RADIOPAQUE MATERIAL FOR 3D PRINTING SCAFFOLDS

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Abstract

The so called "Additive manufacturing" is a new manufacturing process which consists in translating virtual solid model data into physical models in a quick and easy process. The most known example is 3D printing. In the present work, this novel technology will be used to print scaffolds with biomaterials.

Due to the problems that arise when controlling the clinical course of an implant, graft or polymer inside the human body, an innovative idea has emerged: it consists in incorporating particles of barium sulfate in order to increase the radiopacity of the polylactide (PLLA) and thus making these materials visible to X-rays.

Accordingly, $BaSO_4$ loaded PLLA composites were prepared via melt-blending and then injected for further characterization by thermal transitions, mechanical properties, morphology and radiopacity. X-ray analyses confirmed the enhanced radiopacity of the $BaSO_4$ filled composites in comparison to their unfilled counterparts. It is demonstrated that the loads not only contribute to the material's radiopacity, but also dramatically improve its ductility. As an illustration, the incorporation of 10 wt.% of $BaSO_4$ particles resulted in an outstanding 1647% and 3338% increase in toughness and elongation of PLLA matrix, respectively. In view of the good properties of these materials, they will be used for 3D printing. Through this technique it can be molded with any shape in a matter of minutes, making the use of this technology appealing for further innovations.

1. Introduction

Tissue engineering emerged from the need to repair a tissue or organ failure due to damage or injury. This area of knowledge comprehends different fields, such as the Materials Engineering, the Biology and the Medicine. During the last decade the number of studies related to tissue engineering has significantly increased. Due to all these efforts, currently, many different tissues and organs such as vascular graft [1–3], skin graft [4–6] and bone [7–9] amongst others can be replaced, resulting in the improvement of the quality of life of the human being. It should be highlighted that the idea of combining materials engineering and biology began in 1960 with treatments for skin burns. The idea was to use a synthetic skin for burns victim like a symptomatic therapy. However, it was in 1980 when a great leap on this topic was performed [10].

Focusing on biomaterials, during the last decade the tissue engineering applications have moved forward to the use of biodegradable and bioactive materials. One application for these materials can be the graft or bone implants. Unlike traditional metal implants, polymer implants have the advantage of enabling the regeneration of the tissue or the bone, and disappearing some time after the procedure through the absorption by the body. Therefore, in the last years the polymers and especially the biocompatible polymers have experienced a great increase in both research and practical applications. One of the most used polymers nowadays are the polyesters because of their great diversity. Amongst the most used polyesters for medical applications, it can be cited the polylactide (PLA) and their derivatives [11].

Despite all the advantages that these materials offer in comparison to others, their use has been limited so far, due to the fact that it is not possible to monitor the implant properly. In order to overcome this problem, it was decided to mix these polymers with radiopaque markers. As a consequence, the polymer becomes visible to the X-rays. It should be noted that X-ray visible substances are those with high atomic weight, such as barium sulphate ($BaSO_4$), bismuth salts, tantalum or tungsten.

Although alternative radiopaque markers have been proposed,[12-15] barium sulphate ($BaSO_4$) is currently the most commonly used in medical applications [16]. The addition of radiopaque markers like $BaSO_4$ to the polymer matrix is a method extensively used by surgeons for accurate placement and it also enables the surgeon to monitor any migration of the implant over time [17,18]. Several studies have investigated the effect of $BaSO_4$ on the mechanical properties of different polymers, such as polymethylmethacrylate [19-21], polypropylene [22], or polyurethane [23]. It has been demonstrated that a large amount of $BaSO_4$ (30-40 %) has a detrimental effect on both the static and fatigue strength of the bone cement[20]. Such formulations are used for spine reconstructive surgery, while bone cement used to fix joint prostheses contains between 9-13 % $BaSO_4$, being a value of 10% the most common percentage [24,25].

As mentioned before, these materials can be used for tissue regeneration. For that purpose, they will be converted and manufactured into 3D scaffolds. However,

3D printing is one of the most promising techniques. The additive manufacturing process, which has experimented a rapid growth during the last decade, is usually defined as the conversion of a computer aided design (CAD) model into a real model through a quick and easy process. The most widespread example of this technology is the 3D printing, which has been already implemented in various applications for the automotive and aerospace industries and also within the medical field. The use of this technology has gained a great importance in recent years, and different modes of printing have been developed specifically for this field. The different types of 3d printings depend on the mode in which the printing is performed. In the present work we carried out a 3D impression by deposition of the melted material (FDM) layer by layer.

Using this technique, practically any material can be printed. Moreover, it allows to control the geometry and the pore size of the scaffolds which are crucial parameters for promoting cell growth and differentiation.

The aim of the present study is to make scaffolds with radiopaque composite materials. In order to achieve this goal, a 3D-bioploter printer is used. As this printer is based on the FDM technology, the thermal and rheological behaviour of the materials has been studied.

Once the scaffold is printed, the mechanical properties of the scaffold are studied. By adding radiopaque particles, the mechanical properties of these scaffolds are improved in comparison to the scaffolds of unfilled PLLA.

2. Experimental part

For appropriate use of the 3D printing it is necessary to study the rheological and thermal behavior of polymers. The parameters involved in the process of printing must be controlled in order to guarantee the correct performance of the printed product. Printing has to be performed within very strict ranges of temperature, printing rate and pressure; otherwise good printing will not be achieved: as a consequence a proper study of the basic properties of the material has been performed.

The first step to perform is the processing. The $BaSO_4$ particle sizes ranged from 0.75 to 1 µm. PLLA samples containing 10.0 wt.% of $BaSO_4$ were prepared by melt blending. Firstly, the composites were obtained using a Vertical DSM Xplore Model 5 mini-mixer. Subsequently, dumbbell-shaped samples were prepared by a mini-injection in a Micro Injection Moulding Machine 10cc, in order to obtain the mechanical properties of the material. Unfilled PLLA specimens, processed in the same conditions mentioned above, were used as a test control.

Once the material is processed, the thermal and rheological characterization of the material was performed. Thermal transitions of the samples were determined by means of differential scanning calorimetry on a DSC 2920 (TA instruments), and thermogravimetric analyzer (TGA Q50-0545, TA Instruments) under a nitrogen flux of 60 mL min_1. Regarding the rheological properties, the dynamic viscoelasticity was analysed in order to determine the frequency and temperature limits of the terminal zone, with the aid of an ARES-G2 rheometer (TA instruments).

Scanning Electron Microscope (SEM) and Transmission Electron Microscopy (TEM) were used to study the morphology and dispersion of the $BaSO_4$ particles in the composites.

Due to the fact that it is a radiopaque material, radiographs were taken to determine the RO of the polymer with a standard clinical machine. Five 1 mm thick specimens were irradiated with the X-radiographic standard clinical machine to get a radiograph. Subsequently, the relative RO was determined by comparing the RO exhibited by a PLLA sample containing 90 wt.% of $BaSO_4$ particles. The free image editing software ImageJ was used to measure the gray values of the $BaSO_4$ and the composites in the resulting image. The relative RO of the disc was calculated by using the equation (1):

$$RO = \left[\frac{G_c - G_b}{(0.90 \times G_{BaSO_4}) - G_b}\right] \times 100\ \%$$

Where Gc, Gb, and G_{BaSO4} are the gray values of PLLA/$BaSO_4$, background and $BaSO_4$ respectively, for the same specimen thickness.
Once all the characteristics of the material are known, the impression begins. After the printing, the scaffold was characterized thermally and mechanically.

3. Results

As a common practice in the composite materials field, the dispersion of the samples was analyzed. Figure 1 shows the dispersion of the composites by TEM. These images reveal individual particles of $BaSO_4$ randomly and homogeneously dispersed as a consequence of the fine dispersion in the PLLA matrix.

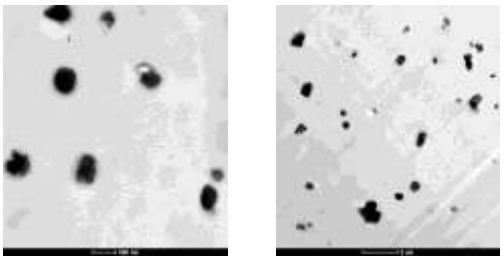

Figure1. *TEM microscopy images of PLLA/BaSO4 composites containing 10 wt. % of BaSO4.*

With regard to the thermal properties, the presence of $BaSO_4$ in the composite did not promote the overall crystallinity of the PLLA, whose values stayed practically constant. In contrast, the thermal stability of the materials increased slightly when the loads were added.

Moreover, it was observed an outstanding improvement in the ductility of the material processed by injection. For instance, PLLA/BaSO4 composites with 10 wt. % of $BaSO_4$ showed around 135 % of elongation at break. Against the fragility that PLLA has. PLLA has around 4% of elongation before failure.

$BaSO_4$ (%)	E (MPa)	σ_r (MPa)	ε_r (%)	TT (J/m^3)
0	1315±119	45.3±9.4	3.9±0.3	3.6±0.2
10	1426±137	54.5±3.5	134.1±6.5	62.9±4.6

Table 1. *Mechanical properties of neat PLLA and PLLA/ PLLA/$BaSO_4$ 10.0 wt. % of $BaSO_4$.*

Table 1 shows the mechanical properties of neat PLLA and PLLA/$BaSO_4$ composites containing 10.0 wt. % of $BaSO_4$. An increase in the amount of $BaSO_4$ within the composite leads to better monotonic mechanical properties. This fact is of paramount importance regarding the ductility parameters such as the elongation at break, being obtained an increase of 3338 % (from 3.9±0.3 to 134.1±6.5) when comparing neat PLLA and PLLA/$BaSO_4$ composite with 10 wt. % $BaSO_4$. For this case, the monotonic strength parameters such as the ultimate tensile strength increase moderately, roughly 20.5% (from 45.3±9.4 MPa to 54.5±3.5 MPa). Regarding the tensile modulus, an increase of 8% (from 1315±119 to 1426±137 MPa) was observed.

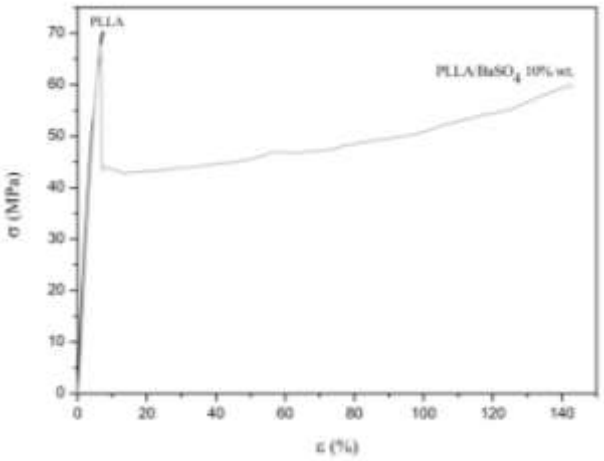

Figure 2.*Tensile stress-strain behavior of a) neat PLLA, and PLLA/$BaSO_4$ composites with b) 10.0 wt. % of $BaSO_4$*

In the Figure 2 the monotonic stress-strain curves of neat PLLA and PLLA/$BaSO_4$ composite are shown together. As it can be observed, the PLLA alone shows the typical behavior of brittle materials, with the final rupture at the end of the elastic deformation, showing no plasticity at all. However, the PLLA/$BaSO_4$ composite with 10 wt. % $BaSO_4$ shows a dramatically different behavior, that of a plastic material, with a much higher plastic zone. As a consequence, the tensile toughness, that is, the energy stored per unit volume within the material in the moment of the final rupture, can be mathematically interpreted in terms of the area bellow the stress-strain curve. The tensile toughness increased by 1647 % from 3.6±0.2 J/m^3 for neat PLLA to 62.9±4.6 J/m^3 for PLLA/$BaSO_4$ composites with 10 wt. % of $BaSO_4$. These results explain the modest increase in terms of strength parameters, and the outstanding enhancement of the ductility parameters

By the addition of $BaSO_4$ to the PLLA matrix, an increase in radiopacity could be observed. As it has been commented previously, the $BaSO_4$ content to fix prostheses is between the range 9-13 %. Figure 3 shows X-radiographies of neat PLLA and PLLA/$BaSO_4$ composite with 10 wt. % of $BaSO_4$. The analysis of the images calculated by eq. 1 showed an increase of 15 % in RO.

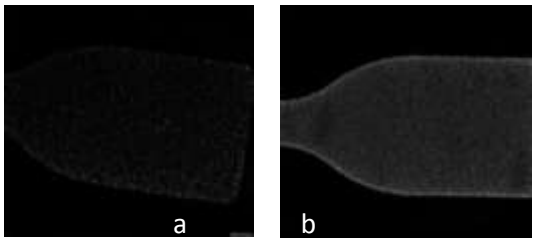

Figure 3. *Radiopacity of a) neat PLLA and b) PLLA/$BaSO_4$ composites with 10.0 wt. % of $BaSO_4$.*

The viscosity of the material is a critical criterion for 3D printing as it determines the feasibility of the impression (the maximum viscosity that the machine admit was 10^5 Pa s). Thus, the viscosity of the composite was determined via rheology measurements. As expected its viscosity was higher than PLLA alone, but still in the range for impression

As the properties of the material are suitable for the impression, it begins with the construction of scaffolds. As shown in Figure 4, these can be obtained by this method of processing materials.

Figure 4. *Scaffold of PLLA/$BaSO_4$ manufactured by 3D printing*

4. Conclusions

Polylactide/barium sulphate composite system, that has good properties obtained in solid state (i. e. injected pieces or sheets obtained by compression molding) could be 3D printed.

Due to the radiopacity and the great toughness of this material, a broad range of possibilities of applying this composite as fixation devices or bone reconstruction in the biomedical field should be considered for future studies.

Acknowledgments

Authors are thankful for funds of Basque Government (GV/EJ) Department of Education (IT-927-16) and from MINECO (MAT 2016-78527-P). N. Sadaba is thankful

for the predoctoral fellowship to POLYMAT Fundazioa-Basque Center for Macromolecular Design and Engineering.

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