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Solution blow spun poly(lactic acid)/hydroxypropyl methylcellulose nanofibers with antimicrobial properties

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ABSTRACT

Poly(lactic acid) (PLA) nanofibers containing hydroxypropyl methylcellulose (HPMC) and tetracycline hydrochloride (THC) were solution blow spun from two different solvents, chloroform/acetone (CA, 80:20 v/v) and 2,2,2-triflouroethanol (TFE). The diameter distribution, chemical, thermal, thermal stability, water sorption, and antimicrobial properties were examined for the fibers. Fibers spun from CA generally had larger fiber diameters and wider fiber diameter distributions than those spun from TFE. Fourier transform infrared (FTIR) spectroscopy results indicated successful incorporation of HPMC and THC into the fibers. Also, phase separation occurred between PLA and HPMC in the fibers. Fibers containing higher HPMC concentrations showed greater water sorption values, due to HPMC being more hydrophilic than PLA. In addition, fibers containing HPMC had larger inhibitory zones against *Escherichia Coli* and *Listeria monocytogenes* than those without HPMC. This was due to THC having better miscibility with HPMC than PLA and HPMC being able to swell and release more THC when in contact with water. Fibers spun from TFE and CA had comparable inhibitory zones, indicating the solvents did not affect antimicrobial properties. All fibers remained effective against bacteria even after six days.

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1. Introduction

Solution blow spinning is a newly developed and alternate technique to electrospinning for producing nano- and microfibers. It offers some advantages over electrospinning, including the elimination of high voltage use, an increase in fiber production rate, and a wider range of materials that can be used as collectors. The blow spinning apparatus consists of concentric nozzles, with the polymer solution pumped into the inner one and high pressure gas injected into the outer one [1]. The high pressure gas then serves as the driving force to stretch the polymer solution into thin strands. The solvent evaporates from the solution and dry fibers are deposited onto a collector.

Solution blow spinning had been used to produce fibers from different synthetic and natural polymers. This includes poly(methyl methacrylate) [1], polystyrene [1], PLA [1–5], PLA/pollock gelatin blend [5], poly(D,L-lactide) [6], polyaniline/PLA blend [1], poly(vinyl pyrrolidone) [7], polyacrylonitrile [8], soy protein isolate/nylon-6 blend [9], cellulose [10], poly(ethylene oxide) (PEO) [2,3,11], PEO/PLA blend [4], and poly(ε-caprolactone) [3]. Core–shell fibers using solution blow spinning had also been produced, with cellulose core and PEO shell [10] as well as soy protein isolate/nylon-6 core and nylon-6 shell [9]. However, only a couple of studies had examined solution blown fibers for controlled-release applications. Oliveira et al. [2] incorporated progesterone into PLA nanofibers

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for controlled delivery to livestock. Martinez-Sanz et al. [5] incorporated an essential oil, carvacrol, as well as an antibiotic, tetracycline hydrochloride, into PLA and PLA/pollock gelatin blend nanofibers and examined their antimicrobial properties. The authors found that blending pollock gelatin with PLA greatly improved the antimicrobial properties of the nanofibers against *Listeria monocytogenes*.

PLA nanofibers had been examined as a matrix for controlled-release applications due to PLA's biological compatability and biodegradability. However, PLA is hydrophobic and does not encapsulate hydrophilic drugs well. In fact, previous studies had shown that hydrophilic drugs, such as tetracycline hydrochloride [12] and doxorubicin hydrochloride [13,14], remained on the surface of electrospun PLA fibers. This resulted in an initial burst release of the drug and little release afterwards. Different strategies had been used to improve control-release of hydrophilic drugs from PLA-based fibers. This included blending PLA with more hydrophilic polymers that could encapsulate the drugs to a greater extent [5,15,16] and using co-axial electrospinning with drug core and PLA shell [12].

HPMC is a hydrophilic polymer that is widely used in the pharmaceutical industry to encapsulate and control-release drugs [17]. When the HPMC matrix comes into contact with water or biological fluids, it swells and allows the fluid to diffuse into it. The drugs can then diffuse out of the matrix. However, there had been few studies on producing HPMC nanofibers [18–20]. Only a couple of studies had examined using HPMC-based fibers for controlled-release applications. Verreck et al. [18] incorporated water insoluble itraconazole into HPMC fibers and characterized their release in an HCl solution. Uslu et al. [20] electrospun HPMC/poly(vinyl alcohol)/poly(vinyl pyrrolidone) iodine/PEO fibers and incorporated aloe vera as a wound healing agent.

In this study, we use solution blow spinning to produce PLA and PLA/HPMC nanofibers containing THC using two solvents, chloroform/acetone and TFE. We use scanning electron microscopy (SEM) to characterize the fiber diameter distributions. We also use FTIR spectroscopy, differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and dynamic vapor sorption (DVS) to examine the chemical, thermal, thermal stability, and water sorption properties of the nanofibers, respectively. In addition, we use overlay diffusion tests to determine the antimicrobial properties of solution blow spun fibers against *Escherichia Coli* and *L. monocytogenes*.

2. Materials and methods

2.1. Sample preparation

All blow spinning solutions contained 10% (w/w) solids. Two solvents were used to prepare the solutions, 80% (v/v) chloroform/20% (v/v) acetone (CA) and 2,2,2-trifluoroethanol (TFE). Chloroform and acetone were obtained from Fisher Scientific (Philadelphia, PA) and TFE was obtained from Sigma–Aldrich (St. Louis, MO). For each solvent, a neat PLA (Polylactide Resin 4042D, Natureworks LLC, Minnetonka, MN) sample was prepared by adding PLA to the solvent and then stirring overnight at room temperature (23 °C). For CA samples, the HPMC (Methocel E15, Dow Chemical, Midland, MI) concentrations in HPMC/PLA blends were 0, 20, 40, and 50 wt% with respect to PLA and HPMC. For TFE samples, the HPMC concentrations in HPMC/PLA blends were 0 and 20 wt% HPMC with respect to PLA and HPMC. Tetracycline hydrochloride (Sigma –Aldrich, St. Louis, MO) was added to the HPMC samples at a concentration of 20 wt% with respect to total solids.

Each sample is named according to wt% PLA (relative to PLA and HPMC)-wt% HPMC (relative to PLA and HPMC)-THC content-solvent. For instance, the fiber sample containing 80 wt% PLA, 20 wt% HPMC, and THC spun from chloroform/acetone is termed 80PLA–20HPMC–THC–CA.

2.2. Solution blow spinning

The solution blow spinning system consisted of a source of compressed air, a 10 mL Becton–Dickinson (Franklin Lakes, NJ) syringe placed in a KD Scientific (Holliston, MA) 780101 model syringe pump, a spinning apparatus of concentric nozzles, and a rotating drum collector [1]. The syringe pump was set to 15.0 μL/min with the solution from the syringe entering the inner nozzle of the spinning apparatus. The air pressure of the compressed air was set to 80 psi with the air entering the outer nozzle. The rotating steel drum collector was covered with aluminum foil and was attached to an IKA Labortechnik (Wilmington, NC) RW20 motor set to a rotation speed of 600 rpm. The distance between the nozzle tip and the drum was set at 20 cm.

2.3. Scanning electron microscopy

A Hitachi (Pleasanton, CA) S-4700 SEM was used to observe the samples. The voltage was set to 2.0 kV or 4 kV and the current was set to 10 μA. A Denton (Moorestown, NJ) Desk II Sputter Coater was used to apply a gold/palladium coating to blow spun samples that were affixed to stubs. The samples were sputter coated for 45 s with the discharge current set at 20–30 mA. The vacuum chamber was lowered to a pressure of less than 100 mTorr. Media Cybernetics (Bethesda, MD) Image Pro 6.3 software was used to characterize the fiber diameters from SEM images.

2.4. Fourier transform infrared spectroscopy

A Perkin Elmer (Waltham, MA) 2000 FTIR Spectrometer was used to characterize chemical changes of blow spun samples. The samples were placed in a DuraSamplIR attenuated total reflectance attachment (ASI SensIR Technology, Danbury, CT). Each IR spectrum contained an average of 50 scans over a 10 min period with a resolution of 4 cm^{-1}.

2.5. Differential scanning calorimetry

A Perkin Elmer (Waltham, MA) 8000 DSC was used to characterize the thermal properties of the blow spun samples. The samples were conditioned in a 50% relative humidity chamber at 23 °C for at least 48 h prior to each test. The chamber was maintained at these conditions by using a saturated solution of calcium nitrate tetrahydrate (Fisher Scientific, Philadelphia, PA), $Ca(NO_3)_2{\cdot}4H_2O$, in