

Study of *in vitro* degradation properties of new bioactive amorphous calcium ortho/pyrophosphate materials in various acellular media

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ABSTRACT

Among inorganic materials for bone substitution, amorphous materials have attracted a lot of attention, due to their metastability that improves their (bio)chemical reactivity and the subsequent release of active ions and/or dissolution/precipitation reactions leading to apatite formation at their surface. Even if bioactive silicate glasses have been extensively described [1,], phosphate-based amorphous materials have also been developed. Two families of materials are referenced in the literature: phosphate-based glasses that are generally melt-derived, with tunable chain length from ultraphosphate (phosphate 3D network) to invert glasses (isolated pyrophosphates / orthophosphates) and amorphous calcium phosphates; the latter can be synthesized at ambient temperature, in water and without further high temperature treatment. Recently, CIRIMAT has developed new mixed calcium orthophosphate/pyrophosphate amorphous materials prepared by soft chemistry [2] with structural properties close to those of materials mentioned above. The pyrophosphate entities can be hydrolyzed into orthophosphates by specific enzymes naturally occurring *in vivo*, or in presence of acidic pHs and thus contributing to bone regeneration. This intrinsic property is a major asset for the fine control of these biomaterials degradation and then their biological properties. The aims of this study are to i) determine the rate of *in vitro* degradation of different compositions of these amorphous materials in cell-free media, ii) understand the physico-chemical mechanisms associated to this *in vitro* evolution, in order to adapt the material composition to the required bone substitute application.

Mixed ortho/pyrophosphate amorphous materials were synthesized by soft chemistry in 4 major steps: controlled addition of a calcium solution into a phosphate solution, centrifugation, washing and drying at 70°C. The degradation tests were carried out at 37°C for 15 days in increasingly complex aqueous media (water, acidified water, simulated body fluid and culture medium) with a solid/ liquid ratio of 1.5 g/L [3]. Materials and media recovered after different degradation times were analyzed separately by XRD, Raman spectroscopy, SEM and elemental titrations.

We have shown that synthesis parameters, such as the ortho/pyrophosphate precursors ratio in solution and their concentrations, influence the nature of the final material (composition, crystallinity, morphology) and its degradation properties/ rates which are directly correlated. These results are a first step to understand and control the biodegradability and osseo-integration of these materials *via* an enzymatic degradation (study currently in progress).

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