

Degradation of Poly(D,L-lactic acid)-*b*-poly(ethylene glycol)-*b*-poly(D,L-lactic acid) Copolymer by Electron Beam Radiation

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ABSTRACT: This article investigates the effects of electron beam (EB) radiation on poly(D,L-lactic acid)-*b*-poly(ethylene glycol) copolymer (PLA-*b*-PEG-*b*-PLA). The copolymer films were EB irradiated at doses from 0 to 100 kGy. The degradation of these films was studied by measuring the changes in their molecular weight, mechanical and thermal properties. The dominant effect of EB radiation on PLA-*b*-PEG-*b*-PLA is chain-scission. With increasing irradiation dose, recombination reactions or partial crosslinking may occur in addition to chain scission. The degree of chain scission G_s and crosslinking G_c of sample are calculated to be 0.213 and 0.043, respectively. A linear

relationship is also established between the decreases in molecular weight with increasing irradiation dose. Elongation at break of the irradiated sample decreases significantly, whereas its tensile strength decreases slightly. The glass transition temperature (T_g) is basically invariant as a function of irradiation dose. Thermogravimetric analysis shows that its thermal stability decreases with increasing dose. © 2009 Wiley Periodicals, Inc. *J Appl Polym Sci* 112: 2981–2987, 2009

Key words: block copolymer; crosslinking; degradation; low energy electron beam; free radical

INTRODUCTION

Poly(lactic acid) (PLA) is a typical biodegradable and biocompatible polymer, studied in a wide variety of applications, from implantable medical devices and drug release matrices to environmentally friendly packaging materials.^{1,2} However, when PLA is used as hydrophilic drug delivery carrier and tissue engineering material, its hydrophilicity was must be improved.

Poly(ethylene glycol) (PEG), well known for its water-solubility, lack of toxicity and excellent biocompatibility, has been authorized by USA Food and Drug Administration (FDA), and usually chosen as the hydrophilic buoy block whose role is to provide a hydrated steric barrier.³ Therefore, by introducing PEG into PLA through copolymerization, the synthesis of poly(lactic acid)-*co*-poly(ethylene glycol) becomes an important way to improve the hydrophilicity of PLA.^{4,5} Attention is also paid to the degradation of micro- and nanoparticles prepared from

PEG-PLA, which have the most suitable combination of properties for use as drug delivery matrix.^{6,7} Conventionally, the degradation rate for this biopolymer is controlled by altering such chemical parameters as comonomer ratio and polymer molecular weight.^{8–10}

Radiation has been known to alter the physical properties of polymers through main-chain scission and crosslinking. According to the principles of radiation chemistry, free radicals are formed when macromolecules of polymers are excited under ionizing radiation, where they are then free to react with one another or initiate further reactions among the polymeric chains, thus giving rise to changes in material properties. The combination of two radicals leads to crosslinking or recombination in the amorphous and crystalline regions, respectively, whereas chain transfer and the subsequent splitting results in chain scission. Usually both these processes take place simultaneously for many polymers.¹¹ Some people^{12–14} have studied the degradation behavior of gamma and electron beam (EB) irradiated PLA, reporting that PLA has a high sensitivity to radiation, whose thermal and mechanical properties decrease significantly due to the drastic decrease in the molecular weight. Recently, some studies^{11,15,16} report an approach to control the degradation rate of PLA and poly(lactide-*co*-glycolide) (PLGA) using EB radiation,

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and the relationship between irradiation dose and the degradation rate is established. Therefore, EB radiation can be a useful tool to control the degradation behavior of these biopolymers.

Although some studies have been reported on the effects of gamma and EB irradiation on PLA and its copolymers, to our best knowledge, no investigation has been reported so far regarding the effects of EB radiation on the mechanical, thermal and molecular weights of PLA-PEG copolymer. In this article, average molecular weight (M_n and M_w), mechanical properties, glass transition temperature (T_g) and thermal stability were measured as a function of irradiation dose. The radiation chemical yields for chain scission (G_s) and crosslinking (G_x) were evaluated, and the relationship between its molecular weight and irradiation dose was also established.

EXPERIMENTAL

Materials

D,L-lactic acid (85–90 wt % aqueous solution) and poly(ethylene glycol) (PEG) with molecular weight 6000 (PEG 6K) were purchased from Tianjin Bodi Chemical Co., Ltd. (China). Tin(II) chloride dihydrate ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$) was purchased from Chongqing Chemical Reagent Company (China). *p*-toluenesulfonic acid (TSA) was purchased from Chengdu Kelong Chemical Reagent Factory (China). Acetone, dichloromethane (DMC) and methanol were laboratory reagents. All reagents were analytical grade and used without further purification.

Synthesis of PLA-*b*-PEG-*b*-PLA

The synthesis of a copolymer of D,L-lactic acid with PEG 6K was carried out by a modification of existing literature techniques and procedure,¹⁷ as shown in Figure 1.

A total of 100 g of D,L-lactic acid (85–90 wt % aqueous solution) was dehydrated at 100°C, first at atmospheric pressure for 1 h, then at a reduced pressure of 20 Torr for 1 h, and finally under a pressure of 5 Torr for another 4 h at 150°C. Then, a viscous liquid of oligo(D,L-lactic acid) (ODLLA) was formed quantitatively.

A 200 mL pear-shaped three-necked flask was equipped with a mechanical stirrer and a reflux condenser that was connected to a vacuum system through a cold trap. A total of 45 g of ODLLA, 5 g of PEG 6K (11 wt % relative to ODLLA), 0.18 g of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (0.4 wt % relative to ODLLA), and 0.14 g of TSA (an equimolar ratio to $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$) were charged into the flask. The reaction mixture was stirred under a pressure of 5 Torr at 180°C for 18 h and was subsequently cooled to room temperature.

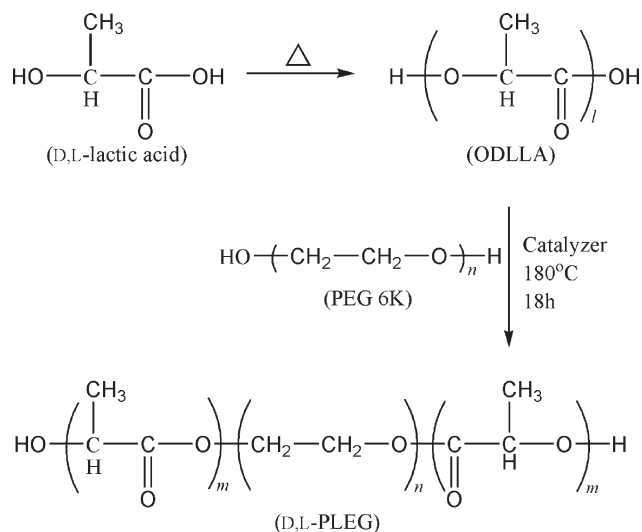


Figure 1 Synthesis of PLA-*b*-PEG-*b*-PLA copolymer by melt polycondensation.

The resulting copolymer was dissolved in acetone, precipitated in a mixture of methanol and distilled water ($v/v = 1 : 6$), and filtered, and then dried under vacuum.

Preparation of samples and irradiations

The prepared copolymer was dissolved in DCM, its content was 20 wt %. Then, the sample was treated to form the film with thickness of 48 μm by solution casting method. Finally, the film was dried in a vacuum oven at 40°C for 36 h.

The film samples were irradiated by a Curetron[®] EBC-200-AB-TW electron beam accelerator (NHV Corp., Japan). The accelerating voltage was 150 kV with a beam current of 5 mA. A transport system was used with a conveyor speed of 27 m min^{-1} . The dose rate was 20 kGy per pass. The irradiation doses of the samples were calculated by multiplying 20 kGy by the number of passes irradiated. The irradiations of the samples were performed at room temperature under the nitrogen atmosphere with the content of oxygen of less than 100 mg L^{-1} . Irradiated samples were kept in sealed packages at room temperature for at least a week to decay radicals completely and dried in vacuum before measuring the properties.

Characterization

FTIR spectra were measured on Thermo Nicolet 380 Fourier Transform Infrared Spectrometer (Thermo Electron Corp.) in KBr pellets at 4000–400 cm^{-1} in air atmosphere. The spectra profile was recorded by using OMNIC software supplied by Nicolet Instrument Corp.

$^1\text{H-NMR}$ spectra were recorded at room temperature using a 300 MHz Bruker spectrometer. CDCl_3 was used as the solvent; chemical shifts (δ) are given in ppm using tetramethylsilane (TMS) as an internal reference.

Molecular weights were determined by a Waters gel permeation chromatography (GPC). The analyzer was composed of a Waters 1515 isocratic HPLC pump and a Waters 2415 refractive index detector. Samples were dissolved in tetrahydrofuran (THF) at a concentration of 1 mg mL^{-1} . A Waters Styragel HT 4 THF column ($7.8 \text{ mm} \times 300 \text{ mm}$) with linear range of molecular weight from 5,000 to 600,000 g mol^{-1} was used in series with HPLC grade THF as eluent at a flow rate of 1.0 mL min^{-1} . The internal and column temperature were kept constant at 35°C . Calibration was accomplished with polystyrene standards. Molecular weight was determined by Empower 2 software.

According to ISO 1184, mechanical properties were analyzed with a KDIII-500 electron tensile testing machine (Shenzhen Kaiqiagli Testing Instruments Co., Ltd, China) at room temperature. The rectangular strip-shaped specimens were extended at a crosshead speed of 50 mm min^{-1} . The tensile property values represented an average of the results from tests run on three specimens. The data were analyzed with KPTest V4.0 controlling software supplied by Shenzhen Kaiqiagli Testing Instruments Co., Ltd.

Calorimetric studies were carried out on a DSC Q200 thermal analyzer (TA Instruments) by using nitrogen as a purge gas (50 mL min^{-1}) at scan rate of $10^\circ\text{C min}^{-1}$ from -10 to 160°C . The instrument was calibrated with an indium standard (melting temperature 156.6°C , $\Delta H_f = 28.45 \text{ J g}^{-1}$) and an empty pan was used as reference. The samples ($\sim 6 \text{ mg}$) were tested in hermetic TA aluminum pans. Thermograms were analyzed with Universal Analysis 2000 software (Version 4.4A, TA Instruments).

The thermal decomposition temperature was measured by using a TGA Q500 thermogravimetric analyzer (TA Instruments). The sample ($\sim 10 \text{ mg}$) was stacked in an open platinum sample pan, and the experiment was conducted under a nitrogen atmosphere (100 mL min^{-1}) at scan rate of $10^\circ\text{C min}^{-1}$ from 40 to 500°C . Thermograms were also analyzed with Universal Analysis 2000 software (Version 4.4A, TA Instruments).

RESULTS AND DISCUSSION

Composition of PLA-*b*-PEG-*b*-PLA

The FTIR spectrum of PLA-*b*-PEG-*b*-PLA is shown in Figure 2. An absorption band at 3502 cm^{-1} is representative of the terminal hydroxy group (OH). The

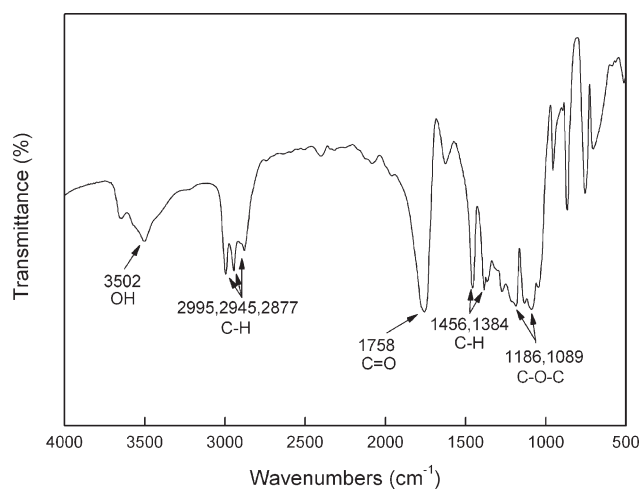


Figure 2 The FTIR spectra of PLA-*b*-PEG-*b*-PLA synthesized by melt polycondensation.

bands at $2995, 2945, 2877 \text{ cm}^{-1}$ and $1456, 1384 \text{ cm}^{-1}$ are attributed to the saturated C-H stretch in copolymer. The bands at 1186 and 1089 cm^{-1} are attributed to the (C-O-C) stretch in ester and ether groups. A strong absorbance is seen at 1758 cm^{-1} which confirms the presence of the ester via the (C=O) stretch. The typical $^1\text{H-NMR}$ spectrum of PLA-*b*-PEG-*b*-PLA is shown in Figure 3. The bands at 1.56 and 5.17 ppm are attributed to the methyl and methine protons of PLA blocks, respectively, whereas the band at 3.64 ppm is characteristic of main chain methylene in the PEG blocks. The existence of a covalent bond between PLA and PEG block is evident from a low-intensity multiplet at 4.25 ppm , which represents methylene protons of the acylated end unit of PEG chain ($-\text{CH}_2-\text{O}-\text{CO}-$).⁸ The number average molecular weight of PLA-*b*-PEG-*b*-PLA is $44,723$, and its polydispersity index (PDI) (M_w/M_n) is 1.76 as evaluated by GPC. These data indicate the feasibility of preparing well defined copolymer under controlled conditions.

Molecular weight of irradiated samples and degree of chain scission and crosslinking

A common phenomenon in radiation-induced processing of polymers is the scission of weaker bonds in macromolecules. The energy supplied by radiation is absorbed by exposed material and excited macromolecules are produced. The GPC plots for PLA-*b*-PEG-*b*-PLA samples under EB radiation are shown in Figure 4. The plots suggest several things regarding the irradiated samples. First, it can be seen that the retention time increases with increasing irradiation dose, which can indicate the reduction of molecular weight. Second, the GPC flow curve of pure PLA-*b*-PEG-*b*-PLA has a symmetrical peak.

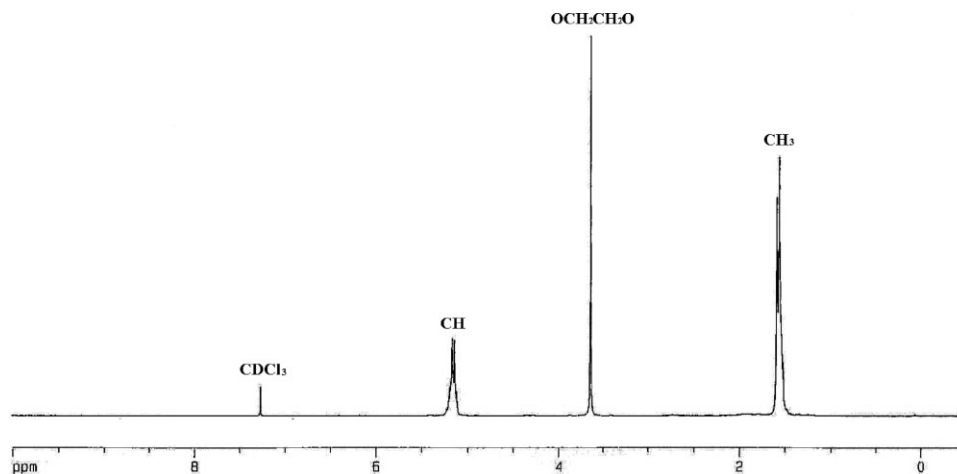


Figure 3 The $^1\text{H-NMR}$ spectra of PLA-*b*-PEG-*b*-PLA synthesized by melt polycondensation.

After EB radiation, a small shoulder on the low retention time side of the peak is observed, and it augments with increasing dose. This indicates an approximate increase in molecular weight because of the formation of a small amount of crosslinking between copolymer molecular chains. In addition, the peaks of irradiated samples become broader and asymmetric. This shows that crosslinking and chain scission occur simultaneously. Irradiation of PLA causes mainly chain scission at doses below 200 kGy, for higher doses, crosslinking reactions increase as a function of dose,¹⁸ and similar observations are made for copolymers of lactide glycolide and lactide ϵ -caprolactone.¹⁹ Although chain scission reactions of the irradiated PLA-*b*-PEG-*b*-PLA occur at doses of 0–100 kGy, its crosslinking reactions increase with increasing dose.

Figure 5 plots the number and weight average molecular weight (M_n and M_w) of the irradiated

samples against dose. The results show the decrease in average molecular weight with increasing dose. This indicates that chain scission is the dominant process upon EB radiation. It can also be observed that the extent of molecular weight decrease is not so drastic. It could be explained as following two different radiation-induced mechanisms. The decrease in molecular weight is due to backbone main chain scission, where some long polymeric backbone chains break into shorter chains, because the energy from the radiation exceeds the attractive forces between the atoms.²⁰ This happens because the excited states dissipate some of the excess energy by bond scission, resulting in the formations of alkyl free radicals in the polymer. Hydrogen abstraction is also a key radiation-induced scission mechanism. Because of a small quantity of oxygen diffuses into the polymer, the alkyl free radicals react with oxygen to form peroxy free radicals.^{21,22} These peroxy

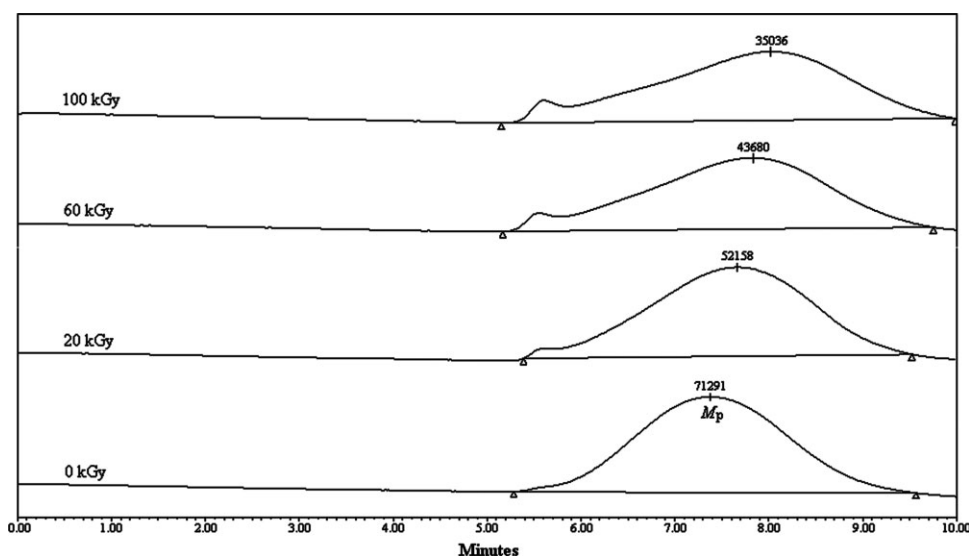


Figure 4 GPC plots of PLA-*b*-PEG-*b*-PLA samples irradiated at various doses.

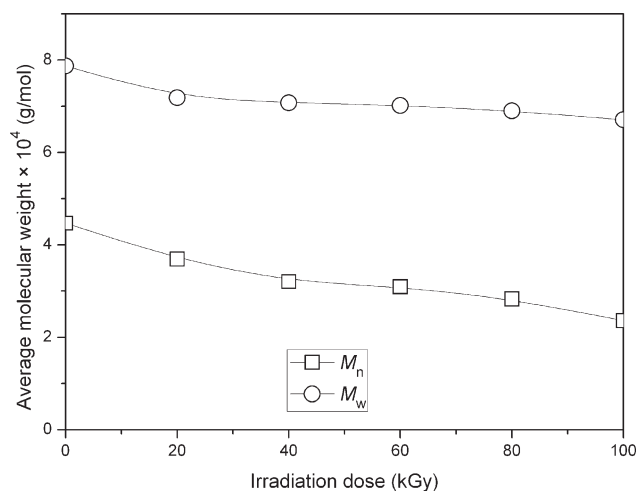


Figure 5 Number and weight average molecular weight (M_n and M_w respectively) of PLA-*b*-PEG-*b*-PLA as a function of irradiation dose.

free radicals thereby cause chain scission through hydrogen abstraction. Unlike main chain scission, in which a drastic decrease in molecular weight is observed, the decrease in molecular weight by chain scission through hydrogen abstraction is less pronounced. Another possibility is that there is a relative increase of crosslinking to chain scission, which can be confirmed from the GPC plots (see Fig. 4). The number of alkyl free radicals present is larger than the number of peroxy free radicals formed because of limited oxygen diffusion into the polymer. Alkyl free radicals are less effective in causing chain scission compared with peroxy free radicals, and they are more likely to recombine or crosslink in the polymer.

The $M_{n,0}/M_{n,t}$ ratio of molecular weight of the unirradiated sample ($M_{n,0}$) to molecular weight of the irradiated sample ($M_{n,t}$) shows the degree of degradation as a function of EB radiation (see Fig.

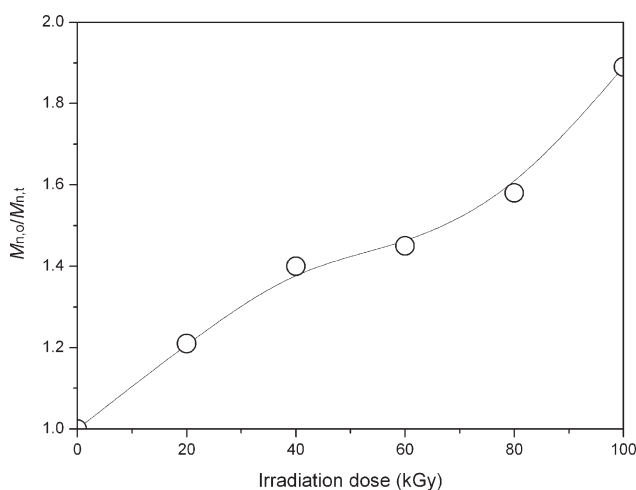


Figure 6 Plots of $M_{n,t}/M_{n,0}$ against irradiation dose.

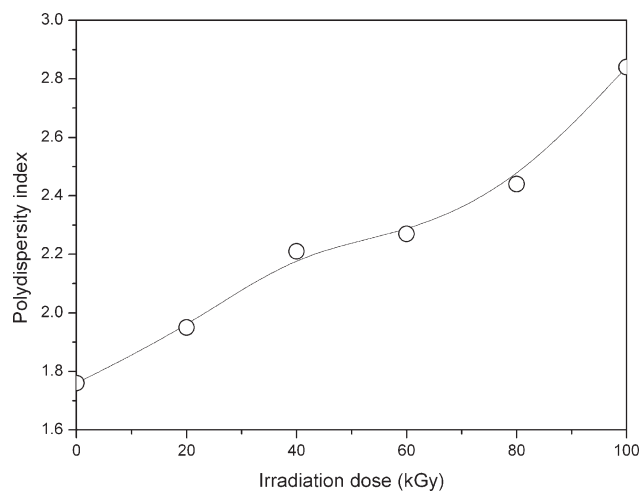


Figure 7 Change in the polydispersity indices of PLA-*b*-PEG-*b*-PLA as a function of irradiation dose.

6). The deviation of $M_{n,t}$ from $M_{n,0}$ implies that a proper degradation has occurred, which results in an increase of $M_{n,0}/M_{n,t}$ ratio. Figure 7 plots the polydispersity index of PLA-*b*-PEG-*b*-PLA against dose. The results show the increase in polydispersity index for polymer with increasing dose. This is due to the poorer chain uniformity resulting from chain branching. Chain branching arises from the crosslinking or recombination of free radicals. The high polydispersity index at 100 kGy indicates an extensive chain branching.

Ionizing radiation causes the formation and breaking of polymer bonds as a result of intermolecular crosslinking and scission in the polymer. The radiation chemical yields for chain scission (G_s) and crosslinking (G_x), which is defined as the number of such reactions per 100 electron volts of absorbed energy, therefore determines the extent of chain scission and crosslinking during irradiation. It can be calculated approximately from the following equations²³:

$$1/M_{w,t} = 1/M_{w,0} + (G_s/2 - 2G_x)D \times 1.038 \times 10^{-6} \quad (1)$$

$$1/M_{n,t} = 1/M_{n,0} + (G_s - G_x)D \times 1.038 \times 10^{-6} \quad (2)$$

where $M_{w,0}$ and $M_{n,0}$ are the weight and number average molecular weight of copolymer before irradiation. $M_{w,t}$ and $M_{n,t}$ are the number average molecular weight after irradiation. D is irradiation dose (kGy). A ratio of G_s/G_x greater than four would indicate that chain scission is more dominant.²⁴ The plots of $(1/M_{n,t}) - (1/M_{n,0})$ and $(1/M_{w,t}) - (1/M_{w,0})$ against D give linear relationships, as shown in Figure 8. From the slope of line (1.79×10^{-7} and 1.86×10^{-8} respectively). The values of G_s and G_x for irradiated PLA-*b*-PEG-*b*-PLA are obtained by using eqs. (1) and (2), and calculated as 0.213 and 0.043, respectively. The ratio of G_s/G_x is 4.95, which further illustrates the

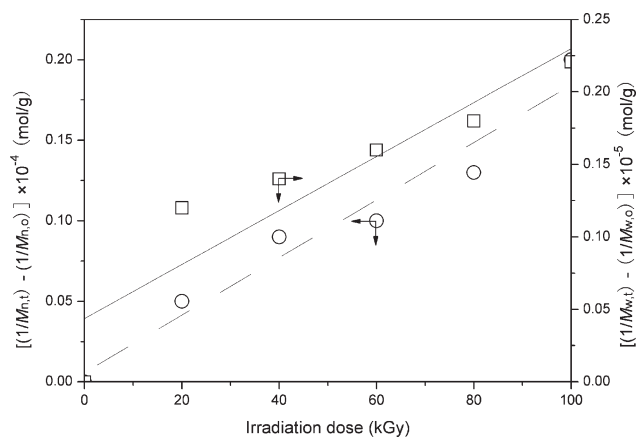


Figure 8 Plots of $1/M_{n,t} - 1/M_{n,0}$ and $1/M_{w,t} - 1/M_{w,0}$ against irradiation dose.

dominance of chain scission in irradiated sample. The G_s value of poly(L-lactic acid) (PLLA) irradiated in the same conditions have been reported to be 0.830,¹² which is larger than our result for PLA-*b*-PEG-*b*-PLA. The difference in G_s may be due to their different structure, and PLLA is more sensitive to radiation than PLA-*b*-PEG-*b*-PLA under nitrogen atmosphere.

When the reciprocal of number average molecular weight is plotted against dose, as required in the calculation for G_s and G_x , a strong linear sample correlation coefficient of 0.98 for PLA-*b*-PEG-*b*-PLA is obtained (see Fig. 8). This means that the decrease in number average molecular weight can be quantified accurately with respect to dose. Using this linear equation, the change in $M_{n,t}$ in terms of irradiation dose for this copolymer can be accurately written as

$$1/M_{n,t} = 1/M_{n,0} + (1.79D + 5.71) \times 10^{-7} \quad (3)$$

for irradiation doses from 0 to 100 kGy. The standard deviation (SD) of this estimate is 6.83×10^{-6}

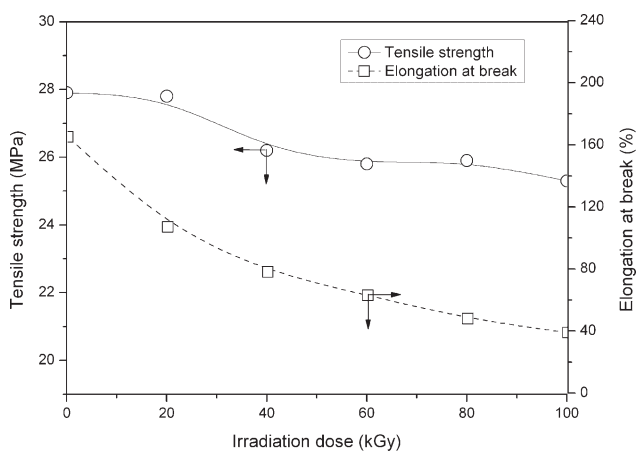


Figure 9 Plots of tensile strength and elongation at break of PLA-*b*-PEG-*b*-PLA samples against irradiation dose.

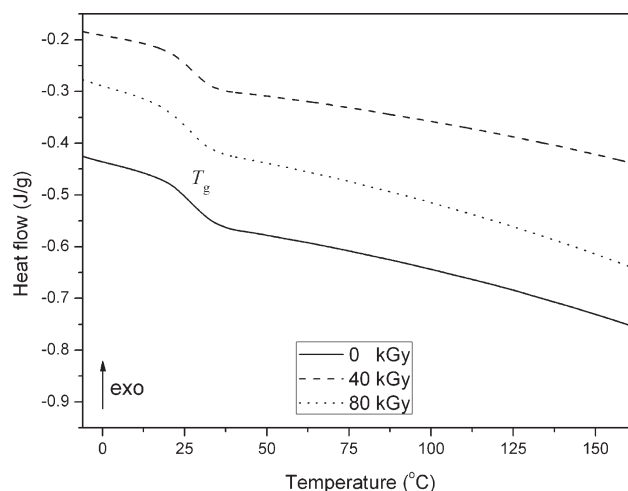


Figure 10 DSC heating curves of PLA-*b*-PEG-*b*-PLA irradiated at 0, 40, and 80 kGy.

mol g^{-1} . This equation will therefore allow for an accurate prediction of the resulting number average molecular weight after EB radiation.

Effects of irradiation on mechanical properties

The influence of irradiation on the mechanical properties of polymers differs widely depending on whether the polymer crosslinks or degrades. Radiation degradation almost always causes deterioration in the mechanical properties of polymers. EB radiation of poly(lactic acid) with a relatively high concentration of ester groups in the backbone is not result in crosslinking of the polymer, but it can be overcome by its copolymerization with the polymers which have a lower concentration of ester groups in the backbone.²⁵ Figure 9 shows the plots of tensile strength and elongation at break of PLA-*b*-PEG-*b*-PLA against dose. At doses from 0 to 100 kGy, the tensile strength decreases slightly from 27.9 MPa to 25.3 MPa. However, the elongation at break decreases sharply. This is attributed to the fact that the crosslinking to chain scission ratio for irradiated PLA-*b*-PEG-*b*-PLA aliphatic polyester increases as a function of increasing $-\text{CH}_2-$ to $-\text{COO}-$ ratio in the main chain.²⁶ The GPC flow curves of PLA-*b*-PEG-*b*-PLA under EB radiation also confirms this fact (see Fig. 4).

Thermal properties

The quantitative evaluation of thermal transitions of radiated PLA-*b*-PEG-*b*-PLA samples with various doses was investigated by DSC. Figure 10 shows the DSC heating curves of PLA-*b*-PEG-*b*-PLA. The unirradiated copolymer shows only a glass transition temperature ($T_g \sim 27^\circ\text{C}$), without any exothermic peak of crystallization and melting peak. Similar observations are made for PLA-*b*-PEG-*b*-PLA

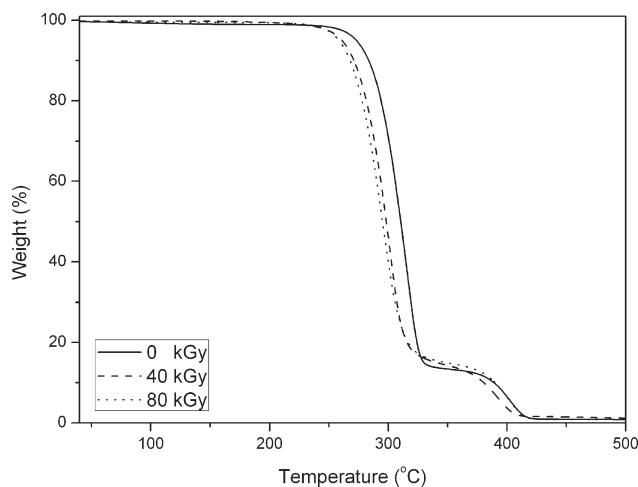


Figure 11 TGA curves of PLA-*b*-PEG-*b*-PLA irradiated at 0, 40, and 80 kGy.

irradiated at 40 and 80 kGy, and T_g is found to be $\sim 27.2^\circ\text{C}$ and $\sim 27^\circ\text{C}$, respectively. This means that EB radiation has little effect on T_g for this copolymer. It is due to the simultaneous occurrence of chain scission and crosslinking in copolymer chains, as shown in Figure 4. However, at doses below 100 kGy, there is an obvious decrease in T_g for PLA and PLGA due to the drastic decrease in their molecular weight.¹¹

The thermal stability of PLA-*b*-PEG-*b*-PLA was studied by TGA. The TGA profiles of copolymer irradiated at various doses are shown in Figure 11. It can be observed that all copolymer samples decompose in two stages. The first stage is probably due to the decomposition of copolymer molecular chains. The second degradation step involves the lactic acid and ethylene oxide segments and leads to complete polymer volatilization. It is also found that 5 and 10% weight loss temperature (T_5 and T_{10}) for unirradiated sample are 273°C and 284°C . After irradiation, T_5 and T_{10} decrease to 257°C and 267°C at 40 kGy, then to 254°C and 264°C at 80 kGy, respectively. It can be seen that EB radiation lowers the thermal stability of PLA-*b*-PEG-*b*-PLA. The decomposition temperature decreases with increasing dose because of the decrease in molecular weight.

CONCLUSIONS

PLA-*b*-PEG-*b*-PLA degrades through chain scission when exposed to EB radiation under nitrogen atmosphere. This causes a decrease in average molecular weights (M_n and M_w) and a relative increase in crosslinking with increasing dose. The radiation chemical yields for chain scission (G_s) and crosslinking (G_x) are 0.213 and 0.043, respectively. The decrease in molecular weight is observed to have a linear relationship with dose. The tensile strength of sample decreases slightly, while its elongation at break decreases sig-

nificantly. T_g is basically unchanged as a function of dose. Results of thermogravimetric analyses show that the thermal stability of PLA-*b*-PEG-*b*-PLA decreases with increasing dose.

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