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Fabrication and properties of L-arginine-doped PCL electrospun composite scaffolds

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ABSTRACT

The article describes fabrication and properties of composite fibrous scaffolds obtained by electrospinning of the solution of poly(ε-caprolactone) and arginine in hexafluoro-2-propanol for the first time. The influence of arginine content on structure, mechanical, surface and biological properties of the scaffolds was investigated. It was found that arginine addition reduces diameter of the scaffold fibers and doesn't impair mechanical properties of the polymer. Porosity and water contact angle of the scaffold were independent from arginine content. The best adhesion and viability of multipotent mesenchymal stem cells was shown on scaffolds with arginine concentration from 0.5 to 1% wt.

1. Introduction

Electrospun fibrous scaffolds are common material for cardiovascular grafts. Owing to high biocompatibility and good mechanical properties, poly(ε-caprolactone) is the one of the most widely used polymers for these devices. The main disadvantages of PCL cardiovascular grafts are high risk of thrombosis and low endothelialization rate [1]. To overcome these drawbacks, a number of methods of surface and bulk modification of PCL grafts were developed.

Application of L-arginine for modification of cardiovascular implants is promising as L-arginine is natural substrate for a family of enzymes called NO-synthases. By NO-synthases L-arginine is being metabolized to citrulline and nitric oxide (II) [2]. With that, nitric oxide (II) is one of the most important substances in cardiovascular system [3]. It is known that L-arginine immobilization on the surface of polymer films decreases their thrombogenicity by reducing blood calcification rate, thus improving their hemocompatibility [4]. The disadvantage of the surface immobilization of L-arginine is reduce of pharmacological activity during graft degradation and substitution by self-tissues.

Thus, the development of biodegradable L-arginine-doped polymer composites (in particular, PCL-based) is a relevant task. The most significant limitation concerning this problem is the absence of common solvents for PCL and L-arginine. By our group it was found that hexafluoro-2-propanol dissolves both PCL and L-arginine giving an opportunity of developing novel composite materials. The aim of the present work is to obtain new composite materials based on PCL and L-arginine using hexafluoro-2-propanol as a common solvent and to fabricate electrospun fibrous composite scaffolds.

2. Materials and methods

For scaffold fabrication poly(ε-caprolactone) M_w = 80 kDa, (PCL, Sigma-Aldrich), L-arginine (≥99%, Sigma-Aldrich) and hexafluoro-2-propanol (≥99%, Sigma-Aldrich) as a solvent were used. Six groups of materials were formed during the study depending on L-arginine concentration in composite: 0, 0.1, 0.5, 1, 3, 7% wt.

Composite scaffolds were fabricated using NANON-01 installation (MECC Co., Japan) at the following parameters: voltage – 20 kV, feed rate – 2 ml/h, 18G syringe tip, distance between syringe

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tip and collector – 150 mm. The collector was presented as a steel cylinder with length of 200 mm and 5 mm diameter. Thickness of the fabricated scaffolds was 137 ± 12 μm.

Grafts morphology was investigated using scanning electron microscopy (JCM-6000Plus, Jeol, Japan). The samples were precoated with gold (SmartCoater, Jeol, Japan). Obtained SEM-images were analyzed by using Image J software (National Institutes of Health, USA). Average fiber diameter was calculated from not less than 400 measurements from the SEM-images of ten areas of the scaffold. Water contact angle of the grafts surface was measured by sitting drop method (EasyDrop, Kruss, Germany). Arginine on the grafts surface was visualized by reaction with 1% ninhydrin solution in ethanol. Thermograms of the obtained materials were recorded in the range of 0–120 degrees using DSC 204F1 Phoenix equipment (NETZSCH, Germany). Degree of crystallinity was measured using the following formula: $X_c = \frac{\Delta H_m}{\Delta H_m^0} \times 100\%$, where X_c is degree of crystallinity, %; ΔH_m^0 is melting enthalpy of 100% crystalline polymer (135.5 J/g for PCL); ΔH_m is melting enthalpy of the composite, J/g. Mechanical properties of the grafts were studied under uniaxial extension using Instron 3369 installation with 50N loading cell (model 2519-102, Instron, USA) at a loading rate of 10 mm/min. Porosity of the scaffolds was measured at room temperature by using the liquid intrusion method. Statistical analysis of the obtained data was conducted by means of GraphPad Prism 6 software (GraphPad Software, Inc., USA) using non-parametric Kruskall-Wallis test with 0.05 level of significance.

Adhesion and viability of multipotent mesenchymal stem cells (MMSC) were studied as previously described [5]. Statistical analysis was performed using Mann-Whitney and ANOVA tests.

3. Results and discussion

SEM-images, average fiber diameter, its distribution and water contact angles of the fabricated PCL/L-arginine grafts are shown in Fig. 1. Grafts formed from PCL without L-arginine addition are presented by fibers with bimodal distribution of diameter (Fig. 1a).

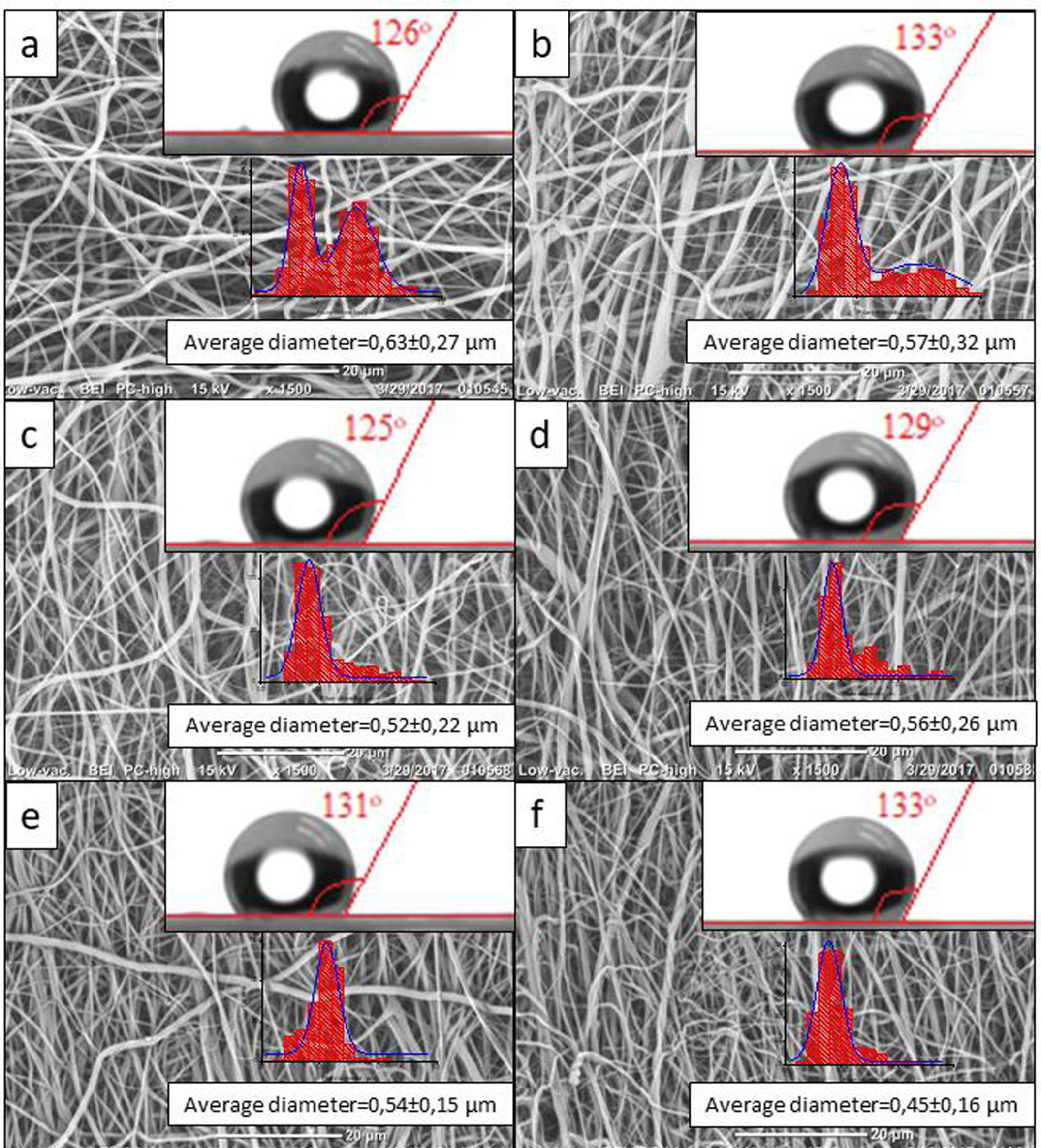

Fig. 1. SEM-images, fiber diameter distribution histograms and water contact angles of PCL/L-arginine scaffolds depending on L-arginine content (a-f – 0, 0.1, 0.5, 1, 3, 7% wt, respectively).