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Microwave-assisted Synthesis of Highly Crystalline Mesoporous Hydroxyapatite with a Rod-shaped Morphology

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Mesoporous hydroxyapatite (MHA) with a rod-shaped morphology has been successfully synthesized for the first time employing cetyltrimethylammonium bromide (CTAB) as a template and $CaCl_2$ and K_2HPO_4 as the precursors for hydroxyapatite under alkaline medium at the reaction temperature of 120 °C via microwave method. The obtained material exhibits a disordered mesoporous structure with a high crystallinity and highly uniform rod-like morphology with an average size of ca. 25 nm in width and 100 nm in length.

Hydroxyapatite (HA) is the prominent inorganic constituent in the human natural bone and dental system and is extensively employed as filling material for cavities and defects in human bone.[1–3] Therefore, synthesis of HA with excellent biocompatibility and bioactivity is of great interest among the researchers in the area of biomedical sciences and nano-biotechnology.[4,5] In addition to biocompatibility, the material should have a good resistance to corrosion, excellent mechanical strength, and chemical stability in physiological environment in the human body system.[6,7] Several methods have been developed for the synthesis of nonporous HA with high crystallinity.[4,5] However, poor physical parameters limit their performance in various applications including drug delivery, catalysis, and biomedical devices.

Since the emergence of mesoporous materials in the early 90s by mobile and Japanese research groups, much attention has been given to mesoporous materials due to their outstanding properties such as high surface areas, well-ordered and tunable pore sizes, and large pore volumes.[8–10] These properties are important for the materials to be employed as catalysts and adsorbents, and in separation, sensors, and drug delivery systems including the delivery of antitumor agents and antibodies for the treatment of osteomyelitis. These interesting features triggered active researchers to fabricate several mesoporous biomaterials such as HA, bioactive glasses, and bioceramics by soft-templating in which polymeric, ionic, or nonionic structure-directing agents are used as templates via hydrothermal approach.[11–13] However, this approach needs a long synthesis time and is not eco-friendly. These drawbacks can be overcome by the use of microwave irradiation combined with the soft-templating process which can offer volumetric and uniform heating and is eco-energy friendly and cost-effective.

In this communication, we report for the first time on the synthesis of mesoporous HA (MHA) with a high crystallinity employing microwave irradiation with fine temperature programming using CTAB as a structure-directing agent at the reaction temperature of 120 °C. The obtained MHA material possesses mesopores, a large pore volume, a high surface area, and uniform rod-like morphology with a high purity and crystallinity.

In a typical synthesis, K_2HPO_4 (1.37 g) and CTAB (1.92 g) were dissolved in 25 mL of deionized H_2O and kept stirring until a milky solution is formed. To this, a solution of $CaCl_2$ (1.11 g) in 15 mL of deionized H_2O was added dropwise and stirred at room temperature. The pH of the mixture was adjusted by adding 3.5 mL of 12 M NaOH and stirred for 1 h before transferring the whole mixture into a Teflon autoclave covered with a ceramic protector in a microwave oven (Milestone Ethos EX microwave lab station). The synthesis was carried out under microwave radiation with a fine temperature control at the reaction temperature of 120 °C with a ramp of 10 °C per minute and kept at the same temperature for the period of 8 h. The obtained reaction mixture was filtered, washed several times with H_2O, and dried at 100 °C in a hot air oven followed by calcination at 550 °C for 16 h. Finally, a white colored solid product was obtained that was denoted MHA-120.

Figure 1 shows the lower and wide-angle powder X-ray diffraction (XRD) patterns of MHA-120 prepared under microwave-assisted process. As can be seen in Figure 1, the sample shows a broad peak at a low angle, a characteristic of disordered

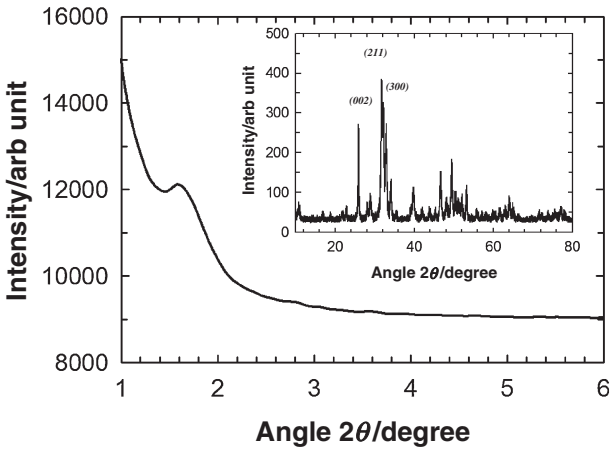

Figure 1. Low-angle powder XRD pattern for MHA-120. Inset: Wide-angle powder XRD pattern for the same sample.

mesoporous material, confirming that the sample contains mesoporous structure. The absence of higher order peaks and a broadness of the lower angle peak indicate that the mesopores of the materials are disordered. The reason for the formation of disordered mesopores in the materials is not known at present. However, we speculated that this is caused by the poor condensation of the P and Ca precursors on the surface of the cationic surfactant during the self-assembly process.

The sample was also characterized by wide-angle powder XRD measurement in order to find out the formation of pure HA along the wall structure of MHA-120, and the data are also displayed in Figure 1 (inset). The sample displays the typical diffraction peaks of HA including several high intense peaks that are located at 25.8, 31.8, and 32.9°. These peaks can be indexed to the (002), (211), and (300) reflections of the hexagonal $P6_3/m$ space group, respectively and are in good agreement with those of standard HA (JCPDC #9-432) and other data reported elsewhere.[14–16] The intensity of the peaks at higher angle and the absence of the impurity phases in the wide-angle XRD pattern further reveal that the sample is not only mesoporous but also highly pure and crystalline. It should be noted that the sample prepared by hydrothermal method under similar conditions exhibits no lower-angle peak but shows only higher-angle peaks with a low intensity, indicative of poor crystallinity with no features of mesoporosity (Figure 1S[17]). These results confirm the importance of the microwave-assisted process which offers the uniform and volumetric heating with the microwave irradiation and help the crosslinking of the precursors as well as the ionic interaction with the structure-directing agent that promotes the quick formation of the mesoporous structure with a high crystallinity.

Figure 2 shows the morphology of MHA-120 which displays cylindrical nanorod particles with an average size of 25 nm in width and 100 nm in length. The formation of highly uniform particles with a nanosize can be attributed to the influence of microwave radiation which can offer uniform and volumetric heating and enhance the condensation of the inorganic precursors. As can be seen in Figures 2A and 2B, all the particles are very small and interconnected, unlike the MCM-41 or SBA-15 particles which are always in the size range of 1 to 5 µm. The mesopores are also clearly seen in the particles throughout the samples, and the interconnection also generated large mesopores which is critical for catalytic or drug delivery applications. It is also interesting to note that the particle size of the sample prepared by the hydrothermal method is much larger than that of the sample prepared by the microwave-assisted process (Figure 2S[17]). In addition, the shape of the particles is not regular and they are agglomerated. This is a typical problem for hydrothermal synthesis as it does not supply uniform heating which is critical for the nucleation of the particles in a perfect shape and size. These results further confirm the role of the microwave radiation for the synthesis of HA with a small particle size with uniform size and mesoporosity.

The textural parameters of the MHA-120 were measured using a nitrogen adsorption isotherm. Figure 3 shows the nitrogen adsorption–desorption isotherm of MHA-120. The sample displays type IV isotherm with a broad capillary condensation step at a higher relative pressure, characteristic of mesoporous material with disordered mesoporous structure. It should be noted that a steep rise in the amount of nitrogen adsorption is observed for the sample at a higher relative pressure. This is mainly attributed to the presence of complementary porosity with large mesopores which are originated from the voids generated by the small mesoporous nanoparticles. It is interesting to note that the sample also exhibits bimodal distribution centered at 2.5 and 3.7 nm that are created by the decomposition of the organic structure-directing agent from the HA matrix (Figure 3 inset) during the calcination. As can be seen in Figure 3, the pore size distribution is quite broad, revealing the presence of disordered pores. This is in agreement with the data obtained from the powder X-ray measurements. This is due to the fact that some of the pores are damaged during calcination. The BJH pore size distribution also confirmed that the sample indeed contains a lot of complementary mesopores with a size in the range of 12 to 14 nm. Similar pores are also seen in the HRSEM images of the same sample. The specific surface area amounts to 60.5 $m^2 g^{-1}$ whereas the specific pore volume and the BJH desorption pore diameter are 0.16 $cm^3 g^{-1}$

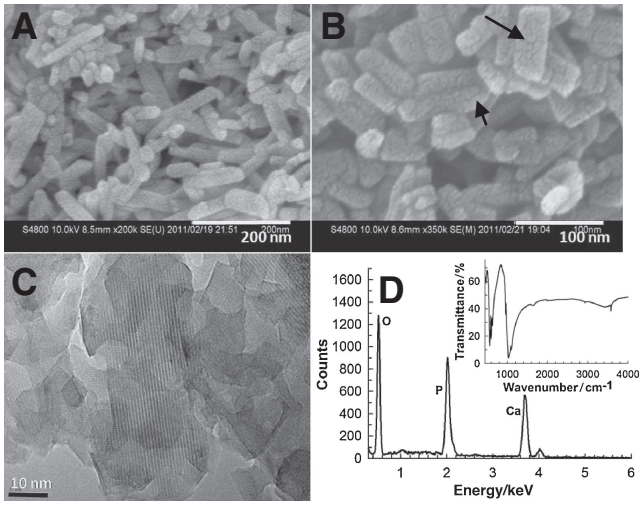

Figure 2. HRSEM (A,B), HRTEM (C) images and EDX (D) pattern of MHA-120. Inset: FT-IR spectrum of MHA-120.

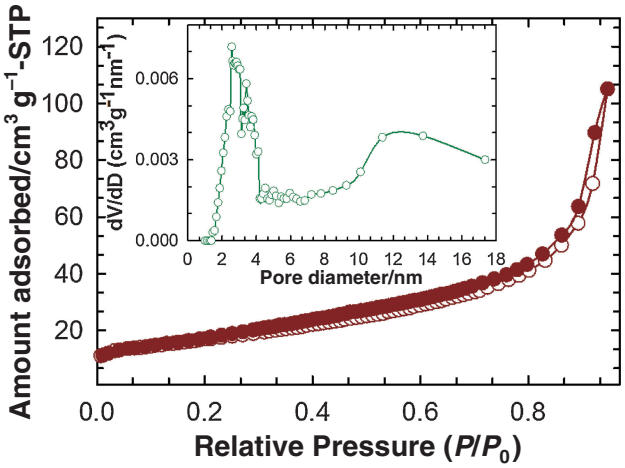

Figure 3. Nitrogen adsorption–desorption isotherm of MHA-120 and (inset) the corresponding BJH desorption pore size distribution.

and 3.73 nm (2.5 nm), respectively. On the other hand, the specific surface area, the specific pore volume, and the pore diameter of the sample prepared under hydrothermal treatment are 25.43 $m^2 g^{-1}$, 0.13 $cm^3 g^{-1}$, and 2.97 nm, respectively (Figure 3S[17]). These values are much lower than those of the sample prepared by microwave method.

The elemental composition of the material was analyzed by EDX. It has been found that the sample contains only Ca, P, and O which rules out the possibility of having impure phases in the sample. The absence of peaks other than Ca, P, and O in the EDX pattern confirms the purity of the mesoporous HA. The weight percentage of the Ca, P, and O is calculated to be 17, 13, and 70%, respectively. The Figure 2C shows the HRTEM image of MHA-120. The image displays the mesoporosity and several lattice fringes within the nanorod confirming each particle is composed of mesoporous structure with a high crystallinity. The shaded fringes observed in the HRTEM images represent the boundaries of mesopores formed within the rod-like particle, and the size of the pores calculated from the HRTEM image is similar to that obtained from the nitrogen adsorption measurement. These pores are aligned lengthwise within the nanorods and originated upon the removal of CTAB template during calcination.

The FT-IR spectrum of MHA-120 is shown in Figure 2D (inset). The sample exhibits phosphate absorption bands located at 1102, 1042, 962, 600, 562, and 467 cm^{-1}, and hydroxide absorption band at about 3567 cm^{-1}, which are all characteristics of a typical FT-IR spectrum of pure and highly crystalline HA.[14–16] The peaks at 600 and 562 cm^{-1} are ascribed to the triply degenerated bending vibration of the O–P–O bond (δPO_4^{3-}) whereas the peaks at 1102, 1042, and 962 cm^{-1} are attributed to the symmetric stretching vibration induced by the O–P–O bond in νPO_4^{3-}. In addition, there are several other peaks which are centered at 3568 and 3680 cm^{-1} which can be assigned to the vibration mode of OH groups whereas the band at 1703 cm^{-1} is assigned to the deformation vibration mode of moisture in air. These results indicate that the sample contains a lot of free OH and PO_4^{3-} groups and is indeed pure HA.

In conclusion, we strikingly demonstrate for the first time on the preparation of mesoporous hydroxyapatite via microwave-assisted process using cationic surfactant as a template. The prepared material is highly crystalline and exhibited highly uniform rod-like particles with a nanosize. The purity of the prepared sample was confirmed by wide-angle powder XRD, FT-IR, and EDX. The microwave radiation with a controlled temperature programming helped the formation of highly ordered mesoporous structure with a high crystallinity and an excellent morphology. We strongly believe that this novel approach can be extended for the fabrication of HA with different mesoporous structure and morphology using different structure-directing agents at various temperatures, which could further be used in various applications including drug delivery, catalysis, and biomedical devices.

References and Notes

1 A. S. Posner, *Physiol. Rev.* **1969**, *49*, 760.
2 D. M. Dabbs, I. A. Aksay, *Annu. Rev. Phys. Chem.* **2000**, *51*, 601.
3 S. V. Dorozhkin, M. Epple, *Angew. Chem., Int. Ed.* **2002**, *41*, 3130.
4 G. Grimandi, P. Weiss, F. Millot, G. Daculsi, *J. Biomed. Mater. Res.* **1998**, *39*, 660.
5 A. Uchida, N. Araki, Y. Shinto, H. Yoshikawa, E. Kurisaki, K. Ono, *J. Bone Jt. Surg., Br. Vol.* **1990**, *72B*, 298.
6 M. Vallet-Regí, *C. R. Chim.* **2010**, *13*, 174.
7 N. F. Fahim, M. F. Morks, T. Sekino, *Electrochim. Acta* **2009**, *54*, 3255.
8 T. Yanagisawa, T. Shimizu, K. Kuroda, C. Kato, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 988.
9 D. Zhao, Q. Huo, J. Feng, B. F. Chmelka, G. D. Stucky, *J. Am. Chem. Soc.* **1998**, *120*, 6024.
10 J. S. Beck, J. C. Vartuli, W. J. Roth, M. E. Leonowicz, C. T. Kresge, K. D. Schmitt, C. T.-W. Chu, D. H. Olson, E. W. Sheppard, S. B. McCullen, J. B. Higgins, J. L. Schlenker, *J. Am. Chem. Soc.* **1992**, *114*, 10834.
11 J. Yao, W. Tjandra, Y. Z. Chen, K. C. Tam, J. Ma, B. Soh, *J. Mater. Chem.* **2003**, *13*, 3053.
12 S. M. Schmidt, J. McDonald, E. T. Pineda, A. M. Verwilst, Y. Chen, R. Josephs, A. E. Ostafin, *Microporous Mesoporous Mater.* **2006**, *94*, 330.
13 Y. F. Zhao, J. Ma, *Microporous Mesoporous Mater.* **2005**, *87*, 110.
14 S. Zhang, Y. Wang, K. Wei, X. Liu, J. Chen, X. Wang, *Mater. Lett.* **2007**, *61*, 1341.
15 Z. Xia, L. Liao, S. Zhao, *Mater. Res. Bull.* **2009**, *44*, 1626.
16 H. Wang, L. Zhai, Y. Li, T. Shi, *Mater. Res. Bull.* **2008**, *43*, 1607.
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