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Phosphate glass fibre scaffolds: Tailoring of the properties and enhancement of the bioactivity through mesoporous glass particles

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ABSTRACT

Novel bone glass fibre scaffolds were developed by thermally bonding phosphate glass fibres belonging to the P_2O_5-CaO-Na_2O-SiO_2-MgO-K_2O-TiO_2 system ($TiPS_{2.5}$ glass). Scaffolds with fibres of 85 or 110 μm diameter were fabricated, showing compressive strength in the range of 2–3.5 MPa, comparable to that of the trabecular bone. The effect of different thermal treatments and fibre diameters and length on the final scaffold structure was investigated by means of micro-CT analysis. The change of the sintering time from 30 to 60 min led to a decrease in the scaffold overall porosity from 58 to 21 vol.% for the 85 μm fibre scaffold and from 50 to 40 vol.% when increasing the sintering temperature from 490 to 500 °C for the 110 μm fibre scaffold. The 85 μm fibres resulted in an increase of the scaffold overall porosity, increased pore size and lower trabecular thickness; the use of different fibre diameters allowed the fabrication of a scaffold showing a porosity gradient.
In order to impart bioactive properties to the scaffold, for the first time in the literature the introduction in these fibre scaffolds of a bioactive phase, a melt-derived bioactive glass (CEL2) powder or spray-dried mesoporous bioactive glass particles (SD-MBG) was investigated. The scaffold bioactivity was assessed through soaking in simulated body fluid. CEL2/glass fibre scaffold did not show promising results due to particle detachment from the fibres during soaking in simulated body fluid. Instead the use of mesoporous bioactive powders showed to be an effective way to impart bioactivity to the scaffold and could be further exploited in the future through the ability of mesoporous particles to act as systems for the controlled release of drugs.

1. Introduction

Bone tissue shows an intrinsic potential of self-healing in response to injury [1]. However, there are clinical situations in which the spontaneous bone regeneration process is not sufficient to properly repair the tissue damage, such as in the case of impaired bone regeneration, compromised regenerative process (e.g. osteoporosis) or in the presence of large defects (e.g. caused by trauma, infection, tumour resection). In these cases, the common surgical procedure involves the use of bone grafts from autogenous (i.e. gold standard) or allogenic tissues, which however implies patient discomfort and could lead to complications as well as rejection and infection transmission risk [2].

Synthetic bone scaffolds, which are three-dimensional (3-D) constructs of synthetic or natural-derived materials, are good alternatives to the use of bone grafts. Bone scaffolds should meet specific requirements such as a high biocompatibility of both the material and its degradation products, a degradation rate matching that of the bone regeneration and sufficient mechanical properties. Moreover a scaffold should possess a porous structure with an interconnected porosity of 40–70 vol.% for bone tissue ingrowth and vascularization and pore size favouring cell migration (100 μm), new vessels and direct bone formation (200–300 μm) [3].

Glass and glass-ceramic materials containing calcium and phosphorous are the most widely studied materials for bone scaffold fabrication owing to their similarity with natural bone both in terms of chemical composition and achievable mechanical properties [4]. Since the development of Bioglass® (SiO_2-Na_2O-CaO-P_2O_5 system) by Prof. L. Hench and co-workers [5], bioactive glass and glass-ceramic materials showed a great potential for the treatment of bone, as well as for soft tissue repair [6,7]. When in contact with physiological fluids, bioactive glasses are able to induce on their surface the precipitation of hydroxyapatite (HA), the mineral phase of natural bone, thus creating a strong interfacial bond with the surrounding tissue [8]. In the last decade a lot of different bioactive and/or bioresorbable silicate, borate, borosilicate and phosphate glasses have been developed for the fabrication of bone scaffolds [9–11].

The most common procedures to obtain glass ceramic porous scaffolds involve the use of melt-derived glass powder as starting material, which are deposited around a sacrificial template that is burnt out

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through a thermal treatment that lead to the glass sintering and partial crystallization [12]. The sacrificial template can be a polymeric foam (i.e. sponge replication technique), polymeric particles (i.e. burn out of a porogen agent method) or ice crystals created by the freezing of a slurry containing the glass particles [13–16]. Moreover, the scaffold porosity could also be obtained by the air bubbles created through foaming a slurry containing the glass powder, followed by gelation to stabilize the bubbles (i.e. gel-cast foaming process) [17]. Afterwards the ice crystals can be removed by means of lyophilisation before sintering the glass [18]. Other more recent techniques involve additive manufacturing technologies [19].

Pirhonen et al. [20] proposed a novel method for obtaining porous scaffolds using glass fibres as starting materials. The fibres were cut and randomly arranged into a mould forming a three-dimensional structure with the porosity originating from the free space between fibres without any further material addition or process before sintering. The porous scaffold is obtained simply by thermally bonding the glass fibres upon their softening. Not all bioactive glasses can be drawn into fibres as this ability is strongly dependent on the glass composition. For example, obtaining Bioglass® fibres by the conventional melt-spinning technique is quite challenging, due to the very narrow sintering window of Bioglass® [12], which corresponds to the temperature range between the glass transition and the onset crystallization temperatures. A large sintering window is highly desirable for fibre drawing, since no crystallization should occur upon heating when the glass reaches the suitable viscosity for fibre drawing [21]. Silicate (e.g. 13-93), borate (e.g. 13-93B3) and borosilicate glasses have a wider working window compared to Bioglass® and have thus been proposed for the development of glass fibrous scaffolds [20,22–27].

Recently, phosphate glass fibres bonded with chitosan (i.e. not thermally treated) have been proposed for the fabrication of three dimensional bone scaffolds with an overall porosity of 87 vol.% and yield stress of 0.38 MPa [28]. In the present work, for the first time to best of the authors knowledge, thermally bonded phosphate glass fibres are proposed, to fabricate porous 3-D scaffolds. Metaphosphate glasses (i.e. P_2O_5 50 mol.%) show a structure composed of long chains of PO_4 tetrahedra, linked by modifying ions which allow a good quality fibre drawing [29]. Moreover, the resorption kinetics of phosphate glasses can be tailored through the glass composition itself. In this work, a resorbable glass (glass code $TiPS_{2.5}$: 50 P_2O_5-30 CaO-9 Na_2O-3 SiO_2-3 MgO-2.5 K_2O-2.5 TiO_2, mol.%) was chosen for the fibre drawing. This glass can be drawn into fibres and has previously shown an excellent biocompatibility with both hard and soft tissue cells [30–32]. In the present work, different fibre sizes were produced in order to investigate the effect of the fibre diameter on the final scaffold structure. Finally, the incorporation of different types of bioactive glass powders into the fibre-based scaffold was investigated with the aim of imparting bioactive properties to the scaffold. The bioactive glasses proposed at this purpose were a melt derived silica-based glass (CEL2) developed by C. Vitale-Brovarone and co-workers and a spray-dried mesoporous glass (SD-MBG), which were previously tested by our group for their bioactivity [13,14,33].

2. Materials and methods

2.1. Glass preparation

2.1.1. $TiPS_{2.5}$ phosphate glass fibres

Fibres of $TiPS_{2.5}$ glass (50 P_2O_5-30 CaO-9 Na_2O-3 SiO_2-3 MgO-2.5 K_2O-2.5 TiO_2, mol.%) were fabricated by means of the preform drawing approach, using a drawing tower developed in-house as described elsewhere [30]. Briefly, high-purity reagents (P_2O_5, $Ca_3(PO_4)_2$, NaH_2PO_4, SiO_2, MgO, K_2HPO_4, TiO_2, Sigma-Aldrich) were melted in a furnace in Pt/Rh (90/10 wt.%) crucible (1350 °C, 3 h, 10 °C·min^{-1}) and the glass was cast on a brass plate. The glass was then re-melted in a furnace in a Pt/Rh crucible and cast in a pre-heated brass mould and subsequently annealed (410 °C, 15 h) to obtain a glass cylindrical preform (diameter 11 mm) for fibre drawing. The preform was polished, mounted on the drawing tower and heated under a flow of nitrogen until a fibre formed (about 580 °C), which was then collected on a rotating drum. Fibre diameters of 85 and 110 μm were obtained using different preform feeding speeds (0.7 and 1 mm·min^{-1}, respectively) and drawing speeds (12 and 10 m·min^{-1}, respectively). After the drawing process, the diameter of 20 fibres of each type, obtained by cutting pieces along the fibre length, were measured using Reichert-Jung MeF3 optical microscope equipped with Leica Qwin image software in order to measure the obtained fibre diameter.

2.1.2. CEL2 melt-derived bioactive glass

Silica-based bioactive glass CEL2 (45 SiO_2, 3 P_2O_5, 26 CaO, 7 MgO, 15 Na_2O, 4 K_2O mol.%) [13,14] was produced by melt quenching. Briefly, high purity reagents (SiO_2, $Ca_3(PO_4)_2$, $CaCO_3$, $4MgCO_3Mg(OH)_25H_2O$, Na_2CO_3, K_2CO_3, Sigma-Aldrich) were placed in a Pt crucible, melted in a furnace at 1500 °C for 1 h (10 °C·min^{-1}) and quenched in cold water to obtain a frit that was then ball milled and sieved to a grain size below 20 μm.

2.1.3. Spray-dried mesoporous bioactive glass particles

Spray-dried mesoporous bioactive glass particles (SD-MBG, 80 SiO_2, 20 CaO mol.%) were produced combining the sol-gel method with the aerosol-assisted spray-drying technique, as previously reported [32]. A solution of 2.2 g of Pluronic P123 and 8.0 g of ethanol was prepared and mixed with a solution of 10.4 g of TEOS (tetraethyl orthosilicate) pre-hydrolysed for 20 min with 5.4 g of diluted hydrochloric acid (pH 2) and 12.0 g of ethanol and stirred for 20 min. Then a solution of 2.95 CaNT (calcium nitrate tetrahydrate) pre-dissolved in 3.4 g of ethanol was mixed with the previous one and stirred for 20 min before spraying using a Mini Spray-Dryer B-290, equipped with the Inert-Loop B-295(Büchi). The obtained powder was then calcined at 700 °C for 5 h to remove the surfactant.

2.2. Hot stage microscopy

Hot stage microscopy (HSM, Misura Expert System Solutions, Modena, Italy) was carried out (air atmosphere, heating rate 10 °C·min^{-1}) in order to study the sintering process of $TiPS_{2.5}$ glass (cubic sample 5 × 5 × 5 mm of pressed glass powder).

2.3. Characterization of the SD-MBG powder

Nitrogen adsorption analysis at 77 K (Quantachrome Autosorb 1) was performed on SD-MBG powder. Specific surface area was obtained by applying the Brunauer-Emmett-Teller (BET) method in the relative pressure 0.04–0.1 range and the average pore size was evaluated through the Density Functional Theory (DFT) method. The glass powder was outgassed at 423 K for 5 h before analysis.

Particle size distribution of the SD-MBG powder was measured using a particle size analyzer (Particle Sizer Malvern 3600D). The sample was dispersed in water and sonicated for 10 min before the analysis.

2.4. $TiPS_{2.5}$ scaffolds

To fabricate the fibrous scaffolds, bundles of $TiPS_{2.5}$ fibres were cut at precise length, weighted and randomly placed inside a zirconia cylindrical mould with the help of a funnel. Since we observed that the construct of fibres was able to maintain its structure also without the presence of the mould, the sintering treatment for $TiPS_{2.5}$ scaffolds was carried out removing the zirconia mould (Fig. 1-a).

2.4.1. 85 and 110 μm diameter scaffolds

Scaffolds using fibre diameter of 85 μm (750 mg, 3 mm) or 110 μm (900 mg, 3 mm) were prepared. The optimization of the sintering