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Heterogeneous electrospun polycaprolactone/polyethylene glycol membranes with improved wettability, biocompatibility, and mineralization

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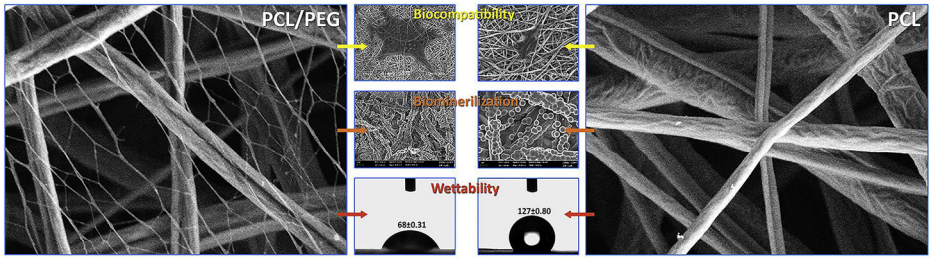
HIGHLIGHTS

- Heterogeneous fibrous membrane was reported from PCL/PEG first time via electro-spinning/netting (ESN).
- Heterogeneous membrane was consisting of thicker/backbone fibers and ultrathin nano-nets.
- Hydrophilicity and mineralization were improved with incorporation of PEG into PCL fibers.
- Heterogeneous scaffolds showed better support for cell activities.

GRAPHICAL ABSTRACT



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ABSTRACT

Polycaprolactone (PCL) based electrospun membranes possess many favorable characteristics such as flexibility, high mechanical properties, and non-toxicity, all of which are required for tissue engineering applications. However, their hydrophobic nature and low biocompatibility limit their uses. To overcome these drawbacks, we propose highly biocompatible and hydrophilic heterogeneous scaffolds from a blend of PCL with polyethylene glycol (PEG) that is composed of nano-nets along with backbone/main fibers via an electro-spinning/netting (ESN) technique. Different scaffolds were fabricated by varying the mass composition of PCL to PEG and evaluated physicochemically and biologically. Scanning electron microscopy showed that the PCL/PEG membranes were of a bimodal structure consisting of backbone/main fibers (diameter range = 350–600 nm) and ultrathin nano-nets while the pure PCL mat was composed of only backbone fibers (diameter range = 550–800 nm). The nano-nets were composed of ultrathin nano-wires with an average diameter of 10–20 nm, shaped in a hexagonal form. We have also prepared the PCL/PEG membranes without nano-nets and compared them to heterogeneous membranes in order to describe the effect of the nano-nets by well distinguishing the effect of PEG on tissue engineering applications such as wettability, biocompatibility, and biomineralization. The results showed that heterogeneous scaffolds exhibit enhanced wettability, mechanical stability, biocompatibility, and mineralization compared to pure PCL and PCL/PEG scaffolds without nano-nets, which confirmed that the nano-nets in the membranes had

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positive effects for tissue engineering applications. Findings from this study have revealed that the heterogeneous fibrous membrane could be useful in the design and tailoring of a suitable structure as a scaffold for bone tissue engineering.

1. Introduction

Electrospinning is a promising technology that can be used to create versatile fibrous scaffolds for biomedical [1], drug delivery [2], air filtration [3] and sensing [4] applications. The scaffold obtained by electrospinning is composed of fibers of mainly submicron sizes. This technique is a simple, versatile and cost-effective way of producing nano-fibers in a controlled manner [1,2,5,6]. The basic principle of electrospinning is the application of an electrical field to eject a polymer solution from a reservoir to a collector producing non-woven fiber networks [1,2,5–7]. These fibers resemble the native extracellular matrix structure that serves as an excellent framework for cell adhesion, proliferation, and differentiation [1,5]. In the past few years, electro-spinning/netting technique (ESN), a variant of electrospinning, has become a promising technique to generate a heterogeneous network structure that consists of three-dimensional electrospun nanofibers along with nano-nets (diameter less than 50 nm) [8–11]. These unique fibrous structures were achieved by changing the solvent system, solution parameters and processing parameters [8,11,12]. Ultrathin fibers obtained from ESN have an extremely large specific surface area, high porosity and good pore interconnectivity [8–12]. In addition, fibers supported by nano-nets have been reported to exhibit higher mechanical properties [9] and enhanced cellular activities [1,13] compared to scaffolds without nano-nets. Because of these intriguing characteristics, these architectures evoke much interest in various fields including tissue engineering. However, detailed studies on the feasibility of bimodal fibers obtained by ESN for tissue engineering applications have yet to be completely understood. Thus, the collective assessments of the heterogeneous fibrous constructs in biocompatibility, biomineralization, mechanical stability and hydrophilicity for tissue engineering applications are greatly anticipated.

Tissue engineering is a promising field that studies repairing and regeneration of damaged tissues by utilizing cell-scaffold interactions [14]. Therefore, scaffolds must possess basic characteristics such as biocompatibility, sufficient mechanical properties, and nontoxicity. Several polymers such as polylactide [15], PCL [16,17] and poly(lactic-co-glycolic) acid (PLGA) [18] can be used to fabricate tissue scaffolds by electrospinning. PCL is a semi-crystalline and hydrophobic polymer that has been approved by the Food and Drug Administration (FDA) for biomedical applications and offers excellent mechanical properties and slow biodegradation, making it an appropriate material for use as a scaffold for tissue engineering [16]. However, PCL scaffolds lack many cell recognition sites and have low hydrophilicity, limiting their applicability. Several strategies have been implemented to overcome these shortcomings of PCL scaffolds. Li et al. [16] fabricated an electrospun PCL scaffold with a porous surface structure to enhance biocompatibility. Incorporation of various bioactive compounds such as gelatin [17], zein [19], calcium carbonate [20,21], hydroxyapatite [22], serum albumin [23] and growth factors [24] into PCL fibers have been reported in order to enhance their biocompatibility. Recently we have reported a bimodal polycaprolactone/human serum albumin (PCL/HSA) fibrous membrane consisting of conventional fibers (main fiber) and nano-nets via ESN [25]. It was found that the albumin contributed mainly to the formation of the ultrathin nano-nets whereas the PCL contributed to the formation of the main fibers due to phase separation during ESN. The preliminary experiment suggested that bimodal membranes allow for better cell adhesion compared to PCL fibers [25]. Li et al. [26] developed polyethylene oxide (PEO) incorporated ultra-porous PCL fibers using electrospinning which exhibited excellent cell compatibility. However, the idea of developing heterogeneous fibrous structures via ESN using different ratios of PEG to PCL is novel and can be promising in overcoming the drawbacks of PCL fibers and is one of the basic goals of the present work. PEG is a hydrophilic polymer known to support cell attachment and is frequently added into synthetic scaffolds to enhance cellular activities [27,28]. Moreover, since PEG is more readily available and cheaper compared to HAS, it was used as a substitute for HSA for the study of heterogeneous membranes in tissue engineering applications. Here, we hypothesize that the use of PEG in combination with PCL may lead to products with a heterogeneous fibrous structure that exhibit enhanced mineralization, hydrophilicity, mechanical stability and biocompatibility.

In this paper, we report the fabrication of a heterogeneous fibrous structure using a novel blend of PCL and PEG. Different mass ratios of PCL and PEG were blended to fabricate the membranes. The structural, morphological, physicochemical and biological properties of the fabricated scaffolds were evaluated. PCL/PEG heterogeneous membranes were compared to PCL/PEG membranes (without nano-nets) and pristine PCL mat to illustrate the role of nano-nets in tissue engineering applications.

2. Materials and methods

2.1. Materials

Poly (ε-caprolactone) (PCL, Mw = 70,000–90,000) was purchased from Sigma–Aldrich (USA). 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP, Matrix Scientific, USA), Polyethylene glycol (PEG20000, Samchun, Korea), fetal bovine serum (FBS, Gibco, USA), trypsin (0.25% Gibco, USA) and cell-counting kit (CCK-8, Dojindo, Japan) were used as received. All other chemicals used in the experiment were of analytical grade.

2.2. Preparation of the electrospinning solutions

The electrospinning solutions were prepared by blending PCL (8 wt%, prepared in HFIP) and PEG solutions (10 wt%, prepared in double deionized water) at different mass ratios so that the mass composition of PCL and PEG in the final solutions were 100:0, 90:10, 80:20 and 60:40. The solution conductivity and viscosity were measured using a programmable electro conductivity meter (Hanna, USA) and rheometer (DV-III Ultra, Brookfield, UK), respectively. The solutions were continuously stirred overnight prior to electrospinning.

2.3. Electrospinning process and scaffolds characterization

The electrospinning solution was withdrawn into a 12 mL syringe. In a typical experimental setting, the feeding rate was kept