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Extrusion as a manufacturing process for polymer micro-tubes for various bio-medical applications

Abstract: In various biomedical applications extrusion represents a common manufacturing process for polymeric semi-finished products. Extrusion allows the processing of a wide range of biomaterials, as well as different cross-sectional geometries. The present work focuses on the development of an extrusion process for polymer micro-tubes used for medical devices manufacturing, e.g. microstents for minimally invasive glaucoma therapy. Semi-finished products were manufactured by means of extrusion and dip-coating. Morphology was investigated using biaxial laser measurement and scanning electron microscopy (SEM). For the analysis of mechanical and thermal properties of the specimens uniaxial tensile testing and differential scanning calorimetry (DSC) were performed. While dip-coated micro-tubes reveal a smooth and homogeneous surface, SEM micrographs of extruded micro-tubes exhibit some longitudinal grooves. Mechanical properties of extruded and dip-coated micro-tubes are comparable, so that the presented extrusion process can be regarded suitable for the manufacturing of polymer micro-tubes in a sub-millimeter scale. A future improvement of nozzle design will allow for a smooth surface of extruded semi-finished products.

Keywords: extrusion; dip-coating; PLLA; ChronoSil; microstent; glaucoma drainage device

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1 Introduction

Glaucoma represents the leading cause of irreversible blindness worldwide [1]. Therapeutic approaches are based on the lowering of intraocular pressure (IOP). A reduction of baseline-IOP by at least 30% usually prevents progressive damage of retinal ganglion cells [2].

Currently, glaucoma drainage devices are available in various sizes, materials and designs with or without an IOP regulating valve. Based on previous work, extrusion is being investigated and evaluated as an alternative to dip-coating methods for the manufacturing of micro-tubes [3]. In the present work, these two manufacturing processes for tubular semi-finished products as a basis for glaucoma drainage devices were compared. For this purpose, biodegradable poly-L-lactide (PLLA) and non-biodegradable thermoplastic silicone-based polyurethane (ChronoSil) were fabricated.

2 Materials and Methods

2.1 Extrusion

Extrusion was conducted using a HAAKE MiniLab II (Thermo Fisher Scientific, Karlsruhe, Germany) extruder with contra-rotating twin screws. A 2-axis laser scanner (ZUMBACH Elektronik, Orpund, Switzerland) was used to monitor the outer diameter of the extrudate during the extrusion process.

The polymers used and the corresponding extrusion parameters are summarized in Table 1. A nozzle with an outer and inner diameter of 2.30 mm and 1.75 mm was used for the shaping of the extrudate, respectively. The haul-off speed was selected accordingly so that outside diameters ranging between 300 µm and 400 µm were achieved.

Table 1: Setting parameters of the extrusion process for ChronoSil 80A and PLLA-Resomer L210

Material	Extruder setting parameters
ChronoSil 80A	T_E = 210°C, n_E = 15 1/min T_D = 205°C, n_A = 32.9 mm/s T_{FF} = 16°C, n_{FF} = 5%
PLLA-Resomer L210	T_E = 210°C, n_E = 8 1/min T_D = 225°C, n_A = 16.9 mm/s T_{FF} = 16°C, n_{FF} = 5%

T_E – Temperature of the extruder, n_E – Rotation speed of extruder screws,
T_D – Temperature of the nozzle, n_A – Haul-off speed
T_{FF} – Temperature of the force feeder, n_{FF} – Power of force feeder

2.2 Dip-coating

Manufacturing of the base body was conducted, using semiautomatic dip-coating process (KSV NIMA Dip Coater, Biolin Scientific Holding AB, Stockholm, Sweden) and dipping mandrels with a diameter of 0.2 mm. A polymer solution based on 4% (w/v) ChronoSil 80A (AdvanSource Biomaterials Corp., Wilmington, MA, USA) in chloroform (Sigma Aldrich Corp., St. Louis, MO, USA) was used. The humidity and temperature during processing were 37% and 23.3°C. On average, one mandrel was dipped 6 times in total. After removal of dipping mandrels the base bodies were stored in a vacuum drying cabinet for four days at 40°C.

2.3 Morphological characterization

The outer tube diameter was measured in 0.2 mm increments by means of a two-axis laser scanner (ODAC 32 XY, Zumbach Electronic AG, Orpund, Switzerland). The samples were each prepared with 40 mm length, $n = 10$. The measurement of the inner diameter was performed in tubing cross-sections. Wall thickness was measured on the basis of cross-sectional images by means of a stereomicroscope with UC30 digital camera (Olympus SZX16, Hamburg, Germany) and the software Stream 1.7.

Scanning electron microscopy (SEM) (Quanta FEG 250, FEI/Thermo Scientific) was used for cross-sectional and surface analysis. In some cases, the images were used to also check outside and inside diameters and wall thickness.

2.4 Mechanical characterization

The material tests were performed using a universal testing machine Zwick/Roell Z2.5/TN (Zwick GmbH & Co. KG, Ulm, Germany) with a 10 N load cell. According to stent application testing temperature was kept at 37°C. For this, the tubes were cut to a length of approximately 40 mm. When calibrating the universal testing machine, it was ensured that the clamping length was set to 10 mm. A cross-head speed of 1 mm/min and 40 mm/min was used for an elongation up to 0.25% and for further elongation, respectively. The following parameters are determined: elastic modulus E, tensile strength σ_m and elongation at break ε_B.

2.5 Thermal characterization

The analysis of the thermal behavior of extruded and dip-coated tubes was carried out using differential scanning calorimetry DSC1 (Mettler Toledo, Greifensee, Switzerland) in a temperature range of 25 – 210°C and with a heating rate of 10 K/min for PLLA. ChronoSil 80A was analyzed in the temperature range -50 – 200°C and at a heating rate of 10 K/min. The sample weights were ranging from 1.7 mg to 2.5 mg. The data was analyzed with respect to glass transition (T_g) and melting temperature (T_M).

3 Results and Discussion

3.1 Morphological characterization

For all samples, a uniform outer diameter in the range of 0.3 mm to 0.4 mm could be achieved (see Figure 1).

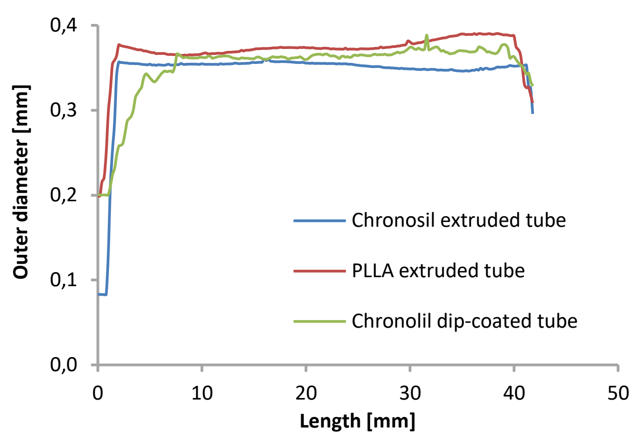

Figure 1: Representation of the average (n = 10) outer diameter per length as an overview of extruded samples of PLLA L210, Chronosil 80A and dip samples of Chronosil 80A.

The microscopical and SEM cross-sectional images were used to determine the wall thickness of tubes (see Figure 2). Five cross sections were examined randomly. For each cross-section five values for wall thickness were noted and an average value was determined from the data. The mean values are summarized in Table 2.

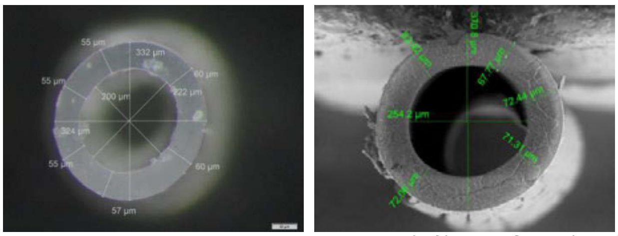

Figure 1: Representative microscopical (left) and SEM (right) cross-section of an extruded sample Chronosil 80A with measurement of outer diameter, inner diameter and wall thickness

Table 2: Mean values with standard deviation of outer diameter, inner diameter and wall thickness of the extruded samples PLLA L210, ChronoSil 80A and dip-coated samples ChronoSil 80A

	PLLA L210 extruded tube	**ChronoSil 80A extruded tube**	**ChronoSil 80A dip-coated tube**
Outer diameter [µm]	384 ± 11	374 ± 17	366 ± 7
Inner diameter [µm]	320 ± 8	255 ± 12	183 ±3
Wall thickness [µm]	31 ± 7	57 ± 11	92 ± 5

The dip-coated micro-tubes had an average inner diameter of 183 µm. The reduction is due to the fact that when removing tubes from mandrels (0.2 mm diameter), the semi-finished products have slightly contracted due to inner tension.

SEM cross-sectional images show the differences in wall thickness. While dip-coated micro-tubes show a smooth and homogeneous surface, the extruded micro-tubes show some longitudinal grooves. The reason for this is probably the nozzle surface texture. The slightly roughened surface of submerged tubes is related to evaporation of the chloroform.

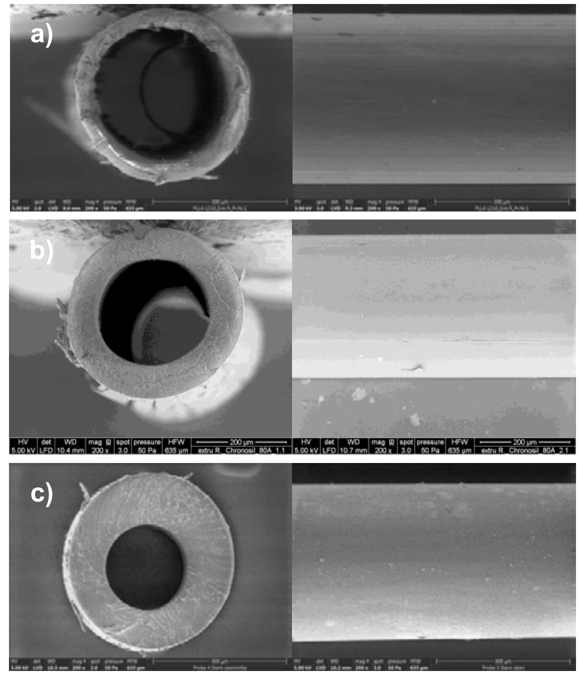

Figure 2: Representative SEM image of cross-section (left) and surface (right) of extruded tubes made of PLLA L210 (a), Chronosil 80A (b) and dip-coated samples made of Chronosil 80A (c)

3.2 Mechanical characterization

For mechanical characterization, 10 samples were tested from each of the three batches. The previously determined cross-sectional geometry was taken into account in the tensile tests. From the measurement curves elastic modulus E, tensile strength σ_m and elongation at break ε_B were determined. The results are summarized in Table 3.

Table 3: Mean values with standard deviation of elastic modulus E, tensile strength σ_m, elongation at break ε_B and cross sectional area A for the extruded samples PLLA L210, ChronoSil 80A and dip-coated samples ChronoSil 80A

	PLLA L210 extruded tube	**ChronoSil 80A extruded tube**	**ChronoSil 80A dip-coated tube**
E [MPa]	2142 ± 352	5,8 ± 0,6	6,1 ± 1,3
ε_B [%]	367 ± 133	671 ± 146	602 ± 88
A [mm^2]	0,03 ± 0,00	0,05 ± 0,00	0,08 ± 0,01
σ_m [MPa]	256 ± 111	225 ± 90	223 ± 75

As expected, elastic modulus of PLLA (2142 ± 352 MPa) is substantially higher compared to ChronoSil samples with a value of 5.8 ± 0.6 MPa. However, there were no changes in the mechanical properties due to the manufacturing process.

3.3 Thermal characterization

Figure 4 shows DSC curves of extruded und dip-coated tubes of ChronoSil 80A compared to extruded PLLA tubes. The glass transition temperature of the ChronoSil samples is identical at approx. -32°C despite different manufacturing processes. Extruded ChronoSil samples show an endothermal peak at approx. 60°C , while this peak only appears at approx. 90°C and another one at 150°C in the dip-coated samples. This effect may be explained by the different manufacturing processes. PLLA shows cold crystallization at approx. 90°C due to the rapid cooling during extrusion.

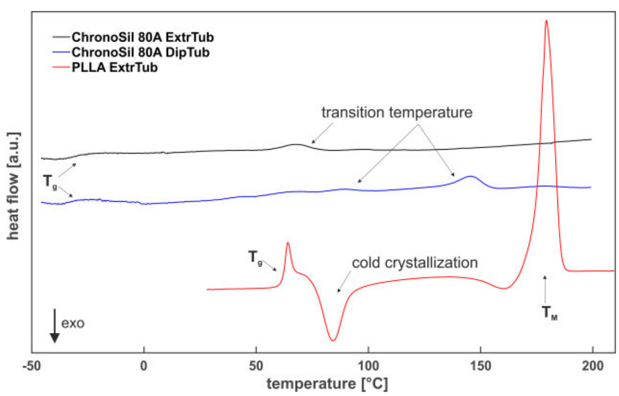

Figure 3: DSC curves of the extruded (black) and dip-coated ChronoSil 80A (blue) compared to extruded PLLA (red)

4 Conclusion

The results show that the presented extrusion process is suitable for the manufacturing of polymer micro-tubes in a sub-millimeter scale. Advantages of extrusion include: a reduced production time, only a single process step and absence of chloroform. The geometry and surface finish of extruded semi-finished products can be improved in the future by improving the nozzle quality. The mechanical tests with ChronoSil micro-tubes demonstrate that the manufacturing process has no influence on the mechanical properties. However, ChronoSil samples show differences during thermal analysis, which may be explained by the manufacturing process. However, this effect will have to be investigated more closely in the future.

Author Statement

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