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Wet synthesis and characterization of modified hydroxyapatite powders

R.N. CORREIA, M.C.F. MAGALHÃES*, P.A.A.P. MARQUES*, A.M.R. SENOS
*Departamento de Engenharia Cerâmica e do Vidro, and *Departamento de Química, Universidade de Aveiro, PT-3810 Aveiro, Portugal*

Hydroxyapatite powders with reproducibly different Ca/P ratios and powders with varying amounts of co-precipitated magnesium, sodium and potassium were synthesized by a wet method. Solids composition, particle size and morphology, crystalline structure, sintering behaviour and microstructure were investigated in order to understand the effect of composition in the properties of the powders. Under the present conditions of synthesis, it was concluded that magnesium, sodium and potassium will enter the hydroxyapatite lattice in vestigial amounts. Magnesium gives rise to a co-precipitated amorphous phase which crystallizes as β-whitlockite on calcining. A relationship was found between the Ca/P ratio in hydroxyapatite and its sinterability. The sintering process of pure and alkali-containing hydroxyapatites is completed at 1300 °C and leads to dense ceramics in the case of pure and sodium–containing hydroxyapatites but not in potassium-containing material.

1. Introduction

Hydroxyapatite (HAp) is, thermodynamically, the most stable calcium phosphate at the pH, temperature and composition of physiological fluids [1]. This solid belongs to the apatite mineral group with the general formula $Ca_5(XO_4)_3$ (Cl, F, OH), in which X = As, P, V; the phosphate group may be partially substituted by carbonate, silicate or sulphate ions; and calcium may be partially substituted by a large number of metal ions. Bone hydroxyapatite contains, in its lattice, magnesium, sodium, carbonate and traces of fluoride ions [2]. Synthetic HAp, in several physical forms, is being used in implantology because of its compatibility with osseous and soft tissues and bone ongrowth and ingrowth capability. Substitutions affect crystallinity, morphology and stability of the apatite structure [3]. Based on these characteristics and on the interest of HAp as implant material, it was considered of importance to investigate the effect of magnesium, sodium and potassium substitutions on the properties of HAp powders.

2. Experimental procedure

All chemicals used for the preparation of the samples were E. Merck *pro analysi* and the standards for inductively coupled plasma (ICP) analysis were BDH Spectrosol. Ultra–pure water from a Sation 9000 deionizer was used in all preparations and washings.

2.1. Preparation

A method for synthesizing HAp was optimized on the basis of co-precipitation methods already described [4, 5]. It consists in the dropwise addition of 500 cm^3 of 0.19 mol dm^{-3} diammonium hydrogen phosphate solution to 500 cm^3 of 0.32 mol dm^{-3} continuously stirred calcium nitrate solution, at controlled temperatures of 50 and 75 °C, in a flask (2 dm^3) with one charge funnel, a thermometer and a reflux condenser fitted with a CO_2 trap. Temperature was kept constant with a glycerol thermostat bath. During the addition the pH was kept at 8–10, using concentrated aqueous ammonia solution. The saturation of the flask atmosphere with ammonia also prevented incorporation of carbonate during synthesis. The mixture was then stirred for 4–6 days, at the same temperature and pH. The precipitate was filtered, washed thoroughly with water and finally air dried at 100 °C overnight. In the synthesis of HAp powders prepared in the presence of Mg^{2+} and K^+, nitrate salts were used, whereas sodium hydroxide was used for the synthesis with Na^+. In all these cases the same synthesis procedure was applied, introducing these ions in different concentrations in the initial calcium solution. Table I summarizes the preparation conditions of a set of solids.

2.2. Characterization

The as-dried powders were dissolved in nitric acid aqueous solutions and these analysed by ICP using

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TABLE I Preparation conditions of hydroxyapatites

No.	pH	θ (°C)	Ageing time (days)	$[Ca^{2+}]$ [a] (mol dm^{-3})	$[Na^+]$ [b] (mol dm^{-3})	$[Mg^{2+}]$ [a] (mol dm^{-3})	$[K^+]$ [a] (mol dm^{-3})	$[HPO_4^{2-}]$ [c] (mol dm^{-3})
A17	8–10	50	6	0.32	–	–	–	0.19
A21	9–10	75	4	0.32	–	–	–	0.19
A22	9–10	75	4	0.32	0.05	–	–	0.19
A23	9–10	75	4	0.32	–	–	0.05	0.19
A6	8–10	50	6	0.29	–	0.029	–	0.19
A15	8–10	60	6	0.32	–	0.05	–	0.19
A16	8–10	60	6	0.32	–	0.006	–	0.19

[a] As nitrate salts
[b] As sodium hydroxide
[c] As ammonium hydrogen phosphate

a Jobin Yvon 70 Plus spectrometer for the determination of total calcium, magnesium, potassium, sodium and phosphorus content in the solids. Thermogravimetric analysis in air up to 900 °C were performed at 5 °C min^{-1} using a Mettler TG50 thermobalance operated by a Mettler TC10A TA Processor. Specific surface area was determined by three-point nitrogen adsorption analysis (BET) using a Quantasorb apparatus. Characterization of as-dried and calcined powders (900 °C for 1 h, in air) was done by infrared (IR) analysis on HAp/KBr pellets in a Fourier transform IR (FTIR) spectrometer Mattson 7000 processed by computer, X-ray diffraction (XRD) with CuK$_\alpha$ radiation using a Rigaku Geigerflex Dmax-C diffractometer equipped with a curved graphite monochromator crystal and scanning electron microscopy (SEM) imaging using a Hitachi S4100 field-emission microscope. The sintering behaviour of the as-synthesized powders was qualitatively assessed by dilatometry in air, in a Linseis L75 apparatus operating at 5 °C min^{-1} up to 1300 °C, on pellets cold-isostatically pressed at 300 MPa in a Stansted press.

3. Results and discussion

Composition, molar ratio, specific surface area (S) and the temperature of the onset of densification (T_{in}) values, for the prepared solids, are given in Table II.

3.1. Factors affecting the synthesis of non-substituted hydroxyapatite

Several methods of synthesis of stoichiometric hydroxyapatite with different degrees of crystallinity and various nucleation and growth rates have been reported [6–12]. Experiments were carried out in the present work in order to find a reproducible method of synthesis and it was found that the composition of the final powder is influenced by the nature of the reagents, pH of solutions, ageing time and temperature. The reproducibility of the process was achieved by close control of these parameters. Ammonium and nitrate (instead of the commonly used chloride) salts were used in order to eliminate the possibility of uptake by the precipitates of ions other than calcium, phosphate and hydroxide.

TABLE II Molar ratio and specific surface area (S) of powders, and temperature (T_{in}) of the onset of densification

Sample	Ca/P	Mg/Ca	Na/Ca	K/Ca	S (m^{2}g^{-1})	T_{in} (°C)
A17	1.62	–	–	–	58.9	530
A21	1.66	–	–	–	45.9	800
A22	1.65	–	1.7×10^{-3}	–	39.8	680
A23	1.63	–	–	8×10^{-4}	35.5	680
A6	1.52	0.06	–	–	9.1	–
A15	1.52	0.05	–	–	10.9	530
A16	1.58	2.6×10^{-3}	–	–	43.7	530

The pH of the solutions was kept above 9 to avoid the crystallization of calcium-deficient hydroxyapatites, as a result of the introduction of hydrogenophosphate ions in the apatitic lattice [13].

The ageing time of the precipitates is related with the temperature of the experiment. A variety of combinations exist between these two parameters, and several authors have studied their correlations. Vitus *et al.* [5] showed that crystallization of hydroxyapatite with a molar ratio Ca/P of 1.656 ± 0.023 is obtained by refluxing the solution at 100 °C for 2 h. Jarcho *et al.* [6] arrived at the conclusion that an ageing time of 7 h at 25 °C was enough to obtain stoichiometric hydroxyapatite, and Eanes *et al.* [14] observed that boiling the reactional mixture for 1 h was equivalent to keeping it overnight at 25 °C.

The present method of synthesis was thus optimized after considering and testing all the above factors. From data in Tables I and II, the comparison of samples A17 and A21, where the reagents had been mixed in the Ca/P molar ratio of 1.67, shows the major influence of experimental conditions on the stoichiometry of the final compound.

3.2. Synthesis in the presence of foreign cations

The amount of magnesium ions in the precipitates is related to the composition of the initial solutions (Tables I and II), as may be seen from the comparison of A6 or A15 with A16. Yet, the amount of magnesium precipitated was only a small fraction of its contents in aqueous solution. The yield of precipitated alkaline ions is smaller than for magnesium, so that only vestigial amounts are detected in the powders. Further work [15] indicates that the incorporation of potassium is virtually independent of its concentration in solution.

On the basis of ionic radii alone the substitution of Na^+ (95 pm) for Ca^{2+} (99 pm) should occur in the HAp lattice; however, the charge difference, with the concomitant creation of anion vacancies, will limit the solubility of sodium. Potassium (ionic radius 133 pm), on the other hand, will substitute calcium to a very low extent due to both charge and ionic radius effects. Not surprisingly, the presence of potassium has not been reported in synthesized hydroxyapatites from aqueous solutions containing high potassium concentrations [10, 16]. With respect of Mg^{2+} (65 pm) the difference in ionic radius must limit its exchange with Ca^{2+} in the HAp lattice, as discussed below. The presence of Mg^{2+} in aqueous solution has indeed been reported as inhibiting the formation of hydroxyapatite [17].

3.3. Structural and morphological characterization

IR spectra of as-dried powders are similar to those published for HAp, CO_3^{2-} lines being absent. X-ray diffractographs of all as-synthesized powders show well-defined HAp lines. An extra line at $2\theta \approx 14°$ is present only in powders which show a CO_3^{2-} absorption line in the IR spectra. In calcined powders this reflection disappears. From TG curves no unequivocal transformation effect could be found up to 900 °C.

Calcination brings about some modifications in the peak height of some HAp lines, together with the appearance of β-tricalcium phosphate in all Mg-containing powders as deduced from the appearance of strong lines at $2\theta = 31.1°$ and $34.5°$, together with coincidence for other weak lines (Fig. 1), the presence of tetracalcium phosphate being ruled out. The amount of this second phase increases noticeably from A16 to A15 (or A6), indicating that the substitution of Mg^{2+} for Ca^{2+} in the rhombohedral whitlockite structure as easier than in hydroxyapatite.

SEM/EDS of sintered magnesium-containing samples detected the presence of a Mg-free matrix and Mg-containing zones (1.5–3 at % Mg). In these Mg-rich regions the (Ca + Mg)/P measured ratio lies between 1.8 and 2.1; this result, which would point towards the presence of tetracalcium phosphate, is, however, subject to criticism, since a deviation towards high Ca/P ratios (2–2.5) has also been arrived at when analysing HAp crystals.

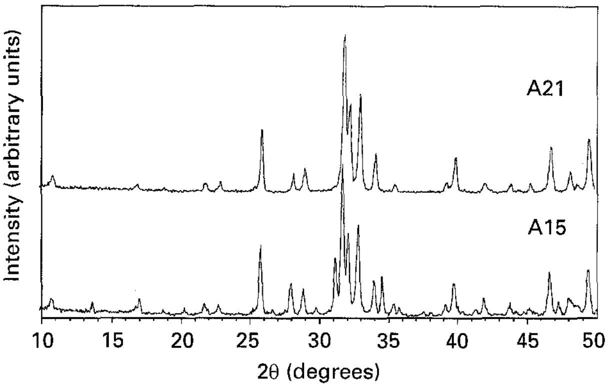

Figure 1 XRD patterns of calcined powders A21 (stoichiometric HAp) and A15 (HAp + tricalcium phosphate).

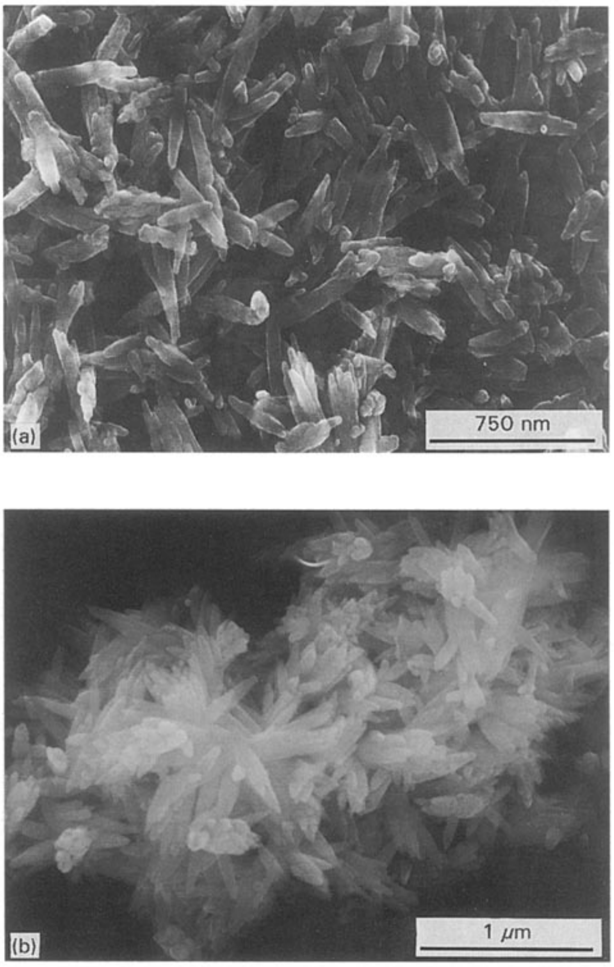

Figure 2 SEM micrograph of as-synthesized powders (a) A21 and (b) A15.

The precipitated powders have a rod-like shape with lengths of about 50 nm and an aspect ratio of about 10 and tend to form agglomerates (Fig. 2a). This tendency is thought to influence the results obtained in BET measurements (Table II) in some of the powders. In the Mg-containing powders the specific surface area decreases with increasing Mg content, which points towards the formation of strong agglomerates; this is evidenced in micrographs (Fig. 2b) and appears to be linked to the presence of an adherent and very fine, initially amorphous, phase.

3.4. Sintering behaviour

The dilatometric curves show that the temperature T_{in} for the onset of densification (Table II) varies between 530 and 800 °C, increasing with the Ca/P ratio: a ratio less than or equal to 1.62 leads to lower T_{in}, whereas the highest temperature is attained for stoichiometric HAp; other factors like specific surface area of the starting powders and presence of foreign cations do not play a clear role. In pure HAp powders or in powders with traces of Na^+ or K^+ densification saturates at 1260–1300 °C. In Fig. 3 it is seen that calcium-deficient HAp (A17) starts its densification and attains final density before stoichiometric HAp (A21). The final grain size of A17 is also somewhat greater than that of A21 (Fig. 4).

The higher sinterability of A17 is thought to be due to enhanced diffusion caused by the presence of calcium and hydroxyl vacancies. Sodium-containing samples also densify to near full density, but in potassium-containing material the plateau density is only about 90%; this latter sample presents clusters of pores whose origin needs further investigation, but no chemical segregation is observed. In all cases no abnormal grain growth is verified.

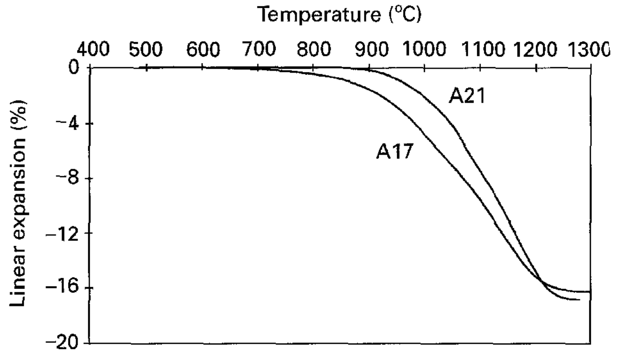

Figure 3 Dilatometric curves for pure hydroxyapatites A17 (Ca/P = 1.62) and A21 (Ca/P = 1.66).

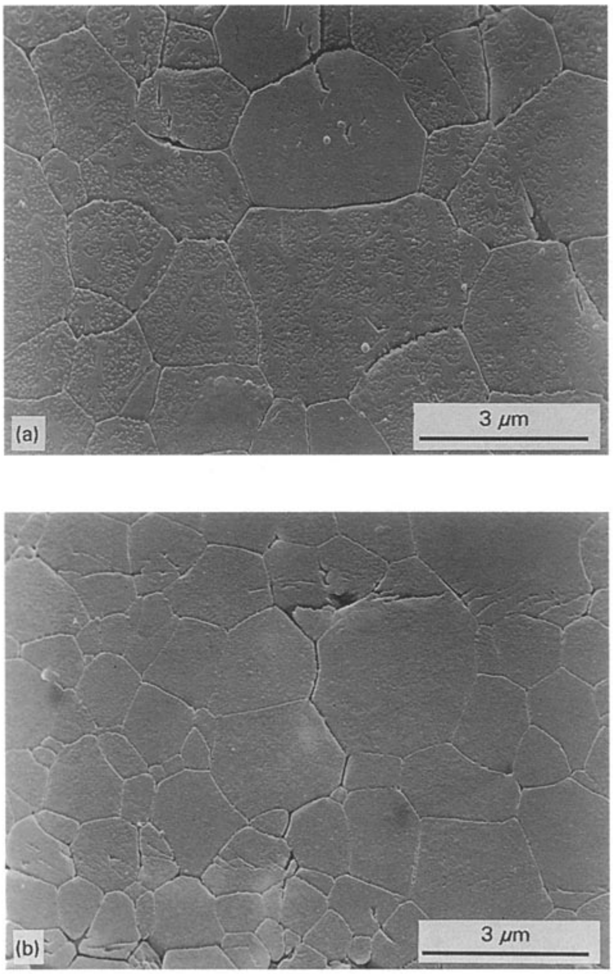

Figure 4 SEM micrographs of sintered hydroxyapatites (a) A17 and (b) A21. Etchant: 0.1 mol dm^{-3} lactic acid in aqueous solution, 30s.

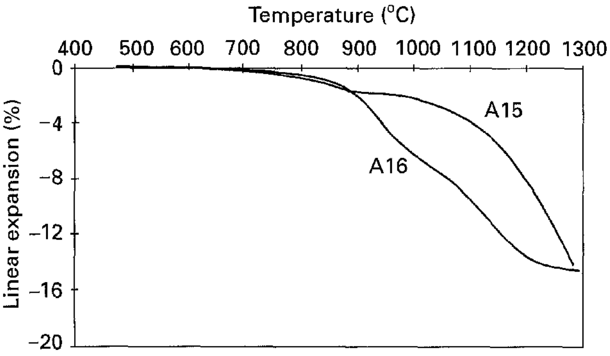

Figure 5 Dilatometric curves for Mg-containing powders A15 (Mg/Ca = 5×10^{-2}) and A16 (Mg/Ca = 2.6×10^{-3}).

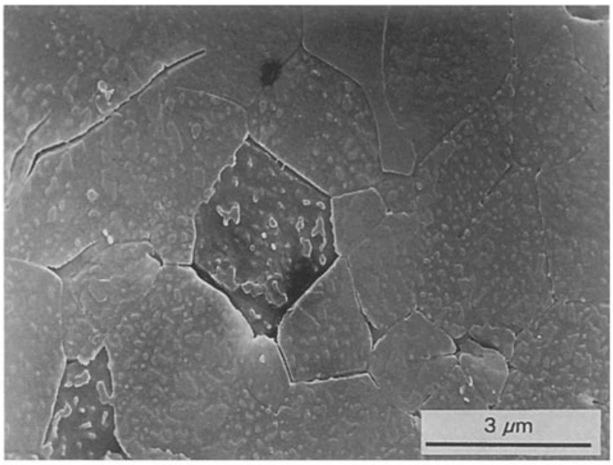

Figure 6 SEM micrograph of sintered sample A16, showing the darker Mg-rich phase. Etched as in Fig. 4.

Changes in densification rate are observed in all the curves, although more pronounced in magnesium-containing materials: since the possibility of a second phase is ruled out in all powders without magnesium, it is thought that this effect is due to preferential sintering of agglomerates [18–19], given the high values of S in the powders. The presence of a second phase retards densification: after the first 2% linear shrinkage, the shrinkage rate of A15 is lower than that of the lower β-whitlockite-containing A16 (Fig. 5). The presence of the second phase in A16 is visible in Fig. 6. This phase is presumed to form during the synthesis as a fine amorphous precipitate, leading to the agglomeration of powders.

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