EVALUATING BIODEGRADATION RATES IN NEAT PCL- AND PCL/PLA-BASED BIOCOMPATIBLE TUBULAR SCAFFOLDS

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ABSTRACT

Vascular grafts are synthetic tubular structures that play an important role in replacing damaged vessels in the treatment of cardiovascular diseases. Existing grafts, especially in small-diameter vessels, face persistent issues such as thrombosis, immune rejection, and mechanical limitations. Vascular grafts designed with an innovative perspective to overcome these deficiencies are tubular scaffolds with a biodegradable structure and a layered design that mimics the native artery structure. This study focuses on the development of biodegradable and biocompatible tubular scaffolds with randomly distributed and radially oriented fibers in different layers to replicate the native structure of artery, utilizing neat polycaprolactone (PCL) and PCL/polylactic acid (PLA) blend with 4/1 polymer blend ratio. Electrospinning technique is employed to fabricate tubular fibrous structures. The biodegradation profiles of these scaffolds are assessed at 3, 6, and 9 months, with comparative analyses conducted to explore how polymer type and orientation level influence degradation rates and the structural integrity of the materials over time. The findings reveal that scaffolds with randomly distributed fibers exhibit higher biodegradation rates compared to those with oriented fibers, particularly in the PCL/PLA blends. Specifically, the study identifies PCL_R as having the highest degradation rate at 61% weight loss by the 9th month. Importantly, while PCL is known for its slow degradation, the high molecular weight of PLA leads to a slower degradation profile in the PCL/PLA samples. These insights underscore the critical role of scaffold morphology and composition in optimizing the performance and functionality of vascular grafts, highlighting the need for scaffolds that support cellular activities while effectively degrading to facilitate tissue regeneration without toxic effects.

KEYWORDS

Polycaprolactone; Polylactic acid; Tissue engineering; Electrospinning; Biodegradability.

INTRODUCTION

Tissue engineering aims to develop scaffolds that serve as effective substitutes for damaged tissues by facilitating biological activities and controlled biodegradation during tissue regeneration, while maintaining mechanical integrity [1]. The design of advanced biomaterials and the integration of implants with tissues are intricately linked to cell-scaffold interactions. Three-dimensional (3D) fibrous scaffolds that mimic the extracellular matrix (ECM) are essential, as they support critical cellular activities such as attachment, migration, proliferation, and differentiation necessary for tissue regeneration [2] [3]. On the other hand, cardiovascular diseases have become a major health problem, causing high rates of death and disability worldwide. The inadequacy of autologous vessels and the problems such as mismatch, thrombosis and occlusion in small-diameter replacements of existing commercial grafts have triggered the need for tissue-engineered vascular grafts [4-6].

Biodegradable polymers offer considerable advantages over non-biodegradable materials by minimizing the need for surgical removal and reducing the necessity for long-term immunosuppressive treatments [7]. The design of biodegradable vascular grafts focuses on fostering the development of an autologous vessel concurrently with scaffold degradation. In particular, the formation of a regenerated structure that will replace the damaged vessel and the realization of endothelialization require a long-term process, and at this point the importance of biodegradability in vascular graft structures emerges. The biodegradability period of the vascular graft should be slow enough to allow time for new tissue formation, but it should not cause a toxic effect during this process [8]. This approach aims to address issues related to immunogenicity and thrombus formation by

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ensuring that the scaffold's degradation rate is synchronized with the rate of neovascularization [9]. The degradation kinetics of the scaffold are influenced by several factors, including the choice of polymer, production techniques, and scaffold architecture. Thus, achieving a balance between degradation and tissue regeneration is critical for maintaining the scaffold's mechanical properties and functional performance throughout the regenerative process. In this context, the choice of material becomes pivotal. Although synthetic polymers such as polyurethane (PU), poly(ethylene glycol) (PEG), poly(glycolic acid) (PGA), poly(lactic acid-co-glycolic acid) (PLGA), poly(vinyl alcohol) (PVA), PLA, poly(L-lactic acid-co-ε-caprolactone) (PLCL), and PCL exhibit varying biodegradation times, they are frequently preferred in tissue engineering applications due to their high strength and comparatively slow degradation rates relative to natural polymers [10]. Among these materials, PCL and PLA are particularly noteworthy for their biocompatibility, adjustable degradation rates, and mechanical properties, making them highly cited in the literature as preferred polymers in various vascular graft applications [11-14].

On the other hand, using layered structures in vascular grafts and designing each layer to mimic the native artery structure is important in terms of obtaining the desired physical, mechanical and biological properties [15]. In this context, at least a two-layer graft design is envisaged and the inner layer is produced with random fiber distribution to mimic the *tunica intima*, the inner most layer of an artery that is in contact with blood, while the outer layer contains fibers with radial orientation to mimic the *tunica media*, the middle layer of an artery responsible for mechanical features [16]. This structural property, in addition to the material type, has an impact on the biodegradable values of the grafts [17].

This study investigates the biodegradation behavior of biocompatible scaffolds designed for vascular graft application. Utilizing electrospinning techniques, tubular scaffolds with randomly distributed and radially oriented fibers made from both neat PCL and PCL/PLA blend are developed. The biodegradation of these scaffolds is assessed over 3, 6, and 9 months. The biodegradability rates of the developed scaffolds are discussed comparatively, taking into account PLA addition and fiber orientation.

EXPERIMENTAL

Materials

PCL (Mn 80,000), PLA (Mn 230,000; Ingeo 2003 D with 4.3 mol% D-lactide content), and the components of solvent systems (chloroform (CHL), ethanol (ETH), and acetic acid (AA)) are supplied from Sigma Aldrich.

Methods

Scaffold fabrication

Neat PCL and PCL/PLA blend are dissolved in CHL/ETH/AA (8/1/1 wt.) solvent system, and polymer concentrations are kept constant at 8%. Blend ratio is selected as 4/1 by weight for PCL/PLA. Each polymer solution system is stirred for 2 hours at room temperature. Tubular structures with 6 mm diameter are fabricated using electrospinning set-up with a custom designed rotating feeding unit (Nanospinner, Basic System, Inovenso, Turkey). Scaffolds are produced at 200 rpm for randomly distributed fibers and 10,000 rpm for randomly oriented fibers. Randomly distributed fibers are indicated with the suffix _R, whereas surfaces with oriented fibers are denoted with the suffix _O.

Scaffold Sterilization

Samples are sterilized by washing once in 70% ethanol, followed by three rinses in sterile phosphate buffered saline (PBS). The fibrous webs are then exposed to UV light for 30 minutes on both sides. All UV sterilization processes are conducted in a laminar flow cabinet.

Biodegradation Analysis

Sterilized surfaces are cut into 1x1 cm pieces, with measurements taken at 3rd, 6th, and 9th months. Initial weights are recorded using a precision balance. The samples are placed in 24-well plates with 300 µl of PBS and incubated at 37°C in a 5% CO_2 humidified incubator (Panasonic, Osaka, Japan). Degradation rates are determined by measuring the mass loss of the samples over the 9-month period.

RESULTS

The biodegradation results of fibrous samples featuring randomly distributed and oriented fibers are presented in Figures 1 and 2. It is observed that scaffolds with randomly distributed fibers degrade more rapidly than samples with aligned fibers, owing to their loosely packed structure. The densely packed arrangement of the scaffolds, together with aligned fibers, establishes a barrier that impedes PBS penetration, thereby effectively decelerating the degradation process [18]. In the present study, it is noted that in both sample groups—PCL and PCL/PLA—the surfaces with randomly distributed fibers exhibited higher degradation rates, especially at the 6th and 9th months, compared to samples with radially orientated fibers. In a 12-month biodegradation assessment, Oztemur et al. (2024) observed that electrospun PCL surfaces with randomly distributed fibers displayed a relatively higher degree of degradation than their aligned fiber counterparts [16]. Similarly, Mirzaei et al. (2020), in a study utilizing blends of polyethylene oxide (PEO) and PCL, found that by the 7th day, surfaces with randomly distributed fibers demonstrated a slightly

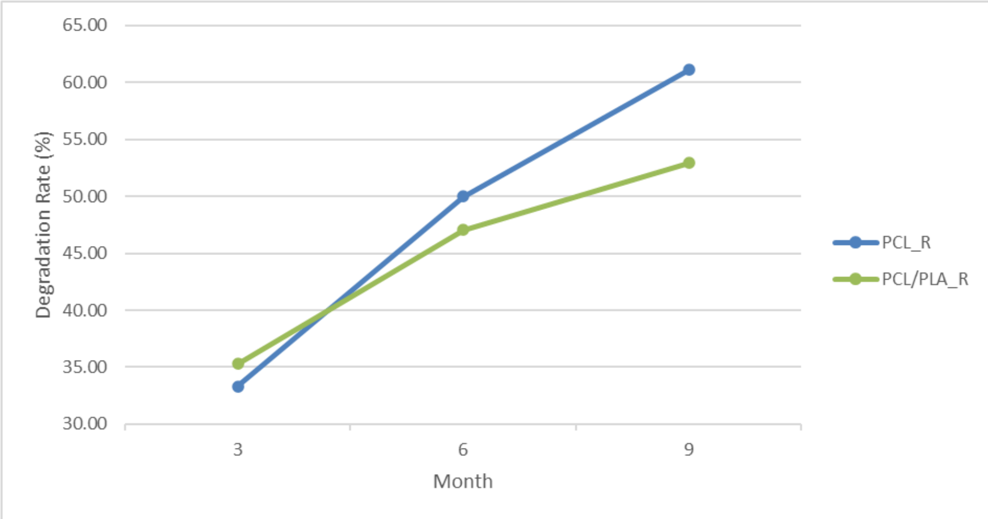

Figure 1. Biodegradation rates of PCL_R and PCL/PLA_R scaffolds.

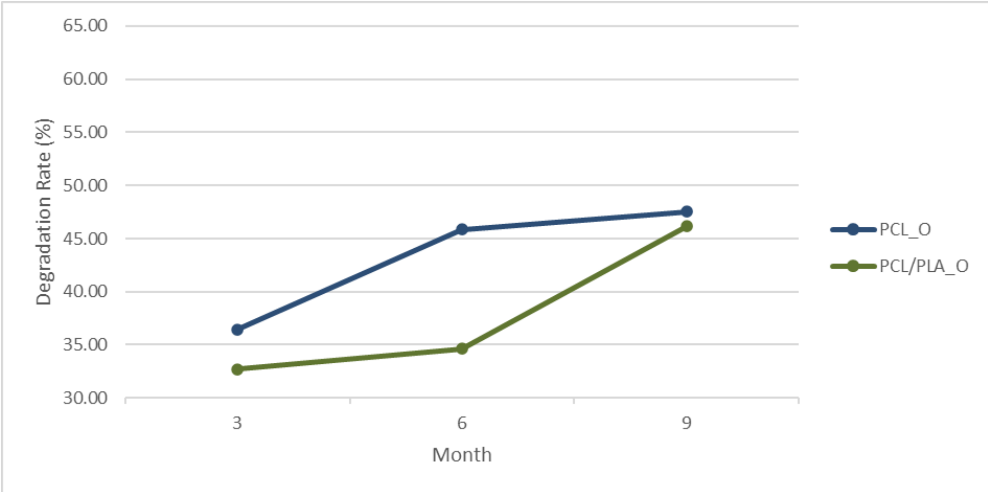

Figure 2. Biodegradation rates of PCL_O and PCL/PLA_O scaffolds.

higher degradation rate, independent of the blending ratio [19].

From a material-centered perspective, when the sample groups are compared, it is observed that both the scaffolds with randomly distributed fibers and those with radial orientation exhibit similar degradation rates within the initial 3 months. PCL degradation primarily occurs through the hydrolytic cleavage of ester bonds, which is generally a slow process taking approximately two to three years [20]; however, in the present study, PCL_R displays a more rapid degradation trend by the 6th and 9th months. This accelerated degradation rate in the PCL sample may be attributed to its substantially lower molecular weight in comparison to PLA. Molecular weight is a crucial factor in the hydrolytic degradation rate of polymers; higher molecular weights are known to correspond to a more stable degradation rate. Conversely, when molecular weight decreases below a specific threshold, degradation accelerates due to increased molecular mobility, a greater presence of hydrophilic groups, and enhanced water diffusion [19]. Additionally, among the radially oriented samples, while PCL_O exhibits a significant increase in degradation rate from the 3rd to the 6th month in comparison to PCL/PLA_O, by the end of the 9th month, both PCL_O and PCL/PLA_O have reached comparable values, with degradation rates of 47% and 46%, respectively.

CONCLUSION

In this study, the influence of fiber orientation and material type on the biodegradation profiles of electrospun scaffolds is evaluated to refine scaffold design for enhanced control over degradation kinetics in tissue engineering applications specifically, in vascular grafts. Through an analysis of fiber alignment and molecular weight variations, the study offers critical insights for optimizing scaffold composition to achieve precise biocompatibility and functional longevity in targeted biomedical applications. In this context, it is necessary to emphasize the following points as the key outcomes of the study:

- Fiber orientation significantly influences biodegradation behavior, with PCL_R and PCL/PLA_R, which possess randomly distributed fibers, exhibiting greater degradation compared to the oriented fiber counterparts, PCL_O and PCL/PLA_O, by the end of the 9-month period.
- Among all samples, PCL_R demonstrated the highest degradation rate at 61% weight loss by the end of the 9th month.
- Although PCL is generally recognized as a relatively slow-degrading biopolymer, the high molecular weight of PLA utilized in the PCL/PLA sample groups resulted in slower degradation rates in this study.

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