Acta Biomaterialia 6 (2010) 2035–2044

Contents lists available at ScienceDirect

Acta Biomaterialia

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

Degradation studies on segmented polyurethanes prepared with HMDI, PCL and different chain extenders

L.H. Chan-Chan [a], R. Solis-Correa [a], R.F. Vargas-Coronado [a], J.M. Cervantes-Uc [a], J.V. Cauich-Rodríguez [a,*], P. Quintana [b], P. Bartolo-Pérez [b]

[a] Centro de Investigación Científica de Yucatán, A.C., Calle 43 # 130 Col. Chuburná de Hidalgo, Mérida, Yucatán, Mexico
[b] Centro de Investigación y Estudios Avanzados del I.P.N., Unidad Mérida, A.P. 73 Cordemex, Mérida, Yucatán, Mexico

ARTICLE INFO

Article history:
Received 8 June 2009
Received in revised form 30 October 2009
Accepted 4 December 2009
Available online 22 December 2009

Keywords:
Polycaprolactone
Segmented polyurethanes
Cardiovascular
Chemical degradation
Thiol chain extender

ABSTRACT

Biodegradable segmented polyurethanes (BSPUs) were prepared with poly(caprolactone) as a soft segment, 4,4′-methylene bis (cyclohexyl isocyanate) and either butanediol (BSPU1) or dithioerythritol (BSPU2) as a chain extender. BSPU samples were characterized in terms of their physicochemical properties and their hemocompatibility. Polymers were then degraded in acidic (HCl 2 N), alkaline (NaOH 5 M) and oxidative (H_2O_2 30 wt.%) media and characterized by their mass loss, Fourier transform infrared (FTIR), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), X-ray diffraction (XRD) and scanning electron microscopy (SEM). Undegraded BSPU1 and BSPU2 exhibited different properties, such as the glass transition temperature T_g of the soft segment (−25 vs. 4 °C), mechanical properties (600% vs. 900% strain to break) and blood coagulating properties (clotting time = 11.46 vs. 8.13 min). After acidic and alkaline degradation, the disappearance of the 1728 cm^{-1} band of polycaprolactone (PCL) on both types of BSPU was detected by FTIR. However, the oxidative environment did not affect the soft segment severely as the presence of PCL crystalline domains were observed both by DSC (melting temperature T_m = 52.8 °C) and XRD (2θ = 21.3° and 23.7°). By TGA three decomposition temperatures were recorded for both BSPU samples, but the higher decomposition temperature was enhanced after acidic and alkaline degradation. The formation of the porous structure on BSPU1 was observed by SEM, while a granular surface was observed on BSPU2 after alkaline degradation.

1. Introduction

The various applications of segmented polyurethanes (SPUs) in the biomaterials field are based on their good physicochemical and mechanical properties while exhibiting an acceptable biological performance. These polymers are particularly useful in blood contact applications such as vascular grafts, hearth valves and pacemakers [1]. In spite of these properties, SPUs exhibit poor fatigue properties and long-term oxidative degradation in their various forms (metal ion induced, auto-oxidation, environmental stress cracking, macrophages/phagocytic cell mediated, etc.), especially those based on polyether type polyols [2]. In order to improve SPU properties, the soft segments have received a great deal of attention as they are the most vulnerable part of the polymer. Resistance to oxidative degradation has been achieved by using ether and ester-free polyurethanes through the incorporation of polycarbonate [3,4] or butadiene diol terminated as soft segments [5–8]. However, hydrolysis of the carbonate group is still possible in addition to long-term calcification [9], whereas butadiene diol polyurethanes render highly hydrophobic and segregated structures [6].

Recently, polyester-based polyurethanes such as those based on polycaprolactone have been investigated for tissue engineering purposes. This is motivated by the fact that the ester group is susceptible to chemical and enzymatic hydrolysis, a condition that is easily achieved in vivo. In this way, segmented polyurethanes containing polycaprolactone as a soft segment have been prepared with aliphatic or aromatic diisocyanates such as hexamethylene diisocyanate [10], 1,4-butane diisocyanate [11], 4,4′-methylene bis (cyclohexyl isocyanate) [12], L-lysine diisocyanate [13], toluene diisocyanate [14], 4,4′-diphenylmethane diisocyanate [15,16] and isophorone diisocyanate [17].

In this paper, the synthesis of a biodegradable segmented polyurethanes (BSPUs) based on a low-molecular-weight polycaprolactone (PCL), 4,4′-methylene bis (cyclohexyl isocyanate) (HMDI) and either butanediol (BD) or dithioerythritol (DTE) as a chain extender is reported. HMDI is proposed not only as it renders a highly amorphous segmented polyurethane at low rigid segment content, but also because it leads to harder and stronger elastomers that can

* Corresponding author.
E-mail address: jvcr@cicy.mx (J.V. Cauich-Rodríguez).

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doi:10.1016/j.actbio.2009.12.010

be used to prepare composites with low modulus and high strength [18]. Furthermore, HMDI has been shown to be less hydrolytically stable than MDI and will render products which are less toxic [19]. DTE was used as thiol-bearing chain extender since this type of chemical group is reported to have the ability to exchange endogenous nitric oxide [20]. PCL of low molecular weight was used as a biodegradable soft segment as it is known that it can be degraded faster than highly crystalline high-molecular-weight PCL and because its degradation products are non-toxic to cells.

The synthesized polyurethanes were characterized physicochemically and also in terms of their hemocompatibility. We also report on the properties of the degraded polymer after being exposed to acidic, alkaline and oxidative conditions. Although there are several reports on the in vitro [21,22] and in vivo [23–25] degradation of polyurethanes, to our knowledge there is no reference on the degradative behaviour of both HMDI:BD:PCL and HMDI:DTE:PCL segmented polyurethanes for biomedical purposes.

2. Materials and methods

2.1. Polyurethane synthesis

Materials for polyurethane synthesis were purchased from Aldrich (Milwaukee, WI, USA). BSPUs with a molar ratio of 2.05:1:1 (HMDI:BD or DTE:PCL) were prepared in dimethylformamide solution by a two-step procedure. In the first stage, diol-terminated PCL (M_n = 1250 as provided by the supplier) was mixed, in a glass reactor at 60 °C under nitrogen atmosphere, with a molar excess of 4,4′-methylene bis (cyclohexyl isocyanate) in the presence of 0.15 wt.% stannous octoate in order to form an NCO-terminated prepolymer. In the second stage, BD or DTE was used as an extender to form the hard segments (they will be referred as BSPU1 and BSPU2, respectively). The reaction time for the prepolymer formation was 4 h at 60 °C while the second stage lasted 2 h. After this time, the polymer was precipitated and washed with distilled water and then dried at 60 °C. The rigid segment contents of BSPU1 and BSPU2 were 34.9% and 36.9%, respectively. Fig. 1 shows their proposed structures. Model polyurethanes were synthesized by one-step polymerization using HMDI–BD or HMDI–DTE only.

2.2. Physicochemical characterization of BSPUs

2.2.1. ^{1}H NMR and Fourier transform infrared (FTIR) spectroscopy

Proton nuclear magnetic resonance spectra were obtained with a 300 MHz Varian spectrometer (Palo Alto, CA) using deuterated chloroform as solvent and tetramethylsilane as reference.

Infrared spectra of the BSPUs were obtained after casting a film on KBr disc with a Nicolet Protégé 460 FTIR (Madison, WI) in the spectral range from 4000 to 400 cm^{-1}, averaging 50 scans with a resolution of 4 cm^{-1}.

2.2.2. Thermal properties

The thermal behaviour was evaluated with a DSC 7 from Perkin-Elmer (Norwalk, CT) using 5 mg of the polymer encapsulated on aluminum pans. The polymer was heated from 40 to 160 °C at 5 °C min^{-1} under nitrogen atmosphere. First and second thermograms were recorded. For thermogravimetric analysis (TGA), 20 mg of the sample were heated from 50 to 550 °C at 10 °C min^{-1} under nitrogen atmosphere using a TGA 7 from Perkin-Elmer (Norwalk, CT). From the first derivative, decomposition temperatures (T_d) were obtained.

The glass transition temperature (T_g) was obtained by dynamic mechanical analysis with a Perkin-Elmer DMA 7 (Norwalk, CT) in the extension mode. Strips of 20 × 3 × 0.1 mm were heated from −50 to 100 °C at 5 °C min^{-1} using a static force of 60 mN and a dynamic force of 40 mN at 1 Hz.

2.2.3. Mechanical properties

Tensile mechanical properties were obtained on rectangles of 75 × 10 × 0.1 mm with a Shimadzu universal testing machine (Kyoto, Japan) using a cross-head speed of 500 mm min^{-1} according to ASTM D-412. The Young's modulus at 100% (E_{100}), tensile strength (σ) and strain to failure (ε) are reported.

2.2.4. X-ray diffraction (XRD)

XRD measurements were carried out with a D-5000 Siemen diffractometer (Karlsruhe, Germany) using monochromatic radiation (Cu Kα λ = 1.5418 Å) at 35 kV and 24 mA. The samples were registered in the range 5° < 2θ < 60° with a step count of 3 s and a step size of 0.02° (2θ). For these experiments 1 cm^2 films were used.

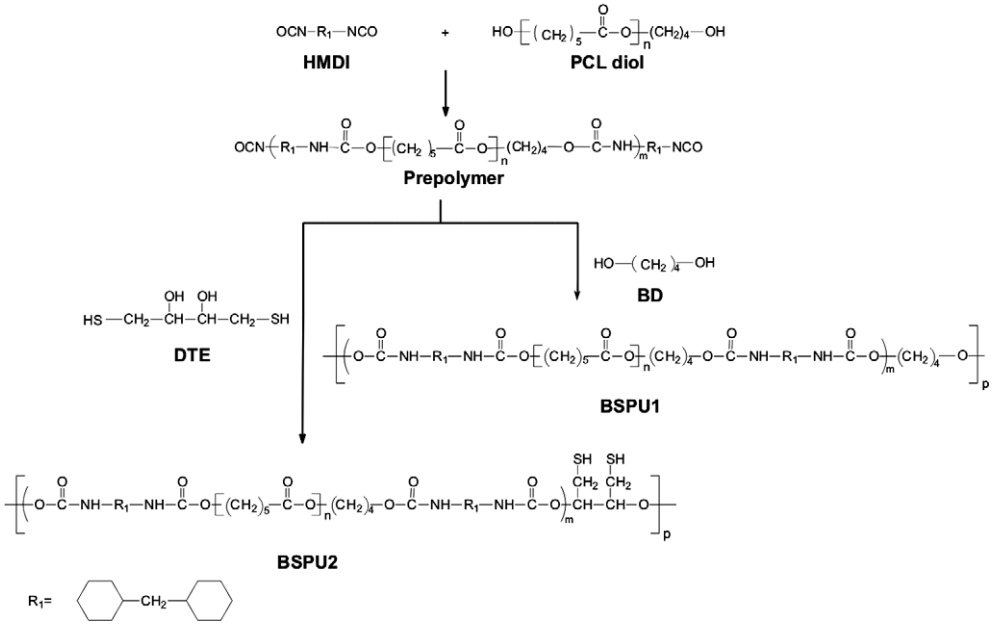

Fig. 1. Chemical reactions leading to BSPUs synthesis.