RADIATION STABILITY OF BIODEGRADABLE LACTIC ACID POLYMERS

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INTRODUCTION

Polylactic acid was the first synthetic absorbable polymer found suitable for biomedical applications. Homo polymers and copolymers of lactic acid are known to be biologically active compounds and are widely used in medicine, dentistry, pharmacy, etc., because of biocompatibility and biodegradability. For this purpose, extensive studies of the physicochemical characterization of poly(L-Lactic acid) (PLLA) and poly(D,L-lactic acid (PDLLA) for biomedical applications have been carried out. One prerequisite for the use of biomaterials is proper sterilization. This may be defined as many process which results in total destruction of all forms of microbial organism (bacteria and spores). Usage of energy irradiation has emerged as the preferred method due to high efficiency, negligible thermal effect and because article may be packaged and sealed before sterilization due to the deep penetration of high energy irradiation. PLLA and PDLLA are hydrolytically unstable and do not withstand to humid heat. It is therefore known that the most suitable sterilization method is high energy irradiation (γ-rays, electron beams) for biomaterials made of this polymer[1]. A promising means of sterilization is provided by gamma-irradiation which, however, is known to induce structural changes such as scission and crosslinking in irradiated polymers. The extend of radiation induced changes are modified by environmental conditions and it may be possible to negate the irradiation damage by the use of appropriate conditions during irradiation.

Much attention has been directed in recent years to thermal and hydrolytical stability and scope of lactic acid polymers by many workers[2-4] and in the radiation sterilization studies, it is found that undergo main random chain scission[1,5]. In our study, radicals produced during irradiation terminate by recombination, and an equation for variation of the second order rate constant with time derived by Plonka gives the best fit[6]. However, there is no so much information on the radiation induced crystallinity damage of lactic acid polymers. Thus it was considered to be some interest to study the effects of radiation on the crystallinity damaged of semi-crystalline PLLA.

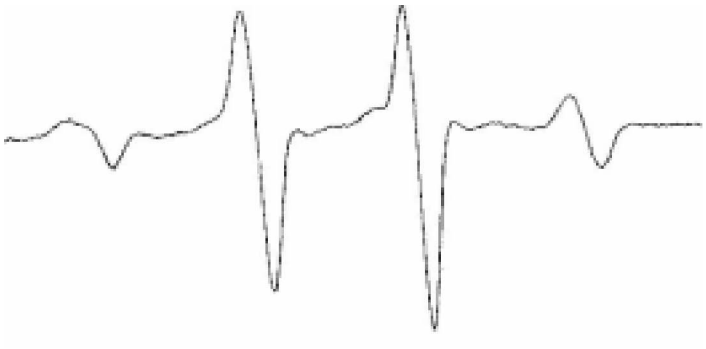
EXPERIMENTAL

Semi-crystalline poly(L-lactic acid) (PLLA) (M_n=31,600, M_w=52,000) and amorphous poly(D,L-lactic acid) (PDLLA) (M_n=22,900, M_w=33,600) which are used in this study was supplied from Sandoz Pharma. Thermal analysis of polymer samples were carried out under dynamic conditions; 20 mL/min of flow rated nitrogen gas at 20 °C/min as optimum heating rate[7] using a Du Pont DSC-910 module equipped with TA-9900 data acquisition system. SAXS diffractograms were obtained under 30 kV, 45 mA conditions by means of a Rotaflex 18 kW rotating anode source using a Rigaku SAXS. ESR spectra have been recorded with a varian E-L 9" X-band spectrometer equipped with a V-4532 dual sample cavity at a power of 4 mW with 100 kHz modulation. The relative peak intensity and g-factor of radicals have been adjusted by using strong pitch (g=2.0028). Poly(L-lactic acid) (PLLA) powder samples were irradiated in air and vacuum (10^{-7} torr) to 10, 25, 50 and 80 kGy at room temperature and at dose rate 0.59 kGy/h by cobalt 60 gamma rays. The irradiated polymer samples were analyzed by differential scanning calorimeter (DSC) and small angle x-ray spectrometer (SAXS) to follow the change in crystallinity, crystalline and melting enthalpy values of PLLA and to better understand the physical effects of radiation on semi-crystalline PLLA. Lactic acid polymers were also contacted with ESR analysis to follow the radical kinetic and to identify the radical species generated by gamma rays.

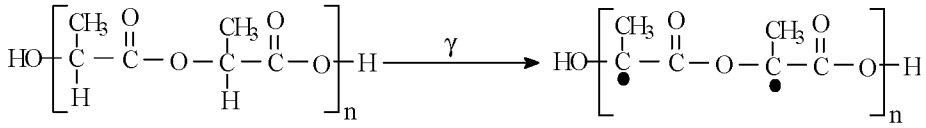
RESULTS AND DISCUSSIONS

The typical ESR spectra of PLLA and PDLLA samples irradiated in vacuum and recorded in vacuum are shown in Figure 1. The radical given rise to these spectra are assumed to be due to the following structures.

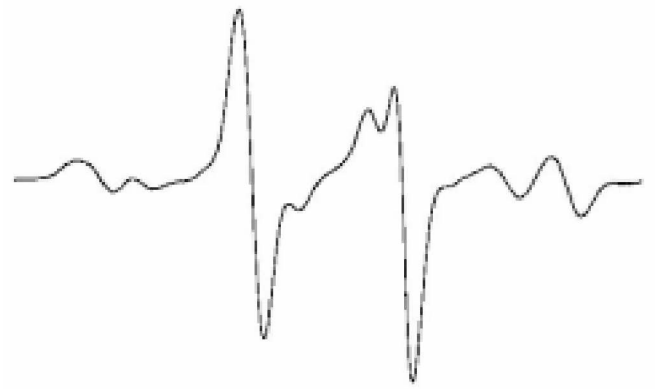
The possible radical was found as ~[C•(CH3)COO]~ for PLLA and PDLLA. And also radical location was found that one of the nearest radical was on the upper and the other one was on the lower plane of PDLLA. This difference in radical location was assumed to be the reason of the splitting and hiperfine splitting value difference between PLLA and PDLLA. The decay of bulk irradiated lactic acid polymers is best described by the non-classical second-order equation with time-dependent rate constant.



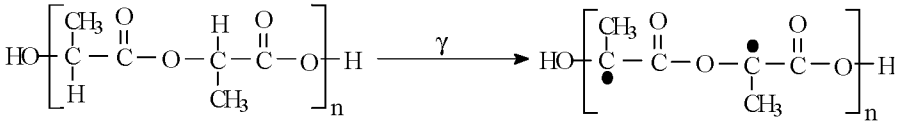
PLLA



PLLA PLLA



PDLLA



PDLLA PDLLA

Figure 1. ESR spectra and possible radical species of PLLA and PDLLA.

In order to determine the effect of radiation on the crystallinity, small angle x-ray and differential scanning calorimetric analysis were made. SAXS diffractogram and DSC thermogram of semi crystalline PLLA are shown in Figure 2 and 3, respectively.

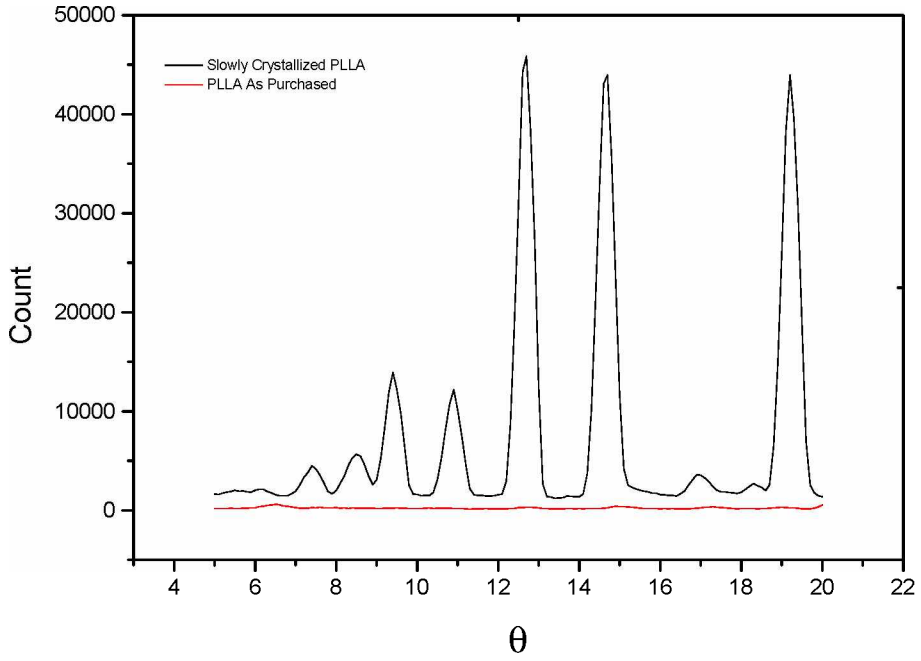


Figure 2. SAXS diffractogram of fully crystallized and original PLLA sample.

As It's seen in Figure 3, by conducting of polymers with gamma rays, some changes on the heat properties were observed. One of the properties is the glass transition temperatures (T_g) were determined for PLLA irradiated to various doses (0, 10, 25, 50 and 80 kGy) in air and vacuum. T_g was found to be 58 °C and 60 °C for samples irradiated in air and vacuum, respectively. And it was also found that it was independent of dose within the interval studies. On the other hand, a decrease is seen in crystallization and melting enthalpy values with increasing dose. The samples analyzed after irradiation showed no significant changes in both the crystalline melting temperature (T_m) and the glass transition temperature (T_g). This is attributed to the morphology of a semi-crystalline PLLA. The morphology of partially crystalline PLLA is usually composed of all three types of micro-conformations (crystalline, amorphous arising from chain-fold). T_g value can be only measured for PDLLA by DSC, due to the amorphous structure of PDLLA and found to be °44 C for air and vacuum irradiated samples.

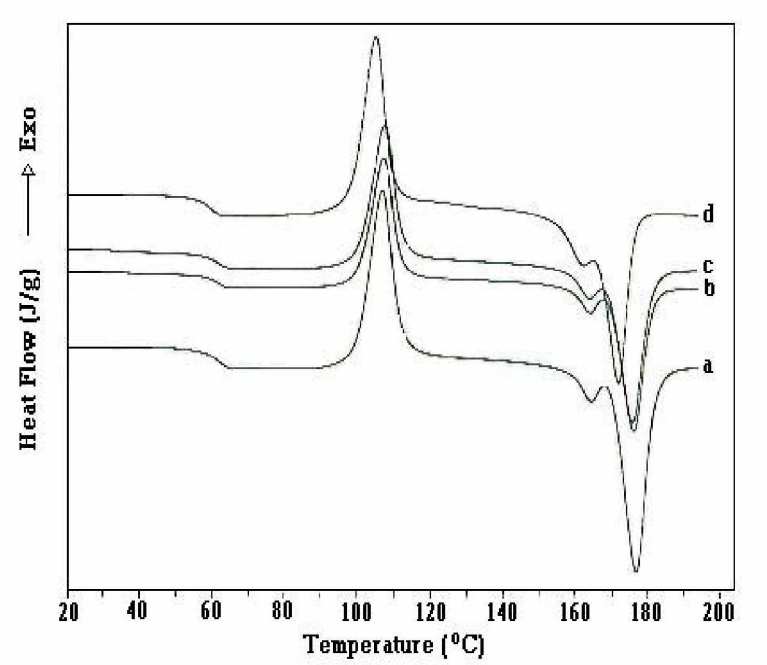


Figure 3. DSC thermograms of PLLA samples irradiated to (a) 0, (b) 10, (c) 25 and (d) 80 kGy in vacuum.

During the re-crystallization process, PLLA chains well organized. This sample analyzed by SAXS and observed that the sample was fully crystallized (Figure 2). Then DSC thermogram of this sample was taken over above mentioned temperature interval and it was found to be 75.57 J/g.

In this equation, ΔH_{ir}, ΔH_{100} denote the crystallization enthalpy values of irradiated sample and

$$\%Crystallinity = \frac{\Delta H_{ir}}{\Delta H_{100}} x100 \quad \text{.....(1)}$$

that of fully crystallized sample, respectively.

Fraction of undamaged units in the crystalline region (X) by radiation is determined from these crystallinity values. This fraction is simply equal to

$$X = \chi_{cf} / \chi_{co} \quad \text{.....(2)}$$

where, χ_{co} and χ_{cf} represent the percent crystallinity of unirradiated and irradiated samples,

$$G(-u) = \frac{(1-X)}{D} \frac{N}{M} \frac{10^2}{6x10^{18}} \quad \text{.....(3)}$$

respectively. The number of units of polymer damaged in crystalline region (G(-u)) per 100 eV of energy absorption can be calculated by using following equation[9].

In this equation, N, M and D denote the Avogadro's number, the molecular weight of repeating unit and the dose in terms of kGy respectively and $6x10^{18}$ corresponds to the conversion factor of kGy to eV. In plotting of the graph versus (1-X) to D, slopes are proportional to the damage in crystalline regions, account of amorphous regions must be made.

The fraction of damaged units of irradiated samples in air and vacuum were plotted versus the dose. The slope of straight-line gives G(-u) value according to equation 3. The slopes were calculated as $5.3x10^{-6}$ and $4.2x10^{-6}$ for PLLA irradiated in vacuum and air, respectively. Then G(-u) values were found to be 0.74 and 0.58 for PLLA irradiated in vacuum and air, respectively. As the thermogram obtained in the scanning of irradiated PLLA samples showed that the crystallinity of the formed crystals were not effected significantly by 100 eV energy absorption, these main chain scissions would occur equally in the amorphous and crystallization regions of the polymer.

CONCLUSION

The possible radical was found as ~[C•(CH3)COO]~ for PLLA and PDLLA. And also radical location was found that one of the nearest radicals was on the upper and the other one was on the lower plane of PDLLA. This differences in radical location was assumed to be the reason of the splitting and hiperfine splitting value difference between PLLA and PDLLA. The decay of bulk irradiated lactic acid polymers is best described by the non-classical second-order equation with time-dependent rate constant.

The glass transition temperature (T_g) of L-lactic acid polymers irradiated to various doses in air and vacuum have been found that it is independent of irradiation atmosphere and dose. The fraction of damaged units of PLLA per unit of absorbed energy G(-u)) is found to be 0.74 and 0.58 for PLLA samples irradiated in vacuum and air, respectively.

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