Acta Biomaterialia 7 (2011) 3277–3284

Contents lists available at ScienceDirect

Acta Biomaterialia

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

# Melt electrospinning of biodegradable polyurethane scaffolds

Ari Karchin [a], Felix I. Simonovsky [a], Buddy D. Ratner [a,b], Joan E. Sanders [a,*]

[a] Department of Bioengineering, Box 355061, University of Washington, Seattle, WA 98195, USA
[b] Department of Chemical Engineering, Box 351750, University of Washington, Seattle, WA 98195, USA

ARTICLE INFO

*Article history:*
Received 28 February 2011
Received in revised form 26 April 2011
Accepted 16 May 2011
Available online 20 May 2011

*Keywords:*
Aliphatic polyurethanes
Biodegradable polymer
Melt electrospinning
Tissue engineering
Scaffolds

ABSTRACT

Electrospinning from a melt, in contrast to from a solution, is an attractive tissue engineering scaffold manufacturing process as it allows for the formation of small diameter fibers while eliminating potentially cytotoxic solvents. Despite this, there is a dearth of literature on scaffold formation via melt electrospinning. This is likely due to the technical challenges related to the need for a well-controlled high-temperature setup and the difficulty in developing an appropriate polymer. In this paper, a biodegradable and thermally stable polyurethane (PU) is described specifically for use in melt electrospinning. Polymer formulations of aliphatic PUs based on $(CH_2)_4$-content diisocyanates, polycaprolactone (PCL), 1,4-butanediamine and 1,4-butanediol (BD) were evaluated for utility in the melt electrospinning process. The final polymer formulation, a catalyst-purified PU based on 1,4-butane diisocyanate, PCL and BD in a 4/1/3 M ratio with a weight-average molecular weight of about 40 kDa, yielded a nontoxic polymer that could be readily electrospun from the melt. Scaffolds electrospun from this polymer contained point bonds between fibers and mechanical properties analogous to many in vivo soft tissues.



## 1. Introduction

A number of polymers have been used in melt electrospinning. However, the use of polyurethanes (PUs) in melt-electrospun scaffolds is not well represented in the literature despite the attractive properties of this class of polymers [1]. The seminal melt electrospinning work of Larrondo and Manley [2–4] focused on polyethylene and polypropylene. Other polymers that have been melt-electrospun include polyester [5], poly(lactic acid) [6], poly(ethylene glycol) [7], and a blend of poly(ethylene oxide-block-caprolactone) with polycaprolactone (PCL) [8]. PUs contain properties that are superior to many commonly used polymers for tissue engineering scaffolds [9]. They can be designed such that the finished material is thermally stable, degradable, nontoxic and with tunable mechanical properties [10–12]. A subclass of PUs, segmented linear elastomeric biodegradable urethane block copolymers consisting of alternating backbone hard and soft segments, are attractive for tissue engineering, primarily due to their molecular design flexibility, which provides a broad range of properties, including biodegradability. Most commercially available linear PU block copolymers are based on aromatic diisocyanates such as 4,4′-diphenylmethane diisocyanate and toluene diisocyanate [11]. Although several medical devices composed of PU elastomers containing aromatic cycles in their hard segments have been approved by the regulatory authorities in past years for medical applications, these are not biodegradable formulations and the products of decomposition (if, indeed, decomposition occurs) may be toxic [13,14]. Some groups have worked to develop less toxic degradable aliphatic diisocyanate-based PUs [15–17]; however, such a polymer has yet to be melt electrospun.

The goal of the current work was to develop a novel degradable and biocompatible aliphatic PU that could be formed into scaffolds via melt electrospinning. The PU formulations investigated in this study were based on various combinations of PCL diol, with a number-average molecular weight (MW) of about 1250 Da, 2,6-diisocyanato methyl caproate (lysine diisocyanate, LDI), 1,4-butanediisocyanate (BDI), 1,4-butanediamine (BDA) (putrescine) and 1,4-butanediol (BD). PU copolymers based on $(CH_2)_4$-content diisocyanates, such as LDI and BDI, are expected to be nontoxic since the product of hydrolytic degradation, BDA, is nontoxic [18]. Similarly, the use of PCL as the soft segment is common due to its biocompatibility and biodegradability [10]. The polymer composition and weight-average MW ($M_w$) were optimized for melt electrospinning. The final polymer was evaluated for cytotoxicity, and the mechanical properties of electrospun scaffolds were determined.

## 2. Materials and methods

### 2.1. Polymer synthesis

All chemicals were purchased from Aldrich Chemical Company, Inc. (Milwaukee, WI), unless otherwise noted. The synthesized

* Corresponding author. Tel.: +1 206 221 5872; fax: +1 206 616 2509.
*E-mail addresses:* jsanders@uw.edu, jsanders@u.washington.edu (J.E. Sanders).

1742-7061/$ - see front matter © 2011 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.actbio.2011.05.017

polymers were made via the standard procedure of multi-step addition polymerization in N,N-dimethylacetamide (DMAc) solvent, described elsewhere [22,23]. This general method allows PUs with a variety of compositions to be synthesized with precision and reproducibility [19,20]. The polymerization pathway can be briefly described by three main steps:

- The reaction between PCL and a variable molar excess of isocyanate (NCO) groups of either LDI or BDI yields intermediates end-capped with isocyanate groups (prepolymers).
- Either BDA or BD with a variable molar excess of amino ($NH_2$) or hydroxyl (OH) groups was used as chain extenders to provide a polymerization with the isocyanate prepolymer in DMAc to create a low MW PU end-capped with either $NH_2$ or OH groups. A reaction between aliphatic NCO groups of the prepolymer and $NH_2$ groups of BDA was carried out at room temperature in DMAc. Dibutyltin dilaurate (DBTDL) served as the catalyst accelerating the reaction between aliphatic NCO groups of the prepolymer and OH groups of BD at approximately 80 °C in DMAc.
- The low MW PU was then combined with a monomeric diisocyanate in a gradual approach to stoichiometry [21,22] to yield a high MW polymer of specific $M_w$.

The simplified scheme of the urethane polymerization process based on PCL, BDI and BD is presented in Fig. 1.

### 2.2. Polymer purification

In order to remove methanol-soluble catalyst after the last synthesis step, the polymer was precipitated in an excess of methanol at room temperature. After filtration, remaining polymer was washed three more times in fresh methanol at room temperature (12 h washing steps). These steps were followed by two 12 h rinses in fresh, circulating deionized (DI) water to remove the methanol and DMAc. The polymer was finally dried under vacuum at approximately 60–65 °C for at least 12 h.

### 2.3. Electrospinning

Scaffolds were electrospun using a custom apparatus described previously [23]. Briefly, the apparatus consists of a melt chamber mounted on an enclosure that housed a collecting surface and electrode. The melt chamber was made up of a metal sleeve that terminated in a 0.5 mm diameter nozzle. A pair of band heaters were secured around the melt chamber to heat the as-received purified and dried polymer. A grounding rod was placed inside the polymer which terminated at the external surface of a custom-made poly(ether ether ketone) cap screwed onto the melt chamber. The positive electrode was mounted below the collection surface. The collection surface, an adhesive-backed copper strip affixed to a glass microscope slide, was mounted on a three-axis stage (404150XR, Parker Daedal, Harrison City, PA) that moved the collector in concentric circles beneath the electrospinning nozzle. A high-voltage power supply (RP-50-100, Del, Valhalla, NY) supplied a potential of 30 kV between the grounding rod and the positive electrode.

The distance between the positive and ground electrodes was set at 13 cm, and the melt temperature set at 220–240 °C for all runs. The reason a 30 kV voltage and a 13 cm electrode distance were used was that they provided an electric field of sufficient strength to form fibers into an electrospun mat on the collector. A lower electric field strength was not strong enough to overcome the surface tension of the polymer droplet [24], while a higher electric field strength increased the bending instability of the electrospun fiber. For a given applied voltage, a larger distance between electrodes did not result in the formation of a Taylor cone and subsequent fiber formation, while a shorter electrode distance caused the fiber to miss the target collector.

After electrospinning, samples were immediately transferred to a 60 mm Petri dish, sealed with Parafilm and placed in a desiccator

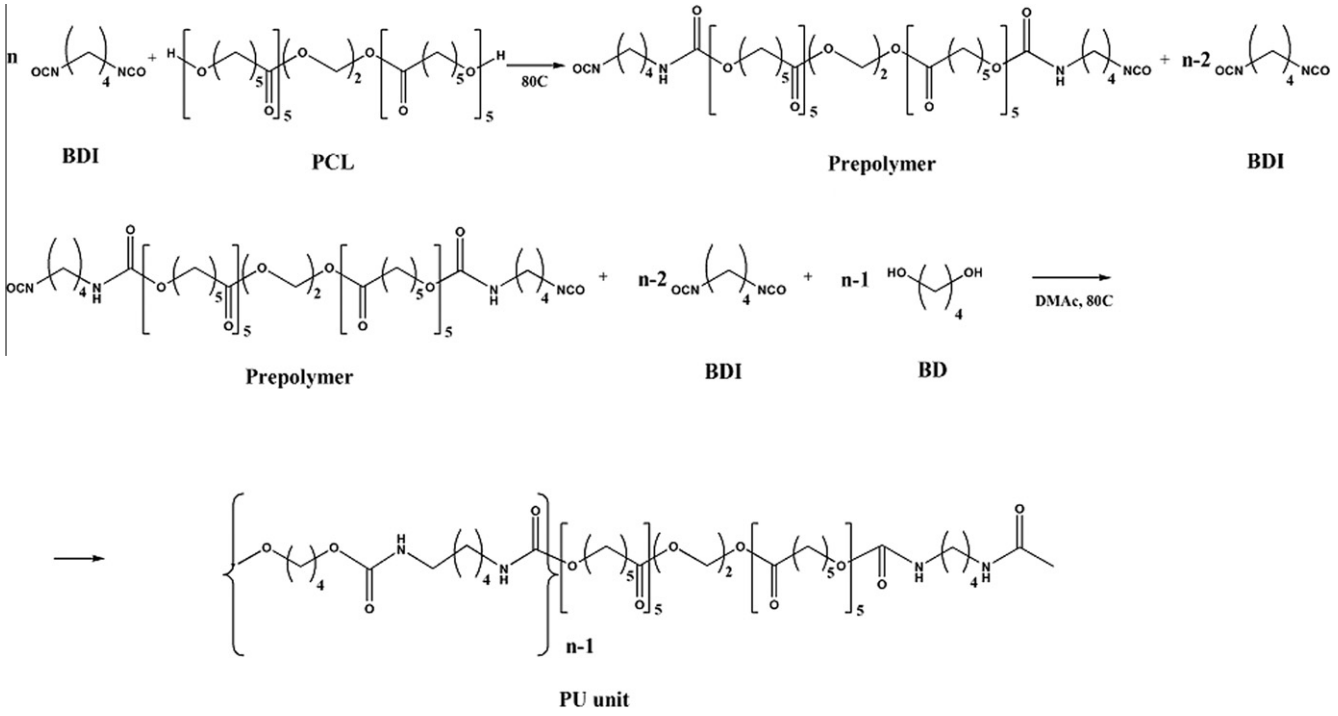


**Fig. 1.** Simplified synthesis scheme of a thermally stable polyurethane based on BDI, PCL and BD.