

An algorithm for preparing bioactive fluorinated hydroxyapatite coatings by sol gel technique

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Fluorinated hydroxyapatite [Ca₁₀(PO₄)₆(OH)_xF_{1-x}] implantologic structures could constitute an alternative to classic hydroxyapatite [Ca₁₀(PO₄)₆(OH)₂] ones in medical applications due to their bioactivity and low solubility. Bioactive apatites are usually used as coatings onto surface of biocompatible metals, leading to implants which take advantage of the coating's bioactivity and good mechanical properties of metals. In this work, powders and apatite type films were prepared on Ti6Al4V medical grade alloy using three sol-gel chemical routes by mixing different calcium and phosphorous precursors Ca(NO₃)₂, P₂O₅ and C₆H₁₅PO₃, and two fluoride reagents: HPF₆ and NH₄F. The resulting calcium phosphates and fluorapatite/hydroxyapatite solid solution (FHA) compounds were investigated by SEM, XRD and evaluated in vitro in SBF Kokubo solution. An efficient preparation algorithm was designed for the Ca(NO₃)₂+ C₆H₁₅PO₃+ NH₄F chemical route which produced monophasic powders with a high crystallinity degree. This chemical route led to FHA sol-gel coatings with bioactive potential.

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1. Introduction

Sol-gel is a flexible method for preparing biocompatible films with complex structures. [1] It has been known for almost half a century that ceramics made of calcium phosphate salts can be used successfully for replacing and augmenting bone tissue. [2] The most widely used calcium phosphate based bioceramics are hydroxyapatite [HA - Ca₁₀(PO₄)₆(OH)₂] and β-tricalcium phosphate or β-whitlockite [β-TCP, Ca₃(PO₄)₂], and recently it is fast developing the flour doped hydroxyapatites: fluorapatite [FA, Ca₁₀(PO₄)₆F₂] and fluorinated hydroxyapatite or fluor-hydroxyapatite [FHA, Ca₁₀(PO₄)₆(OH)_xF_{1-x}] available in pastes, putties, solid matrices, granules and thin films. For osseointegration purposes, fluorapatite could be a material of interest because of its similarity to bony apatite and lower solubility in aqueous solutions like body fluid in comparison to HA and β-TCP respectively. On the other part, metallic based implants have high strength and fracture toughness, but their bonding ability to bone tissue is very low. In this paper we have studied different chemical routes, varying the process parameters for preparing thin bioactive flour-hydroxyapatite (FHA) films onto metallic substrates and pure and fine monophasic powders. Thus FA/HA films would facilitate joining between the prosthesis and the osseous tissue, and increase the long-term stability and integrity of the implant due to its chemical similarity to the calcium phosphate minerals in biological hard conjunctive tissue, and its ability to form a strong chemical bond with bone. [3] The morphology and the composition of the thin films and powders can be relatively easy to be controlled by sol-gel processing parameters such as starting pH of the sol, annealing for crystallization temperature [4] and addition of auxiliary chemical reagents. [5] The roughness of the metallic

surface, in order to improve the adherence between the substrate and the ceramic coating, can be obtained by promoting the formation of a TiO₂ layer after a cleaning/pasivating chemical treatment. [6], [7]. This study aimed at the preparation of bioactive FHA films on Ti6Al4V substrates through three different chemical routes using various Ca/P precursors and F promoting reagents. The resulting powders and thin layers were qualitatively and quantitatively evaluated by SEM and XRD. Their bioactive potential was tested by using in vitro Kokubo test.

2. Materials and methods

The powders and the thin films were prepared by three chemical routes, with different combinations of calcium and phosphorous precursors and fluorine reagents. The dip-coating velocities were also varied (between 0.3 and 1.2 mm/s). The films and powders were annealed in air at 500, 600 and 950 °C. A biphasic Ti6Al4V alloy was used as substrate. Structural and morphological characterization (XRD, Rigaku D/Max RA) with a scan speed of 1°(2θ)/min and a step of 0.02° and SEM, Hitachi S-4100 with Rontec Energy dispersive spectroscopy) were performed, and the bioactive potential was estimated by SBF Kokubo test. The chemical sol-gel routes were as follows: (i) mixing a refluxed phosphoric pentoxide ethanol solution with a calcium nitrate tetrahydrate ethanol solution and using hexafluorophosphoric acid as F precursor reagent; (ii) mixing a phosphoric pentoxide in a water-ethanol solution and using ammonium fluoride as precursor for F; (iii) dissolving calcium nitrate tetrahydrate and triethyl phosphite in a water-ethanol solution and adding gradually ammonium fluoride as precursor for F. The films were submerged in Kokubo solution for

characterizing the fluorine incorporation influence upon bioactivity.

3. Results and discussion

In the first route calculated amounts of phosphoric pentoxide (P_2O_5 , Riedel-deHaen) and calcium nitrate tetrahydrate ($Ca(NO_3)_2 \cdot 4H_2O$, Riedel-deHaen) were dissolved in absolute ethanol (C_2H_6O , Merck) to form 2 M solutions. These two solutions were mixed in Ca/P molar ratio of 1.67. Hexafluorophosphoric acid (HPF_6 , Aldrich, AR) prepared in 6.78 M aqueous solution was chosen as the fluorine containing reagent. Controlled amounts of HPF_6 were gradually added to the Ca-P solution, and finally refluxed for 24 hours.

After refluxing, the resulting sol became foggy and latter white opaque. The dipping sols could remain stable for 24 hours before precipitation occurred. When the dipping sol derived from the initial mixed precursor solution with HPF_6 was used for the preparation of films, all of the resulting films showed a small amount of apatite and two calcium phosphates phases in their XRD patterns.

Calcium species have a strong tendency to react with HF to form CaF_2 . [8] The HF produced in the reaction is rapidly consumed by the calcium species forming fine CaF_2 particles even in case of refluxing the mixture. The formation of solid CaF_2 causes the foggy aspect of the refluxed mixture. The XRD patterns of the gel state demonstrated that the solid product formed is CaF_2 .

By the condensation reaction, the potential FHA sol was transformed in a light yellow gel, which displayed CaF_2 lines in X-ray diffraction investigation. The gel was transformed into powders by applying different heat treatments in order to observe and to obtain different phases and degrees of crystallinity. Three different heat-treatments in air were used: 600 °C for 1 hour (the powder obtained was dark grey), 600 °C for 15 minutes (the powder was black) and 950 °C for 1 hour (the powder was light grey). At 600 °C and 950 °C for 1 hour from XRD patterns were distinguished two calcium phosphates with low crystallinity peaks: the orthorhombic calcium pyrophosphate $Ca_2P_2O_7$ and the monoclinic dicalcium phosphite $Ca_2(PO_3)_2$. After a shorter heat treatment in air at 600 °C for 15 minutes, besides the calcium phosphates mentioned previously, low intensity peaks of hydroxyapatite could be also identified. We supposed that the initial high sol acidity (pH~0.96) led to a multiphase low crystalline coatings less suitable for medical applications.

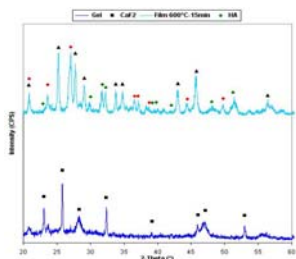


Fig. 1. XRD patterns of the first chemical route: gel and HA/FA film heat-treated at 600 °C for 15 minutes.

A scanning electron microscopy analysis has been performed on dip-coated samples of titanium alloy. This has provided supplementary information regarding the chemical composition and the morphological structure of the deposits. The investigated coated samples have been prepared by immersion in the FHA dipping sol with various speeds between 0.5 and 3 mm/s, and then dried and heat-treated.

The structure presented multiple cracks, due to the high acidity (pH~0.96) of the dipping sol and to the vibrations existing during the immersion of the samples, and certain domains with crystallized particles. The surface morphology was rough and comprised agglomerates of nano-particles. The heat-treatment that offered better results was the one applied to the samples at 600 °C for 15 minutes in air, the withdrawal speed from the dipping sol being 0.5 mm/s. The surface morphology of these samples had a more smooth appearance, and contained zones without cracks.

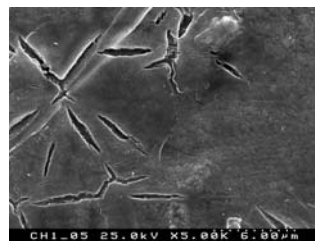


Fig. 2. Scanning electron microscopy image of a FHA / Ti6Al4V structure annealed at 600 °C for 15 minutes in air, withdrawal speed of 0.5 mm/s.

Fig. 3 shows SEM photos taken to coated titanium based alloy sample maintained for 21 days in SBF solution. The morphology of the immersed sample demonstrates that even the small amounts of the apatite type compounds present in the coating induced the creation of new bonds and the growth of calcium phosphates onto the sample surface, due to its bioactivity. Energy dispersive spectrometry (EDS) analysis allowed us to distinguish the presence of calcium and phosphorous on the substrate coated with sol, proving once more that the surface ingrowths consist of calcium phosphates.

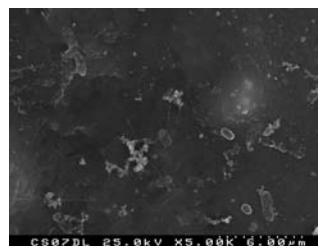


Fig. 3. Scanning electron microscopy image for the 1st route FHA coated sample immersed in simulated body fluid for 3 weeks.

For the second route the sol was prepared mixing a 0.6 M phosphoric pentoxide (P_2O_5 , Riedel-deHaen) in

ethanol – water solution, 2M calcium nitrate tetrahydrate ($\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, Riedel-deHaen) ethanol solution and 0.4 M ammonium fluoride (NH_4F , Riedel-deHaen,)

After aging at 38 °C the sol became strongly precipitated, being separated in two distinct parts: a transparent supernatant liquid and a gelatinous white precipitate due to the strong tendency of the calcium species to form CaF_2 molecules. The reaction developed more slowly in comparison with the first case, when the HPF_6 was used as fluorine reagent. The first signs of precipitations occurred approximately after 36 hours. In order to perform the dip-coating of the titanium alloy samples, the sol was stirred and heated at 75 °C for 3 hours. Thus a stable, white-transparent dipping sol was obtained, without any sign of precipitation along 6 weeks. The gel state was obtained by maintaining a small amount of liquid dipping sol in an oven at a constant temperature of 80 °C for 48 hours. The gel and the fluor-hydroxyapatite coatings on Ti6Al4V substrates prepared by the sol-gel method using the organo-metallic precursors and the fluorine reagent mentioned above were characterized by X-ray diffraction and scanning electron microscopy.

The XRD patterns of the coatings and the calcinated powder obtained at 500 °C in air (Fig. 4) presented besides the majoritary apatitic phase other bioactive calcium phosphates phase as whitlockite [$\text{Ca}_3(\text{PO}_4)_2$]. [9] The main problem is the high solubility of $\text{Ca}_3(\text{PO}_4)_2$ and its fast resolvable properties, making the coating less suitable for anchoring the new formed bone at the surface of the substrate.

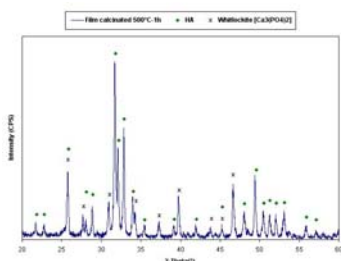


Fig. 4. XRD patterns of 2nd route FHA thin layers deposited by sol-gel method onto Ti6Al4V alloy substrates.

The SEM morphology (Fig. 5) revealed an inhomogeneous surface with agglomerated nanoparticles.

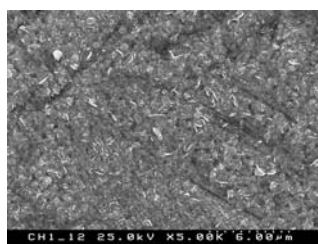


Fig. 5. Scanning electron microscopy image of a 2nd route dip coated sample at a withdrawal speed of 1.2 mm/s.

In the third chemical route the dipping sol was prepared by mixing calcium nitrate tetrahydrate

($\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, Riedel-deHaen) + triethyl phosphite ($\text{C}_6\text{H}_{15}\text{PO}_3$, Aldrich) + ammonium fluoride (NH_4F , Riedel-deHaen).

The obtained sol was maintained in a controlled pH range of 8 – 10, in order to have a preferred formation of the fluor-hydroxyapatite, and keep a high stability of the reaction. The dipping sol was subsequently fed into an oven, where it was held at a constant temperature of 80 °C for 2 days which represented suitable conditions for the condensation process to take place, leading to the formation of the fluor-hydroxyapatite gel.

The basic pH values provided a large number of OH^- ions to the solution. The OH^- surely acted as capturing the released H^+ , rendering the solution less acidic and more importantly accelerating the reaction in forward direction.

The XRD investigations (Fig. 6) confirmed the presence of apatite signals in the gel structure.

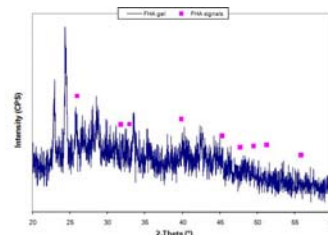


Fig. 6. XRD patterns of the 3rd route FHA gel.

Thus, after a series of different heat-treatments the gel has been transformed in powders with different colors and grain size depending of the applied temperature. The resulting powders were characterized by X-rays diffraction (XRD).

The best results have been obtained after the calcination at 950 °C in ambient air. The obtained powders were white and presented a fine appearance.

The XRD analysis (Fig. 7) showed a high crystalline, monophasic apatite compound, with no impurity or other residual calcium phosphates phase's or traces of CaO or CaF_2 present.

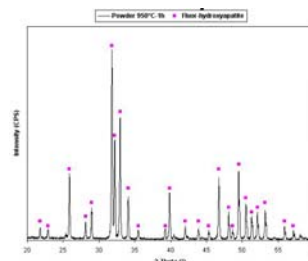


Fig. 7. XRD patterns of 3rd route fluor-hydroxyapatite powder calcinated in air at 950 °C.

The lattice parameters were calculated in order to establish if the compound obtained is fluorapatite/hydroxyapatite solid solution. The calculated “a” parameter with an average value of 9.388 (Table 1) demonstrated that the powders obtained in this work were indeed fluor-hydroxyapatite type.

Table 1. Comparative table between HA (PDF #09-0432), FA (PDF #15-0876) and respectively the experimental FHA's lattice parameters.

Lattice parameter	HA ASTM	FA ASTM	FHA exp. average
a=b (Å)	9.42	9.36	9.38
c (Å)	6.88	6.88	6.88

These encouraging results obtained for the FHA powders were continued by the films preparation. The 3rd chemical route coatings were prepared respecting approximately the same procedure as for the previous two routes. The substrates were immersed / withdrawn vertically into/ from the dipping sol at a constant speed of 0.3 mm/s. The as-dipped structure was dried at 80 °C for 1 hour, and the dried structure was annealed at 500°C for 1 hour in ambient air. The deposition run was repeated in order to increase the FHA film thickness.

The XRD patterns for these types of coatings annealed at 500 °C in air (Fig. 8) presented a crystalline majoritary FHA structure with a few signals owned to the metallic substrate. Such structure should have a good influence on the acceptance by human body of the implant to be coated with, due to a high purity that conducts to low controlled dissolution rate.

