COMPOSITE & HYBRID (BIO)MATERIALS BASED ON BIOACTIVE GLASS: TOWARD OPTIMISED SUBSTITUTE FOR BONE BIO-ENGINEERING

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Introduction

From the need of support -as screws or plates (devices that must be easily shaped in 3D and that exhibiting specific mechanical properties)-, to the used of "gel-based device" -fillable or conformable, cellularized and/or cellularizable biomaterials (that exhibit highly hydrated properties with specific architecture in volume)-, bone regeneration necessitates various strategies and solutions to face complex, singular and multiparametric situations. Beside these specific requirements, bone substitute materials must present “osteo-properties”: from osteocompatibility to osteogenic and osteocompetency. In this context, due to its ability to release ions in solution and triggering signaling pathways that lead to osteoresponse [1], bioactive glass (BG) appear as a versatile, pertinent and universal solution whatever the bone material and the bone strategy developed. Moreover, its composition can be tuned in order to tailor its dissolution properties and/or to favor release of therapeutic ions.

Here we present the development of two different BG-systems: i) a composite based on PLA and ii) an hybrid based on gelatin (where the covalent linking between the organic and inorganic phases is insured by the (3-Glycidyloxypropyl)trimethoxysilane (GPTMS) [2]. For each system, two BG particles composition are used, 13-93 and 13-93B20 (13-93 with 20% of the SiO_2 replaced with B_2O_3).

Materials and Methods

Each system contains 70% of organic matrix (PLA or gelatin) and 30% of BG (13-93 or 13-93B20 particles weight %). The composites were processed by co-extrusion whereas the hybrids were synthetized by sol-gel transition. First, the gelatin is functionalized with the GPTMS and then the BG is added in the solution. Different proportions of GPTMS/gelatin (molar ratio) were tested in order to vary the degree of connectivity between the organic and inorganic phases.
The dissolution of both composites and hybrids materials was studied in Simulated Body Fluid (SBF) up to two weeks. The change in the SBF pH was studied and correlated to ion release, measured by Inductively Coupled Plasma - Optical Emission Spectrometry (ICP-OES). Scanning Electron Microscopy coupled with Energy Dispersive X-ray (SEM-EDX) confirmed the bioactivity related to the precipitation of an apatite layer at the materials’ surface when immersed in aqueous solution. Mass loss of the hybrids was measured and correlated to the degree of cross-linking between the gelatin and the BG particles.

Cell assays were performed in order to assess the osteoinductive potential of the materials. Osteopontin and myosin immunostainings as well as the alizarin staining were done after 14 days of incubation.

Results and Discussion

For the composites, over two weeks of immersion in SBF, the Si content in the solution increases due to the BG dissolution. The [P] and [Ca] concentration decreases overtime, suggesting the precipitation of a reactive layer. The reactive layer was further confirmed to be apatite. Precipitation of apatite was greater for the composites with boron containing glass, due to its faster dissolution rate. Myoblastic cells culture on the composites exhibits a decrease of myosin and increase of osteopontin. This indicates that the myoblastic cells in presence of BG go toward an osteoblastic lineage. Moreover, the neosynthese of a mineral matrix is evident (FIG. 1).

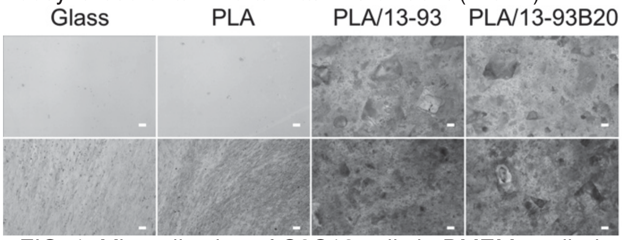

FIG. 1. Mineralization of C2C12 cells in DMEM studied with Alizarin red S staining after 14 days of incubation on glass, PLA, PLA/13-93, PLA/13-93B20 without cells (top line) or with cells (bottom line). Scale bare 200 µm.

For the hybrids, compare to a reference without bioactive glass and/or crosslinking, the mass loss is significantly lowered. This confirms the covalent linkages between the gelatin and the BG and the benefit in terms of stability. Moreover, higher is the ratio of GPTMS/gelatin, higher is the gels stability. *In vitro* dissolution of the scaffolds, performed in SBF, showed again precipitation of an apatite like-layer from BG dissolution (FIG. 2).

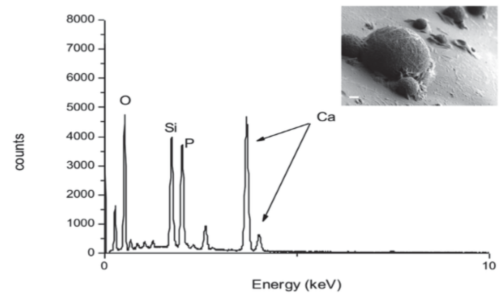

FIG. 2. EDX analysis of the nodules appearing on hybrid surfaces after two weeks of immersion in SBF.

Conclusions

These results demonstrate that the bioactivity of the BG was maintained in both composites and hybrids. Moreover, boron inclusion in the formulation allows a smart tailoring of the dissolution rate of the BG. Osteoinductive potential shown permits to conclude that such materials are promising for bone application.

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