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Sonochemical synthesis of calcium phosphate powders

M. de Campos · F. A. Müller · A. H. A. Bressiani · J. C. Bressiani · P. Greil

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Abstract β-tricalcium phosphate (β-TCP) and biphasic calcium phosphate powders (BCP), consisting of hydroxyapatite (HA) and β-TCP, were synthesized by thermal decomposition of precursor powders obtained from neutralization method. The precursor powders with a Ca/P molar ratio of 1.5 were prepared by adding an orthophosphoric acid (H_3PO_4) solution to an aqueous suspension containing calcium hydroxide ($Ca(OH)_2$). Mixing was carried out by vigorous stirring and under sonochemical irradiation at 50 kHz, respectively. Glycerol and D-glucose were added to evaluate their influence on the precipitation of the resulting calcium phosphate powders. After calcination at 1000°C for 3 h BCP nanopowders of various HA/β-TCP ratio were obtained.

1 Introduction

Calcium phosphates are an important class of inorganic compounds for application as bulk material and coating in medical implant applications. Chemical and structural similarity to the mineral phase of bone tissue provides biological capability to promote bone integration. The most widely used synthetic calcium phosphates are hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH)_2$) and β-tricalcium phosphate (β-TCP, $Ca_3(PO_4)_2$) [1, 2].

HA is stable in physiological body fluids and shows very slow biodegradation in vivo, which makes it a widely used coating material on metallic implants with an increased rate of bone integration [3, 4]. In some applications however, accelerated implant degradation with simultaneous bone in growth is necessary to substitute natural bone by a synthetic material. In vivo modifications of calcium phosphate ceramics result either from a cellular chemical dissolution/reprecipitation processes during interactions with biological fluids or from bioresorption due to cellular activity of osteoclasts. β-TCP shows an in vivo solubility 3–12 times faster than HA [5, 6]. Biphasic calcium phosphate (BCP), consisting of a mixture of HA and β-TCP, has been considered to be a well applicable bone substitute due to its tailorable degradability [2, 7]. It has been demonstrated that the bioactivity of BCP may be adapted to the local situation by manipulating the HA/β-TCP ratio [6]. However, it is difficult to produce a dense sintered ceramic body from precursor powders in the micronscale because the maximum sintering temperature of β-TCP is limited to temperatures below 1125°C [8, 9]. At higher temperatures the β to α phase transformation prevents TCP from further densification [10, 11]. Consequently, to obtain a sintered BCP material of high density at lower temperatures the particle size has to be reduced to the submicronscale to increase the rate of solid-state sintering [12].

M. de Campos · F. A. Müller (✉) · P. Greil
Department of Materials Science, University of Erlangen-Nuernberg, Martensstr. 5, Erlangen 91058, Germany
e-mail: Frank.Mueller@ww.uni-erlangen.de

M. de Campos · A. H. A. Bressiani · J. C. Bressiani
Instituto de Pesquisas Energéticas e Nucleares-IPEN, Av. Prof. Lineu Prestes 2242, Cidade Universitária, São Paulo, SP 05508-000, Brazil

M. de Campos
University of Mogi das Cruzes, Technological Research Center, Av. Dr. Cândido Xavier de Almeida Souza 200, Mogi das Cruzes, SP 08780-911, Brazil

The properties of the HA, β-TCP and BCP powders such as crystal morphology, crystallinity, thermal stability, and solubility have been shown to be strongly influenced by the route of fabrication [13]. β-TCP powders were prepared by solid-state reaction from amorphous calcium phosphate (ACP) or thermal decomposition of calcium-deficient apatite (CDHA) [2]. BCP powders were produced by mechanical mixing of HA with TCP powder or by calcinating CDHA with a Ca/P molar ratio of 1.5–1.65 above 700°C [14].

Ultrasound was shown to be a promising tool to facilitate the reactions to prepare homogeneous and fine ceramic powders from aqueous solution [15]. Ultrasonic irradiation enables the generation of high energy in a solution from acoustic cavitation resulting in the formation, growth, and implosive collapse of bubbles in liquids. Cavitation serves as a means of concentrating the diffuse energy of sound producing hydroxyl radicals $^{\cdot}OH$ and atomic hydrogen $H^{\cdot}$. The 'hot spot' theory [16] assets that cavitation bubbles act as local 'hot spots' that generate temperature exceeding 5000°C and pressures of more than 100 MPa during their compression or collapse phase. Treatment with ultrasonic irradiation is considered to enhance the chemical reactivity resulting in the acceleration of the heterogeneous reactions between liquid and solid reactants of inorganic, organic or organometallic reactions [17–19].

In this work the sonochemical effect was successfully applied to obtain calcium phosphate nanopowders by a wet chemical reaction of orthophosphoric acid and calcium hydroxide. Glycerol and D-glucose were added to control the HA/β-TCP ratio of the resulting BCP powders.

2 Experimental procedure

2.1 Powder synthesis

Synthesis of calcium phosphate powders by neutralization was achieved by drop wise addition (0.8 ml/min) of a 0.3 M aqueous solution of orthophosphoric acid (H_3PO_4) to 0.1 M aqueous suspension of calcium hydroxide ($Ca(OH)_2$) at room temperature. The reagents were mixed with a Ca/P molar ratio of 1.50. Two series of experiments were realized for a homogeneous mixing of the reagents during the drop wise addition of H_3PO_4 solution: in the first series, the suspension of $Ca(OH)_2$ was submitted under vigorous mechanical stirring and in the second series the suspension of $Ca(OH)_2$ was irradiated by ultrasound at a frequency of 50 KHz for 2 h in an ultrasonic trough. The $Ca(OH)_2$ suspensions were prepared in three different media: (N) in distilled water, (GLY) in a solution containing 40 vol% glycerol and (GLU) 40 wt% D-glucose, respectively. The slurries were aged for 24 h. The solutions were homogenized for 1 h before starting the drop wise addition of H_3PO_4. The pH was measured immediately after homogenization and after 1, 2 and 24 h, respectively. The slurries were filtrated and dried at 100°C for 24 h. The resulting powders were calcinated at 1000°C for 3 h. The experimental conditions used in this work to obtain different calcium phosphate powders are depicted in Fig. 1.

2.2 Characterization

The specific surface area of dried and calcinated powders were measured by gas adsorption in N_2 atmosphere (BET method, Micromeritics ASAP 2000, USA). Fourier transform infrared spectroscopy (FTIR, Nicolet Impact 420, USA) from the powders dispersed in spectroscopic grade KBr with a KBr:CaP weight ratio of 300:1, was applied to characterize absorption bands corresponding to functional groups in the calcinated products. Crystalline phases of the materials were analyzed by X-ray diffraction with monochromatic CuKα radiation (XRD, Siemens D500, D). A semi quantitative phase analysis software (Bruker AXS Diffract Plus, USA) was applied to quantify HA and β-TCP phases fractions by using the internal I/Icor standards of 1.25 and 1.06 for β-TCP (JCPDS 70–2065) and HA (JCPDS 73–0294), respectively. The temperature of HA to β-TCP phase transition was determined by high temperature X-ray diffraction (Siemens D500 equipped with a Anton Paar HTK 10 chamber, A). A heating rate of 10°C/min was applied from room temperature up to 1000°C, and the spectra were taken in the 2θ range between 19° and 39° every 200°C without holding time. The powder morphology was evaluated by scanning electron microscopy (SEM, FEI Quanta 200, CZ).

3 Results and discussion

Figure 2 shows the pH measured immediately after homogenization and after 1, 2 and 24 h, respectively. During synthesis the pH decreased to a final level of 6.5 in the case of GLY and GLU and 5.5 in the case of N, respectively. Ultrasound treatment did not change the pH at any time of synthesis.

HT-XRD revealed that apatite (HA) is the only crystalline phase in the reaction product powder N up to 600°C. Above 600°C the powder transformed into

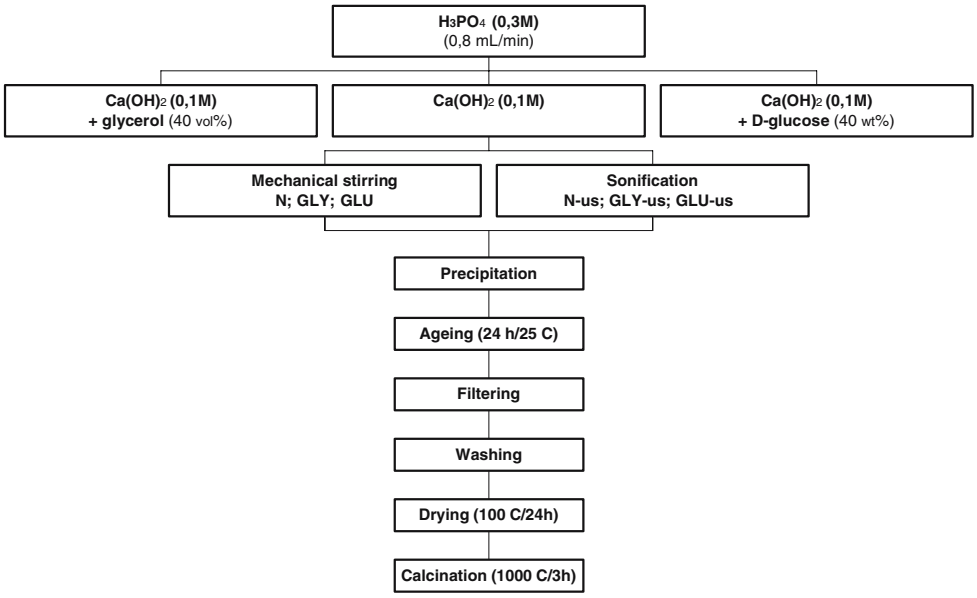

Fig. 1 Flow chart of powders synthesis. Mechanical stirring (N, GLU, and GLY); Sonication (N-us, GLU-us, and GLY-us)

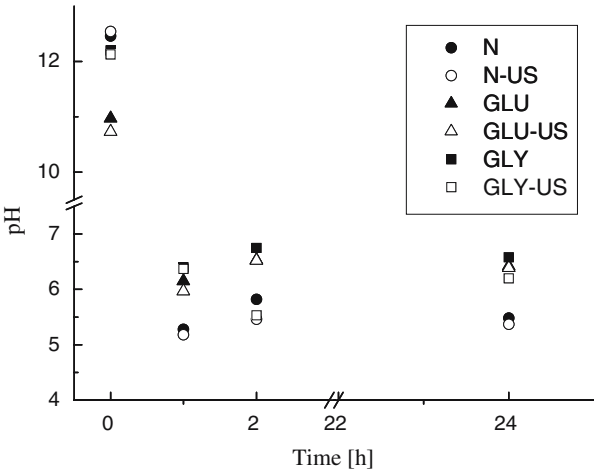

Fig. 2 Equilibrium pH of the medium during synthesis with ultrasound irradiation (us) and mechanical stirring as a function of time

β-TCP, Fig. 3a. The ultrasonicated powder N-us showed the same crystalline structure as HA between 100 and 600°C. Above 600°C, however, a transformation into biphasic calcium phosphate (BCP) was observed, Fig. 3b.

The powders N and N-us dried at 100°C for 24 h showed specific surface areas of 80 and 100 m^2/g, respectively. After calcination at 1000°C for 3 h the specific surface area decreased to 2 m^2/g in N and 4 m^2/g in N-us. While powder N, which was produced by rigorous mechanical stirring showed an average particle size of 300 nm after calcination the particle size in the ultrasonicated N-us decreased significantly down to 50 nm.

Powders N, GLU, and GLY, obtained by magnetic stirring and subsequently calcinated at 1000°C for 3 h consist of single-phase β-TCP (Fig. 4a). The powders N-us and GLY-us obtained in sonochemical condition are BCP consisting of HA and β-TCP of different ratios (Fig. 4b and Table 1).

The powders obtained by mechanical stirring only showed absorption bands characteristic for β-TCP. OH^{-1} bands at 633 and 3600 cm^{-1} characteristic for HA were not detected (Fig. 5a). In contrast the N-us and GLY-us powders, produced under sonification, clearly revealed these characteristic OH^- bands. The intensity of the absorption band in N-us is higher than in GLY-us, which indicates a higher concentration of OH^- groups in N-us. In GLU-us only bands characteristic of crystalline β-TCP phase were detected by FTIR. The absorptions of OH^- stretching at 3600 and 630 cm^{-1} that are characteristic for the HA phase were not detected (Fig. 5b).

Figure 6 shows SEM micrographs of GLU and GLY powders after calcination at 1000°C for 3 h. The average particle size of powder GLU and GLY was 800 and 700 nm, respectively. The average particle size of sonificated powders GLU-us and GLY-us were 750 and 600 nm, respectively.

The results of XRD analysis reveal the presence of β-TCP after calcination at 900°C. β-TCP cannot be directly obtained from aqueous systems but by solid-state reaction or thermal decomposition from ACP with a Ca/P molar ratio of 1.5 or CDHA above 700°C [2, 20]. The conditions of synthesis used in this work produced non-stoichiometric apatite, $Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$. For $0 < x < 1$ this apatite exhibits the

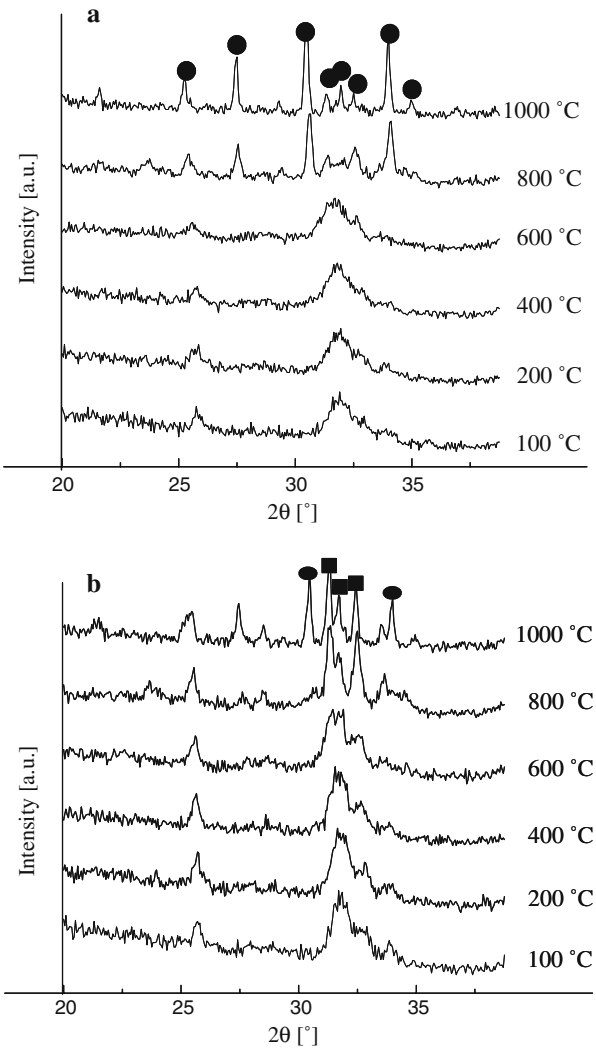

Fig. 3 HT–XRD patterns for the transformation of apatite produced by neutralization method (**a**) N; (**b**) N-us. (●) β-TCP and (■) HA crystalline phases

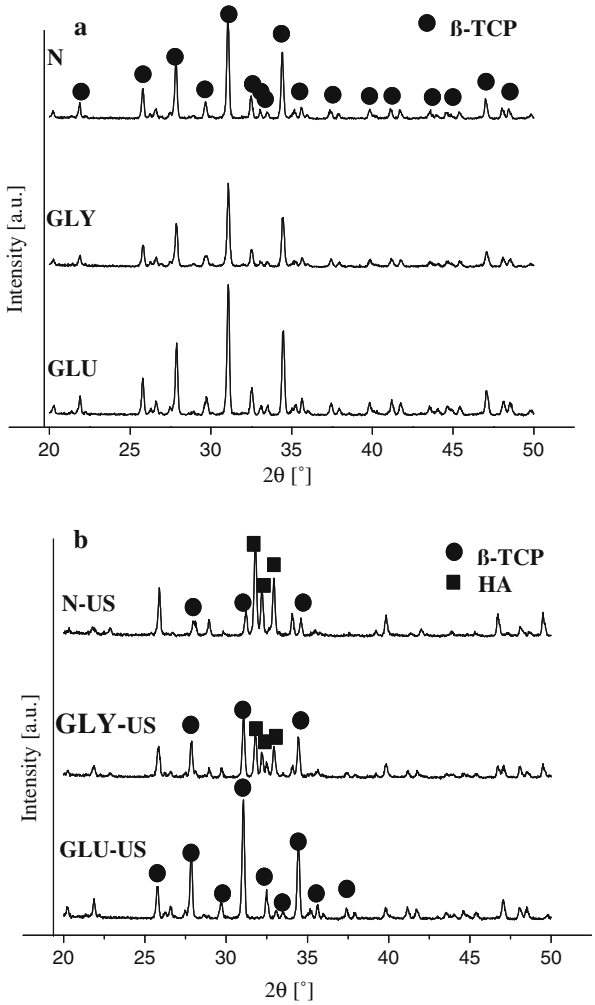

Fig. 4 XRD patterns of the powders obtained and calcinated at 1000°C for 3 h: (**a**) mechanical stirring and (**b**) sonification. (●) β-TCP and (■) HA crystalline phases

same crystal structure as stoichiometric HA. It is known, that HPO_4^{2-} groups in CDHA will be converted into $P_2O_7^{4-}$ ions ($2HPO_4^{2-} \rightarrow P_2O_7^{4-} + H_2O$) when heated to 650°C [8]. $P_2O_7^{4-}$ will then react with OH^- ($P_2O_7^{4-} + 2OH^- \rightarrow 2PO_4^{3-} + H_2O$). Thus, CDHA is supposed to decompose into β-TCP and HA according to [8]

$$Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x} \rightarrow 3x\ Ca_3(PO_4)_2 + (1-x)\ Ca_{10}(PO_4)_6(OH)_2 + H_2OM \quad (1)$$

Equation 1 is characterized by a slow reaction rate, starting at 650°C and proceeding even above 1000°C [8]. The concentration of $P_2O_7^{4-}$ might play an important role on the decomposition of CDHA. Since $P_2O_7^{4-}$ could be detected by FTIR even at temperatures up to 750°C, it seems that the rate of CDHA conversion into β-TCP and HA may depend on the reaction rate between $P_2O_7^{4-}$ and OH^- instead of HPO_4^{2-} condensation [2, 8]. In this work the composition corresponded to $x = 1$, so that after calcinating above 700–800°C CDHA in N powder transformed into β-TCP [9, 14, 20].

Table 1 XRD quantitative analyses for powders calcinated at 1000°C for 3 h

Experiment	Phase content [Vol %]	
	HA	β-TCP
N-us	80	20
GLY-us	45	55
GLU-us	–	100

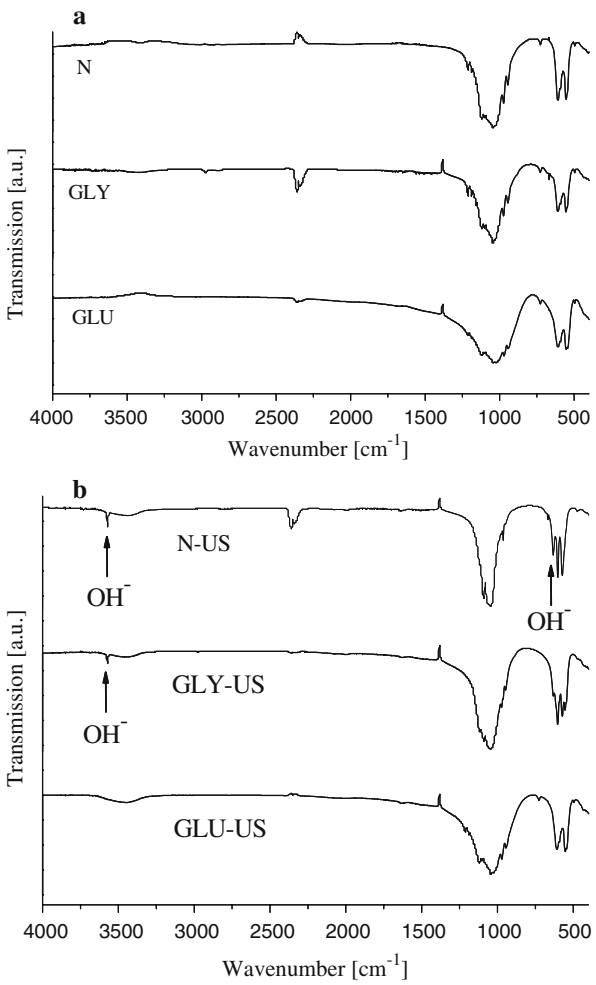

Fig. 5 FTIR absorption spectra of powders obtained and calcinated at 1000°C for 3 h: (**a**) mechanical stirring; (**b**) sonification

$$Ca_9(HPO_4)(PO_4)_5(OH) \rightarrow 3\ Ca_3(PO_4)_2 + H_2O \quad (2)$$

β-TCP powders obtained by neutralization after calcination at 1000°C exhibited thermal stability and single-phase composition with no traces of HA. The characteristic FTIR absorption bands of β-TCP were confirmed by 1096 and 1041 cm^{-1}, assigned to the components of the triply degenerate, antisymmetric P–O stretching mode. The bands at 604 and 560 cm^{-1} are assigned to components of the triply degenerate O–P–O bending mode. Adsorbed water bands were detected at 3400 cm^{-1}. The powders produced by neutralization method N consisted of homogeneous strongly spherical particles with an average grain size of 300 nm after calcination. The small particle size may be caused by the slow rate of water removal during drying and calcination treatment. Due to the submicron crystallite size extended agglomerate formation due to sintering occurred during annealing at 1000°C.

N-us experiment is the result most interesting for sonic effects by producing BCP crystalline phase. In N-us synthesis the condition was expected to yield β-TCP only, but HA was detected as a second phase in addition to β-TCP crystalline phase. Kim et al. [15] supposed that under sonochemical condition the nucleating phase in solution was dicalcium phosphate ($CaHPO_4$, DCPA) present in the medium with calcium carbonate ($CaCO_3$) producing oxi-calciumphosphate ($Ca_4(PO_4)_2O$),

$$2\ CaHPO_4 + 2\ CaCO_3 \rightarrow Ca_4(PO_4)_2O + 2\ CO_2 + H_2O \quad (3)$$

The $CaCO_3$ forms by reaction of Ca^{2+} with carbon dioxide (CO_2) from atmosphere dissolved in the solution [20]. Another explanation for the presence of $CaCO_3$ during synthesis can be related to a reaction between $Ca(OH)_2$ and CO_2. Calcination of $Ca_4(PO_4)_2O$ at 1000°C in ambient atmosphere e.g. in H_2O containing atmosphere finally originates the formation of HA [9]

$$3\ Ca_4(PO_4)_2O + H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 2\ CaO \quad (4)$$

It is believed that above a critical ultrasonic energy of 20 kHz $^{\cdot}OH$ radicals are formed by hemolytic dissociation [16, 21, 22, 23]. Since $^{\cdot}OH$ radicals are free-radical intermediate precursors for many hydroxide products generated by sonification HA is likely to be formed [9, 20]

$$3CaHPO_4 + 2\ Ca^{2+} + {}^{\bullet}OH \rightarrow Ca_5(PO_4)_3OH \quad (5)$$

Additionally very small amounts of CO_3 substituting HPO_4 in the CDHA lattice lead to an increase of the Ca/P molar ratio, e.g. $Ca_9(HPO_4)_{0.96}(PO_4)_5(CO_3)_{0.04}(OH)$ has a Ca/P molar ratio of 1.51. Annealing of these powders to temperatures above 750°C would lead to a composite consisting of 90% TCP and 10% HA. During ultrasonic irradiation a higher amount of $Ca(OH)_2$ may react with CO_2 to form CO_3^{2-} compared to magnetic stirring due to the better intermixing at higher energies. This carbonate can be incorporated into the crystal lattice and thus increase the Ca/P molar ratio. In case of GLU-US and GLY-US the Ca/P molar ratio is lower than that of N-us. The presence of complex organic molecules, specifically glucose, ethanol and proteins, has been shown to enhance carbon dioxide incorporation [24].

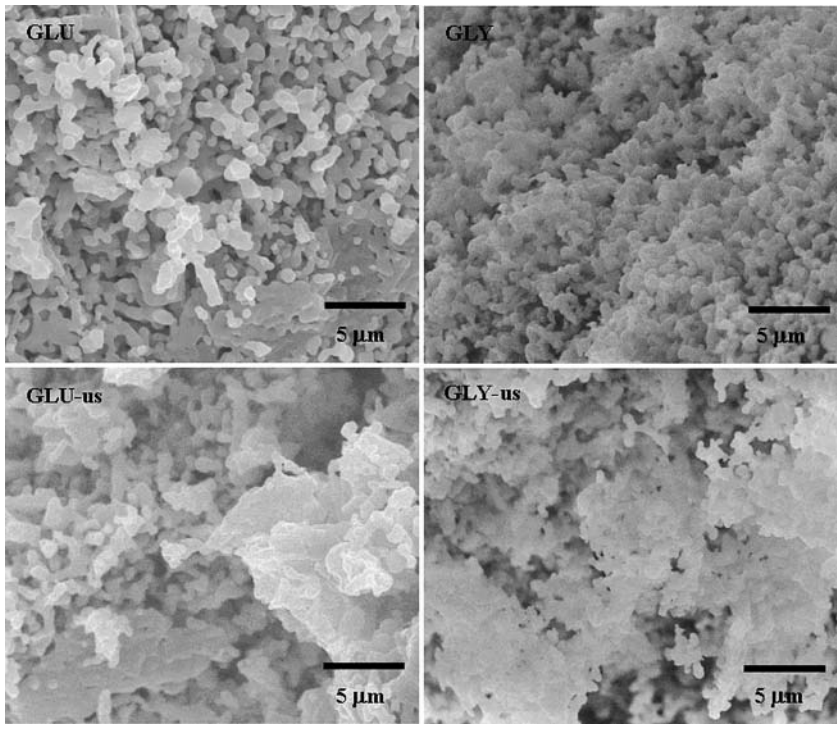

Fig. 6 SEM micrographs of powders calcination at 1000°C for 3 h. (GLU and GLY) prepared by mechanical stirring; (GLU-us and GLY-us) prepared by sonification

4 Conclusions

The neutralization method with a Ca/P molar ratio of 1.5 was effective to produce calcium deficient apatite powder that transforms into highly pure β-TCP between 600–800°C. The neutralization method associated with ultrasound irradiation was performed to produce BCP with higher concentration of HA crystalline phase. The association of neutralization method with ultrasound irradiation was effective to produce homogeneous nanopowders with 50 nm in N-us. Organic additives glycerol and D-glucose are effective tools to control the HA/β-TCP ratio of the resulting powders. The organic additives increase the particle size independently of mechanical stirring or sonification. The glycerol additive reduces the resulting HA content. D-glucose inhibits the formation of HA.

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