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Tailoring the morphology of hydroxyapatite particles using a simple solvothermal route

Maïssa Dardouri[a,b], João Paulo Borges[c,*], Amel Dakhlaoui Omrani[b,d,**]

[a] Institut National des Sciences Appliquées et de Technologies, INSAT, Centre Urbain Nord BP 676 - 1080 Tunis Cedex, Tunisia
[b] Laboratory of Physical Chemistry of Mineral Materials and their Applications, National Center of Research in Material Sciences, CNRSM, Technologic Park of Borj-Cedria B.P. 73, 8020 Soliman, Tunisia
[c] CENIMAT/I3N, Departamento de Ciência dos Materiais, Faculdade de Ciências e Tecnologia, FCT, Universidade Nova de Lisboa, Portugal
[d] Department of Chemistry, Faculty of Sciences Khulais, University of Jeddah, P. O. Box 355, Jeddah 21921, Saudi Arabia

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ABSTRACT

Nanometric and sub-micrometric monodispersed hydroxyapatite (HAp) particles with different morphologies (spheres and rods) were synthesized via a simple solvothermal method using $Ca(NO_3)_2{\cdot}4H_2O$ and P_2O_5 as starting materials without any requirement to use organic templates. The growth, evolution and purity of the nanoparticles were investigated by controlling the synthesis conditions, including the alkalinity and the temperature of the solvothermal treatment. The increasing of the alkaline ratio results in a great change of the elaborated particles' morphology that evolved from anisotropic forms (nanorods, sub-micrometric rod) at pH 9, short rod particles at pH 9.5 to spherical ones at higher pH (pH≥10).

Powder X-Ray diffractometry (XRD), Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FTIR) and Nitrogen adsorption and desorption studies (BET) were used to characterize the structure and composition of the as-prepared samples.

The thermal analysis of the synthesized particles conducted by differential scanning calorimetry (DSC) shows a good stability for all morphologies with a degradation temperature reaching 1300 °C.

1. Introduction

Due to its important properties including bioactivity, biocompatibility, osteoconductivity and biodegradability, hydroxyapatite (HAp) constitutes the best candidate in biomedical applications especially for bone and teeth regeneration [1–4]: as its mineralogical composition resembles to that of natural bone and teeth, $HAp(Ca_{10}(PO_4)_6(OH)_2)$ is one of the most important members of calcium phosphate group. It has been extensively investigated and used in bone tissue engineering and regeneration, clinical orthopedic surgery, production of ceramics and scaffolds which are at present the best substitutes of the hard human tissues [1,2,5–7]. Several techniques have been used to produce HAp such as the solid-state and mechano-chemical methods, chemical precipitation, hydrolysis, sol–gel, hydrothermal treatment, emulsion and sonochemical methods as well as high temperature processes such as combustion, pyrolysis and synthesis from biogenic sources [8–10]. Among these numerous methods, researchers opt frequently for the sol–gel technique due to its simplicity and its low cost [11]. Unfortunately, to synthesize well-crystallized HAp, sol–gel process requires a high sintering temperature which could causes removal of hydroxyl ions, loss of the morphology, formation of β-TCP and CaO phases [12,13]. In order to overcome these problems, solvothermal technique is currently used. As it has been reported in the literature, the solvothermal method could be a potentially superior alternative for low-cost production of well crystallized HAp with highly homogeneous composition and uniform morphology and size at low temperature and without requiring of high sintering temperatures [11,14,15]. With this technique HAp can be easily obtained which is of potential importance for bone Tissue Engineering since the bone itself is a composite consisting of HAp nanorods integrated in a collagen matrix. The rod shaped HAp nanoparticles enhance the resorbability of the protein and possess desirable biocompatibility and bioactivity due to their better absorbability. Finally, the inclusion of 1-D nanostructured HAp in scaffolds could significantly enhance their toughness and mechanical properties [8,16–18]. A lot of researchers used to use an organic template with inorganic precursors to privilege the elongated growth of the HAp. As example, Parthiban et *al.*[19] used the hydrothermal method to prepare HAp nanorods using the thiosalicylic acid. Zhang

* Corresponding author.
** Corresponding author at: Department of Chemistry, Faculty of Sciences Khulais, University of Jeddah, P. O. Box 355, Jeddah 21921, Saudi Arabia.
E-mail addresses: jpb@fct.unl.pt (J.P. Borges), dakhlaoui_amel@yahoo.fr (A.D. Omrani).

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et al. [20] studied the influence of some organic additive (EDTA and CTAB) on the morphology and the length of HAp nanoparticles under hydrothermal treatment. They conclude that the use of CTAB results in rod-like HAp particles whereas with EDTA Hap whiskers are obtained. However, the use of these organic templates as a structure directing agent to induce the anisotropic growth of the HAp poses a threat to many biological systems, as they are known to be cytotoxic [21,22]. Qi et al. [23] have obtained various HAp morphologies (including nanoparticles, microrods, nanorods and nanorod-assembled flower-like hierarchical structures), without any organic templates, using an expensive and organic phosphorus source (Adenosine 5′-monophosphate sodium salt (AMP))by solvothermal treatment in different solvents. One of the solvents used was N, N-dimethylformamide (DMF) which is not good for biomedical applications.

This paper reports, a protocol based on a simple, reproducible and low-temperature solvothermal technique, without using any organic templates or toxic solvents for the synthesis of highly crystalline HAp nanoparticles, using two inorganic and inexpensive precursors:phosphorous pentoxide (P_2O_5) and calcium nitratetetrahydrate ($Ca(NO_3)_2{\cdot}4H_2O$). Nanometric and submicrometrical particles with different morphologies (spherical and rod-like) were obtained just by changing the pH.

The anisotropic growth of the HAp particles is determined by simple adjusting of the synthesis parameters. The growth mechanism of the HAp particles was proposed on the basis of the evolution of the morphology of the elaborated particles in relation to the synthesis parameters: pH and temperature. Our study is focused on varying only the pH and the temperature, since these variables are among others (concentration of reactants, solvents or additives) are the most widely used to control powder size and morphology under hydrothermal condition [14]. In addition Earl et al. [24] proof that the treatment time had no effect on the particle's morphology or size within the reaction time range of 24–72 h. The crystallites were measured to be within the size range 100–600 nm in length and 10–60 nm in diameter. Also Wang et al. [25] uphold and explain that the main two factors responsible to the purity and the growth of the HAp crystal are the temperature and the pH.

Furthermore, the study of Ding et al. [26] on the Hydrothermal synthesis of nanorod-assembled porous microspheres of hydroxyapatite/casein using ATP as a phosphorus source and casein sodium salt as a template confirms that the time is not the most important parameter in the hydrothermal method: so, after 2, 12, 24, 36, 72 h always microspheres are obtained and the only changes were noticed on their surface (change from smooth to rough to porous surface). In addition Wu et al. [27] compare the morphology of HAp at 40 °C without hydrothermal treatment and after hydrothermal treatment at 160 °C for 18 h. In the two cases they found nanorods and the growth occurs via c-axis, emphasizing that the time of hydrothermal treatment is not the main important factor in the hydrothermal or solvothermal treatment. Nagata et al. [28] confirm that temperature and the pH are determinant factors in the formation and growth of HAp via c-axis of the HAp.

2. Experimental details

2.1. Materials

The principal precursors used here are: calciumnitrate tetrahydrate ($Ca(NO_3)_2{\cdot}4H_2O$) (Sigma Aldrich; purity 99–103%] and phosphorus pentoxide [P_2O_5, from Sigma-Aldrich; purity > 98%]. For the preparation of the precursor solutions, absolute ethanol [C_2H_5OH, from Fisher Chemical] and Ammonia [NH_3 25%, from Sigma-Aldrich] were used as received.

2.2. Synthesis of the hydroxyapatite particles

Hydroxyapatite (HAp) particles were prepared according to the following process: the calcium nitrate and phosphorus pentoxide solutions were prepared separately in ethanol. The calcium nitrate solution together with 25% ammonia solution were added simultaneously at ambient conditions drop by drop to the phosphorus solution, using syringe pumps, during 1 h until [Ca]/[P]=1.67. The pH of the final solutions was in the range of 8.5 to 10. The milky mixture obtained was then transferred to a Teflon lined stainless steel autoclave and heated at different temperatures (140, 160, 180 and 200 °C) for 20 h.

At the end of the reaction the autoclave was cooled down to room temperature. The precipitate obtained was washed several times with Millipore water (to eliminate the NH_4^+), collected by centrifugation and dried at 60 °C overnight. The dried samples were heat treated for 2 h at 500 °C, 600 °C, 1050 °C and 1300 °C. The treatment temperatures were established based on the purity of the samples (X-ray diffraction) and differential thermal analysis data.

2.3. Characterization

The as-synthesized products were characterized using different techniques. Their crystal structure was obtained by X-ray diffraction (XRD) employing a Panalytical X'Pert PRO MPD diffractometer equipped with a copper anticathode ($\lambda_{Cu k\alpha}$=1.5418 Å). The average crystallites size was calculated using the Scherrer's relation $L=\frac{0.9\lambda}{\beta\cos\theta}$, where: λ is the wavelength of the X-ray radiation, θ is the Bragg angle of the corresponding peak, $\beta=\sqrt{\beta_M^2-\beta_S^2}$ is the full width at half-height (FWHM) of the sample, β_M, corrected for the instrumental broadening, β_S, inferred from the standard Si sample.

Scanning Electron Microscopy (SEM) micrographs were obtained using an ULTRA 55 field emission scanning electron microscope (Zeiss, Auriga). Acquisitions were carried out at room temperature applying a voltage of 5.00 kV. The free working distance (FWD) varied from 5.9 to 30 mm. The samples were thoroughly dispersed in ethanol then deposited on silicon substrates. Prior to observation all the samples were previously coated with iridium (Ir) conductive film to avoid charge effects.

Fourier Transform Infrared (FTIR) analysis was done using a Nicolet 6700 equipped with a Smart Orbit™ (Thermo Electron Corporation, Madison, WI) diamond crystal. The samples were examined in ATR (attenuated total reflectance) mode with a resolution of 4 cm^{-1}.

Differential Scanning Calorimetry (DSC) measurements were carried out with a Simultaneous Thermal Analyzer (TGA-DSC - STA 449 F3 Jupiter), in the temperature range of 30–1300 with 10 °C/min. The collected data was analyzed with the NETZSCH Proteus software.

The specific surface area and the pore size of the HAp particles were determined by Brunauer–Emmett–Teller (BET) nitrogen gas adsorption at 77 K on powder degassed at 300 °C and Barrett-Joyner-Helenda (BJH) methods respectively using Micromeritics ASAP 2010 equipment.

3. Results and discussion

Several synthesis parameters such as the pH of the reaction medium and the temperature of the solvothermal treatment have been varied in this study resulting, in certain conditions, in the formation of pure hydroxyapatite (HAp) particles with different sizes and shapes (spheres, short nanorods and rods) as summarized in Table 1.

3.1. Effect of the temperature

To determine the ideal temperature for the preparation of pure