Degradation behavior of poly (l-lactide-co-glycolide) films through gamma-ray irradiation

Sun-Young Jo a, Jong-Seok Park a, Hui-Jeong Gwon a, Young-Min Shin a, Myung-Seob Khil b, Young-Chang Nho a, Youn-Mook Lim a,*

a Advanced Radiation Technology Institute, Korea Atomic Energy Research Institute, 1266 Sinjeong-dong, Jeongeup, Jeonbuk 580-185, Republic of Korea
b Department of Organic Materials and Fibers Engineering, Chonbuk National University, Jeonju 561-756, Republic of Korea

Article info

Article history:
Received 26 May 2011
Accepted 15 March 2012
Available online 24 April 2012

Keywords:
Gamma-ray
PLGA
Degradation
Chain scission

Abstract

Gamma-ray irradiation is a very useful tool to improve the physicochemical properties of various biodegradable polymers without the use of a heating and crosslinking agent. The purpose of this study was to investigate the degradation behavior of poly (l-lactide-co-glycolide) (PLGA) depending on the applied gamma-ray irradiation doses. PLGA films prepared through a solvent casting method were irradiated with gamma radiation at various irradiation doses. The irradiation was performed using 60Co gamma-ray doses of 25–500 kGy at a dose rate of 10 kGy/h. The degradation of irradiated films was observed through the main chain scission. Exposure to gamma radiation dropped the average molecular weight ($M_n$ and $M_w$), and weakened the mechanical strength. Thermograms of irradiated film show various changes of thermal properties in accordance with gamma-ray irradiation doses. Gamma-ray irradiation changes the morphology of the surface, and improves the wettability. In conclusion, gamma-ray irradiation will be a useful tool to control the rate of hydrolytic degradation of these PLGA films.

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1. Introduction

Polymer degradation generally occurs via a scission of the main or side polymer chains, and is induced through photodegradation, oxidation, or hydrolysis. The degradation of certain polymers takes place in biological environments including soil and water, as well as within the bodies of humans and animals. These polymers have been applied to various biomedical fields, e.g., drug delivery, gene delivery, and tissue engineering (Fugita, 2003). Recently used biodegradable polymers include polyesters, and their copolymers. Aliphatic polyesters of both natural and synthetic origins are among the biodegradable polymers that have been most intensively investigated (Garkhal et al., 2010; Shin et al., 2010; Lee et al., 2011).

Polyesters that include a hydrolysable ester bond in their backbone are considered the best biomaterials with regard to their design and performance. Polyesters are biocompatible, biodegradable, and non-toxic materials. Their products of degradation are also biocompatible and are eliminated from the body through either the respiratory or urinary systems. Polyesters degrade through a hydrolytic attack of the ester bond (Fugita, 2003; Lee et al., 2011).

Polymers are all hydrolytically unstable. In the case of PCL (poly(l-caprolactone)), while they are enzymatically degradable in earth environments, in living bodies, they are non-enzymatically degradable. Poly (l-lactic acid), on the other hand, is non-enzymatically degraded both in earth environments and in living bodies. Polymers degrade through a hydrolytic cleavage of their ester bonds. In the human body, lactic and glycolic acids enter Kreb’s cycle as hydrolysates and are metabolized. Afterwards, they are removed from the human body as carbon dioxide and water (Loo et al., 2004).

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Polystyrene polymers are all hydrolytically unstable. In the case of PCL (poly(l-caprolactone)), while they are enzymatically degradable in earth environments, in living bodies, they are non-enzymatically degradable. Poly (l-lactic acid), on the other hand, is non-enzymatically degraded both in earth environments and in living bodies. Polymers degrade through a hydrolytic cleavage of their ester bonds. In the human body, lactic and glycolic acids enter Kreb’s cycle as hydrolysates and are metabolized. Afterwards, they are removed from the human body as carbon dioxide and water (Loo et al., 2004).

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such as cations, anions and radicals, can react with one another, or are able to initiate further reactions among the polymeric chains, thus giving rise to changes in material properties. As a consequence, cross-linking reactions or the chain scission through the breaking of chemical bonds can occur, depending on the radiation dose. In general, aromatic polymers are more resistant to sterilization by high-energy radiation than aliphatic polymers, while the presence of impurities and additives may enhance degradation and/or crosslinking (Suljovruji et al., 2003).

The responses of biodegradable aliphatic polyester to radiation depend on the presence or absence of methyl side group. Main chain scission occurs predominantly by the irradiation of poly (hydroxy buthylate) (PHB) (Mitomo et al., 1995) and PLLA (Pramono et al., 2001) that have methyl groups. While, polyesters such as poly (ε -caprolactone) (PCL) (Darmawan et al., 1998) and poly (butylene succinate) (PBS) (Song et al., 2001) that have no methyl group are radiation crosslinkable. The degradation rate of polymeric biomaterials due to γ-ray irradiation is linked to radical formation (Martinez-Sncho et al., 2004).

The aim of this work was to investigate the effects of gamma-ray irradiation on poly (l-lactide-co-glycolide) (PLGA), including hydrophilicity, mechanical strength, chemical composition and surface morphology.

2. Experimental

2.1. Materials

Biodegradable polymers, Poly (l-lactide-co-glycolide) (PLGA 85/15), was purchased from RESOMER® (Boehringer Ingelheim Pharma GmbH &Co.KG, Germany) (Fig. 1). Chloroform (CHCl3, Showa Co. Ltd., Japan) was selected as a solvent.

2.2. Preparation of the polymer films

Polymer films were prepared using a solution casting method. PLGA (2 wt%) was dissolved in chloroform which was used as a solvent. The polymer solutions were then casted onto a well-cleaned glass plate. After solvent evaporation in air at room temperature, the films were separated from the glass plates and dried in a vacuum oven at room temperature, for 24 h. For gamma-ray irradiation, the prepared films were packed in aluminum sealing bag with nitrogen gas. The gamma-ray irradiation was carried out using a 60Co source (MDS Nordion, Canada, IR 221) at a dose rate of 10 kGy/h. For the preparation of the films, the gamma-ray irradiation were measured at room temperature, for 24 h. For gamma-ray irradiation, the prepared films were packed in aluminum sealing bag with nitrogen gas. The gamma-ray irradiation was carried out using a 60Co source (MDS Nordion, Canada, IR 221) at a dose rate of 10 kGy/h. The second run heating was observed for these samples from –50 to 250 °C.

2.3. ATR-FTIR measurement

ATR spectra for biodegradable polymers irradiated with gamma-ray were obtained using an ATR-FTIR spectrophotometer (Bruker TEMSOR37, Bruker AXS, Inc., Germany). The spectra were measured in the region of 500–4000 cm⁻¹ at a resolution of 4 cm⁻¹ in the ATR mode.

2.4. Thermal properties

The thermal properties of the polymer films were recorded through a difference scanning calorimetry (DSC). DSC thermograms of the obtained films were measured using a DSC Q100 TA instrument in the temperature range from –50 to 250 °C in a nitrogen atmosphere; the heating rate was 5 °C/min. Then, the sample pans were cooled at room temperature. The second run heating was observed for these samples from –50 to 250 °C.

2.5. Average molecular weight

Molecular weights were determined using a gel permeation chromatography (GPC, PL-GPC110, Polymer Laboratories Ltd., UK) equipped with columns of PL gel Guard column 5 μm, PL gel 10 μm Mixed B and PL gel 5 μm 10,000 A (Polymer Laboratories Ltd., UK) calibrated with polystyrene. Chloroform was used as a mobile phase at a flow rate of 1.0 ml/min at 40 °C. Variation in molecular weight is related to the radiation yields of crosslinking (Gc) and chain scission (Gs), which determines the extent of chain scission or crosslinking during gamma-ray irradiation, and can be calculated from the following equations (Sen et al., 2003):

\[
\frac{1}{M_w} = \frac{1}{M_{w,0}} + \left(\frac{G_s}{2 - 2G_s}\right)D_\gamma 1.038 \times 10^{-6}
\]

\[
\frac{1}{M_n} = \frac{1}{M_{n,0}} + \left(\frac{G_s - G_c}{2 - 2G_c}\right)D_\gamma 1.038 \times 10^{-6}
\]

where \(M_{w,0}\) and \(M_{n,0}\) are the molecular weight and number of average molecular weight of unirradiated films, respectively. \(M_w\) and \(M_n\) are the corresponding values following exposure to irradiation dose, \(D_\gamma\) (unit: kGy). A \(G_s/G_c\) ratio of greater than 4 would indicate that chain scission is more prominent (Sen et al., 2003). Eq. (1) can be applied for any initial molecular weight distribution of the polymer, but Eq. (2) can only be applied for an initial most probable distribution (\(M_{w,0}/M_{n,0}\) of the used PLGA is about 1.3, obtained G values by these equations are approximated values.

2.6. Mechanical properties

The mechanical properties of the films were measured based on ASTM D 882 using a Universal Tensile Machine (Instron Model-4443). All films had a gage length of 31.8 mm, width of 5.3 mm and different thicknesses of 30–40 μm, and were stretched at a crosshead speed of 50 mm/min.

2.7. Surface characterization

The surface morphology of the prepared samples was first examined using a field-emission scanning electron microscope (Jeol JSM-6390, Jeol Ltd., Japan). The film pieces were coated with a 40–50 nm layer of gold using a metal ionizer (Jeol FineCoat Sputter JFC-1100, Jeol Ltd., Akishima, Japan), allowing surface and cross-section visualization. All the samples were examined at an accelerating voltage of 1 kV. The contact angles of tap on the polymer film surfaces after gamma-ray irradiation were measured at room temperature using a contact-angle meter (Phoenix-300, Surface electro optics Ltd., Korea).
3. Results and discussion

3.1. ATR-FTIR

ATR-FTIR spectra of PLCL are plotted in Fig. 2. The characteristic bands for ester carbonyl stretching (C=O) at 1747 cm\(^{-1}\), C–O stretching at 1128 cm\(^{-1}\), and the C–O–C group at 1082 cm\(^{-1}\) were found for unirradiated PLGA and the different irradiation films (Jose et al., 2009). The IR spectra did not demonstrate any significance in the gamma-ray irradiated films because the IR spectra of polyesters are inherently broad and weak, and it is very hard to detect minor chemical changes occurring on the polymer chain. Although the effects of gamma-ray irradiation on polyesters are well known, gamma-ray irradiation as evaluated by the IR spectra did not cause a significant degradation in the polyester.

3.2. Scanning electron microscopy (SEM) analysis

As shown in Fig. 3, SEM images of the PLGA films describe changes in surface morphology depending on the gamma-ray irradiation. The morphological changes indicate a superficial degradation that affects the surface roughness. It can be seen that a non-irradiated film has a smooth surface (Fig. 3a). The appearance of globules formed on the irradiated film surfaces can also be seen in Fig. 3 (c–f for 50–500 kGy). When the PLGA films were irradiated with \(\gamma\)-rays, it was observed that the globules appeared from a dose amount of 50 kGy (Fig. 3c). The average size of the globules for 50 kGy irradiated PLGA film is 0.1 \(\mu\text{m}\), which slightly increases with gamma-ray irradiation of about 0.3 \(\mu\text{m}\). This is probably due to the formation of new crystallites consisting of low molecular weight PLGA formed by main chain scissions, by the similar mechanism of the radiation induced crystallization of polytetrafluoroethylene (PTFE) (Bhateja et al., 1995).

3.3. Water contact angle

The results of water contact angle measurements are described in Fig. 4. The wettability of all of the samples improved following gamma-ray irradiation. The water contact angle of the films is dependent on the gamma-ray irradiation. The contact angle of unirradiated PLGA is about 74°, which indicates a hydrophobic material. After irradiation, the water contact angle decreased to 44°. Gamma-ray irradiation shows a drastic variation in the PLGA surface. It seems it is due to the changes in surface morphology rather than the changes in chemical structure of PLGA by gamma-ray irradiation, because there is no indication of the formation of hydrophilic groups as
shown in Fig. 2. While the irradiation causes significant enhancement of surface roughness of PLGA as explained earlier, the newly formed crystallites increase the surface roughness and surface energy. There is a relationship between contact angle and the surface roughness as expressed in Eq. (3).

$$\cos \theta = R \cos \theta$$  \hspace{1cm} (3)

where $\theta$ is the contact angle of the original smooth surface (about 74°) and $R$ is the surface roughness factor (Wenzel, 1936). Thus, $\theta$ decreases with increasing surface roughness. Consequently, gamma-ray irradiation enhances wettability of PLGA.

3.4. Thermal analysis

A chain scission due to gamma-ray irradiation results in variations in the physical properties of PLGA. Fig. 5 shows the DSC thermograms for PLGA films irradiated by gamma-rays. The thermogram of the PLGA before irradiation shows a glass transition ($T_g$) and melting peaks ($T_m$), whereas after irradiation it shows additional cold crystallization ($T_c$) and displays two distinctly separate $T_m$ peaks. The formation of the two $T_m$ peaks in PLGA is due to the structural changes in the PLGA chains by irradiation. The degree of crystallinity of the original unirradiated PLGA is low because it is a high molecular weight ($M_w$: 962,800) copolymer. Thus, the $T_c$ of the unirradiated PLGA is unclear. The reduction of molecular weight by irradiation facilitates crystallization, resulting in the increased crystallinity and clear $T_c$. The formation of the two $T_m$ peaks by irradiation is also caused by the reduction of molecular weight. The simultaneous main chain scissions of PLGA chains occur in the crystal region and amorphous regions with the same probabilities per unit molecular weight. The molecular weights of PLGA chains in the amorphous regions are higher than those of the crystal region because the high molecular weight polymers are hard to crystallize compared with the lower molecular weight polymers. The decomposed lower molecular weight polymers in amorphous regions crystallize to form new crystalline regions as explained earlier. Thus, two crystalline regions are found after irradiation, the original crystallites and the newly formed crystallites. The molecular weight of the latter is higher than that of the former due to higher molecular weight of the original PLGA in the amorphous regions. It is well known that the $T_m$ of polymer decreases with decreasing number of average molecular weight (Mn) of the polymer in crystal Nielsen, (1962). Thus, the two $T_m$ peaks are observed in the irradiated PLGA thermogram, $T_m$ and $T_c$ decrease with increasing irradiation dose due to the decreasing molecular weight with dose.

3.5. Molecular weight measurement

The changes in average molecular weight ($M_w$ and $M_n$) of PLGA by the irradiation are given in Fig. 6. As shown in Fig. 6, the molecular weight decreases with an increasing radiation dose due to the main-chain scission of the PLGA by the irradiation.

A large $G_s/G_x$ value ($G_s/G_x = 34.667$), from Table 1, indicates that the extent of main-chain scission is predominant in irradiated PLGA films. The $G_s$ and $G_x$ tend to decrease with increasing irradiation dose.
3.6. Mechanical strength

Fig. 7 shows the mechanical properties of the PLGA films both before and after irradiation. Unlike an unirradiated PLGA film, the tensile strength and Young’s modulus of the irradiated films decrease with an increase in irradiation dose due to the main chain scission of PLGA chains in the amorphous regions. These are generally observed in the radiation degradation of polymers such as PTFE and polypropylene.

4. Conclusion

PLGA degradation through chain scission depending on the amount of gamma-ray irradiation doses was investigated. The main degradation mechanisms seem to be a main chain scission in the backbone. These results led to a decrease in the average molecular weight ($M_n$ and $M_w$), and therefore a decrease in the $T_c$ and $T_m$ of the PLGA. They also lead to the lower mechanical strength of PLGA. The $G_s$ and $G_x$ tend to decrease with increasing irradiation dose. The $G_s/G_x$ value through molecular weight confirmed that the chain scission is superior to the crosslinking during gamma-ray irradiation. Since the main-chain scission of PLGA by gamma-ray irradiation increases causes the formation of crystallites that alters the morphological properties of the surface, resulting in the enhancement of the wettability of PLGA increases the obtained measurements of the water contact angle. In conclusion, gamma-ray irradiation can therefore be a potential tool to control the rate of hydrolytic degradation of these biopolymers.

Acknowledgments

This work was supported by Nuclear R&D program through the Korea Science and Engineering Foundation funded by the Ministry of Education, Science and Technology, Korea.

References


