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Synthesis and characterization of hydroxyapatite/β-tricalcium phosphate nanocomposites using microwave irradiation

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Abstract

Microwave assisted synthesis method is a relatively new approach employed to decrease synthesis time and form a more homogenous structure in biphasic calcium phosphate bioceramics. In this study, nanocrystalline HA/β-TCP composites were prepared by microwave assisted synthesis method and, for comparison reason, by conventional wet chemical methods. The chemical and phase composition, morphology and particle size of powders were characterized by FTIR, XRD and SEM, respectively. The use of microwave irradiation resulted in improved crystallinity. The amount of hydroxyapatite phase in BCP ranged from 5% to 17%. The assessment of bioactivity was done by soaking of powder compacts in simulated body fluid (SBF). The decreasing pH of the solution in the presence of β-TCP indicated its biodegradable behavior. Rod-like hydroxyapatite particles were newly formed during the treatment in SBF for microwave assisted substrate synthesis. In contrast, globular particles precipitate under same conditions if BCP substrates were synthesized using conventional wet chemical methods.

Keywords: Microwave processing; Hydroxyapatite; β-tricalcium phosphate; Chemical synthesis

1. Introduction

Bioceramics such as alumina, zircon, calcium phosphates and bioglass have great importance in biological environments. Research and development on such bioceramics have made significant contributions to the health and quality of human life. Such biomaterials can be used in the human body to substitute for damaged segments of human skeleton system [1,2]. Calcium phosphates are broadly used in medicine due to the apatite-like structure of enamel, dentin and bones known as ''hard tissue'' [3]. Furthermore, hydroxyapatite crystals with chemical formula of $Ca_{10}(PO_4)_6(OH)_2$ and Ca/P ratio of 1.67, can generally make up to 69% of the weight of the natural bone. Hydroxapatite has a hexagonal structure and is the most stable phase among various calcium phosphates. Hydroxyapatite is stable in body fluid as well as in dry or moist air up to 1200 °C. It does not decompose and has shown to be bioactive. The β-tricalcium phosphate (β-TCP), represented by the chemical formula of $Ca_3(PO_4)_2$ with Ca/P ratio of 1.5, has also a hexagonal crystal structure [1]. The biocompatibility and similarity of calcium phosphates like hydroxyapatite and tricalcium phosphate to the mineral composition of human bone and teeth have made them suitable for substitution of damaged segments of human skeleton system [2–6]. Bioactivity of calcium phosphate materials depends on many factors during the synthesis procedure including precursor reagents, impurity contents, crystal size and morphology, concentration and mixture order of reagents, pH and temperature. Such conditions are application specific and should be controlled by synthesis preparation parameters [7]. As discussed before, HA is stable in the body fluid while TCP is rather soluble. The dissolution rate of HA in body fluid is too low but that of β-TCP is too fast for bone bonding. Therefore biphasic calcium phosphate consisting of HA and TCP can be used to control the bioresorbability and achieve optimal results. Biphasic calcium phosphate composites, BCP, consisting of HA and β-TCP have many applications in human body [8–14]. There are many techniques for production of such biomaterials including wet chemical methods [10,15–17], hydrothermal processes [18–21], solid-state reaction [22–24], and sol–gel synthesis [15,25]. The degree of success in preparing HA is significantly different

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for each method [1]. These methods have some disadvantages such as being time-consuming, having low quality control and chemical contamination [2,26–28]. Microwave synthesis methods can be used to limit and reduce such disadvantages and be able to easily control the condition of production process. By using microwave as an assisted method, the powders can be produced faster by employing an improved and efficient heat transfer throughout the volume [29–33]. It is the aim of this research to investigate microwave assisted synthesis of nanopowders for biphasic calcium phosphate composites and characterize the resulting powders by XRD, FTIR and SEM techniques. For the purpose of comparison, another set of nanopowders was synthesized by conventional wet chemical precipitation method.

2. Materials and methods

Calcium hydroxide (Merck) and orthophosphoric acid (Merck) were used as the starting materials. HNO_3 (Merck) and NaOH (Merck) were used to control the pH of the solution mixture during the process. Two different synthesis methods were used for preparation of the BCP powders: (1) Nanopowders wet chemical, acid–base reaction [27] and (2) Microwave radiation based chemical reaction [32]. To prepare BCP by acid base reaction method, orthophosphoric acid solution was added dropwise to the calcium hydroxide suspension under stirring conditions. The suspension was centrifuged, dried out in an oven at 90 °C overnight and calcined at 900 °C for 1 h. On the other hand, to prepare the biphasic calcium phosphate by microwave assisted synthesis, the solution mixture was immediately transferred to a domestic microwave oven (2.45 GHz, 800 W) and irradiated for 45 min. At the end of the irradiation, the white precipitation was centrifuged and dried at 90 °C. The powders were calcined at 900 °C for 1 h. The initial Ca/P ratios and the conditions for preparation of BCP powders are given in Table 1. We studied the effects of microwave irradiation on the growth of hydroxyapatite particles on BCP samples by immersion in a simulated body fluid (SBF). The SBF analysis was adopted from Kokubo et al. who conducted similar experiments with a simulated chemically prepared body fluid (SBF) solution. He designed the solution to imitate human body fluid with ion concentrations similar to those of the inorganic constituents of human blood plasma to demonstrate the similarity between *in vitro* and *in vivo* behavior of bioceramic compositions. Each liter of SBF was prepared by dissolving of NaCl (7.996 g), $NaHCO_3$ (0.350 g), KCl (0.224 g), $K_2HPO_4{\cdot}3H_2O$ (0.228 g), $MgCl_2{\cdot}6H_2O$ (0.305 g), $CaCl_2$ (0.278 g), Na_2SO_4 (0.071 g) and TRIS-$C_4H_{11}NO_3$ (6.057 g) into distilled water. The pH value of 7.25 was maintained by adjusting amount of HCl. Its composition is comparable with the ionic composition of human blood plasma. Also, the samples' containers were placed in an incubator to keep the temperature of the solution at 37 °C [34].

Table 1
The condition for preparation of BCP powders.

Sample		Initial Ca/P ratio	pH	Aging time
BCP1	HA	1.67	11	24 h
BCP2	HA-Riched-BCP	1.54	9	10 h
BCP3	β-TCP-Riched-BCP	1.53	8	6 h
BCP4	β-TCP	1.51	6	3 h
MBCP1	HA + Microwave	1.67	11	45 min
MBCP2	HA-Riched-BCP + Microwave	1.54	9	45 min
MBCP3	β-TCP-Riched-BCP + Microwave	1.53	8	45 min
MBCP4	β-TCP + Microwave	1.51	6	45 min

2.1. Sample characterization

Phase analyses of composite powders were determined by X-ray diffraction (Siemens D 500 diffractometer, Cu-Kα radiation, 40 kV, 30 mA and 0.02° s^{-1} step scan). Fourier transform infrared spectroscopy (Vector 33) using pellets of powdered samples mixed with KBr was performed to evaluate the functional groups of specimens. The FTIR spectra were obtained over the region 400–4000 cm^{-1}. The stoichiometry of the HA was checked using differential thermal analysis (PL-STA 1640) method at a heating rate of 10 °C/min between 25 and 1100 °C in the air atmosphere to analyse the endothermic and exothermic reactions. α-Alumina was used as the reference material. Simultaneous thermogravimetric analysis was used to find the weight loss during the heating using procedures similar to those described above. Scanning electron microscopic analysis (Philips XL30) was used for morphological observations. The pH of the SBF solution was measured at predefined intervals (7, 14 and 21 days) of time after soaking powder compacts in SBF under a controlled environment of 37 °C and pH 7.25. Finally, the morphologies of hydroxyapatite crystals after immersion in SBF solution were characterized using SEM.

3. Results and discussions

3.1. Phase characterization

The XRD patterns of samples are shown in Figs. 1 and 2. Powders exhibited sharp diffraction peaks indicating a high

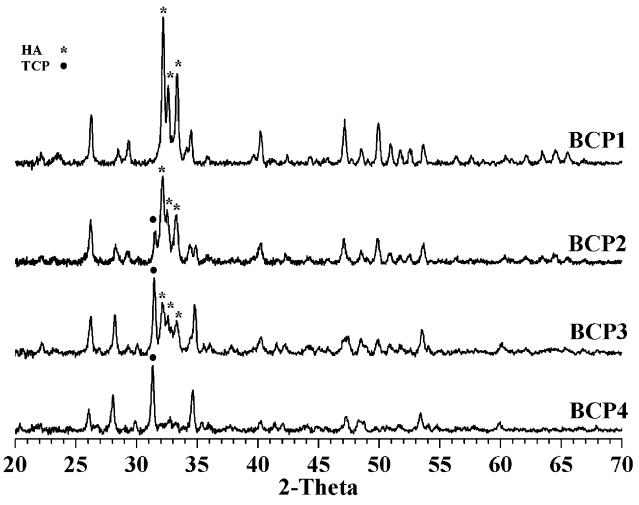

Fig. 1. XRD patterns of BCP samples.

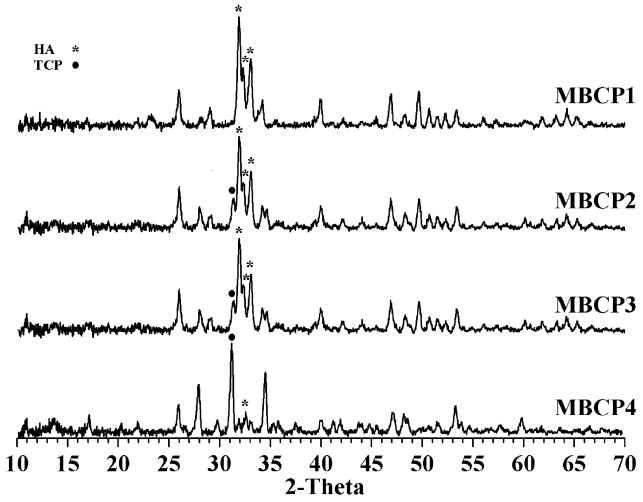

Fig. 2. XRD patterns of MBCP samples.

crystallinity. The peaks of TCP and HA are indexed according to standard patterns. The pattern for BCP1 in Fig. 1 shows well-characterized peaks of pure HA (hereafter BCP1 is called as pure HA) and the peaks were indexed according to the standard pattern (JCPDS 09-0432). The diffractograms of the samples BCP2 and BCP3 show additional peaks rather than the HA peaks. The peaks were identified to be corresponding to β-TCP and indexed according to the standard value (JCPDS 09-0169). The intensity of the additional peaks increases from BCP1 to BCP3 indicating that the amount of β-TCP increases as the excess amount of the phosphate solution is increased during the preparation procedure. The sample BCP4 shows peaks of β-TCP and the Ca/P ratio of this sample approaches the value of stoichiometric TCP. This indicates that single phase β-TCP was successfully synthesized at temperatures 900 °C [31]. The pattern in Fig. 2 indicates the two phases of HA and TCP according to standard patterns (JCPDS cards) and shows how easy it is to produce BCP powders by microwave assisted method.

The percentages of volume fraction of β-TCP and HA present in all the samples were calculated using the relative intensity ratio (RIR), Eq. (1), for the HA/β-TCP in biphasic calcium phosphate, where I_{TCP} and I_{HA} represent the normalized intensity of (2 1 1) and (2 0 1 0) peaks of HA and β-TCP respectively [27,35] and the results are given in Table 2. The behavior of dipole moment of the hydroxyl ions in HA structure could be responsible for the dielectric nature of hydroxyapatite. OH^- groups absorbed more

Table 2
Percentage of HA and β-TCP phases in BCP powders.

Sample	HA%	β-TCP%
BCP1	100	0
BCP2	64	36
BCP3	42	58
BCP4	0	100
MBCP1	100	0
MBCP2	75	25
MBCP3	44	56
MBCP4	13	87

Table 3
The amount of crystallinity of HA and TCP powders.

Sample	$2\theta^\circ$	Variable	Intensity	$\%X_c$
BCP1	32.93	I_{300}	2950	79.66
	32.75	$V_{(112/300)}$	600	
MBCP1	32.85	I_{300}	503	81.11
	32.5	$V_{(112/300)}$	95	

Sample	$2\theta^\circ$	Variable	FWHM	$\%X_c$
BCP4	25.802	$\beta_{(1010)}$	0.375	26.21
MBCP4	25.802	$\beta_{(1010)}$	0.3125	45.3

microwave radiation that indicates the development of HA phase [36–40]. The XRD and FTIR patterns also illustrate this result. The crystallinity degree, corresponding to the fraction of crystalline HA phase present in the examined volume, was evaluated by the Eq. (2), where I_{300} is the intensity of (3 0 0) reflection and $V_{112/300}$ is the intensity of the hollow between (1 1 2) and (3 0 0) reflections, that completely disappears in non-crystalline samples. For this method being sensitive to the crystallite dimensions, verification can be done with the Eq. (3) where K is a constant found to be equal to 0.24 for TCP powders, and β_{002} is FWHM of reflection (0 0 2). Table 3 shows the amount of crystallinity in HA and TCP powders by using both Eqs. (2) and (3), respectively [41]. The crystallization process is controlled by diffusion. It seems that by using microwave as an external source, increasing temperature influences the rate of atomic motion and decreases the diffusion barrier. So the atoms are easily transported to the lattice site and the crystallinity is increased.

$$\mathrm{RIR} = \frac{I_{\beta-\mathrm{TCP}}}{I_{\beta-\mathrm{TCP}} + I_{\mathrm{HA}}} \quad (1)$$

$$X_C = 1 - (V_{112/300}/I_{300}) \quad (2)$$

$$\beta_{(1\,0\,\underline{1}\,\underline{0})}\sqrt[3]{X_c} = K \quad (3)$$

The broadening of a diffraction peak can be related to the crystallite size via the Scherer equation relying on Eq. (4). The (0 0 2) and (1 0 $\underline{1}$ $\underline{0}$) peaks of HA and β-TCP were chosen respectively for the analysis of the broadening of the Bragg line [42–44]. The crystallite size of hydroxyapatite and β-tricalcium phosphate in BCP1, MBCP1, BCP4 and MBCP4 are given in Table 4. These results clearly indicate that using microwave and increasing temperature result in increasing crystallite size of the powders. The lattice parameters of HA and β-TCP were calculated using the XRD data. Lattice parameters of all the samples were listed in Tables 5 and 6. Using microwave irradiation leads to a slight increase in the a lattice parameter, whereas the c lattice parameter does not show any significant difference [32].

$$\beta = \frac{0.9\lambda}{t\cos(\theta)} \quad (4)$$

The FTIR spectra of BCP powders are shown in Figs. 3 and 4. The spectra illustrate the hydroxyl bond stretch at 3550 cm^{-1} and HOP_4^{2-} at 970 cm^{-1} corresponding to HA and β-TCP

Table 4
The effect of synthesis condition on crystal size.

Sample	Δ (2θ°)	FWHM	2θ°	Cos(θ)	Crystal size (Å)
BCP1	0.5	0.008726646	26.039	0.974293	163.0673666
MBCP1	0.375	0.006544985	25.9	0.974566	217.3623499
BCP4	0.375	0.006544985	25.802	0.974757	217.3196923
MBCP4	0.3125	0.005454154	25.89	0.974586	260.8295868

structure respectively. The vibrational bands of the phosphate ions are observed in all of the samples. As there is insignificant amount of hydroxyapatite in BCP4 and MBCP4 samples, the hydroxyl band disappears and forms a relatively broad band stretch over the range of 3300–3800 cm^{-1} due to the adsorbed molecules of water. By increasing the amount of tricalcium phosphate phase in BCP2, BCP3 and BCP4 samples, the hydroxyl band at 633 cm^{-1} reduces in peak area. The hydroxyl vibrational band disappears in BCP4 sample [32]. The powders prepared by microwave assisted method have the FTIR patterns similar to the previous results [32]. Also the vibrational bonds of OH^- decrease in spectra because of TCP forming. In addition, the bond of HPO_4^{2-} at 980 cm^{-1} increases by showing an increase in phosphate group forming TCP. The in situ formation of BCP is confirmed by these FTIR spectra.

3.2. Thermal analysis

The TG/DTA analysis of BCP3 and MBCP3 powders are shown in Figs. 5 and 6, respectively. The thermogram shows a decreasing path that is related to the removal of the water from the precipitated powders. The results show no exothermal peak that indicates there is no decomposition reaction taking place in the BCP3 sample. The XRD and FTIR patterns show that HA and TCP phases are present in the powders and the DTA indicates the in situ formation of BCP. By using microwave as an external source, the endo peak at 700 °C shows the formation of HA. The behavior of dipole moment of the hydroxyl ions in HA structure is the root cause of dielectric nature of hydroxyapatite that indicates the development of HA phase by using microwave method [36–40].

Table 5
List of lattice parameters (*a* and *c*) of HA.

Sample	*a* (Å)	*c* (Å)
BCP1	9.42	6.85
BCP2	9.389	6.848
BCP3	9.39	6.87
MBCP1	9.425	6.869
MBCP2	9.403	6.861
MBCP3	9.402	6.865

JCPDS (09-0432): *a* (Å) = 9.418 and *c* (Å) = 6.884.

Table 6
List of lattice parameters (*a* and *c*) of β-TCP.

Sample	*a* (Å)	*c* (Å)
BCP2	10.401	37.23
BCP3	10.38	37.148
BCP4	10.41	37.48
MBCP2	10.428	37.003
MBCP3	10.3839	37.186
MBCP4	10.436	37.26

JCPDS (09-0169): *a* (Å) = 10.429 and *c* (Å) = 37.38.

3.3. Morphological observation

The scanning electron micrograph of BCP2, BCP3, MBCP2 and MBCP3 powders are illustrated in Fig. 7. They demonstrate many agglomerations of small spherical particles in nanometric scale, but samples produced with microwave

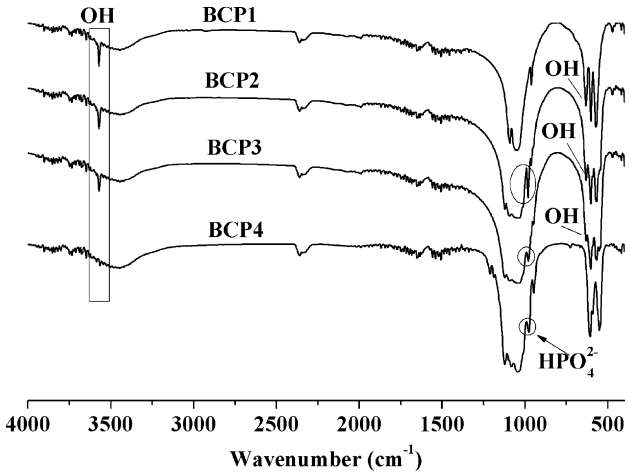

Fig. 3. FTIR spectra of BCP samples.

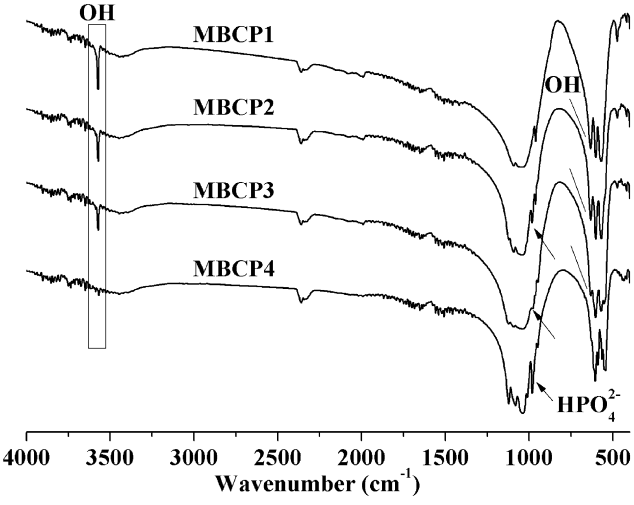

Fig. 4. FTIR spectra of MBCP samples.

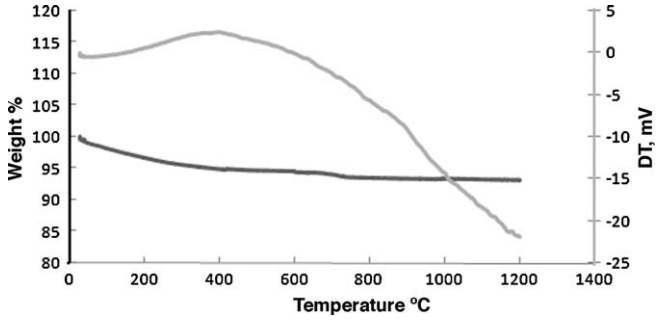

Fig. 5. TG/DTA graph of BCP3 powders.

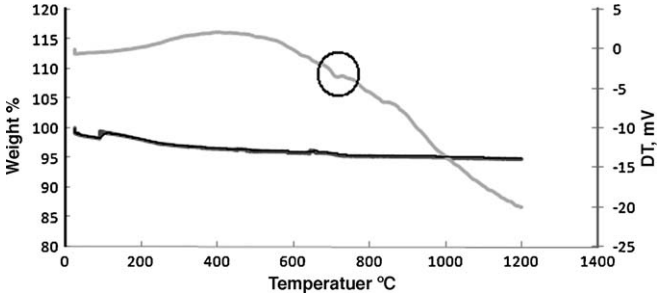

Fig. 6. TG/DTA graph of MBCP3 powders.

become fine and more homogeneous. The grain size measurement reveals that the grain size of powders produced with microwave assisted method is around 43 nm to 55 nm and the grain size of powders produced by acid–base reaction method is around 57–67 nm.

The morphology of hydroxyapatite crystals after soaking in the SBF is shown in Fig. 8. After immersion (21 days), the shape of grains precipitating on the original grain surfaces differed. In BCP3 sample that is prepared by acid–base reaction, the HA crystals has spherical shape in SBF solution. On the other hand, a precipitated HA rod and cubic like layer formed on the surface of MBCP3 prepared by the microwave assisted method. These results could be due to the effect of microwave on the surface energy of powders that in turn increases the suitable sites for nucleation.

3.4. In vitro assessment

The SBF solution was used to characterize the biodegradable behavior of samples under a controlled environment of 37 °C and pH 7.25 [45]. For this experiment sintered powder compacts were employed. The pH values were recorded at regular time intervals shown in Fig. 9. The extent of dissolution in SBF *in vitro* is much higher for the β-tricalcium phosphate ceramic compared to that of the hydroxyapatite ceramic. Thus, the extent of dissolution of BCP composite depends on the HA/β-TCP ratio. However, biphasic calcium phosphate composite with similar HA/β-TCP ratios could present different dissolution rates depending on the grain size, crystallinity and lattice defects. This phenomenon may be caused by processing techniques such as using microwave which could affect the crystallinity and microstructure [46]. The BCP2 sample shows a decrease in the pH value but less than that of BCP3. This is due to the presence of more tricalcium phosphate phase in the BCP3 sample converted to a stable HA phase causing the release of acidic ion of HPO_4^{2-}. Also, the sample prepared by microwave assisted method shows less decrease in the pH value indicating its higher stability by an increase in crystallinity [32,47].

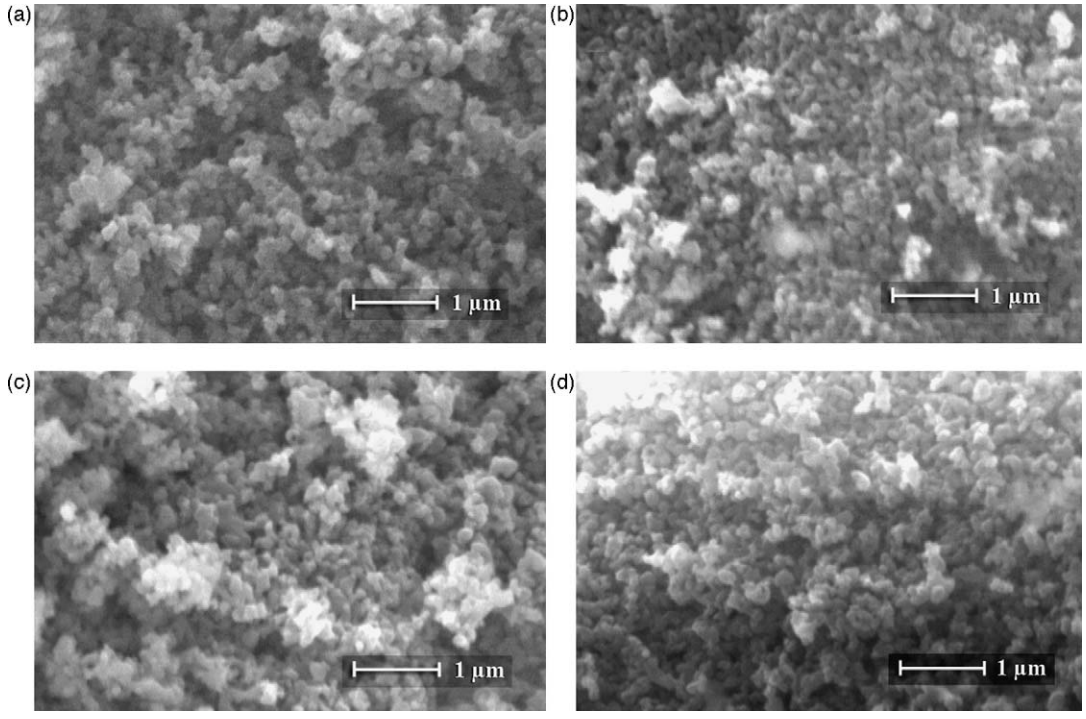

Fig. 7. SEM images of BCP powders (a) BCP2, (b) MBCP2, (c) BCP3 and (d) MBCP3.

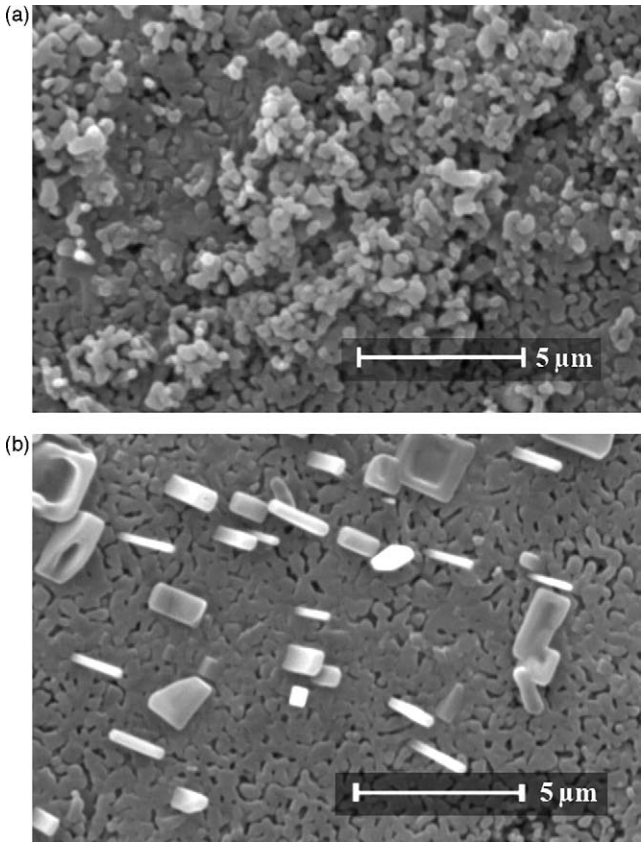

Fig. 8. SEM images of prepared samples after soaking in SBF for 21 days (a) BCP3 and (b) MBCP3.

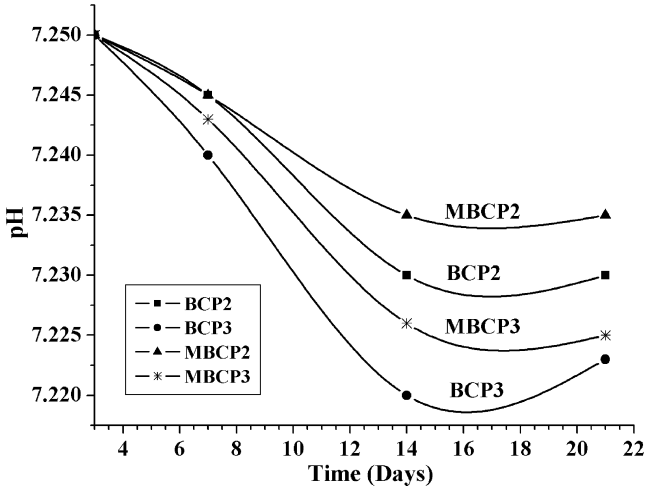

Fig. 9. The pH value variations of SBF due to the immersion of the powders.

4. Conclusion

By using microwave heating, biphasic calcium phosphate powders can be prepared in situ in a shorter time compared to traditional methods. The variation in the Ca/P ratio during the preparation has resulted to the variation in the HA/β-TCP ratio. The results showed that the use of microwave improves crystallinity where the crystallite size ranged from ≈16 nm to ≈27 nm. Also, using microwave irradiation as an assisted method increases the amount of HA phases in biphasic calcium phosphate. In SBF, the pH of the solution was decreased with the presence of β-tricalcium phosphate due to its biodegradable behavior. So, the dissolution rate of the biphasic calcium phosphate powders was strongly dependent on the β-TCP content. The precipitated hydroxyapatite particles formed after soaking in SBF solution have rod-like shapes once the powder compacts produced by microwave assisted synthesis have been employed. By adjusting the β-tricalcium phosphate percentage, the bioresorbability of the calcium phosphate powders can be controlled.

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