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Short communication

Formation and characterization of porous spherical biphasic calcium phosphate (BCP) granules using PCL

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Abstract

We developed a process to fabricate porous spherical BCP granules using different volumetric ratios of polycaprolactone (PCL). This technique takes advantage of the formation of spherical drop shapes that occur for any liquid. The method to produce porous granules is based on the liquid immiscibility effect of a PCL solution and distilled water. Granules were sintered at 1300 °C and 1400 °C using conventional and microwave sintering techniques. Using this approach, the granules showed a good pore-interconnected relation and granules with a porosity that ranged from 36.12% to 59.8%, inner pore sizes that ranged from 30 μm to 250 μm, and a granular size of about 1.5 mm could be obtained. Granules were characterized for microstructure, phase composition and porosity. Using this novel approach, we were able to achieve desirable porous characteristics that simulate natural bone structure.

Keywords: Granules; BCP; Porous ceramic; Pore size distribution

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1. Introduction

Porous biphasic calcium phosphate (BCP) containing hydroxyapatite (HAp) and tricalcium phosphate (α/β-$Ca_3(PO_4)_2$) ceramics are extensively used in biomedical applications, including bone tissue engineering, cell proliferation, and drug delivery [1–3], because they have a chemical composition similar to the inorganic phase of human bones tissue [4]. In bone tissue engineering, they are excellent candidates for bone graft substitutes due to their resorption in the body fluid upon implantation and provide an interfacial bond between an implant and the surrounding tissues [5,6]. In some cases, osteoinductivity was reported to be more efficient than for HAp alone for the repair of periodontal defects [7] whereas, BCP consisting of HAp and β-TCP was shown to have better osteoinduction than single phase HAp or β-TCP [8,9]. With these advantages in mind, a few researchers have recently developed and fabricated porous BCP bodies by the ceramic foaming technique, the polymeric sponge method, and microwave processing [1,10,11].

Recently, the use of porous spherical BCP granules as drug delivery systems and injectable bone substitute (IBS) has attracted a great deal of attention [12–14]. The delivery and application of drugs using particulate systems claimed to have enhanced biocompatibility, predictable therapeutic response, greater efficacy, safety and prolonged drug release time [13,15–17]. Rounded granules with smooth shapes are also favorable for defect tissue filling [18]. Furthermore, it has been reported that porous bioceramic structures that allow tissues to infiltrate and enhance implant tissue attachment and resorbability provide fast bone ingrowths due to high surface area [19,20]. Due to the growing number of potential applications of porous granules as bioactive ceramics, many researchers have fabricated porous spherical HAp granules with diameters

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ranging between 0.2 and 2 mm using techniques such as the drip-casting process or granulation process [18,21].

Among the spherical granule fabrication methods that have been developed bioceramic materials, the formation of drops from particle-laden liquids has received little attention in the field of ceramic manufacturing [22,23]. Moreover, it was reported that viscosity is an especially important parameter, which may influence particle morphology as well as mixing behavior [24]. In this study, we were interested in extending the technology of spherical granule fabrication and in developing a novel method to fabricate porous BCP spherical granules based on the formation of drops from PCL solutions containing BCP powder. Conventional and microwave sintering methods were used to sinter the granules at different temperatures. Microwave sintering may lead to some benefits including fine control over microstructure, reduced manufacturing costs due to energy savings, and shorter processing time. The geometry, microstructure, crystalline phases and material properties of porous BCP granules were characterized as a function of the processing conditions.

2. Materials and fabrication methods

2.1. Materials

BCP powder was prepared by the precipitation method with reagent-grade calcium hydroxide ($Ca(OH)_2$) and phosphoric acid (H_3PO_4) as starting materials following a microwave assisted process.

Commercial-grade $Ca(OH)_2$ (Aldrich Chemical, 99.995%) and reagent grade H_3PO_4 (85–87.0% H_3PO_4, Dongwoo Fine Chemicals, electronic grade) were used for the synthesis of BCP powders. A molar ratio Ca/P = 1.67 powder was mixed homogeneously by stirring it in de-ionized distilled water for 2 h. The pH of the solution was adjusted to 10. Subsequently, the pH controlled suspension was placed in a microwave oven (LG Electronics Co., Korea), operated at 2.45 GHz frequency while the operating power was maintained at 700 W, for 25 min at 300 °C. After cooling to room temperature, the precipitate was washed thoroughly with de-ionized distilled water several times and dried in an oven at 90 °C for 24 h. Finally, the calcinations were carried out at 750 °C in air. Details of the preparation route are described in our previous report [25].

2.2. Porous spherical granule preparation

To make BCP/PCL slurries volume ratios of 70/30, 60/40, and 50/50, PCL (poly caprolactone, purity >99.9%, Aldrich, USA) granules were first dissolved in acetone contained in beakers using an ultrasonic machine to produced different solutions. The machine was set at 50 °C for 3 h to dissolve the PCL granules. The beakers were covered with Al_2O_3 paper to avoid acetone evaporation. Subsequently, PCL solutions were stirred for 4 h, and then added to the BCP slurries drop by drop using a pipette. The slurries were mixed homogeneously for 12 h. Finally, these homogeneous slurries were dripped into de-ionized distilled water using a pipette with a diameter of approximately 0.5 mm. The slurries were continuously stirred during this process to avoid agglomeration. The drops of slurry were then dried, resulting in the formation of spherical or near-spherical granules. The obtained granules were dried in an oven, at 40 °C for 24 h, burnt out at 600 °C for 2 h in air to remove the PCL binder and sintered at 1300 °C and 1400 °C in a conventional furnace for 2 h in a microwave furnace for 20 min, respectively.

To determine the phase composition, porous sintered BCP granules were crushed into powders, then together with the calcination powder, were analyzed using X-ray diffraction (XRD, D/MAX-250, Rigaku, Japan). Thermo-gravimetric and differential thermal analysis (TG/DTA, SDT Q600, TA instruments), was conducted at a heating rate of 10 °C/min in air to investigate the decomposition behavior. The porosity of the spherical granules was measured using the Archimedes method. The microstructure and morphology of porous granules were observed by SEM (JSM-635F, JEOL, Tokyo, Japan).

To observe the inner microstructure of porous spherical BCP granules, they were covered with a slurry shell made of a

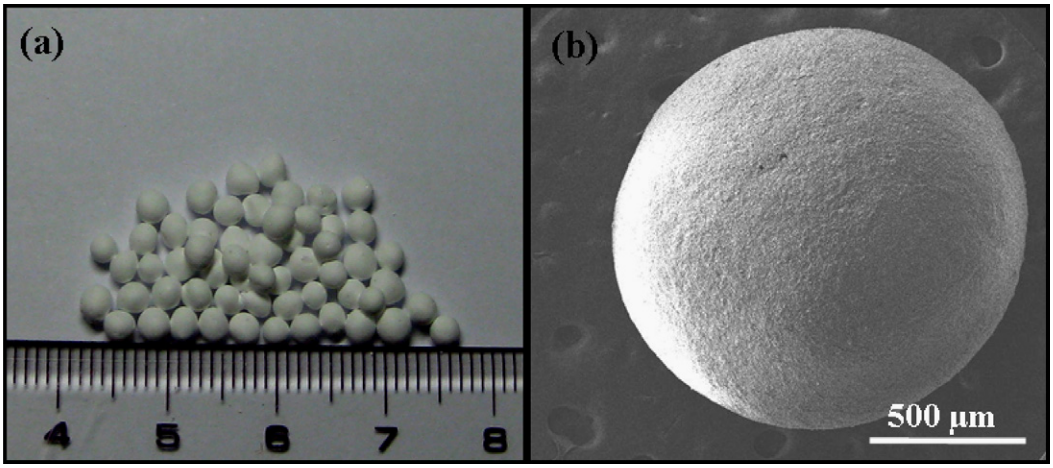

Fig. 1. Micrographs of the porous spherical BCP granules fabricated using 30 vol.% PCL before burning out (a) and (b) after sintering by conventional furnace at 1300 °C, respectively.

mixture of Epoxy resin (Epon 812, polysciences, Inc.), dodecenyl succinio anhydride (DDSA ($C_{16}H_{28}O_3$), Polysciences, Inc.), nadic methyl anhydride (NMA ($C_{10}H_{10}O_3$), polysciences, Inc.), and tris (dimethylamino-methyl) phenol (DMP-30 ($C_{15}H_{27}N_3O$), polysciences, Inc.) at a volume ratio of 48/31/21/2, respectively. The slurry was then dripped on to the cavities of a plastic mould to produce ready-made shells for the porous spherical BCP granules. The BCP granules containing the outer covers were subsequently dried in an oven for 48 h at 60 °C. Finally, these BCP granules that resulted covered with hard shells were polished and prepared for SEM micrographs.

3. Results and discussion

Fig. 1(a) and (b) shows the micrographs of the BCP granules fabricated using 30 vol.% PCL as the forming agent before the burn-out and after being sintered at 1300 °C for 2 h in a conventional furnace, respectively. Most granules were spherical or near spherical and had an average diameter of about 1.5 mm after sintering as shown in Fig. 1(b).

Fig. 2 shows the TG/DTA profiles of PCL. This figure shows that the weight percentage of PCL decreased as the temperature increased to 250 °C, and when the temperature was higher than 500 °C, PCL was completely removed. In contrast, an endothermic reaction was observed around 65 °C in the DTA profile, and three exothermic reactions around 250 °C, 270 °C, and 370 °C due to the decomposition of PCL.

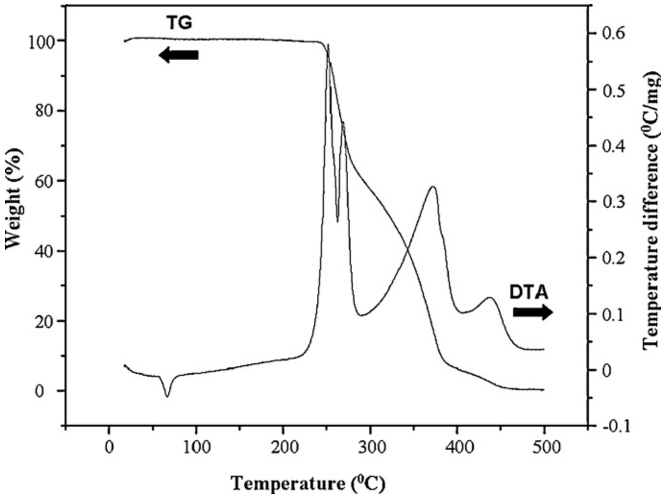

Fig. 2. TG/DTA profile of PCL.

Figs. 3 and 4 show the SEM micrographs of the surfaces of porous BCP granules. The porosity of the BCP granules, which were sintered in conventional for 2 h and microware furnaces for 20 min at 1300 °C and 1400 °C, depended on the volumetric ratio of PCL used during fabrication. The SEM micrographs show a porous structure with many pores due to the removal of the PCL pore-forming agent during the burning out at 600 °C in air atmosphere. These pores were distributed homogeneously on the sphere surfaces with a size in the range from 1 to 12 μm.

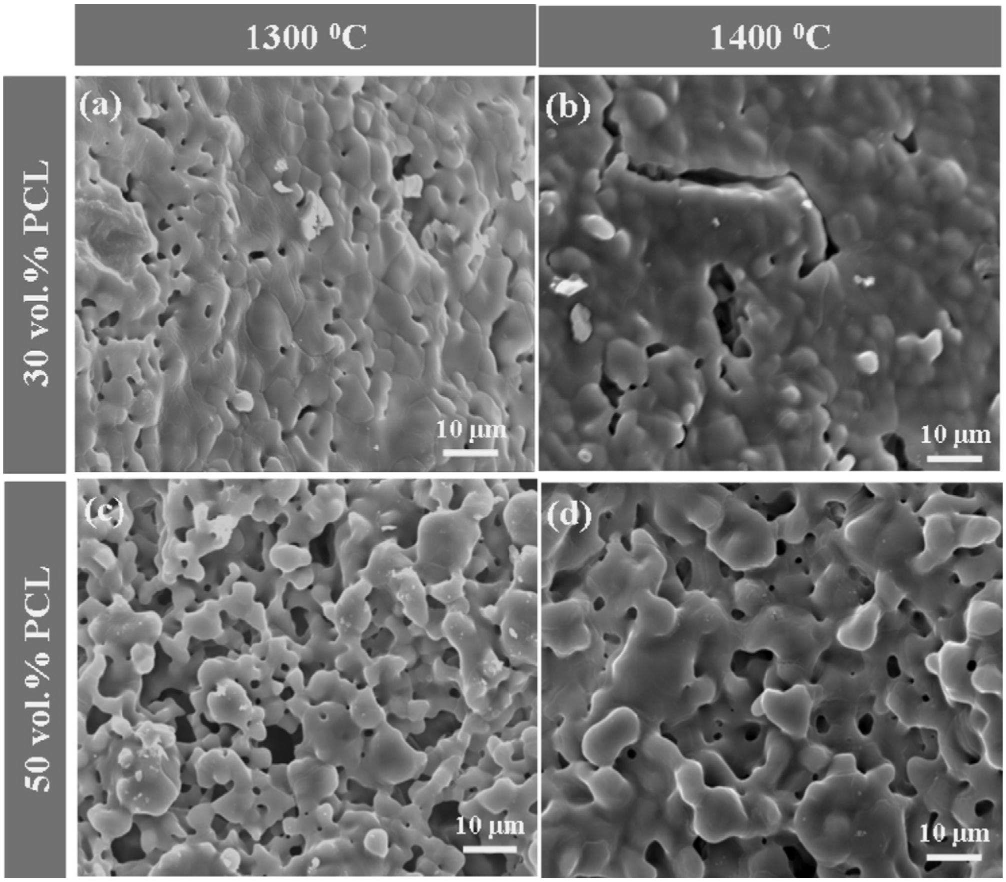

Fig. 3. SEM micrographs of the rough surface of porous spherical BCP granules sintered at 1300 °C and 1400 °C for 2 h by a conventional furnace, respectively.

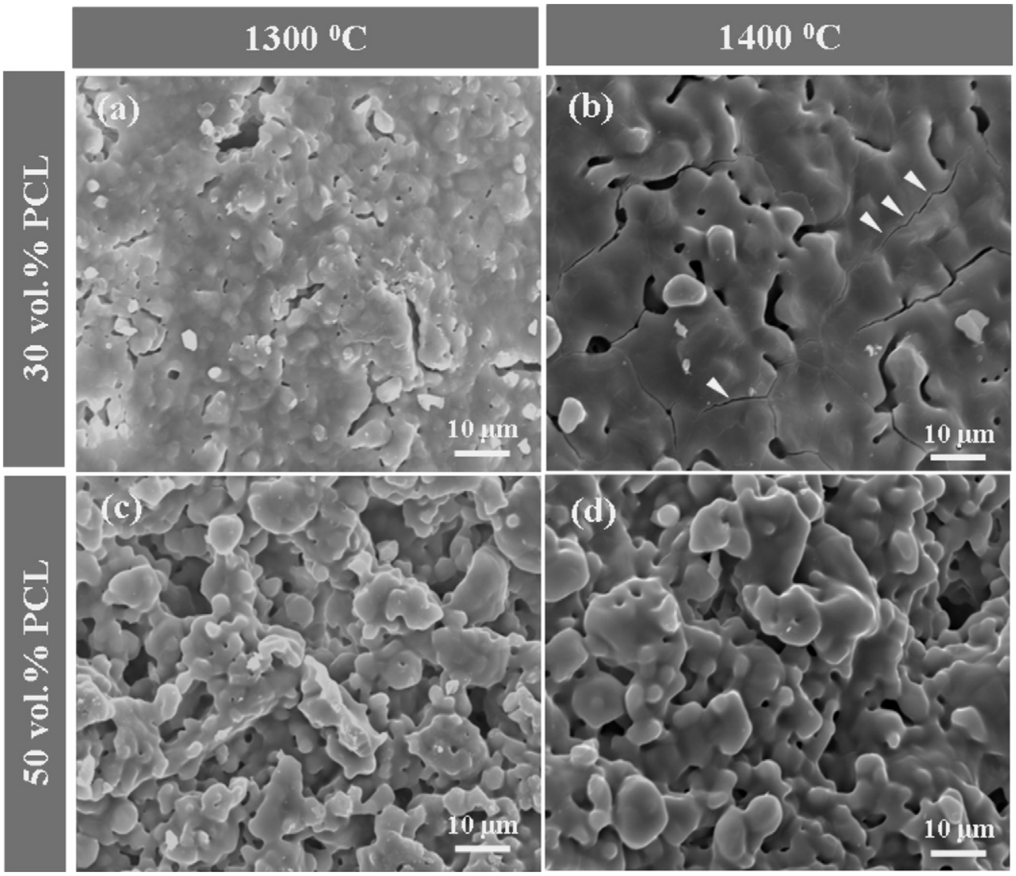

Fig. 4. SEM micrographs of the rough surface of porous spherical BCP granules sintered at 1300 °C and 1400 °C for 20 min by a microwave furnace, respectively.

Figs. 3 and 4 also show that increased PCL content lead to an increase in the pore content. These SEM micrographs show a distinct difference in the microstructure of porous granules sintered at 1300 °C or 1400 °C in conventional and microwave furnaces. The PCL powders with the same PCL content sintered at 1300 °C or 1400 °C in the microwave furnace show a denser microstructure compared with those sintered at 1300 °C or 1400 °C in the conventional furnace as shown in Fig. 3(a) and (b) and (c) and (d) or Fig. 4(a) and (b) and (c) and (d), respectively. However, there was a distinct microstructural feature at a sintering temperature of 1400 °C when the microwave furnace was used. Under these conditions, the microstructure exhibited some evidence of cracking as indicated by the arrowheads in Fig. 4(b) at 30 vol.% PCL, whereas, this was not observed at 50 vol.% at the same sintering temperature as shown in Fig. 4(d). This denser microstructure may be explained by the fact that microwave heating is a more rapid sintering process than the conventional heating techniques so that energy can be deposited volumetrically throughout the material rather than relying on thermal conduction from the surface [11].

Fig. 5 shows the XRD profiles of raw BCP powder and porous BCP granules, which depended on the different sintering temperatures and methods used during fabrication. The major β-TCP, HAp and minor α-TCP peaks were observed as shown in Fig. 5. When the samples were sintered at 1300 °C, a phase transformation of β-TCP to α-TCP was observed, however, this phase transformation was not remarkable, as shown in Fig. 5(b and c). The intensities of the α-TCP peaks were detected more strongly at a sintering temperature of 1400 °C in the conventional furnace as shown in Fig. 5(d). It has been reported that the use of a microwave furnace instead of a conventional furnace results in a lower crystalline degree when

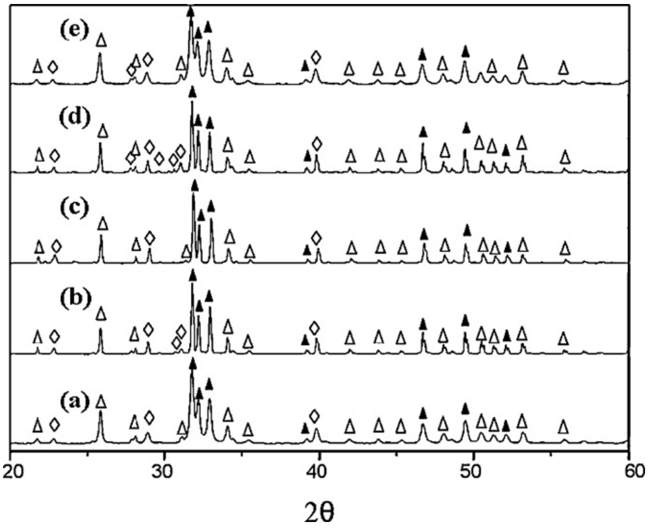

Fig. 5. XRD profiles of the porous spherical BCP granules (a) calcination at 750 °C (b and d) sintered at 1300 °C, 1400 °C by a conventional furnace, and (c and e) sintered at 1300 °C, 1400 °C by a microwave furnace, respectively.

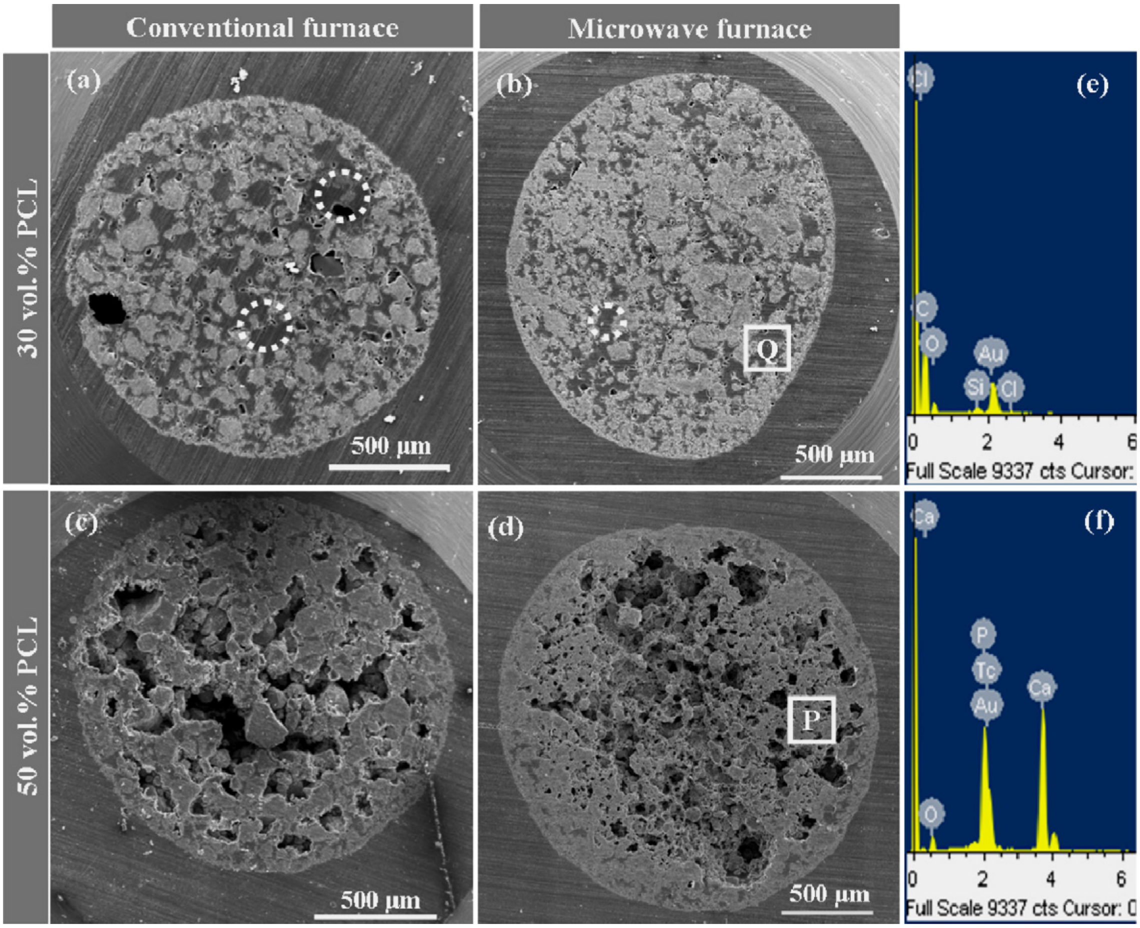

Fig. 6. SEM micrographs and EDS profiles of the polished surfaces of the porous spherical BCP granules sintered at 1300 °C for 2 h by a conventional and a microwave furnace, respectively.

the samples are sintered at the same temperature. Therefore, using microwave furnaces may have improved the bioactivity of the bioactive ceramic material [11].

Fig. 6 shows SEM micrographs and EDS profiles of the microstructure of polished surfaces of porous spherical BCP granules, which depend on the volumetric ratio PCL and sintering temperatures used during fabrication. From the SEM micrographs of the polished porous spherical BCP granules fabricated with 50 vol.% PCL, a porous inner structure was observed with many pores, which were distributed randomly on the polished surfaces and had pore sizes between 30 and 250 μm (Fig. 6(c) and (d)). At 30 vol.% PCL, a denser microstructure with smaller pore sizes was observed as shown in Fig. 6(a) and (b). These SEM micrographs also show that a lot of the pores have a black contrast, which is indicated by the dotted circles in Fig. 6(a) and (b). This may have occurred if the pores filled up with the powder of the hard shells of porous BCP granules during the polishing process. Furthermore, from the EDS profiles shown in Fig. 6(e) and (f), which were taken from the regions marked Q and P in Fig. 6(b) and (d), respectively, elements C and O (in black) and elements Ca and P (in white) were observed in these regions. Therefore, the almost black regions are most certainly organic compounds, whereas, the white regions consist primarily of BCP powder. On the other hand, when 30 vol.% PCL was used during fabrication, the polished surfaces contained near circle shapes (Fig. 6(a) and (b)), while almost circle shapes were observed when 50 vol.% PCL was used during fabrication (Fig. 6(c) and (d)). This may be explained the fact that the viscosity of the BCP/PCL slurry at a volume ratio of 70/30 was higher than for a volume ratio of 50/50.

Fig. 7 shows SEM micrographs of the grain size on the rough surface of sintered porous BCP granules using both conventional and microwave sintering methods, respectively. Microwave sintering shows a much smaller and more uniform grain structure compared with those in conventional sintering. The grain size varied from 2 to 3 μm in microwave sintering with 20 min holding time at 1300 °C and 1400 °C; however, the variation in grain size ranged from 2 to 6 μm in conventional sintering with a 2 h holding time at the same temperatures. It was reported that microwave sintering of HAp ceramics led to the reduction of grain size [26], which is in agreement with the findings of this study. Therefore, the decrease of grain size was due to the rapid heating, which should be responsible for the finer grain size. In addition, it has also been reported that small grain size is effective at increasing the mechanical strength of the sample. Therefore, it may provide advantages in regards to biomedical applications.

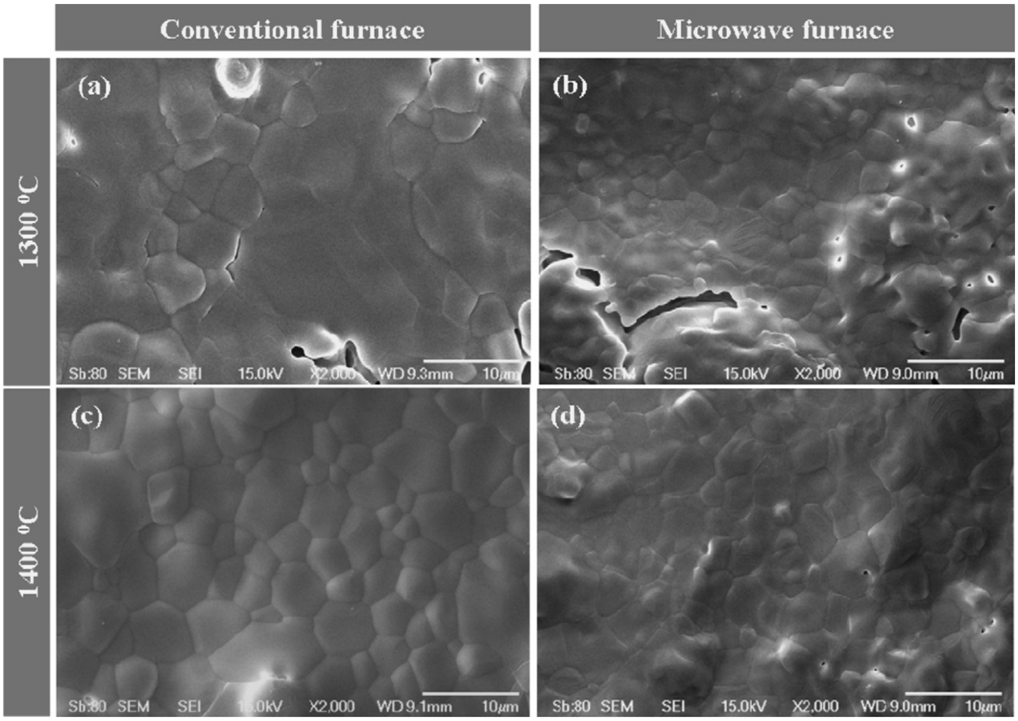

Fig. 7. SEM micrographs of rough surface of porous BCP granule using 30 vol.% PCL sintering by conventional furnace and microwave furnace, respectively.

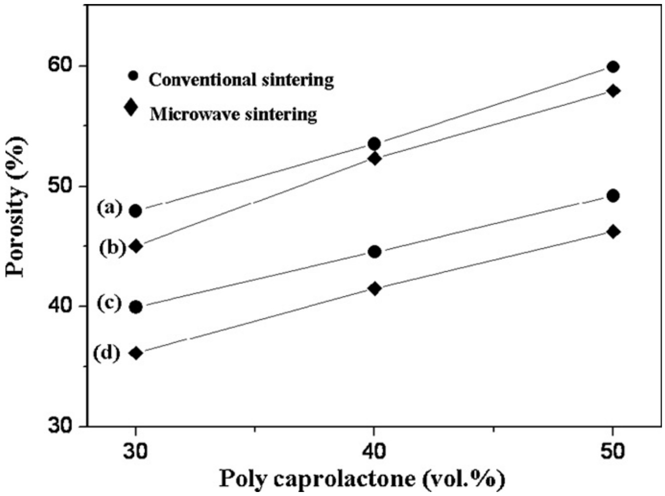

Fig. 8. Porosity of the porous spherical BCP granules depending on PCL contents (a), (b) sintered at 1300 °C and (c), (d) at 1400 °C by a conventional and a microwave furnace, respectively.

Fig. 8 shows the relationship between porosity and the PCL volume content, which depended on the sintering methods and sintering temperatures. The relationship between porosity and PCL contents sintered at 1300 °C and 1400 °C was almost linear. Furthermore, a remarkably different porosity between porous BCP granules using conventional and microwave furnace was observed (Fig. 8). At the same sintering temperatures, the conventional furnace gave a higher porosity than the microwave furnace. Experimental results also show that the minimum and maximum porosity values of porous granules sintered at 1300 °C by conventional and microwave methods were about 47.5%, 45% and 59.8%, 57.5%, whereas, at 1400 °C they were 39.95%, 36.12% and 49.9%, 46.2%, respectively.

4. Conclusion

Porous spherical BCP granules were successfully fabricated using the dripping process at different volumetric ratios of PCL. This is a simple fabrication method that is based on the formation of spherical drop shapes, which can occur for any liquid. The granules exhibited a controllable porosity and porous character, depending on PCL content. Porous granules sintered at 1300 °C and 1400 °C in a conventional furnace for 2 h and microwave furnace for 20 min, respectively, had a particle diameter of approximately 1.5 mm. The porosity of granules sintered at 1300 °C in conventional and microwave furnaces ranged from 45% to 59.8%, whereas, the porosity ranged from 36.12% to 49.9% when sintered at 1400 °C. The pore size ranged from 1 to 12 μm, the inner pore sizes ranged from 30 μm to 250 μm, and the pores displayed good interconnectivity. Using this approach, porous granule structures can be specifically made to simulate of the porous structure of the living bone, which is expected to be highly beneficial for biomedical applications.

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