Multifunctional polymeric microfibers with prolonged drug delivery and structural support capabilities

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A B S T R A C T

The strength and stability of hybrid fiber delivery systems, ones that perform a mechanical function and simultaneously deliver drug, are critical in the design of surgically implantable constructs. We report the fabrication of drug-eluting microfibers where drug loading and processing conditions alone increase microfiber strength and stability partially due to solvent-induced crystallization. Poly(l-lactic acid) microfibers of 64 ± 7 μm diameter were wet spun by phase inversion. Encapsulation of a model hydrophobic anti-inflammatory drug, dexamethasone, at high loading provided stability to microfibers which maintained linear cumulative release kinetics up to 8 weeks in vitro. In our wet spinning process, all microfibers had increased crystallinity (13–17%) in comparison to unprocessed polymer without any mechanical stretching. Moreover, microfibers with the highest drug loading retained 97% of initial tensile strength and were statistically stronger than all other microfiber formulations, including control fibers without drug. Results indicate that the encapsulation of small hydrophobic molecules (<400 Da) may increase the mechanical integrity of microfibers whose crystallinity is also increased as a result of the process. Multifunctional drug-eluting microfibers can provide an exciting new opportunity to design novel biomaterials with mechanical stability and controlled release of a variety of therapeutics with micron-scale accuracy.

1. Introduction

Polymeric fibers have many medical uses, such as surgical sutures, dialysis devices, wound dressings and tissue engineering scaffolds. Advances in polymer and drug delivery sciences have led to the evolution of engineered fibers for use as drug delivery vehicles. Over the past decade, research towards the design of therapeutically active fibers has increased [1–6]. While there are many techniques to make polymeric fibers, only a small subset of these methods is suitable for drug encapsulation. Wet spinning is one such technique that lends itself to drug delivery technologies since it can be done at ambient temperatures and is most similar to conventional microsphere-based encapsulation techniques. Wet spinning also produces micron-sized fibers that have the potential to be woven, knitted, braided or embroidered into macro-level scaffold superstructures for the clinical reconstruction of damaged tissues/organs.

Wet spun microfiber delivery systems have been achieved by impregnating therapeutics into the core of hollow microfibers, entrapping therapeutics within microfibers, and chemically crosslinking or adsorbing therapeutics to the surfaces of microfibers. A broad range of biologically active therapeutics including antibiotics [7–9], heparin [10], proteins [6,11–14], growth factors [4,15], genes [16,17] and even viruses [18,19] have been incorporated into wet-spun microfibers. Recent efforts have focused on the biocompatibility and biological activity of therapeutics delivered from wet-spun microfibers. However, the effect of drug incorporation on the mechanical integrity of wet-spun microfibers is not well understood [9,20–22]. The mechanical properties of engineered microfibers for drug delivery and tissue engineering applications are important to their functionality in vivo. For clinical applications, therapeutic fibrous drug delivery implants must retain structural integrity during surgical implantation, and provide mechanical and pharmaceutical support in vivo throughout the process of tissue integration and implant degradation, which can occur over several months up to a year. Mechanical cues are also important for the organization, growth and maturation of reconstructed tissues. Even small changes in the mechanical properties of the local microenvironment have been shown to influence cell behaviors by altering cell–cell and cell–matrix interactions [23].

In this study, we examined the dynamic mechanical properties of drug-eluting wet-spun microfibers. Dexamethasone (DXM), a potent anti-inflammatory drug, served as the model therapeutic...