3D Printing of Poly Lactic Acid Bone scaffold combined with Poly Ethylene Glycol for tissue engineering applications

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Abstract. Additive Manufacturing (AM) is a new trend in manufacturing in which computer aided design (CAD) 3D model file is used to make a solid physical model of the designed part. Fused deposition modelling (FDM) a technique in additive manufacturing has revolutionized engineering in various applications. One of the significant impacts of this technology is on the medical industries. The most substantial reason is because of this technology’s facility to convert 3D medical imaging data into solid objects. The productional cost of an implant and other instruments reduced because of the ease of this technology which significantly reduced the cost charged from the patients. Polylactic acid (PLA) is conceivable one of the best-known polymers shaped from renewable raw materials such as sugar cane and corn starch. Poly(ethylene glycol) (PEG) is an FDA approved low toxicity material which is in re water-soluble liquid state or waxy solid-state. It is used in preparations of cosmetics and pharmaceuticals. Most of the emulsifying or wetting agents and lubricants are manufactured using PEG. Also, PEGs are suitable plasticizers owing to their low glass transition temperature. PLA/PEG has a hopeful probable for large-scale manufacture of green composites towards various applications in biomedical fields. In this research work, PEG reinforced polylactic acid composite were produced in 2, 5 and 10 wt. % PEG content by a single-screw extruder in filament form. The results obtained during the experiment indicated that PEG concentration enhances the processing of PLA, but changes in various features like relevant surface, geometry ad structure were observed. The addition of PEG in PLA had significantly changed the rate of degradation of the FDM fabricated scaffolds.

Keywords: Additive Manufacturing, Poly Lactic Acid, Fused Deposition Modelling, Poly Ethylene Glycol, Bone Scaffolds

1. Introduction

Additive Manufacturing (AM) is a new trend in manufacturing in which computer aided design (CAD) 3D model file is used to make a solid physical model of the designed part [1]. The growing opportunities and innovative challenges in 3D printing has attracted industrialists towards rapid prototyping for various components and academics to learn the fabricating of 3D models with this technology, as this uses trifling detrimental chemicals during manufacturing a component [2–4]. The AM has paved a new
way of manufacturing with optimized use of materials, FDM is widely used because of ease of printing models by extruding a thermoplastic filament and printing it layer by layer.

Recent research on 3D printed scaffolds exhibits the scope of various degradable polymers such as polylactic acid (PLA), polyglycolic acid, polycaprolactone, chitosan and their copolymers being used in AM fabricated scaffolds. [5]. Currently, most biomedical applications use PLA as a biodegradable polymer which is approved by the FDA [6-7]. Though numerous researches have used this polymer and extensively studied, the usage of this polymer for 3D printed scaffolds in tissue engineering applications through FDM is scarcely reported. All the recent reports of PLA -based scaffold fabricated through FDM use the control of temperature during the print process along with freeze-drying as a post-processing technique to set in molecular modifications in the PLA matrix. [10]. Poly (ethylene glycol) (PEG) is an FDA approved low toxicity material which is in re water-soluble liquid state or waxy solid-state. It is used in preparations of cosmetics and pharmaceuticals. Most of the emulsifying or wetting agents and lubricants are manufactured using PEG. Also, PEGs are suitable plasticizers due to their low glass transition temperature [8-9].

In this work the blending of PLA and PEG for various composition ratios and 3D printing of porous scaffold with the PLA/PEG composite through FDM with greater structural and degradable properties is discussed.

2. Experimental

2.1. Materials

Extrusion grade Poly Lactic Acid (PLA) polymer (trade-name Ingeo 2003D) was purchased. The material has a specific gravity of 1.24 and yield Modulus of 3.5GPa (as provided by the manufacturer) Pure Pharma grade Poly ethylene Glycol (PEG 400) was purchased. The specifications and properties as per the manufacturer report are with a density of 1.127 kg/litre, Molecular Weight 380-420 and the viscosity is 6.8 -8.0 cSt.

2.2. Materials processing and sample preparation

2.2.1. Compounding

The Polylactic acid and PEG were solvated separately in chloroform (5%w/v) with addition of PEG in concentrations (0, 2, 5, 10% w/w) and the composites were named PLA-2, PLA-5 and PLA-10 respect to the PEG concentrations. A homogeneous polymer blend solution was achieved by placing the prepare composites for 48hours on an orbital mixer.

2.2.2. Filament extrusion

The blended composites were fed into single screw extruder (screw diameter = 3.175mm, L/D ratio = 20 and rod die diameter =3mm). The rotation speed of the screw and collection rate were controlled to acquire a final diameter of the extruded filament of 1.75mm with a screw speed at 20 rpm. The Table 1 depicts the details of process control parameters for different samples.
Table 1. Conditions used to produce PEG-filled PLA

| Composite Name | PEG wt % | Extruder Temperature (˚C) | Motor Speed (rpm) |
|----------------|----------|----------------------------|-------------------|
| PLA            | 0        | Hopper: 148, Screw: 175, Die: 175 | 20                |
| PLA-2          | 2        | Hopper: 148, Screw: 170, Die: 170 | 20                |
| PLA-5          | 5        | Hopper: 142, Screw: 170, Die: 170 | 20                |
| PLA-10         | 10       | Hopper: 145, Screw: 170, Die: 170 | 20                |

2.2.3. Scaffold Design and Fabrication

The PLA/PEG scaffolds were fabricated using a Flashforge Desktop 3D Printer. The feed to the 3D printer was the filaments prepared using the extruder. However, since there is fluctuation in filament diameter during extrusion, not all prepared filaments were printable. As shown in figure [1] The doubled layer scaffolds, which are Orthogonal displaced with the distance between struts D=400μm and each layer of height Φ=200μm. The samples of neat PLA, PLA-2, PLA-5 and PLA-10 were successfully printed with the following printing parameters: 100% object infill; no raft; 0.35 mm nozzle diameter; 0.20 mm layer height; 220°C nozzle temperature and 55°C bed temperature.

![Figure 1. Axial and cross-section view of designed 3D scaffold of orthogonal scaffolds: D = 400 μm; Φ = 200 μm](image)

2.3. Scaffold Characterization

2.3.1. Differential Scanning Calorimetry

Differential Scanning Calorimetry tests were carried out to measure the glass transition temperature and degree of crystallinity. The samples were initially heated from 15°C to 220°C at a rate of 100°C/min and then it was kept for an isothermal stay at 220°C for 5 minutes. Then the temperature of the samples was reduced from 220°C to -15°C at a rate of -10°C/min and reheated at the same temperature from -15°C to 220°C. Then the glass transition temperature (Tg) was measured.

2.3.2. Morphological SEM study

The morphological study of the fabricated scaffolds and the prepared samples were observed under a scanning electron microscope (SEM). The prepared polymer film samples were kept in simulated body fluid (SBF), and the SEM was inspected after t= 0, 2, 4, 6 and 8 weeks for possible surface
modifications during the degradation. This analysis was primarily done to evaluate the scaffold's key parameters like structural solidity of the intermediate layers and struts, surface morphology and design of the 3D scaffold. The morphology analysis plays a vital role in the quality assessment of the porosity in the theoretical geometry and the fabricated scaffold.

2.3.3. Mechanical Properties

The mechanical properties were evaluated using a Universal Testing Machine (Instron 5567) was used to study and compare the mechanical properties of all the prepared PLA/PEG bio-composites at room temperature. The tensile specimen and the tests were conducted according to the ASTM D638 standards.

![Universal Testing Machine (Instron 5567)](image)

**Figure 2.** Universal Testing Machine (Instron 5567)

2.3.4. Porosity

The porosity evaluation for the fabricated scaffolds of varying composition of PEG in the PLA matrix was performed by calculating the theoretical volume porosity percentage (%Vol theoretical) with the considered design (Fig.1). An assumption that there is no touching due to the blend between struts from end-to-end was made so that the values of layer height and strut diameter was the same.

$$\%\text{Vol theoretical} = \left(1 - \left(O^2/4 \pi N_c N_l / (wh) \right) \right) \times 100\%$$

Where $O$, $w$ and $h$ refer to the strut diameter, scaffold width and scaffold height in millimetres as per the scaffold design. Moreover, $N_c$ denotes the number of cylinders (struts) per layer, while $N_l$ denotes the number of layers per scaffold.
3. Results and Discussions

3.1. Morphological SEM Study and Porosity Evaluation

From the SEM analysis it was observed that there was a striking variation between the three scaffolds of varying PEG concentration. Upon increasing the PEG concentration, there was a shift from the designed initially squared pores into slightly rounded ones. The Neat PLA scaffold had an even flat exterior whereas the PLA-10 had a slightly irregular coarse spherical structure. During the degradation process, i.e. after 8 weeks of absorption of the scaffolds in Simulated Body Fluid, Neat PLA did not show any degradation, and the surface remained the same. In the other case, PLA-10 shows great contrasts in terms of their exterior morphology and intense degradation with several cracks at the surface.

Figure 3 shows the SEM micrograph of PLA-5 which indicates the scaffolds surface showing the micro porosity due to the evaporation of the solvent. Figure 4 presents the theoretical volume porosity percentages of the PLA/PEG scaffolds fabricated with the varying concentration of PEG in the PLA matrix. From the graph, we can interpret that the porosity of the scaffold decreases from 98.5% (Neat PLA) to 86.5% (PLA-10) as PEG concentration increases from 0 to 10% (w/w).

![Fig 3. SEM image of PLA-5 showing micro porosity](image1)

![Fig 4. Theoretical Porosity % for 3D Printed scaffolds](image2)
3.2. Differential Scanning Calorimetry Analysis

The thermal characteristics of Neat PLA and PLA/PEG composite samples are shown in Table 2. Here the results obtained from the DSC analysis exhibit that increase in the concentration of PEG in the PLA matrix increases the percentage of crystallinity (Xc), i.e. increase in the hardness and density of the composite but decreases the Glass transition temperature (Tg). For the increase in the PEG concentration from 0% to 10% (w/w), the value of Tg decreases from 57.59ºC (Neat PLA) to 29.25ºC (PLA-10), and Xc substantially increases from 2.1% (Neat PLA) to 22.13% (PLA-10).

| Samples     | Tg ( ºC) | Xc (%) |
|-------------|----------|--------|
| Neat PLA    | 57.59    | 2.10   |
| PLA-2       | 50.78    | 7.62   |
| PLA-5       | 41.6     | 14.40  |
| PLA-10      | 29.25    | 22.13  |

Table 2. Glass transition temperature (Tg) and Crystalline fraction (%Xc) of PLA/PEG blends

A gradual rise of Tg values along the degradation rate was reported, particularly for the materials with a higher concentration of PEG. During the degradation period in SBF, at t=4 weeks Neat PLA showed a gradual increase whereas the PLA-5 exhibited a steeper increase which depicted an improvement in crystallinity. Overall, the addition of PEG has a strong influence on the degradation rate of the fabricated scaffold.

3.3. Mechanical Properties Evaluation

The comparison of the mechanical properties of the neat PLA and PLA/PEG composite samples are shown in Table 3. The measured mechanical properties of the neat PLA are Young's Modulus of 3306 MPa, elongation at the breakpoint is 3.8% and the yield strength of 61.0MPa. As previously stated,
'increase in the concentration of the PEG increases the hardness', leading to the decrease of yield strength and Young's Modulus but with least change in the values of elongation at the breakpoint. This least change occurs because of the variation in the chemical structure of PLA and PEG. Thus it can be understood that stiffness and strength of the PLA/PEG composite, gradually reduced during the variation of PEG from 2-10% wt.

| Samples | Stress at Break (MPa) | Elongation at Break (%) | Young’s Modulus (Mpa) |
|---------|-----------------------|-------------------------|----------------------|
| Neat PLA | 61.0                  | 3.8                     | 3306                 |
| PLA-2   | 53.6                  | 4.1                     | 3751                 |
| PLA-5   | 48.9                  | 3.2                     | 3568                 |
| PLA-10  | 35.3                  | 3.5                     | 3042                 |

4. Conclusions

Biopolymer composites consisting of a polylactic acid matrix reinforced with Poly ethylene glycol was synthesized successfully and filaments were extruded to make the 3D scaffolds. The preliminary results indicate that polymer composites can be achieved with direct mechanical mixing of PLA and PEG. An extensive work on the addition of the PEG in the PLA matrix was done to achieve a novel bio-composite and has been investigated to develop a 3D printed Bone scaffold through Fused Deposition Modelling (FDM) for tissue engineering applications. The modernity of the research was by optimizing some basic parameters like material printability, thermal stability, printing conditions and design. This supported the fabrication of the 3D printed PLA/PEG scaffold with the variation of PEG concentration (2, 5, 10% w/w). The morphological, structural, thermal and mechanical characterization was conducted on both the film samples (2D) and the fabricated scaffolds (3D).

The results achieved through the work make apparent that the addition of various weight percentage of PEG gives rise to notable changes in the Structure and degradation rate of the PLA/PEG composite. With more weight percentage of PEG, there is a significant increase in the hardness, stiffness, surface roughness and wettability which reduces the mechanical properties like yield strength, Young's modulus of the fabricated 3D scaffold. The blending of 5% (w/w) PEG with PLA is an efficient method for the realistic approach for 3D printing of Bone scaffolds as it weaves the structural, thermal properties and degradation rate with fair stability.

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