Fill molding in Capillaries (FIMIC) with new precursors for hydroxyapatite (HAp) biomineralization

1 Introduction

It is a great challenge to synthesize scaffold biomaterials for application in bone tissue engineering, which can mimic both the structure and the mechanical properties of natural bone. The mineral Calcium Phosphate and in particular **Hydroxyapatite** (**HAp**) is one of the most widely investigated materials in this field, due to its chemical similarity to the inorganic matrix of the natural bone, its bioactivity and its excellent osteoconductivity[1]. A novel monomer called **PhosMA**, a methacrylate derivative containing **phosphonate** groups, has been recently investigated due to its ability to provide nucleation sites for the formation of Hap, in close collaboration with researchers from the University of Potsdam; Katrin Bleek and Andreas Taubert[2].

Poly(ethylene glycol) (PEG) is nontoxic, cytocompatible material, which displays protein repellent behavior and, therefore, shows minimal cell–substrate interactions[3,4]. **PEG-based hydrogels**, due to their unique properties, are widely used, for example, for tissue engineering replacements, drug and growth factor delivery among other applications[5].

In this study, **novel PEG-based polymer blends (PEG-PhosMA) and composite (PEG-PhosMA-nHAp) hydrogels** were prepared. These **"bioactive" gels** are expected to have the property to promote HAp biomineralization, which make them promising **biomaterials** for tissue engineering applications, such as bone repair.

Moreover, to design materials with variable surfaces properties is capital for investigatingcell-substrate interactions in biomimetic and biological materials, which can facilitate to understand the bone and tooth formation mechanisms. With this aim, the FIMIC process[6] (Figure 1) has been successfully adapted to a new set of polymerizable precursors in order to obtain **FIMIC-micropatterned materials** with tunable properties, e.g. chemical surface patterns of bioactive alongside bioinert materials.

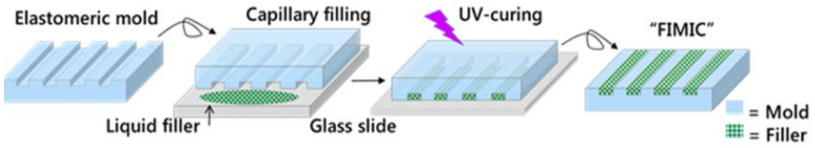

Figure 1: Schematic representation of the FIMIC method.

2 Results and Discussion

2.1 PEG-PhosMA-nHAp composite materials for HAp biomineralization

The effect of the phosphonate groups were evaluated by comparing the SEM images of PEG-PhosMA-nHAp composite hydrogels with different ratios of PhosMA after 1 day incubation in simulated body fluid (SBF) (Figure 2). These pictures show that higher contents of PhosMA (i.e. more presence of phosphonate groups) (Figure 2A) lead to greater generation of HAp on the surface of the sample.

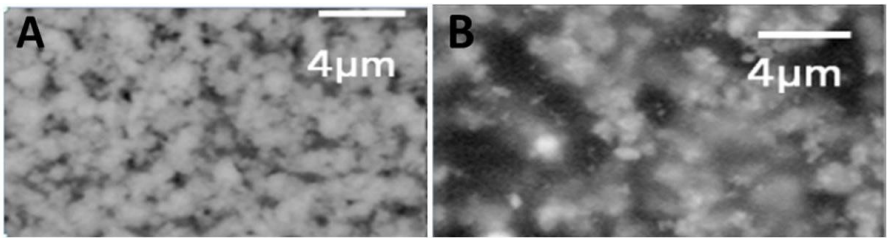

Figure 2: SEM images of PEG-PhosMA-nHAp composite hydrogels with different PEG : PhosMA weight ratios: A) 5:1, B) 9:1. Both samples were incubated 1 day in SBF.

2.2 Surface patterning via FIMIC Method

Figure 3 presents optical images of successful FIMIC substrates prepared with PEG as mold and different composite materials as filler: PEG PhosMA nHAp (Figure 3d), PEG PhosMA (Figure 3c) and PEG (Figure 3b). These pictures show the border between the filled and the still empty channels, which correspond to the typical profile for capillary filling.

These results, when compared with previously reported pure PEG FIMIC samples, confirmed that PEG-PhosMA-nHAp composites can also be used to generate FIMIC samples. The combination of PEG and this novel composite in a FIMIC substrate has the potential to generate patterned surfaces with defined bioinert areas alongside with bioactive ones, after HAp formation via incubation in SBF solution. Further experiments will focus on this research line.

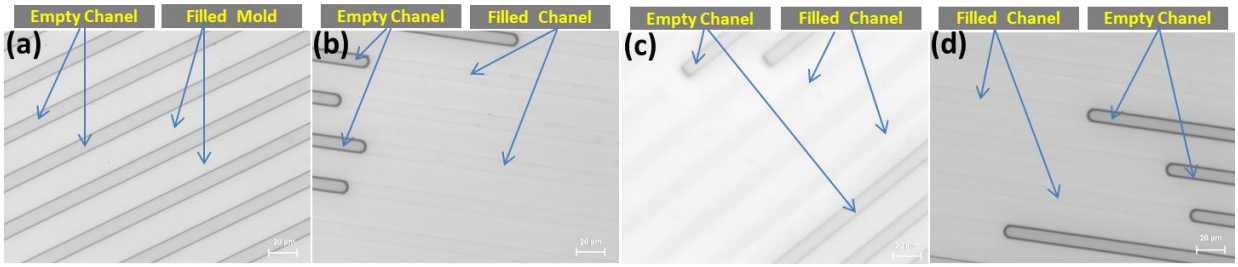

Figure 3: Optical images of: (a) PEG patterned mold, FIMIC samples: (b) PEG in PEG, (c) PEG-PhosMA in PEG and (d) PEG-PhosMA-nHAp in PEG. Scale bar: 20µm.

2.3 Atomic Force Microscopy (AFM) characterizations of the FIMIC samples

AFM analysis demonstrates that PEG-PhosMA-nHAp in PEG FIMIC samples exhibit a lateral micropattern, which corresponds to the dimensions of the PEG and the composite lines (Figure 4). A slight topographic unevenness, in the order of 400 nm, is observed as well (sample measured in dry state). Such a topography is inherent to the FIMIC method.

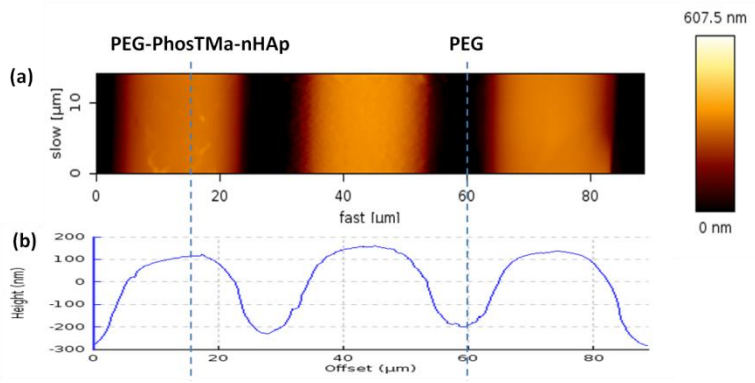

Figure 4: Topographical imaging in dry state of prepared PEG-PhosMA-nHAp in PEG FIMIC platforms, (a) Height image, (b) Height profile.

3 References

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