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Poly-ε-caprolactone/hydroxyapatite for tissue engineering scaffold fabrication via selective laser sintering

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Abstract

Rapid prototyping (RP) techniques are becoming more popular for fabricating tissue engineering (TE) scaffolds owing to their advantages over conventional methods, such as the ability to fabricate scaffolds with predetermined interconnected networks without the use of organic solvents. A versatile RP technique, selective laser sintering (SLS), offers good user control of scaffold microstructure by adjusting the process parameters. This research focuses on a the use of biocomposite material, consisting of poly-ε-caprolactone (PCL) and hydroxyapatite (HA), to fabricate TE scaffolds using SLS. Biocomposite blends with different percentage weights of HA were physically blended and sintered to assess their suitability for fabrication via SLS. Optimal sintering conditions for the powders were achieved by varying parameters such as laser power and scan speed. Studies of the sintered specimen morphology were performed by scanning electron microscopy. Thermogravimetric analysis confirmed the homogeneity of the biocomposite blend. Simulated body fluid (SBF) samples show the formation of hydroxy carbonate apatite, as a result of soaking HA in a SBF environment. Cell culture experiment showed that Saos-2 cells were able to live and replicate on the fabricated scaffolds. The results show the favorable potential of PCL/HA biocomposite as TE scaffolds that are fabricated via SLS.

Keywords: Rapid prototyping; Selective laser sintering; Poly-ε-caprolactone; Hydroxyapatite; Tissue scaffold

1. Introduction

Tissue engineering (TE) merges many aspects of engineering and life sciences, aiming towards the primary understanding of cell functions and the advancement of biological substitutes. TE assists the body to repair itself by delivering the necessary cells, scaffolds and biological environments to damaged or diseased tissues and organs [1]. The growing interest in TE is motivated by the potential of customizing tissue implantation for organs such as heart, bone, liver, cartilage, skin, muscles and pancreas islets [2–5]. The intention of TE is to relieve limitations due to the shortage of organs for transplantation, as well as short-term treatments, where temporary implants are needed until a patient's own tissues heal completely [6–9].

TE scaffolds serve as artificial substitutes for extracellular matrices, which are essential for cell attachment, guiding cell growth and maintaining cell characteristics during tissue or organ regeneration. These scaffolds give shape to regenerated tissue and temporarily fulfil the structural functions of the native tissue. In addition to fitting into the anatomical defect, they have to possess sufficient strength and stiffness that will bear *in vivo* loads so that the scaffolds can function before the growing tissue replaces the gradually degrading scaffold matrix. Appropriate composition and microstructural porosity of the scaffolds enhances the growth of tissue within them. Studies have shown that the porosity of the scaffolds and the type of materials used significantly influence biological responses [10]. Scaffold architecture, material composition

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and porosity can be controlled through design and fabrication, and this ability is crucial to future success in tissue engineering [10–12]. The materials used should not provoke inflammation or toxicity and must be removed from the body through metabolic pathways, while their degradation rates and the concentrations must be at tolerable levels. Suitable materials include ceramics, natural/synthetic polymers as well as their composites [13,14].

Conventional methods for making scaffolds include solvent casting, fiber meshes, phase separation, melt molding and gas foaming [15]. These techniques lack precise control of pore shape, pore geometry and spatial distribution. Some methods also require the use of organic solvents that leave undesirable residues in the finished products, and may thus create host reactions due to inflammation or toxicity [15].

One of the technologies being explored to improve the manufacturing process of scaffolds is rapid prototyping (RP). Using computer-control of design data, RP is able to overcome many of the limitations encountered by conventional methods [16–18]. RP is an excellent alternative as it can provide the consistency, flexibility in geometry and reproducibility in physical properties without any use of organic solvents. Selective laser sintering (SLS) is one of the most versatile RP systems in terms of material usage and structural stability. SLS builds up models layer-by-layer using powders which are selectively bonded when a laser beam scans the powder across each layer's cross-sectional area [19]. SLS settings and parameters can be optimized through experiments to achieve the desired mechanical properties of the TE scaffolds.

Modeling materials for SLS are commercially available but they are non-biocompatible. Hence, novel biomaterials suitable for processing via SLS are needed for scaffold fabrication. Theoretically, powdered biomaterials that are not degraded by the laser beam during sintering have the possibility to be successfully processed by SLS. Polymers are highly elastic and low in stiffness while ceramics are rigid and brittle. By combining polymers and ceramics into composites, the mechanical properties will be greatly enhanced, as the problem of brittleness and the difficulty of shaping hard ceramics can be overcome. Studies done using SLS have involved sintering hydroxyapatite (HA) powders coated with polymeric binders [20,21].

Poly-ε-caprolactone (PCL) is a Food and Drug Administration (FDA)-approved bioresorbable polyester with potential applications for bone and cartilage repair. It is semicrystalline with high thermal stability and a degradation time of about two years [22]. Pure PCL has been investigated for fabrication using SLS and it has shown to possess sufficient mechanical properties for TE applications for bone and cartilage regeneration [23,24].

HA is a ceramic material that is biocompatible due to its similarity to the mineral constituents of human bone and teeth. Owing to its high bioactivity and biocompatibility, HA is commonly used as filler in polymer-based bone substitutes [25,26].

The interest in PCL/HA composites for use in bone regeneration is evident. Initial attachment of primary human osteoblasts on PCL/HA composite films has also shown favorable interactions between the cell and material for bony tissues [25,27].

This paper presents the development of powdered PCL and HA biocomposite for SLS using improved blending methods. The feasibility of using such biocomposite powders on SLS and the influence of SLS process parameters on the sintering effect of the specimens were studied. Characterization of the specimens was carried out and analyzed.

2. Materials and methods

2.1. PCL

PCL powder was supplied by CAPA 6501, Solvay Caprolactones, UK. It is a linear polyester derived by the ring-opening polymerization of caprolactone with a high molecular weight of 50,000. It has a low melting-point of 58–60 °C and low viscosity; 99% of its particles are less than 100 μm. Its density is ~1.15 g/cm^3.

2.2. HA

HA powder was supplied by Plasma Biotal Ltd. Two types were used, namely reactor powder CAPTAL® 'R' and sintered powder CAPTAL® 'S', to assess the suitability of different HA powder-types on SLS. CAPTAL® 'R' has a 'spikey' crystal morphology which gives the material a relatively high surface area of 15–20 m^2/g for powders of d(50) ~5 μm when measured by the Brunauer–Emmet–Teller (BET) method. CAPTAL® 'S' is highly crystalline, with approximately 10% higher crystallinity by X-ray diffraction than CAPTAL® 'R'. The surface area of powder d(50) ~5 μm is approximately 1–2 m^2/g. The purity and crystallinity for both types ensures low resorption rates when used *in vivo* with excellent biocompatibility when used in bony sites.

2.3. Preparation of PCL/HA biocomposite

Different compositions of PCL and HA by wt.% were mixed. The powders were mixed into portions of 50 g and put into 500 ml polypropylene containers. Proportions of PCL were higher as PCL acts as a binder. HA was added to make up 10, 20 and 30 wt.% content in the powder blends. To ensure thorough mixing of the powders, mixing was performed using a mixing roller (CZ98174, US Stoneware, East Palastine, OH). The rollers were set to run at 40 rpm for a period of 3 h [28].

2.4. Design and fabrication of test specimens

The test sintering specimens fabricated were in the shape of circular discs, with a diameter and thickness of 15 mm and 1 mm, respectively. This size was chosen to ensure that

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