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3D-Bioactive aerogel scaffolds for bone tissue engineering

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1. Introduction

Bone tissue engineering (BTE) aims to regenerate this tissue at critical-sized defect sites. An ideal bone scaffold should mimic the bone extracellular matrix and provide suitable mechanical properties to preserve the physiological and anatomical function of the damaged area [1]. Alginate scaffolds are biocompatible and suitable for cell colonization but they lack the bioactivity needed for bone regeneration [2]. Accordingly, hydroxyapatite (HA) is commonly used as a bioactive component in BTE to promote cell adhesion. In general, mechanical and biological properties of bone substitutes can be enhanced by crosslinking strategies. Specifically, glutaraldehyde (GA) is a chemical crosslinker commonly employed on biopolymeric scaffolds to improve their mechanical properties and stability.

Different techniques have been proposed to obtain BTE scaffolds. Among others, three-dimensional (3D) printing is a reproducible and precise technology for the manufacturing of bone scaffolds with patient-specific shapes [3]. Furthermore, alginate bioinks have been widely employed in BTE scaffolds because of its easy and fast crosslinking ability. Nevertheless, one of the current 3D-printing technical limitations is the lack of nanostructuration in the end structures. Aerogel technology could help to solve this problem but the production of these nanoporous materials with a customized external structure is still a remarkable challenge [4].

In this work, alginate-HA aerogels were obtained by the combination of 3D-printing and supercritical drying techniques. GA post-crosslinking was performed on aerogel scaffolds. Biocompatibility, bioactivity and textural properties of aerogels were then measured and assessed for BTE applications.

2. Materials and methods

Scaffolds were printed from different alginate-HA aqueous inks (6 wt.% alginate aqueous solutions with HA-to-water ratios of 0, 8, 16, or 24 wt.%) using a grid pattern (20x20x1 mm) with 3 layers. After the printing process, scaffolds were put directly in contact with 1 M CaCl2 for aging. The 3D-aerogels were obtained after solvent exchange to ethanol and supercritical drying (120 bar, 40 ºC, 5 g/min, 3 h). GA crosslinking was performed in aerogel scaffolds for 1 h under room temperature and vacuum. The effect of GA treatment on the textural parameters of the scaffolds was evaluated by SEM analysis. Biocompatibility was assessed in BALB 3T3 cells after 24 and 48 h of incubation using this cell line as positive control. Bioactivity assays were performed in simulated body fluid (SBF) at 37 ºC for 28 days.

3. Results and Discussion

Homogeneous and customized 3D-structures formed by filaments arranged in layers were successfully obtained by the technological combination herein proposed (Fig. 1). The initial 3D-structure and porosity of the printed gel were preserved in the resulting aerogel scaffolds, with mesopores and macropores clearly recognized.

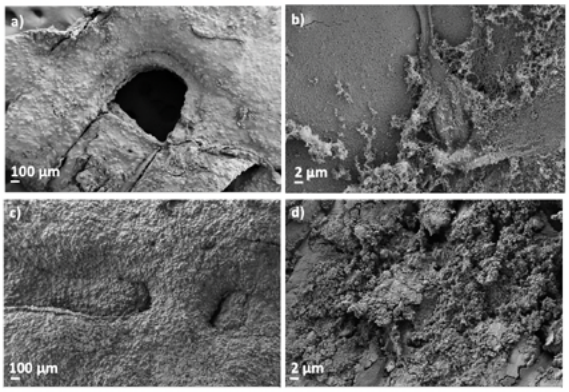

Figure 1: SEM images of alginate-HA aerogels. (a,b) AlgHA16 %. (c,d) AlgHA16 %,GA.

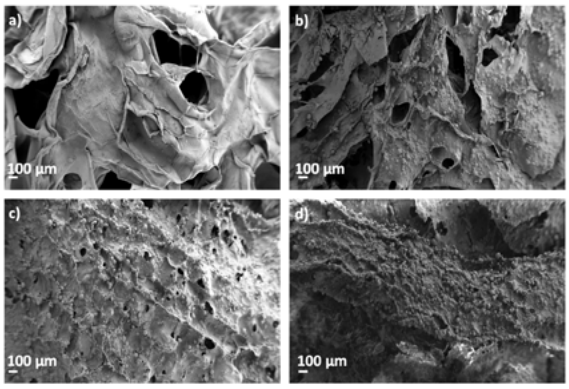

Figure 2: SEM images of alginate-HA aerogels after SBF treatment for 28 days. (a) AlgHA0 %, GA; (b) AlgHA8 %,GA; (c) AlgHA16 %,GA and (d) AlgHA24 %,GA.

Excellent results of viability of BALB cells were found for all aerogel formulations, without observing statistical significance (t-test, $p < 0.05$) with respect to the positive controls, thus confirming the lack of cytotoxicity. Finally, apatite formation was found at all HA concentrations studied thus confirming the long-term bioactivity of the aerogel scaffolds (Fig. 2). An increasing HA content in the scaffolds resulted in a higher apatite growth.

4. Conclusions

Macroporous alginate-HA aerogel scaffolds following a customized pattern were obtained by the technological combination of 3D-printing and supercritical drying. Lack of cytotoxicity and high apatite formation were found at all formulations studied, thus confirming the excellent biocompatibility and bioactivity of alginate-HA aerogel scaffolds and also their potential for BTE applications.

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