Invited paper

MICROWAVE-ASSISTED SYNTHESIS, DRYING AND SINTERING OF PHOSPHATE-BASED BIOCERAMIC MATERIALS

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Abstract

Recent developments in nanotechnology have demonstrated that nano-bioceramics play an important role in the biomedical field due to their superior biological and mechanical properties compared to that of conventional bioceramics. However, a long sintering duration and high temperature used in conventional sintering have remained as a challenge to preserve the nano-structure of the sintered materials. Microwave synthesis, drying and sintering of phosphate-based bioceramics have emerged in recent years as new methods which offer significant benefits against conventional methods. As a prelude, a brief discussion on the fundamental aspects of microwave and microwave heating is also introduced. Subsequently, the applications of microwave in phosphate-based bioceramics are evaluated in detail.

Keywords: Bioceramics, Mechanical properties, Microwave, Sintering, Synthesis

Introduction

Conventionally, bioceramics such as hydroxyapatite (HA), β-tricalcium phosphate (β-TCP), and biphasic calcium phosphate (BCP) powders are mainly synthesized using wet-chemical methods [1,2] and solid-state processes [3,4]. However, the synthesis of bioceramics by the wet-chemical method is complicated, time consuming and inefficient, whilst the solid-state process usually needs high temperature for calcination and sintering, which in turn leads to particle agglomeration or decomposition. It is, therefore, necessary to develop more efficient synthesis methods which are simpler, of shorter duration and produce high purity products [5, 6].

The low mechanical strength of conventional HA bioceramic generally restricts its use for load-bearing applications. For conventional sintering, a higher temperature is necessary to attain high-density parts with superior mechanical properties. However, HA tends to transform to tricalcium phosphate (TCP, $Ca_3(PO_4)_2$) and/or CaO phases during sintering, particularly above 1200 °C. The presence of these impurity phases in HA can further influence both mechanical and biological properties [7]. In contrast to conventional sintering, microwave sintering of bioceramics can offer certain advantages such as rapid heating rates, time and energy savings, reduction of sintering temperatures and fine microstructures. Hence, these lead to improved mechanical properties for better product performance [8]. Therefore, microwave is expected to be a tool to overcome the problems in synthesis and sintering of bioceramics. The advantages of the application and prospective use of nanosized and nanocrystalline bioceramics for clinical applications had been reported [7,9,10], such as greater viability and better proliferation of various types of cells, good biocompatibility and bone integration ability. Using microwave sintering, nano-bioceramic materials had been obtained with significant improvement of mechanical strength and bioactivity [8]. Figure 1 shows the use of microwave sintering in ceramics and bioceramics in the last decade. It is evident that microwave sintering have been widely applied for ceramics, whilst the use of microwave sintering for bioceramics is still limited.

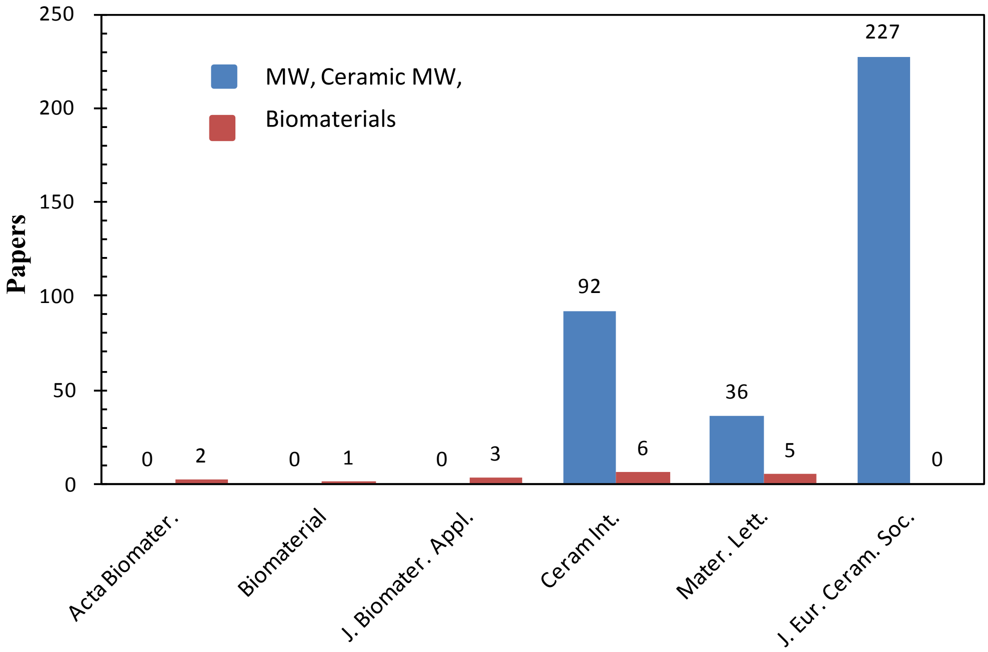

Figure 1. Distribution of research papers on microwave sintering of ceramics and bioceramic materials in different journals from 2000-2011

Numerous review papers on the applications of microwave, such as microwave sintering of ceramics [9], microwave treatment of minerals [11] and microwave polymer synthesis, as a tool in biomaterials science [12] etc., are available. However, no review paper on the microwave synthesis and sintering of bioceramics have been found up to date. Thus, a review paper on the applications of microwave in bioceramics is necessary so as to provide an overall perspective of the progress, as well as the potential applications, of microwave in bioceramic materials in the future.

Microwave Heating Principle

Microwave Radiation

Microwaves are a group of electromagnetic energy with a frequency range of 0.3 to 300 GHz and wavelengths of 1 m to 1 mm. This frequency range falls just above the radio waves and below the visible light in the electromagnetic spectrum. Most of the microwave frequency band is used for communications and radar. Microwave heating is usually applied at frequencies normally employed for industrial, scientific and medical applications, namely 0.915 and 2.45 GHz. Microwave furnaces that use variable frequencies from 0.9 to 18 GHz have been developed for material processing [11,13], and recently, more specifically for biomaterials processing [8,14].

Microwave Interaction with Different Materials

The interaction between microwaves and materials obey the laws of optics, where microwaves can be transmitted, absorbed or reflected depending on the type of material. Microwaves are reflected and cannot penetrate metals and, therefore, do not heat metals. Metals in general have a high conductivity and are classed as conductors. Materials which are transparent to microwave are classed as insulators. Materials which are excellent absorbers of microwave energy are easily heated and are classed as dielectrics [15].

The way microwave heats a material, to a great extent, depends on its ‘dissipation’ factor, which is the ratio of dielectric loss or ‘loss’ factor to dielectric constant of the material. The dielectric constant is the ability of the material to retard microwave energy as it passes through; the loss factor is the ability of the material to dissipate the energy. Therefore, a material with high ‘loss’ factor is easily heated by microwave energy [16]. In addition, the extent of microwave heating is also dependent on the size of the material. For instance, microwave cannot heat bulk metals but can heat up metallic powders [17].

When microwaves penetrate and propagate through a dielectric material, the internal field generated within the effected volume induces translational motions of free or bound charges such as electrons or ions, and rotates charge complexes such as dipoles. As a result, elastic and frictional forces resist these induced motions and cause losses, a consequence of which is volumetric heating. More detailed fundamentals and interactions between microwave and materials had already been reported [18,19].

Advantages and Difficulties of Using Microwave in Heating Materials

The use of microwave energy for materials processing was reported to have major potential and proven advantages over conventional heating, principally its rapid heating, which consequently led to time and energy savings [17, 20]. However, at room temperature, many ceramics do not absorb 2.45 GHz microwave energy appreciably [19, 21]. In many research works, absorbing constituents (e.g., SiC, carbon and organic binders) were added to increase their absorption to microwave [21, 22], as shown in Figure 2. Additionally, microwave also creates a potential problem where large thermal gradients may take place during heating, and this results in stresses which lead to the cracking of the materials.

The temperature gradient problem can be overcomed by maintaining the environment temperature as that of the sample through a simultaneous application of microwave and conventional heating. A hybrid microwave furnace, which consists of microwave and conventional resistant electric components was used to simultaneously sinter $BaTiO_3$ ceramic in order to avoid the temperature gradient problem [23]. Poor absorption of microwave by ceramics at room temperature can also be improved by increasing their temperatures using hybrid heating, where the ceramics are heated initially using conventional methods. For instance, a SiC-rod susceptor was used in a microwave hybrid furnace to accelerate the initial heating of Al_2O_3, ZrO_2 and Si_3N_4 at low temperatures. Once the ceramic is heated to its critical temperature, Tc, microwave absorption becomes sufficient to cause self-heating. The hybrid heating method can also yield a much more uniform temperature distribution than those resulting from stand-alone microwave sintering or conventional sintering methods [18]. Hybrid heating can also be achieved either by using an independent heat source, such as a gas or electric furnace in combination with microwave, or through the use of an external susceptor that couples with the microwave furnace [23]. In the latter, the material is exposed simultaneously to microwave and radiant conventional heating produced by the susceptor.

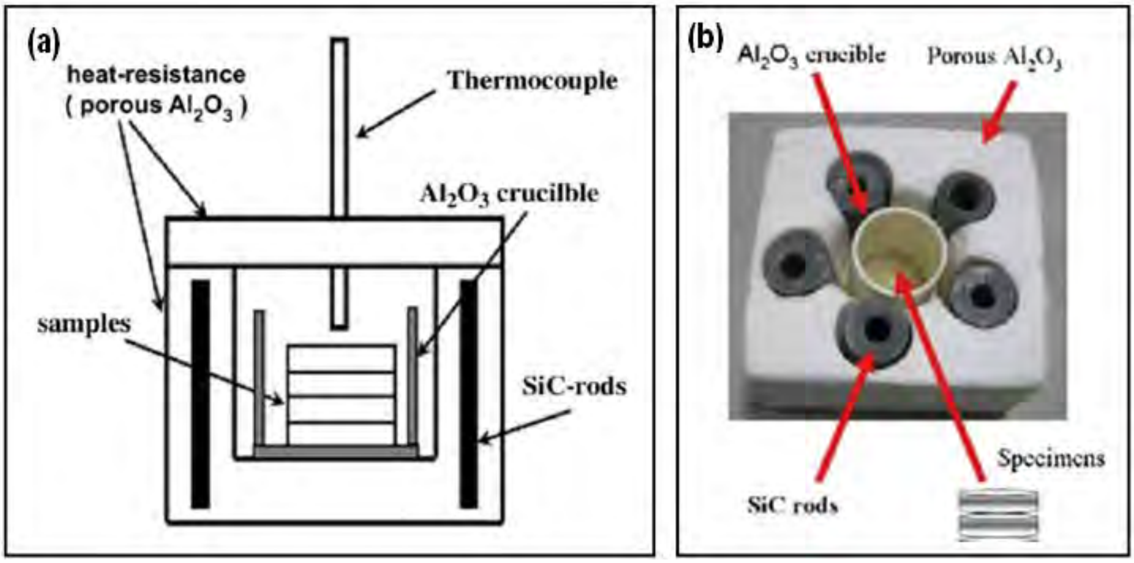

Figure 2. Microwave hybrid heating (a) a schematic illustration, and (b) an actual illustration of the components being heated [22]

Microwave-Assisted Synthesis

Synthesis of Hydroxyapatite

HA which exhibits excellent biocompatibility is an ideal candidate for orthopedic and dental implants or components of implants. Synthetic HA has been widely used in repair of hard tissues, bone augmentation, as well as coating of implants or acting as fillers in bone or teeth [7-8]. Microwave synthesisS of ceramics and bioceramic materials such as HA has been known for more than two decades. Recently, microwave was also applied in the synthesis of bioceramic materials [24]. Microwave synthesis of bioceramics offers the benefits of uniform heating throughout the volume with very efficient transformation of energy. In addition, the reaction duration of aqueos solution under microwave is much shorter than those required for conventional synthesis, and therefore, results in a very fine and uniform particles of the final products.

HA nanorods was reported [24] to be synthesizd by heating an aqueos solution of $CaNO_3$. $4H_2O$ and Na_2HPO_4 with EDTA complexing reagent in a household type microwave oven of 700 W power for 30 min. Uniform HA nanorods were formed with an average diamater of 40 nm and a length up to 400 nm, as shown in Figure 3. Similarly, a high purity HA nanostrips were also rapidly synthesized under microwave using $CaNO_3$. $4H_2O$, Na_2HPO_4 and CTAB complexing reagent [6] in a short duration of 5 min. TEM investigations showed that the fabricated nanostrips had a width and length of about 10 and 55 nm, respectively. This rapid syntheses of HAs were also reported in other research works, the duration being 3 min [25] and even 1 min [26].

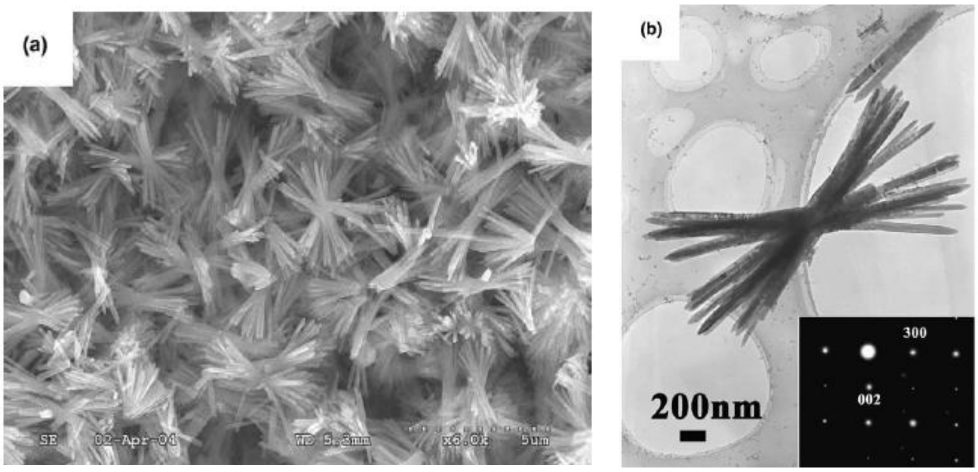

Figure 3. SEM and TEM images of HA nanostructures prepared from a solution with pH 11 (a) SEM image showing bowknot-like HA nanostructures (b) TEM image of a typical bowknot-like bundle of HA. Inset: SAED pattern taken from individual HA nanorod from the bowknot-like HA nanostructures [24]

Microwave power, interaction duration and synthesis temperature show significant effects on the thermal stability, size and shape of the as-synthesized HA. In another research work [27], HA polycrystals were synthsized from H_3PO_4, glucose and $Ca(NO_3)_2$. $4H_2O$ using a domestic microwave oven for different reaction duration of 5, 30, 60 and 120 min. It has been found that the thermal stability of HA increases with an increase of aging time, duration and microwave power. The XRD patterns of samples with different microwave powers at a calcination temperature of 1200 ^{o}C showed that the phases formed were β-TCP and HA at 70 W. On the other hand, only a small amount of β-TCP was formed together with a dominant HA phase at 210 W. Subsequently, a single-phase HA was formed at 700 W. In addition, Wang et al. [26] also reported that single-phase HA nanoparticles were obtained using microwave-hydrothermal method at a temperature range of 100-140^{o}C. The particle size of the as-synthesized HA powder increased with increasing synthesis temperature and duration. Furthermore, the morphology of the as-synthesized HA powder was observed to transform from rod-like to prism-like nature with an increase of the reaction temperature.

The change in shape and size of the as-synthesized HA with microwave power was also reported by Han et al. [28]. They found that the synthesis of HA was strongly dependent on the experimental parameters such as the applied microwave powers. In the case of relatively low microwave power of 450 W, mixed calcium phosphate compounds such as $Ca(OH)_2$, $CaHPO_4$ and HA were detected in the as-synthesized powders. However, at 550 W, the synthesized powder showed a monophase HA having two kinds of morphologies. One was a needle shape with 4-15 nm in width and 20-50 nm in length, and the other was a spherical shape of 10-30 nm in diameter. The variation of particle size and shape of the as-synthesized HA with the microwave power was cleary observed in another research work [29]. In that work, the result at 175 W showed needle-like particles with a length of 39-56 nm and width of 12-14 nm, whilst at 525 W the respective dimensions of the plate-like particles were 10-16 nm in length and 10-12 nm in width. The sample at 660 W power showed platelet shapes of 32-42 nm in lengths and widths of 12-25 nm. All these results are shown in Figure 4.

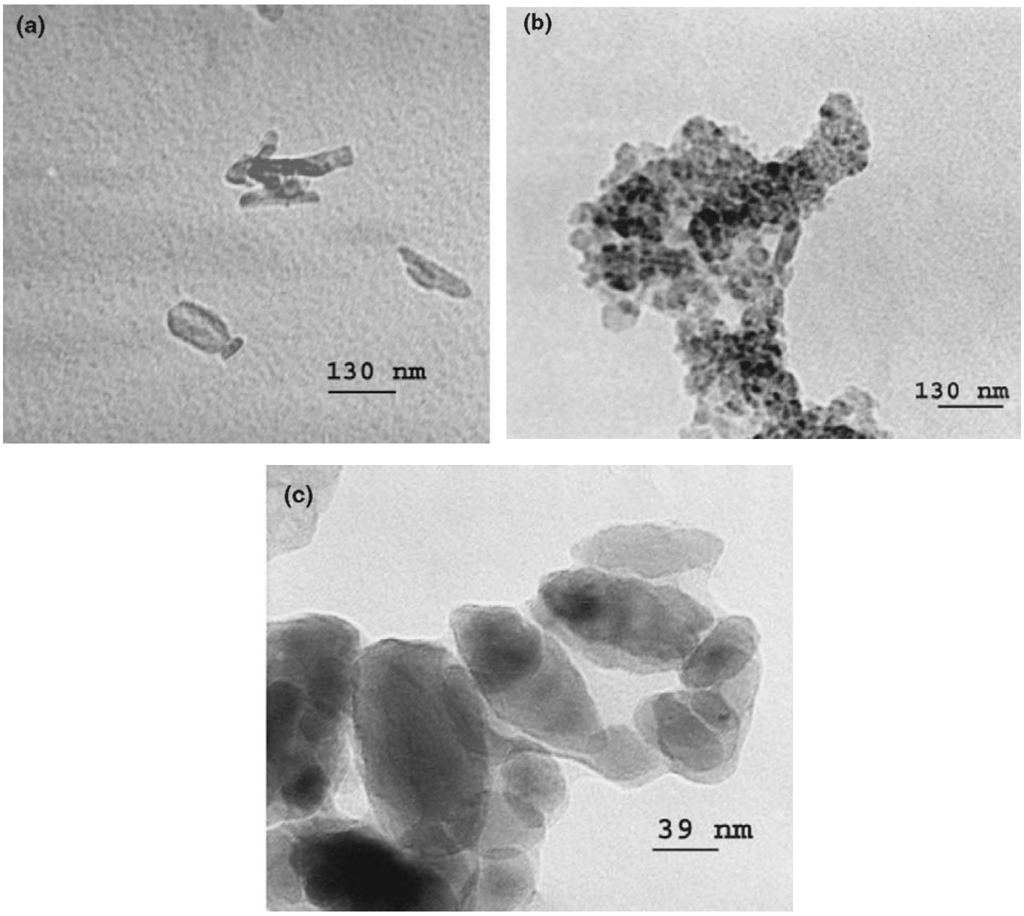

Figure 4. TEM bright field images of as-synthesized HA nanoparticles at various microwave powers: (a) 175 W, (b) 525 W and (c) 660 W [29]

Synthesis of B-TCP and B-TCP Composites

Although numerous research work had been carried out on the synthesis of HA using microwave, the synthesis of β-TCP using microwave is limited. A new fabrication technique, microwave-assisted co-precipitation, had been used to fabricate β-TCP [5]. An aqueous suspension of $Ca(NO_3)_2$. $4H_2O$ and $(NH_4)_2HPO_4$ was subjected to a microwave for 40 min at a temperature of 50 ^oC. As a result, spherically shaped β-TCP nanoparticles of about 60-70 nm were uniformly formed. After calcination at 800 ^oC, single-phase β-TCP was observed in the XRD pattern. TEM image clearly showed that the morphology of the β-TCP was a short rod-like shape with a size of about 80-150 nm in width and 200-300 nm in length. In another research work, biodegradable poly (lactide-co-glycolide) (PLGA)/β-TCP composites were synthesized through polymerization under microwave for 2 h at a power of 100 W (around 150 ^oC) [29]. The results indicated that the PLGA/β-TCP composites were formed with uniform dispersion of β-TCP in the PLGA matrix of up to 30% content. The compressive strength of the PLGA/β-TCP composites also showed a much higher value compared to that of the PLGA matrix.

Synthesis of Biphasic Calcium Phosphate (BCP)

HA has been known to possess the capacity for direct chemical bonding to bone, whilst β-TCP has high resorption properties. Due to the remarkable biocompatibility, high bioactivity and, in some cases, osteoinductivity, BCP containing HA and TCP phases, had been reported to be more efficient than HA or β-TCP alone for the repair of periodontal defects, certain orthopedic applications and maxillofacial surgery [14, 31]. Therefore, BCP ceramics appear to be preferable as bone graft substitutes, and have recently attracted much attention [14, 31]. BCP can also be used to control the bioresorbability, and hence, achieve optimal results due to the combination [32].

In an earlier research work [33], the *in situ* formation of BCP ceramic with various ratios were synthesized by placing a solution mixture of $(NH_4)_2HPO_4$ and $Ca(OH)_2$ in a domestic microwave oven for 40 - 45 min at a power of less than 400 W. XRD and FTIR results confirmed that BCP was formed without other phases apart from HA and β-TCP. A thermal study indicated that no decomposition took place. The HA/β-TCP ratio can be easily changed to form BCP with desired properties. Rameshbabu and Rao [34] also reported that microwave synthesis is a useful method for the synthesis of nanostructured BCP with the possibility of changing the degree of solubility for the needs of different applications. Lee et al. [35] reported that *in situ* BCP nanoparticles were synthesized using a microwave-assisted process. The results showed that the microstructures and crystal structures were dependent on the pH of the starting solutions. The as-synthesized particles were spherical in shape with an average size in the range of 50-90 nm. HA and β-TCP phases were found to co-exist in the pH range of 6-12. The yield of HA was also reported to increase remarkably as the pH of the solution increased, whereas α-TCP or/and β-TCP yields decreased. At pH 12, monolithic HA nanoparticles was obtained.

Due to the short synthesis duration, microwave synthesis of bioceramics has been shown to offer advantages over conventional methods. In a recent research work [36], it was reported that the formation of in situ BCP powders was much faster (45 min) using microwave synthesis as compared to that of conventional methods (24 h). In addition, the application of microwave during the synthesis process also improved the crystallinity of the BCP where the crystallite size ranged from 16 - 27 nm. The amount of the HA phase in BCP was found to increase when using microwave synthesis.

Synthesis of Carbonated Hydroxyapatite (CHA)

Carbonate substitution in the HA structure is of special interest, because the CO_3^{2-} ion has an impact on different pathologies of human tissue, such as dental caries. CHA was also reported to be more soluble in vivo than HA and increases the local concentration of calcium and phosphate ions that are necessary for new bone formation [37, 38]. Moreover, CHA was resorbed by osteoclasts and replaced with new bone, whereas HA was not resorbed by osteoclasts and thus would not be replaced by new bone [39]. CHA with low crystallinity and of nano size are suitable for the processing of bone-resembling materials. Thus, the development of a new synthesis technique for CHA with controlled morphology and chemical composition is of a great importance [40]. Kumar et al. [41] reported that CHA was successfully synthesized by the substitution of $CaCO_3$ (10, 20, 30 and 40 mol %) for $Ca(OH)_2$ during the reaction with $(NH_4)_2HPO_4$ under microwave. The results showed that CHA was formed after 45 min of reaction under microwave. Interestingly, the authors also reported that the preparation technique may be employed even in operation theaters for instant preparation of CHA if sterilization condition was attended to.

Microwave Sintering

Phase Stability under Microwave Sintering

The stability of HA during microwave sintering was investigated by Ramesh et al. [42]. In this research work, the as-prepared nano HA powder was uniaxially compacted into disc samples, and were subsequently cold isostatically pressed at 200 MPa before microwave sintering at a temperature range of 1000-1300^{o}C for 30 min. As a result, no secondary phases were observed and the phase stability of HA was maintained up to 1300 ^{o}C without any decomposition by microwave heating. In another research work [9], the thermal stability of monophase microwave-sintered HA (MS-HA) was reported to be stable in the temperature range of 900-1200 ^{o}C. The sinterability of both MS-HA and conventionally sintered HA (CS-HA) were also investigated in another research work [43]. The results showed that both the MS-HA and CS-HA compacts were stable up to 1350 ^{o}C with no sign of HA decomposition, but the dehydroxylation of HA had taken place in CS-HA samples.

The key issue in conventional sintering of HA was the dehydroxylation behavior which led to phase transformation upon heating at higher temperatures. Ruys et al. [44] found that the dehydroxylation behaviour of HA started at a temperature lower than 800 ^{o}C; at 800-1350^{o}C, dehydroxylation was accelerated; at 1350^{o}C, dehydroxylation reached the critical point before decomposition took place. So far, there are no reports on the decomposition of MS-HA at such temperature. Pattanayak et al. [45] found that the thermal stability of CS-HAs were only up to 600 ^{o}C, and at higher sintering temperatures, CS-HAs dissociated into other non-stoichiometric phases such as TCP, calcium pyrophosphate ($Ca_2P_2O_7$) and calcium hydrogen phosphate ($CaHPO_4$). In that work, TCP was found to be the major phase above 1000 °C. Similarly, Han et al. [46] also reported that β-TCP, α-TCP and CaO were also found in HA samples after sintering at 1200^{o}C for 3 h using conventional sintering.

Microstructure and Grain Size

Fang et al. [47] reported that the microstructures and grain sizes of microwave-sintered materials were significantly different from that of conventionally-sintered materials. In their research work, HA powder was prepared from $CaHPO_4$. $2H_2O$ and $CaCl_2$, and subsequently sintered at 1200 ^oC for 5 and 10 min, as well as at 1300 °C for 20 min using a 500 W, 2.45 GHz commercial microwave furnace. For comparison, conventional sintering of the same material was also carried out at the same temperatures for 2 h. The morphologies of MS-HA and CS-HA are shown in Figure 5. The morphology of CS sample is shown in Figure 5 (a) in which the entire surface area was reportedly described as rough and uneven, the grains being angular with boundaries shown by straight lines. In contrast, the surface area of MS-HA (Figure 5 (b)) was also reported to show unique features: the entire area looked flat and smooth. The rough and uneven sintered surfaces of conventional sintering was attributed to a higher residual surface area which imply a lesser degree of sintering. A similar morphology of MS-HA was also observed in other research works [8,43]. In addition, the morphology of MS-HA was also reported to be uniform.

The particle sizes of MS-HA reported by different researchers varied with sintering temperatures. In this review paper, the particle sizes of different MS-HAs are plotted as a function of sintering temperature in Figure 6 together with CS-HAs for comparison. It can be seen that the particle sizes of MS-HAs are significantly finer than that of CS-HAs at the same sintering temperature. Figure 6 also indicates that the grain growth or particle sizes of CS-HA increases rapidly with increasing sintering temperature [43] as compared to that of MS-HA. This was proposed as the advantage of MS in preventing grain growth at high sintering temperatures [43].

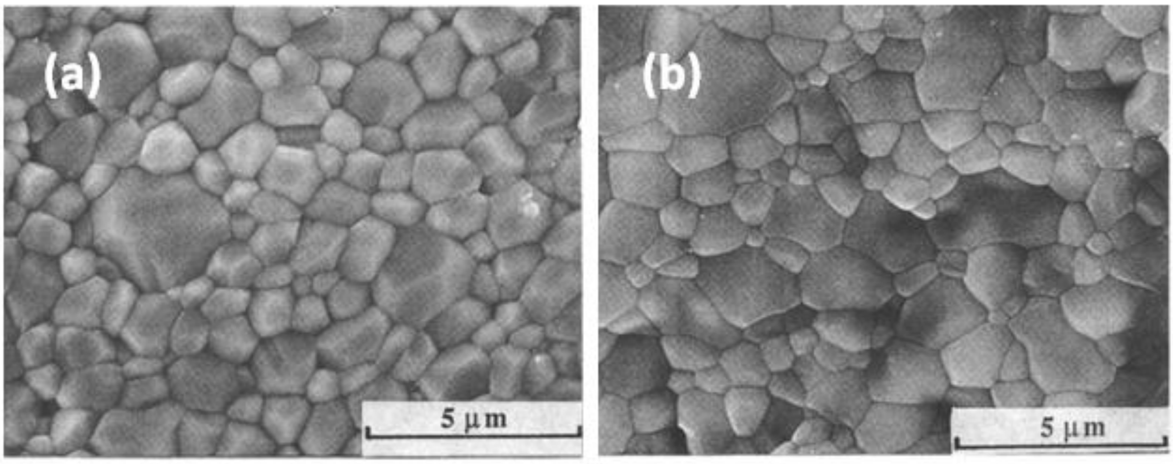

Figure 5. SEM micrographs of sintered HAp: (a) conventionally/1200 °C/2 h,
(b) microwave/1200 °C/10 min [47]

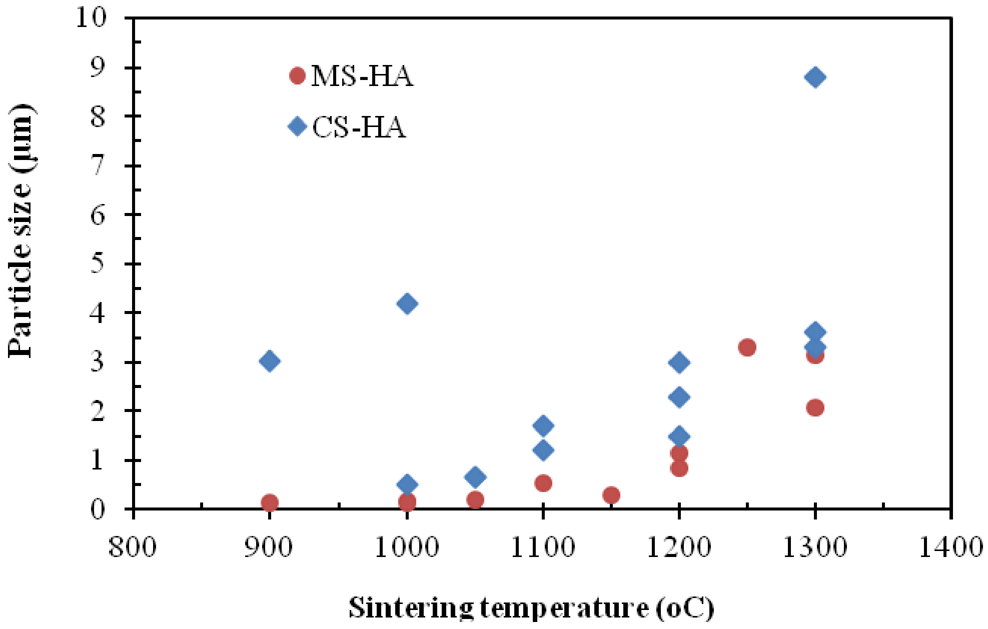

Figure 6. Comparison particle size of MS-HA and CS-HA. The values are extracted from the literature : MS-HA [8,9,26,34] and CS-HA [27,48]

Mechanical Properties

Numerous research work [8,43,46] had indicated that at the same sintering temperature, higher densities were achieved in MS-HA samples for much shorter duration compared to that of CS-HA. The relative density of sintered HA samples from different research works are plotted in Figure 7 as a function of sintering temperature for both microwave sintering and conventional sintering. Figure 7 clearly shows that at sintering temperature below 1250 ^{o}C, the relative density of MS-HA is significantly higher than that of CS-HA. It was suggested that grain boundary diffusion between the HA particles was substantially enhanced by microwave irradiation [43]. At sintering temperatures above 1200^{o}C, the densities of HA samples obtained by both microwave sintering and conventional sintering appear to be similar. Vijayan and Varma [48] reported that the density of HA samples achieved 95% and 98 % of the theoretical density after 5 and 15 min of microwave sintering, respectively. Ramesh et al. [42] also reported that the rapid sintering of nano HA via MS achieved densities above 96% theoretical density at a temperature of 1100 °C for 30 min, whilst maintaining a fine-grained microstructure. The relative density of the compacts in that work varied between 90% and 98% (1000-1300 °C), however, the higher values of 96% and 98% density were attained in samples consolidated at 1100 and 1300 ^{o}C, respectively.

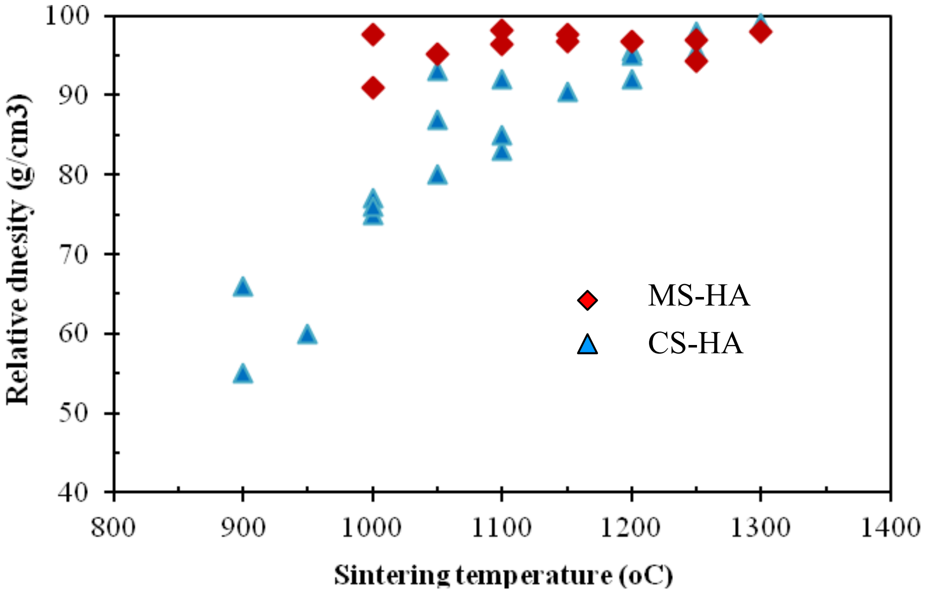

Figure 7. Comparison of relative densities (%) of sintered HA bioceramics using microwave sintering and conventional sintering adapted from the literature (microwave sintering [8,26] and conventional sintering [27]

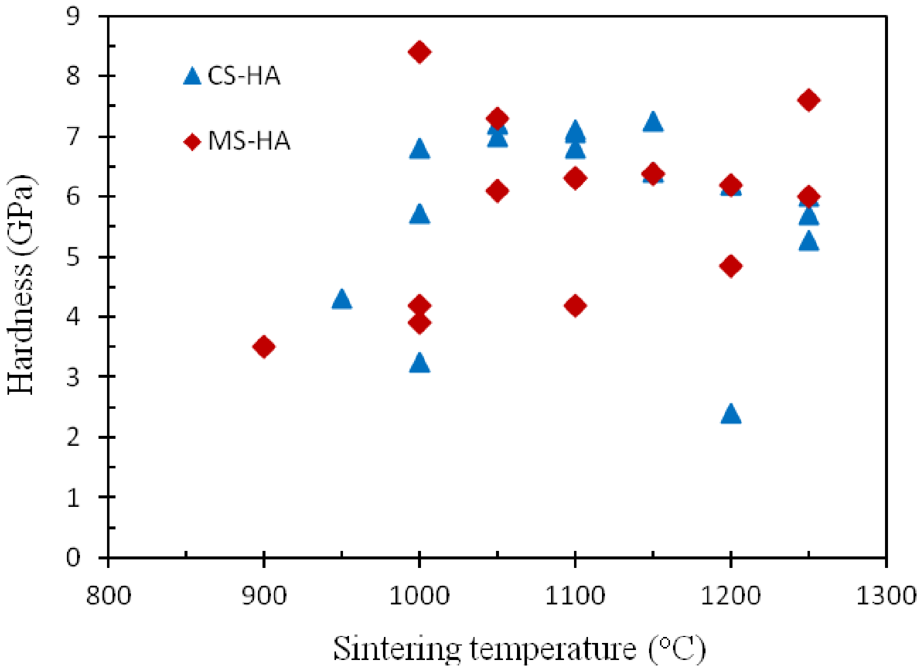

Figure 8. Hardness of sintered HAs using MS and Cs from the literature, MS [8,9, 27] and CS [9,27]

The hardness values of MS-HA and CS-HA from different research work are plotted together in Figure 8 as a function of sintering temperature. It can be seen that the hardness of MS-HA and CS-HA are comparable and within the range of 3-8.4 GPa. The maximum hardness of MS-HA is 8.4 GPa at a sintering temperature of 1000°C for 20 min [8], whilst that of CS-HA is 7.2 GPa at a sintering temperature of 1150 °C for 120 min [49]. This indicates that a higher hardness of HA can be obtained using microwave sintering at a sintering temperature less by 150 °C in a much shorter duration compared to that of HA using conventional sintering. In addition, a very high compressive strength of 395 MPa for HA was also reported when using microwave at 1000 °C for 20 min [8].

The fracture toughness of MS-HA from different research work are also plotted as a function of sintering temperature in Figure 9 together with CS-HA for comparison. The fracture toughness values of MS-HA are significantly higher than that of CS-HA at the same sintering tempature. It can be seen that the fracture toughness of both MS-HA and CS-HA decreases with increasing sintering temperature. However, the maximum fracture toughness of MS-HA is 1.9 MPam$^{1/2}$ [8], whilst that of CS-HA is 1.52 MPam$^{1/2}$ [50]. The improvement in fracture toughness of MS-HA was explained due to both the improved properties of the as-synthesized HA powders, as well as the improved sinterability of these powders with limited grain growth during microwave sintering [8,46].

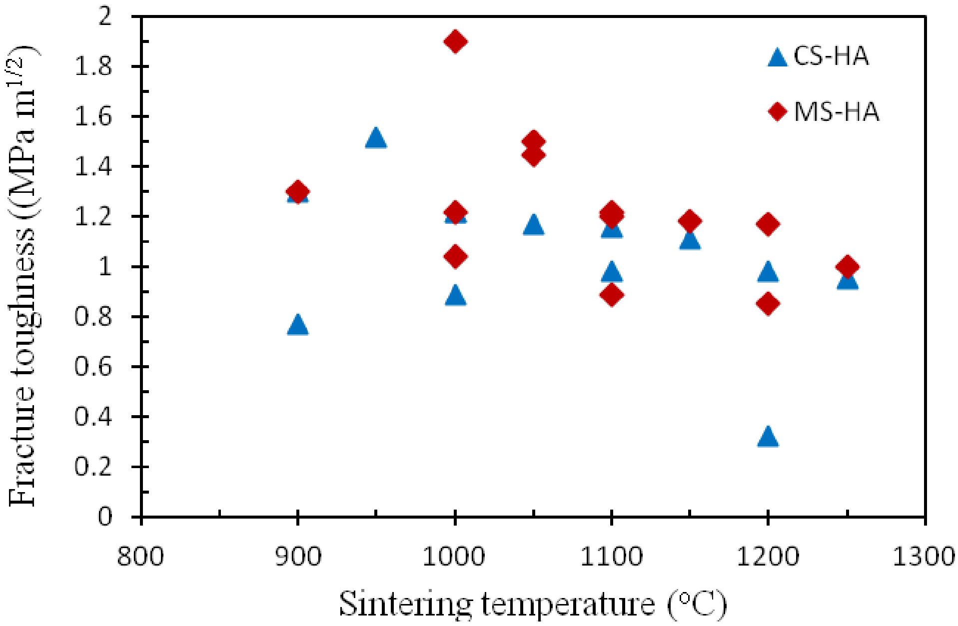

Figure 9. Fracture toughness of sintered HAs using MS and Cs from the literature, MS [8,9,27] and CS [9,27]

Microwave Sintering Of Porous Bioceramic

Porous BCP containing HA and α/β TCP ceramics had been reported to demonstrate excellent properties in biomedical applications, such as in bone tissue engineering, cell proliferation and drug delivery [51]. However, the production of porous BCP ceramics was generally based on a sintering process with a long duration and high temperature, whereby the bioactivity of the final product could be reduced [14,52].

By using microwave sintering, Wang et al. [14] reported that porous BCP with an average crystal size of 300 nm, porosity of 65%, and compressive strength of 6.40 MPa was formed within a short duration. Initially, the porous green BCP body was fabricated from wet-synthesized BCP powders by H_2O_2 foaming under a temperature of 40-80 °C and dried at 100 °C for 12 h. Subsequently, the BCP green bodies were sintered in a microwave oven at 900 to 1300 °C for 5 min. As a result, the MS-BCP samples showed much smaller grain sizes and more uniform microstructures. The compressive strength is comparable to that obtained by CS at the same temperatures but for 2 h at 5 ^{o}C/min heating rate. A similar process was also adopted to form porous, nanostructured carbonated BCP ceramics by Li et al. [52]. SEM observation of MS-BCP revealed a structure of interconnected pores with an average grain sizes of ~86 nm (Figure 10). This research work also indicated that carbonated BCP nanograins can be easily obtained by rapid microwave sintering with a compressive strength which is comparable to that obtained by the conventional sintering for a much longer sintering duration.

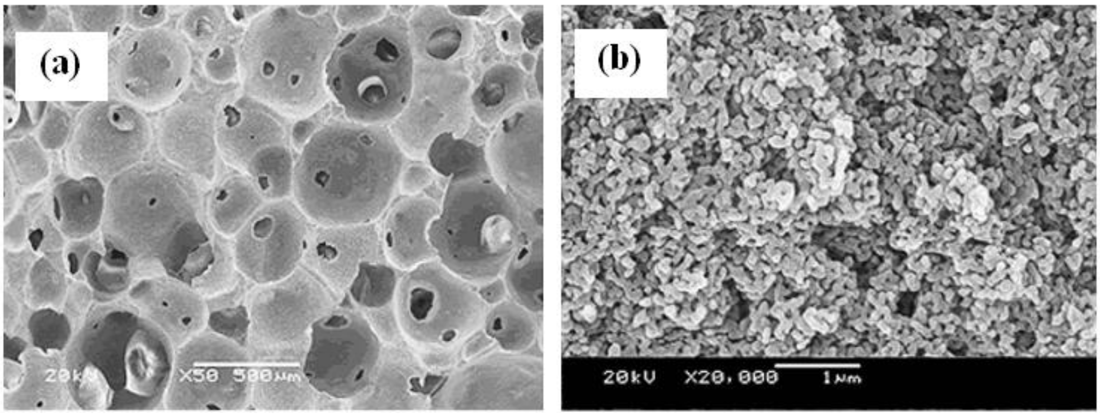

Figure 10. Typical scanning electron micrographs of the nanoporous carbonate BCP at different magnifications: (a) 50 X and (b) 20,000 X [53]

Kim et al. [53] reported that 3D porous TCP-coated Al_2O_3 scaffolds was formed using a polyurethane (PU) foam replica method by coating TCP on Al_2O_3 scaffolds and followed by microwave sintering. The Al_2O_3 scaffold was dipped into a TCP slurry and dried at 80 °C for 8 hours The dipping-and-drying steps were repeated three times. The body obtained was then heat-treated to burn out the sponge and binder at 600 °C for 3 hours. Afterwards, the TCP-coated Al_2O_3 scaffold was then sintered using microwave at 1300 ^{o}C with a heating rate of 45 ^{o}C/minute for 30 minutes to generate a porous surface morphology. The pore sizes obtained were in the range of 100-600 µm, which is ideal for cellular proliferation. The results also indicated that TCP-coated Al_2O_3 scaffold enhanced its mechanical strength, bioactivity, osteoconductivity, and cellular proliferation. A similar research work [51] reported that porous spherical BCP granules was fabricated using different volumetric ratios of polycaprolactone (PCL). The method to produce porous granules was based on the liquid immiscibility effect of a PCL solution and distilled water. Granules were sintered at 1300 °C and 1400 °C using CS (2 hours) and microwave sintering (20 minutes) methods. The results showed that the porosity of the granules sintered at 1300◦C by conventional sintering and microwave sintering ranged from 45% to 59.8%, whereas, the porosity ranged from 36.12 % to 49.9 % when sintered at 1400 ^{o}C. The pores were interconnected and the inner pore size ranged from 30 to 250 µm.

In another research work [55], a porous scaffold of gelatin–starch–nano HA composites was fabricated through microwave vacuum drying and crosslinking with three different percentages of nano HA: 20%, 30% and 40%. Gel samples of gelatin-starch polymer network with nano HA were placed in a vacuumed cylindrical drum with a microwave generator. The drum was rotated with a rotation speed of 5-10 rpm whilst microwave was simultaneously applied to assist the drying process. The results showed that the time required for drying the wet gel was only 40-45 min. Mechanical tests on the gelatin-starch polymers did not show any fracture; rather, it underwent densification even when the brittle nano HA was added up to 40 wt.%. The compressive strength of the scaffold increased with increasing nano HA content with a maximum value of around 10 MPa at 40 wt.% nano HA. The composite scaffolds reported in this work could be loaded with antibiotic drugs, and so have potential for use in wound healing and hard tissue regeneration.

In-Vitro Biocompatibility and Osteoconductivity

Fine particle sizes of bioceramics obtained via rapid microwave synthesis and sintering do not only improve the mechanical properties, but also improve the bio-properties of the materials. Bose et al. [8] reported that nano MS-HA compacts simultaneously improved the mechanical and *in vitro* biological properties of HA. *In-vitro* studies of bone cell material interactions of MS-HA using a human osteoblast bone cell line showed that the formation of vinculin-positive focal adhesion plaques increased gradually with cell culture time. The highest fluorescence staining of vinculin was observed in MS-HA substrate having 168 nm grains and the lowest amount of vinculin expression for 1.16 µm-grained MS-HA substrate, as shown in Figure. 11. The increase in bone cell adhesion and proliferation with decreasing grain size was explained due to the presence of a higher number of grain boundaries. The smaller grain size influences surface properties in which surface energy increases with decreasing grain size. Higher surface energy positively influences bone cell attachment and growth significantly even if there is no difference in composition. Li et al. [53] also reported that compared with the microscale porous BCP formed by conventional sintering, the results showed that nanophase scaffolds promoted cell proliferation and differentiation, respectively, and SEM observation showed that the nanoscale structure clearly promoted cell adhesion. The BCP ceramics prepared using microwave also demonstrated other advantages such as good tissue biocompatibility without adverse effects [56]. The BCP ceramic has a controlled biodegradability, thus producing calcium ions in the microenvironment which induces bone formation and gradual remodeling of the new bone.

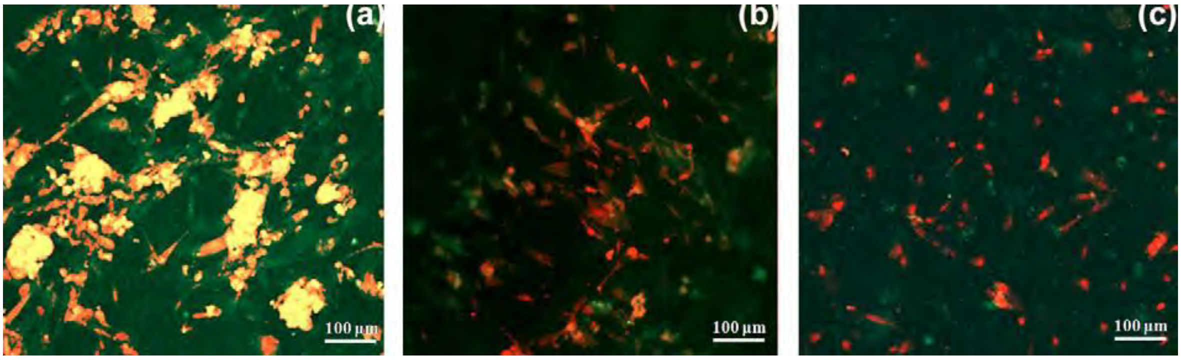

Figure 11. Confocal micrographs of vinculin expression in human osteoblast cells cultured on HA compacts with different grain size: (a) 0.168 µm, (b) 0.52 µm and (c) 1.1 µm after 5 days [8]

New Approaches and the Future of Microwave in Bioceramics

The conventionally synthesized bioceramics, such as HA, CHA and β-TCP, were normally dried in an oven for a long duration of one or a few days after synthesis [37, 57-60]. The drying process of the as-synthesized bioceramics will need an even longer duration for a large-scale production. A long drying process also lead to a delay in the subsequent processes such as compaction, shape forming, etc.. In addition, the lengthy drying of bioceramics in the oven is energy consuming and costly. The drying process in the oven can also be non-uniform due to the thermal gradient especially if it is on a large-scale production. Hence, microwave with rapid and more uniform heating, coupled with possible energy savings, can be a potential method for drying bioeceramics. Literature reports on the use of microwave in drying bioceramics is scarce. However, recently, Thevi et al. [61] reported that milled mixture of β-TCP and $CaCO_3$ with trisodium citrate and water was rapidly dried using microwave oven for 60-70 min, and followed by conventional sintering to form HA scaffolds. In another research work, Sundaram et al. [55] showed that gelatine-starch scaffolds with nano HA composite had been formed after drying the wet gel for 40-45 min under microwave vacuum.

Most of the microwave synthesis of bioceramics were conducted using domestic microwave ovens. This method is simple and low cost. However, the temperature in household microwave oven during the synthesis was not properly controlled and rarely reported. Therefore, a microwave oven with better control features should be designed for the synthesis of biceramics in order to control their properties. The application of microwave in bioceramics was much less than that for ceramic materials. However, the use of microwave in bioceramics is increasing over the years. Recent research work had shown that the use of microwave in bioceramics is a promising approach with obvious advantages over the conventional processes.

Recently, researchers have focused on the fabrication of substituted-HAs, such as CHA [3, 37] and Si-HA [62, 63], but the difficulties in sintering these materials are of serious concerns, such as decomposition due to high sintering temperatures and long duration [64]. It is expected that microwave will be a suitble method to solve this problem by rapid sintering at lower sintering temperature, whilst still achieving mechanical properties comparable to that obtained by conventional sintering without decomposition.

Conclusions

The use of microwave has been demonstrated to be useful as a tool for sythesizing high purity nano-bioceramics in a short duration of 30 min, even in 1 min, instead of a much longer duration when using conventional methods. The size and shape of the as-synthesized HA powders had been shown to vary with the microwave powers. The shape can be transformed from needle, acicular, spherical, rod-like and prism-like shapes. The particle sizes of the as-synthesized bioceramic powders increased with increasing synthesis temperature using microwave, whilst the thermal stability increases with increasing applied microwave duration and power.

Microwave sintering of bioceramics is a rapid process with finer grain size and higher thermal stability compared to that of conventional sintering. Rapid microwave sintering of bioceramics prevents grain growth, which results in a much finer grain size and improved mechanical properties. The grain boundary diffusion between the HA particles is substantially enhanced during microwave sintering and this can lead to a higher density of the bulk HA compared to that of conventional sintering. High fracture toughness of microwave sintering samples is due to the better sinterability and less grain growth compared to conventionally sintered samples. Microwave sintering of bioceramics also consumes much lower energy compared to that of conventional sintering. Low temperature, rapid heating and short duration have demonstrated that microwave sintering can be a new promising method for sintering CHA. Microwave sintering of nano-bioceramics promotes bone cell adhesion, proliferation and good tissue biocompatibility.

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