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Combustion synthesis of calcium phosphate bioceramic powders

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Abstract

Calcium phosphate (hydroxyapatite and tri-calcium phosphate) bioceramics closely resembling, in chemical composition, those found in vivo in human bones have been synthesized by using novel synthetic body fluid solutions via the self-propagating combustion synthesis (SPCS) method. Powder characterization was performed by XRD, ICP-AES, FTIR and SEM. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Calcium hydroxyapatite (HA: $Ca_{10}(PO_4)_6(OH)_2$), the major inorganic phase of bones, is a member of the “apatite” family. However, biological apatites, which comprise the mineral phases of calcified tissues (enamel, dentin and bone), differ from pure and synthetically produced calcium hydroxyapatite (HA) in stoichiometry, composition, crystallinity, and also in other physical and mechanical properties.[1] Minor elements, such as, Na^+, Mg^{2+}, K^+, acid phosphate $(HPO_4)^{2-}$, Cl^-, and F^-, and some divalent trace elements, such as, Sr, Ba, Cu, Zn, or Fe, are also associated with biological apatites and may be seen as substituents in the apatite structure. On the other hand, the smaller presence of resorbable calcium phosphates in human bones (such as, tricalcium phosphate, TCP: $Ca_3(PO_4)_2$) is explained by the need for a mineralized framework for bone remodeling.

HA or TCP powders have generally been synthesized from aqueous solutions for use in bioceramic applications. It is known[2] that calcium hydroxyapatite is the least soluble and the most stable calcium phosphate phase in aqueous solutions at pH values higher than 4.2. HA has been synthesized either in neutral or highly alkaline media[3–10] to ensure the thermal stability of the formed phase after high-temperature (1100–1300°C) sintering. Synthesis of HA in neutral[5] or slightly acidic media[8] is known to be a more complicated and difficult task. The synthesis of bi-phasic mixtures of HA and TCP has also been achieved by aqueous coprecipitation.[11]

The synthetic body fluid (SBF) prepared in accord with the chemical analysis of human body fluids, with ion concentrations simulating the human blood plasma, was first used by Kokubo and his co-workers,[12–14] to prove the similarity between in vitro and in vivo behaviors of certain glass-ceramic compositions. Tas[15,16] has recently synthesized nanosized HA powders, under the biomimetic conditions of 37°C and $pH = 7.4$, by using synthetic body fluids (SBF), instead of water, as the precipitation medium.

Self-propagating combustion synthesis (SPCS) is an established technique for powder synthesis, first used by Kingsley and Patil[17] for the preparation of high-purity α-alumina powders. The combustion being both rapid and energy-saving has attracted much interest and been successfully utilized in the synthesis of $LaCrO_3$,[18] $YBa_2Cu_4O_8$[19] and Y–Ba–Cu–O phases.[20] Recently, combustion methods using “glycine” as the fuel,[21] and “urea” as the fuel,[22,23] have also been reported for the preparation of Ca-doped $LaCrO_3$, pure $LaAlO_3$ and the binary phases of the $CaO–Al_2O_3$ system, respectively. A similar combustion route was also demonstrated for the synthesis of YAG:Cr and Y_2O_3:Eu,[24] and of YAG:Nd and YIG:Nd[25] powders using both of the above-mentioned fuels.

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The purpose of this study is to prepare powders of HA/TCP calcium phosphate bioceramics by using the technique of combustion synthesis in synthetic body fluid solutions containing dissolved calcium nitrate tetrahydrate and di-ammonium hydrogen phosphate salts, and to investigate their high temperature (600–1150°C) calcination and phase evolution behavior in a stagnant air atmosphere.

2. Experimental

The chemical composition of the novel synthetic body fluid (SBF) solutions[26] used during the combustion synthesis experiments is given in Table 1.

The reagent-grade (>99.5%, Merck, Darmstadt, Germany) chemicals listed in the second column of this table were first added (by the amounts given in the third column) into a 700 ml volume of previously boiled de-ionized water in the order given in the first column. The solution was heated to 37±1°C in a water bath and then completed to 1 l, by slowly adding aliquots of a total of 10 ml of 0.7 M HCl (for pH adjustment to 7.4) together with the required amount of de-ionized water. Prior to adjusting the volume to 1 l and HCl addition, the nominal ion concentrations in the SBF solutions were as given in Table 2 (with the only exception of Cl^-, which is going to be higher (i.e. 132 mM) than the value given there due to the titration with HCl solution). Human plasma is also known to contain small amounts of elements, like Fe, Cu, and Zn,[27] and these elements are accordingly present in this SBF solution.

The solutions used during the combustion synthesis were prepared as shown in Table 3, in six groups of experiments (each repeated thrice for reproducibility). First, a 50 ml portion of the above-described SBF solution was placed in a clean Pyrex® beaker of 250 ml capacity. $Ca(NO_3)_2.4H_2O$ and $(NH_4)_2HPO_4$ salts, of the amounts given in Table 3, were then respectively added. The resulting opaque solution was then made clear, by adding 0.5 ml of concentrated (36 vol.%) nitric acid (99.9%, Merck) while stirring on a stir-plate at room temperature. Three grams of urea were finally added to the clear solution, and following 2 min of stirring at room temperature, the beaker was directly placed in an electrical box furnace pre-heated to 500±10°C. The beaker was taken out of the furnace after 15 min. The foam-like, crisp products of the combustion reaction were lightly ground in an agate mortar/pestle by hand into a fine powder and then calcined on clean α-alumina plates, in a stagnant air atmosphere, over the temperature range of 600–1150°C, with 17 hours of soaking at the selected temperature.

Phase characterization was performed on both the as-is and calcined samples by powder X-ray diffraction. A powder diffractometer (Rigaku, DMax/B, Tokyo, Japan) was used with monochromatic $CuK_{\alpha1}$ radiation and step size of 0.02° and a preset time of 5 s. The Infrared spectra of the powder samples were collected by an FTIR spectrometer (Nicolet, DX-510, USA) in the transmission mode, collecting 64 scans in the 4000–400 cm^{-1} range, with 2 cm^{-1} resolution. Dried (at 90°C) calcium phosphate samples were mixed in an agate mortar with 3 wt.% KBr prior to pellet formation for FTIR analyses. Particle size and morphology of the

Table 1
Preparation of synthetic body fluids[a]

Order	Reagent	Amount (gpl)
1	NaCl	6.429
2	$NaHCO_3$	2.520
3	KCl	0.373
4	$Na_2HPO_4.2H_2O$	0.178
5	$MgCl_2.6H_2O$	0.305
6	$CaCl_2.2H_2O$	0.368
7	$ZnCl_2$	0.136
8	$CuSO_4.5H_2O$	0.125
9	$FeC_6H_5O_7.3H_2O$	0.897
10	$(CH_2OH)_3CNH_2$	6.057

[a] Patent pending:[26] Turkish Patent Institute, TR 1999 0037, 11 January 1999.

Table 2
Ion concentrations of synthetic body fluids[a]

Ion	Concentration (mM)
Na^+	142
Cl^-	125
HCO_3^-	30
K^+	5
Mg^{2+}	1.5
Ca^{2+}	2.5
HPO_4^{2-}	1
Cu^{2+}	0.5
Fe^{2+}	3
Zn^{2+}	1
SO_4^{2-}	0.5

[a] Patent pending:[26] Turkish Patent Institute, TR 1999 0037, 11 January 1999.

Table 3
Experimental compositions studied by SPCS

Sample	$Ca(NO_3)_2{\cdot}4H_2O$ (g)	$(NH_4)_2HPO_4$ (g)	Ca/P (atomic)
1	1.457	0.479	1.70
2	1.457	0.494	1.65
3	1.457	0.509	1.60
4	1.457	0.526	1.55
5	1.457	0.543	1.50
6	1.457	0.562	1.45

powders were investigated by SEM (Jeol, JSM6400, Tokyo, Japan). The samples were sputter-coated with an approximately 25 nm-thick layer of Au-Pd alloy, prior to SEM analyses. Chemical analyses of the synthesized calcium phosphate powders were performed by ICP-AES (Perkin Elmer, Plasma-1000, UK). The residual C and N contents of the phosphate powders were determined by the combustion-IR absorption method (Eltra, CS-800, Germany).

3. Results and discussion

Nitrate solutions usually decompose at temperatures less than 700°C with the evolution of gases, such as NO_2, NO and N_2O_5.[20] Urea is also known[20,23] to decompose into biuret (H_2N–CO–NH–CO–NH_2, i.e. $C_2H_5N_3O_2$), cyanuric acid (HCNO), and ammonia (NH_3), when it is heated to about 200°C. Biuret itself then decomposes when heated at temperatures >300°C. Therefore, in an aqueous mixture of a metal nitrate and urea, the gaseous decomposition products are expected to consist of nitrous oxides, NH_3 and HCNO. This gaseous mixture will spontaneously ignite when the ambient temperature reaches about 500°C.[23] This ignition was believed to instantaneously increase the local temperature of the dried foam to about 1300°C,[20] which, in a sense, is similar to the case of flash pyrolysis.

The calcium-phosphate solutions placed into the furnace at 500°C in Pyrex® beakers have initially undergone boiling and dehydration followed by decomposition, with swelling and frothing, resulting in a voluminous, beige foam which ruptures with a flame and glows to incandescence.[17] The entire process was complete in less than 15 min.

Fig. 1 shows the XRD spectra of the combustion-synthesized calcium phosphate compositions listed in Table 3. The samples of this figure were all calcined in air at 1150°C for 17 h, following the SPCS process. The variation in the nominal Ca/P (molar) ratio in the starting SPCS solutions was found to provide a useful control in the final phase assemblage (in terms of the distribution of HA and TCP phases) of the 1150°C-calcined powders. Single-phase HA powders were only obtained, as expected, for the Ca/P ratios (in the initial solutions) which were in excess of 1.65. Samples prepared from solutions with Ca/P <1.667 all yielded (after 1150°C calcination) bi-phasic mixtures of HA-TCP. In other words, the amount of TCP (as evaluated by the quantitative interpretation of XRD peak heights and widths) in the two phase mixtures increased as a function of decreasing Ca/P ratio, as follows; 10% at 1.65, 19% at 1.60, 35% at 1.55, 80% at 1.50 and 95% at 1.45. Phase assemblage in these samples consisted of a mixture of both α- (high-T) and β- (low-T) polymorphs of tri-calcium phosphate. The powder synthesis method presented in this study may be regarded as a quick way (as compared to chemical precipitation processes[4,11]) of

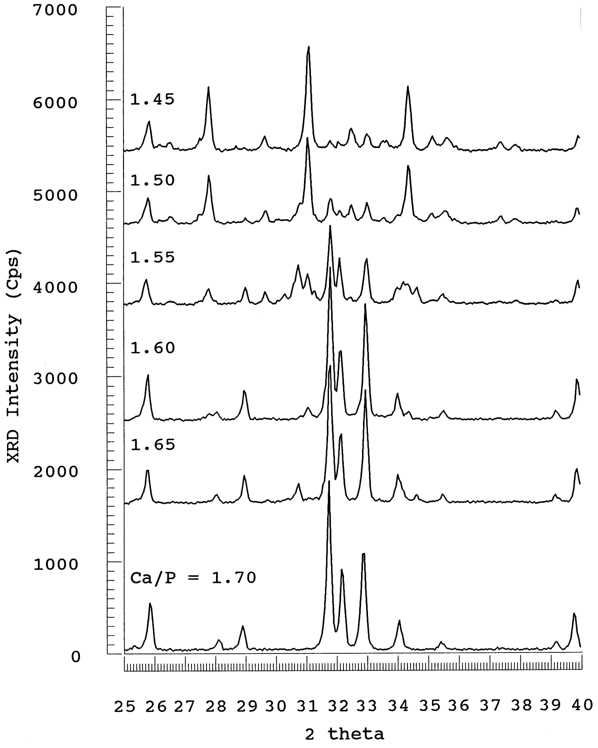

Fig. 1. XRD spectra of combustion-synthesized calcium phosphate compositions of Table 2 (1150°C, air, 17 h).

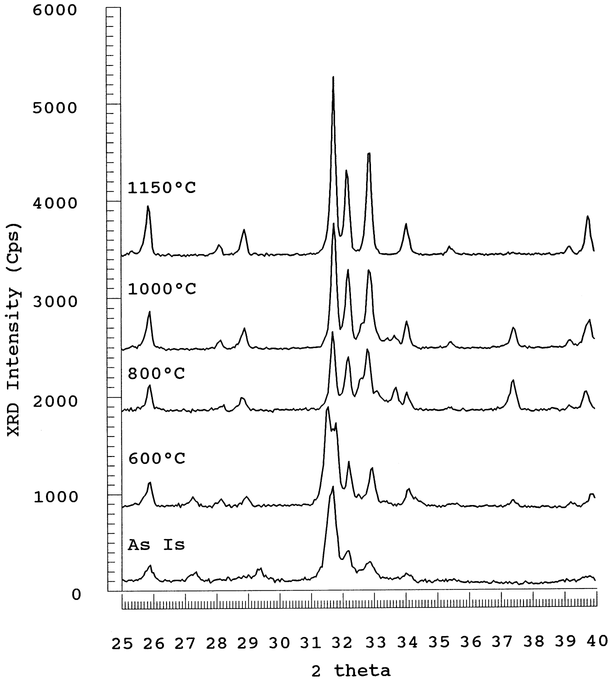

Fig. 2. XRD spectra showing the crystallization behavior of combustion-synthesized powder samples having the initial solution composition of (Ca/P =) 1.70. (Air, 17 h each heating.)

producing the powders of bi-phasic mixtures of HA and TCP, as well of single-phase HA.

Fig. 2 shows the XRD spectra of the combustion-synthesized powder samples obtained with an initial (solution) Ca/P ratio of 1.70, after being heated at different, consecutively increasing temperatures. The "as-is" powders obtained immediately following the CS process were found to be crystalline, and they basically consisted of the phases of $Ca_8H_2(PO_4)_6.5H_2O$ (ICDD PDF 26-1056), $Ca(OH)_2$ (PDF 4-733) and CaO (PDF 4-777). After heating (15°C/min: heating and 5°C/min: cooling) these powders in a stagnant air atmosphere at 600°C for 17 h, the above phase assemblage was almost retained. Calcination of the same powders at 800° and 1000°C caused the initial formation of HA phase (ICDD PDF 9-432), and the powders heated at 1150°C were found to consist of single-phase calcium hydroxyapatite. The lattice parameters of the 1150°C-calcined HA samples were measured as $a = 9.431$ and $c = 6.884$ Å. These values were in good agreement with those reported[28] for natural bone apatites.

Table 4
Results of ICP-AES analysis of 1150°C-calcined HA samples

Element	Wt.%
Ca	39.415
P	18.348
Mg	0.113
Na	0.072
K	0.009
Cl	0.109
Fe	0.014
Zn	0.005
Cu	0.003

The results of the ICP-AES analysis performed on the 1150°C-calcined, combustion-synthesized HA powder samples were given in Table 4. The powder samples were first dissolved in HNO_3 and the ICP-AES analyses were then performed on these solutions.

The presence of elements other than Ca and P in the calcined HA sample seen in Table 4 was purely due to the use of novel SBF solutions during combustion synthesis experiments. The atomic Ca/P ratio was found to be 1.6601 for these powders. In the 'as is' (uncalcined) precursor samples of Ca/P = 1.70 composition, the carbon level was about 240 ppm, and the nitrogen

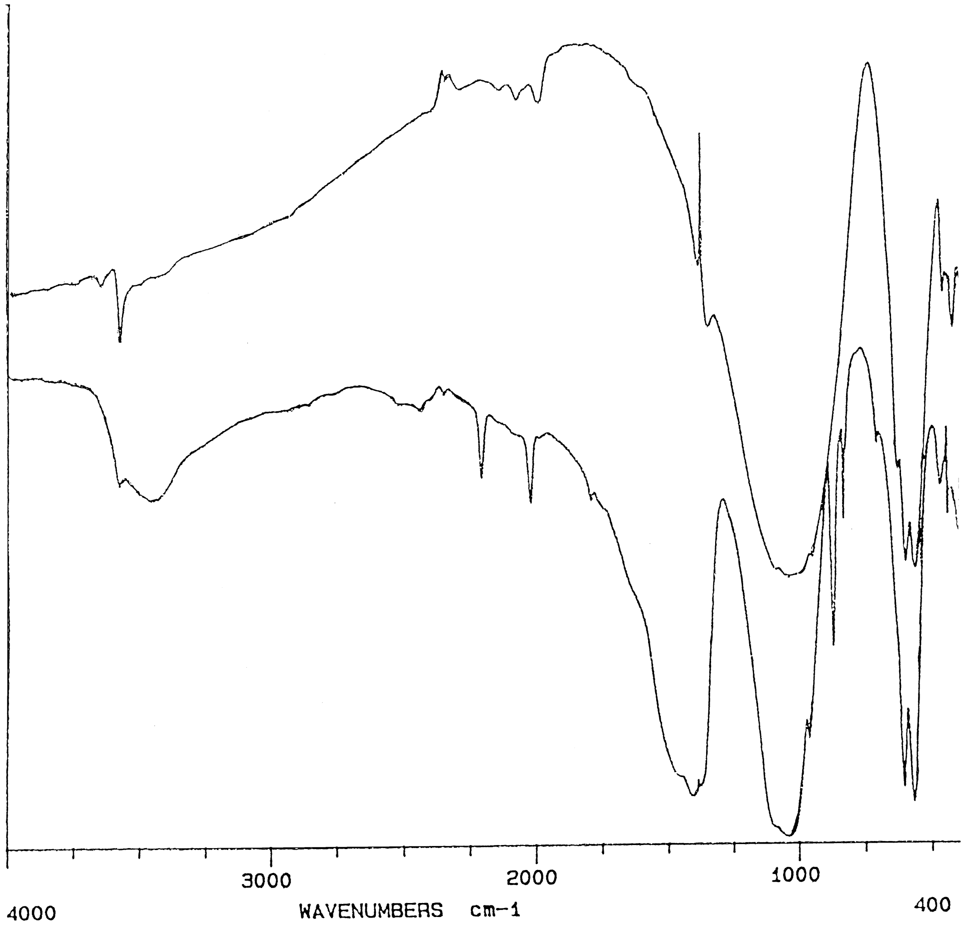

Fig. 3. FTIR spectra of the combustion-synthesized powder samples having the initial solution composition of (Ca/P =) 1.70. (Top: 1150°C-calcined; bottom: as-is powders.)

content was in the vicinity of 1.3 wt.%. Both values have then dropped below 100 ppm (i.e. the detection limit of the equipment used for C and N analyses) upon calcination at 1150°C in air for 17 h.

Although a crystallographic study of the mechanism(s) of incorporation of the divalent transition elements (i.e. Fe, Cu and Zn) into the crystal structure of calcium hydroxyapatite is beyond the scope of this paper, these cations (together with Mg^{2+}) are expected to substitute on the Ca-sites of the structure as previously reported, for Mn^{2+}, by Hughes et al.[29] Cl^- ions are also expected to substitute on the OH^- sites of the structure[30]. On the other hand, in vivo animal experiments on these samples are still strongly needed to check their biocompatibility with the natural bones, in comparison to synthetic HA samples prepared via pure water.

Fig. 3 shows the typical FT–IR spectra of "as-is" and "1150°C-calcined HA" powder samples (sample 1 of Table 3). The bottom spectrum of the "as-is" powders displayed the NO_3^- bands at 2213 and 2034 cm^{-1} (as an inevitable result of the SPCS method), and a significant CO_3^{2-} presence indicated by the large bands at 1470–1420 and 880 cm^{-1}. The top spectrum (Fig. 3) of "1150°C-calcined" sample had the OH^- stretching vibration at 3571, OH^- bending vibration at 636, and the PO_4 bands at 1096, 1045 (v_3), 962 (v_1), 603, 570 (v_4) and 470 (v_2) cm^{-1}, which are typical for the HA phase, respectively. The most important observation from the comparison of these two spectra would be that upon calcination at 1150°C, the samples were almost decarbonated and the nitrate bands disappeared.

Fig. 4 shows a typical SEM photomicrograph of the combustion-synthesized calcium phosphate precursor powder sample (sample 1 of Table 3), after being heated at 200°C, as a loose powder body, for 6 h. The powders were then ultrasonically (Misonix, XL2015, USA) dispersed in isopropyl alcohol (5 mg powder in 10 ml alcohol) and a single drop of this suspension was dried at 100°C on a clean glass slide, prior to the Au-Pd coating and SEM study. The particles were observed to be sub-micron and non-agglomerated, with an average particle size of 0.45 μm.

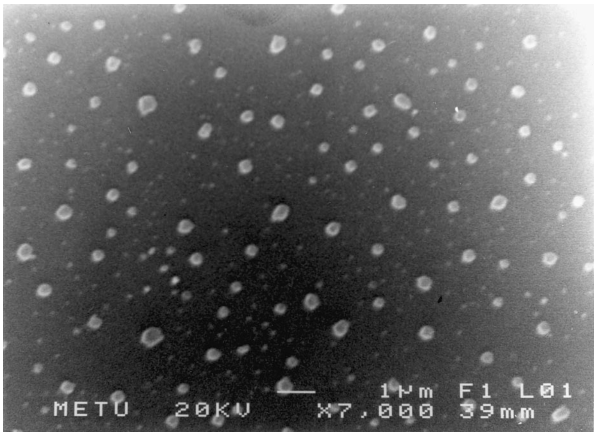

Fig. 4. A typical SEM micrograph of combustion-synthesized calcium phosphate powder samples having the initial solution composition of (Ca/P =) 1.70. (200°C, 6 h.)

4. Conclusions

A new chemical recipe for the preparation of synthetic body fluids (SBF), which contains small concentrations (at the levels of human blood plasma) of transition elements, such as Fe, Cu and Zn, has been developed. These novel SBF solutions were used for the synthesis of single-phase HA and bi-phasic HA-TCP bioceramic powders by the self-propagating combustion method.

The combustion process was shown to be an alternative and quick way of synthesizing the sub-micron (0.45 μm) powders of calcium phosphate bioceramics, starting with SBF solutions which contain calcium nitrate tetrahydrate, di-ammonium hydrogen phosphate and urea. Combustion-synthesized HA and/or TCP bioceramic powders were found to contain (after calcination at 1150°C in air) Mg, Cl, Na, K, Fe, Zn and Cu, all being at the ppm levels similar to the chemical composition of natural bones.

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