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Research Paper

Designing highly structured polycaprolactone fibers using microfluidics

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ARTICLE INFO

Article history:
Received 29 October 2015
Received in revised form
2 April 2016
Accepted 5 April 2016
Available online 20 April 2016

Keywords:
Polymer microfibers
Microfluidic approach
Hydrodynamic focusing
Polycaprolactone

ABSTRACT

Microfibers are becoming increasingly important for biomedical applications such as regenerative medicine and tissue engineering. We have used a microfluidic approach to create polycaprolactone (PCL) microfibers in a controlled manner. Through the variations of the sheath fluid flow rate and PCL concentration in the core solution, the morphology of the microfibers and their cross-sections can be tuned. The microfibers were made using PCL concentrations of 2%, 5%, and 8% in the core fluid with a wide range of sheath-to-core flow rate ratios from 120:5 μL/min to 10:5 μL/min, respectively. The results revealed that the mechanical properties of the PCL microfibers made using microfluidic approach were significantly improved compared to the PCL microfibers made by other fiber fabrication methods. Additionally, it was demonstrated that by decreasing the flow rate ratio and increasing the PCL concentration, the size of the microfiber could be increased. Varying the sheath-to-core flow rate ratios from 40:5 to 10:5, the tensile stress at break, the tensile strain at break, and the Young's modulus were enhanced from 24.51 MPa to 77.07 MPa, 567% to 1420%, and 247.25 MPa to 539.70 MPa, respectively. The porosity and roughness of microfiber decreased when the PCL concentration increased from 2% to 8%, whereas changing the flow rate ratio did not have considerable impact on the microfiber roughness.

1. Introduction

Fiber systems are becoming increasingly important for numerous biological applications, such as tissue engineering, as the fibers are able to guide cell growth, alignment, and migration (Chung et al., 2012; Hwang et al., 2008a). Additionally, the design of microfibers gives them the correct properties in order to perform drug delivery and drug release in the human body for medical purposes (Caplin et al., 2015; Tiwari et al., 2010). The fibers have high surface area-to-volume and strength-to-weight ratios. Some of them are permeable and can be woven into textiles (Boyd et al., 2013b). These properties allow microfibers to carry even delicate materials, such as water-soluble drugs, throughout

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http://dx.doi.org/10.1016/j.jmbbm.2016.04.005
1751-6161/

a biological medium with good accuracy (Kraitzer et al., 2008; Saraf et al., 2010). This makes for safe insertion and transmittance of material used for treatment, demonstrating the effectiveness of microfibers in medicine. The method of generation of the microfibers plays a role in determining its viability in these types of applications.

Several approaches exist for the fabrication of microfibers from naturally derived or synthetic materials such as electrospinning, wetspinning, biospining, meltspinning, and the microfluidic techniques (Tamayol et al., 2013). Electrospinning is relatively a simple method and it is feasible to efficiently scale-up and control the involved parameters such as flow rate and voltage. However, there are some difficulties in the fabrication of thick, complex 3D scaffolds with this method (Deng et al., 2012; Hwang et al., 2008a). Additionally, electrospun microfibers are generally not easy to align and it requires extra care to ensure that the fibers are accurately aligned, especially because the randomly aligned fibers are not desirable for applications like growing nerve cells (Jung et al., 2009). Wetspinning is an efficient method for fabricating fibers with a wide range of diameters by changing the needle(s) diameter. Nevertheless, long exposure to chemicals during the fabrication process is required, which can be harmful to cells (Enea et al., 2011). Biospinning method is the process of fabricating silk fibers by insects. Silk has high tensile strength and is biodegradable. In addition, after chemical processing, it is non-cytotoxic and non-inflammatory. The major challenges of using biospun fibers are the limitation of resources, which makes it difficult for the scale-up process, as well as the fact that the process of silk fiber fabrication is time consuming (Reddy and Yang, 2010). In the meltspinning approach, various synthetic polymers can be used for fiber fabrication with this method. Fibers created by meltspinning have high mechanical properties. However, the meltspinning process is in a high temperature range (150–300 °C) and requires using expensive equipment. Using high temperatures during the fiber fabrication process prevents the cell or protein from being loaded onto the fiber in order to deliver the bioactive molecules in biomedical applications (Ella et al., 2011). Additionally, because the viscosity of the melted polymer is relatively high, a high pressure difference is needed to move the melted polymer through the spinneret (Akbari et al., 2011; Yim et al., 2006).

Using microfluidics to fabricate fiber is a relatively new approach in which the fiber is created in a microchannel using coaxial flow of core (pre-polymer) and sheath fluids. The key benefits of using this method include versatility of size, continuity of the fiber fabrication process, and simplicity of cell, protein or drug incorporation. This process is straightforward, cost-efficient, reproducible, and suitable for many biological applications since the fiber is created without using high temperature, high pressure, high voltages, or toxic materials. By changing the flow rate and flow rate ratio, the fiber size and aspect ratio can be simply controlled (Bai et al., 2014; Daniele et al., 2013; Goodrich et al., 2015; Hwang et al., 2008a). The microfluidic fiber fabrication can be employed to create fibers with various materials using different cross-linking mechanisms such as photopolymerization (e.g., polyethyleneglycol diacrylate, 4-hydroxybutyl acrylate) (Daniele et al., 2014a, 2014b; Jeong et al., 2004; Oh et al., 2006), ionic gelation (e.g., alginate) (Shin et al., 2007), and thermal phase transition (e.g., agar) (Khademhosseini et al., 2006; Vunjak-Novakovic et al., 2004). However, there are some studies which employ phase inversion process instead of cross linking method to solidify the polymer (Bai et al., 2014; Hwang et al., 2008a). Hwang et al. (2008a) used the solution of poly(lactic-co-glycolic acid) (PLGA) in dimethyl sulfoxide (DMSO) and mixture of glycerin and distilled water as the core and sheath fluids, respectively. At the fluid–fluid interface in the channel, the DMSO in the core fluid is replaced by water in the sheath fluid and the polymer is solidified. Likewise, Bai et al. (2014) dissolved gelatin in DMSO and showed that by exchanging the DMSO in the core fluid and ethanol in the sheath fluid, the gelatin can be solidified.

This approach makes it feasible to fabricate fibers with different shapes of solid (Bai et al., 2014; Daniele et al., 2013; Hasani-Sadrabadi et al., 2013), tubular (Choi et al., 2011; Kang et al., 2011), hybrid (Jung et al., 2009), and flat (Boyd et al., 2013a; Cho et al., 2012) dimensions for divergent applications such as cell encapsulation, alignment, and immobilization. There are different physical and chemical methods for solidification of fibers including diffusion-limited solidification by solvent extraction, diffusion-limited solidification by chemical cross-linking, and photo polymerization (Bai et al., 2014; Choi et al., 2011; Daniele et al., 2015; Yoo et al., 2015, 2012). The fibers fabricated by photopolymerization are not easily degraded and metabolized in biomedical applications. In addition, ultraviolet radiation (UV) has damaging effects on bioactive species (Jun et al., 2014). It was demonstrated by Hwang et al. (2008b) that the concentration of photo-initiator has adverse impacts on the cell viability. The negative aspects of UV-light can be minimized by decreasing the exposure time and using less-harmful wavelengths than the standard one (Panda et al., 2008). Due to these limitations, photopolymerization is not the most desired approach for fabrication of fibers in cell encapsulation applications.

Although some thermoplastic polymers have been used in microfluidic fiber fabrication such as PLGA (Hwang et al., 2008a) and poly(methyl methacrylate) (PMMA) (Thangawng et al., 2009), there is no report on microfluidic fabrication of PCL fibers. PCL is a Food and Drug Administration (FDA) approved polymer which is widely used as a biomaterial due to its biocompatibility and biodegradability (Acar et al., 2014; Li et al., 2014; Soliman et al., 2010). Due to slower degradation rate of this polymer, for instance compared to PLGA, it possesses no adverse impacts on cell viability and migration because it does not change the PH of the environment during the degradation sharply (Sung et al., 2004). This polymer also has good mechanical properties, is not toxic, and its rate of degradation can be controlled. Furthermore, PCL does not trigger immune responses in the body (Hong and Kim, 2013).

In this paper, we have employed solvent extraction to fabricate biocompatible and biodegradable PCL microfibers in a microfluidic platform for the first time. PCL grants us the advantage of having a biocompatible and strong material from which to make fibers. Using microfluidics, we are able to avoid the constraints of other methods such as electrospinning (Hwang et al., 2008a). We can produce fibers with different cross-sectional shapes while the fabrication is continuous and stops only when the core and sheath solutions stop flowing. By fabricating PCL using a microfluidic microchannel, we are