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Fabrication of PCL/PLA composite tube for stent manufacturing

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Abstract

This work presents the effect of Dip Coating process over the tube's features to obtain a PCL/PLA tube to stent purpose. The effects of withdrawal speed, number of cycles, and solutions concentration were studied. Four different tubes were fabricated and analyzed by Dynamic Mechanical Analysis (DMA), Degradation Rate, Surface Roughness, Thickness, and Uniformity.

Results have shown the strong influence of withdrawal speed and polymer's concentration over the tube's features. DMA and degradation results showed the limitations of PCL and PLA as material for the stent purpose, meanwhile the PCL/PLA composite tube showed a behavior closer to the stents requirements.

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Keywords: Dip Coating, Biodegradable Stent, Composite

1. Introduction

Since their introduction in the market in the early 1990s, nobody was able to predict the advantages that will occur in stent technology over the upcoming decades. Nowadays, stents are the main treatment modality for atherosclerosis. The coronary stent global market, primarily balloon-expanded, bare metal (BMS), and drug eluting stents (DES), was approximately $7.5 billion in 2015 and forecast stent sales will grow at double digit rates [1]. Since stenting appearances it became evident that this approach has significant limitations, such as vessel occlusion, restenosis or migration of the prosthesis. These problems have improved with the development of BMS and more recently, the DES both based on metallic structures.

Although metallic stents are effective in preventing acute occlusion and reducing late restenosis after coronary angioplasty, many concerns still remain, such as thrombosis and restenosis. Bioresorbable stents (BRS) were introduced to overcome these limitations with important advantages: complete bioresorption, mechanical flexibility, etc.

In the design of biodegradable stents several types of materials are currently been investigated: poly-L-lactic acid (PLLA) and magnesium have been the most promising materials [2], although there are other polymers suggested such as polycaprolactone (PCL) [3]. Regardless of material choice, the challenges associated with biodegradable materials remain similar; the mechanical properties, manufacturing process, and biocompability.

Due to these needs, there are numerous authors whose have been analyzing the properties of some different polymeric biodegradable materials. Wiggins et al. [4] found that the degradation rate of polyurethane increased with cyclic strain rate, whereas strain magnitude has essentially no effect employing a circular membrane devices in which vacuum was applied to one side of the membrane. This device applied bi-axial strain to the membrane in the middle region, and largely uniaxial strain in the outer region. Meital et al. [5] studied the effect of degradation on tensile mechanical properties and morphology of PLLA, PDS, and PGACL where PLLA emerged as the most promising materials of the study. Ruben et al. [6] demonstrated that the addition of POSS nanocores to the PCU imparts a type of protective, extending its resistance to degradation. Niels Grabow et al. [7] designed and produced a biodegradable slotted tube stent based on PLLA and P4HB polymers, carried out mechanical and degradation experiment.

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The results showed that the PLLA/P4HB stent allows rapid balloon-expansion and exhibited adequate mechanical scaffolding properties suitable for a broad range of vascular and nonvascular applications. Yang et al. [8, 9] studied the effect of cyclic loading on the in vitro degradation of PLGA scaffolds for 12 weeks. Their mode of deformation was unconfined compression of <5% strain at 1Hz for 8 h per day for 12 weeks and compared results with static controls. The authors have found that water absorption was higher in dynamic conditions and observed markedly higher reductions in mass, dimensions, and molecular weight when compared with static conditions. Vieira et al. [10] studied the evolution of mechanical properties of PLA-PCL fibers during degradation based on experimental data. The decrease of tensile strength followed the same trend as the decrease of molecular weight. More recently, Chu et al. [11], have analyzed the effect of fluid shear stress in the in vitro degradation rate of PLGA membranes. Their work showed that the fluid shear stress affects over the viscosity of the degradation solution, the ultimate strength and has a great effect on the surface morphology of PLGA membranes.

Despite, the efforts for understand and develop news fully biodegradable materials for medical applications, nowadays is still necessary to continue the study of new material or configuration of them, and the employed manufacturing process. In the stent industry, many steps are require until achieve an implantable stent. The original material should be dissolved to make the tube, by dip coating, for the subsequent laser cutting process, ending by a cleaner and sterilization processes. The effect of the parameter involved in these processes over the material properties are still unclear.

The ideal stent should be uniform, has smooth surface for a better vessel placing, fully corrosion resistant, vascular compatible, fatigue resistant, and visible using standard X-Ray and MRI methodology, and a good relation between hardness and soft. The above properties are interrelated and sometimes contradictory, requiring careful compromise.

The authors aim to analyze the effect of process parameters over the tube's physical features to obtain a PCL/PLA composite tube that accomplish with the stents requirement. The effect of withdrawal speed, the number of cycles, and the solutions concentration was studied. Four different tubes were made, namely, PCL, PLA, PCL/PLA, and PLA/PCL. The tubes were analyzed by Dynamic Mechanical Analysis (DMA), Surface Roughness, Dimensional Uniformity, in order to find the best tube for the stent purpose.

2. Material and Method

2.1. Dip Coating Machine

Dip coating techniques can be described as a process where the substrate to be coated is immersed in a liquid and then withdrawn with a well-defined withdrawal speed under controlled temperature and atmospheric conditions. Taking advantage of a 3D Printer Machine, we developed a Dip Coating Machine. A male stainless steel cores of 4 mm outer diameter are lodged in a superior support grip to the vertical axis. The process is defined by the start-up time, withdrawal speed, evaporation time, and number of cycles **(Fig. 1)**.

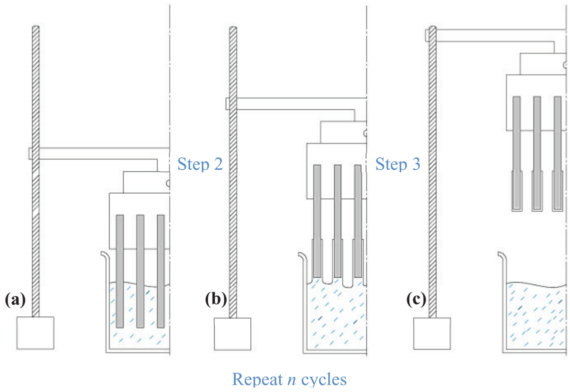

Fig. 1. Dip Coating Method (a) Start-up time (b) Withdrawal speed (c) Evaporation time

2.2. Materials

Polycaprolactone (PCL) Capa 6500® supplied by Perstorp and Polylactide (PLA) 3251D® supplied by NatureWorks were used as material for the experiments. PCL is a biodegradable polyester with a low melting point (60ºC) and a glass transition of about -60ºC. PLLA is a biodegradable thermoplastic aliphatic polyester derived from renewable resources, such as corn starch, or sugarcane. Their melting point is about 173–178 °C with a glass transition of 60–65 °C. Both PCL and PLA degradation is produced by hydrolysis of its ester linkages in physiological conditions and has therefore received a great deal of attention for using it as an implantable biomaterial for long term implantable devices, such stents, because of their properties **(Table 1).** The solvent employed were $CHCl_3$.

Table 1. Material Properties.

Material	Molecular Weight [g/mol]	Young Modulus [MPa]	Strain at Break [%]	Degradation Time [Months]
PCL	50000	470	700	>24
PLA	90000	108	3.5	12-24

2.3. Characterization

2.3.1. Physical Properties

To study the physical tube's characteristics, the samples were examined using Roughness Mitutoyo SurfTest SV-2000 Machine to measure the R_a along the longitudinal axis, Optical Microscope Nikon SMZ – 745T attached to a digital camera CT3 ProgRes to check the radial uniformity, and Micrometer Micromar 40EWV to measure the tube's thickness. Three measurements of each test were carried out to obtain more accurate results.

2.3.2. Mechanical Properties

The mechanical characteristic were measured by DMA employing the METTLER TOLEDO SDTA861e Machine. The dynamic storage modulus (E') are analyzed. The loss tangent is the ratio of loss modulus and storage modulus, which indicate the viscosity and elastic properties of material, respectively. The peak of loss tangent curve appears and can be defined as the glass transition temperature (T_g) of material. Three measurements of each sample were carried out to obtain more accurate results.

2.3.3. Degradation Rate

The degradation study were carried out submerging the samples in Phosphate Buffered Solution (PBS) at 37 ºC during 6 weeks. The samples were recovered after, 2, 4, and 6 weeks under the same conditions. Weight loss were evaluated by weighing in a METTLER TOLEDO Sartorius 2MP Scale, taking into account the original tube's weight after dip coating process (W_o), and the residual weight, after degradation that had completely dried (W_r). Weight loss percentage, $W_L\%$ was estimated with the following equation:

$$W_L\% = \frac{W_0 - W_r}{W_0} \cdot 100 \quad (1)$$

2.4. Design of Experiment

Based on a Central Composite Design (CCD) with 6 center points and alpha 1.22, 20 PCL tubes and 20 PLA tubes were made, (3 replicas of each one). Table 2 collects the levels selected. Analyzing the physical properties we selected the best parameters to obtain a tube for the stent purpose, namely, a uniform tube with the minimal Ra. All experiment were conducted in controlled room condition at 25 ºC and 50 % of humidity. The samples were dried in oven at 35 ºC for 48 hours to remove all the solvent content.

Table 2. Design of Experiment Levels.

Level	Withdrawal Speed (mm/min)	Polymer Concentration (w/v)	Cycles (#)
Low	50	3	40
Med	250	5	50
High	450	7	60

3. Results and discussion

3.1. Dip Coating Parameter Effects

Results have shown the strong influence of withdrawal speed over the layer thickness (Figure 2a). Both the PCL and the PLA have shown similar behavior. At low speeds the $CHCl_3$ contained in the solution dissolves part of the previous layer, making impossible the formation of a uniform wall. On the contrary, at fast speeds, the slight vibrations produced in the axis, generate inequalities on the tube's radial shape as can be seen from Figure 3. With regard to the polymer's concentration, its increase, raises the layer thickness following a near linear trend (Figure 2b). The best results were achieved with a concentration of 5% (w/v) both for PCL and PLA. Lastly, for a polymer concentration and withdrawal speed fixed, the number of cycles, seem to do not affect over the layer thickness directly, due to it mainly depends both on the polymer concentration and the withdrawal speed.

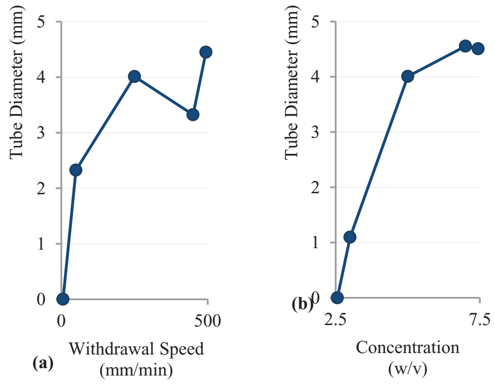

Fig. 2. Main effect plot for thickness (a) Withdrawal speed (b) Polymer concentration

Analyzing the roughness, its shows a downward trend according to withdrawal speed increases. With regards to the polymer's concentration, its reduction, lower the solution viscosity, helping to a better layers deposition, thus a minor roughness. According to the number of cycles, the results show an increases of the superficial roughness according to cycles raise. The increase of cycles, makes that the solution is exposed longer, increasing their concentration due to the $CHCl_3$ evaporation.

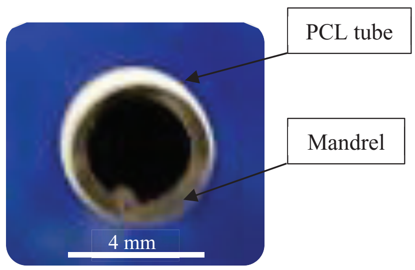

Fig. 3. Front View of the tube (tube's radial shape)

With regards to the uniformity, the samples have been strongly influenced by the withdrawal speed and solution concentration, where the lower data have left the best results.

3.2. PCL-PLA Composite fabrication

Based on the previous results, the parameter selected to develop the PCL – PLA composite tubes were 250 mm/min withdrawal speed both for PCL and PLA, 5 % (w/v), 10 cycles per layer, both for PCL and PLA to obtain 100 µm layers. Table 3 shows the tubes composition.

Table 3. Tubes Composition Layer

Sample	Layer 1 (100 µm)	Layer 2 (100 µm)	Layer 3 (100 µm)	Layer 4 (100 µm)
1	PCL	PCL	PCL	PCL
2	PLA	PLA	PLA	PLA
3	PCL	PCL	PLA	PLA
4	PLA	PLA	PCL	PCL

3.3. Physical Properties

The results have corroborated the behavior described in the section *3.1. Dip Coating Parameter Effects*. Nevertheless, it seems that the order of the layer deposition affect over the union of PCL - PLA. When the first layers are PCL (sample number 3) the resultant tubes have a largest R_a and a visible heterogeneity on their surface than the tubes which have PLA as first layer (sample number 4).

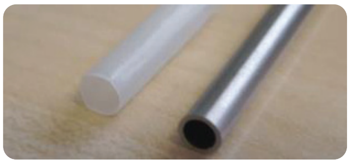

Fig. 4. PLA tube (left) and Dip Coating 316 SS mandrel

3.4. Dynamics Mechanical Analysis

The DMA results (Figure 5) have shown the strong different between PCL and PLA make clear their difficulty for the stent purpose. Nevertheless, the PCL – PLA composite has shown a middle E' that would be more appropriate for stent manufacture [12]. In this case, the order in the deposition layer did not show any influence over the dynamic modulus E'.

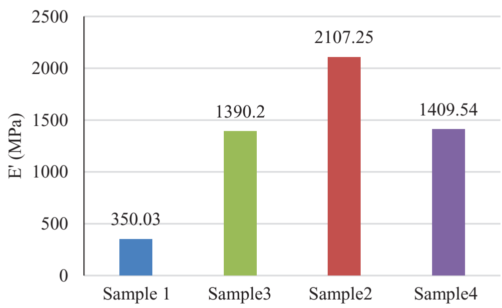

Figure 5. DMA Results

3.5. Degradation Rate

Results have shown the differences between PCL and PLA degradation rates. The composite tubes, both PCL-PLA as PLA-PCL have shown a medium weight losses, which make them, a good material for the stent purpose.

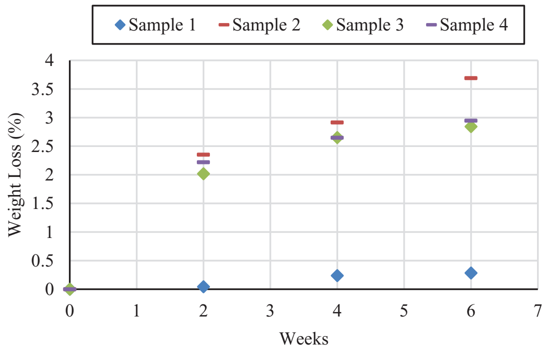

Fig. 6. Degradation rate of tubes

4. Conclusions

In this study, the dip coating parameters has been studied and selected to fabricate a PCL/PLA composite tube for stent manufacture.

The effect of withdrawal speed, the number of cycles, and the solution's concentration over the physical properties were studied. The results have shown the strong influence of withdrawal speed and polymer's concentration over the layer thickness and superficial roughness.

Four different tubes were fabricated with different order of layers, namely, PCL, PLA, PCL/PLA, and PLA/PCL. The tubes were analyzed by Dynamic Mechanical Analysis (DMA), Surface Roughness, Dimensional Uniformity, and Degradation Study in order to find the best tube for the stent purpose.

DMA results showed the limitations of PCL and PLA as material for the stent purpose, meanwhile the composite PCL/PLA tube showed a behavior close to the stent requirements. The degradation study corroborated the statement that the PCL/PLA composites could be a promise material for the biodegradable stents purpose.

This work is only a preliminary study that allow us to believe that a composite tubes made from PCL and PLA would be a good solution for the biodegradable stent market. Although the tests carried out are only one of many test that a stent should be go through to say that their properties are adequate, the work present is a good approximation of the potential of composite tubes.

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