5° coBeF Congresso Brasileiro de Engenharia de Fabricação

ABCM COMPROMETIDA COM A PROMOÇÃO DO DESENVOLVIMENTO DA ENGENHARIA E DAS CIÊNCIAS MECÂNICAS
ASSOCIAÇÃO BRASILEIRA DE ENGENHARIA E CIÊNCIAS MECÂNICAS

V CONGRESSO BRASILEIRO DE ENGENHARIA DE FABRICAÇÃO
14 a 17 de abril de 2009 - Belo Horizonte - Minas Gerais - Brasil

MANUFACTURING OF DRUG DELIVERY DEVICE BY SELECTIVE LASER SINTERING USING OF POLYCAPROLACTONE AND POLYETHYLENE

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Abstract: *The selective laser sintering is a technical that uses powder form material for built specimens through of the sintering by laser beam, layer-by-layer. Between differents applications, highlight in the biomedical area, as in manufacture of the scaffolds and controlled drug delivey device, because it allows the built of matrix porous of the biocompatible ans biodegradable materials. In this work, high density polyethylene and polycaprolactone specimens were built by selective laser sintering with different particle sizes (106-125 µm and 150-212 µm), for application as drug delivery device. The specimens were characterized by density measurements, scanning electronic microscopy (SEM) and flexural test. The results showed that the specimens with small particle size had a significant level of open pores, as shown by microscopy and density analyses. The mechanical properties of specimens prepared with bigger particles presented lower values flexure modulus and stress due to a lower sinter degree, compared the size of particles smaller.*

Keywords*: Rapid Prototyping, Selective Laser Sintering, drug delivery devices, high density polyethylene, polycaprolactone.*

1. INTRODUCTION

Selective Laser Sintering (SLS) is a Rapid Prototyping technique that creates 3D objects by the sinter of powder materials using infrared laser beams (Jacobs, 1993; Upgraft and Fletcher, 2003; Jacob, 1999; Jacob, 1999; Yeong et al, 2004; Hur et al, 2001; Gibson and Shi, 1997; Salmoria et al, 2007; Tan et al, 2003; Salmoria et al, 2008).

Low et al. (2001) investigated the construction of drug delivery devices by the technique of selective laser sintering (SLS). An important criterion required in the devices architecture are interconnected pores which can enable drugs to be embedded before the implantation and diffused into the biological enviroment. Using the technique of RP, macrostructure and porosity of the devices can be controlled varying the parameters of process (Low, 2001).

In drug delivery devices, the pore size is an important factor for controlling the release (Massod, 2007). Salmoria et al. (2007) studied the construction of porous parts, built by SLS, with different particle sizes of the high density polyethylene. This study showed that the pore size is a function of the particle size and the sintering degree. Williams et al (2005) investigated the built of the porous PCL scaffolds fabricated via selective laser sintering (SLS) and that show great potential for replacement of skeletal tissue. According to the authors PCL scaffolds have previously been created with a variety of solid free-form fabrication techniques, however, the fabrication and characterization of PCL scaffolds with varying internal architectures and porosities made through SLS has not been reported.

High density polyethylene (which can be used as implant) is stable, extremely inert, with minimal foreign body reaction, and it does not degrade over time (Quatela et al, 2008). PCL is a polar bioresorbable polymer presenting low glass transition and melting temperature (-60 and 60^{o} C). The PCL amorphous phase presents high molecular mobility at body temperature what can aid its degradation by hydrolysis. The hydrolyzed products are reabsorbed by the body with minimal reaction of tissue (Tay, 2007). In this work, high density polyethylene and polycaprolactone specimens were built by selective laser sintering using particles size of 106-125 and 150-212 µm. The specimens were characterized by density measurements, scanning electronic microscopy (SEM) and flexural test.

2. MATERIALS AND METHODS

2.1 Polymeric materials

The powder polymers used in this study was the High Density Polyethylene (HDPE), HD7555 Ipiranga, which has a melting temperature (Tm) of 127.7 °C (according to differential scanning calorimetry) and Polycaprolactone (PCL), which is provided by the Sigma-Aldrich company, with molecular weight 80,000 g / mole and melting temperature of 60 oC. The PCL was grinded cryogenically in a mechanical grinder and sieved. The particle size ranges used for two polymers were 106-125 and 150-212 μm.

2.2 Specimens fabrication

The specimens were manufactured in a prototype equipment of selective laser sintering, installed in CIMJECT laboratory. This equipment has a CO_2 laser with 9W power and beam diameter of 250 μm. The work was performed in air atmosphere. The laser scan strategy used was single direction type (i.e. "zague type"). The HDPE sintering was performed using 4.9 W, which gives 0.44 $J.mm^{-2}$ as energy density, and 44.5 mm/s of laser scan speed. On the other hand, the PCL was processed with 1.8 W, representing 0.18 J.mm-2 as energy density, and 39.8 mm/s of laser scan speed. The specimens for both polymers were built with approximately 200 μm layers.

2.3 Scanning Electronic Microscopy

The morphology of the surface and cryogenic fracture surface of the specimens were examined with a scanning electron microscope (SEM), model Phillips XL30. In addition, the specimens were coated with gold in a Bal -Tec Sputter Coater model SCD005.

2.4 Density determination

The apparent density was obtained using a pycnometer of 50 cm^3. It was used four specimens with 35 x 5 x 1.4 mm that was immersed during four hours in isopropyl alcohol to obtain the average measurement. The volumetric density was calculated using the dimension and mass values.

2.5 Mechanical test

The specimens were tested in a single cantilever clamp, with controlled force rate of 2N/min, using a DMA Q800 equipment from TA instruments.

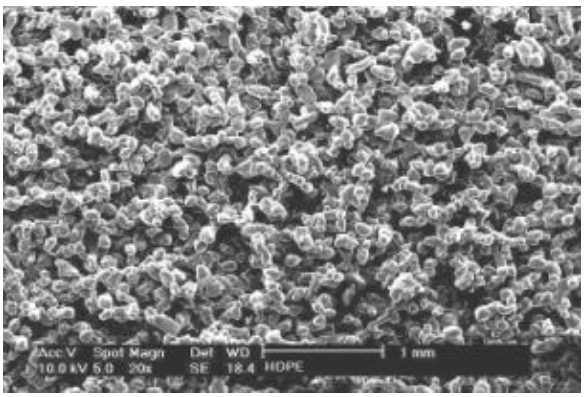
3. RESULTS AND DISCUSSIONS

The figures (1) and (2) show, respectively, the micrographs of the HDPE and PCL specimen surface and its cryogenic fracture. It was observed in SEM analysis of the HDPE specimens the coalescence particles and that the sintered HDPE specimens presented interconnected pores distributed throughout the structures. The micrographs of its cryogenic fracture show that the specimens present microstructure with a high sintering degree within large necks between the particles.

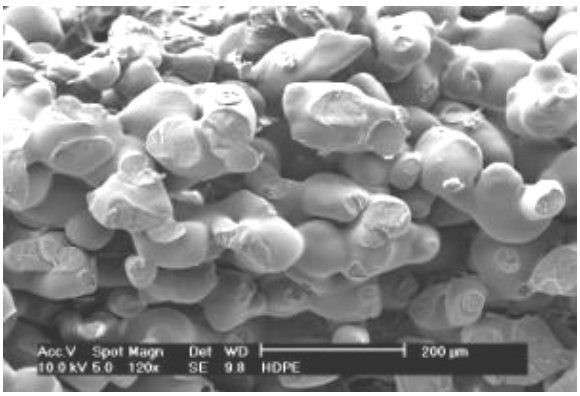
The PCL specimens with particles of 106 – 125 μm presented strong coalescence of the particles due to the lower melting temperature compared to HDPE and the higher absorbance of laser energy by the polar esters groups. The sintered PCL specimens presented interconnected pores distributed throughout the structures as can be noted by the micrographs of its cryogenic fracture.

The table (1) presents the theoretic, volumetric and apparent density values for these two materials, prepared with different particles sizes. The measured volumetric densities were 0.512 and 0.560 g/cm3 for HDPE, and 0.577 and 0.510 g/cm3 for PCL specimens with particles size of 106 – 125 and 150 – 212 μm, respectively. The measured apparent densities were 0.774 and 0.749 g/cm3 for HDPE and 0.911 and 0.708 g/cm3 for PCL specimens, respectively, for the same particles sizes as described above.

The general porosity (open and close porous) was from 40 to 56 % of porosity in the specimens. The relationship between values of apparent density (close porous) and volumetric density (porosity total) indicates the existence of a significant level of open porosity, 28 and 20% for HDPE; 29 and 17% for PCL with particles size of 106 – 125 and 150 – 212 μm, respectively. The specimens built with large particles size had higher volume of close porosity.



106 - 125µm



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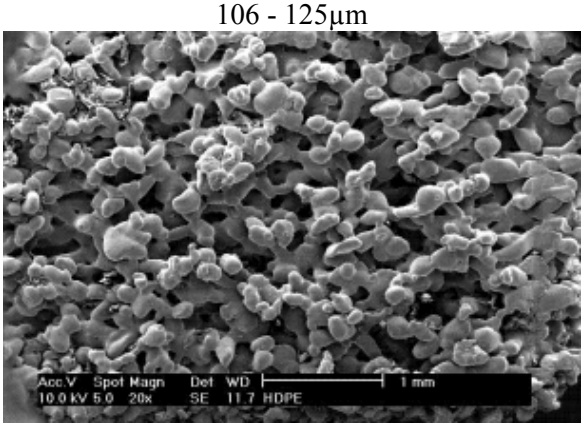
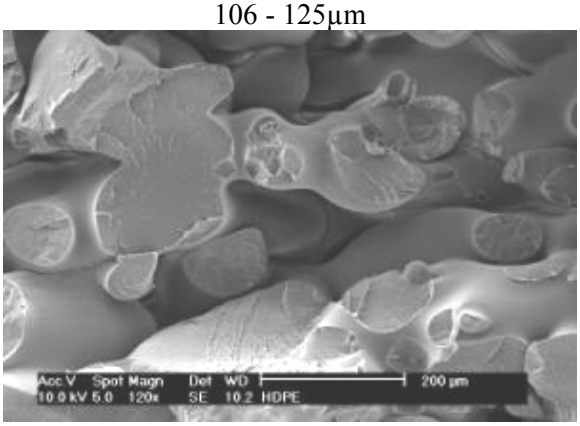
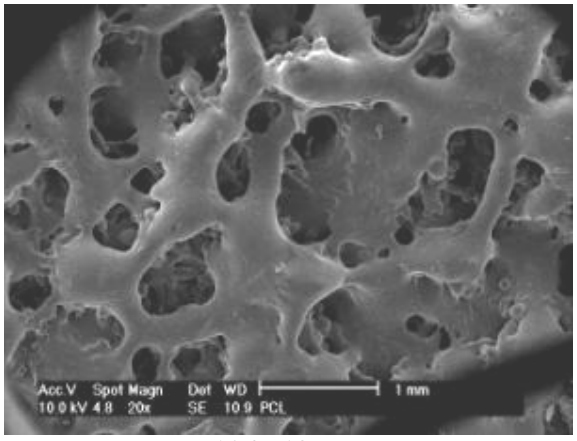


150 - 212µm

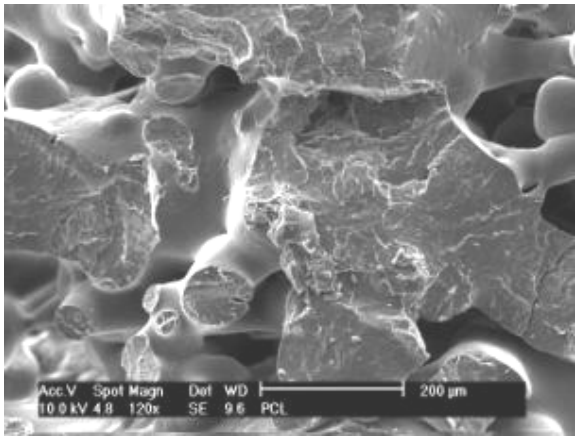


150 - 212µm

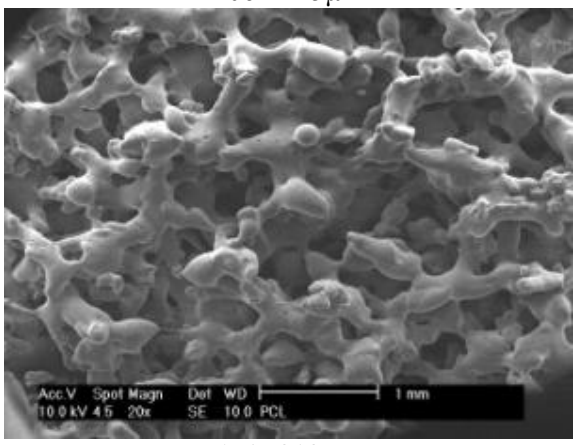
Figure 1 - Micrographs of HDPE specimens surface (left) and its cryogenic fracture (right).



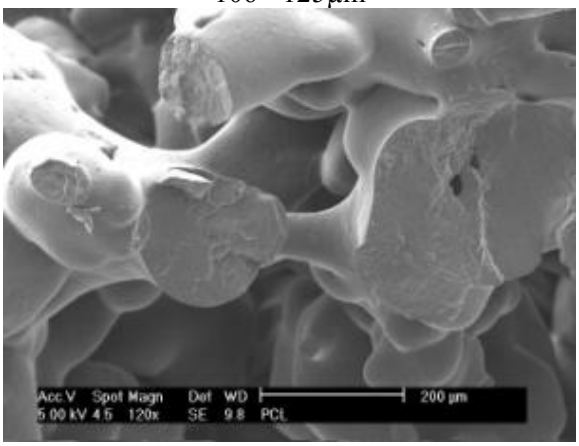
106 - 125µm



106 - 125µm



150- 212µm



150- 212µm

Figure 2 - Micrographs of PCL specimens surface (left) and its cryogenic fracture (right).

Table 1. Values of theoretic, volumetric and apparent density of the HDPE and PCL specimens prepared with different particles size.

Material (particle size)	$\rho_{theoretic}$ (g/cm^3)	$\rho_{volumetric}$ (g/cm^3)	$\rho_{apparent}$ (g/cm^3)
HDPE (106-125 μm)	0.950	0.512	0.774
HDPE (150-212 μm)	0.950	0.560	0.749
PCL (106-125 μm)	1.145	0.577	0.911
PCL (150-212 μm)	1.145	0.510	0.708

The Figure (3) shows stress versus strain curves for the specimens fabricated with different particle sizes of the HDPE and PCL. Since the equipment had a limited force, the failure was not verified on PCL specimens; the stress values were standardized and obtained at 12% for HDPE and PCL. The HDPE and PCL specimens presented a higher average flexural modulus for 106-125 μm particle size (105.1 for HDPE and 349.2 MPa for PCL) than the 150-212 μm particle size (103.6 and 130.7 MPa), as shown in Tab. (2).

This result is expected due to the higher degree of sintering and the number of necks per area of the lower size particles. The average value of strain was higher for the large particles size (150-212 μm). As the results suggested, the smaller particles size have a larger surface contact area, contributing to the increase the sintering degree (particle connections) and resulting in more number of necks per area.

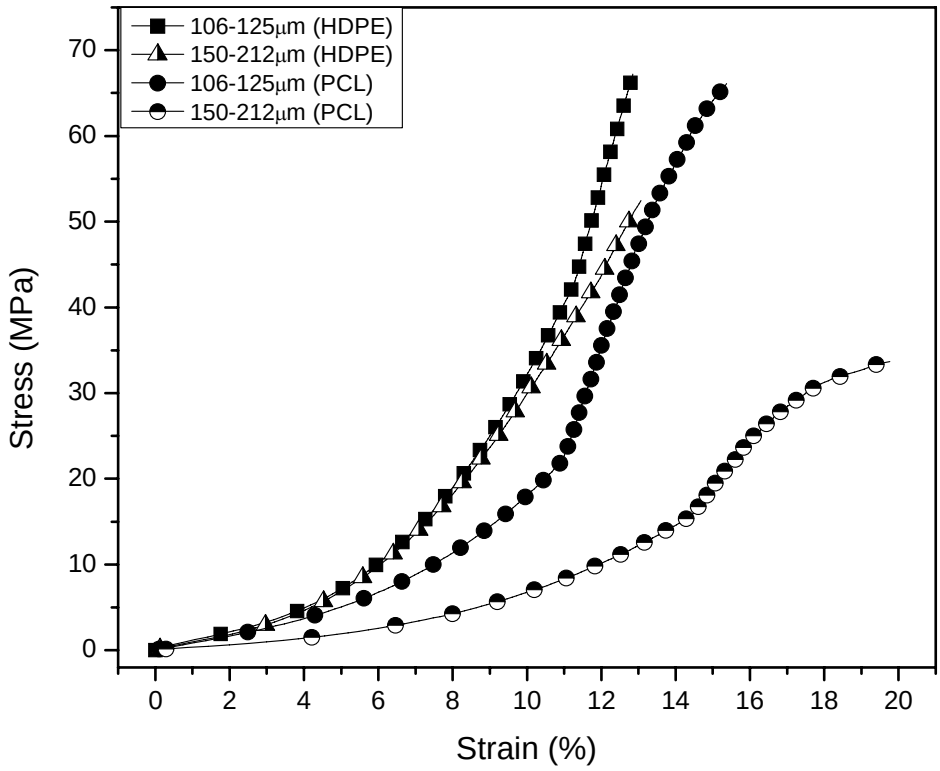


Figure 3. Stress versus strain curves for the HDPE and PCL specimens prepared with different particles size.

Table 2. Average mechanical properties of the HDPE and PCL specimens prepared with different particles size.

Material (particle size)	Flexure Modulus (MPa)	Stress (MPa) at 12%
HDPE (106-125 μm)	105.1	55.62
HDPE (150-212 μm)	103.6	43.74
PCL (106-125 μm)	349.2	41.16
PCL (150-212 μm)	130.7	12.05

4. CONCLUSION

The characterization by microscopy and density of HDPE and PCL specimens, prepared by SLS using different particle sizes, showed that the specimens have a significant level of open pores. The mechanical properties of specimens prepared with bigger particles presented lower values of flexural modulus and strength due to a lower sintering degree, compared with smaller particles size.

This study showed that the SLS technology can be applied in areas such as drug delivery devices manufacturing, considering that it generates porous specimens and permits for that the use of inert and bioresorbable materials, like as HDPE and PCL.

5. ACKNOWLEDGEMENTS

The authors would like to thank FAPESC, CAPES, CNPq and FINEP for the financial support.

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7. RESPONSIBILITY NOTICE

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