

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

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ABSTRACT

This paper investigates the effects of electron beam irradiation on poly(D,L-lactic acid)-*b*-poly(ethylene glycol) copolymer (PLEG) and poly(L-lactic acid) (PLLA). The dominant effect of EB irradiation on both PLEG and PLLA is chain-scission. With increasing dose, recombination reactions or partial cross-linking of PLEG can occur in addition to chain-scission, but there is no obvious cross-linking for PLLA at doses below 200 kGy. The degree of chain-scission of irradiated PLEG and PLLA is calculated to be 0.213 and 0.403, respectively. The linear relationships are also established between the decrease in molecular weight with increasing dose. The present of poly(ethylene glycol) (PEG) chain segment in PLEG is the key factor in its greater stability to EB irradiation compared to PLLA.

Keywords: biopolymer; cross-linking; degradation; electron beam irradiation; molecular structure

1. Introduction

Biodegradable polymers have become of interest from the standpoints of pharmaceutical and biomedical applications as well as environmental application. Various properties such as good mechanical property, good biocompatibility, controlled degradability and good safety are desired for biodegradable medical materials¹. Poly(D,L-lactic acid)-*b*-poly(ethylene glycol) copolymer (PLEG) and poly(L-lactic acid) (PLLA) are the most widely utilized class of biodegradable and bioabsorbable polymers in the field of biomedical materials and have been used clinically in wound closure, tissue repair and regeneration and drug delivery²⁻⁵. PLEG and PLLA are both hydrolytically unstable. Although insoluble in water, they degrade by hydrolytic attack of their ester bonds. Through this hydrolytic attack, random chain scission

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occurs in the polymeric biomaterial, causing it to degrade into lactic and ethylene glycol for PLEG and lactic acid for PLLA. In human body, lactic and ethylene glycol enter the tri-carboxylic acid cycle and are metabolized and subsequently eliminated from the body as carbon dioxide and water. The rate of degradation of PLEG and PLLA is dependent on their degree of polymer morphology and their glass transition temperature⁶. Conventionally, the degradation rate for these biopolymers is controlled by altering such chemical parameters as comonomer ratio and polymer molecular weight using chemical synthesis method⁷⁻¹¹. However, this process is time-consuming, complexity of control and needs post-treatment.

Radiation has been known to alter the physical properties of polymers through main-chain scission and cross-linking. 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 cross-linking 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 polymers¹². Especially, Electron beam (EB) irradiation has been well known as a very convenient, efficient and environmental-friendly tool for modification of polymers through degradation technique. Besides, EB irradiation can cause in parallel sterilization of the materials¹³, which is very important for medical applications. Some people have studied the degradation behaviour of gamma irradiated PLLA, reporting that PLLA has a high sensitivity to gamma radiation, whose thermal and mechanical properties decrease significantly due to the drastic decrease in the molecular weight¹⁴⁻¹⁷. Recently, some studies report an approach to control the degradation rate of PLLA and poly(lactide-*co*-glycolide) (PLGA) using EB irradiation under air atmosphere^{6,12,18,19}. The results show that PLLA undergoes chain scission upon irradiation but to a lesser degree compared to PLGA, and PLLA is of greater stability to EB irradiation compared to PLGA. Meanwhile, the relationship between irradiation dose and the degradation rate is also established.

It is widely accepted that PLEG and PLLA undergoes hydrolytic degradation, but to our best knowledge, no investigation has been reported so far regarding the differences in the effects of EB irradiation on properties of PLEG and PLLA under nitrogen atmosphere. In this paper, average molecular weight (M_n and M_w) and molecular structure were measured as a function of irradiation dose. The radiation chemical yields for chain scission (G_s) and cross-linking (G_x) were evaluated, and the relationships between the molecular weight and irradiation dose were also established.

2. Experimental

2.1. Materials

Poly(L-lactic acid) (PLLA) was purchased from Shenzhen Brightchina Industry Co., Ltd. (China). Poly(D,L-lactic acid)-*b*-poly(ethylene glycol) copolymer (PLEG) was synthesized according to our reported method²⁰. Poly(ethylene glycol) with molecular weight 6000 (PEG6000) were purchased from Tianjin Bodi Chemical Co., Ltd. (China). Dichloromethane (DCM) was analytical grade and used without further purification.

The biopolymer films of PLLA and PLEG were prepared by a simple solvent casting method. PLLA and

PLEG were first dissolved in DCM at a weight ratio of 1:4. Then, the polymer solution was spread over a glass plate to give a wet film. The solvent was evaporated slowly in air at room temperature for 12 h to prevent the formation of air bubbles. Finally, The polymer films were dried in a vacuum oven at 40 °C for 36 h. The films were of approximately 50 μm in dry thickness.

2.2. Electron beam irradiations

The film samples were irradiated by a Curetron[®] EBC-200-AB-TW electron beam accelerator (NHV Corporation, 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.

2.3. Measurements

The intrinsic viscosity [η] was determined at a concentration of 0.125 g/dL in DCM at 30 °C using an Ubbelohde viscometer with capillary diameter of 0.38 mm (Shanghai Shenyi Glass Products Co., Ltd., China).

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 × 300 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 were determined by Empower 2 software.

Attenuated total reflection infrared (ATR-IR) spectra of films were measured on Thermo Nicolet 380 Fourier Transform Infrared Spectrometer (Thermo Electron Corporation) at 4000-400 cm⁻¹ in air atmosphere. The spectra profile was recorded by using OMNIC software supplied by Nicolet Instrument Corp.

¹H-NMR spectra were recorded at room temperature using a 300 MHz Bruker spectrometer. CDCl₃ was used as the solvent; chemical shifts (δ) are given in ppm using tetramethylsilane (TMS) as an internal reference.

3. Results and Discussion

3.1. Intrinsic viscosity of irradiated samples

The changes in intrinsic viscosity [η] of PLLA, PLEG and PEG6000 under EB irradiation are shown in Fig. 1. At doses from 0 to 100 kGy, the irradiation causes a drastic decrease in PLLA's [η] from 1.52 dL/g to 0.45 dL/g. However, a slight decrease in PLEG's [η] from 0.73 dL/g to 0.52 dL/g is observed. Meanwhile, it can be seen that PEG6000's [η] almost does not change as a function of EB irradiation. Therefore, PLEG has a better radiation resistance compared to PLLA mainly due to the PEG6000 chain

segment in PLEG.

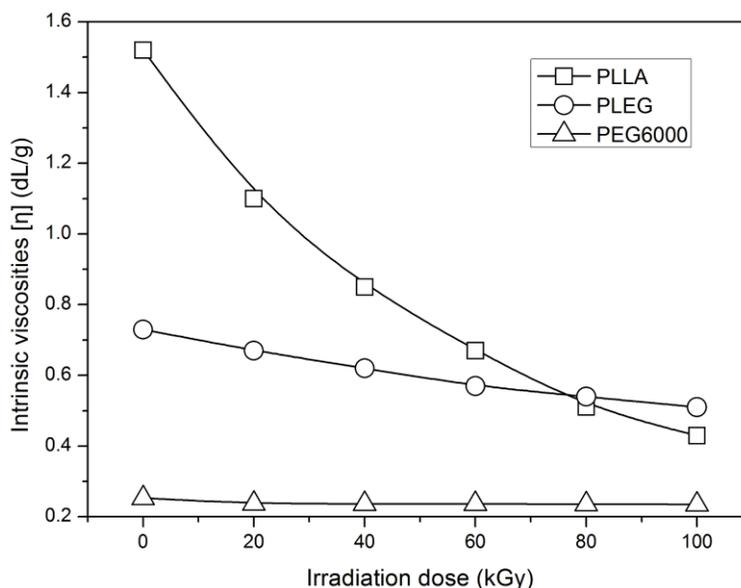


Fig. 1. The relationship of $[\eta]$ and irradiation dose.

3.2. Molecular weight of irradiated samples and degree of chain-scission and cross-linking

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 PLLA and PLEG samples under EB irradiation are shown in Fig. 2. The plots suggest several things regarding the irradiated samples. First, it can be seen that the retention time of irradiated PLEG and PLLA increases with increasing irradiation dose, which can indicate the reduction of molecular weight. Second, the GPC flow curve of PLEG has a symmetrical peak. After EB irradiation, a small shoulder on the low retention time side of the peak is observed at low dose of 20 kGy, and it augments with increasing dose. This indicates an approximate increase in molecular weight due to the formation of a small amount of cross-linking between PLEG molecular chains. However, for PLLA, no small shoulder on the low retention time side of the peak is observed at doses below 200 kGy. Therefore, irradiation of PLLA causes mainly chain-scission, for higher doses, cross-linking reactions can increase as a function of dose. Although chain-scission reactions of the irradiated PLEG occur at doses of 0-100 kGy, its cross-linking reactions increase with increasing dose. These results are consistent with the reported conclusion that the cross-linking to scission ratio for aliphatic polyesters increased upon irradiation as a function of increasing $-\text{CH}_2-$ to $-\text{COO}-$ ratios in the main chain²¹.

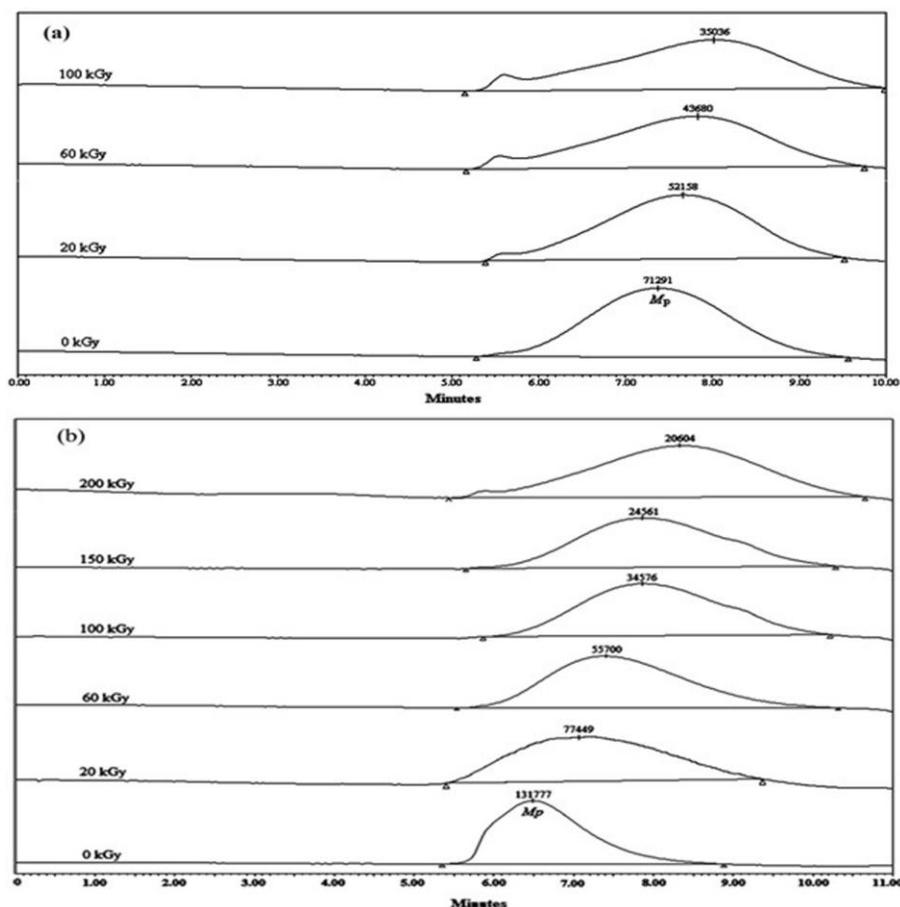


Fig. 2. GPC plots of samples irradiated at various doses, (a) PLEG, (b) PLLA.

Fig. 3a and Fig. 3b plots the number and weight average molecular weight (M_n and M_w) of the irradiated PLEG and PLLA against dose, respectively. The results show the decrease in average molecular weight with increasing dose. This indicates that chain scission is the dominant process upon EB irradiation. It can also be observed that the extent of molecular weight decrease of irradiated PLEG is not so drastic. However, a drastic decrease in molecular weight of irradiated PLEG is observed as a function of dose. These phenomena are accordance with the variation trends of $[\eta]$ in Fig. 1. 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 atoms²². 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. Due to a small quantity of oxygen diffuses into the polymer, the alkyl free radicals react with oxygen to form peroxy free radicals^{23,24}. These peroxy 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 cross-linking to chain scission, which can be confirmed from the GPC plots (see Fig. 2a). 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 to peroxy free radicals, and they are more likely to recombine or cross-link in the polymer. Meanwhile, compared to PLEG, PLLA is more prone to chain scission as a function of dose because of the relatively high concentration of ester groups in PLLA backbone²⁵.

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 irradiation (see Fig. 3c). 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. It can also be seen that the degree of degradation of PLLA is much more significant than that of PLEG. Fig. 3d plots the polydispersity index of PLEG and PLLA 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 scission and chain branching. Chain branching arises from the cross-linking or recombination of free radicals.

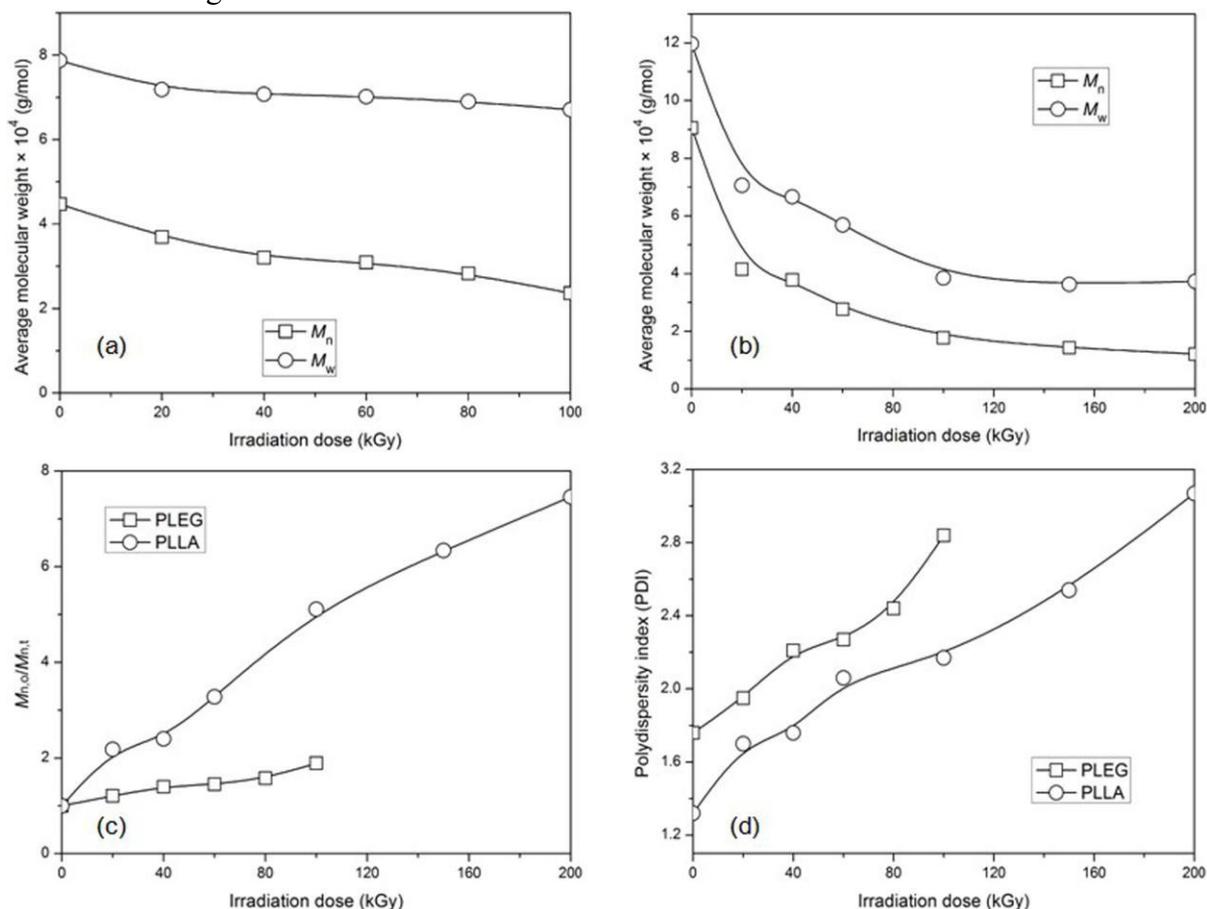


Fig. 3. Changes in the molecular weight and polydispersity indices (PDI) of samples as a function of irradiation dose, (a) molecular weight of PLEG, (b) molecular weight of PLLA, (c) $M_{n,0}/M_{n,t}$, (d) PDI.

Ionizing radiation causes the formation and breaking of polymer bonds as a result of intermolecular cross-linking and scission in the polymer. The radiation chemical yields for chain scission (G_s) and cross-linking (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 cross-linking during irradiation. It can be calculated approximately from the following equations²⁶:

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

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

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 4 would indicate that chain scission is more dominant²⁷.

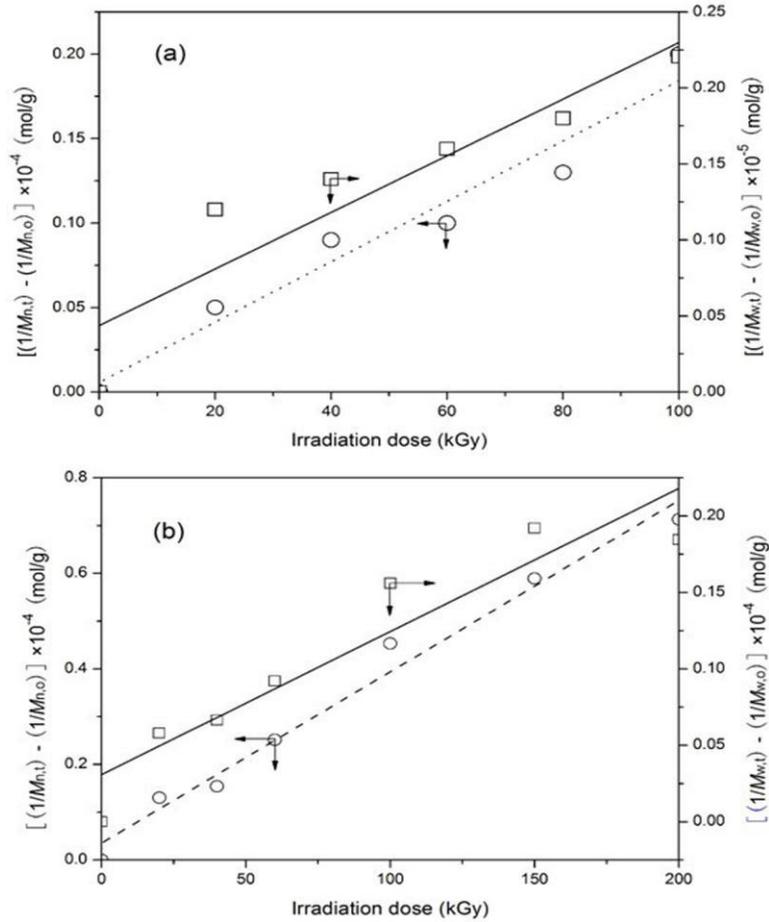


Fig. 4. Plots of $(1/M_{n,t}) - (1/M_{n,0})$ and $(1/M_{w,t}) - (1/M_{w,0})$ of PLEG and PLLA against irradiation dose, (a) PLEG, (b) PLLA.

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 Fig. 4. From the slope of line (1.79×10^{-7} and 1.86×10^{-8} respectively for PLEG, 3.59×10^{-7} and 9.36×10^{-8} respectively for PLLA). The values of G_s and G_x for irradiated PLEG and PLLA are obtained by using Eqs. (1) and (2), and tabulated in Table 1. The large G_s/G_x ratios, from Table 1, further illustrate the dominance of chain scission in irradiated PLEG and PLLA samples, and this thereby increases the solubility of these polymers in DCM after EB irradiation.

Table 1 Chain scission (G_s) and cross-link (G_x) radiation yields of EB irradiated PLEG and PLLA

Polymer	G_s	G_x	G_s/G_x
PLEG	0.213	0.043	4.95
PLLA	0.403	0.053	7.60

The ratio of G_s/G_x differs for PLEG and PLLA, as shown in Table 1. The results show that PLLA has a higher G_s/G_x ratio compared to PLEG, indicating that PLLA is more susceptible to EB irradiation degradation than PLEG under nitrogen atmosphere. This can be explained in terms of their different structure, since PLEG contains long PEG chain segment, which has the ability of radiation resistance as a function of dose (see Fig. 1). Therefore, this factor plays an important role in reducing the extent of EB degradation in PLEG.

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 and 0.99 for PLEG and PLLA respectively is obtained (see Fig. 4). 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. The equations obtained for PLEG (Eq. (3), 0-100 kGy) and PLLA (Eq. (4), 1-200 kGy) are:

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

$$1/M_{n,t} = 1/M_{n,0} + (0.36D + 3.54) \times 10^{-6} \quad (4)$$

The standard deviation (SD) of this estimate is $6.83 \times 10^{-6} \text{ mol g}^{-1}$ and $3.93 \times 10^{-6} \text{ mol g}^{-1}$ for PLEG and PLLA respectively. These equations will therefore allow for an accurate prediction of the resulting number average molecular weight after EB irradiation.

3.3. Structure analyses

Fig. 5 plots the % transmittance of infrared against the infrared frequency for samples. There are some distinctive differences in the ATR-IR spectra of PLEG and PLLA before and after EB irradiation. Irradiation results in the increase in peak intensity for peak 2880 cm^{-1} (PLEG) and $2872, 2942 \text{ cm}^{-1}$ (PLLA). The increase in peak intensity mainly corresponds to an increase in $-\text{CH}_2-$ and $-\text{CH}_3$ groups formed during irradiation.

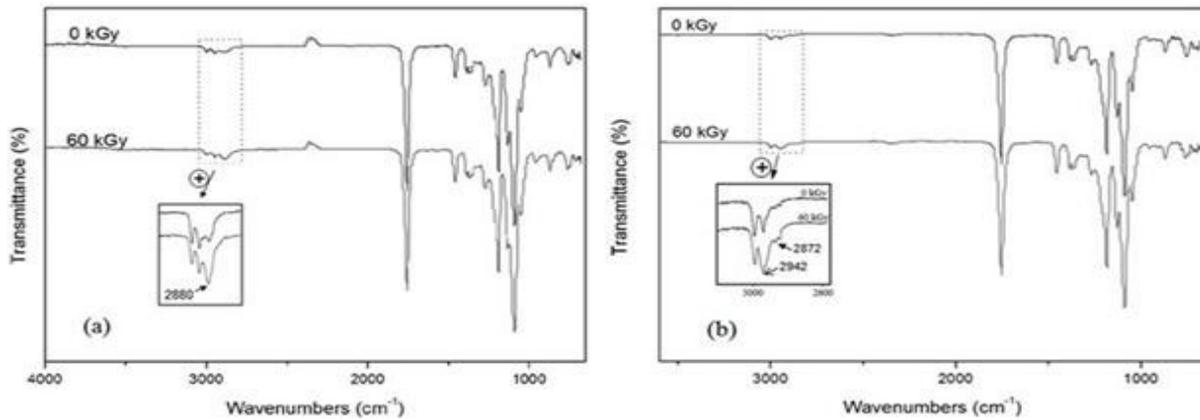


Fig. 5. ATR-IR spectra of samples before and after EB irradiation, (a) PLEG, (b) PLLA.

Fig. 6 plots the $^1\text{H-NMR}$ spectra of PLEG and PLLA irradiated at 60 kGy, which is found to be similar to the $^1\text{H-NMR}$ spectra of unirradiated samples. For PLEG, the bands at 1.56 and 5.17 ppm are attributed to the methyl and methane protons, 3.64 ppm is characteristic of main chain methylene in the PEG blocks. For PLLA, the signals of the methane bond and methyl group are located at 5.11 ppm and 1.50 ppm, respectively. The magnification of $^1\text{H-NMR}$ spectra of irradiated samples from 1.0 ppm to 2.8 ppm, where the only difference between the unirradiated samples and irradiated samples is observed. Each of the labeled peaks (a-g) indicates the formation of a new chemical bond formed during irradiation. Table 2 summarizes the possible chemical structures for each of these $^1\text{H-NMR}$ peaks, arising possibly due to free radical recombination¹². The proposed chemical structures have been reconfirmed with the $^1\text{H-NMR}$ simulation software ChemDraw Ultra 8.0 (CambridgeSoft Corporation) and the simulated ppm values are close matches to the actual $^1\text{H-NMR}$ peak ppm values.

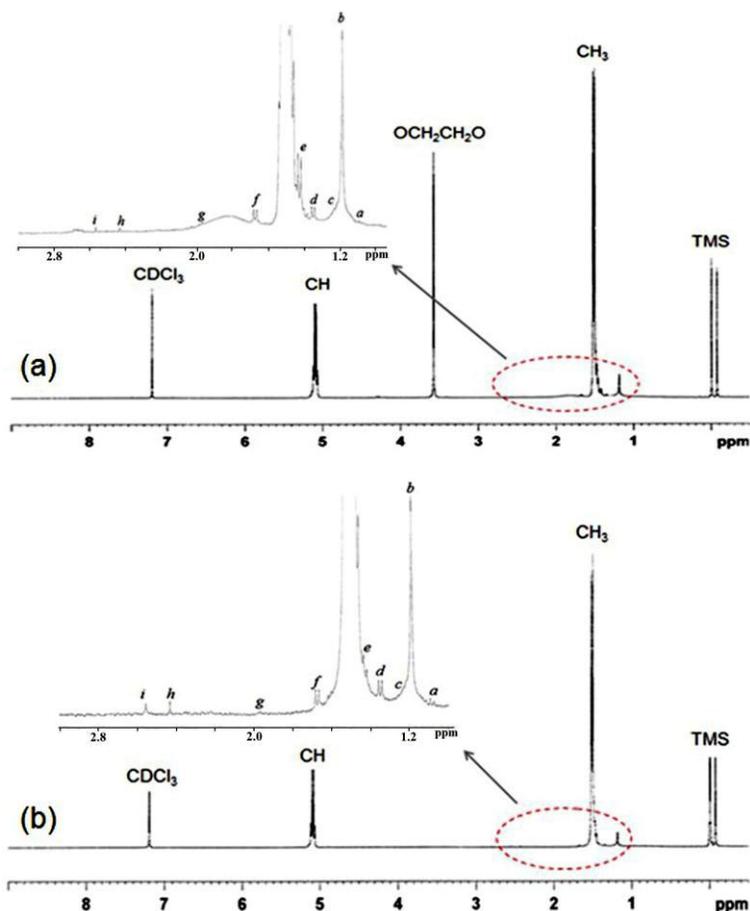


Fig. 6. $^1\text{H-NMR}$ spectrum of samples irradiated at 60 kGy, (a) PLEG, (b) PLLA.

Table 2 Identification of the possible chemical structures of the new peaks formed on the $^1\text{H-NMR}$.

Peak / δ (ppm)	Proposed structure
<i>a</i> / 1.10	$\begin{array}{c} \text{CH}_3 \\ \\ \text{H}-\text{C}-\text{O}- \\ \\ \text{H} \end{array} \quad / \quad \begin{array}{c} \text{CH}_3 \quad \text{O} \\ \quad \\ \text{H}-\text{C}-\text{C}-\text{O}- \\ \\ \text{H} \end{array}$
<i>b</i> / 1.19	$\begin{array}{c} \text{CH}_2 \quad \text{CH}_2 \quad \text{O} \\ \quad \quad \\ -\text{O}-\text{C}-\text{C}-\text{C}-\text{O}- \\ \quad \\ \text{H} \quad \text{CH}_2 \end{array} \quad / \quad \begin{array}{c} \text{H} \quad \text{H} \quad \text{O} \\ \quad \quad \\ -\text{O}-\text{C}-\text{C}-\text{C}-\text{O}- \\ \quad \\ \text{CH}_2 \quad \text{H} \end{array}$
<i>c</i> / 1.23	$\begin{array}{c} \text{CH}_3 \quad \text{H} \quad \text{O} \\ \quad \quad \\ -\text{O}-\text{C}-\text{C}-\text{C}-\text{O}- \\ \quad \\ \text{CH}_3 \quad \text{H} \end{array}$
<i>d</i> / 1.38	$\begin{array}{c} \text{CH}_3 \quad \text{CH}_2 \quad \text{O} \\ \quad \quad \\ -\text{O}-\text{C}-\text{C}-\text{C}-\text{O}- \\ \quad \\ \text{H} \quad \text{CH}_2 \end{array}$
<i>e</i> / 1.45	$\begin{array}{c} \text{CH}_2 \quad \text{O} \\ \quad \\ -\text{O}-\text{C}-\text{C}-\text{O}- \\ \\ \text{CH}_2 \end{array}$
<i>f</i> / 1.68	$\begin{array}{c} \text{OH} \quad \text{O} \\ \quad \\ -\text{O}-\text{C}-\text{C}-\text{O}- \\ \\ \text{CH}_2 \end{array}$
<i>g</i> / 1.95	$\begin{array}{c} \text{OH} \quad \text{O} \\ \quad \\ -\text{O}-\text{C}-\text{C}-\text{O}- \\ \\ \text{H} \end{array} \quad / \quad \begin{array}{c} \text{OH} \quad \text{O} \\ \quad \\ -\text{O}-\text{C}-\text{C}-\text{O}- \\ \\ \text{CH}_3 \end{array}$
<i>h</i> / 2.43	$\begin{array}{c} \text{CH}_3 \quad \text{H} \quad \text{O} \\ \quad \quad \\ -\text{O}-\text{C}-\text{C}-\text{C}-\text{O}- \\ \quad \\ \text{CH}_3 \quad \text{H} \end{array}$
<i>i</i> / 2.54	$\begin{array}{c} \text{H} \quad \text{H} \quad \text{O} \\ \quad \quad \\ -\text{O}-\text{C}-\text{C}-\text{C}-\text{O}- \\ \quad \\ \text{CH}_3 \quad \text{H} \end{array}$

4. Conclusion

PLEG and PLLA degrade through chain-scission when exposed to EB irradiation under nitrogen atmosphere. This causes a decrease in average molecular weight (M_n and M_w) of the biopolymers. With increasing dose, recombination reactions or partial cross-linking of PLEG can occur in addition to

chain-scission, but there is no obvious cross-linking for PLLA at doses below 200 kGy. The decrease in molecular weight is observed to have a linear relationship with dose. Compared to PLEG, PLLA is more susceptible to EB irradiation degradation, since PLEG contains long PEG chain segment, which has the ability of radiation resistance as a function of dose. ATR-IR and ¹H-NMR spectra indicate the formation of a new chemical bond during EB irradiation mainly due to the chain scission of lactic acid units in PLEG and PLLA backbone.

Acknowledgements

The authors would like to express their special appreciation to Sichuan Santai Gurui Enterprise Co., Ltd. (P. R. China) and Mr. Zhifu Huang for the ATR-IR and GPC measurements. This work was supported by International Cooperative Project with NHV Corporation (Grant No. 08H0783).

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