

Microwave-assisted synthesis of calcium phosphate nanowhiskers

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Calcium phosphate [single-phase hydroxyapatite (HA), single-phase tricalcium phosphate (TCP), and biphasic HA-TCP] nanowhiskers and/or powders were produced by using a novel microwave-assisted “combustion synthesis (auto ignition)/molten salt synthesis” hybrid route. This work is an example of our “synergistic processing” philosophy combining these three technologies while taking advantage of their useful aspects. Aqueous solutions containing NaNO_3 , $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and KH_2PO_4 (with or without urea) were irradiated in a household microwave oven for 5 min at 600 watts of power. The as-synthesized precursors were then simply stirred in water at room temperature for 1 h to obtain the nanowhiskers or powders of the desired calcium phosphate bioceramics.

I. INTRODUCTION

Calcium hydroxyapatite¹ [HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$], the major inorganic phase of bones, is a member of the “apatite” family. However, biological apatites (e.g., enamel, dentin, and bone), differ from pure and synthetically produced calcium hydroxyapatite in stoichiometry, composition, crystallinity, and also in other physical and mechanical properties.¹ Minor cations (e.g., Na^+ , K^+ , Mg^{2+} , Sr^{2+} , Ba^{2+} , Cu^{2+} , Zn^{2+} , or Fe^{2+}), and anions (e.g., HCO_3^- , HPO_4^{2-} , Cl^- , and F^-) are also associated with biological apatites. These can be considered ionic substituents in the apatite structure. The more resorbable β -tricalcium phosphate [β -TCP, $\text{Ca}_3(\text{PO}_4)_2$], when present in synthetic bone substitute materials, helps improving the resorption and bioactivity of the implanted bioceramics, and increase their ability in taking part in the in vivo bone remodeling processes.

HA or single-phase tricalcium phosphate (TCP) powders have generally been synthesized from aqueous solutions for use in bioceramic applications. It is known² 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^{3–6} to ensure the thermal stability of the formed phase after high-temperature (1100–1300 °C) sintering. Synthesis of HA in neutral or slightly acidic media⁷ is known to be a more complicated and difficult task. The synthesis of biphasic mixtures of HA and TCP has also been achieved by aqueous coprecipitation.⁸ HA-TCP biphasic bioceramics, due to the higher in vivo solubility of beta-TCP,

display increased bioactivity as compared to more stable pure HA samples.⁹

This work utilizes a microwave-assisted “auto ignition” process to synthesize the aforementioned materials.^{10,11} The auto ignition synthesis has been referred to as combustion synthesis (CS) by Kingsley and Patil¹² for the preparation of high-purity α -alumina powders. We prefer to use the term auto ignition to distinguish it from “combustion synthesis” or “self-propagating high temperature synthesis,” using mostly solid reactants.^{13,14} The process, which used urea (H_2NCONH_2) as the fuel in a $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and $(\text{NH}_4)_2\text{HPO}_4$ system of starting chemicals, was previously used to synthesize calcium phosphate powders.¹⁵ A variant procedure [citric acid and ethylene glycol, mixed with $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and $\text{NH}_4\text{H}_2\text{PO}_4$] based on the Pechini process¹⁶ was also shown to work well for the synthesis of calcium phosphate powders.¹⁷ However, both the combustion synthesis (or auto ignition)¹⁵ and Pechini-like process¹⁷ required high-temperature calcination steps (at 1000–1200 °C for prolonged periods) for the formation of the calcium phosphate phases (i.e., HA, TCP, or biphasic). This is where the advantage can be taken of molten salt synthesis. The molten salt synthesis technique,¹⁸ which uses a molten flux, was shown to form monodispersed whiskers of HA upon heating and cooling of a mixture of HA powders and K_2SO_4 from 1100 to 1200 °C, followed by washing in water to remove the K_2SO_4 glass and expose the HA whiskers.^{19,20}

The present communication reports the development of an extremely simple and rapid microwave-assisted, molten salt-combustion (auto ignition) synthesis hybrid procedure to manufacture nanowhiskers and nanopowders of HA, TCP, and HA-TCP biphasic bioceramics. The work is an example of our “synergistic processing”

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technique, which utilizes the useful features of the aforementioned processes.

II. EXPERIMENTAL PROCEDURE

Aqueous solutions containing dissolved NaNO_3 , $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, KH_2PO_4 , concentrated HNO_3 , and urea (all reagent-grade, Fisher Chemicals, Fairlawn, NJ) were prepared in 10 ml of deionized water in 30 ml-capacity Pyrex beakers, as shown in Table I. The first chemical added and dissolved in water was NaNO_3 , while the last one was urea. Small amounts of concentrated nitric acid were added for the sole purpose of dissolving back any colloidal calcium phosphates that might have formed following the addition of Ca- and phosphate-salts into the NaNO_3 solution. Thus, for each case shown in Table I, clear-transparent solutions were obtained.

Small sample beakers were then placed onto $10 \times 10 \times 1$ cm alumina insulating fiberboards and covered with an upside down 250 ml-capacity glass beaker. To proceed with the auto ignition-molten salt process, the above-mentioned sample assemblies were placed into a household microwave (MW) oven (Sunbeam, max. power 600 W, 2.45 GHz, Boca Raton, FL) for only 5 min. The MW oven was always operated at its maximum power setting. At the end of 5 min of MW heating within a well-ventilated fume hood, the sample beakers were taken out and their contents were let to cool down to room temperature (RT) in ambient atmosphere over the next 10–15 min. The substance in the sample beaker was then scraped off with a spatula, and directly placed (without grinding) into 500 mL of deionized water at RT ($22 \pm 1^\circ\text{C}$) and vigorously stirred for 1 hour. Formed suspension was filtered by using a vacuum-assisted Buechner funnel, and washed with 2 L of water, prior to drying the powders at 80°C for 2 hours. Samples were characterized by powder x-ray diffraction (XRD) (XDS 2000, Scintag, Sunnyvale, CA), Fourier transform infrared (FTIR) (Nicolet 550, Thermo-Nicolet, Woburn, MA), scanning electron microscopy (SEM) (Hitachi S-3500, Tokyo, Japan), FESEM (Hitachi S-4700), and ICP-AES (Thermo Jarrell Ash, Model 61E, Woburn, MA) analysis.

III. RESULTS AND DISCUSSION

Sample solutions placed into the MW oven first went through an initial stage of evaporation and boiling of

TABLE I. Sample preparation for HA, TCP, and HA-TCP biphasic samples.

Sample	NaNO_3 (g)	$\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (g)	KH_2PO_4 (g)	15.69 M			Ca/P
				HNO_3 (ml)	Urea (g)		
HA	5.00	1.00	0.345	0.10	1.75	1.67	
TCP	5.00	1.00	0.384	0.10	...	1.50	
Biphasic	5.00	1.00	0.345	0.10	0.075	1.67	

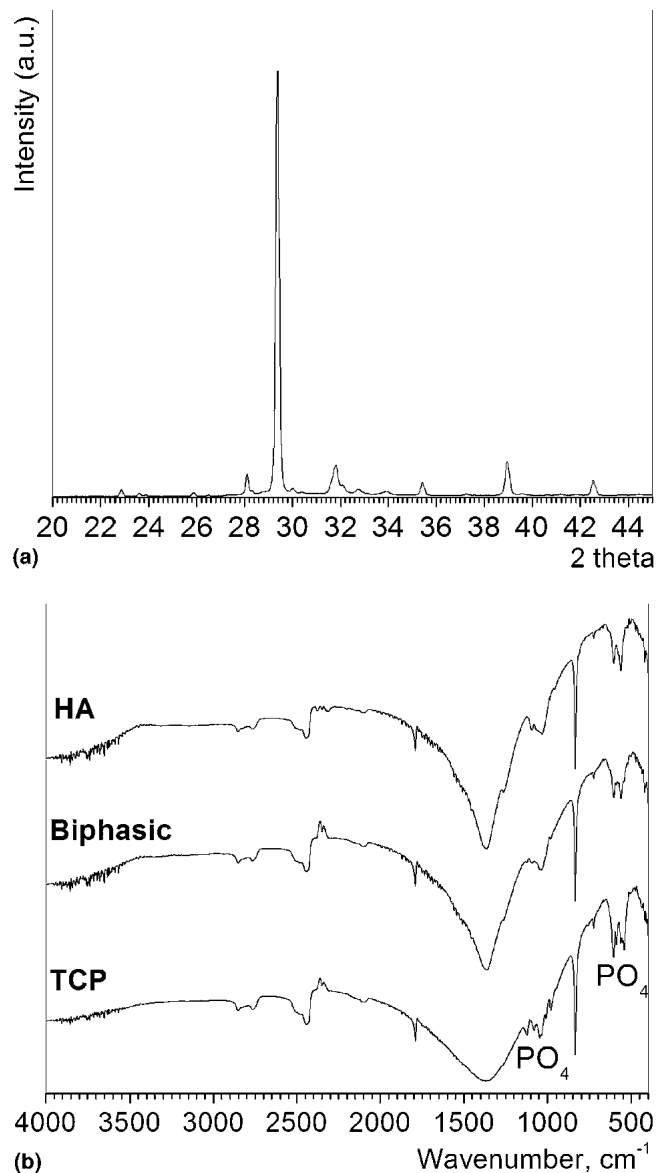


FIG. 1. XRD and FTIR data for the unwashed samples. (a) XRD data: single-phase NaNO_3 . (b) FTIR data: phosphate bands are present in otherwise a typical NaNO_3 trace.

water. This obviously took place within the first minute. Urea is known²¹ to decompose into biuret ($\text{H}_2\text{N}-\text{CO}-\text{NH}-\text{CO}-\text{NH}_2$, i.e., $\text{C}_2\text{H}_5\text{N}_3\text{O}_2$), cyanuric acid (HCNO), and ammonia (NH_3) when it is heated to about 200°C . Biuret itself then decomposes when heated at temperatures $>300^\circ\text{C}$. Nitrate solutions, on the other hand, usually decompose at low temperatures with the evolution of gases, such as NO_2 , NO , and N_2O_5 . Moreover, we used NaNO_3 , which melts at 307°C ,²² at a high concentration in our liquid samples. It would have been possible to lower this salt melting temperature further if we were using mixtures of NaNO_3 and KNO_3 .^{23–29} All the samples glowed red in the MW oven between the 90 and 240 s of heating time. In high urea solutions, intermittent

sparks were also observed within that time period. This is the evidence of occurrence of combustion in this hybrid process. In the solutions containing urea, an exothermic reaction occurs which generates high temperatures leading to deformation of the Pyrex beakers. At the end of 5 min of MW irradiation, the recovered sample beakers only contained a liquid phase of slightly yellowish tint. NaNO_3 did not evaporate and it formed a molten salt. This liquid phase solidified at RT within the following 4–5 min, by forming large dendritic crystals of NaNO_3 on its surface.

Powder XRD data of all the unwashed samples (i.e., after 5 min of microwave heating, but without wash in water) only showed the presence of NaNO_3 as the crystalline phase, as seen in Fig. 1(a). However, as expected, FTIR data of the unwashed precursors revealed the presence of characteristic phosphate infrared (IR) bands [labeled in Fig. 1(b)], as given in detail elsewhere.^{15,19}

The relatively big chunks (20–700 μm) common to all the unwashed samples, are shown in the SEM picture of Fig. 2(a). Scraping off of the reacted substance with a spatula from the inner walls of the reaction beakers led to

that wide size distribution. Following the washing step, these chunks turned porous as seen in Fig. 2(b), upon the dissolution and removal of NaNO_3 . pH values of the washing solutions in situ raised to about 11.5–11.8 at the end of 1 h ($t = 60$ min) of stirring at RT. The pH value of the solutions at $t = 0$ was around 10. Powders were further washed in a Buechner funnel filter unit until the effluent solution has reached a neutral pH value. Figures 2(c)–2(f) display the SEM morphology of the TCP, HA-TCP biphasic, and HA samples, respectively. TCP samples [Fig. 2(c)] mainly consisted of Whitlockite (β -TCP) rhombohedra, with only a small amount of whiskers. The solutions of TCP samples (with a Ca/P molar ratio of 1.50 and solution pH ≈ 0.9) did not contain any urea, and there was almost no combustion observed during MW irradiation. The solutions containing urea (pH ≈ 1.5) lead to the auto ignition-like process, and helped in increasing the temperature of the molten salt phase [Fig. 2(d)]. Growth of nanowhiskers is more readily facilitated within a molten salt of lower viscosity, otherwise equiaxed grains are observed,³⁰ as depicted in Fig. 2(c). XRD and FTIR data for these samples are

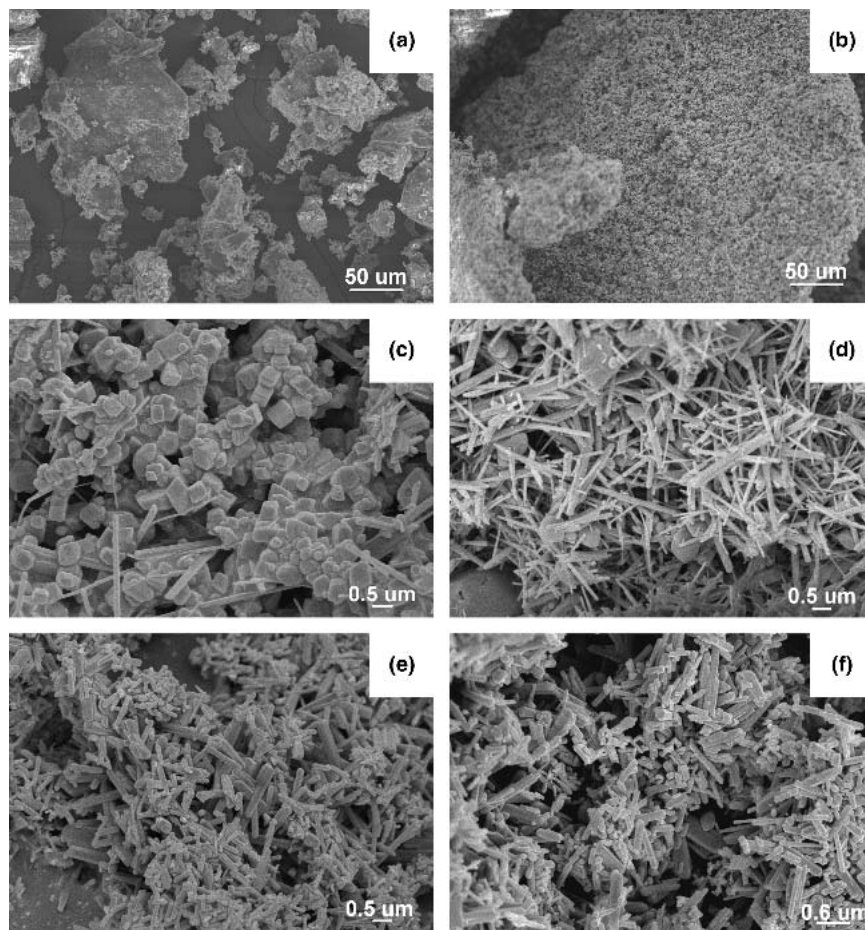


FIG. 2. SEM micrographs of calcium phosphate samples: (a) NaNO_3 -ctg precursors, low magnification, (b) after washing, low magnification, (c) TCP samples, (d) biphasic HA-TCP samples, and (e, f) HA samples.

depicted in Fig. 3. Monodispersed nanowhiskers of HA obtained by this robust and simple process were about 1 μm long and 100 nm thick, as shown in Figs. 2(e) and 2(f). The biphasic samples [Figs. 2(d) and 3(a)] contained around 60% TCP and 40% HA. The volume percentage of the HA phase can easily be adjusted by varying the urea content in the starting solutions, as shown in Fig. 4. Inductively coupled plasma analyses of the HA, TCP, and HA-TCP biphasic samples revealed that they contain around 1.5 wt% Na and 250 ppm K. In the case of HA samples, such ionic substitutions surely cause a deviation from the perfect stoichiometry of $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. However, non-stoichiometry in an

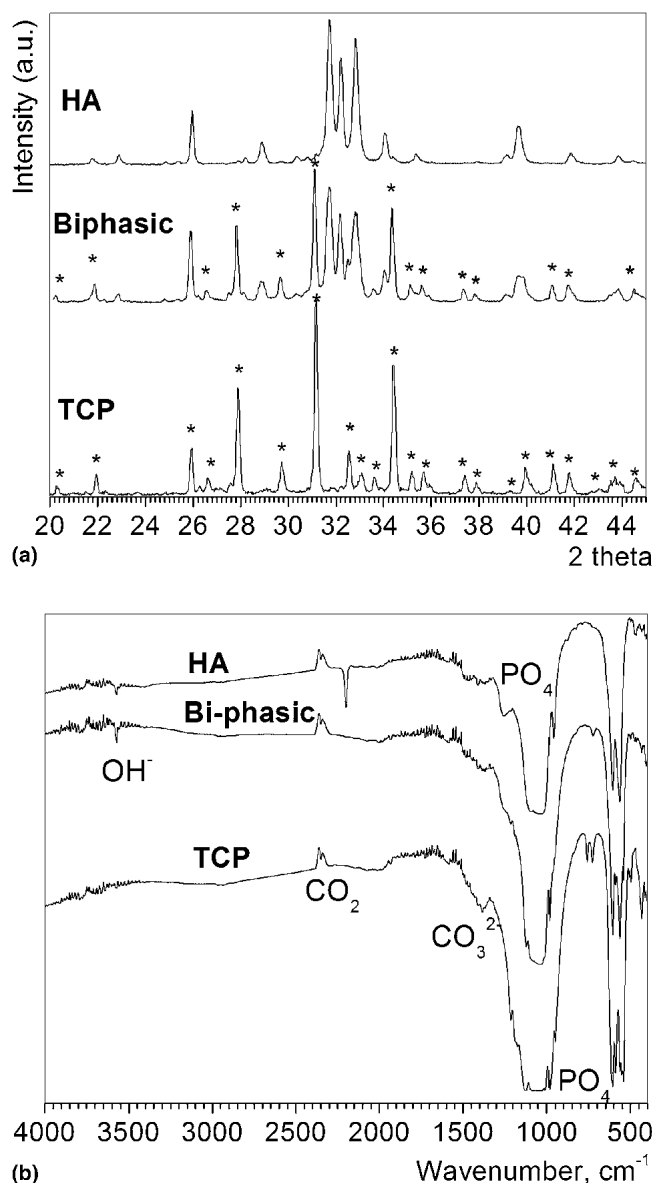


FIG. 3. XRD and FTIR data for calcium phosphate nanopowders and nanorods: (a) XRD traces, where (*) denotes TCP peaks and (b) FTIR traces for TCP, biphasic, and HA samples.

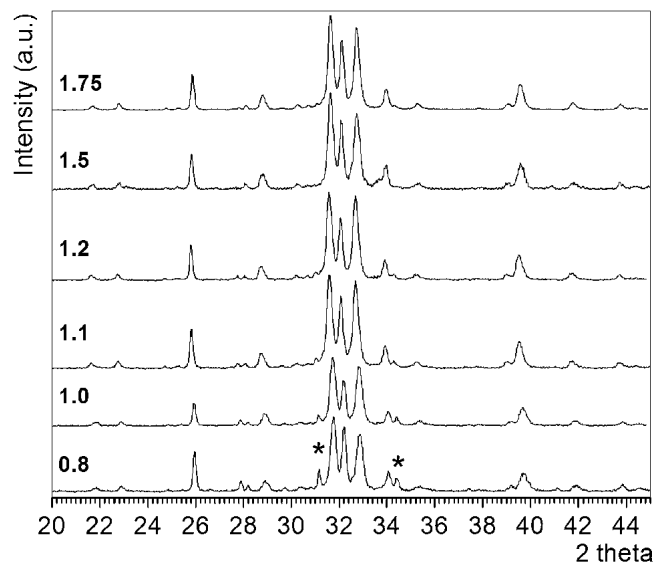


FIG. 4. XRD data showing the gradual elimination of the secondary phase of TCP with an increase in the weight of urea (in grams) during HA nanowhisker synthesis. TCP peaks are denoted by (*).

apatitic calcium phosphate sample is perfectly acceptable if the aim is to produce a synthetic biomaterial which can resorb *in vivo*, and readily take part in the bone-remodeling process.³¹ Human bones contain a total of 1.3 wt% of cations like Na^+ , K^+ , and Mg^{2+} .¹ The process developed here yields bonelike calcium phosphate samples, as confirmed by the FTIR data of Fig. 3(b). Carbonate ion concentration in human bones amounts to a significant 5.8 wt% of the total weight.¹ It is also a well known fact that either synthetic hydroxyapatites³² or human bones³³ heated above 700 $^{\circ}\text{C}$ readily lose their carbonate ions.

An important part of the present work is the assistance of microwave heating. If we were to perform the combustion of our initial solutions (for the biphasic and HA samples) under conventional heating, for instance, in an electrical-resistance heated chamber furnace, the temperature distribution of the solution would be inhomogeneous. This is because the reaction beakers would have been heated by thermal conduction through a container wall, convection, and agitation. Since the synthesis of nanoparticles from their precursors in solutions consist of nucleation and particle growth, it is important that the particle growth is terminated.³⁴ Those processes partly rely on the local temperature distribution within the solution. Any inhomogeneity in the temperature distribution would then cause broad distributions in particle size. MW irradiation should lead to homogeneous, i.e., molecular-level heating of the polar solution system, achieving automatic control of the above two processes required for the preparation of nanowhiskers or nanoparticles.

The liquid phase formed during this process by the

molten NaNO_3 dissolves all of the initially formed calcium phosphate precipitates. Such precipitates form during the initial boiling and evaporation of the excess water. Due to the presence of urea, an auto ignition process is initiated (as evidenced by the observation of intermittent sparks in the irradiated reaction beakers), and these in situ processes raise the extent of superheating in the molten-salt bath. Embryonic particles of calcium phosphate phases are formed through the nucleation and growth processes. As the molten ionic bath cools, while passing through its melting point down to room temperature, rapid crystallization occurs along the preferred growth axes of the ceramic phase. Calcium phosphate nanowhisker growth probably occurs during this rapid process, by a sequential “dissolution–crystallization–whisker-growth” process.

Solubility of the specific calcium phosphates in molten NaNO_3 (which is a function of temperature) has a significant role in the crystallization process to follow. The degree of superheating of the molten NaNO_3 must also have a strong effect on the resultant aspect ratio of the formed whiskers. The morphology of the whiskers growing out of the cooling molten salt bath could be strongly dependent on soaking time at the peak temperature, as well as the cooling rate. Such issues further warrant follow-up studies, which we plan to report in due time.

IV. CONCLUSION

A new microwave-assisted process has been developed for the synthesis of monodispersed nanowhiskers and nanopowders of Na- and carbonate-containing calcium phosphates. This new procedure is a hybrid of the urea-combustion (auto ignition) and molten salt synthesis techniques, and represents the philosophy of synergistic processing. The fluxing agent used was NaNO_3 . Urea was used as the fuel in the combustion part of this process. According to this synthesis route, 5 min of MW heating of aqueous solutions in a household MW oven at 600 watts, followed by 1 h of washing of the irradiated samples in water at RT was sufficient to form nanowhiskers. The 100-nm-thick HA nanowhiskers obtained had an aspect ratio of 10. Procedure was successfully shown to yield single phase TCP, single phase HA, and biphasic HA-TCP samples. Nanowhiskers or powders produced in this study were chemically similar to human bones.

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