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Regenerated cellulose micro-nano fiber matrices for transdermal drug release

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ABSTRACT

In this work, biobased fibrous membranes with micro- and nano-fibers are fabricated for use as drug delivery carries because of their biocompatibility, eco-friendly approach, and potential for scale-up. The cellulose micro-/nano-fiber (CMF) matrices were prepared by electrospinning of pulp in an ionic liquid, 1-butyl-3-methylimidazolium chloride. A model drug, ibuprofen (IBU), was loaded on the CMF matrices by a simple immersing method. The amount of IBU loading was about 6% based on the weight of cellulose membrane. The IBU-loaded CMF matrices were characterized by Fourier-transform infrared spectroscopy, thermal gravimetric analysis, and scanning electron microscopy. The test of ibuprofen release was carried out in an acetate buffer solution of pH 5.5 and examined by UV–Vis spectroscopy. Release profiles from the CMF matrices indicated that the drug release rate could be determined by a Fickian diffusion mechanism.

1. Introduction

Electrospinning is one of the simplest and fastest methods to produce fiber nonwovens in both microscale and nanoscale. Electrospun nonwoven web architecture has remarkable characteristics such as high surface area-to-volume ratios, high interconnected porosities with tunable pore sizes, possibilities for efficient surface functionalization, adjustable surface morphologies, and structural similarities to extracellular matrix [1]. The nonwoven mats formed by electrospun fibers are suitably used as biomedical materials, such as drug delivery carriers, wound dressing, scaffolds for tissue engineering, due to their cost-effectiveness, flexibility, and potential to scale up [2,3]. Among the various potential applications, drug delivery is one of the most popular uses [4]. Electrospun nonwoven mats can be used in a variety of drugs ranging from antibiotics to anticancer agents [5].

In order to load drug on electrospun mats, several techniques were employed, including post-spinning modifications, electrospinning of drug/polymer blenders, emulsion electrospinning, and core-shell electrospinning [6]. Among these methods, post-spinning modification is a straightforward approach for drug-loaded nonwoven matrices. The simplest mechanism for drug loading is drug absorption to an electrospun matrix after an electrospinning of polymer [1,4].

Many natural and synthetic polymers have been used in electrospinning. With a rising awareness of sustainable and renewable materials, much attention has been drawn to applications of natural polymers [7]. As the oldest type of natural polymers extracted from a variety of natural resources (e.g. plants, bacterial, and fungus) [8], cellulose is the most abundant natural polymer on earth, with a bio-production rate estimated to be over 7.5×10^{10} metric tons annually [9,10]. Among cellulose materials, regenerated cellulose nanofibers and microfibers are a type of engineered material with a great application potential from drug delivery, wound dressings, biosensors, to scaffolds for tissue engineering, because of their biodegradability, biocompatibility, low toxicity, excellent mechanical properties and low cost [11–16].

However, non-derivative cellulose is difficult to electrospin because it cannot be dissolved either in water or common organic solvents due to its high crystallinity [17]. Rogers and his group carried out studies on cellulose dissolution in ionic liquids [18,19]. Natural cellulose without derivation can be dissolved in some hydrophilic ionic liquids such as 1-butyl-3-methylimidazolium chloride ([BMIM]Cl) [20,21]. With this approach, electrospinning natural cellulose became possible.

A variety of electrospun matrices prepared from synthetic polymers and derivative cellulose, such as polyvinylpyrrolidone [22], polyvinyl alcohol [4], cellulose acetate [23], and ethyl cellulose [24], are used as drug carriers. Although most of these polymers are biodegradable, they are treated chemically and do not have a low-carbon footprint or low-cost compared to natural cellulose. Little work has been done on electrospun pure natural cellulose matrices as a drug carrier. In the present work,

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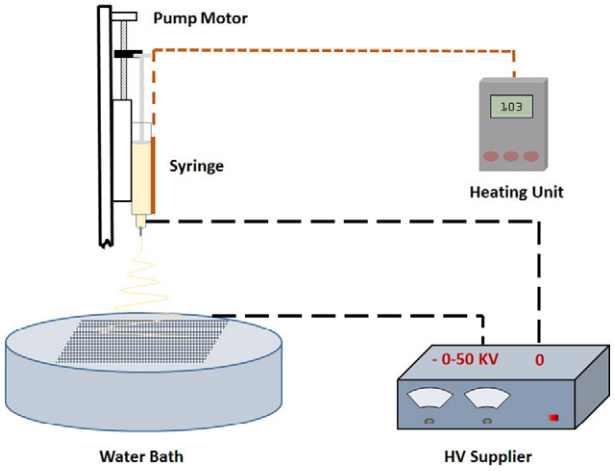

Fig. 1. Schematic diagram of the dry-wet electrospinning device.

cellulose micro-nano fiber (CMF) matrices were fabricated by dry-wet electrospinning. Ibuprofen (IBU) was used as a model drug loaded on the CMF matrices using a simple immersing method. After fabrication, CMF and IBU-loaded CMF (IBU@CMF) matrices were characterized by electron scanning microscopy (SEM), Fourier transform infrared spectroscopy (FT-IR), and thermogravimetric analysis (TGA). Tribological properties, water contact angle and wettability of CMF and IBU@CMF matrices were also studied. The drug release characteristics from IBU@CMF matrices were examined via an in vitro drug releasing study.

2. Materials and methods

2.1. Materials

Raw pulp is a commercial grade south pine kraft pulp with 87% alpha cellulose. [BMIM]Cl with purity > 95% was purchased from Sigma-Aldrich, Inc. Ibuprofen was purchased from Cayman Chemical Co. Other chemicals, ethyl alcohol, acetic acid and sodium acetate were purchased from Thermo Fisher Scientific Inc.

2.2. Formation of cellulose microfibers matrices

Solid [BMIM]Cl was heated to 80 °C in a water bath until melted. The pulp cellulose was ground and added into the melted [BMIM]Cl. Complete cellulose dissolution in [BMIM]Cl, yielding a transparent solution,

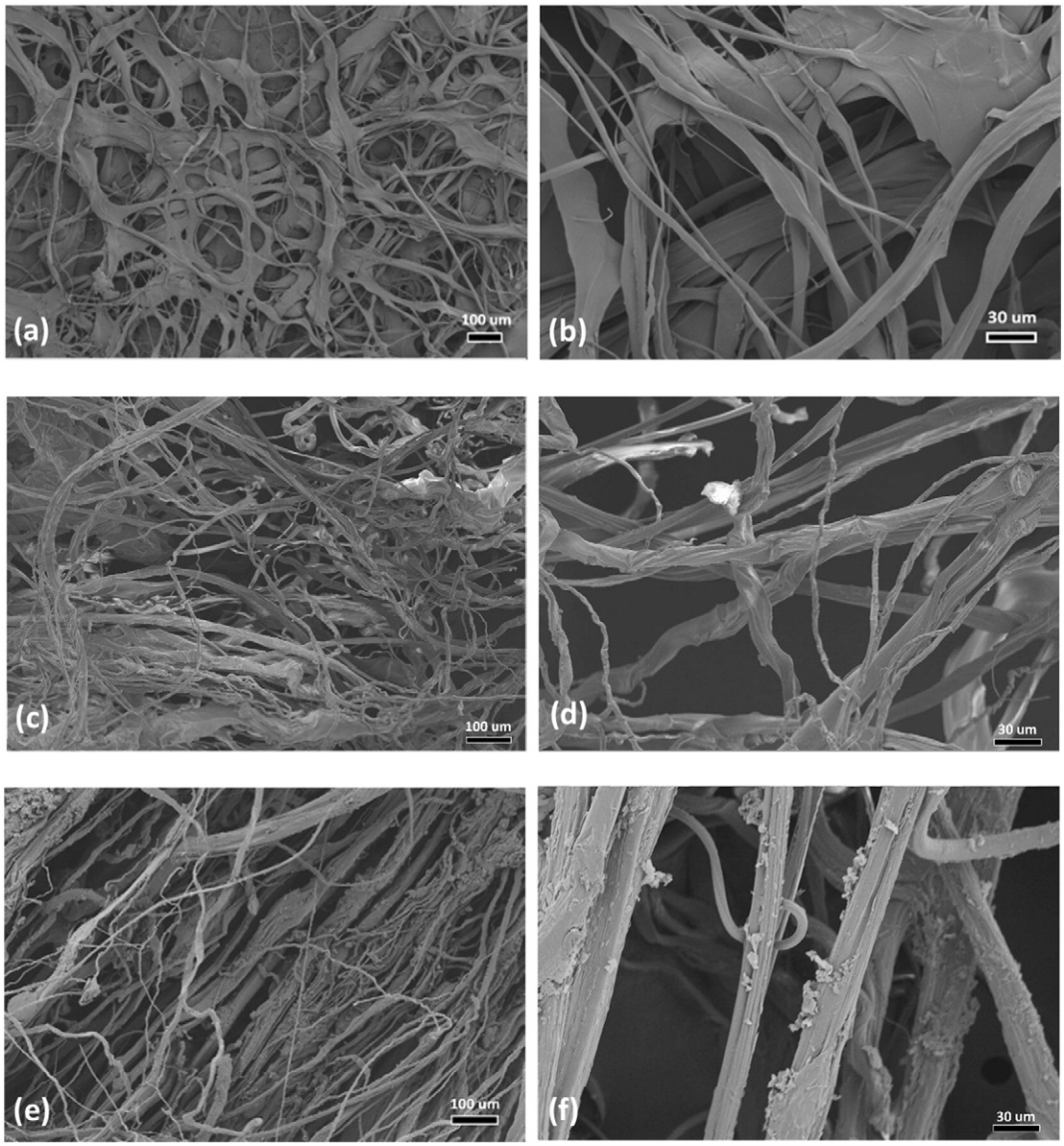

Fig. 2. SEM images of 2% CMF (a and b), 3% CMF (c and d) and IBU@3% CMF matrices (e and f).