

Preparation and Degradability of Poly(lactic acid)–Poly(ethylene glycol)–Poly(lactic acid)/SiO₂ Hybrid Material

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ABSTRACT: Poly(lactic acid)–poly(ethylene glycol)–poly(lactic acid) (PLA-PEG-PLA)/SiO₂ hybrid material is prepared by sol–gel method using tetraethoxysilane (TEOS) and PLA-PEG-PLA as raw material. From Fourier transform infrared spectroscopy (FTIR) and X-ray photoelectron spectroscopy (XPS) spectra, the hydroxyl groups of the silica sol derived from partially hydrolysis of TEOS and the unhydrolyzed ethoxy groups of TEOS can react with PLA-PEG-PLA. Differential scanning calorimetry (DSC) curves imply that the glass transition temperature (T_g) of PLA-PEG-PLA/SiO₂ hybrid material is higher than that of PLA-PEG-PLA and increases with the increase of silica content. X-ray diffraction (XRD) analysis results show that PLA-PEG-PLA and PLA-PEG-PLA/SiO₂

hybrid material are both amorphous. Field scanning electron microscope (FSEM) photographs show that when PLA-PEG-PLA/SiO₂ hybrid material has been degraded for 12 weeks in normal saline at 37°C, a three-dimensional porous scaffold is obtained, which is available for cell growth and metabolism. Moreover, the hydroxyl (–OH) groups on SiO₂ of PLA-PEG-PLA/SiO₂ hybrid material could buffer the acidity resulted from the degradation of PLA, which is beneficial to proliferation of cell in tissue repairing. © 2008 Wiley Periodicals, Inc. *J Appl Polym Sci* 110: 3985–3989, 2008

Key words: PLA-PEG-PLA/SiO₂ hybrid material; preparation; sol–gel process; degradability

INTRODUCTION

Poly(lactic acid) (PLA) is an important biomaterial because of its good biocompatibility and biodegradability.¹ However, some of the other properties, such as hydrophilic properties, degradation rate, mechanical properties, melt viscosity, impact factor, heat distortion temperature, and gas barrier properties, are frequently not good enough for various end-use applications.² Much research has been done to improve its properties,^{3–5} and poly(ethylene glycol) (PEG) has been widely studied to modify PLA.^{6–10} Compared with PLA, the hydrophilicity of PLA-PEG-PLA has been obviously improved, but its mechanical properties are not good¹¹ and easily decrease at the initial degradation stage. Moreover, the acidity resulted from the degradation of PLA may cause inflammatory, which limits the application of PLA-PEG-PLA as a scaffold material in bone tissue engineering. It was reported that the addition of hydroxyapatite (HA), a calcium phosphate that is closely related to the mineral component of bone, could reinforce PLA^{12,13} and

help buffer the acidity resulted from the degradation of PLA.¹⁴ Based mainly on an inorganic polymerization reaction, the sol–gel process is a chemical synthesis method initially used for the preparation of inorganic materials such as glasses and ceramics.¹⁵ In recent years, sol–gel method is also an effective way for the synthesis of hybrid materials.^{16–19} Based on PLA, a few articles have reported preparation of PLA/SiO₂ nanocomposites by sol–gel method²⁰ using tetraethoxysilane (TEOS) or *in situ* polymerization.²¹

In this work, we prepared PLA-PEG-PLA/SiO₂ hybrid material by sol–gel method using TEOS and PLA-PEG-PLA as raw material and investigated the degradation of PLA-PEG-PLA/SiO₂ hybrid material in normal saline. The heat stability and degradability of the PLA-PEG-PLA/SiO₂ hybrid material can be controlled by the adjustment of the ratio of PLA-PEG-PLA and SiO₂; moreover, the hydroxyl (–OH) groups on SiO₂ can buffer the acidity resulted from the degradation of PLA, implying potential as a new scaffold material in bone tissue engineering.

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EXPERIMENTAL

Material

Tetraethoxysilane (TEOS) with analytical purity (SiO₂ = 28.4%) is obtained from Sinopharm Chemical

TABLE I
The Molar Ratio of each Component for
PLA-PEG-PLA/SiO₂ System

Samples	SiO ₂ content (wt %)	PLA-PEG-PLA/TEOS/H ₂ O (molar ratio)
No. 1	2	1 : 14 : 58
No. 2	4	1 : 28 : 116
No. 3	8	1 : 58 : 241

Reagent, Shanghai city, China. Tetrahydrofuran (THF) is purchased from Shantou Xilong Chemical, Guangdong province, China. PLA-PEG-PLA with a total molecular relative weight of 40,000 and PEG with relative molecular weight of 1000 are prepared with ring-opening polymerization²² by ourselves.

Sample preparation

Silica sol

With HCl as a catalyst, the partial hydrolysis and polycondensation of TEOS (molar ratio employed was TEOS/ethanol/H₂O = 1 : 3 : 4.15) were conducted at 45°C in a three-necked round-bottomed flask for 3.5 h. The silica sol was obtained after the by-products were removed away by vacuum.

PLA-PEG-PLA/SiO₂ hybrid material

To PLA-PEG-PLA/SiO₂ hybrid sol, 10.0 g PLA-PEG-PLA was dissolved in 100 mL THF in a three-necked round-bottomed flask, then the measured silica sol was dropped in and the temperature was raised and kept at 60°C for 6 h. Afterward, the hybrid sol was kept in a plastic container at ambient temperature until it changed into hybrid gel completely. After the hybrid gel was heat treated in a vacuum oven at 40°C for 48 h, PLA-PEG-PLA/SiO₂ hybrid material was obtained. Table I shows the molar ratio of each component for PLA-PEG-PLA/SiO₂ hybrid system with different SiO₂ content.

Degradation of PLA-PEG-PLA/SiO₂ hybrid material in vitro

PLA-PEG-PLA/SiO₂ hybrid material tablets sized Ø10 mm × 5 mm were prepared with TDP1.5 single punch tablet press. The degradation of PLA-PEG-PLA/SiO₂ hybrid material was conducted in 100 mL normal saline at 37°C for 12 weeks.

Measurements

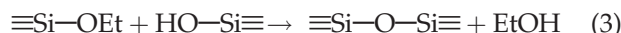
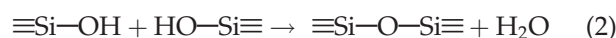
Fourier transform infrared (FTIR) spectra were measured with a Nicolet (Wisconsin, USA) Nexus-

870 spectrometer. X-ray photoelectron spectroscopy (XPS) was performed with Mg K α radiation from a VG (West Sussex, UK) ESCALAB MKII X-ray photoelectron spectrometer. Differential scanning calorimetry (DSC) was conducted with a Mettler Toledo (Im Langacher, Switzerland) DSC-821E under nitrogen atmosphere at a flow of 80 mL/min. Field scanning electron microscopy (FSEM) photographs were taken on a Jeol (Jeol, Japan) JSM-6700F field scanning electron microscope. X-ray diffraction (XRD) analysis was measured with a Risaku (Tokyo, Japan) D/max- γ B rotating diffractometer with the Cu K α line (λ = 0.15418 nm) and the diffractograms were scanned in 2θ from 10 to 70°C at a rate of 6°C/min.

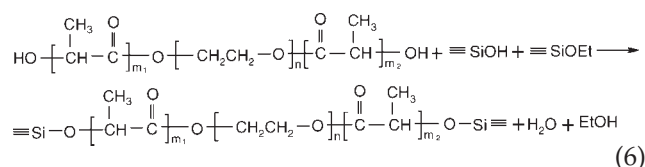
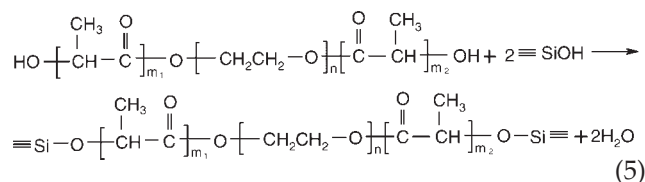
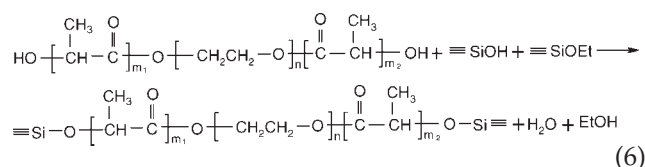
RESULTS AND DISCUSSION

PLA-PEG-PLA/SiO₂ hybrid mechanism

With HCl as a catalyst, the silica sol was synthesized by partial hydrolysis and polycondensation of TEOS in ethanol medium as following:



The hydroxyl groups of the silica sol derived from partially hydrolysis of TEOS and the unhydrolyzed ethoxy groups of TEOS can react with PLA-PEG-PLA to form PLA-PEG-PLA/SiO₂ hybrid material as following:



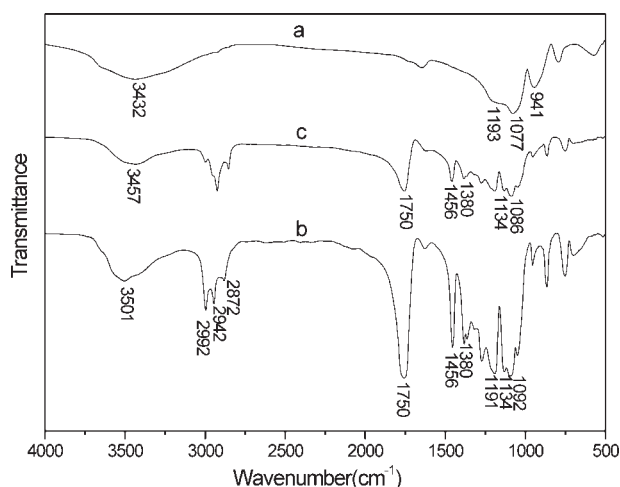


Figure 1 FTIR spectra of samples. (a) silica sol, (b) PLA-PEG-PLA, and (c) PLA-PEG-PLA/SiO₂ hybrid material.

FTIR analysis

Figure 1(a-c) shows the FTIR spectra of silica sol, PLA-PEG-PLA, and PLA-PEG-PLA/SiO₂ hybrid material, respectively. As shown in Figure 1(a), the characteristic peaks for the silica sol are present: $\nu(-OH)$ at 3432 cm⁻¹, $\nu Si-O-Si$ at 1077 cm⁻¹, $\nu_{as}Si-O-C$ at 1193 cm⁻¹, and $\nu_s Si-O-C$ at 941 cm⁻¹. As shown in Figure 1(b), the characteristic peaks for PLA-PEG-PLA are shown: $\nu(C=O)$ at 1750 cm⁻¹, $\nu_{as}C-O-C$ at 1134 cm⁻¹, $\nu_s C-O-C$ at 1191 and 1092 cm⁻¹, $\nu(-CH_3)$ at 2992 and 2942 cm⁻¹, $\delta(-CH_3)$ at 1380 cm⁻¹, $\nu(-CH_2)$ at 2872 cm⁻¹, and $\delta(-CH_2)$ at 1456 cm⁻¹. Compared with Figure 1(a,b), the characteristic peaks for the formation of the Si-O-Si bands $\nu Si-O-Si$ at 1134 and 1086 cm⁻¹ and the characteristic peak of Si-O-C at 1185 cm⁻¹ are shown in Figure 1(c), which overlapped $\nu_{as}C-O-C$ and $\nu_s C-O-C$ and became broad,

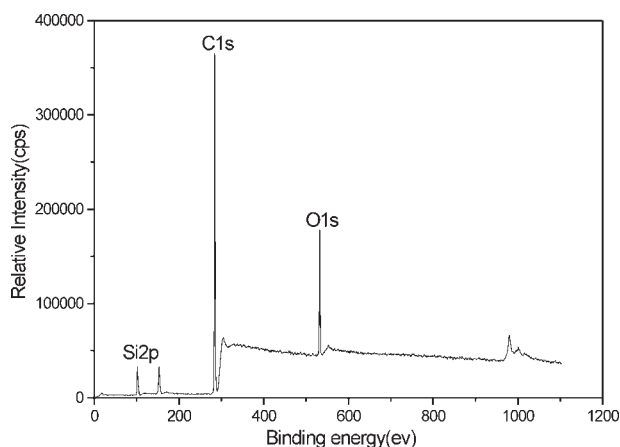


Figure 2 XPS full-scan spectrum of PLA-PEG-PLA/SiO₂ hybrid material.

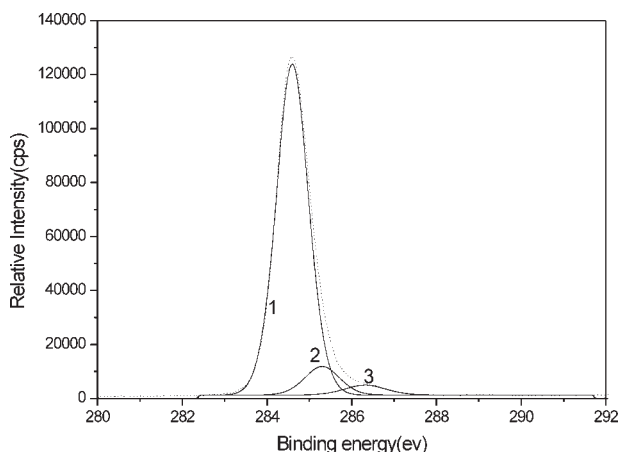
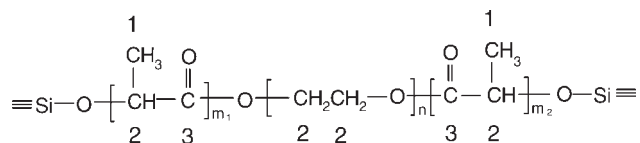


Figure 3 Curve-fitted XPS C1s spectrum of PLA-PEG-PLA/SiO₂ hybrid material.

implying that the silica sol has reacted with PLA-PEG-PLA and formed PLA-PEG-PLA/SiO₂ hybrid material.

XPS analysis

Figure 2 illustrates the XPS full-scan spectrum of PLA-PEG-PLA/SiO₂ hybrid material. In Figure 2, the peaks Si2p, C1s, and O1s are at 101.74, 285.05, and 532.08 eV, respectively. When peak C1s is fitted, three peaks at 284.6, 285.3, and 286.32 eV are obtained, as shown in Figure 3, corresponding to three different carbons (C1-C3) in PLA-PEG-PLA/SiO₂ molecular structure as following:



Peaks Si2p, C1s, and O1s signify that PLA-PEG-PLA/SiO₂ hybrid material are made up of Si, C, and O elements, implying that the hydroxyl groups of the silica sol derived from partially hydrolysis of TEOS and the unhydrolyzed ethoxy groups of TEOS can react with PLA-PEG-PLA and formed PLA-PEG-PLA/SiO₂ hybrid material. This fact agrees well with the conclusions drawn from FTIR analysis.

DSC analysis

Figure 4(a-d) shows the DSC heating scans for PLA-PEG-PLA and PLA-PEG-PLA/SiO₂ hybrid material for 2, 4, and 8 wt % SiO₂, respectively. The peak at about 21.7°C in Figure 4(a) corresponds to glass transition temperature (*T_g*) of PLA-PEG-PLA, whereas the peaks at about 24.0, 25.3, 28.1°C in Figure 4(b-d) correspond to *T_g* of PLA-PEG-PLA/SiO₂

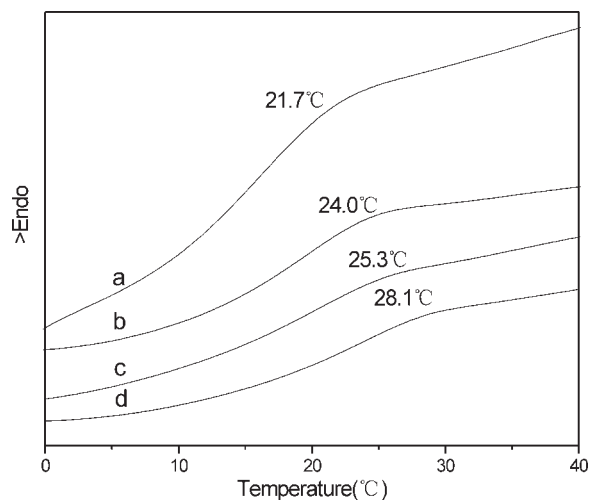


Figure 4 DSC curves of samples. (a) PLA-PEG-PLA, (b) PLA-PEG-PLA/SiO₂ hybrid material for 2 wt % SiO₂, (c) PLA-PEG-PLA/SiO₂ hybrid material for 4 wt % SiO₂, and (d) PLA-PEG-PLA/SiO₂ hybrid material for 8 wt % SiO₂.

hybrid material for 2, 4, and 8 wt % SiO₂, respectively. It is obvious that the T_g of PLA-PEG-PLA/SiO₂ hybrid material is higher than that of PLA-PEG-PLA and increases with the increase of silica content. The reason is that the SiO₂ hybridized on PLA-PEG-PLA chain limits the moving of PLA-PEG-PLA segments.

XRD analysis

Figure 5(a,b) shows the XRD patterns for PLA-PEG-PLA and PLA-PEG-PLA/SiO₂ hybrid material, and no significant difference is found between these two patterns. It is obvious that both PLA-PEG-PLA and PLA-PEG-PLA/SiO₂ hybrid material are amorphous, implying that the addition of SiO₂ did not change the form of PLA-PEG-PLA.

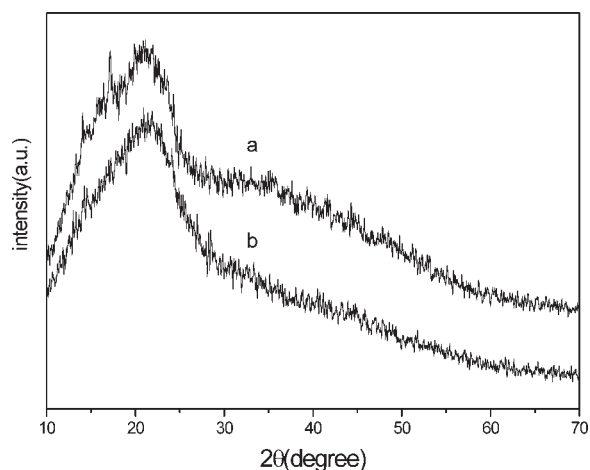


Figure 5 XRD patterns for samples. (a) PLA-PEG-PLA and (b) PLA-PEG-PLA/SiO₂ hybrid material.

Morphology of PLA-PEG-PLA/SiO₂ hybrid material degraded in normal saline

To investigate the application future of PLA-PEG-PLA/SiO₂ hybrid material in bone tissue engineering, we investigated the morphology change of PLA-PEG-PLA/SiO₂ hybrid material degraded in normal saline at 37°C. It can be seen in Figure 6(a) that SiO₂ is integrated well with PLA-PEG-PLA matrix and no obvious phase separation is observed before degradation. Six weeks later, because of the degradation of PLA, many low molecular PLA-PEG-PLA, PLA-

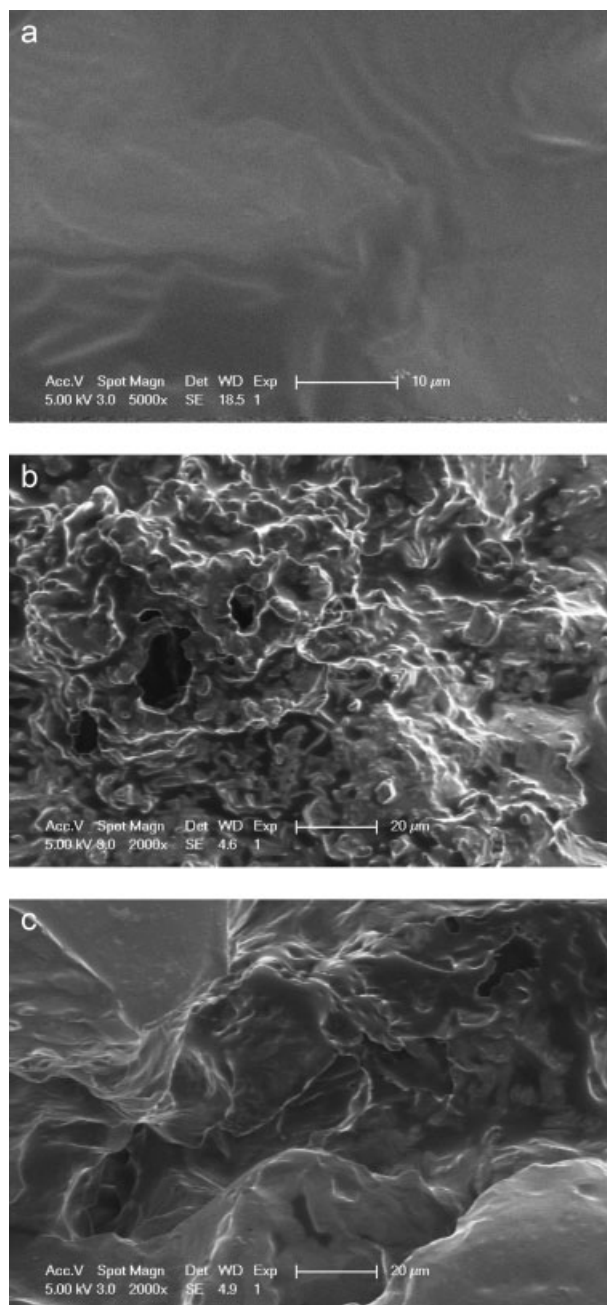


Figure 6 SEM photographs for samples degraded in normal saline at 37°C. (a) degraded, (b) 6 weeks later, and (c) 12 weeks later.

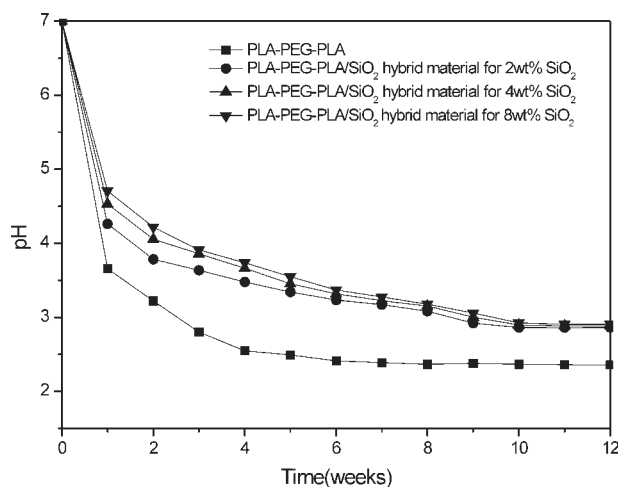


Figure 7 Relationships between pH of degradation solution and time for samples.

PEG, or PEG fragments were produced. When these fragments dispersed in degradation solution, lots of slots and pores appeared as shown in Figure 6(b). Twelve weeks later, as the degradation of PLA was conducted from surface to interior, these slots and pores were enlarged and deepened to form a three-dimensional porous scaffold as shown in Figure 6(c), which are available for cell growth and metabolism.

pH change for degradation solution

Figure 7(a–d) illustrates the relationships between the pH of degradation solution and degradation time of PLA-PEG-PLA and PLA-PEG-PLA/SiO₂ hybrid material for 2, 4, and 8 wt %SiO₂, respectively. Figure 7(a) shows that the pH of degradation solution of PLA-PEG-PLA decreased faster at initial stage (first 4 weeks), slower at medium stage (5–8 weeks), unobviously at later stage (9–12 weeks), and kept stable at about 2.4 finally. At initial stage, the degradation occurred mainly on the surface, and the degradation rate was faster. As degradation continuing, the degradation was conducting from surface to interior, meanwhile, the degradation rate was lowered because of the diffusion of low molecular PLA-PEG-PLA, PLA-PEG, or PEG fragments. Compared with Figure 7(a), Figure 6(b,c) illustrates that the pH of degradation solution of PLA-PEG-PLA/SiO₂ hybrid material is higher than that of PLA-PEG-PLA at each given degradation time and keep stable at about 3.0 finally, implying that the hydroxyl (–OH) groups on SiO₂ can buffer the acidity resulted from the degradation of PLA, which may decrease the inflammatory caused by acidity and is beneficial to proliferation of cell in tissue repairing.

CONCLUSIONS

PLA-PEG-PLA/SiO₂ hybrid material is successfully synthesized by sol–gel process. The hydroxyl groups of the silica sol derived from partially hydrolysis of TEOS and the unhydrolyzed ethoxy groups of TEOS can react with PLA-PEG-PLA to form PLA-PEG-PLA/SiO₂ hybrid material. The T_g of PLA-PEG-PLA/SiO₂ hybrid material is higher than that of PLA-PEG-PLA and increases with the increase of silica content. The addition of SiO₂ did not change the form of PLA-PEG-PLA. After PLA-PEG-PLA/SiO₂ hybrid material has been degraded for 12 weeks in normal saline at 37°C, a three-dimensional porous scaffold was obtained, which was available for cell growth and metabolism. Moreover, the hydroxyl (–OH) groups on SiO₂ of PLA-PEG-PLA/SiO₂ hybrid material can buffer the acidity resulted from the degradation of PLA, which is beneficial to proliferation of cell in tissue repairing.

References

- Hutchinson, F. G.; Furr, B. J. A. In *Drug Delivery Systems: Fundamentals and Techniques*; Johnson, P., Lloyd-Jones, J. G., Eds.; Ellis Horwood: Chichester, England, 1987; p 106.
- Ogata, N.; Jimenez, G.; Kawai, H.; Ogiwara, K. *J Polym Sci Part B: Polym Phys* 1997, 35, 389.
- Wang, H.; Li, Y.; Shi, T.; Sheng, M.; Zhai, L.; Wang, J. *Chin J Appl Chem (Chinese)* 2005, 22, 976.
- Sinha Ray, S.; Yamada, K.; Okamoto, M.; Ueda, K. *Polymer* 2003, 44, 6633.
- Kylmä, J.; Härkönen, M.; Seppälä, J. V. *J Appl Polym Sci* 1997, 63, 1865.
- Mohammadi-Rovshandeh, J.; Farnia, S. M. F.; Sarbolouki, M. N. *J Appl Polym Sci* 1998, 68, 1949.
- Ruan, G.; Feng, S. S. *Biomaterials* 2003, 24, 5037.
- Lim, D. W.; Park, T. G. *J Appl Polym Sci* 2000, 75, 1615.
- Deng, X. M.; Xiong, C. D.; Cheng, L. M.; Huang, H. H.; Xu, R. P. *J Appl Polym Sci* 1995, 55, 1193.
- Sasatsu, M.; Onishi, H.; Machida, Y. *Int J Pharm* 2005, 294, 233.
- Chen, W. N.; Yang, J.; Wang, S. G.; Bei, J. Z. *Acta Polym Sin (Chinese)* 2002, 5, 695.
- Kasuga, T.; Maeda, H.; Kato, K.; Nogami, M.; Hata, K.; Ueda, M. *Biomaterials* 2003, 24, 3247.
- Ignjatovic, N.; Uskokovic, D. *Appl Surf Sci* 2004, 238, 314.
- Agrawal, C. M.; Athanasiou, K. A. *J Biomed Mater Res, Appl Biomater* 1997, 38, 105.
- Han, Y.; Lin, J.; Zhang, H. *Mater Lett* 2002, 54, 389.
- Tian, D.; Dubois, P.; Jerome, R. *Polymer* 1996, 37, 3983.
- Novak, B. M.; Grobbs, R. H. *J Am Chem Soc* 1988, 110, 7542.
- Eusworkth, U. W.; Novak, B. M. *J Am Chem Soc* 1991, 113, 2756.
- Wang, H.; Shi, T.; Yang, S.; Hang, G. *Mater Res Bull* 2006, 42, 298.
- Perry, C. C.; Eglin, E.; Ali, S. A. M.; Downes, S. *Mater Res Soc Symp Proc* 2002, 726, 67.
- Yan, S. F.; Yin, J. B.; Yang, Y.; Dai, Z. Z.; Ma, J.; Chen, X. S. *Polymer* 2007, 48, 1688.
- Quan, D. P.; Gao, J. W.; Liao, K. R.; Lu, Z. J. *J Funct Polym (Chinese)* 2002, 15, 391.