Nanostructured calcium phosphate apatites for biomedical applications: structure and properties.

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Abstract – Synthetic calcium phosphate with particle size smaller than 50nm may be synthesized under controlled conditions. The structure and the crystallization process of hydroxyapatite nanoparticles are characterized. The decrease of particle size improves hydroxyapatite chemical reactivity and its biological response. Consequences to hard tissue bioengineering are discussed.

Hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$, HA, is actually one of the most promising biomaterials for hard tissue engineering. In vivo studies have demonstrated the ability of calcium phosphate bioceramics in stimulating osteogenesis by promoting the migration of mesenchymal cells to the implanted area, increasing their adhesion and proliferation rates and stimulating their differentiation to osteoblasts. Great efforts have been made in order to improve bioactivity and mechanical properties of hydroxyapatite and other calcium phosphates: physicochemical and morphological treatment of HA surface, association of calcium phosphate with inorganic radicals and metals, adsorption of signaling proteins such as growth factors and bone morphogenetic proteins, adhesion of polysaccharides, composites of calcium phosphates and polymers, and association of complex scaffolds with cells.

In the last years several studies have been reported concerning the properties of bioceramics with nanometric particle size. The approach involving nanoparticles is a new attempt to improve the biological response of hydroxyapatite and to develop new drug delivery devices using HA nanoparticles. In parallel, numerous investigations have dealt with the nucleation of nanostructured synthetic HA with crystal size similar to bone apatite (<50nm). Those studies intended to biomimic bone apatite formation by using synthetic calcium phosphates produced by different chemical routes. In this direction, some questions immediately arise concerning the ultra-structure of these nanosized particles and the minimum size of HA particle possible to be synthesized.

The reduction of particle size induces important changes on the hydoxyapatite behavior, when it is in contact with the biological fluid. As particle dimensions are reduced chemical activity of HA surface and protein adsorption are expected to be drastically enhanced. In addition, crystallinity, dissolution rate and sintering are affected by particle size. The driving force for sintering is the reduction of the system free energy due to the decrease in surface energy. Thus, nanosized bioceramics require less energy contribution to be sintered, meaning sinterability at lower temperatures. All these physicochemical properties linked to the decrease of particle dimensions have great influence on hydroxyapatite, *in vitro and in vivo*, behavior and consequently on its clinical use.

In this work, recent experimental techniques to synthesize hydroxyapatite nanopowders and HA nano films are discussed. We present some experimental results, in special from high resolution transmission electron microscopy HRTEM, which introduce new information concerning: i) HA and carbonated apatite nanoparticle structure and ii) particle transformation from amorphous calcium phosphate to crystalline HA. The stoichiometry, dissolution rate and capability to adsorb molecules of as-precipitated nanosized HA particles are compared with HA synthesized in normal conditions and sintered at high temperatures. We evaluated the *in vivo* behavior of nanoHA and the potential of this nanostructured material for biomedical applications.