

Hydrolytic degradation of electron beam irradiated high molecular weight and non-irradiated moderate molecular weight PLLA

Say Chye Joachim Loo ^{a,*}, Hui Tong Tan ^b, Chui Ping Ooi ^b, Yin Chiang Freddy Boey ^a

^a Nanyang Technological University, School of Materials Science and Engineering, Nanyang Avenue, Singapore 639798, Singapore

^b Division of Bioengineering, School of Chemical and Biomedical Engineering, Nanyang Avenue, Singapore 639798, Singapore

Received 21 June 2005; received in revised form 10 October 2005; accepted 19 October 2005

Abstract

The purpose of this study is to examine the hydrolytic degradation of electron beam irradiated ring-opening polymerized (ROP) poly(L-lactide) (PLLA-ir) and non-irradiated melt polycondensation polymerized poly(L-lactic acid) (PLLA-pc). It was observed that irradiation increases the hydrolytic degradation rate constant for ROP PLLA. This was due to a more hydrophilic PLLA-ir, as a result of irradiation. The degradation rate constants (k) of PLLA-ir samples were also found to be similar, regardless of the radiation dose, and an empirically formulated equation relating hydrolytic degradation time span to radiation dose was derived. The k value for PLLA-pc was observed to be lower than that for PLLA-ir, though the latter had a higher molecular weight. This was due to the difference in degradation mechanism, in which PLLA-ir undergoes end group scission, through a backbiting mechanism, during hydrolysis and thus a faster hydrolysis rate. Electron beam irradiation, though accelerates the degradation of PLLA, has been shown to be useful in accurately controlling the hydrolytic time span of PLLA. This method of controlling the hydrolytic degradation time was by far an easier task than through melt polycondensation polymerization. This would allow PLLA to be used for drug delivery purposes or as a temporary implant that requires a moderate time span (3–6 months).

© 2005 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.

Keywords: PLLA; Melt polycondensation polymerization; Electron beam radiation; Hydrolytic degradation; Chain end scission

1. Introduction

Poly(L-lactide) and poly(L-lactic acid) (both termed PLLA) are biodegradable aliphatic polyesters synthesized from ring-opening polymerization (ROP) of L-lactide or polycondensation of L-lactic acid, respectively, producing high molecular weight PLLA and low molecular weight PLLA from the respective synthesis technique [1]. Because of the excellent biodegradability, biocompatibility and non-toxicity properties of PLLA, it has generated immense interest and its applications for biomedical and pharmaceutical purposes have been well documented [1,2]. Some examples of its biomedical applications are as drug carriers for controlled drug release and stents [3,4].

High molecular weight PLLA is usually synthesized by ring-opening polymerization of the cyclic diester of lactide [5]. There are many advantages of this polymerization method, one of which includes the elimination of dehydration of the polymerization system [1], thereby giving high molecular weight PLLA. Low molecular weight PLLA, on the other hand, is usually synthesized through melt polycondensation of L-lactic acid [1], which is a more cost effective technique than ROP. However, low molecular weight PLLA usually has low mechanical strength and very fast rates of hydrolytic degradation, thus limiting its usage in many applications. In recent years, there has been a breakthrough in producing moderately high molecular weight PLLA through direct melt polycondensation (PLLA-pc) using binary catalysts system of stannous(II) chloride dihydrate and *p*-toluene sulphonic acid monohydrate (SnCl₂/TSA), in a relatively short reaction time. It

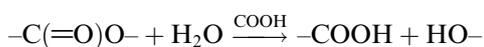
* Corresponding author. Tel.: +65 67904044; fax: +65 67909081.

E-mail address: joachimloo@ntu.edu.sg (S.C.J. Loo).

has been reported that $M_w > 100,000$ g/mol and $M_w \sim 40,000$ g/mol of PLLA were obtained by Moon et al. [6] and Gao et al. [7], respectively, through this synthesis technique. The synthesis of moderately high molecular weight PLLA may therefore help overcome some of the disadvantages of low molecular weight PLLA, by improving on their hydrolysis rate and thus allowing for applications where a moderate hydrolytic degradation time span (3–6 months) is required.

PLLA synthesized by ROP has a long hydrolytic degradation time [1], which may be unsuitable for usage in applications where a moderate degradation time span is required. In our previous work, we have studied and reported the decrease in molecular weight of ROP PLLA by electron beam irradiation, through chain scission in the polymer [8]. The reduction of molecular weight through irradiation could therefore be another possible alternative for obtaining PLLA of moderate hydrolytic degradation time span; since it is well established that hydrolytic degradation rate is dependent on parameters such as degree of crystallinity and molecular weight [1,9]. However, with the dearth of work conducted on the hydrolytic degradation of irradiated ROP PLLA, little is known of the effects of irradiation on its hydrolytic degradation, and how molecular structural modifications, such as the decrease in molecular weight through irradiation, can affect its rate of hydrolysis and subsequently, its hydrolytic degradation time.

Besides obtaining PLLA polymers with moderate hydrolytic time span, the use of radiation could also provide a way of controlling the hydrolytic degradation time of PLLA, through its accurate decrease of its molecular weight [8]. It is generally accepted in recent papers [10–13] that the hydrolysis of most polyesters proceeds according to the reaction:



And the hydrolytic degradation of polyesters therefore observes this equation:

$$\ln M_n = \ln M_{n,0} - kt \quad (1)$$

where $M_{n,0}$ is the initial number average molecular weight of the polymer before hydrolytic degradation, k is the hydrolytic degradation rate constant and t is the hydrolytic degradation time. The ability to control the hydrolytic degradation time of PLLA with radiation would be extremely useful for applications such as controlled drug release or temporary implants, such as stents, where a specific hydrolytic degradation life span is desired. Though there is a possibility that toxic components, such as free radicals, could be released from irradiated PLLA during hydrolytic degradation, such an effect was not studied in this paper.

To our knowledge, there have also been no studies that compare the hydrolytic degradation rate and time of irradiated high molecular weight ROP PLLA (PLLA-ir) and

melt polycondensation synthesized PLLA (PLLA-pc) of relatively similar molecular weights. This paper therefore seeks to discuss the hydrolytic degradation rate and time of these PLLA polymers and at the same time, establish a plausible relationship between the hydrolytic degradation time and radiation dose for PLLA-ir.

2. Materials and methods

2.1. Synthesis of PLLA through melt polycondensation

The material used for the synthesis of PLLA-pc is 80 wt.% L-lactic acid in aqueous solution, and the catalysts used were stannous(II) chloride dihydrate (SnCl_2) and *p*-toluene sulphonic acid monohydrate (TSA), all of which were purchased from Sigma–Aldrich. Chloroform solution and diethyl ether were purchased from Sigma–Aldrich and Merck, respectively. All reagents were used as received.

In the apparatus setup, a 250 ml three-neck flask was placed on a round-based mechanical stirrer and connected to a vacuum system through a cold trap. During the first synthesis step (oligomerization), the L-lactic acid solution was first heated to 150 °C at atmospheric pressure in the flask for 2 h to remove any free water. The pressure of the reaction system was then reduced to and maintained at 100 Torr for the next 2 h. This was followed by another pressure reduction to 30 Torr for a further 4 h. The reaction temperature was kept at 150 °C throughout the entire oligomerization process, and the product obtained was a transparent viscous oligomer gel.

Next, the catalysts were added to the oligomer, and the resulting mixture was mechanically stirred. The pressure was then reduced to 10 Torr and the temperature increased to 180 °C, with the polymerization process kept at this condition for 12 h. The final product was then dissolved in chloroform and precipitated in diethyl ether. The polymer was then filtered from diethyl ether and dried under vacuum to yield the purified PLLA-pc.

2.2. ROP PLLA and PLLA-pc films

The high molecular weight (i.v. = 4.37) ROP PLLA (residual monomer less than 0.1%) used in this study was purchased from Purac Far East, and was used as received. Films of ROP PLLA and PLLA-pc were prepared by a simple solvent casting method, which first involves dissolving the polymer in dichloromethane (DCM), purchased from E. Merck, at a weight ratio of 1:12. The polymer solution was then poured into a mould and the solvent was evaporated slowly in air at room temperature for 48 h to prevent the formation of air bubbles. Any remaining solvent was further removed in an oven at 40 °C for a week. The dry thicknesses of the films (8 cm × 3 cm) were then measured, using a film thickness measurement device (Elcometer, model 456) that employs the ultrasound technique, to be about 55 ± 3 μm.

ID	Title	Pages
2183	Hydrolytic degradation of electron beam irradiated high molecular weight and non-irradiated moderate molecular weight PLLA	10

Download Full-Text Now



<http://fulltext.study/article/2183>



Categorized Journals

Thousands of scientific journals broken down into different categories to simplify your search



Full-Text Access

The full-text version of all the articles are available for you to purchase at the lowest price



Free Downloadable Articles

In each journal some of the articles are available to download for free



Free PDF Preview

A preview of the first 2 pages of each article is available for you to download for free

<http://FullText.Study>