Polymer Degradation and Stability 130 (2016) 118–125

Contents lists available at ScienceDirect

Polymer Degradation and Stability

journal homepage: www.elsevier.com/locate/polydegstab

A comparative study on Poly(ε-caprolactone) film degradation at extreme pH values

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ARTICLE INFO

Article history:
Received 19 April 2016
Received in revised form
30 May 2016
Accepted 5 June 2016
Available online 7 June 2016

Keywords:
PCL
Hydrolytic degradation
pH
Hydrolysis

ABSTRACT

The present paper studies the effect of pH on hydrolytic degradation of Poly(ε-caprolactone) (PCL) Degradation of the films was performed at 37 °C in 2.5 M NaOH solution (pH 13) and 2.5 M HCl solution (pH 1). Weight loss, degree of swelling, molecular weight, and calorimetric and mechanical properties were obtained as a function of degradation time. Morphological changes in the samples were carefully studied through electron microscopy. At the start of the process the degradation rate of PCL films at pH 13 was faster than at pH 1. In the latter case, there was an induction period of around 300 h with no changes in weight loss or swelling rate, but there were drastic changes in molecular weight and crystallinity. The changes in some properties throughout the degradation period, such as crystallinity, molecular weight and Young's modulus were lower in degradations at higher pH, highlighting differences in the degradation mechanism of alkaline and acid hydrolysis. Along with visual inspection of the degraded samples, this suggests a surface degradation at pH 13, whereas bulk degradation may occur at pH 1.

1. Introduction

Polycaprolactone (PCL) is a bioabsorbable, semi-crystalline polymer (Tm ≈ +60 °C) with a low glass transition temperature (Tg ≈ −60 °C), which can be degraded by microorganisms, as well as by hydrolytic mechanisms under physiological conditions [1]. Because of its low glass transition temperature, the PCL amorphous phase displays high molecular mobility at body temperature. In comparison with the other commercially available bioresorbable polymers, PCL is one of the most flexible and easy to process materials [2]. Because of its significant degree of crystallinity and substantial hydrophobicity, high molecular weight PCL has shown remarkably long *in vivo* degradation times, in some instances as long as 2 years [3]. As for its tissue compatibility, PCL is known to elicit a rather mild inflammatory response [4].

Polycaprolactone (PCL) was one of the earliest polymers synthesized by the Carothers group in the early 1930s [5] and a resurgence of interest during the 1990s and 2000s has stemmed from the realization that PCL possesses superior rheological and viscoelastic properties over many of its resorbable-polymer counterparts, which renders it easy to manufacture and manipulate into a large range of scaffolds. Surprisingly, despite more than 1000 papers being published during the last decade in the biomaterials and tissue-engineering literature on PCL-based-scaffolds, only a small number of groups have included a study of the degradation and resorption kinetics of PCL scaffolds [6].

The most important role of the use of scaffold *in vivo* is that it persists in a robust state for sufficient time to allow the formation of new tissue, but also ultimately degrades and is replaced by this tissue. Hydrolytic degradation is of crucial importance [7,8] for its successful implementation in applications such as surgical sutures, drug delivery systems, and tissue engineering scaffolds. The rate of degradation has been attributed to a number of polymer characteristics. It is believed that the access of water to the ester bond, rather than intrinsic rates of ester cleavage, govern the time it takes for a polymer to degrade [9]. Water access to the ester bonds is determined by the combined effect of the hydrophobicity of the monomers, the crystallinity of the sample, the molecular weight, the glass transition temperature and the bulk sample dimensions [10–12]. Some studies have also shown the effect of porosity on degradation of PCL samples [13,14] and on degradation of samples based on other polyesters [15,16]. High porosity with a large specific surface could increase the hydrolysis rate and produce large amounts of acid byproducts and also provide a better inter-

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http://dx.doi.org/10.1016/j.polymdegradstab.2016.06.005
0141-3910/

connective pore structure and enhanced fluid permeability [14]. Natu et al. have shown that the processing method does not have a significant effect on the long term degradation of PCL constructs, although there were some differences in the degradation profile for samples prepared by different processing methods of up to 18 months, these differences tended to disappear during the advanced stage (18–36 months) [17].

A closer look at the degradation of polyester materials has revealed that there are still many unsolved problems that hinder us from taking full advantage of these materials [18]. Most of what we know about degradation mechanisms dates back to the early 1980s, when degradable polymers were classified into surface eroding and bulk eroding [19]. Several mathematical models have been developed to predict the degradation of the aliphatic polyesters in an aqueous environment [18,20–23].

The degradation rate also depends strongly on pH. However most degradation studies are usually done in a physiologic saline solution of pH 7.4. After shifts in pH, reaction rates of esters may change some orders of magnitude due to catalysis. Ester hydrolysis can therefore either be acid or base catalyzed [24]. It is therefore important to understand the pH dependent degradation of biomaterials, because they should be able to retain adequate properties under all possible physiologic and pathologic conditions. It is known that the pH of gastric juice in the stomach can go as low as 0.9–1.5, while the pancreatic juice in the duodenum ranges from 7.5 to 8.2 [25]. Hydrolytic degradation of Poly(glycolic acid) has been reported at three different pHs [26]. The comparison of the effect on mechanical properties of pH levels ranging from 5.25 to 10.09 on the hydrolytic degradation of polyglycolic acid and poly(glycolide-lactide) suture materials has also been reported [25]. Accelerated degradation studies in an alkaline medium have previously been reported by a small number of groups for PCL-based polymeric films and devices [27–30]. Tsuji and Ishizaka studied the enzymatic and alkaline degradation of porous PCL films [31]. The degradation of PCLs in acidic and basic media have been studied by Jung et al., who reported variations in the relative viscosities at various pH as a function of time [32].

The objective of this study is to further investigate the hydrolytic degradability of PCL films by assessing the effects of extreme pH (1 and 13) on weight loss, degree of swelling, molecular weight, and calorimetric and mechanical properties, as well as morphological changes, to better understand the influence of the pH medium on the process of degradation and the relationship between bulk and surface characteristics during the degradation period.

2. Materials and methods

2.1. Materials

2.1.1. Poly(caprolactone) films

(PCL) [Polysciences (M_w 43,000–50,000)] in the form of powder was used without further purification. The solvent, tetrahydrofuran (THF) from Aldrich was used as received. Films were prepared from a solution of PCL in tetrahydrofuran (THF) by evaporation of THF at room temperature (for 7 days).

2.1.2. Degradation solutions

Sodium hydroxide, NaOH, and hydrochloric acid, HCl, from Sharlab were used as received. Distilled water with 10 μS conductivity was used as a solvent. 2.5 M degradation solutions were prepared from HCl (pH 1), and NaOH (pH 13).

2.2. Methods

2.2.1. Incubation

The resultant films were cut into discs (diameter, 6 mm; thickness, 2.5 mm) and used for the degradation experiments. After placing the films (≈70 mg) into test-tubes, degradation solution was added at either pH 1 or pH 13; the ratio sample/degradation medium was 1/50 in mass. Triplicates were prepared for each period of degradation for both pH settings to minimize the effects of random errors. After the addition of degradation solution, the test tubes were placed in an oven at 37.0 °C for incubation. At predetermined time intervals three sample replicates were taken out of the solution, washed twice with distilled water, wiped, weighed, and subsequently vacuum dried prior to posterior analyses.

2.2.2. pH

The pH measurements in the degradation medium were carried out using a pH meter equipped with an Ag/AgCl electrode with an accuracy of ±0.01 (XS instruments 510). The instrument was calibrated using buffer solutions at pH 4 and pH 7.

2.2.3. Porosity

Sample porosity (φ) before immersion in degradation solutions was estimated from the apparent volume V_T and PCL volume V_M, defined by the actual amount of polymer (m) and its mean density (ρ) (ρ = 1.14 g/cm3)

$$\varphi(\%) = \frac{V_T - V_M}{V_T} \times 100 = \frac{V_T - \frac{m}{\rho}}{V_T} \times 100$$

Ten replicates were used to obtain mean porosity and standard deviation (SD).

2.3. Degree of swelling and weight loss

The degradation process was followed by determining the water absorption and mass loss of the materials. Samples were washed with distilled water and gently wiped with paper. Wet weight was determined in order to evaluate the evolution of the samples' hydrophilicity. The degree of swelling was determined by comparing the wet weight (w_w) at a specific time with the dry weight (w_d) according to Eq. 1

$$\text{degree of swelling } (\%) = \frac{w_w - w_d}{w_d} \times 100 \quad (1)$$

The percentage of weight loss was determined after drying the samples in a vacuum by comparing dry weight (w_d) at a specific time with the initial weight (w_0) according to Eq. 2

$$\textit{weight loss } (\%) = \frac{w_0 - w_d}{w_0} \times 100 \quad (2)$$

A balance (Mettler Toledo) with a sensitivity of 0.01 mg was used to weigh the samples.

2.4. Scanning electron microscopy (SEM)

To investigate the surface and cross section morphology of dried samples, SEM pictures of degraded and non-degraded samples were taken using a JEOL JSM-5410 scanning electron microscope.