

Development of hydroxyapatite-based biomaterials scaffolds for hard tissue regeneration

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INTRODUCTION: Hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6\text{OH}_2$)¹ has been widely used in tissue engineering specially in bone and cartilage regeneration. Sol-gel technology offers an alternative technique for producing bioactive and osteoconductive HA. Because HA can be described as a multisubstituted calcium-phosphate apatite, the presence of small concentration of ions, such as silicon, play an important role in the biochemistry of the hard tissue. The aim of this research project is to improve HA biocompatibility and bioactivity and to develop a methodology able to tailor HA scaffolds appropriate for any specific biomedical application through controlling composition, impurities concentration, crystal size and morphology.

METHODS:

HA was synthesized by sol-gel method using $\text{PO}(\text{Et})_3$ and $\text{Ca}(\text{NO}_3)_2$ as P/Ca precursors respectively. Silicon was introduced into the HA matrix using TEOS as reactant². The obtained gel was washed in water overnight and freeze-dried to achieve the desired porosity. In order to obtain the HA crystalline phase, samples were calcined for 4 hours at 400°C. HA was tailored into tablet shape using a 5 tones press and bioactivity studies were performed by soaking HA tablets into simulated body fluid (SBF). Cell attachment assays were performed by culturing human mesenchymal stem cells on top of HA and silicon-modified HA tablets.

RESULTS:

HA obtained by the sol-gel method was observed as a porous structure under a SEM. HA tablets modified with 11% silicon were immersed in SBF for one week and analysed by XRD every other day. Diffractograms showed crystallinity peaks increased from day 1 to day 7. SBF samples were also analyzed by electrophoresis to detect Ca release and an increase in Ca concentration was observed due to a Ca delivery from the HA tablet matrix to the SBF. Cell attachment assays showed higher cell density when cultured on silicon modified substrates in all

percentages studied (Figure 1). Samples containing a smaller percentages (4%, 11%) of silicon showed a 4 fold increase on cell attachment compared to non-modified HA, while higher amounts of silicon (28%) showed a 2 fold increase.

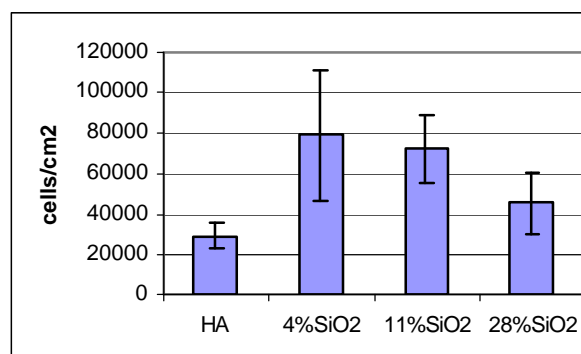


Fig 1: Cell attachment assay on different HA substrates. Cells were counterd 90 minutes after seeding.

DISCUSSION & CONCLUSIONS:

It is possible to obtain different HA porous structures for different applications demonstrating the sol-gel versatility. XRD of silicon modified HA after immersion in SBF showed an increase in HA crystallinity. On the other side, Ca release observed in electrophoresis results showed that the increase in crystallinity may be due to a stoichiometric reorganization in the HA matrix. In addition, the interaction between HA tablets and the SBF is indicative of HA bioactivity. Preliminary cell culture results demonstrate that HA obtained by sol-gel methodology is a biocompatible matrix. The addition of SiO_2 in the matrix may modify biological properties as observed the increase of cell attachment in the performed cell culture assays. Further experiments will be addressed in order to modify HA based biomaterial surfaces to obtain a total integration between the tissue and the scaffold.

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