Journal of the mechanical behavior of biomedical materials 65 (2017) 657–664

Contents lists available at ScienceDirect

Journal of the Mechanical Behavior of Biomedical Materials

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

Systematic characterization of porosity and mass transport and mechanical properties of porous polyurethane scaffolds

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ABSTRACT

One of the key challenges in porous scaffold design is to create a porous structure with desired mechanical function and mass transport properties which support delivery of biofactors and development of function tissue substitute. In recent years, polyurethane (PU) has become one of the most popular biomaterials in various tissue engineering fields. However, there are no studies fully investigating the relations between porosity and both mass transport and mechanical properties of PU porous scaffolds. In this paper, we fabricated PU scaffolds by combining phase inversion and salt (sodium chloride) leaching methods. The tensile and compressive moduli were examined on PU scaffolds fabricated with different PU concentrations (25%, 20% and 15% w/v) and salt/PU weight ratios (9/1, 6/1, 3/1 and 0/1). The mass transport properties of PU scaffolds including hydraulic permeability and glucose diffusivity were also measured. Furthermore, the relationships between the porosity and mass transport and mechanical properties of porous PU scaffold were systemically investigated. The results demonstrated that porosity is a key parameter which governs both mass transport and mechanical properties of porous PU scaffolds. With similar pore sizes, the mass transport and mechanical properties of porous PU scaffold can be described as single functions of porosity regardless of initial PU concentration. The relationships between scaffold porosity and properties can be utilized to facilitate porous PU scaffold fabrication with specific mass transport and mechanical properties. The systematic approach established in this study can be applied to characterization of other biomaterials for scaffold design and fabrication.

1. Introduction

For years, polyurethane (PU) has been extensively used in various implantable devices such as catheters, pacemaker leads, intra-aortic balloons and mammary implants (Grad et al., 2003; Asefnejad et al., 2011). The in vivo molecular stability of PU provides a successful clinical utilization (Hu et al., 2012). In recent years, porous PU scaffolds have become one of the most popular biomaterials in various tissue engineering applications, for example, small diameter vascular graft and regeneration of cartilage and bone tissue (Tsui and Gogolewski, 2009; Xu et al., 2010; Wang et al., 2012; Khorasani and Shorgashti, 2006; Whatley et al., 2011; Hung et al., 2014; Gorna and Gogolewski, 2006; Heijkants et al., 2008). Formation of porous PU scaffolds has been achieved by several methods, such as electrospinning, phase inversion and porogen leaching (Wang et al., 2012; Khorasani and Shorgashti, 2006; Whatley et al., 2011; Hung et al., 2014; Gorna and Gogolewski, 2006; Heijkants et al., 2008). One of the key challenges in porous scaffold design is to create a porous structure with desired mechanical function and mass transport properties which aid delivery of biofactors and development of functional tissue substitutes (Stylianopoulos et al., 2008).

The mechanical properties (Young's modulus in tension and compression) of PU scaffolds have been characterized for their specific applications. The tensile modulus of PU has been examined for the small diameter vascular graft application because of the need of resisting pressure from blood flow (Hayashi et al., 1989). With different formation methods with and without wall reinforcement, the tensile modulus requirement for small diameter vascular grafts is ranged from 0.05 MPa to 4 MPa (Wang et al., 2012; Khorasani and Shorgashti, 2006; Stylianopoulos et al., 2008; Khorasani and Shorgashti, 2006). In the application of cartilage and bone tissue engineering, the porous PU scaffolds are utilized as a temporary extracellular matrix and also provide a sufficient mechanical strength to withstand in vivo stress and loading (Hutmacher, 2001). With various fabrication methods and

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http://dx.doi.org/10.1016/j.jmbbm.2016.09.029
Received 27 June 2016; Received in revised form 12 September 2016; Accepted 22 September 2016
Available online 23 September 2016
1751-6161/

modification, the compressive moduli of PU scaffolds for cartilage tissue engineering are usually ranged from 0.01 MPa to 1 MPa (Grad et al., 2003; Whatley et al., 2011; Hung et al., 2014; Heijkants et al., 2008, 2006; Tsai et al., 2015). Because of different mechanical characteristics between cartilage and bone tissues, PU scaffolds for bone tissue engineering have higher compressive moduli which range from 2.5 MPa to 50 MPa (Bil et al., 2009; Gogolewski et al., 2008). Therefore, creating scaffolds with adequate mechanical properties is important for particular applications.

Mass transport properties (e.g., permeability and diffusivity) of porous scaffolds are also important in maintaining cell health by facilitating exchanges of nutrients and metabolites for tissue engineering applications. Transport of fluid and solutes within porous scaffolds is mainly affected by their hydraulic permeability and solutes diffusivities (Yuan et al., 2009; Jackson et al., 2008). Hydraulic permeability represents a measurement of how easy the fluid can flow through a porous material, while diffusivity is a measurement of solute mobility. Therefore, fully understanding the mass transport properties of porous scaffolds is necessary for successful tissue engineering applications.

Previous studies have showed that permeability and solute diffusivity were highly dependent upon porosity in tissues and scaffold (Jackson et al., 2008; Jackson and Gu, 2009; Kang et al., 2010). Furthermore, it has also been demonstrated that scaffold porosity is strongly associated with mechanical properties (Kang et al., 2010; Jones et al., 2009, 2007; Boccaccini and Fan, 1997; Chen et al., 2014; Gibson, 2005; Harley et al., 2007; Kanungo and Gibson, 2010). Although high porosity is desirable for efficient transport of nutrients in the scaffolds for tissue engineering applications, it reduces the mechanical properties of the scaffolds. Therefore, seeking the balance between efficient mass transport and sufficient mechanical strength is one of the challenges in the scaffold design. By understanding the relationships between porosity and mass-transport and mechanical properties, it allows us to facilitate the design of porous scaffolds with desired mass transport and mechanical properties for tissue engineering applications. However, the relations between porosity and both mass transport and mechanical properties of PU porous scaffolds have not been fully elaborated. Therefore, the objectives of this study were to systemically investigate the mass transport and mechanical properties of the porous PU scaffolds and their relationship with porosity.

2. Materials and methods

2.1. PU scaffold preparation

The PU solution was prepared by dissolving PU pellets (Tecflex® SG-85A, Lubrizol, Wickliffe, OH,) in the N,N-dimethyl formamide (DMF; Sigma-Aldrich, St. Louis, Mo., USA) with 25%, 20% and 15% (w/v) concentration, respectively. Porous PU scaffolds were prepared using a sodium chloride (NaCl; Sigma-Aldrich) salt-leaching method. NaCl crystals were grinded, sieved to sizes smaller than 75 μm and mixed into the PU solution at three different weight ratios (NaCl/PU ratio: 9/1, 6/1 and 3/1). Polytetrahydrofuran (Sigma-Aldrich) was added to the NaCl/PU mixture in 25% (v/v) volume ratio as a soluble filler to enhance interconnectivity in PU scaffolds (Chen et al., 1999). The mixed solution was well stirred and then injected into a plastic rectangular mold. After injection, the mold was placed at room temperature for two hours to evacuate air bubbles and then stored at −80 °C overnight to solidify PU resin. The frozen PU resin was removed from the mold and merged in 65% of ethanol with 1% DMF solution for phase inversion process for 24 h. The porous PU scaffolds were then rinsed in distilled water for another 24 h in order to remove remaining NaCl crystals. After the rinse procedure, PU samples were punched in different sizes for the further analyses of mechanical and mass transport properties. Three independent tests were performed for each experimental group in each analysis. Samples were freshly prepared for individual tests and were not reused for different tests.

2.2. Porosity

To measure porosity, PU samples were air dried and punched into cubic shape (n=3 per NaCl/PU ratio or PU concentration). The length and mass of samples were measured with a digital caliper and scale, respectively. The porosity was calculated by the volume and mass of the sample with the following equation (Heijkants et al., 2008):

$$\varphi = 1 - \frac{\rho}{\rho_{polymer}} \quad (1)$$

Where φ was the porosity, ρ was the density of the porous PU scaffold and the $\rho_{polymer}$ is the density of the pure polymer.

2.3. Scanning Electron Microscopy (SEM)

25% PU samples with different NaCl/PU ratios were prepared (n=3 per NaCl/PU ratio) and the mid-height cross section area of the samples were scanned under the SEM (JSM-6010PLUS/LA, JEOL, Peabody, MA) at the acceleration voltage 1.5 kV. Three random locations of each ratio group were captured for pore size and distribution measurement by ImageJ software. The Saltykov theory was utilized as a stereology analysis for the estimation of 3D pore size distribution (lewis et al., 1973; Shen et al., 2006).

2.4. Mechanical properties

PU samples were prepared in cuboid shape (25 mm×15 mm×3 mm, n=3 per NaCl/PU ratio or PU concentration) for tensile testing which was performed using a single column testing system (Instron, Norwood, MA). With a 5% tensile strain preload, the PU samples were subjected to 10% strain and tensile load was measured after 500 s of relaxation. For compressive testing, the PU samples were prepared in cylindrical shape (diameter: 5.8 mm, height: 3 mm, n=3 per NaCl/PU ratio or PU concentration) using a punch. Compressive testing was performed using a custom-made loading system (Wang et al., 2013) which consisted with a stepper motor (Moog Animatics, Santa Clara, CA) and a high accuracy low profile load cell (OMEGA Engineering Inc., Stamford, CT). Similarly, 5% of compressive strain was used as a preload and compressive load was measured after application of 10% strain with 500 s of relaxation. Young's moduli of PU samples in tension and compression were determined and normalized by that of the scaffold fabricated with phase inversion method only. The relationship between porosity and normalized Young's modulus was determined by the following equation (Chen et al., 2014; Gu et al., 2003):

$$E = c(1 - \varphi)^{\alpha} \quad (2)$$

where c and α are the material parameters, φ is the porosity and E is the normalized Young's modulus in either tension or compression. The material parameters were curve fitted by MATLAB software (MathWorks Inc., Natick, MA).

2.5. Hydraulic permeability

PU samples were prepared in cylindrical shape (diameter: 7.8 mm, height: 1 mm, n=3 per NaCl/PU ratio) and the measurement of hydraulic permeability was performed as described in our previous study (Yuan et al., 2011). Briefly, the PU samples were placed between two compartments in a permeability chamber. By creating a pressure gradient across the PU sample with phosphate-buffered saline (PBS) solution, the hydraulic permeability can be determined by Darcy's law:

$$k = \frac{Qh}{A\Delta P} \quad (3)$$

Where k is the hydraulic permeability, Q is the volume flow rate, h is the thickness of the sample, A is the effective cross section area of the sample and ΔP is the pressure gradient across the PU sample. The