Studies on the interactions of CO_2 with biodegradable poly(DL-lactic acid) and poly(lactic acid-*co*-glycolic acid) copolymers using high pressure ATR-IR and high pressure rheology

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ABSTRACT

Amorphous poly(DL-lactic acid) ($P_{DL}LA$) and poly(lactic acid-*co*-glycolic acid) (PLGA) polymers have been used to fabricate porous scaffolds for tissue engineering applications via a supercritical foaming technique. The chemical composition of the polymers and the morphology (pore size, porosity and interconnectivity) of the scaffolds are crucial because they influence cell filtration, migration, nutrient exchange, degradation and drug release rate. To control the morphology of supercritical foamed scaffolds, it is essential to study the interactions of polymers with CO_2 and the consequent solubility of CO_2 in the polymers, as well as the viscosity of the plasticized polymers. In this paper, we are showing for the first time that well known and useful biodegradable polymers can be plasticized easily using high pressure CO_2 and that we can monitor this process easily via a high pressure attenuated total reflection Fourier transform infrared (ATR-IR) and rheology. High pressure ATR-IR has been developed to investigate the interactions of CO_2 with $P_{DL}LA$ and PLGA polymers with the glycolic acid (GA) content in the copolymers as 15, 25, 35 and 50% respectively. Shifts and intensity changes of IR absorption bands of the polymers in the carbonyl region (~ 1750 cm^{-1}) are indicative of the interaction on a qualitative level. A high pressure parallel plate rheometer has also been developed for the shear viscosity measurements of the CO_2-plasticized polymers at a temperature below their glass transition temperatures. The results demonstrate that the viscosities of the CO_2-plasticized polymers at 35 °C and 100 bar were comparable to the values for the polymer melts at 140 °C, demonstrating a significant process advantage through use of $scCO_2$. The data from the high pressure rheology and high pressure ATR-IR, combined with the sorption and swelling studies reported previously, demonstrate that the interaction and the solubility of CO_2 in PLGA copolymers is related to the glycolic acid content. As the glycolic acid ratio increases the interaction and consequent solubility of CO_2 decreases. The potential applications of this study are very broad, from tissue engineering and drug delivery to much broader applications with other polymers in areas that may range from composites and polymer synthesis through to injection moulding.

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1. Introduction

Biodegradable poly(lactic acid) (PLA) and poly(lactic acid-*co*-glycolic acid) (PLGA) polymers have been used widely for the fabrication of drug delivery and tissue engineering devices [1]. To incorporate biologically active guest species into polymer host with limited loss or change of activity, carbon dioxide (CO_2) has been used as an efficient plasticizer and foaming agent for the fabrication of 3-D $P_{DL}LA$ and PLGA scaffolds [2–5]. A single step $scCO_2$ foaming process using polymer powder samples has been developed to generate porous scaffolds with an interconnected porous structure for growth factor delivery and cell culture [6]. Previous studies on the $P_{DL}LA$ and PLGA foaming process demonstrated that the processing temperature, pressure, soaking time, molecular weight and

composition of polymers have significant effects on the pore size and porosity of the foamed scaffolds [7,8]. The critical parameters for controlling foam development in a CO_2 foaming process include the solubility and diffusivity of CO_2 in the polymers, as well as the viscosity of the polymer/CO_2 mixture [9,10]. These parameters are dependent on the interactions of the polymers with CO_2.

The gas sorption and the consequent polymer swelling of PLA and PLGA/CO_2 systems have been measured using various apparatus and simulated using mathematical models. These include a quartz crystal microbalance [11], an external balance [12] and a pressure decay technique [13]. The mathematical models used include dual-mode sorption model, Flory–Huggins equation [11], perturbed-hard-sphere-chain equation of state [12] and Sanchez–Lacombe equation of state [13]. In our previous work, a view cell equipped with a camera and a magnetic suspension balance were adopted to measure polymer swelling and the gas sorption of $P_{DL}LA$ and PLGA/CO_2 systems up to a high pressure of 200 bar, Sanchez–Lacombe equation of state was also used for modelling [14,15].

FTIR and ATR-IR spectroscopy have been used to study the specific intermolecular interactions between CO_2 and polymers [16–18]. This spectroscopic method has been used for in-situ measurements of gas sorption and polymer swelling [19,20]. The comparison between gravimetric and in-situ spectroscopic methods has been investigated by measuring the sorption of CO_2 in a biocompatible acrylate copolymer and proved that the spectroscopy method is a powerful tool to study the interactions of gas and polymers [21].

Moreover, the viscosity of the polymer/CO_2 mixture plays an important role for the control of porous structures during the CO_2 foaming process. The dissolved CO_2 in the polymers can reduce the viscosity and the glass transition temperature (T_g) of the polymers dramatically [22,23]. These reductions are closely related to the solubility of CO_2 in the polymers. The melt rheology of poly(lactic acid) has been widely investigated [24–28], however, there is no literature reporting the viscosity measurement of CO_2-plasticized amorphous $P_{DL}LA$ and PLGA polymers. A few high pressure viscometers have been adopted to study the viscosity reduction of polymer melts or fluid samples under CO_2. These include high pressure concentric cylinder rotational viscometer [29], high pressure slit die [30] and capillary viscometer [31], and high pressure magnetically levitated sphere rheometer [32].

In this paper, we are showing for the first time that well known and useful biodegradable polymers can be plasticized easily using high pressure CO_2 and that we can monitor this process easily via a high pressure attenuated total reflection Fourier transform infrared (ATR-IR) and rheology. A high pressure ATR-IR was used to study the interactions of PLGA polymers with CO_2 and a high pressure parallel plate viscometer was developed to directly measure the shear viscosity of CO_2-plasticized amorphous $P_{DL}LA$ or PLGA polymers at a temperature below their glass transition temperatures.

2. Experimental section

2.1. Materials

Amorphous $P_{DL}LA$ 15 KD, $P_{DL}LA$ 52 KD and PLGA polymers (the mole percentage of glycolic acid in the copolymers was 15, 25, 35 and 50 respectively) were purchased from Boehringer Ingelheim (Resomer, Germany), Purac (Netherlands) and Lakeshore Biomaterials (USA) and used as received (Table 1). Weight-average molecular weights (M_w) and polydispersity (PDI) of these polymers were measured by Gel Permeation Chromatography (GPC) (PL-120, Polymer Labs) with an RI detector. The columns (30 cm PLgel Mixed-C, two in series) were eluted by THF and calibrated with narrow

Table 1
Polymer characteristics.

Polymers	Supplier	Composition (LA:GA)[a]	Inherent viscosity (dL/g)	M_w[b] (KD)	PDI[c]	T_g[d] (°C)	Form
$P_{DL}LA$ 15 KD	Resomer	100:0	0.26	15	1.66	48.7	Powder
$P_{DL}LA$ 52 KD	Purac	100:0	0.52	52	1.87	46.9	Granular
PLGA 8515	Lakeshore	85:15	0.63	77	1.70	48.6	Pellet
PLGA 7525	Resomer	75:25	0.5–0.7	72	1.75	50.4	Powder
PLGA 6535	Lakeshore	65:35	0.5	52	1.69	49.1	Granular
PLGA 5050	Resomer	50:50	0.55	53	1.59	47.0	Powder

[a] Copolymer composition: the mole ratio of lactic acid (LA) and glycolic acid (GA) in the copolymer.
[b] Weight average molecular weight, determined by GPC.
[c] Polydispersity, determined by GPC.
[d] Glass transition temperature, determined by DSC.

molecular weight distribution polystyrene standards. All calibrations and analyses were performed at 40 °C with a flow rate of 1 mL/min. Glass transition temperatures of these polymers were determined utilising a TA 2920 Differential Scanning Calorimeter (DSC) under nitrogen atmosphere. The tests were performed from −10 to 120 °C, at a heating rate of 10 °C/min. Food grade CO_2 was supplied by Cryoservice and used without further purification.
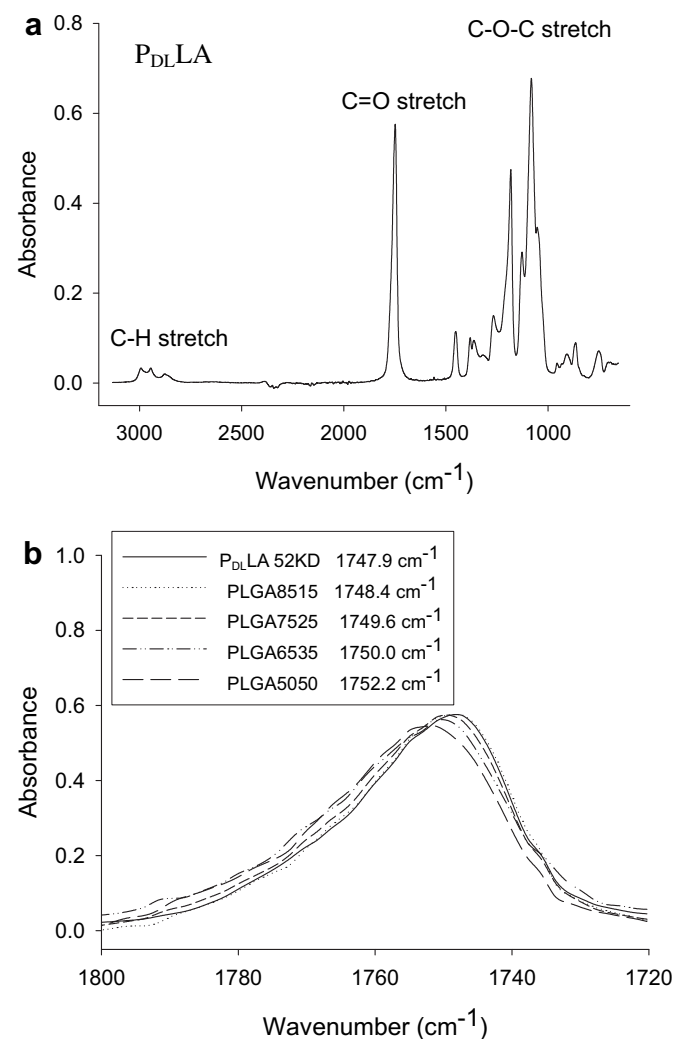

Fig. 1. FTIR spectra of $P_{DL}LA$ and PLGAs. The absorbance bands in the carbonyl region shift to high wavenumber with increasing GA content in the PLGA copolymers. The lack of methyl pendant groups in the PGA polymer chains could have caused this shift.

2.2. High pressure ATR-IR

A commercial Golden Gate ATR-IR supercritical fluid analyzer (Specac Ltd., UK) [20] was used to collect the FTIR spectra of the $P_{DL}LA$ and PLGA polymer films at 35 °C in the absence and presence of CO_2. This ATR-IR supercritical fluid analyzer with diamond crystal and ZnSe focusing lenses has a low volume (28 μL) stainless steel sample cell and can be used at extreme conditions (maximum pressure 400 bar and maximum temperature 300 °C). The ATR-IR method probes a thin layer (~ 1 μm) of the polymer film attached to the ATR crystal, allowing the measurement of the spectrum of the polymer-CO_2 mixture without overlapping with the spectrum of the surrounding gas. To avoid this possible overlapping, good contact between the polymer sample and the ATR crystal is essential. The thin polymer films were formed on the diamond window by solvent casting. The polymer solution (1 wt% in THF) was dropped onto the window and the solvent evaporated leading to a thin layer of the polymer film. All the spectra were recorded with a Nicolet 380 FTIR spectrometer using 4 cm^{-1} resolution and 32 scans. The Omnic software was used for the spectra collection and analysis. The high pressure ATR-IR was pressurized by ISCO 260D syringe pump.

2.3. High pressure parallel plate rheometer

An Anton Paar Physica 301 rheometer was used to perform the rheological study. The pressure cell attachment developed by Anton Paar allows measurements at pressures up to 150 bar and temperatures up to 300 °C. Flichy et al. [29] used this pressure cell attachment with a standard concentric cylinder and special designed vane geometry to study the rheological properties of heterogeneous fluid samples under CO_2. A considerable amount of sample (13 mL) is required for this geometry, thus it needs a long period for CO_2 to saturate the polymers. Moreover, CO_2-plasticized $P_{DL}LA$ and PLGA polymers are highly viscous, thus the standard concentric cylinder geometry is not suitable due to possible overloading, i.e. the torque exceeds the upper limit of this machine (150 mNm). In this work, a parallel plate (20 mm) geometry was first adopted for this high pressure cell to measure the viscosity of the polymer samples subjected to CO_2. Polymer powder/granular (500 mg) or discs (diameter 20 mm, thickness 1 mm) were placed on the bottom plate and the gap distance between the two plates was set as 1 mm for rheological measurements. The polymer discs were prepared using a constant thickness film maker (Specac P/N 15620) at a temperature of 80 °C and pressure of 3 tonnes, then cut into the required diameter (20 mm) for measurements. The high pressure rheometer was also pressurized by ISCO 260D syringe pump.

3. Results and discussion

3.1. High pressure ATR-IR

The absorbance bands of the $P_{DL}LA$ and PLGA polyesters (Fig. 1a) include the C–H stretch (weak) near 3000–2800 cm^{-1}, the C=O stretch near 1750 cm^{-1}, the aliphatic ether C–O–C stretch in the 1275–1050 cm^{-1} region and the long chain CH_2 rocking motion near 730 cm^{-1}. Also present in the spectra are peaks in the region of 1500–1300 cm^{-1} representing CH_2, CH_3, and CH deformation vibrations. The analysis of the spectra in this work was focused on the carbonyl band (C=O) because it is an isolated and strong absorption band and therefore easier to quantify. The absorbance bands in the carbonyl region for $P_{DL}LA$ and PLGA polymers (Fig. 1b)
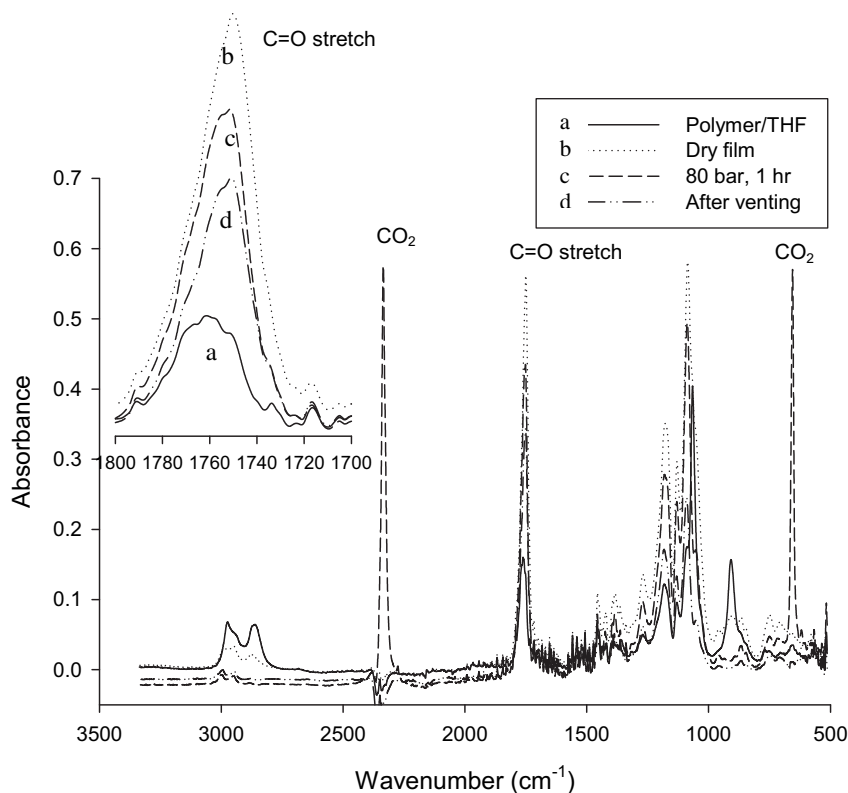

Fig. 2. FTIR spectra of PLGA 6535. (a) Polymer/THF mixture; (b) Polymer dry film, which is dense and compact; (c) Polymer film subject to CO_2, which has swollen and is thus less dense; (d) Foamed polymer film after depressurization. This demonstrates that CO_2 has played the role of a solvent leading to a decrease in the band intensity (c vs b). The further decrease of the band intensity (d vs c) after depressurization (rather than an increase) implies a porous structure was formed.

showed a shift towards high wavenumber from 1747.9 to 1752.2 cm^{-1} for P$_{DL}$LA and PLGA 5050 respectively.

Effect of solvent. As stated in the Experimental section, the polymer films were cast from polymer/THF solutions. The comparison between the spectra for the polymer film before and after solvent evaporation (Fig. 2a and b) indicated a decrease in the band intensity in the presence of solvent due to the increase of the free volume in the polymer matrix. CO$_2$ plasticization can also result in an increase of free volume in the polymer matrix since there is an increase in freedom of motion of polymer chains [21]. Therefore, a decrease in the intensity of the band (Fig. 2c) assigned to the polymer corresponds to a change in the polymer density and thus to a volume change (swelling) of the polymer film. On the other hand, the absorbance of CO$_2$ IR bands at ~2330 cm^{-1} and ~655 cm^{-1} shows sorption (solubility) of CO$_2$ into the polymer (Fig. 2c). In the literature, the v_3 band of CO$_2$ dissolved in polymer (at 2335 cm^{-1}) has been used to calculate the sorption data and the polymer swelling has been determined by analyzing the changes in the absorbance of the v(C=O) band (at 1730 cm^{-1}) of the polymer [21]. Moreover, the further decrease of the band intensity (Fig. 2d) after depressurization (rather than an increase) implied a porous structure formed.

Determination of soaking time. To allow CO$_2$ to saturate the polymer, a sufficient duration of soaking was needed. The experimental results (Fig. 3) indicated that a soaking time of 1 h was sufficient for the very thin polymer films to reach CO$_2$ equilibrium status.

Effect of pressure. In order to investigate the effect of pressure, the intensities of the characteristic absorption bands of CO$_2$ were studied at 80 and 150 bar. While the CO$_2$ pressure was increased from atmospheric to 80 and 150 bar, the intensities of all of the polymer bands decreased, whereas the intensities of the characteristic absorption bands at ~2330 cm^{-1} and ~655 cm^{-1} increased. Fig. 4 illustrates the spectral changes in the carbonyl region and v_3 CO$_2$ band as the pressure of the CO$_2$ increased. This shows a decrease in the polymer band absorbance (Fig. 4a) as a result of the polymer swelling and an increase in the CO$_2$ absorbance (Fig. 4b) as a result of gas sorption. The intensity difference of the spectra under various pressures demonstrated an increase in the swelling and the solubility with an increase in CO$_2$ pressure.

The analysis of the carbonyl band of P$_{DL}$LA under CO$_2$ (Fig. 4a) reveals a small increase in the wavenumber of the band maximum. A similar behavior has also been observed for the PLGA copolymers. Although the shift was small (a few cm^{-1}), it increased with the increase of CO$_2$ pressure. Such high-frequency shifts of IR bands usually indicate a decrease in the interaction of the polymer chains with their environment. Thus, the detected high-frequency shift of carbonyl region band of the polymers under CO$_2$ indicated a weaker inter-chain interaction in the polymers under CO$_2$ environment [20].
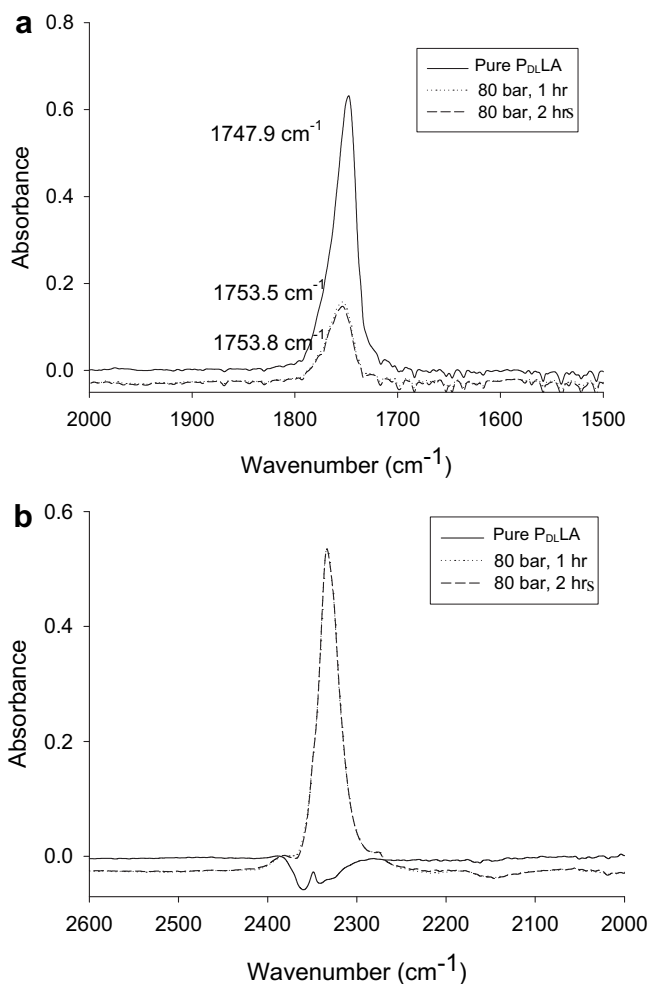

Fig. 3. FTIR spectra of P$_{DL}$LA 52 KD obtained at 35 °C and 80 bar after soaking for 1 h and 2 h. (a) Carbonyl region; (b) CO$_2$ absorbance band. Both sets of data show that the CO$_2$ in the polymer reached equilibrium after soaking for 1 h.
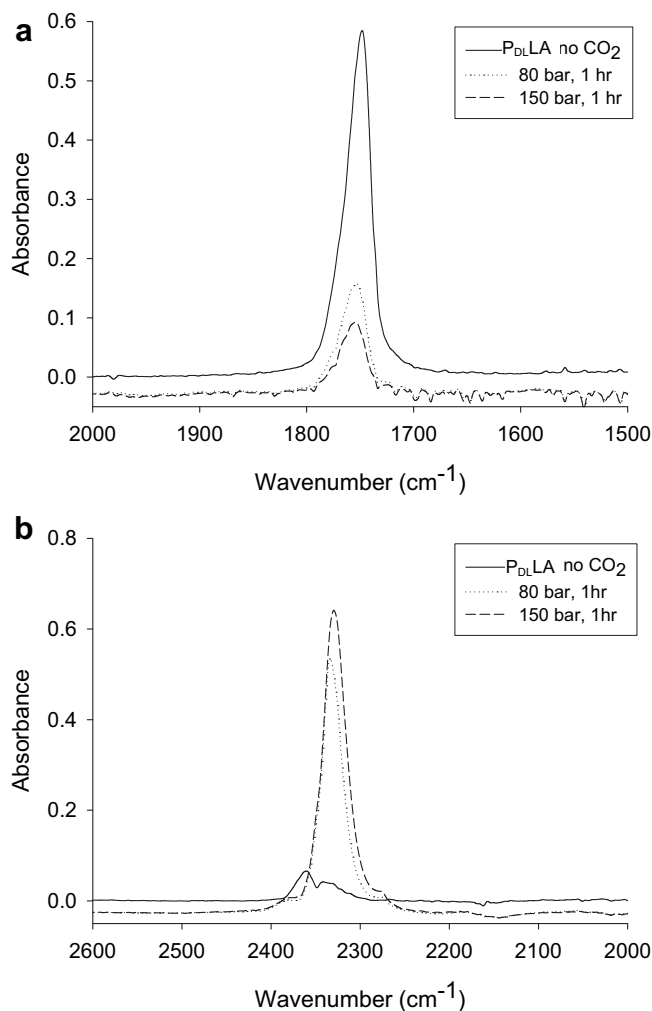

Fig. 4. FTIR spectra of P$_{DL}$LA 52 KD obtained at 35 °C under atmosphere, 80 bar and 150 bar after soaking for 1 h. (a) Carbonyl region; (b) CO$_2$ absorbance band. Note, there is an increase in the volume of the film (a) and in the solubility of CO$_2$ (b) when CO$_2$ pressure is raised.

Effect of polymer molecular weight and composition. The FTIR spectra of plasticized $P_{DL}LA$ 15 KD and $P_{DL}LA$ 52 KD showed no noticeable differences. This is in agreement with previous published sorption and swelling studies [14,15], indicating that two homopolymers with different molecular weight show equivalent interactions with CO_2. The spectra for $P_{DL}LA$ and PLGA polymers were recorded at 35 °C and 80 bar after soaking for 1 h. It was found that the maximum absorptions in carbonyl region bands for all these polymers, analyzed by Omnic software, were located at the similar position at ~1753.5 cm^{-1}. In comparison with the spectra for the pure polymers (Fig. 1b), $P_{DL}LA$ had the largest shift (5.6 cm^{-1}) and PLGA 5050 had the smallest shift (1.3 cm^{-1}). This indicated that $P_{DL}LA$ had the greatest interaction with CO_2 and the interaction decreased with the increasing GA content in the polymers. This is in good agreement with the results obtained from the solubility studies. The solubility of CO_2 in PLGA copolymers was found to decrease with the increase in the glycolic acid content [13,14].

The interaction of polymers with CO_2 is dependent upon the chemical structure. The affinity of CO_2 with polyesters is largely due to the interaction of CO_2 molecules with the carbonyl group on the polymer chains [13,17]. Lactic acid (LA) possesses an extra methyl group which could lead to at least two-opposing consequences. One is to increase the steric hindrance and then lower the interaction between the carbonyl group and the CO_2 molecules; the other one is to increase the available free volume in the matrix due to steric effects. It was hypothesized that the latter factor plays a dominant role in determining the CO_2 behavior in PLGA polymers, leading to a higher solubility for PLGA with a high LA content [13]. The intensity changes of the carbonyl bands of the polymers and CO_2 characteristic bands were also observed with the increase of sorbed CO_2 and are related to the swelling of the polymers and the sorption of CO_2.

3.2. High pressure rheology

Dissolved CO_2 in polymers acts as a plasticizer and reduces the glass transition temperature and the viscosity of polymer/CO_2 mixtures [33]. The viscosity of the plasticized polymer plays an important role in the supercritical foaming process. Scaffold fabrication via CO_2 foaming technique at temperatures of about 35 °C have drawn particular interest in tissue engineering applications. However, to our knowledge, studies on the viscosity of polymer/CO_2 at this low temperature have not been reported. A parallel plate geometry located in a high pressure cell rheometer was used in this study to record the viscosity curves of $P_{DL}LA$ 15 KD, $P_{DL}LA$ 52 KD, PLGA 8515 and PLGA 6535 plasticized by CO_2 at 35 °C.

Effect of soaking time. As demonstrated previously in sorption and swelling studies [14,15] and high pressure ATR-IR studies, it was important to determine the time required to allow CO_2 to saturate the polymer in different measurement techniques. Using the high pressure rheometer, it was found that 1 h soaking time is sufficient to reach equilibrium status for polymer samples in powder and granular form regardless the molecular weight and composition (Fig. 5a). This represents a typical soak time for scaffold fabrication [7]. However, polymer disc samples (1 mm in thickness and 20 mm in diameter) require much longer soaking time because they were fabricated by melt press and have much dense morphology. It was found that $P_{DL}LA$ 52 polymer disc samples reached equilibrium status after 10 h soaking (Fig. 5b).

Effect of pressure. To study the effect of the CO_2 pressure on the viscosity of $P_{DL}LA$ polymer, the viscosity of the plasticized polymer was measured at 25, 75 and 100 bar [34]. Each measurement was performed at 35 °C and a constant soak time of 1 h using 500 mg $P_{DL}LA$ 52 KD granular. Although viscosity measurements are
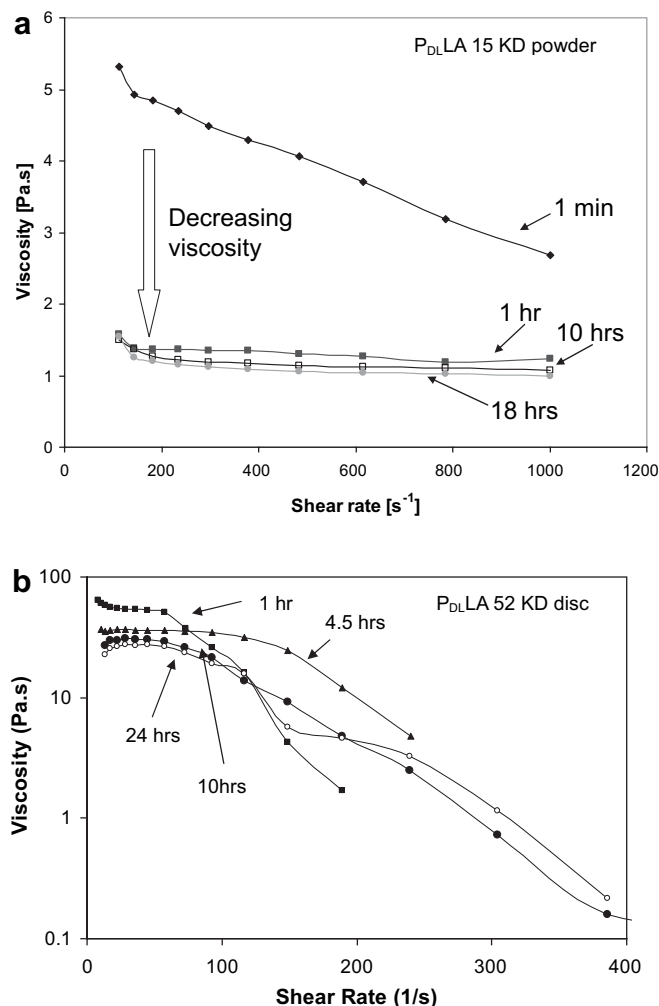

Fig. 5. The effect of soak time on polymer viscosity at 35 °C and 100 bar (a) $P_{DL}LA$ 15 KD powder, the equilibrium status was reached after 1 h soaking; (b) $P_{DL}LA$ 52 KD disc, the equilibrium status was reached after 10 h soaking.

possible at lower pressures, Fig. 6 clearly shows that the CO_2 in the supercritical phase led to a significant viscosity reduction. CO_2 becomes a supercritical fluid at 73.8 bar and 31.1 °C and above these conditions CO_2 density increases dramatically comparing to gas CO_2 leading to higher capability to plasticize $P_{DL}LA$ and reduce the viscosity. This viscosity reduction of the polymer is the result of the dissolved CO_2 lowering the T_g and liquefying the polymer [7]. At 25 bar, when the CO_2 was not in the supercritical phase, the polymer viscosity was several magnitudes higher. Increasing the pressure from 75 to 100 bar showed no obvious difference in the viscosity reduction. This is thought to be because of the limitations in the sensitivity of the rheometer.

Effect of polymer molecular weight. PLA and PLGA polymers are biodegradable and their degradation rate, which is dependent on the M_W, can be tailored to the required application. Consequently, they are of particular interest to biomedical science. Viscosity measurements were obtained at 35 °C for two $P_{DL}LA$ polymers with molecular weight (M_W) of 15 KD (powder) and 52 KD (granular) after soaking for 1 h at 100 bar. The viscosity data obtained (Fig. 7) are in agreement with literature data published for polymer melts at atmospheric pressure [35] as the M_W was increased, the measured viscosity increased. The PLA viscosity increases with M_W, because as the M_W increases, the polymer chain length and the number of chain entanglements increase. An entanglement is
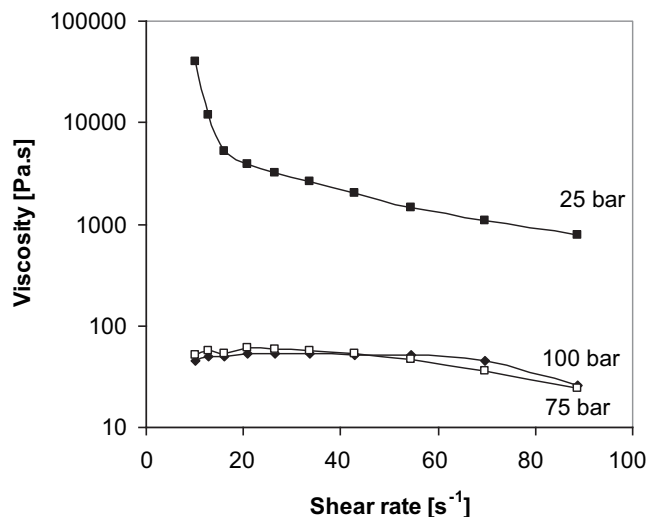
Fig. 6. Effect of CO_2 pressure on the viscosity of $P_{DL}LA$ 52 KD at 35 °C. The CO_2 in the supercritical phase led to a significant viscosity reduction.

a topological interaction between one polymer molecule and its neighbours. These greatly impede the motion of the polymer chains and their ability to relax after deformation. Consequently, entanglements in a polymer melt result in high viscosities [36].

Effect of polymer composition: Polymer disc samples were used in this study. The viscosity measurements were performed every 2 h at 35 °C after overnight soaking under CO_2 at 100 bar. Equilibrium status was reached after 10 h and the viscosity curves (*i.e.* shear viscosity *vs* shear rate) of polymer/CO_2 mixtures were similar in shape to those of pure polymers (Fig. 8). The shear thinning phenomenon was observed for all the polymers, which is important information for extrusion and injection processing of the polymers. A greater viscosity reduction for $P_{DL}LA$ was observed compared to PLGA. This is in agreement with the ATR-IR data confirming that $P_{DL}LA$ has a greater interaction with CO_2 than PLGA polymers and one would therefore predict a larger decrease in viscosity. Comparison of the viscosity of $P_{DL}LA$ and PLGA in the presence and absence of CO_2 (Figs. 8 and 9) shows that at atmospheric pressure it is necessary to heat the polymer to 140 °C to obtain a liquid polymer with a viscosity that is easily processible. By contrast, in the presence of scCO_2 this can be achieved at only 35 °C. It must be emphasized that the viscosity is dependent upon the scCO_2 pressure and hence density. The rheological measurements reported here are limited by the rheometer upper pressure limit (ca. 100 bar). In reality, our processing apparatus typically operates at 200–300 bar giving
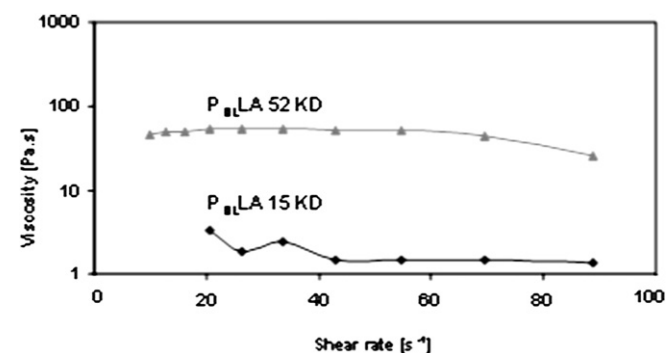
substantially further viscosity reduction, though currently we can observe this only empirically. However, the key advantage of working with scCO_2 is that elevated processing temperature can be avoided thus negating polymer degradation. Furthermore, the ability to use CO_2 to reduce the viscosity of polymers at near ambient temperatures enables heat sensitive materials such as proteins to be incorporated [37]. This viscosity reduction is directly attributed to the dissolved CO_2 (*ca.* 25–30 wt%) in the polymers [14].

The results from the high pressure rheology and high pressure ATR-IR, combined with the sorption and swelling studies reported previously [14,15], demonstrate that the interaction and the solubility of CO_2 in PLGA copolymers is related to the glycolic acid content. As the glycolic acid ratio increases the interaction and consequent solubility of CO_2 decreases. This is in good agreement with our finding on manipulating scaffold fabrications using these polymers, which indicates that the scaffolds produced from PLGA with high glycolic acid content have a lower porosity [7]. A lower porosity is in fact directly connected to a lower CO_2 concentration, and therefore solubility, in the plasticized polymer.
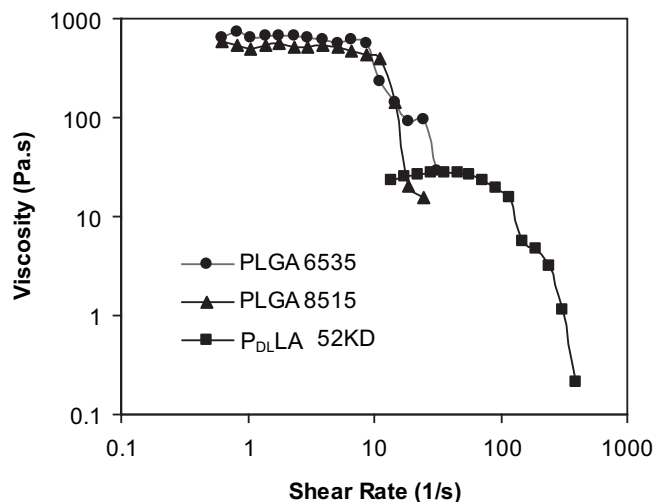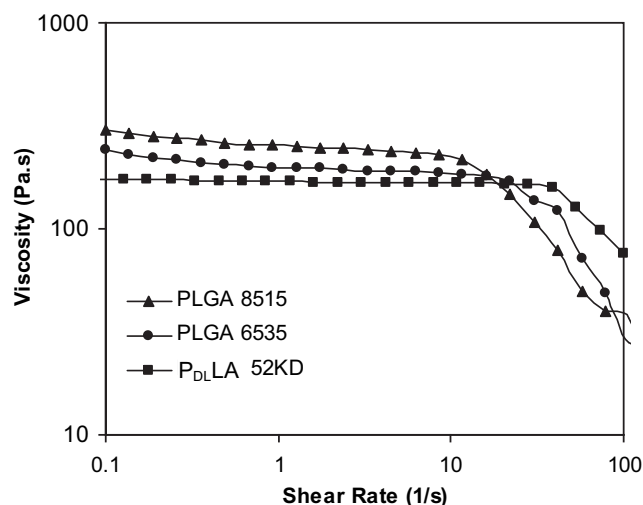

Fig. 8. Flow curves of $P_{DL}LA$ 52 KD, PLGA 8515 and PLGA 6535 plasticized by CO_2 at 35 °C and 100 bar after soaking for 24 h, which demonstrate CO_2 has a stronger interaction with $P_{DL}LA$ than PLGA polymers resulting in a reduced viscosity.

Fig. 7. Viscosity profiles showing that as expected the viscosity of the plasticized polymer increases as the M_w is increased.

Fig. 9. Shear viscosity of $P_{DL}LA$ 52 KD, PLGA 8515 and PLGA 6535 without CO_2 at 140 °C and atmosphere pressure.

4. Conclusion

A high pressure attenuated total reflection Fourier transform infrared (ATR-IR) and a high pressure parallel plate rheometer have been successfully developed to study the interactions of CO_2 with a series of amorphous $P_{DL}LA$ and PLGA polymers with different compositions (glycolic acid content as 15, 25, 35 and 50% respectively). Shifts of the maximum absorption of carbonyl groups (C=O) of the polymers and the absorption intensity changes of both carbonyl and CO_2 bands show clearly the effect of CO_2 upon the polymers. The viscosity of CO_2-plasticized polymers has been measured directly using a high pressure parallel plate rheometer and the data obtained demonstrate that the interactions of CO_2 with PLGA polymers decrease with increasing GA content in the copolymers. This investigation provides further fundamental understanding of the control of the foaming process for the fabrication of $P_{DL}LA$ and PLGA porous scaffolds and is in a good agreement with our previous findings on manipulating scaffold fabrications by altering the fabrication conditions and polymer compositions. The potential applications of this study are very broad, from tissue engineering and drug delivery through potentially to much broader applications with other polymers in areas that may range from composites and polymer synthesis through to injection moulding.

Acknowledgement

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