Preparation and Characterization of Poly(L-lactide) Membranes Prepared by γ-Radiation-Induced Grafting of *N*-Vinyl Pyrrolidone

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ABSTRACT: A copolymer, poly(L-lactide)-*g*-poly(*N*-vinyl pyrrolidone) (PLLA-*g*-PVP) was prepared with poly(L-lactide) (PLLA) and *N*-vinyl pyrrolidone in the presence of methanol as a solvent by γ-ray irradiation. The structure of PLLA-*g*-PVP was characterized by ^{1}H-NMR and Fourier transform infrared spectroscopy. The PLLA-*g*-PVP graft ratio calculated by the percentage increase in weight increased with the increase of absorbed dose, and the percentage crystallinity of PLLA-*g*-PVP decreased with increasing graft ratio. The introduction of the poly(*N*-vinyl pyrrolidone) chain into PLLA resulted in a decrease in the contact angle of PLLA-*g*-PVP with increasing graft ratio. *In vitro* degradation testing showed that PLLA-*g*-PVP had a higher degradation rate both in the weight-loss test and molecular weight measurement because of a lower crystalline percentage and higher hydrophilicity compared to PLLA. © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 114: 3152–3157, 2009

Key words: biomaterials; graft copolymers; irradiation

INTRODUCTION

Poly(L-lactide) (PLLA) has been extensively used for orthopedic devices, controlled release carriers, and packaging materials because of its good performance, such as its high mechanical properties and biocompatibility.[1,2] However, the degradation rate of PLLA as an implantation material is comparatively low because of its high crystallinity percentage and poor hydrophilicity.[3,4] Conventionally, the copolymers of functionalized PLLA grafted by free-radical copolymerization with other monomers, such as *N*-vinyl pyrrolidone (NVP) and *tert*-butyl acrylate, have been prepared under a variety of conditions.[5–7] The degradation behavior of poly(lactic acid) grafted with methacrylate and oligo(D,L-lactide) grafted with dextrans has been tentatively investigated.[8,9] It was found that both the hydrophilicity and the degradation rate of graft copolymers increased with increasing graft ratio.

Compared to chemical grafting initiated by an initiator, the radiation graft that is initiated directly by a high-energy ray is safer and more environmentally friendly. Thus, this method has attracted considerable attention for the surface modification of the membrane materials, especially for biomedical materials. To improve the surface properties of the polymer, plasma-induced graft polymerization has been widely used, such as in the production of modified poly(ether sulfone) membranes by low-temperature, plasma-induced graft polymerization and polysulfone membranes by ammonia plasma treatment.[10–12] PLLA is a semicrystalline, hydrophobic polymer. As a biomedical material, there are two drawbacks, a low degradation rate and poor hydrophilicity. To overcome the drawbacks of PLLA, many studies have been done. Recently, it was reported that the cell adhesion of PLLA and poly(lactic-*co*-glycolic acid) could be improved by plasma surface modification.[13,14] Although considerable studies were carried out on the effect of γ-ray irradiation on the molecular weight, crystallization behavior and thermal stability of PLLA and poly (D,L-lactide),[15,16] there are few reports on grafting of PLLA induced by γ-ray irradiation, because γ-ray irradiation usually results in the decreased

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mechanical properties, especially when the absorbed dose is more than 10 kGy.

To improve the surface hydrophilicity and degradation rate of PLLA, a poly(L-lactide)-*g*-poly(*N*-vinyl pyrrolidone) (PLLA-*g*-PVP) copolymer was prepared by ^{60}Co γ-ray irradiation at a low absorbed dose in the presence of methanol as a solvent and then characterized with nuclear magnetic resonance (^{1}H-NMR), Fourier transform infrared (FTIR), and differential scanning calorimetry (DSC). The degradation rate and surface properties of PLLA-*g*-PVP were also determined.

EXPERIMENTAL

Materials

L-Lactide and tin octoate were supplied by Sichuan Dikang Scitech Pharmaceutical Industry Co., Ltd. (Chengdu, People's Republic of China), and Sinopharm Chemical Reagent Co., Ltd. (Shanghai, People's Republic of China), respectively. NVP (Alfa Aesar A. Johnson Matthey Co, USA) was purified by vacuum distillation before use. The solvents, including chloroform, acetone, ethanol, and methanol, purchased from Kelong Agent Co. (Chengdu, People's Republic of China), were used directly without further purification.

Synthesis of PLLA

All syntheses were carried out in 10- or 20-mL ampule, and tin octoate was used as an initiator in the polymerization of L-lactide. Ampules were loaded with freshly recrystallized L-lactide and tin octoate with a molar ratio (monomer to initiator) of 12,000, then sealed in a high vacuum, and left in a temperature-controlled oil heating bath at 160°C for 24 h. The final products were allowed to cool to room temperature, then dissolved in chloroform, precipitated in methanol, and dried to a constant mass *in vacuo*.[17]

Measurement of the molecular weight

The molecular weight of PLLA was approximated from the viscosity of the polymer solutions in chloroform by an Ubbelohde glass capillary viscometer (Zhengyuan Glass Co., Chengdu, China) in a water bath at 25 ± 0.1°C. The viscosity-average molecular weight (M_η) was calculated from the intrinsic viscosity (η) as follows:

$$\eta = 5.45 \times 10^{-4} \times M_\eta{}^{0.73} \quad (1)$$

Graft copolymerization

PLLA (Mη = 610,000) membranes were soaked in acetone for 24 h and then put into a vacuum oven for 12 h (30°C). PLLA membranes (0.5 g, 0.2–0.21 mm) were added to the mixture of 6 g of NVP and 14 mL of methanol in 25-mL ampules. Ampules were sealed off under a nitrogen atmosphere before they were irradiated by γ rays at room temperature. After copolymerization, the PLLA membranes were washed with deionized water and then ethanol to remove poly(*N*-vinyl pyrrolidone) (PVP) and monomer and dried *in vacuo*. The graft ratio was determined by the percentage increase in weight as follows:

$$\text{Graft ratio } (\%) = \frac{W_1 - W_0}{W_0} \times 100\% \quad (2)$$

where W_0 and W_1 represent the weights of the initial and grafted PLLA membranes, respectively.

Characterization of PLLA-*g*-PVP

FTIR spectra were obtained on an FTIR spectrometer (MX-1E FTIR, Nicolet Co., Ltd, USA). The structures of PLLA and PLLA-*g*-PVP were characterized with a Bruker Avance 600 spectrometer (Bruker Co., Ltd., Fallanden, Switzerland) with a proton frequency of 600 MHz. Deuterated chloroform was used as a solvent, and tetramethylsilane was used as an internal standard. The crystallization behaviors of the samples were examined with a differential scanning calorimeter from Mettler–Toledo Instruments (TA Co., Ltd, USA). Samples were first heated from room temperature to 200°C. Then, DSC thermograms of the same samples cooled to 20°C were taken over the same temperature interval. All data were accumulated at 10°C/min in a dynamic nitrogen atmosphere.

Contact angle

To determine the surface properties of samples, the sessile drop method with a Contact Angle System OCA (Dataphsics, Bad Vibel, Germany) was used. Samples with dimensions of 25 × 50 mm^2 and thicknesses of 0.2–0.21 mm were used for the determination of the surface hydrophilicity. The data were recorded, and the average values of the contact angle were calculated by a computer when ultrapure water dropped to different places of the sample surface for 3 s.

In vitro degradation of PLLA-*g*-PVP

The *in vitro* degradation test was carried out by determination of the weight loss of polymers under the chosen conditions. Into cone cups (2000 mL) sealed with rubber plugs were added 8.00 g of sodium chloride, 0.20 g of potassium chloride, 1.44 g of sodium phosphate, 0.24 g of potassium dihydrogen phosphate, and 1000 mL of distilled water. The

cone cups were put into an autoclave (0.1 MPa) at 145°C for 40 min and then cooled to room temperature. Polymer membranes were put into the buffer solution sealed with glass plugs, and the temperature of the solution was kept at 70 ± 1°C. The membranes were taken out at various time points, washed with distilled water, and then dried *in vacuo* at 40 ± 1°C for 24 h. The weight loss was calculated as follows:

$$\text{Weight loss } (\%) = \frac{W_0 - W_1}{W_0} \times 100\% \qquad (3)$$

where W_0 and W_1 represent the weight of polymers before and after degradation, respectively.

RESULTS AND DISCUSSION

Graft ratio of the copolymers

The relationship between the graft ratio and the absorbed dose in the graft process of NVP onto PLLA at a monomer concentration of 30% in the presence of methanol as a solvent is shown in Figure 1. The graft ratio increased with increasing absorbed dose in the range from 0 to 20 kGy and then leveled off when the dose was higher than 20 kGy. The graft ratios were 14.9 and 47.6% at doses of 5 and 20 kGy, respectively. However, in the systems without methanol, such as PLLA/NVP, PLLA/NVP/ethanol, and PLLA/NVP/H_2O, few copolymers were obtained. So methanol played an important role in initiating the graft reaction, and graft sites may have been located in the methine of PLLA. We assumed that the active hydrogen atoms were formed by the radiolysis of the methanol; then, the hydrogen of the methine of PLLA was abstracted by the active hydrogen free radical from methanol. Macromolecular free radicals of PLLA were formed and initiated the graft reaction. The viscosity of the methanol solution increased with increasing absorbed dose, which means that the homopolymerization of PVP increased with increasing absorbed dose. The high viscosity of the reaction system held the graft copolymerization back. So the graft ratio was kept constant above 20 kGy.

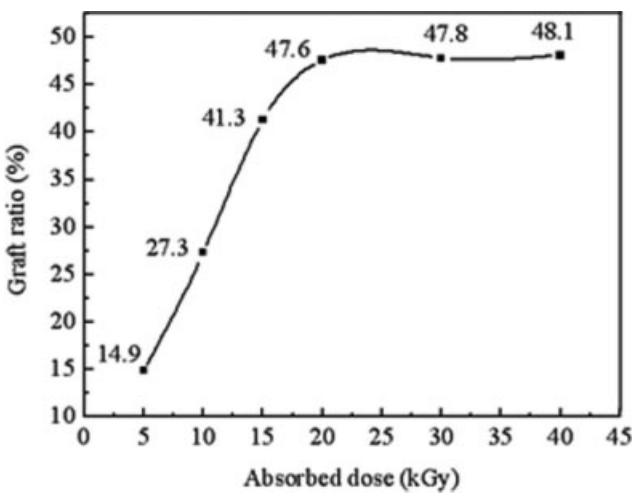


Figure 1 Effect of the absorbed dose on the graft ratio of PLLA-*g*-PVP.

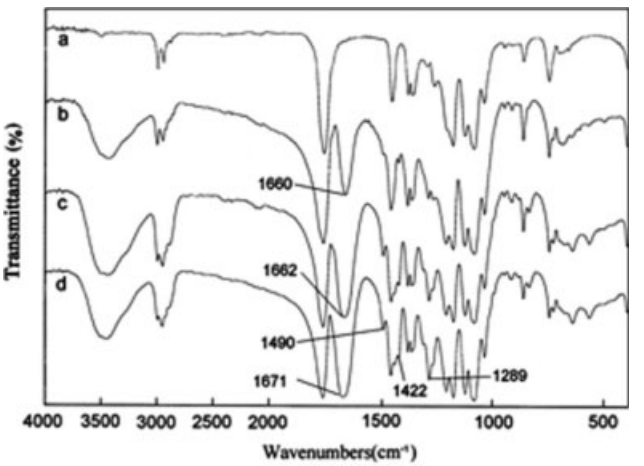


Figure 2 FTIR spectra of (a) PLLA and (b–d) PLLA-*g*-PVP with graft ratios of 14.9, 41.3, and 48.1%, respectively.

FTIR study

Figure 2 shows the FTIR spectra of PLLA and PLLA-*g*-PVP with different graft ratios. Compared to the PLLA spectrum [Fig. 2(a)], the dramatic change of peaks was at 1422 cm^{-1}, which arose from the methylene wagging mode, and 1660–1671 cm^{-1}, which arose from the stretching mode of C=O. The peaks centered at 1490 and 1289 cm^{-1} were characteristic of the pyrrolidone ring.[18] The C=O stretching mode of the pyrrolidone ring shifted to higher wave numbers with increased absorbed dose, that is, 1660 cm^{-1} at 5 kGy, 1662 cm^{-1} at 15 kGy, and 1671 cm^{-1} at 40 kGy; these were lower than the homopolymer of PVP. Moreover, the peaks centered at 3434 cm^{-1} were attributed to hydroxyl arising from water because of the better hydrophilicity of PVP chains.

^{1}H-NMR study

^{1}H-NMR was used to investigate the structure and graft ratio of PLLA-*g*-PVP. ^{1}H-NMR spectra taken from samples with different graft ratios are shown in Figures 3 and 4. For samples of PLLA-*g*-PVP, the appearance of peaks centered at 2.0 (peak d), 2.36 (peak e), 3.25 (peak f), 3.74 (peak g), and 1.69 (peak c) indicated that the pyrrolidone ring was successfully grafted onto PLLA by comparison to PLLA with the appearance of peaks centered at 1.58 ppm

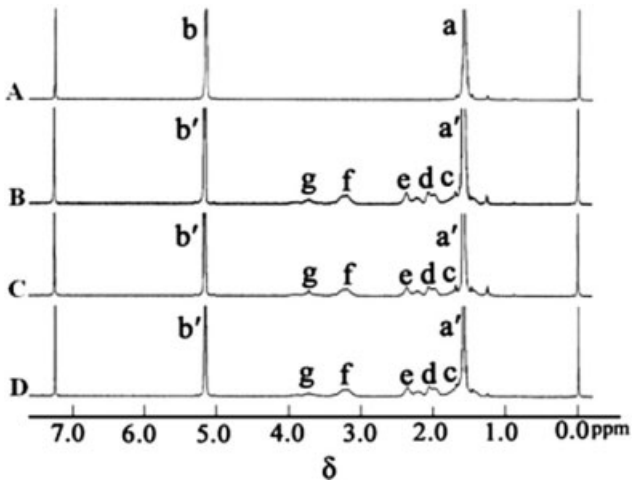


Figure 3 ^{1}H-NMR spectra of (A) PLLA and (B–D) PLLA-*g*-PVP with graft ratios of 14.9, 41.3, and 48.1%, respectively.

(peak a′) and 5.18 ppm (peak b′), respectively.[18] With the assumption that the amount of hydrogen atoms on the methine groups of PLLA did not change after grafting, through eq. (4), we calculated the molar ratio of PLLA to PVP units to be 9.4 : 1, which corresponded to a graft ratio of 16.4 wt %. However, the peak area ratio of hydrogen protons of methyl to methine in the PLLA chains was up to 3.27 : 1, which indicated that part of the hydrogen proton of methine in PLLA was lost. Accordingly, the structure of PLLA-*g*-PVP was believed to be formed as shown in Scheme 1. However, the detailed reaction mechanism still needs further investigation:

$$\text{Graft ratio } (\%) = \frac{M_2 S_f}{2 M_1 S_{b'}} \times 100\% \qquad (4)$$

where M_1 and M_2 represent the relative molecular weights of the construction unit of PLLA and NVP, respectively, and S_f and $S_{b'}$ represent the peak areas of peak f and peak b′, respectively.

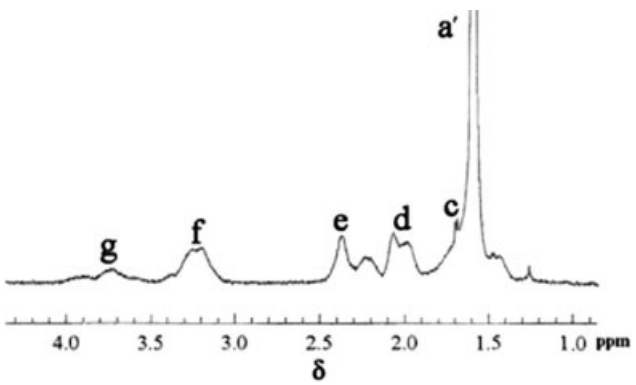
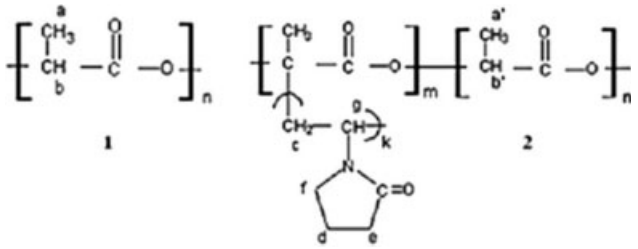


Figure 4 ^{1}H-NMR expanded spectrum of PLLA-*g*-PVP with a graft ratio of 14.9%.



Scheme 1 Structural formulas of (1) PLLA and (2) PLLA-*g*-PVP.

DSC analysis

To investigate the crystallization behavior of PLLA-*g*-PVP, DSC thermograms of the copolymers were taken over the same temperature interval. Previous studies showed that as a semicrystalline polymer, PLLA suffering from γ irradiation underwent random main-chain scission and a substantial decrease in the crystallization and melting enthalpy values. However, no significant changes in the melting temperature (T_m) and glass-transition temperature (T_g) were observed until a dose of 80 kGy was applied.[19,20] The T_g, crystallization temperature, T_m, and enthalpy values of PLLA-*g*-PVP with different graft ratios are shown in Figure 5. As shown in Figure 5, PLLA-*g*-PVP showed no significant changes in T_g; however T_m decreased with increasing graft ratio from 177°C (14.9%) to 172°C (48.1%). The melting enthalpy, crystallization enthalpy, and percentage crystallinity calculated according to Omer's method[21] are shown in Table I.

The melting enthalpy values of PLLA (sample A) irradiated at the dose of 5 kGy was the highest among all of the treatments, the melting enthalpy

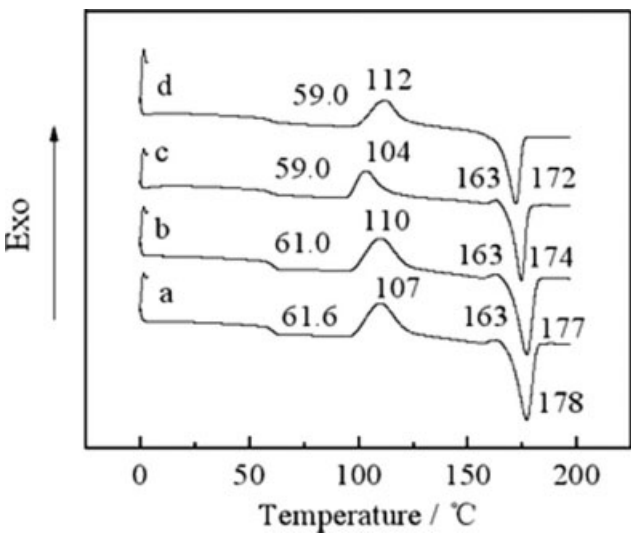


Figure 5 DSC curves of (a) PLLA at a dose of 5 kGy and (b–d) PLLA-*g*-PVP with graft ratios of 14.9, 41.3, and 48.1%, respectively.

TABLE I
Crystallization and Melting Enthalpy Data for PLLA-*g*-PVP

Sample	Graft ratio (%)	Melting enthalpy (J/g)	Crystallization enthalpy (J/g)	Crystallinity (%)
A	0.0	52.2	35.9	69.1
B	14.9	37.2	31.4	49.2
C	41.3	22.2	18.3	29.4
D	48.1	16.4	13.8	21.7

values of PLLA-*g*-PVP (samples B–D) sharply decreased with increasing graft ratio in the range from 14.9 to 48.1%, and the percentage crystallinity of PLLA-*g*-PVP decreased with increasing graft ratio. There were two factors that resulted in decreases in the crystallinity percentage of the copolymers with increasing graft ratio. One was the same as the irradiated PLLA mentioned earlier; the other was the formation of the side-chain structures, which destroyed the regularity of molecular structure.

Surface properties of PLLA-*g*-PVP

The contact angle is useful for evaluating the surface hydrophilicity of a polymer. The value of contact angle greatly depends on the structure and properties of the graft chain. Generally, a higher hydrophilicity results in a lower contact angle. The relationship between the contact angle and the graft ratio of the polymers is listed in Table II. The contact angle of PLLA-*g*-PVP decreased with increasing graft ratio, which was in good agreement with the result that the better hydrophilicity reflected a higher graft ratio. The contact angle decreased from 75.1° (graft ratio = 0.0%) to 65.3° (graft ratio = 14.9%), which was attributed to the better hydrophilicity of the PVP chain.

In vitro degradation of PLLA-*g*-PVP

To investigate the degradation over a short time, an accelerated degradation test was performed. The percentage weight loss and M_η of PLLA and PLLA-*g*-PVP were used to estimate the accelerated degradation rate. The relationship between the weight loss and degradation time is listed in Table III. The weight loss of PLLA and PLLA-*g*-PVP induced by

TABLE II
Contact-Angle Values for PLLA and PLLA-*g*-PVP

Sample	Graft ratio (%)	Contact angle (°)
A	0.0	75.1
B	14.9	65.3
C	27.3	58.2
D	41.3	50.3

TABLE III
Weight-Loss Data at Different Degradation Times

Time (h)	Weight loss (%)		
	PLLA	PLLA at a dose of 5 kGy	PLLA-*g*-PVP with a graft ratio of 14.9%
12	2.20	2.83	2.13
24	3.80	2.02	5.45
36	4.97	3.25	9.10
48	3.07	2.60	12.60
72	3.73	2.93	24.03
96	4.40	3.53	25.53
120	4.90	3.26	33.45
144	6.85	2.87	35.10
168	6.97	2.53	38.20

γ-ray irradiation at a dose of 5 kGy increased with increasing degradation time. For PLLA, the weight loss was up to 6.97% after 168 h. The weight loss of PLLA-*g*-PVP was up to 5.45% for 24 h, 24.03% for 72 h, and 38.21% for 168 h, which was attributed to the lower crystallinity and the better hydrophilicity compared to PLLA. However, the weight loss of irradiated PLLA at a dose of 5 kGy remained stable with the increase of degradation time and only 2.53% for 168 h.

The M_η values of PLLA and PLLA-*g*-PVP at different degradation times are listed in Table IV. The M_η of PLLA and irradiated PLLA at a dose of 5 kGy gradually decreased with increasing degradation time. However, for the samples of PLLA-*g*-PVP, a drastic decrease in molecular weight was observed when the samples were soaked for 12 h. Subsequently, a more steady decrease in molecular weight was observed when the degradation time was greater than 12 h. Both the weight residue and change in M_η indicated that the degradation rate of PLLA-*g*-PVP greatly increased compared to that of PLLA without graft modification. This was attributed to a lower crystallinity and better hydrophilicity compared to those in PLLA.

TABLE IV
M_η Values at Different Times

Time (h)	M_η ($\times 10^4$)		
	PLLA	PLLA at a dose of 5 kGy	PLLA-*g*-PVP with a graft ratio of 14.9%
0	61.00	23.80	24.10
12	57.70	21.00	2.88
24	63.40	24.20	2.88
36	52.90	19.90	2.20
48	52.20	16.30	1.86
72	37.80	12.50	1.55
96	33.60	10.40	1.26
120	25.50	7.45	2.53
144	20.10	6.10	1.55
168	18.10	4.00	1.26

CONCLUSIONS

To improve the degradation rate and hydrophilicity of PLLA, a graft copolymer, PLLA-*g*-PVP was prepared at low dose by γ-ray irradiation. The graft ratio of the copolymers increased with increasing absorbed dose. The T_m, melting enthalpy, and crystallinity percentage of PLLA-*g*-PVP were lower than those of PLLA without graft modification. Through the introduction of a hydrophilic PVP chain onto the PLLA chain, the contact angle of PLLA-*g*-PVP at a graft ratio of 14.9% decreased to 65.3° compared to PLLA. The weight loss of the PLLA-*g*-PVP membranes was up to 38.21%, and M_η decreased to 12,000 from 241,000 when the sample was soaked in buffer solution for 168 h. PLLA-*g*-PVP with a good hydrophilicity and an appropriate degradation rate could possibly be used for medical materials with a controllable degradation rate.

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