INFLUENCE OF POLYMER TYPE AND BLENDING ON MECHANICAL PROPERTIES OF COAXIAL ELECTROSPUN VASCULAR GRAFTS

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Abstract

The field of tissue engineering has witnessed significant progress in the development of vascular grafts for critical applications in cardiovascular surgery; however, the current vascular grafts still suffer from certain inadequacies such as thrombosis, intimal hyperplasia, and compliance mismatch. Among the various fabrication techniques, coaxial electrospinning has emerged as a promising method to produce vascular grafts due to its ability to tailor the architecture and composition of fibers for creating core-shell fibers, enabling the incorporation of both miscible and immiscible polymers and functional properties within the same fiber. The importance of material selection in coaxial electrospinning for vascular graft applications lies in determining the graft's mechanical properties, biocompatibility, and degradation characteristics, crucial factors that directly impact its long-term performance and success in cardiovascular tissue engineering. The mechanical properties of vascular grafts are important as they directly influence graft durability, stability, and biomechanical compatibility, critical factors for ensuring successful integration and long-term functionality within the cardiovascular system. This study focuses on the effect of polymer selection and blending for the core and shell parts of the fibers on the tensile strength, burst strength, and compliance of monolayer vascular grafts. The scaffolds have coaxial fibers with polycaprolactone (PCL) and polylactic acid (PLA), and their blends either in the core or shell part are fabricated. The results showed that the polymer selection and the fiber arrangement significantly affect the mechanical features. Using PLA shell and implementing PCLPLA blend in core result in enhanced strength values and elasticity of the material.

Keywords: Vascular grafts, coaxial electrospinning, compliance mismatch

1. INTRODUCTION

Cardiovascular diseases maintain their status as the foremost cause of death in developed nations, surpassing the combined annual mortality rates of cancer and chronic lower respiratory diseases [1]. The main treatment involves using blood vessel transplants, but a shortage of autologous vessels makes it difficult to meet clinical requirements. Consequently, developing artificial blood vessels is of utmost importance [2]. While synthetic grafts like polytetrafluoroethylene (ePTFE, Gore-Tex) and poly(ethylene terephthalate) (PET, Dacron) have found clinical utility as substitutes for large-diameter arteries, their effectiveness in smaller diameter blood vessels is limited primarily due to the elevated risks of thrombosis, restenosis, infection, and compliance mismatch [3,4]. An optimal small-diameter vascular prosthesis should exhibit a combination of desirable attributes to be used in clinical applications. This includes robust mechanical strength and compliance to endure the challenges of hemodynamic stress, suturability for surgical ease, immediate availability in various dimensions for potential emergencies, user-friendly handling to minimize surgical duration, costs, and associated risks, resilience against thrombosis and infections, biocompatibility, long-term functionality, fast endothelialization, and adequate porosity to facilitate easy cell diffusion [5]. Developing vascular grafts that replicate the distinctive characteristics of native blood vessels represents a promising approach in the field of regenerative medicine [6]. Concerning blood vessels, endothelial cells located in the *tunica intima* are organized parallel to the direction of blood flow, while smooth muscle cells are aligned circumferentially in the *tunica media* [7]. The utilization of electrospinning has gained prominence in the creation of vascular grafts in recent times, primarily because they can closely replicate the framework of extracellular matrix [8]. When designing electrospun vascular grafts, there are two main categories of parameters to consider that directly influence the mechanical and biological response of the scaffolds: structural parameters, which include fiber diameter, pore size, porosity, fiber orientation, wall thickness, the number of layers, and material selection [9]. The mechanical properties of the scaffold, including its suturability, compliance, tensile strength, burst pressure, and blood permeability, are heavily affected by its design and composition [10]. Within the structural parameters, fiber orientation stands out as a highly significant feature of scaffolds because it influences both cellular alignment and the mechanical properties [10,11]. Circumferentially aligned fibers within the vascular scaffolds exhibit enhanced modulus, tensile strength, burst strength, and decreased compliance when subjected to hemodynamic forces, primarily due to the material's rigidity [12]. On the other hand, synthetic polymers typically possess greater mechanical strength than their naturally derived counterparts, rendering them promising for vascular applications that necessitate scaffolds that can bear blood pressure [13]. Among synthetic polymers, PCL is recognized as a non-toxic, elastic, and cell-friendly scaffold material with long-term biodegradation, whereas PLA offers both biocompatibility and mechanical strength, and it can be customized in terms of biodegradation [14]. In principle, it is possible to achieve resistant and elastic scaffolds that also demonstrate an ideal biodegradation rate by utilizing the blending or copolymer form of PCL and PLA [15]. However, it is mentioned that achieving the desired mechanical performance in blends of PCL/PLA can be a challenge due to the immiscible characteristics of these polymers. As another approach, coaxial electrospinning, a modified version of traditional electrospinning, involves the use of a specialized spinneret with two coaxial needles to simultaneously feed two different polymer solutions, thereby achieving core-shell fibers [16]. In contrast to fibers that are coated or blended, coaxially electrospun fibers have demonstrated improved biocompatibility and mechanical characteristics [17]. Additionally, it is discovered that the mechanical features of the fiber are less affected by its core polymer characteristics and more influenced by the interaction that exists between the core and the shell [18]. The compatibility of the solutions holds great significance in the context of coaxial electrospinning. It is crucial for the two solutions to either be immiscible or partially miscible in order to create a steady Taylor cone at the needle tip [19]. In this study, monolayer vascular grafts composed of radially oriented core-shell fibers, including the neat or blended forms of PCL and PLA either in core or shell, are produced by coaxial electrospinning. The tensile properties, burst pressure, and compliance of the fabricated scaffolds are assessed to observe the effect of using the selected polymers either in neat or blended form and their placement within the core or shell regions on the mechanical properties. It is aimed to achieve a promising monolayer graft that can imitate the *tunica media* layer in native blood vessels and be used in multilayered scaffolds.

2. EXPERIMENTAL PART

2.1 Materials

The pristine and the blended form of PCL (Mn 80,000) and PLA (Mn 230,000) are dissolved in a solvent composition comprising chloroform, acetic acid, and ethanol, in an 8:1:1 weight ratio, reaching a concentration of 8% w/w. All the polymers and chemicals are sourced from Sigma Aldrich. The blending ratio employed for PCL/PLA solution is established as 50/50.

2.2 Methods

Coaxial electrospinning of vascular grafts

To fabricate the fibrous vascular prostheses with 5 mm diameters via coaxial electrospinning, neat PCL and PLA solutions are used either in the core or shell part (PCL_PLA and PLA_PCL), whereas the PCL/PLA blend is only utilized in the core region of bicomponent fibers (PCLPLA_PCL and PCLPLA_PLA). The coaxial needle consists of inner and outer needles with inner diameters of 0.6 and 0.8 mm, respectively. The rotational speed of the collector is determined at 10,000 rpm to obtain radially oriented bicomponent fibers. Both the core and the shell solutions are delivered at a rate of 1 mL/h and subjected to a voltage of 11±0.5 kV for 40 minutes to fabricate the scaffolds with sufficient wall thickness for mechanical assessments. Samples are produced at a temperature of 26±2°C with a relative humidity of 50±5%.

Wall Thickness

The Standard Gage Electronic External Micrometer (Hexagon Metrology, Turkey) is used to gauge the wall thickness of tubular grafts.

Tensile Strength and Strain

Tensile strength and strain of scaffolds are assessed using a Zwick-Roell Z005 universal testing machine equipped with a 200N load cell (Zwick-Roell, Germany). The measurements are performed on both axial (0) and radial directions (90) in planar form and also on the axial direction in tubular form (T0) to simulate the prosthesis position after implantation. Planar pieces are prepared by cutting tubular samples into dimensions of 10mm in width and 15mm in length. Tubular pieces with a length of 1.5 cm are prepared to be tested. Tensile testing is realized with a cross-head speed of 10 mm/min and a gauge distance of 5 mm.

Burst strength and Compliance

To measure the burst pressure, tubular scaffolds are first cut into 4 cm segments. Next, a balloon is inserted through all the sample sections. Following this, the ends of the samples are secured to the air nozzles using sleeves to prevent any air from escaping. When pressure is introduced through the air inlets, the samples start to expand. The moment the sample bursts, the burst pressure value is observed on the screen and recorded. The experiments are performed a minimum of three times for each individual graft.

In the compliance test, physiological pressure is generated within the vascular graft at diastolic and systolic pressure levels ranging from 80 to 120 mmHg via a custom-designed testing machine, as outlined in the ISO 7198:2016 standard. A camera system captures images of the samples under these pressure conditions, and the testing machine is used to measure their diameters at each pressure point. Subsequently, the system calculates the compliance values using Equation (1). This entire process is conducted for each vascular graft, with compliance measurements being repeated at least three times for accuracy.

$$\%compliance = \frac{\frac{R_{p_2}-R_{p_1}}{R_{p_1}}}{p_2-p_1} \times 10^4 \tag{1}$$

where C is the compliance (%/100mmHg), R_{p1} *and* R_{p2} *are* the radii at diastolic and systolic pressure, respectively (mm) and p_1 *and* p_2 are the diastolic and systolic pressures, respectively (mmHg).

3. RESULTS AND DISCUSSION

3.1 Wall thickness

The wall thickness values are given in **Table 1**. It can be seen that the scaffolds have sufficient wall thickness values for the mechanical testing and can be considered as one of the layers in multilayer graft designs that can mimic *tunica media*. In a study by Valence et al. (2012), the wall thickness of the layers varies between 167 and 413 µm [20]. If it is necessary, the wall thickness can be adjusted by changing the production time.

3.2. Tensile Strength and Strain

The tensile testing results (**Table 1**) revealed that achieving radial fiber orientation results in an enhancement in tensile strength in the radial direction, whereas lower strain values are observed when compared with the axial direction. It has been shown in many studies in the literature that if the fibers are oriented in any direction, they can resist the applied stress better in the same direction and have lower elongation as they possess fewer fiber junctions [12,21,22]. In addition, the use of PLA at the shell part of the bicomponent fibers generally affects the tensile strength positively. However, the usage of PCL at the shell part contributed to the strain values when compared with the samples with PLA shells, as PCL is a flexible polymer, whereas PLA is known for its stiffness and strength [23]. Viscusi et al. (2021) fabricated bicomponent fibers (the one with a PCL-curcumin core/PLA shell and the other with a PLA-curcumin core/PCL shell). They also reported that the usage of PLA as a shell resulted in better Young's modulus and tensile strength, whereas it caused lower elongation at break [24]. Also, it is clear that the PCLPLA_PLA sample has enhanced properties when compared with the PCL_PLA scaffold. Thus, using a blended form of PCL and PLA in the core region enhanced the tensile strength and flexibility of the material. It is also stated in the literature that utilizing the blended form of PCL with PLA can decrease the brittleness of PLA while also improving the strength of PCL [25].

3.3. Burst strength & compliance

In Table 1, it can be seen that samples where PLA is used at the shell part (PCL_PLA and PCLPLA_PLA) have higher burst strength values compared to the ones where PCL is used at the shell region (PLA_PCL and PCLPLA_PCL). Also, the usage of the PCLPLA blends in the core region contributes to the burst strength of the scaffolds when they are compared with their neat counterparts. For example, PCL_PLA has a burst strength of 1144 mmHg, whereas PCLPLA_PLA has a burst strength value of 1386 mmHg. As a result, when the PLA proportion is raised within the entire scaffold, there is a notable increase in the burst strength value. According to the findings by Johnson et al. in 2019, an optimal vascular graft should possess a burst strength exceeding 1000 mmHg [26], thus the produced grafts seem convenient for further consideration.

On the other hand, when PLA is used at the shell part of the fibers, the tubular webs show lower compliance values, which can be attributed to the stiffness of the material [27]. In the case of compliance, fibers with a PCL shell result in more compliant tubular scaffolds. In addition, the utilization of the PCLPLA blend in the core region enhanced the compliance of the vascular grafts when compared with the fiber with neat core and shell parts. The results show that the compliance values fall within a range of 0.7-1.5%/100 mmHg, which is the limit for the human saphenous vein [28].

Table 1 Mechanical testing results of vascular grafts with the wall thickness values

Sample code	Wall thickness (µm)	Test direction	Tensile strength (MPa)	Tensile strain (%)	Burst strength (mmHg)	Compliance (%/100mmHg)
PCL_PLA	151±21	0	1.61±0.14	176.39±28.02	1144±90	0.862±0.475
		90	5.26±0.52	78.29±12.73		
		T0	1.80±0.17	296.09±116.83		
PLA_PCL	108±16	0	2.57±0.30	253.25±11.84	1078±175	1.732±1.359
		90	5.08±0.82	91.05±32.71		
		T0	2.48±0.37	306.09±14.44		
PCLPLA_PLA	111±23	0	2.02±0.12	168.73±28.60	1386±305	1.103±0.557
		90	6.25±0.47	111.16±15.06		
		T0	2.00±0.22	234.52±56.93		
PCLPLA_PCL	192±52	0	2.75±0.04	381.27±56.56	1085±245	1.800±0.880
		90	4.61±0.52	282.43±21.09		
		T0	1.92±0.66	392.82±204.56		

4. CONCLUSION

In this study, the effect of the polymer type used in the core and shell parts of the bicomponent fibers on the mechanical properties of vascular grafts is investigated. The results show that utilizing a strong polymer in the shell and a PCLPLA blend in the core enhances the strength of the material. Also, the PCL shell and PCLPLA core contribute to the elasticity and compliance values of the scaffolds. Thus, these grafts are considered sufficient in terms of mechanical properties and can also be evaluated for further cellular and biodegradation evaluations for optimization.

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