

021

Intermolecular interactions between carbon dioxide and the carbonyl groups of polylactides and poly(ϵ -caprolactone)

S.P. Nalawade¹, F. Picchioni², J.H. Marsman², D.W. Grijpma¹, J. Feijen¹, L.P.B.M. Janssen²

¹Institute for Biomedical Technology, Polymer Chemistry and Biomaterials, Faculty of Science and Technology, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands, e-mail: s.p.nalawade@tnw.utwente.nl.

²Department of Chemical Engineering, University of Groningen, The Netherlands

Summary

Fourier transform infrared (FT-IR) spectroscopy was used to reveal weak intermolecular interactions between carbon dioxide (CO₂) and the carbonyl groups of several polymers. This interaction affects the solubility of CO₂. The polymers used in this study were poly(L-lactide) (PLLA), poly(D,L-lactide) (PDLLA) and poly(ϵ -caprolactone) (PCL). In the presence of CO₂, the wavenumber of the carbonyl groups shifted to a higher value and in the bending mode region of CO₂ a new absorption band appeared. For PCL, the effect of CO₂ dissolution on the melting point depression could clearly be observed, even at low pressures.

Introduction

Detailed attention has been given to the synthesis and processing of biodegradable polymers. Especially aliphatic polyesters are frequently used due to their favourable mechanical properties, biocompatibility and degradability. Examples of applications are sutures, drug delivery systems, and scaffolds in tissue engineering. However, these polymers are susceptible to thermal degradation at elevated temperatures, which makes processing difficult. In drug delivery systems encapsulation of a thermally sensitive drug in these polymers at high temperatures is also an important concern.

In the synthesis and processing of various polymers, CO₂ has been established as a solvent [1]. Attractive advantages of CO₂ are its inert nature and its easy removal by simple depressurization. At or above supercritical conditions (31 °C and 7.38 MPa), gas-like diffusivity and liquid-like density allows CO₂ to be used as a conventional solvent. Dissolution of CO₂ in a polymer

Table 1
The glass transition temperature (T_g) and melting point (T_m) of the polymers used

Polymers	T_g (°C)	T_m (°C)
PDLLA	47	–
PLLA	59	181
PCL3	–60	57
PCL50	–61	60

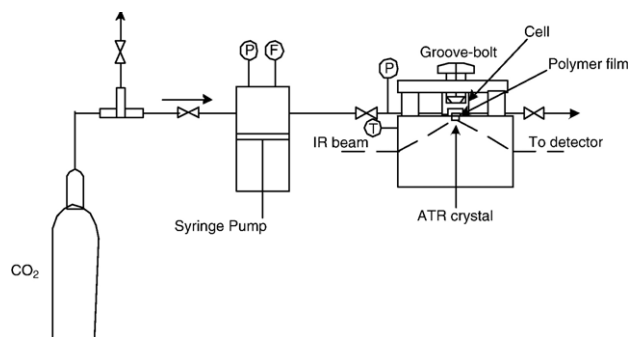


Fig. 1. The high pressure FT-IR (golden gate) unit.

depresses its melting point and hence reduces its viscosity. This melting point depression is caused by an increase of the polymer free volume in the presence of CO₂. This then allows the polymer to be processed at a lower temperature. The amount of CO₂ that can be dissolved in a polymer is generally interpreted thermodynamically in terms of temperature and pressure.

The intermolecular interaction between CO₂ and the polymer carbonyl groups is a Lewis acid–base interaction. Polymers containing ester bonds in general show good solubility of CO₂ [2–4]. Fourier transmission infrared spectroscopy (FT-IR) is a good tool to study these interactions. In this study, a high pressure FT-IR unit was used to reveal the interaction between CO₂ and the carbonyl groups of PLLA, PDLLA and PCL.

Materials and methods

PCL of a weight average molecular weight (M_w) of 3000 g/mol (PCL3) and 50,000 g/mol (PCL50) were supplied by Solvay, UK. Poly(D,L-lactide) (PDLLA) and Poly(L-lactide) (PLLA) were supplied by Purac, The Netherlands. The viscosity average molecular weight (M_v) of PDLLA and PLLA were respectively 135,000 and 148,000 g/mol as determined from the intrinsic viscosity measurements (chloroform, 25 °C). Table 1 shows the glass transition temperatures (T_g) and the melting points (T_m) of the polymers. Analytical

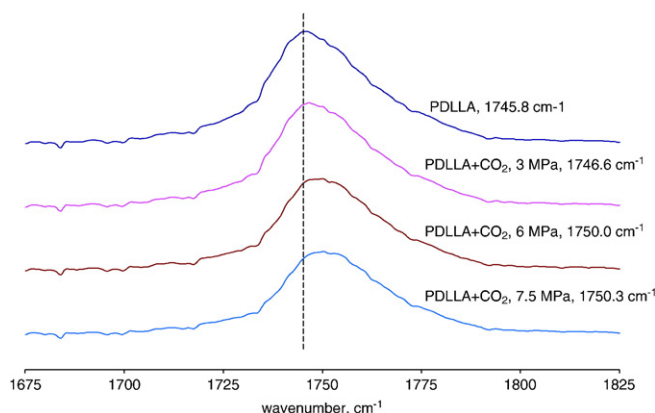


Fig. 2. The absorption spectra of PDLLA carbonyl groups at different CO₂ pressures.

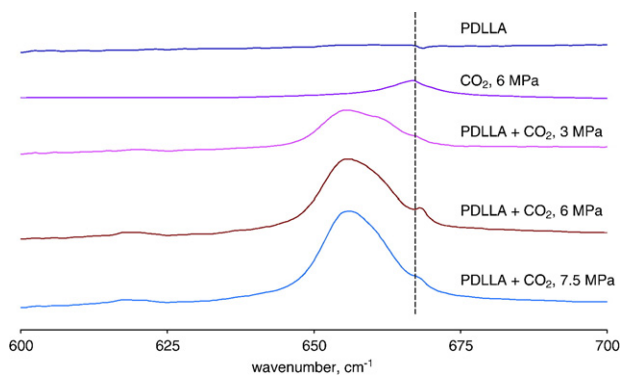


Fig. 3. The absorption spectra of the bending mode (ν_2) of CO_2 and dissolved at different pressures in PDLLA.

grade chloroform (CHCl_3) was purchased from Aldrich, The Netherlands. High purity CO_2 , 99.99%, was used in the FT-IR experiments.

A schematic of the high pressure FT-IR unit is shown in Fig. 1. This unit consists of an FT-IR apparatus (golden gate type, Spectrum 2000, Perkin Elmer, UK), a CO_2 cylinder, a high pressure syringe pump (Isco, USA), and a high pressure cell and valves. The high pressure cell was home-built and can withstand pressures up to 9 MPa. The cell, inlet lines, exit lines and valves were heated using a heating element. The scanning range available in our FT-IR set up is $500\text{--}4000\text{ cm}^{-1}$. Polylactide films were cast onto the (diamond) crystal from chloroform solutions, and the PCL polymer films were prepared by directly melting the polymer on the crystal.

The FT-IR experiments were carried out at $40\text{ }^\circ\text{C}$. Spectra were recorded in the absence of CO_2 and at different CO_2 pressures (3–8 MPa). The spectra were scanned at the resolution of 2 cm^{-1} , and an average of 60 scans was acquired.

Results and discussion

In the presence of dissolved CO_2 , the wavenumber corresponding to the carbonyl group ($\text{C}=\text{O}$) of PDLLA, at approximately 1745 cm^{-1} , shifted to higher values. With increasing pressure, the amount of dissolved CO_2 in a polymer increases. The effect of pressure on the stretching vibrations of the carbonyl group can be seen in Fig. 2. This shift is in agreement with what has been reported for poly(methyl methacrylate) [2–3].

Evidence of the interaction between CO_2 and the carbonyl groups was also observed in the bending mode (ν_2) region of CO_2 . Fig. 3 shows the absorption spectra of the bending mode of CO_2 and of the CO_2 dissolved at the different pressures. A new band at 655 cm^{-1} can be observed upon dissolution of CO_2 . For CO_2 only this band is observed at 667 cm^{-1} .

Similar results were obtained for PLLA and PCL. In the future, we will quantitatively analyze the spectra to determine the strength of these interactions.

Fig. 4 shows the spectrum of PCL3 and PCL50 at different CO_2 pressures. For the PCLs, the effect of CO_2 solubility on the depression of T_m could be observed in the crystalline and amorphous regions of the IR spectra. The shape of the spectra of PCL3 and PCL50 change at a CO_2 pressure of 3 and 6 MPa, respectively. The lower pressure required in the case of PCL3 is related to its lower molecular weight. Such changes were not observed for PDLLA and PLLA. PDLLA is an amorphous polymer and PLLA has a much higher melting temperature than PCL.

Conclusions

Using FT-IR, a shift in the wavenumber corresponding to the absorption of the carbonyl groups of polylactides and PCL was found upon dissolution of CO_2 . A new absorption band in the bending mode region of CO_2 was observed as well. This is indicative of an interaction between the carbonyl groups of the polymers and CO_2 . For PCL, a depression in the melting temperature, which depends on polymer molecular weight, could be observed. These results suggest that CO_2 has great potential as a solvent in the processing of polylactides and PCL.

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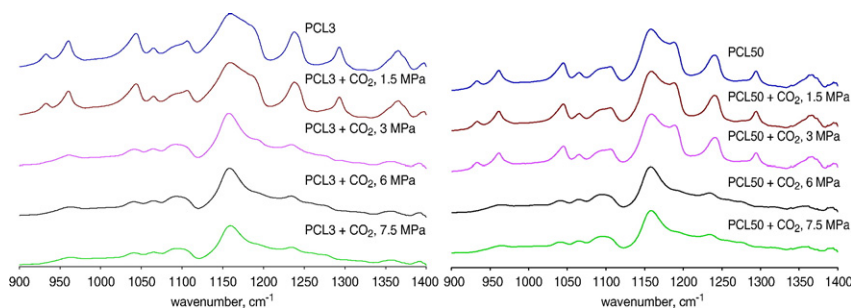


Fig. 4. The absorption spectra of PCL3 and PCL50 in the absence and in the presence of CO_2 at different pressures.

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022

Self-assembly of PEG-oligo-lactates with monodisperse hydrophobic blocks

M.G. Carstens^{1,2}, C.F. van Nostrum¹, A. Ramzi¹, L.G.J. de Leede², D.J.A. Crommelin¹, W.E. Hennink¹

¹*Dept. of Pharmaceutics, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, P.O. Box 80082, 3584 CA, Utrecht, The Netherlands, e-mail: m.g.carstens@pharm.uu.nl*
²*OctoPlus Technologies BV, Leiden, The Netherlands*

Summary

Methoxypoly(ethylene glycol)-b-oligo-L-lactates (mPEG-b-OLA) with monodisperse OLA blocks were obtained by preparative HPLC of the polydisperse oligomers. These block oligomers formed nanoparticles with a hydrodynamic radius of 130–300 nm at concentrations above the critical aggregation concentration of 0.4–1 mg/ml. Detailed analysis of the particles demonstrated that they consisted of a hydrated core of mPEG-b-OLA block oligomers and a thin outer PEG layer. This novel type of particles is expected to be suitable for pharmaceutical applications.

Introduction

The nature of the two building blocks of PEG-b-PLA, the hydrophilic and non-immunogenic PEG, and the hydrophobic and biodegradable PLA confer this amphiphilic polymer attractive properties for pharmaceutical applications. The polymer self-assembles in water into nanoparticles, which have been extensively studied, for example by Gref et al. [1] and Yamamoto et al. [2]. These studies mainly focused on high molecular weight PEG-b-PLA. In this study we present the preparation of low molecular weight block oligomers with monodisperse hydrophobic blocks [3]. Their critical aggregation concentration, particle formation and temperature sensitivity were studied and the particles

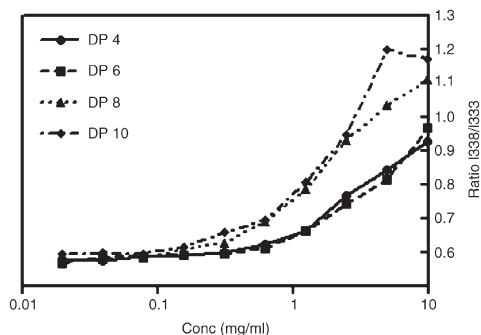


Fig. 1. Fluorescence intensity ratio I338/I333 of pyrene as a function of the concentration of mPEG550-b-oligo-L-lactate with different OLA block lengths.

were investigated by static light scattering and ¹H NMR in D₂O.

Experimental methods

Synthesis and characterization of mPEG-b-OLA

Polydisperse block oligomers were synthesized by ring opening polymerization of L-lactide initiated by mPEG (*M_w* of 350, 550 or 750) as shown in Scheme 1. The polydisperse oligomers were fractionated by preparative reversed phase (RP) HPLC, using a water–acetonitrile gradient. The identity of the collected fractions was established by electrospray mass spectrometry (ESI-MS) and ¹H NMR in CDCl₃ and the purity by analytical RP-HPLC. The glass transition temperature (*T_g*) and the melting temperature (*T_m*) of the oligomers were determined by differential scanning calorimetry (DSC).

Behaviour in water

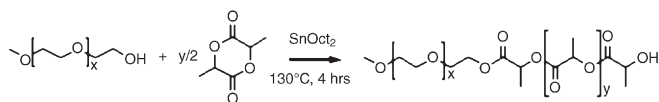
The critical aggregation concentration of the fractionated oligomers was determined using pyrene as a fluorescent probe [4]. Samples were prepared in 10 mM ammonium acetate buffer pH 5. Particles were formed by the hydration of an block oligomer film at a concentration of 10 mg/ml in the same buffer.

Characterization of the mPEG-b-OLA nanoparticles:

The size and polydispersity of the mPEG-b-OLA particles were measured by dynamic light scattering (DLS). The samples were analyzed at 25 °C directly after preparation and after incubation at room temperature for several days. Some of the samples were investigated in more detail with multiangle static light scattering (SLS) and by ¹H NMR in D₂O.

Results and discussion

Fractionation of the polydisperse mPEG-b-OLAs yielded block oligomers with monodisperse OLA blocks, with a degree of polymerization (DP) of 4, 6, 8 and 10, as assessed by ESI-MS and ¹H NMR. The purity of the samples was 80–90%, determined from the relative peak areas in analytical HPLC.



Scheme 1. Synthesis of mPEG-b-OLA.