

Microwave-Assisted Fabrication of Poly (L-lactic acid)/ Hydroxyapatite Composites as Artificial Bone Materials

Yuko Takeoka^{1*#}, Kaori Arai¹, Masahiro Yoshizawa-Fujita¹, Mamoru Aizawa², and Masahiro Rikukawa^{1#}

¹Department of Materials and Life Sciences, Sophia University, 7-1 Kioi-cho, Chiyoda-ku, Tokyo 102-8554, Japan

²Department of Chemistry, Meiji University, 1-1-1 Higashi-mita, Tama-ku, Kanagawa 214-8571, Japan

#Equally Contributed

Commentary

Received date: 22/10/2016

Accepted date: 22/11/2016

Published date: 28/11/2016

*For Correspondence

Yuko Takeoka, Department of Chemistry, Meiji University, 1-1-1 Higashi-mita, Tama-ku, Kanagawa 214-8571, Japan

E-mail: y-tabuch@sophia.ac.jp

Keywords: Hydroxyapatite; Poly (L-lactic acid); Bulk polymerization; Ring-opening polymerization; L-lactide

ABSTRACT

The composites of poly (L-lactic acid) (PLLA) and hydroxyapatite (HAp) were easily fabricated by ring-opening polymerization of L-lactide in porous HAp disks under microwave irradiation without any additional catalyst. Ring-opening polymerization of L-lactide in the porous HAp proceeded efficiently at relatively lower reaction temperatures and for shorter times. By use of the MW methods, PLLA/HAp composites with excellent mechanical properties, which were higher than those of pristine HAp were obtained.

COMMENTARY

Hydroxyapatite ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$; HAp) has been currently used in hard tissue engineering due to its excellent biocompatibility and osteoconductivity [1-3]. However, the brittleness and relatively low mechanical properties of HAp limit its usefulness in bone implants. Thus, much attention has been focused on the hybridization of HAp with suitable polymers in order to obtain high mechanical properties enough to match those of human bones [4,5]. Among them, composites of HAp and poly (L-lactic acid) (PLLA) or PLLA based copolymers have been extensively studied due to the favorable characteristics of PLLA [6]. Most of the reported PLLA/HAp composites were fabricated from hybridization of HAp with pre-synthesized PLLA using various catalysts such as organometallic compounds and lipases [7-10]. The toxicity of organometallic compounds and the poor reproducibility of lipase catalysts are also problems that hinder obtaining biomaterials desired for applications.

We have previously succeeded in preparing PLLA/HAp hybrids by ring-opening bulk polymerization of L-lactide in porous HAp without any catalysts [11]. Because OH groups on porous HAp surfaces can act as activation sites for the ring-opening polymerization of L-lactide, PLLA can directly hybridize with HAp by our method. Although the mechanical properties were superior to those of pristine HAp, the polymerization needed 7 days at 130°C, and the hybridizing processes have not been simplified and optimized yet. On the other hand, there has been growing interest in microwave (MW)-assisted polymerization from the view-point of green chemistry. Although numerous MW-assisted polymerizations have been investigated [12,13], there are few reports relating to the polymerization in inorganic matrices using MW heating, which is expected to occur as localized reactions. Herein, we attempted to fabricate PLLA/HAp composites by MW-assisted ring-opening polymerization of L-lactide in porous HAp without additional catalysts.

Porous HAp pellets with approximately 40% porosity were obtained by sintering fibrous HAp pellets at 1200°C for 5 h [14]. Each porous HAp pellet was immersed in melted L-lactide at 130°C, and the mixture was freeze-thaw degassed three times in order to fill up the pores with L-lactide, as shown in **Figure 1a**. The MW-assisted ring-opening polymerization of L-lactide in porous

HAp was carried out in a CEM Discover monomodal MW oven with a frequency of 2.45 GHz and a maximum output power of 150 W. The porous HAp pellets filled with L-lactide were subjected to MW irradiation for 2 or 8 h at various temperatures (130, 150, 170, 190, or 210 °C). Obtained PLLA/HAp composites were characterized by ¹H NMR, FT-IR, GPC, SEM, and TG-DTA. For ¹H NMR and GPC measurements, PLLA in porous HAp was extracted from ground composites by dissolving in chloroform and tetrahydrofuran, respectively. The filling rate of PLLA in porous HAp, the weight percentage of PLLA filled in the pores of HAp, was determined from the weight loss after the thermal decomposition of PLLA around 200 °C observed by TG-DTA of PLLA/HAp composites. Here, filling rates of PLLA are equivalent to yields of PLLA, and a filling rate of 100% means that the pores are fully covered with PLLA. The mechanical properties of composites were estimated by three-point bending tests. The polymerization of L-lactide in porous HAp under conventional heating was also conducted in oil for comparison.

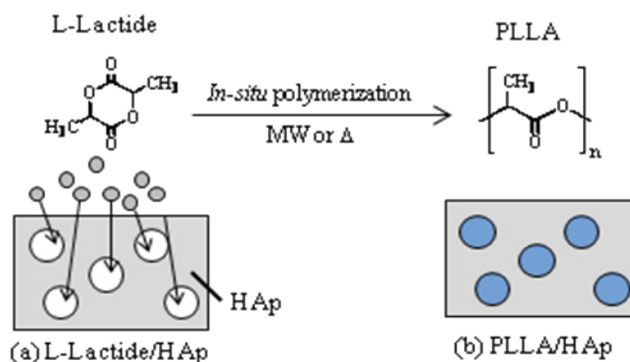


Figure 1. Scheme of *in-situ* polymerization of L-lactide in a porous HAp pellet using MW-irradiation.

Table 1 shows the molecular weights and filling rates of PLLA in the PLLA/HAp composites fabricated by MW or conventional heating for 2 or 8 h at various temperatures. Ring-opening polymerization was successfully achieved in porous HAp for both MW and conventional heating methods by selecting certain reaction conditions. In the ¹H NMR spectra, the PLLA extracted from obtained PLLA/HAp composites showed a chemical shift at 5.17 and 1.57 ppm, while L-lactide showed two chemical shifts at 5.02 and 1.67 ppm. In FT-IR spectra of the PLLA, the peaks assigned to C-H and C=O stretching vibrations are observed at 3000 and 2950 cm⁻¹, and at 1755 cm⁻¹. These results indicate that HAp functions as the catalyst for the ring-opening polymerization of L-lactide. For 2 h at 130 or 150 °C, L-lactide was polymerized by MW nor conventional heating. When the reaction time was extended to 8 h, PLLA was also obtained by the conventional method; however, the M_w was clearly lower than that prepared by MW heating. This result demonstrates that MW accelerates the polymerization of L-lactide. In the case of MW heating, the M_w of PLLA increased with increasing the reaction temperature from 130 to 170 °C and decreased beyond 190 °C. On the contrary, the M_w of PLLA prepared by conventional heating increased with the reaction temperature up to 210 °C. The filling rate of PLLA determined by TG-DTA also depended on the reaction temperature and the heating method. The filling rate for MW heating increased with increasing the reaction temperature from 130 to 170 °C, but decreased beyond 190 °C. The maximum filling rate of PLLA reached to 21% wt at 170 °C. In the case of the conventional heating, the filling rate gradually increased and reached the maximum value at 210 °C. These results suggest that the MW heating at higher temperatures causes decomposition of PLLA, resulting in low molecular weights and filling rates at 190 and 210 °C. Under conventional heating, heat comes from outside through materials, and it takes much time to attain thermal equilibrium. Dipole rotation and ion conduction transfer thermal energy from MW to substances, leading to instantaneous localized superheating regardless of thermal conductivity [15,16].

Table 1. Characteristics of PLLA/HAp composites fabricated by MW or conventional heating methods at various conditions. a) Determined by GPC, b) Determined by TG-DTA. c) MW: Microwave heating, d) Δ: Conventional heating.

Temp/ °C	Time/h	M_w^a		M_w/M_n^a		Filling rate of PLLAb/wt%	
		MW ^c	Δ ^d	MW	Δ	MW	D
130	2	700	-	1.05	-	7.3	0.8
130	8	14,400	2,900	1.51	1.84	18.8	11.6
150	2	7,100	-	4.33	-	15.1	7.3
170	2	15,900	12,200	1.41	2.45	21	14.9
190	2	7,700	17,200	1.37	1.56	16.5	16.9
210	2	12,300	16,200	1.47	1.68	10.2	18.2

Ritter et al. reported that solid particles are rapidly heated under MW irradiation leading to specific heating effects of solid [17]. Similarly, the observed faster polymerization under MW irradiation can be ascribed to specific heating of the hydroxyapatite matrix. As a result, high filling rates of PLLA in porous HAp were obtained under MW irradiation at relatively lower reaction temperatures. **Figure 2** shows the cross-sectional SEM images of the PLLA/HAp composites prepared by MW irradiation for 2 h. After MW-assisted polymerization, the pores in pristine HAp pellets (a) were gradually filled-up with PLLA, and the smoothest surface was observed at 170 °C. The surfaces of composites became rough for the sample prepared at 210 °C. The mechanical properties of PLLA/HAp composites are strongly dependent on the molecular weights and on the filling rates of PLLA. **Figure 3** shows the bending strength and fracture toughness of PLLA/HAp composites fabricated by MW (a) or conventional heating (b)

methods. The bending strength and fracture toughness were higher than those of pristine HAp and were strongly dependent on the reaction temperature, and the maximum values (62.0 MPa and 1.0 MPa m^{1/2}) were obtained at 170°C for the MW heating. For conventional heating, the mechanical properties of composites increased with the reaction temperature. It was found that the MW-assisted polymerization modified the mechanical properties of PLLA/HAp composites more effectively over the temperature range examined in this study compared with the conventional method.

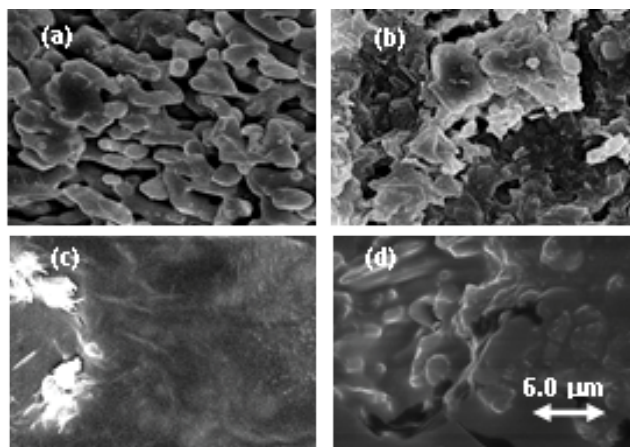


Figure 2. Cross-sectional SEM images of porous HAp (a) and PLLA/HAp composites fabricated by MW heating for 2 h at 130°C (b), 170°C (c), and 210°C (d).

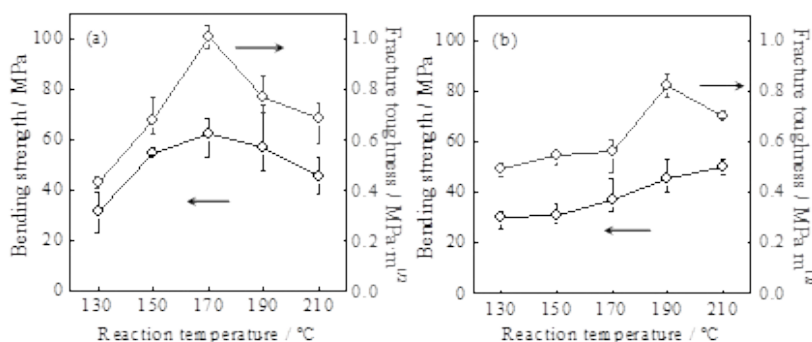


Figure 3. Mechanical properties of PLLA/HAp composites fabricated by MW (a) or conventional methods (b) at various reaction temperatures.

REFERENCES

1. Van Blitterswijk CA, et al. The biocompatibility of hydroxyapatite ceramic: a study of retrieved human middle ear plants. *J Biomed Mater Res.* 1990;24:433-453.
2. Suchanek W and Yoshimura M. Processing and properties of hydroxyapatite-based biomaterials for use as hard tissue replacement implants. *J Mater Res.* 1998;13:94-117.
3. Abidi S and Murtaza Q. Synthesis and characterization of nano-hydroxyapatite powder using wet chemical precipitation method. *J Mater Sci Technol.* 2014;30:307-31.
4. Sugiyama N, et al. Fabrication of Artificial Bone Materials using Bioceramics and Polymers having phosphoric acid groups. *Arch BioCeramics Res.* 2006;6:315-318.
5. Chu K, et al. Preparation and Characterization of Nano-Hydroxyapatite/Poly(ε-caprolactone)-Poly(ethylene glycol)-Poly(ε-caprolactone) Composite Fibers for Tissue Engineering. *J Phys Chem.* 2010;114:18372-18378.
6. Takeoka Y, et al. In-situ preparation of poly (L-lactic acid-co-glycolic acid)/hydroxyapatite composites as artificial bone materials. *Polymer J.* 2015;47:164-170.
7. Albertsson AC and Varma KI. Recent Developments in Ring Opening Polymerization of Lactones for Biomedical Applications. *Biomacromolecules.* 2003;4:1466-1686.
8. Dechy-Cabaret O, et al. Controlled Ring-Opening Polymerization of Lactide and Glycolide. *Chem Rev.* 2004;104:6147-6176.
9. Yan W, et al. In vitro investigation of nanohydroxyapatite/poly(L-lactic acid) spindle composites used for bone tissue engineering. *J Mater Sci Mater Med.* 2016;27:130.
10. Huang J, et al. Evaluation of the novel three-dimensional porous poly(L-lactic acid)/nanohydroxyapatite composite scaffold. *Bio-med Mater Eng.* 2015;26:S197-205.
11. Sugiyama N, et al. Ring-opening polymerization of L-lactide in porous hydroxyapatite. *Chem Lett.* 2007;36:12:1476-1477.

12. Kempe K, et al. Microwave-assisted polymerizations: Recent status and future perspectives. *Macromolecules*. 2011;44:15;5825-5842.
13. Adlington K, et al. Mechanistic investigation into the accelerated synthesis of methacrylate oligomers via the application of catalytic chain transfer polymerization and selective microwave heating. *Macromolecules*. 2013;46:10:3922-3930.
14. Aizawa M, et al. Ultrastructural observation of single-crystal apatite fibers. *Biomaterials*. 2005;26:3427-3433.
15. Bogdal D, et al. Microwave-assisted synthesis, cross-linking, and processing of polymeric materials. *Adv Polym Sci*. 2003;163:193-263.
16. Lidstrom P, et al. Microwave assisted synthesis. *Tetrahedron*. 2001;57:9225-9283.
17. Klink M, et al. Microwave-assisted synthesis of channel-containing polymeric materials. *e-Polymers*. 2005:069.