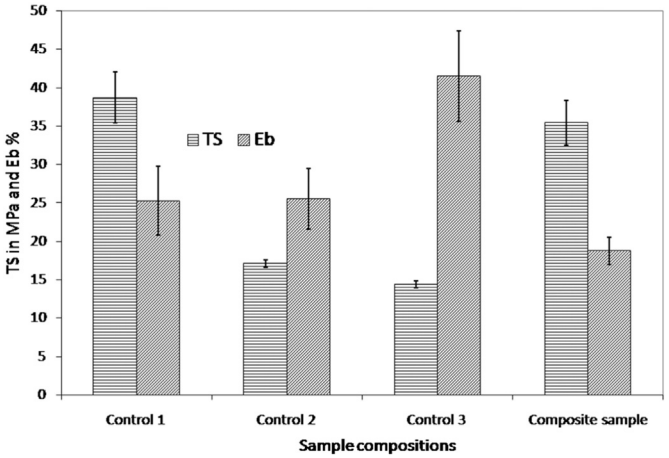

Fig. 2. Comparison of TS and Eb of the developed sample with the base materials.