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45S5 Bioglass®-derived glass–ceramic scaffolds for bone tissue engineering

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Abstract

Three-dimensional (3D), highly porous, mechanically competent, bioactive and biodegradable scaffolds have been fabricated for the first time by the replication technique using 45S5 Bioglass® powder. Under an optimum sintering condition (1000 °C/1 h), nearly full densification of the foam struts occurred and fine crystals of $Na_2Ca_2Si_3O_9$ formed, which conferred the scaffolds the highest possible compressive and flexural strength for this foam structure. Important findings are that the mechanically strong crystalline phase $Na_2Ca_2Si_3O_9$ can transform into an amorphous calcium phosphate phase after immersion in simulated body fluid for 28 days, and that the transformation kinetics can be tailored through controlling the crystallinity of the sintered 45S5 Bioglass®. Therefore, the goal of an ideal scaffold that provides good mechanical support temporarily while maintaining bioactivity, and that can biodegrade at later stages at a tailorable rate is achievable with the developed Bioglass®-based scaffolds.

Keywords: Scaffolds; Bone tissue engineering; Mechanical properties; Bioactivity; Biodegradation; Replication technique

1. Introduction

Tissue engineering seeks to promote the regeneration ability of host tissue through a designed scaffold that is populated with cells and signalling molecules. The specific criteria for ideal scaffolds used in bone tissue engineering are summarised as follows [1–3]: (1) ability to deliver cells, (2) excellent osteoconductivity, (3) good biodegradability, (4) appropriate mechanical properties, (5) highly porous structure: porosity > 90% [4] and pore sizes > 400–500 μm [5], (6) irregular shape fabrication ability, and (7) commercialisation potential.

Bioactive glasses meet the first three criteria: excellent osteoconductivity and bioactivity [6–10], ability to deliver cells [11], and controllable biodegradability [12–14]. These advantages make bioactive glasses promising scaffold materials for tissue engineering [15–17]. Among a variety of processes for fabrication of porous materials [5,18–21], the replication technique [22] (also called the polymer-sponge method) produces porous ceramic structures that are most similar to those of spongy bone [23,24]. This technique also satisfies scaffolds' criteria (5)–(7) mentioned above. Thus, all criteria for an ideal tissue engineering scaffold, except that related to mechanical competence, could be satisfied by 45S5 Bioglass® foams fabricated by the replication method. The replication method has been applied to produce scaffolds of hydroxyapatite (HA) [25–27]. Surprisingly, this technique, however, has never been considered before to produce scaffolds from bioactive glasses. Bioactive glass scaffolds have only been fabricated by dry-powder processing with porogen additions [28–30] and by sol–gel and gel-casting techniques [3,31].

The major hurdle in the production of highly porous Bioglass®-based foam-like scaffolds has been caused by the following apparently irreconcilable issues of this glass: (a) it has been reported that crystallisation of 45S5 Bioglass® turns a bioactive glass into an inert material [32]; (b) full crystallisation of the glass occurs prior to significant densification [33]; (c) extensive densification is required to

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strengthen the struts of a foam, which would otherwise be made of loosely bonded particles and thus be too fragile to handle. According to these three factors, to maintain the bioactivity of 45S5 Bioglass®, one should sinter the foam at a relatively low temperature at which crystallisation does not take place or does not occur to a great extent. However, sufficient densification by sintering will not occur at low temperatures, and therefore a very fragile scaffold made of loosely packed 45S5 Bioglass® particles is produced.

The above dilemma might be solved in light of the recent work of Clupper and Hench [34–37], who carried out quantitative investigations on the effect of crystallinity on the apatite formation on Bioglass® surfaces in vitro. Their findings revealed that the crystal phase $Na_2Ca_2Si_3O_9$ slightly decreased the formation kinetics of an apatite layer on the Bioglass® sample surface but it did not totally suppress the formation of such layer [34]. Moreover, it is recognised that the bioreaction kinetics of a highly porous network can be very different from that of a dense product of the same chemical composition due to a high surface area in the foams. Hence, it might be possible to find a new sintering protocol leading to mechanically competent foams through extensive densification of the struts, while inducing the formation of a bioactive and biodegradable crystalline phase. The objectives of this work, therefore, were to synthesize 45S5 Bioglass® scaffolds using the replication technique, to achieve mechanically stable 3D scaffolds through a tailored sintering schedule, and to assess the bioactivity and biodegradability of the scaffolds. The final goal is to create an ideal scaffold for bone tissue engineering.

2. Materials and experiments

2.1. Materials

The starting material was melt-derived 45S5 Bioglass® powder (particle size ~5 μm). A fully reticulated polyester-based polyurethane foam with 60 ppi (pores per inch) from Recticel UK (Corby) was used as sacrificial template for the replication method. The details of the polyurethane foam used have been reported by other authors [38]. The foam was supplied in large samples of 20 mm in thickness and was cut to size 10 mm × 10 mm × 20 mm for compression strength tests and 10 mm × 10 mm × 60 mm for bending strength tests.

2.2. Scaffold fabrication

The replication method involves preparation of green bodies of ceramic (or glass) foams by coating a polymer (e.g. polyurethane) foam with a ceramic (or glass) slurry. The polymer, having the desired pore structure, simply serves as a sacrificial template for the ceramic coating. The polymer template is immersed in the slurry, which subsequently infiltrates the structure and ceramic (glass) particles adhere to the surfaces of the polymer. Excess slurry is squeezed out leaving a more or less homogeneous coating on the foam struts. After drying, the polymer is slowly burned out in order to minimise damage to the ceramic (glass) coating. Once the polymer has been removed, the ceramic (or glass) network is sintered to a desired density. The process replicates the macrostructure of the starting sacrificial polymer foam, and results in a rather distinctive and well-defined microstructure within the struts. A flowchart of the process is given in Fig. 1.

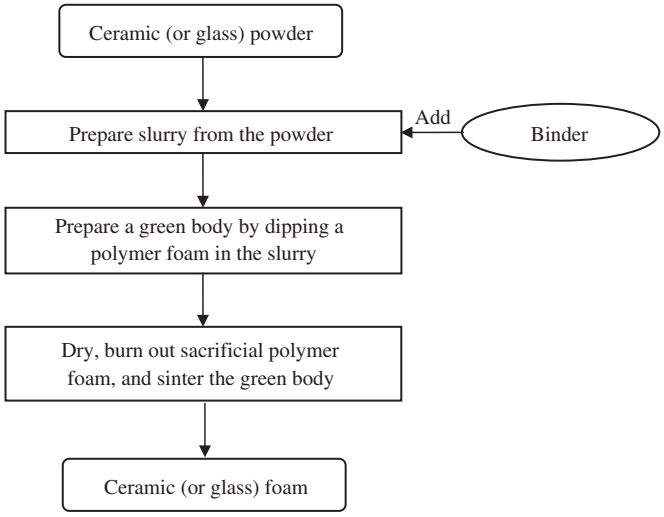

Fig. 1. Flowchart of the polymer-sponge method for fabrication of glass or ceramic foams.

In our experiments, the slurry for the impregnation of the polyurethane foam was prepared using the following recipe. Polyvinyl alcohol (PVA) was dissolved in water, the ratio being 0.01 mol/L. Then 45S5 Bioglass® powder was added to 100 ml PVA-water solution up to concentration of 40 wt%. Each procedure was carried out under vigorous stirring using a magnetic stirrer for 1 h.

The polyurethane foams cut to shape were immersed in the above-prepared slurry and remained in it for 15 min. The foams were manually retrieved from the suspension as quickly as possible, and the extra slurry was completely squeezed out. The samples (called green bodies) were then placed on a smooth surface and dried at ambient temperature for at least 12 h. The coating thickness of a green body could be increased by repeating the above coating procedure. In this work most green bodies were prepared by single coating, but few were made by double coating. The double-coated green bodies will be mentioned where they are used in this paper.

Post-forming heat treatments for the burnout of the polymer template and sintering for the 45S5 Bioglass® structure were programmed, as shown in Fig. 2. The burning condition of the polymer templates was the same for all samples: 400 °C/1 h. Sintering conditions were designed to be 900 °C/5 h; 950 °C/0–5 h; and 1000 °C/0–2 h. The heating and cooling rates were 2 and 5 °C/min, respectively.

2.3. Characterisation

The density ρ_{foam} of the scaffolds was determined from the mass and dimensions of the sintered bodies. The porosity p was then calculated by

$$p = 1 - \frac{\rho_{foam}}{\rho_{solid}} = 1 - \rho_{relative}, \quad (1)$$

where $\rho_{solid} = 2.7\,g/cm^3$ is the density of solid 45S5 Bioglass® [14].

The microstructure of the foams was characterised in a JEOL 5610LV scanning electron microscope (SEM), before and after immersion in simulated body fluid (SBF). Samples were gold- or carbon-coated and observed at an accelerating voltage of 15 kV.

Selected foams were also characterised using X-ray diffraction (XRD) analysis with the aim to assess the crystallinity after sintering and formation of HA crystals on strut surfaces after different times of immersion in SBF. The foams were first ground into a powder. Then 0.1 g of the powder was collected for XRD analysis. A Philips PW 1700 Series automated powder diffractometer was used, employing Cu kα radiation (at 40 kV and 40 mA) with a secondary crystal monochromator. Data were