Hindawi Publishing Corporation
Journal of Nanomaterials
Volume 2013, Article ID 515741, 10 pages
http://dx.doi.org/10.1155/2013/515741

Research Article

Investigation of the *In Vitro* Degradation of a Novel Polylactide/Nanohydroxyapatite Composite for Artificial Bone

Jianghong Huang,[1,2] Jianyi Xiong,[1,2] Jianquan Liu,[1,2] Weimin Zhu,[1,2] and Daping Wang[1,2]

[1] *State Key Department of Orthopedics, The Second People's Hospital of Shenzhen, Shenzhen, Guangdong 518035, China*
[2] *Key Laboratory of Tissue Engineering, Shenzhen, Guangdong 518035, China*

Correspondence should be addressed to Daping Wang; dapingwang1972@163.com

Received 22 April 2013; Revised 7 August 2013; Accepted 20 September 2013

Academic Editor: Anchal Srivastava

Copyright © 2013 Jianghong Huang et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

We prepared the poly-L-lactic acid (PLLA)/nanohydroxyapatite (n-HA) composite and investigated the *in vitro* degradation of pure PLLA material and PLLA/n-HA composites in order to identify a suitable and ideal artificial bone tissue repair material. The water uptake, weight loss, and changes in the PBS pH value and in the mechanical properties of material were measured during the processes that PLLA and PLLA/n-HA biological composites were degraded in PBS. We also performed electron microscopic scanning of the material fracture surface and observed the microscopic morphologies of materials during the degradation process. We found that the degradation rate of the PLLA/n-HA material was slower than the PLLA material, and there was a little degradation of the PLLA/n-HA material at early stages. The PLLA/n-HA material also maintained the initial mechanical strength better than the pure PLLA material. The PLLA/n-HA material is thus a better material for artificial bone than the pure PLLA material.

1. Introduction

The quest for an ideal artificial bone tissue repair material is a hot topic in the bone tissue engineering research field. Polylactic acid is biomedical synthetic material that is most commonly used in bone tissue repair, and it has good biocompatibility, degradability, and processing controllability. However, polylactic acid still has defects such as poor hydrophilicity, generation of acidic degradation products, and insufficient retention time for its mechanical strength [1–3]. Nanohydroxyapatite (n-HA) is a type of bone graft substitute material that has similar physicochemical and biological properties as the human skeleton and can be absorbed by the body and gradually transformed into autologous bone component. n-HA is strongly hydrophilic and is a mildly basic material. Moreover, it can be degraded via the solution-mediated process (dissolved in physiological solutions) and the cell-mediated process (phagocytosis). The calcium and phosphate ions released after degradation participate in the local bone tissue calcification or enter the calcium and phosphorus pools of the body, and they can be subsequently utilized or discharged physiologically. However, as a scaffold material for tissue engineering, the mechanic characteristics of n-HA are weak and cannot match the mechanical strength of human bone. In addition, the degradation of the n-HA is slow [4–6]. PLLA/n-HA composites can be generated using the poly-L-lactic acid (PLLA) as a base material and n-HA particles as reinforcement substances, thus fully utilizing the advantages of the two materials as biomedical engineering materials [7, 8]. The paper focused on the *in vitro* degradation characteristics of pure PLLA and PLLA/n-HA composites in order to provide the ideal bone tissue repair material for bone tissue engineering.

2. Materials and Methods

2.1. Preparation of Composites

2.1.1. Preparation of PLLA. L-lactide (LLA) with high purity (99.95%) was prepared by a combination of distillation technology and washing-recrystallization with lactic acid. PLLA was synthesized via ring-opening polymerization using prepared L-lactide at 140°C for 24 hours. The solution spinning method was used to obtain sheets of the PLLA material (Figure 1).

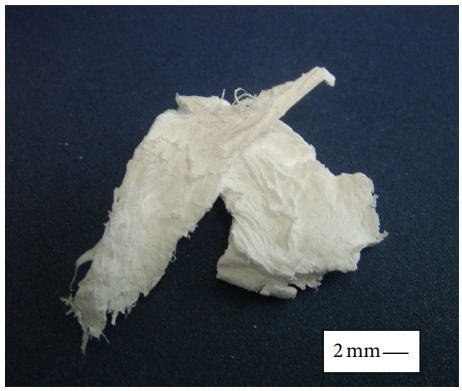


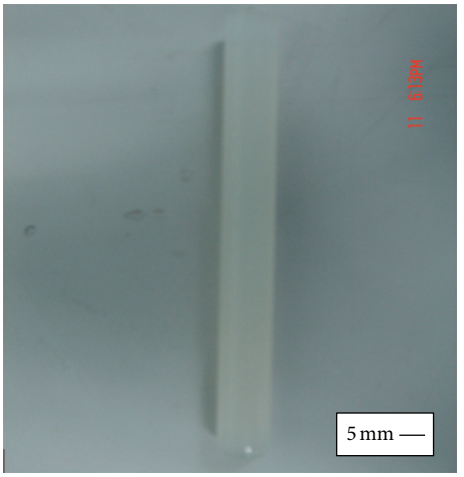
Figure 1: Sheets of the PLLA material.

Figure 2: n-HA powder.

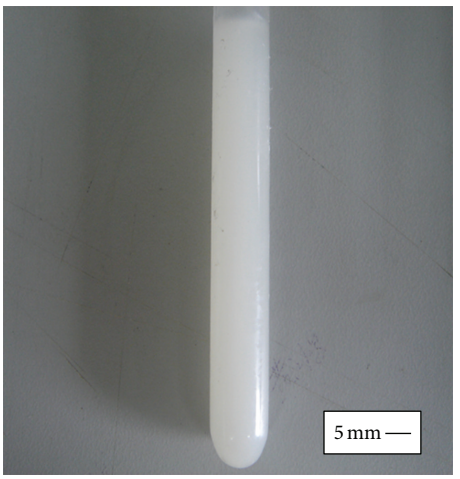
2.1.2. Preparation of n-HA Powder. n-HA was generated from $Ca(NO_3)_2$ and NH_4PO_3 via sol flocculation. During the chemosynthesis of n-HA, aqua ammonia was used to adjust the PH value to 8~13. With dispersant agent and appropriate agitator, the n-HA deposit was separated out of the solution. With series of processes including scouring, filtering, drying, sinter-roasting, and milling, the n-HA powder has been prepared (Figure 2).

2.1.3. Preparation of PLLA/n-HA Artificial Bone. The PLLA/n-HA composite was jointly developed by the Tissue Engineering Laboratory of the Second People's Hospital of Shenzhen and the Powder Metallurgy Research Institute of Central South University. The PLLA/n-HA composite was prepared via melt blending method, which includes 2 steps. Firstly, the PLLA was heated into viscous flow state at 160°C. Then n-HA was mixed with PLLA. The PLLA/n-HA artificial bone material was processed into cylinders (with a length of 10 mm, diameter of 5 mm, and height of 5 mm) (Figure 3) and preserved in vacuum packaging.

2.2. Preparation of the In Vitro Degradation Medium, Phosphate Buffered Saline (PBS). The preparation of PBS solution was carried out according to the following steps:



(a)



(b)

Figure 3: Sample strips after being mold-pressed: (a) PLLA; (b) PLLA/n-HA.

(1) prepare 1/15 mol/L KH_2PO_4, that is, 9.078 g KH_2PO_4 per liter of water;

(2) prepare 1/15 mol/L $Na_2HPO_4{\cdot}2H_2O$, that is, 11.876 g $Na_2HPO_4{\cdot}2H_2O$ per liter of water;

(3) mix 18.2% (volume fraction) of the KH_2PO_4 solution and 81.8% of the $Na_2HPO_4{\cdot}2H_2O$ solution;

(4) adjust the pH of the PBS solution to be about 7.4 by using acid/base solution.

2.3. In Vitro Degradation Experiments. We used the compression molding method to prepare strips of PLLA and PLLA/n-HA composite materials (10 mm × 5 mm × 5 mm with a n-HA content of 20 wt%) (Figure 3). The prepared biological material was cleaned with deionized water and placed in a 40°C vacuum oven. After being sufficiently dried, the sample stripes were weighed, and the weight was recorded as m_0. The weighted and dry strips were divided into two categories based on the material composition (PLLA and PLLA/n-HA). Each category of material was further divided into 10 groups

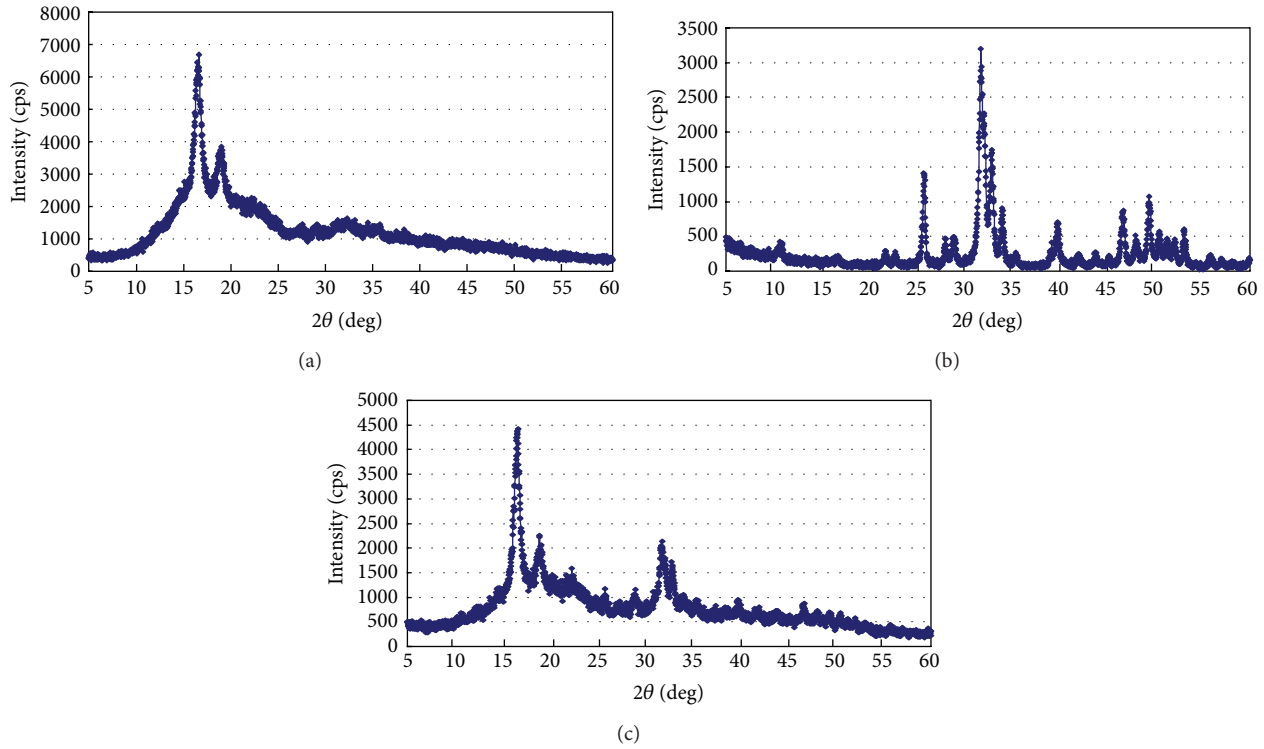


Figure 4: (a) XRD curves of PLLA; (b) XRD curves of HA powder; (c) XRD curves of PLLA/n-HA composite.

based on the degradation time (2 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, 12 weeks, 14 weeks, 16 weeks, 18 weeks, and 20 weeks), and each group contained three samples.

All the samples were placed in clean glass bottles containing PBS, which were then sealed and placed in an electric thermostatic shaker. The shaker temperature was 37 ± 0.5°C, and the vibration speed was 100 rpm.

2.4. Evaluation Indicators

2.4.1. Assessing the PLLA, n-HA Powder, and PLLA/n-HA Composite Using X-Ray Diffraction (XRD). The crystal structure of PLLA, n-HA, and PLLA/n-HA composite was measured by X-ray diffraction system (D/max 2550, Japan). The scanning range is from 0 to 80 degree and the scanning speed is 8.0°/min. Data were acquired using a $CuK_{\alpha 1}$ source at 40 kV and 300 mA.

2.4.2. Assessing the PLLA/n-HA Composite Using Transmission Electron Microscope (TEM). The PLLA/n-HA composite was cut into blocks measuring about 1 mm wide, 1 mm long, and 1 mm thick. The blocks and n-HA powder were post-fixed in 1% osmium tetroxide for 2 h at 4°C. They were rinsed in distilled water for several times, dehydrated in graded series (20~100%) of ethanol and then in propylene oxide, infiltrated with Epon 812, and finally polymerized in pure Epon 812 for 48 h at 65°C. Ultrathin sections were cut on an ultramicrotome using diamond knives, collected on copper grids, and stained with 4% uranyl acetate and Reynolds, lead citrate. Sections were observed under a transmission electron microscope.

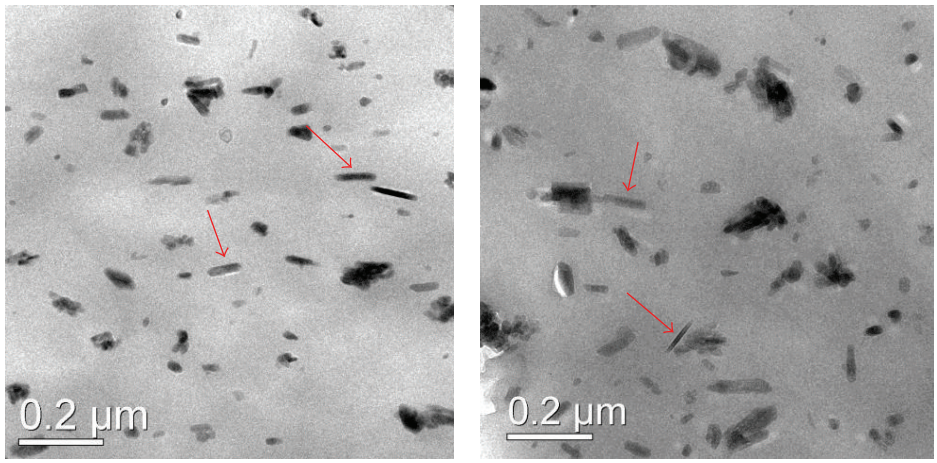
2.4.3. Calculation of the Biological Material Water Uptake Ratio and Weight Loss Ratio. One group was taken for each type of material at various degradation time points (2 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, 12 weeks, 14 weeks, 16 weeks, 18 weeks, and 20 weeks). The sample weight was measured in accordance with the following steps.

The weight of the sample before degradation is called the initial weight (m_0). After a certain period of degradation, the samples were removed, blotted gently with paper to remove the water on the surface, and weighed to get the wet weight (m_1). The degraded experimental samples were vacuum-dried for 24 h at 40°C, and the residual weight (m_2) was then obtained. The sample water uptake ratio (m_A) and the weight loss ratio (m_L) were calculated as follows [9]:

$$m_A\,(\%) = \frac{100\,(m_1 - m_2)}{m_2} \tag{1}$$

$$m_L\,(\%) = \frac{100\,(m_0 - m_2)}{m_0}. \tag{2}$$

2.4.4. pH of the PBS Solution. A digital pH meter (pHS-25 pH meter with digital display, Shanghai REX Instrument Factory) was used to measure the pH value of the PBS solution at different degradation stages.



(a) (b)

Figure 5: (a) TEM micrograph of the n-HA powder; (b) TEM micrograph of PLLA/n-HA composites.

2.4.5. Measurement of Flexural Strength and Modulus. The flexural strength and modulus of each dried sample strip were measured using the three-point bending method on a universal testing machine (Instron-1121, UK).

2.4.6. Scanning Electron Microscopy (SEM) Morphological Features of the Fracture Surface. After measuring the flexural strength, the fracture surface of the sample strip was sprayed with gold, and SEM (field emission scanning electron microscope, Tescan, Czech) was used to observe the changes in the bending fracture microscopic morphology of samples in the degradation process.

3. Results

3.1. XRD Analysis of the PLLA, n-HA Powder, and PLLA/n-HA Composite. Figure 4 shows the XRD curves of PLLA, n-HA, and PLLA/n-HA composite. From Figure 4(a), we can see that PLLA shows its most intense diffraction peaks at 2θ values of 16.6 and 18.96, which is in agreement with 2013 international center for diffraction data (PDF no. 54-1917). Figure 4(b) shows the XRD curve of n-HA. n-HA shows its most intense diffraction peaks at 2θ values of 31.74, 32.12, and 32.9, which coincides with 2013 international center for diffraction data (PDF no. 9-432). Figure 4(c) shows XRD curve of PLLA/n-HA composite. PLLA/n-HA composite shows its most intense diffraction peaks at 2θ values of 16.6 and 18.96, which is in agreement with the PLLA data in PDF no. 54-1917. In addition, PLLA/n-HA shows its most intense diffraction peaks at 2θ values of 31.74, 32.12, and 32.9, which coincides with the n-HA data in PDF no. 9-432.

3.2. TEM Analysis of the n-HA Morphology in the PLLA/n-HA Composite. Results of TEM showed that n-HA presents needle-like structure, which is similar to human bone components (Figure 5(a)). In addition, n-HA was distributed evenly in n-HA/PLLA composite (Figure 5(b)).

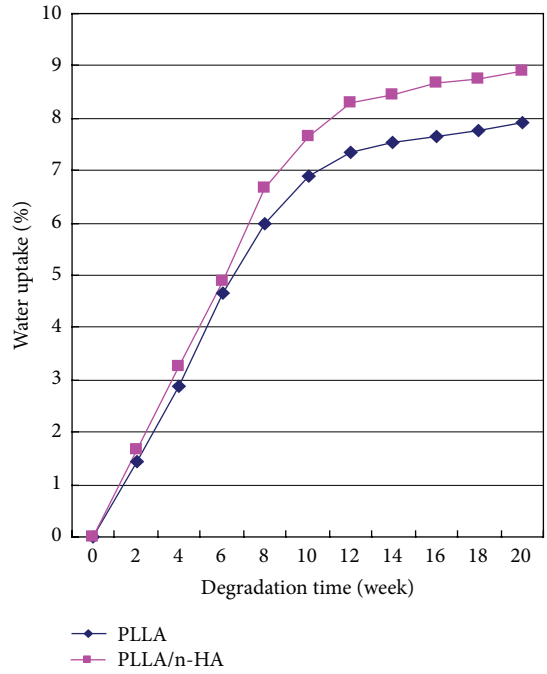


Figure 6: Variation of water uptake of biomaterials with degradation time.

3.3. Changes in the Material Water Uptake Ratio and Weight Loss Ratio. Figure 6 showed that with the extension of the degradation time, the water uptake ratios of the two samples were gradually increased, but the rate of increase in the water uptake ratio became slower. During the entire degradation period, the water uptake ratios of the PLLA/n-HA samples were significantly higher than those of the PLLA samples.

As seen from the curves in Figure 7, the weight loss ratios of the PLLA and PLLA/n-HA materials were relatively low before the 6th week of degradation, and they were 1.038% and 0.698%, respectively. After 6 weeks of degradation, with the rapid increase of the water uptake ratio, the weight loss ratio

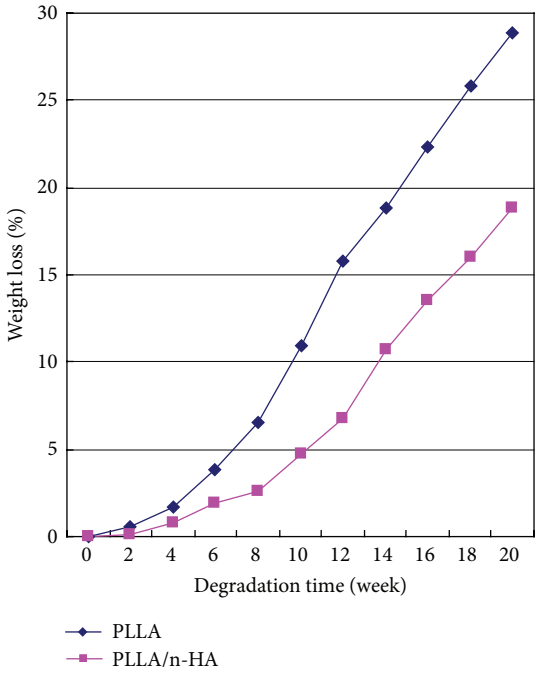


Figure 7: Change of sample weight loss as a function of degradation time.

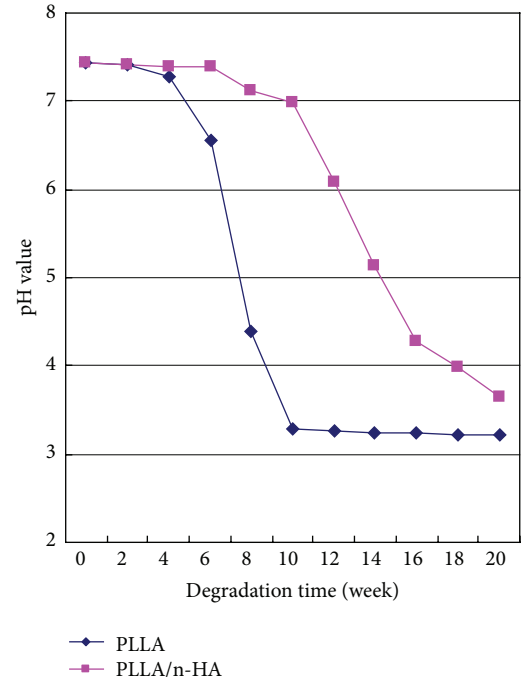


Figure 8: Effect of degradation time on pH value of PBS.

of the pure PLLA material was also increased sharply and showed a linear upward trend with the degradation time. In contrast, the weight loss ratio of PLLA/n-HA composite did not increase with the degradation time until the degradation time reached 10 weeks, and the extent of increase was smaller than the pure PLLA material.

3.4. pH Changes of the PBS Solution. Figure 8 showed the curve that the pH value of the PBS solution changed with the degradation time. It demonstrated that prior to 4 weeks of degradation, the decrease in the pH value was small for all PBS solution. After 4 weeks, the pH value of the PBS solutions containing the PLLA samples began to show the phenomenon of accelerated decrease. This phenomenon became even more significant after the pH value dropped below 6. At the 10th week, the pH value was reduced to about 3. After 10 weeks, the decrease in the pH value became slow and basically stopped decreasing. Before the degradation time reached six weeks, the pH value of the PBS solution containing the PLLA/n-HA sample almost showed no changes. And between 6~12 weeks, the pH value of the buffer was slightly decreased with the extension of degradation time. After 12 weeks, the decrease in the buffer pH was intensified. The pH value at 16 weeks was about 4.2, and after 16 weeks, the decrease in the pH value started to slow down.

3.5. Changes in the Material Mechanical Properties in the Degradation Process. Figures 9 and 10, respectively, demonstrate the curves by which the bending strength and bending modulus of each sample of biological material changes with the degradation time in the process of degradation. As seen from Figure 9, in the early stages of degradation (0–6 weeks), the strengths of all materials showed little reduction. The strength of the pure PLLA material decreased abruptly between 6~12 weeks, and the decrease of strength was alleviated after 12 weeks. The strength of the PLLA/n-HA composite started to show significant decrease after eight weeks and lasted until the end of the degradation experiment. The curves in Figure 10 that depicted the changes of material flexural over the degradation time revealed similar changes as the curves in Figure 9.

3.6. Analysis of the Fracture Morphology of Biological Materials in the Degradation Process. Figure 11 shows the SEM images of the morphologies of the bending fracture of the pure PLLA biological material in the degradation process (×8000). Figure 12 shows the SEM images of the morphologies of the bending fracture of the PLLA/n-HA composite biomaterial in the degradation process (×8000).

Before degradation, the fractures of each biological material sample showed dense structures. After 4 weeks of degradation, the fracture surface of the pure PLLA material did not show significant changes, and the fracture surface was smooth without cracks (Figure 11(b)). After 6 weeks of degradation, a small amount of cracks could be observed in the middle of the fracture, although the fracture edge still showed compact structures (Figure 11(c)). It might be related to that fact that the polymeric material first underwent autocatalytic degradation. After 8 weeks of degradation, the cracks extended to peripheral areas and a large number of the small holes could be observed in the fracture surface (Figure 11(d)), which might be caused by the degradation of the interior of the material. This suggested that the PLLA

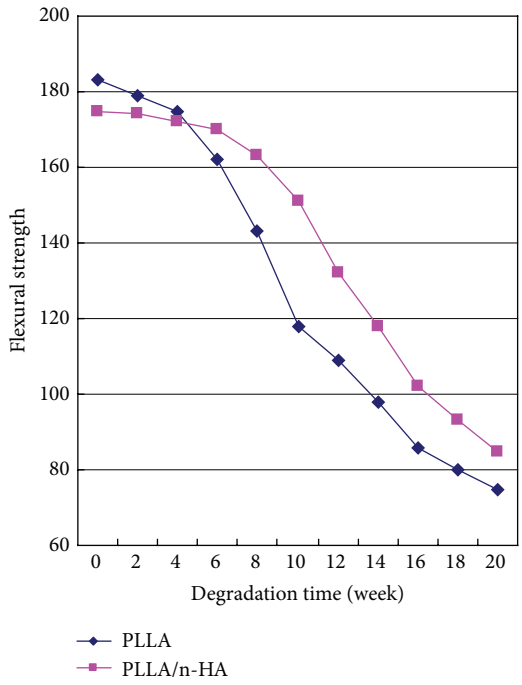


Figure 9: Variations of bending strength of biomaterials with degradation time.

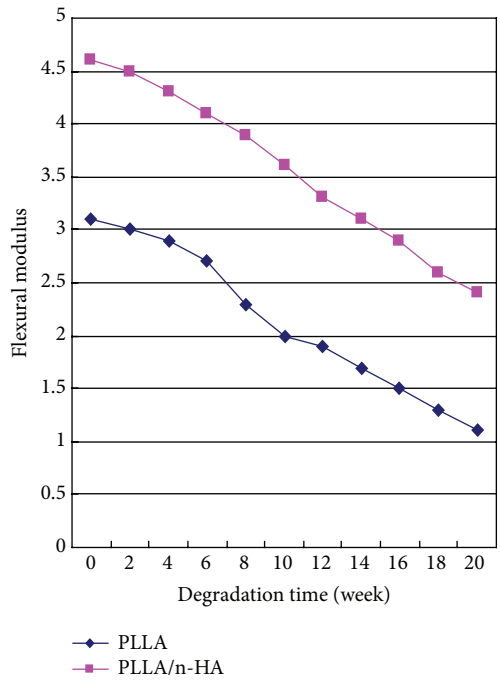


Figure 10: Effects of the degradation time on the bending modulus of biomaterials.

materials had undergone partial degradation. After 12 weeks of degradation, the cracks of the material expanded to form slits, providing passage for the water molecules, thus accelerating the degradation of the PLLA materials. Many holes generated by the degradation process could be observed in the material fracture surface (Figure 11(e)). When the degradation time was further extended, the slits continued to expand, and 18 weeks later, the PLLA material had collapsed, and the material was destructed as a whole (Figure 11(f)).

Figure 12 shows the SEM images of the fracture surfaces of the PLLA/n-HA material. Compared with the morphology of the fracture surface of the pure PLLA material, the fracture surface of the PLLA/n-HA material showed dense structures with only a small amount of cracks prior to 10 weeks of degradation. After 14 weeks, the fracture surface showed a large number of mesh-like holes, accompanied by the generation of large cracks. In addition, exposed HA particles could also be clearly seen, suggesting the occurrence of the degradation and absorption of the PLLA/n-HA materials. With the extension of the degradation time, the PLLA/n-HA material underwent accelerated degradation, and criss-cross cracks appeared on the fracture surface, although exposed HA particles were not found. It suggested that with the progress of the degradation, HA particles were already dissolved in the PBS solution. After 20 weeks, the fracture surface presented more depression, widened and deepened cracks, and loose structures. Large amounts of degradation fragments could not be decomposed in a timely manner and were thus filled into the cracks in the interior of the materials. The composite materials showed significant degradation.

4. Discussion

The biggest advantage of biomedical polymeric materials is its biodegradability and bioresorbabilty. Biocomposite materials not only keep the features of the component materials, but also can acquire new properties that individual component materials do not have. Therefore, the comprehensive properties of the composite materials are better than those of the original component materials [10]. Biodegradability refers to the process that the polymeric chains of solid-state polymeric materials or devices are broken by the complex physiological environment *in vivo*, leading to the generation of large quantities of small molecule fragments and the complete destruction of the polymeric materials or devices. Bioresorbabilty refers to the process that solid-state polymeric materials or devices are biodegraded *in vivo* and that the resulting degradation products are absorbed or excreted via metabolism.

Besides the general characteristics such as good biocompatibility and the lack of antigenicity, rejection reaction, teratogenicity, carcinogenicity, and toxicity and side effects, biodegradable polymeric composites that can be used as an artificial bone tissue repair materials also need to have other features as follows: (1) moderate degradation rate, that is, the degradation rate of the artificial bone tissue repair material must match the rate of bone healing, (2) appropriate biomechanical properties, that is, the biomechanical properties of the implanted artificial bone tissue repair material have to match the mechanical properties of the implant site [11].

Hydroxyapatite (HA), whose chemical formula is $Ca_{10}(PO_4)_6(OH)_2$, is the major inorganic component of human bone. Sixty percent of HA in bone is needle-like and less than 100 nm in size [12]. TEM results demonstrated

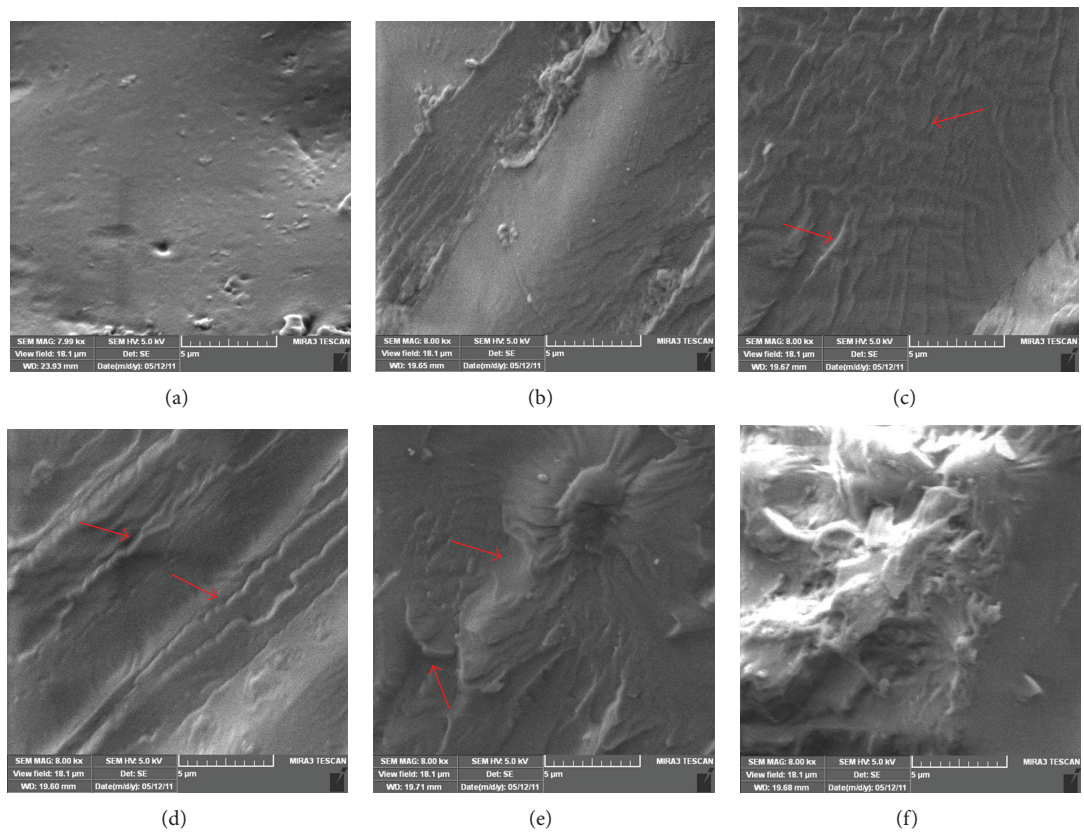


Figure 11: SEM images of fracture surfaces of degraded PLLA biomaterials (×8000) ((a)-0 w; (b)-4 w; (c)-6 w; (d)-8 w; (e)-12 w; (f)-18 w). (a) and (b) smooth fracture surface without substantial cracks; (c) Surfaces showed a small amount of cracks as red arrows indicated, and the fracture edges still had compact structure; (d) the cracks in material surface extended to the peripheral area, and a large number of small holes appeared in the fracture surface as red arrows indicated; (e) the cracks of the material expanded to form slits, and the fracture surface was covered with holes as red arrows indicated; (f) materials had collapsed, and the material was destructed as a whole.

that the n-HA in this study was 50~200 nm in size and showed needle-like appearance, which was close to that of human bone. Results of XRD showed that PLLA and n-HA manufactured in this study are of good degree of crystallization. Furthermore, both PLLA and n-HA keep the integrated structure of crystal in the PLLA/n-HA composite.

Several methods have been used to prepare the PLLA/n-HA composite, such as coating method [13], solvent casting/particulate leaching [14], supercritical CO_2 foaming [15], solution blending method [16], and melt blending method. Organic solvent is often used in the preparation of composites via the above methods except melt blending method. Besides its unfavorable effect on grafted tissues, organic solvent may inactivate biological growth factors and negatively influence cell adherence and proliferation. In order to avoid the negative effect of organic solvent, melt blending method was used in this study.

Varila et al. compared *in vitro* the reactivity of the composites in simulated body fluid, Tris-buffered solution, and phosphate buffered saline (PBS). They concluded that degradation of the composites containing the bioactive glasses was faster in PBS than in the two other solutions [17]. Furthermore, PBS was often used as *in vitro* degradation system in other studies [9, 18–26]. In consistent with previous studies, PLLA/n-HA was put into PBS to observe the water uptake ratio, weight loss ratio, and other biological properties.

There are multiple interfaces between the respective components of the PLLA/n-HA composite material. The interfaces exposed in the medium present the "suction effect" due to the capillary action. As a result, water molecules are prone to diffuse along the interfaces and enter into the inside of the material. Therefore, the water uptake ratio of the PLLA/n-HA composite material is higher than that of the non-interfaced and closely combined pure PLLA material. In addition, the hydrophilic n-HA particles are more conducive for absorption and lead to the increase in the water uptake ratio of the composite material.

As compared to the pure polymeric materials, composite materials have a slower degradation rate. The specific reasons might include the following aspects. First, micropores among the pure PLLA material molecules provide channels for the penetration of water molecules, so that water molecules can easily get access to the interior of the material and accelerate the material degradation. Second, as to the PLLA/n-HA composite material, although the water uptake of the composite material is greater than that of the pure PLLA material, the basic ions released by HA into the PBS buffer can neutralize the acidic substances generated in the PLLA

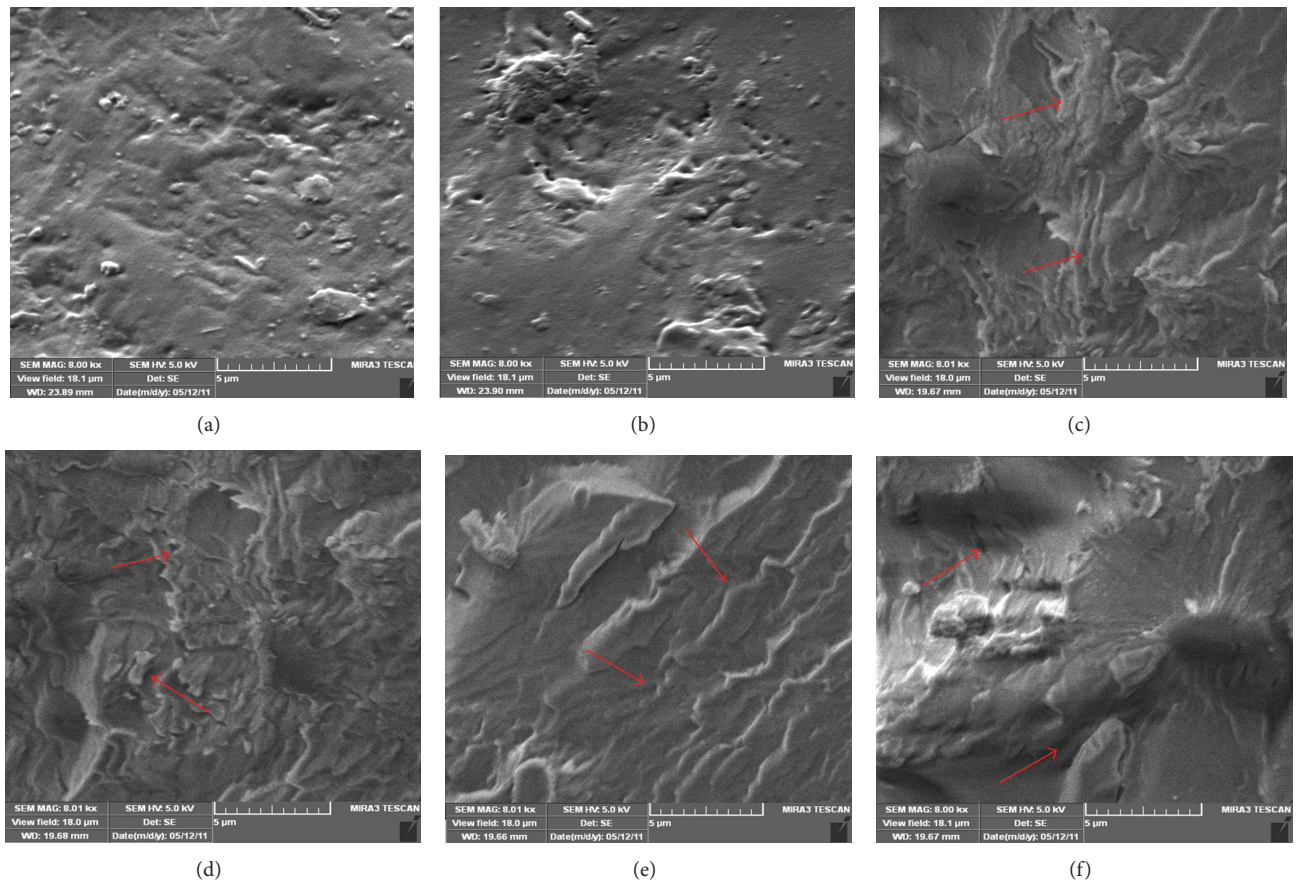


Figure 12: SEM images of fracture surfaces of degraded PLLA/n-HA biomaterials (×8000) ((a)-0 w; (b)-6 w; (c)-10 w; (d)-14 w; (e)-18 w; (f)-20 w). (a) and (b) No significant changes on the fracture surface, which had no substantial cracks; (c) The fracture showed compact structure with only a small number of cracks as red arrows indicated; (d) Fracture surface showed a large number of mesh-like holes, accompanied by the generation of large cracks as red arrows indicated; (e) Criss-cross cracks on the fracture surface as red arrows indicated; (f) Fracture surface showed more depression, widened and deepened cracks as red arrows indicated, loose structure, and significant degradation.

degradation process, slowing the autocatalytically accelerated degradation of the polymeric material in acidic environment and inhibiting the degradation of the polymeric material. As compared to the pure PLLA biological material, the degradation rate of the PLLA/n-HA composite material in the initial stages of degradation is slower, thus delaying the degradation of the PLLA/n-HA composite. Therefore, the weight loss of the composite material is smaller than that of the pure polymer materials in the same period.

The incorporation of n-HA particles successfully reduces the acidity caused by the acidic products of polylactic acid degradation generated in the early phase of degradation. It thus can reduce or avoid the aseptic inflammation caused by the acidic substance, and it can improve the biocompatibility of the polymeric biomaterial. In addition, in the early phase of degradation, due to the slowing down of the degradation rate, the PLLA/n-HA composite material can maintain high initial mechanical strength and provide sufficient supporting effect for new bone tissue. In the late phase of degradation, the degradation of the PLLA/n-HA composite material accelerates, which is conducive to new bone tissue ingrowth in order to achieve good therapeutic effect. Therefore, the prepared polymeric PLLA/n-HA composite material has wide application prospect and practical value.

The ions released from the dissolution of n-HA in the PLLA/n-HA composite material are basic and can neutralize the acidic degradable substances generated during the PLLA degradation process. The autocatalytic degradation effect of acids on the polymeric material can be alleviated, thus slowing down the degradation rate. In the early phases of degradation, the composite material can still maintain relatively high strength. After 6 weeks of degradation, the decrease rate in the composite material flexural strength and modulus accelerated. After 10 weeks of degradation, the composite material had a flexural strength of 151 MPa, equivalent to that of the fresh adult bone (160 Mpa), and it could still provide a good supporting role for the newly generated bone tissue. Thus, the PLLA/n-HA composite material prepared by the addition of n-HA can maintain relatively high flexural strength and modulus in the early and middle phases of degradation. After 16 weeks of degradation, it was still able to maintain a flexural strength of 100 MPa, higher than the minimum flexural strength of the human bones (96 Mpa), thus providing a reliable support for the regeneration of new

bone tissue. In addition, the improvement in the acidic environment can reduce or avoid the occurrence of inflammatory reaction caused by the acidic degradation products. In the late phase of degradation, due to the degradation of the polymeric substance in the composite material, the amount of composite material is gradually reduced, leaving space for new generated bone tissue.

Changes in the material fracture surface morphology revealed that the degradation rate of the PLLA/n-HA material was slower than that of the PLLA material. Most importantly, before the degradation time reached 14 weeks, there was little degradation of the PLLA/n-HA material, and its mechanical strength loss was also small. It thus is able to maintain a high mechanical strength and provide a good supporting role for new bone tissue. This is mainly related to the following reasons. (1) The addition of n-HA particles neutralizes the acidic products generated during the degradation process of polymeric materials and slows down the PLLA autocatalytic degradation. (2) It also effectively reduces the inflammatory response caused by the acidic products and improves the biocompatibility of the composite materials.

The *in vitro* degradation characteristics of our PLLA/n-HA composite material as mentioned above might be beneficial for its application in bone tissue repair. However, since the body's osteogenic process is very complicated, investigation of the physicochemical properties of *in vitro* degradation alone cannot confirm its value in application. It is thus necessary to carry out a series of follow-up experiments focusing on the *in vivo* bone tissue repair and construction, coupling with the bone growth factors and co-culture with osteoblasts *in vitro*.

Acknowledgments

The authors acknowledge the Shenzhen Key Laboratory Enhancement Projects (CXB201104220049A), Shenzhen-Hong Kong Innovation Circle Project Fund (JSE201007190007A), Shenzhen Second People's Hospital Seeding Plan for providing the funding source for this work.

References

[1] C. Zhang, Q. Feng, T. Zhang, J. Chen, C. Lu, and H. Wu, "*In vitro* biologic evaluation on nano-hydroxyapatite/poly (L-lactic acid) biocomposites fabricated using in-situ growth method," *Sheng Wu Yi Xue Gong Cheng Xue Za Zhi*, vol. 29, no. 2, pp. 307–310, 2012.

[2] H. K. Moon, Y. S. Choi, J.-K. Lee, C.-S. Ha, W.-K. Lee, and J. A. Gardella Jr., "Miscibility and hydrolytic behavior of poly(trimethylene carbonate) and poly(Ll-lactide) and their blends in monolayers at the air/water interface," *Langmuir*, vol. 25, no. 8, pp. 4478–4483, 2009.

[3] X. Niu, Q. Feng, M. Wang, X. Guo, and Q. Zheng, "Porous nano-HA/collagen/PLLA scaffold containing chitosan microspheres for controlled delivery of synthetic peptide derived from BMP-2," *Journal of Controlled Release*, vol. 134, no. 2, pp. 111–117, 2009.

[4] S. Ishii, J. Tamura, T. Furukawa et al., "Long-term study of high-strength hydroxyapatite/poly(L-lactide) composite rods for the internal fixation of bone fractures: a 2-4-year follow-up study in rabbits," *Journal of Biomedical Materials Research B*, vol. 66, no. 2, pp. 539–547, 2003.

[5] L. MacArini, P. Milillo, A. Mocci, R. Vinci, and G. C. Ettorre, "Poly-L-lactic acid—hydroxyapatite (PLLA-HA) bioabsorbable interference screws for tibial graft fixation in anterior cruciate ligament (ACL) reconstruction surgery: MR evaluation of osteointegration and degradation features," *Radiologia Medica*, vol. 113, no. 8, pp. 1185–1197, 2008.

[6] M. Ngiam, S. Liao, A. J. Patil et al., "Fabrication of mineralized polymeric nanofibrous composites for bone graft materials," *Tissue Engineering A*, vol. 15, no. 3, pp. 535–546, 2009.

[7] F. Peng, X. Yu, and M. Wei, "*In vitro* cell performance on hydroxyapatite particles/poly(L-lactic acid) nanofibrous scaffolds with an excellent particle along nanofiber orientation," *Acta Biomaterialia*, vol. 7, no. 6, pp. 2585–2592, 2011.

[8] F. Peng, J. R. Olson, M. T. Shaw, and M. Wei, "Influence of pretreatment on the surface characteristics of PLLA fibers and subsequent hydroxyapatite coating," *Journal of Biomedical Materials Research B*, vol. 88, no. 1, pp. 220–229, 2009.

[9] H. Zhao, L. Ma, Y. Gong, C. Gao, and J. Shen, "A polylactide/fibrin gel composite scaffold for cartilage tissue engineering: fabrication and an *in vitro* evaluation," *Journal of Materials Science*, vol. 20, no. 1, pp. 135–143, 2009.

[10] D. D. Wright-Charlesworth, J. A. King, D. M. Miller, and C. H. Lim, "*In vitro* flexural properties of hydroxyapatite and self-reinforced poly(L-lactic acid)," *Journal of Biomedical Materials Research A*, vol. 78, no. 3, pp. 541–549, 2006.

[11] G. Sui, X. Yang, F. Mei et al., "Poly-L-lactic acid/hydroxyapatite hybrid membrane for bone tissue regeneration," *Journal of Biomedical Materials Research A*, vol. 82, no. 2, pp. 445–454, 2007.

[12] M. A. Malik, D. A. Puleo, R. Bizios, and R. H. Doremus, "Osteoblasts on hydroxyapatite, alumina and bone surfaces *in vitro*: morphology during the first 2 h of attachment," *Biomaterials*, vol. 13, no. 2, pp. 123–128, 1992.

[13] T. Tian, D. Jiang, J. Zhang, and Q. Lin, "Fabrication of bioactive composite by developing PLLA onto the framework of sintered HA scaffold," *Materials Science and Engineering C*, vol. 28, no. 1, pp. 51–56, 2008.

[14] T. Kasuga, Y. Ota, M. Nogami, and Y. Abe, "Preparation and mechanical properties of polylactic acid composites containing hydroxyapatite fibers," *Biomaterials*, vol. 22, no. 1, pp. 19–23, 2001.

[15] C. Delabarde, C. J. G. Plummer, P.-E. Bourban, and J.-A. E. Månson, "Biodegradable polylactide/hydroxyapatite nanocomposite foamscaffolds for bone tissue engineering applications," *Journal of Materials Science*, vol. 23, no. 6, pp. 1371–1385, 2012.

[16] X. Deng, J. Hao, and C. Wang, "Preparation and mechanical properties of nanocomposites of poly(D,L-lactide) with Ca-deficient hydroxyapatite nanocrystals," *Biomaterials*, vol. 22, no. 21, pp. 2867–2873, 2001.

[17] L. Varila, T. Lehtonen, and J. Tuominen, "*In vitro* behaviour of three biocompatible glasses in composite implants," *Journal of Materials Science*, vol. 23, no. 10, pp. 2425–2435, 2012.

[18] S. Zhou, B. Song, and X. Li, "*In vitro* degradation and release profiles for poly-dl-lactide film containing paracetamol," *Journal of Materials Science*, vol. 18, no. 8, pp. 1623–1626, 2007.

[19] S. Kobayashi and K. Sakamoto, "Effect of hydrolysis on mechanical properties of tricalcium phosphate/poly-L-lactide composites," *Journal of Materials Science*, vol. 20, no. 1, pp. 379–386, 2009.

[20] M. Mehdikhani-Nahrkhalaji, M. H. Fathi, V. Mortazavi, S. B. Mousavi, B. Hashemi-Beni, and S. M. Razavi, "Novel nanocomposite coating for dental implant applications *in vitro* and *in vivo* evaluation," *Journal of Materials Science*, vol. 23, no. 2, pp. 485–495, 2012.

[21] T. Niemelä, H. Niiranen, and M. Kellomäki, "Self-reinforced composites of bioabsorbable polymer and bioactive glass with different bioactive glass contents. Part II: *in vitro* degradation," *Acta Biomaterialia*, vol. 4, no. 1, pp. 156–164, 2008.

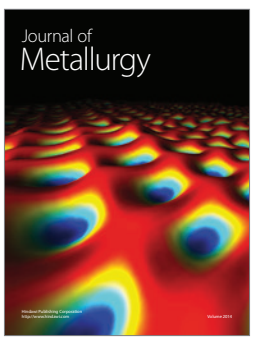
[22] N. A. Weir, F. J. Buchanan, J. F. Orr, and G. R. Dickson, "Degradation of poly-L-lactide. Part 1: *in vitro* and *in vivo* physiological temperature degradation," *Proceedings of the Institution of Mechanical Engineers H*, vol. 218, no. 5, pp. 307–319, 2004.

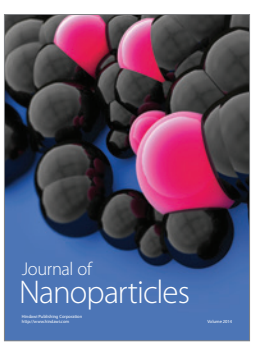
[23] S. Chen, Y. Hao, and W. Cui, "Biodegradable electrospun PLLA/chitosan membrane as guided tissue regeneration membrane for treating periodontitis," *Journal of Materials Science*, vol. 48, no. 19, pp. 6567–6577, 2013.

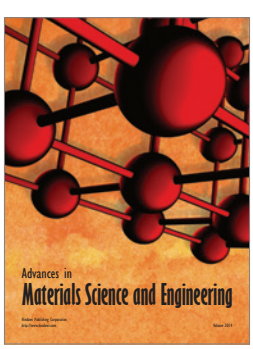
[24] J. Russias, E. Saiz, R. K. Nalla, and A. P. Tomsia, "Microspheres as building blocks for hydroxyapatite/polylactide biodegradable composites," *Journal of Materials Science*, vol. 41, no. 16, pp. 5127–5133, 2006.

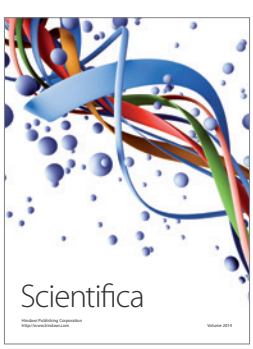
[25] L. M. Ehrenfried, M. H. Patel, and R. E. Cameron, "The effect of tri-calcium phosphate (TCP) addition on the degradation of polylactide-co-glycolide (PLGA)," *Journal of Materials Science*, vol. 19, no. 1, pp. 459–466, 2008.

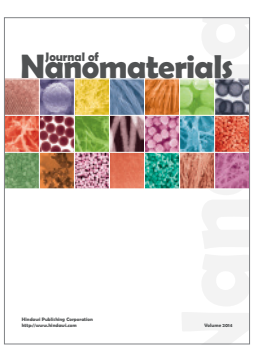
[26] Z. Zhou, Q. Yi, X. Liu, L. Liu, and Q. Liu, "*In vitro* degradation behaviors of poly-L-lactide/bioactive glass composite materials in phosphate-buffered solution," *Polymer Bulletin*, vol. 63, no. 4, pp. 575–586, 2009.

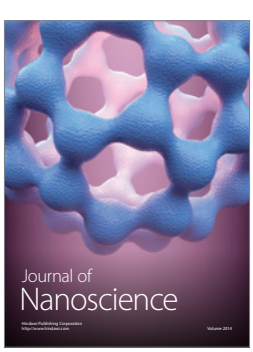


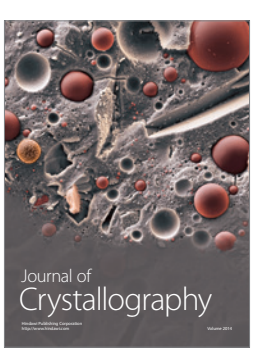


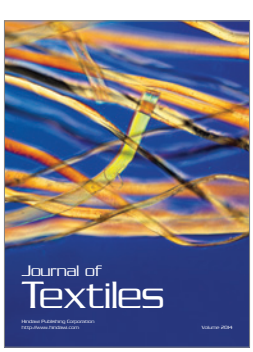












Hindawi

Submit your manuscripts at
http://www.hindawi.com