Sol-Gel Process for Robocast Calcium Phosphate Scaffolds

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Introduction: Biphasic composites of Hydroxyapatite (HA) and β-Tricalcium phosphate (β-TCP) are promising candidates for the fabrication of tailored bone engineering scaffolds based on the preferential dissolution of TCP vs. HA [1,2]. Among the technologies able to produce biphasic calcium phosphate materials with controlled Ca/P ratio, the sol-gel method presents considerable advantages due to its low cost, simplicity and high versatility, for the synthesis of materials with very homogeneous molecular composition [3]. The aim of this work was to combine sol-gel synthesis with direct write assembly (robocasting) to build tissue engineering scaffolds with controlled composition and porosity.

Experimental: The sol-gel process used in this work is summarized in Figure 1. A first solution was prepared by dissolving Calcium Nitrate Tetrahydrate (CNT) into absolute ethanol under vigorous stirring. In parallel, the TriEthyl Phosphite (TEP) precursor was mixed with deionised water and absolute ethanol. Hydrolysis reactions take place in the ethanol-water media leading to phosphoric and calcium forms [3]. Then, CNT and TEP hydrolysed sols were mixed in the Ca/P ratio range from 1.5 to 1.67 to get HA and β-TCP phases after sintering. Finally, water was added to accelerate the hetero-condensation reaction leading to a polymeric solution composed by oligomeric derivatives containing -Ca-O-P- bonds [3]. Evaporation of the solvent allowed the acceleration of polycondensation reactions to get an amorphous powder containing -(Ca-O-P)$_n$- oligomers. Mixed with a solvent, this powder turns into a gel used to print scaffolds by robocasting following a process previously described [4]. In a second step the polymeric solution were used to coat the scaffold internal surfaces by dip-coating.

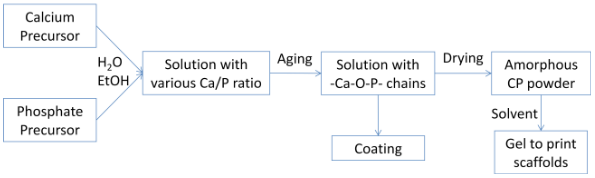

Figure 1: Sol-gel procedure to obtain CP solutions and gels respectively used to coat and print scaffolds.

Results: Three-dimensional scaffolds were successfully patterned by extruding the gel through 250 µm cone tip (Fig. 2). Printed scaffolds consist of macro-pores about 250 µm, i.e. space between lines (Fig. 2a) and 80 µm, i.e. space between layers (Fig. 2b). Such porosity could allow cell seeding and bone formation inside the scaffold as required for tissue engineering applications. The internal surfaces of the scaffolds are rough and the printed lines exhibit micro-pores about 1-2 µm (Fig. 3a). Larger pores (~15 µm) can be formed on the surface of the printed lines by coating the scaffolds using the sol-gel solution (Fig. 3b). According to the literature, the micro-porosity could play an important role in fibrovascular ingrowth, promoting apatite crystallization and cell adhesion, which could accelerate *in vivo* bone formation.

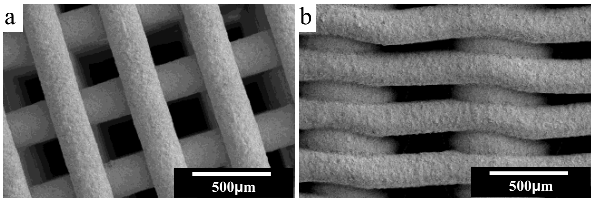

Figure 2: SEM micrograph of a robocasted scaffold: (a) top view and (b) side view.

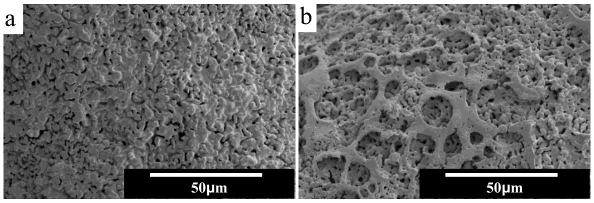

Figure 3: SEM micrographs of scaffold surfaces (a) without coating and (b) with coating.

X-ray diffraction analysis demonstrates that HA/TCP and TCP/Pyrophosphate biphasic scaffolds can be fabricated by manipulating the sol-gel process parameters, i.e. the initial Ca/P ratio and the solvent selection. The overall porosity (micro- and macro-porosity) of the scaffolds ranges between ~72 vol% without coating and ~67 vol% after coating. The compressive strength increases from ~6 to ~12 MPa after coating. Both porosity decrease and mechanical strength increase result from the decrease of micro-porosity after infiltration with the solution.

Conclusion: Highly porous biphasic calcium phosphate scaffolds have been fabricated by combining sol-gel synthesis with robocasting. The method allows an easy control of the scaffold chemistry and porosity. These parameters are key factors in the scaffold performances.

References:

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